An investigation into the impact of cumulative life stress and neuromodulation on adults' cognitive function and subjective well-being.

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Abstract

As healthcare advances, more people are living longer increasing the prevalence of age-related disorders including declining brain function. Acute and chronic stress can also negatively affect brain activity however less is known about the impact of accumulated stress and its interaction with ageing. Interventions that best maintain brain and cognitive health, e.g. exercise and calorie-restriction, are not suitable for everyone.

This research aimed to understand the impact of healthy ageing, cumulative stress and their interaction on executive function and subjective well-being and also to identify and investigate practical interventions. A literature review indicated mindfulness meditation (MM) and transcranial alternating current stimulation (tACS) as appropriate interventions. Their relative efficacy were systematically reviewed and meta-analysed. The following studies were then completed which targeted healthy adults aged 18-85: Study 1 aimed to replicate the finding that cumulative life stress accelerates cognitive ageing as well as evaluate the efficacy of tACS as potential mitigation. Studies 2A and 2B aimed to replicate and confirm Study 1's findings. Study 3 measured the impact of ageing, cumulative stress, resilience and subjective sleep quality on working memory. It also explored the impact of adverse childhood events and it's interaction with cumulative stress on working memory. In Study 4, the well-used cumulative stress index, Social Readjustment Rating Scale (SRRS), central to this work, was modernised and updated whilst remaining compatible with the original, i.e. backwards-compatible. Analyses were conducted with Bayesian and frequentist statistics.

Key meta-analysis findings were a lack of rigour in MM research and no conclusive benefit to subjective well-being or working memory; a lack of standardised protocols in tACS research but an indication that sophisticated tACS protocols can be effective. Key findings for Studies 1 to 3 showed no evidence that cumulative stress has an accelerative ageing effect. However, ageing slowed processing speed. Resilience increased with age. There were no associations between working memory and the independent variables. Study 4 successfully updated and modernised the SRRS.

This thesis provides preliminary evidence that higher levels of cumulative life stress, as measured with the SRRS, are unlikely to accelerate the ageing of older adults' cognitive functioning. It also demonstrates that to draw conclusions in these areas, overall research standards need to be raised by improving rigour and standardisation, employing sophisticated tACS protocols and using an updated, backwards-compatible SRRS. In addition, data collected may serve as an informed Bayesian prior.

Contents

Chapter 1: Ageing, cumulative stress and brain function

Ageing may be defined as the post-maturational biological process where the cells within an organism deteriorate over time (Masoro, 2010). The literature shows that key executive functions such as memory and attention decline as a normal part of ageing (Deary et al., 2009). These changes occur because of reduced efficiencies within functional networks and these, in turn, are linked to deterioration in certain brain structures including the hippocampus and prefrontal cortex (PFC) as well as biochemical changes (Meunier et al., 2014; Morrison & Baxter, 2012). A recent longitudinal fMRI study showed that as one gets older the brain shrinks in size in a number of areas, namely: the hippocampus, the inferior temporal cortex and the entorhinal cortices, and that this shrinkage accelerates with age (Deary et al., 2009; Raz et al., 2005). Moreover, this reduction in volume with increasing age is linear (Fjell & Walhovd, 2010). In addition, because a number of functions within the brain are highly lateralised, such as language, white matter and grey matter structures are asymmetrical (Herve et al., 2013), meaning that age-related changes vary within the brain. While there may be potential within the brain to adapt, maintain and even improve in the face of ageing, it is worth first reviewing the key underlying factors that cause or accelerate cognitive decline, because ageing is a complex, multi-level process and varies considerably between people (McEwen et al., 2016; Meunier et al., 2014).

This chapter is divided into three sections. The first will briefly review key factors that contribute to and/or accelerate biological ageing with examples of research evidence showing how they affect cognition. The second section will provide an overview of the impact of ageing on brain networks and how this affects key executive functions. The third section will consider the brain's resilience and the potential of treatments like neurostimulation and meditation, to improve cognitive performance in older people by harnessing this resilience.

1.1 Section 1: Key factors that contribute to/accelerate biological ageing.

The ageing process begins in a single cell that creates a cascade of effects across different systems within the body, including the brain. Ultimately, the key to a longer life is the ability to mitigate cell damage (Pomatto & Davies, 2017). According to the 'common cause' theory, much of the age-related decline in the mind and body may be attributable to a small number of core biological processes such as: oxidative stress, telomere attrition, immune dysfunction and hormonal dysregulation (Deary et al., 2009). These processes affect particular pathways including the cardiovascular (Paneni et al., 2017) and endocrine systems (Chahal & Drake, 2007), which in turn, affect mental processes and are linked to neurodegenerative diseases such as vascular dementia and Alzheimer's Disease (Bilbo & Schwarz, 2009; Gottesman et al., 2017; Magri et al., 2006; McEwen et al., 2016). These mental processes, namely memory,

attention, language-processing, decision-making and so on, may be regarded as indicators of brain function (Shalev & Arbuckle, 2017). Studies investigating the effects of ageing on cognitive performance typically include a young adult sample, because comparisons between groups yields important information about the level of impact ageing has on cognition.

1.1.1 Neurogenesis

Neurogenesis refers to the self-renewal of neural stem cells that produce, *inter alia*, new neurons which play an important role in mental tasks and brain plasticity. Much of what is known about neurogenesis is based on animal studies. These studies show that neurogenesis appears to follow a quadratic curve, reaching its peak at around 30 years of age in humans and then begins to decline at an accelerating rate (Fjell & Walhovd, 2010; Lazic, 2012). The drop-off of new neurons is not accompanied by any serious cognitive decline (Palmer & Ousman, 2018) and evidence has shown that the number of neurons in frontal and temporal areas remain fairly stable in healthy ageing humans (Fjell & Walhovd, 2010; Freeman et al., 2008). However, the risk with declining neurogenesis is that the brain becomes vulnerable to injury and disease. One of the functions of neurogenesis is to repair damaged cells, for example, in the event of a stroke. With fewer neural stem cells available to generate new astrocytes and oligodendrocytes, the odds of a successful repair are lowered considerably, because the level of production of newly generated cells cannot keep up with the damage, creating potential for vulnerability in cognitive function (Apple et al., 2017). This is particularly

important in the hippocampus, which plays a pivotal role in spatial learning, memory and emotional processing (ibid).

1.1.2 Oxidative Stress and Immune dysfunction

Oxidation is the general process of energy release. Harman (1956) argued that free radicals or oxidants are by-products created during cell metabolism and can harm lipids, proteins and nucleic acids within a cell, causing it to become damaged or die. Oxidative damage is believed to play a central role in ageing and disease (Black et al., 2017). Oxidants are not entirely destructive, they are also used by the immune system to dispose of toxins (Beckman & Ames, 1998). Importantly, the potential for damage depends on the genotype of the cell, it's protective mechanisms and the metabolic organisation of the cell (Gladyshev, 2014). Oxidative and inflammatory stress are closely related (Garrido et al., 2019; Joseph et al., 2005) and a key issue in ageing is the gradual inability of cells to adapt and adjust to these stressors.

As with any biological system, the human body and brain strives to maintain a homeostatic state and possesses inbuilt stress-response mechanisms to enable transient adaptive homeostasis; this process is known as allostasis (Sterling & Eyer, 1988). Allostasis is adaptive because it produces a collective adjustment of the body to a change that takes precedence over localised homeostatic signalling (De la Fuente, 2008; Pomatto & Davies, 2017). With age, complex inflammatory mechanisms that form part of this allostatic response become chronically activated, resulting in low-level inflammation. Homeostatic signalling then becomes cumulatively and progressively less responsive to metabolic and other

stressors; with age, homeostatic responsiveness becomes compressed (Pomatto & Davies, 2017). Neurons that become chronically exposed to the synergistic effect of oxidative stress followed by an inflammatory response followed by more oxidative stress (Pomatto & Davies, 2017), create chemical imbalances that can degrade synapses, thereby impairing the neural networks that they support. An example of this is the hippocampus, which plays a critical role in a range of cognitive functions central to decision-making and learning. The hippocampus is highly malleable in terms of its structure and functionality and is also very sensitive to the impact of chemical stressors. Through a chain-reaction of chemical events, the dendrites retract and simplify (McEwen et al., 2016). As the neural networks become less connected, capillaries shrink back, contributing to a cascade of structural changes and volume loss known to occur in the ageing brain (ibid).

1.1.3 Astrocytes, inflammation and synaptic plasticity

Structural changes observed within the brain may partly relate to glial cells, rather than to neurons themselves (Palmer & Ousman, 2018). Astrocytes line the capillaries of the brain, providing structure and volume. They also form part of the blood-brain barrier, which controls the movement of chemicals to and from the central nervous system (Hancock et al., 2014; Palmer & Ousman, 2018). Importantly, neurons are enclosed in astrocytic processes and astrocytes are also known to play an essential role in synaptic neurotransmission, releasing neuroactive chemicals such as gamma-aminobutyric acid (GABA) and adenosine (Hancock et al., 2014). When the levels of neuro-inflammation increase the phenotype of

the astrocytes changes making them reactive (Palmer & Ousman, 2018). These reactive ageing astrocytes activate the complement system, part of the brain's immune response mechanism, allowing cells to be tagged for phagocytosis. Consequently, synapses, dendrite spines and neurons may fall victim to a strong inflammatory response (ibid). Furthermore, as part of this inflammatory response, the secretions from astrocytes weaken the blood brain barrier (Sarkar et al., 2019). Thus, reactive ageing astrocytes create a potentially toxic environment that increases the risk of developing or accelerating age-related neurodegeneration, which is associated with neuron damage/death. Indeed, it has been argued that this change to neuronal activity is one possible mechanism for memory loss observed in older adults (ibid).

1.1.4 Oligodendrocytes and Myelination

Myelin in the brain comprises oligodendrocytes that wrap around neuronal axons forming a sheath. Myelination greatly enhances the speed and efficiency of signalling throughout the central nervous system. A reduction in the amount (Tse & Herrup, 2017) and quality (Palmer & Ousman, 2018) of myelination has been associated with ageing (Liu et al., 2017; Tse & Herrup, 2017). Myelination is slow to develop and follows a quadratic trajectory with maturation occurring only around 45-47 years of age followed by decline, which starts in frontal areas including the PFC (Gunning-Dixon et al., 2009; Raz et al., 2005). MRI evidence has shown that cognitive processing speed is significantly correlated with the integrity of prefrontal lobe myelination (Lu et al., 2011). Critically, signal delays

caused by disrupted myelin can affect the phase of neural signalling leading to reduced amplitude of the signal (Pajevic et al., 2014).

1.1.5 Telomere length

Telomeres may be defined as "…tandem TTAGGG repeats found at the ends of chromosomes, associated with several telomere-binding proteins." (de Magalhaes & Passos, 2018, p. 3). These binding proteins protect chromosomes from damage. However, each time a cell divides the telomere shortens and eventually reaches cell senescence. Telomere length is adversely affected by chronic stress and age-related cortisol dysfunction. For example, Barha et al. (2017) conducted a study comparing women who had experienced child mortality to those who had not and found that the women who had lost a child had shorter telomeres than controls, indicating that trauma influences telomere length. They also found, across groups, that women with higher cortisol base levels had shorter telomeres. The authors argued that this is evidence of cellular ageing.

1.1.6 Cumulative Life Stress and the hypothalamic-pituitary-adrenocortical axis

"The brain is the organ that decides what is stressful and determines the behavioural and physiological responses, whether health-promoting or health damaging." (McEwen, 2006, p. 368). Events like on-going financial strain and marital difficulties are examples of what most would consider stressful (Holmes & Rahe, 1967) and can have severe negative health consequences. Moreover, early childhood trauma can affect stress reactivity in later years, compounding the perceived level of

threat posed by stressors (McEwen, Bowles, et al., 2015). The hippocampus has a large number of cortisol receptors and is consequently particularly susceptible to the damaging effects of chronic stress (Kim et al., 2015; McEwen et al., 2016). To understand why stress is harmful, it is worth briefly outlining how the adaptive stress response works.

The hypothalamic-pituitary-adrenocortical axis (HPA) forms part of the body's homeostatic system and is regulated by the hypothalamus (Gassen et al., 2017). The HPA operates via a negative feedback system to regulate glucocorticoid levels, which are affected by both endogenous and exogenous events (McEwen, 2006; Sapolsky et al., 1986). Once an individual perceives a situation as stressful, the sympathetic nervous system is activated, releasing adrenaline and noradrenaline into the bloodstream (al'Absi & Arnett, 2000). Glucocorticoids are also released (ibid). The hypothalamus secretes the corticotrophin-releasing hormone (CRH) which triggers the pituitary gland to secrete adrenocorticotropic hormone (ACTH) which, in turn, signals the adrenal cortex to release glucocorticoids into the circulatory system (al'Absi & Arnett, 2000; McEwen, 2006; Sapolsky et al., 1986). Glucocorticoids, such as cortisol, activate target cells via two receptors: the mineralocorticoid receptor and the glucocorticoid receptor (ibid). The increase in cortisol then signals a decrease in production of ACTH and CRH, which down-regulates HPA activity to baseline (ibid). Cortisol levels vary as a function of circadian rhythm and fluctuate over a 24-hour period. Cortisol starts to build up from midnight, peaking by early morning and gradually levelling off over the course of the day, to begin the cycle again at midnight (Chan & Debono,

2010). Rodent studies have demonstrated that aged rats respond adaptively to an acute stressor by efficiently initiating an appropriate activation of the stress response. However, while young rats took about 60 minutes to return to basal stress hormone levels, older rats took up to 24 hours to do the same (Sapolsky et al., 1986).

When the HPA fails to down-regulate glucocorticoid signalling following a stressful event or the stressful event is on-going, this constitutes a dysfunction in the stress response. Research has demonstrated an association between chronic cortisol exposure and depression, anxiety, hypertension, suppressed immune function and early mortality (Gaffey et al., 2016; McEwen et al., 2016) and evidence suggests that this chronic/excessive glucocorticoid exposure is toxic to cells (McEwen et al., 2002; McEwen et al., 2016; Pomatto & Davies, 2017; Swartz et al., 2015). For example, Aschbacher et al. (2013) found in a study of post-menopausal carers versus non-carers that heightened anticipatory cortisol reactivity was associated with greater levels of oxidative damage. In addition, Black et al. (2017) showed, in a large-scale study (n=2858), that oxidative damage is associated with HPA function, inflammation and autonomic nervous system activity and is dose-dependent. Thus, chronic stress may accelerate ageing in a dose-dependent manner. Importantly, these effects may also accumulate over time and one possible mechanism for this is through epigenetics (Gassen et al., 2017). Glucocorticoid response elements regulate gene transcription

and create enduring changes to DNA methylation[1] (Makhathini et al., 2017; Yang et al., 2012), which cells then carry forward when they divide, affecting subsequent responses to glucocorticoids (Gassen et al., 2017).

Reviews of animal and human studies indicate that chronically elevated glucocorticoid levels are associated with structural and functional changes to the hippocampus, prefrontal cortex and the amygdala, which can have lasting effects on cognitive ability and emotional well-being (Gaffey et al., 2016; McEwen et al., 2016; Pomatto & Davies, 2017). In a recent study on rats, Cohen and colleagues (2014) found that alterations to behaviours following a stressful event were closely associated with changes to dendrites in terms of number, length and density; extreme responders showed reductions across these indices in dentate gyrus granular neurons, and CA1 and CA3 pyramidal neurons. A corresponding, significant increase in arborisation occurred in the dendrites of the amygdala, creating a physiological environment for an on-going, highly sensitised stress response.

Congruent with the research showing a toxic impact of prolonged exposure to glucocorticoids are the findings by Marshall and colleagues (2018; 2017; 2016; 2016b; 2015) who examined the impact of experienced (cumulative) stress[2] on cognitive performance and neural network function in young and older adults. They demonstrated that older adults who scored higher on a measure of cumulative life stress performed worse on

[1] DNA methylation/demethylation is the process whereby gene expression is modified without changing the genetic code.
[2] 'experienced stress' is operationalised as the summed/accumulated impact of specific life events, e.g. moving house, marriage, changing job, over one's whole life.

working memory (2015), processing speed, inhibitory control (2016), spatial discrimination (2016b) and spatial working memory (2018) compared to lower-stress older adults and young participants. Critically, the young adults' cumulative life stress scores did not significantly affect performance, indicating that it is the cumulative effect of stressful events that affects cognitive ageing in later life. Their respective studies also investigated correspond eldering oscillatory patterns during the respective tasks using EEG and found altered patterns consistent with the deficits observed in the behavioural data across all studies and at rest (2017) in the older high cumulative life stress group, compared to low-stress older and young participants. These results robustly demonstrate that chronic exposure to glucocorticoids has a far-reaching, progressive impact on neural network efficiency (2018; 2017; 2016; 2016b; 2015), reflecting changes to brain structures, quite possibly starting with the aforementioned processes of oxidative damage and DNA methylation.

Care should be taken when interpreting results of the above work as causality was not proven that stress accelerates ageing. Indeed, other studies show that the effects of ageing can, in certain circumstances, increase stress. Johar et al. (2014) conducted a study (n= 745) with older participants (65 to 90 years) comparing levels of saliva cortisol taken at morning and evening. They found an association between frailty[3] and dysregulation of cortisol levels, which were low in the morning and higher

[3] Frailty is characterized by "unintentional weight loss, feeling of exhaustion and fatigue, physical inactivity, slow gait speed, and low grip strength" Johar, H., Emeny, R. T., Bidlingmaier, M., Reincke, M., Thorand, B., Peters, A., Heier, M., & Ladwig, K. H. (2014). Blunted diurnal cortisol pattern is associated with frailty: a cross-sectional study of 745 participants aged 65 to 90 years. *J Clin Endocrinol Metab, 99*(3), E464-468. https://doi.org/10.1210/jc.2013-3079 .

in the evening, indicating a blunted diurnal cortical response. It is likely that a generally blunted cortisol response may be associated with age-related dysregulation of the suprachiasmatic nucleus, which regulates, *inter alia*, the HPA (Morris et al., 2012; Nakamura et al., 2016).

1.1.7 Section 1 Summary

Biological ageing reflects a progressive decline in the body's ability to adapt and adjust to stressors, which resonates through every level, from singular cells to behaviour. Evidence demonstrates that oxidative stress, telomere attrition, immune dysfunction and hormone dysregulation are key underlying factors. These key factors affect cognition through their profound electro-chemical influence on the expression of genes, which changes the structure and functionality of different brain regions. The impact of stress on the physiology of the hippocampus and amygdala is a case in point. The impact of ageing processes on complex neural networks and the cognitive function they support will be discussed in the following section.

1.2 Section 2: Age-related cognitive decline and neural connectivity

1.2.1 Neurons, synapses and functional connectivity

Neurons are the longest-living human cells (Mertens et al., 2018) and become terminally differentiated post-mitotic early in their development. Interestingly, neurons have the potential to synthesize DNA but are completely resistant to cell division in their post-mitotic state (Aranda-

Anzaldo, 2012). In fact, neurons are very susceptible to DNA damage, because they cannot make use of division-mediated DNA repair to maintain genome stability and are therefore completely reliant on other repair mechanisms (Böhnke et al., 2018). Thus, normal ageing is more closely linked to mitochondrial ageing, caused by increasingly inefficient cellular energy homeostasis, but does not necessarily lead to neuronal death (Böhnke et al., 2018; Toescu & Verkhratsky, 2003). In contrast, neurodegenerative diseases, like Alzheimer's disease (AD), which represents pathological ageing, have been linked to cellular stressors, such as oxidative damage, that trigger neurons to re-enter the cell cycle, inevitably causing them to die (Aranda-Anzaldo, 2012; Böhnke et al., 2018).

Normal age-related cognitive decline is arguably more strongly linked to subtle changes in synaptic activity than the neurons themselves (Morrison & Baxter, 2012). More specifically, when synapses fail, neurons become more likely to degenerate. This is particularly important in the hippocampus and PFC, which play a central role in executive function. Studies on rhesus monkeys' dorsolateral prefrontal cortex (DLPFC) regions show age-related loss of volume not seen in other areas of the PFC and that this phenomenon relates to neuropil[4] rather than neuron loss (Morrison & Baxter, 2012; Peters, 2002). Oh et al. (2016) reviewed animal studies that examined hippocampal CA1 and CA3 pyramidal neuron

[4] "The neuropil is defined as the space between neuronal and glial cell bodies that is comprised of dendrites, axons, synapses, glial cell processes, and microvasculature." Spocter, M. A., Hopkins, W. D., Barks, S. K., Bianchi, S., Hehmeyer, A. E., Anderson, S. M., Stimpson, C. D., Fobbs, A. J., Hof, P. R., & Sherwood, C. C. (2012). Neuropil distribution in the cerebral cortex differs between humans and chimpanzees. *J Comp Neurol, 520*(13), 2917-2929. https://doi.org/10.1002/cne.23074 .

function. They concluded that age-related changes to the CA1-CA3 circuit are caused by altered firing rates of the pyramidal cells. CA3 pyramidal cells progressively increase their firing rate with age, forcing the CA1 pyramidal neurons to attenuate the effect of the bombardment of signals through enhancing post-burst after-hyperpolarisation (AHP), which in turn reduces their effectiveness. The authors argued that the perturbation of this finely balanced system is likely caused by unsuitable levels of intracellular calcium. Intracellular calcium levels are known to mediate synapse activity, which in turn alters firing patterns (Kim & Yoon, 1998), ultimately leading to learning and memory deficits (Morrison & Baxter, 2012). Petralia et al. (2014) argue that older synapses and their circuits lose their overall malleability, and with it, flexibility and variability in cognitive function.

Neurons and synapses form the neural substrate of structural networks which, in turn, provide functional connectivity. Neural networks are time-dependent and are governed by the activity of spatially distinct anatomical structures that are linked together by white matter projections within cortical and sub-cortical areas (Damasio, 1989; Gray et al., 1989; Sporns, 2013; van den Heuvel & Hulshoff Pol, 2010). Research shows that cognition occurs through the dynamic interaction of these neural networks (Damasio, 1989) and that they are context[5]-driven (Bressler & McIntosh, 2007; Bressler & Menon, 2010). It is noteworthy that, despite

[5] Context refers to both neural context, where neural activity is affected by different nodes within the brain, and environmental context, where neural activity responds to stimuli and task demands Bressler, S. L., & McIntosh, A. R. (2007). The Role of Neural Context in Large-Scale Neurocognitive Network Operations. In V. K. Jirsa & A. R. McIntosh (Eds.), *Handbook of Brain Connectivity* (pp. 403-419). Springer Berlin Heidelberg. https://doi.org/10.1007/978-3-540-71512-2_14 .

the energy cost, networks project over long distances in addition to short-distances, showing their critical role in functional connectivity (Sporns, 2013).

These distinct anatomical regions integrate dynamically, allowing different regions of the brain to work together to carry out tasks in a broad repertoire of contexts (Bressler & Menon, 2010; Cohen & D'Esposito, 2016). For example, Cohen and D'Esposito (2016) demonstrated how different tasks recruit different network dynamics in an fMRI study with young adults. Participants completed a motor (sequence-tapping task) and a working memory task (n-back task). Analyses showed that within-network activity mediated motor activity, while the integration of different networks was key to working memory. Indeed, studies have shown that, during more complex tasks, increased network efficiency is associated with less modular activity (Hearne et al., 2017; Kitzbichler et al., 2011; Wen et al., 2015). For example, Kitzbichler and colleagues (2011) showed increased long-range network synchronisation between brain regions in young adults.

Ageing has an impact on these optimising characteristics. Research has shown that in older adults, there is more variable functional connectivity (Sullivan et al., 2019), including less long-range network activity, compensated for by more local network activity (McIntosh et al., 2014; Tomasi & Volkow, 2012; Wang et al., 2018). Evidence points to deteriorating white matter[6] integrity and composition as a significant

[6] White matter includes microstructures such as axonal cell membranes, myelin sheaths, and neurofilaments Bennett, I. J., & Madden, D. J. (2014). Disconnected aging: cerebral

underlying contributing factor (Bennett & Madden, 2014; Gold et al., 2010; Liu et al., 2017; Ziegler et al., 2010). Rather unjustly, late-developing myelin deteriorates first and this would therefore seriously impair long-range network dynamics, by disrupting temporal synchrony, which play a crucial role in higher cognitive functions and memory encoding (Bartzokis, 2004). Moreover, there is less specialisation of regions (Burianová, 2013; Sleimen-Malkoun et al., 2013). Sleimen-Malkoun and colleagues (2013) demonstrated by comparing young and older adults that, in terms of the general slowing hypothesis[7], both motor and cognitive tasks are progressively maintained by the same neural structures. Similarly, Burianová (2013) found differences between young and older adults' face processing outcomes: compared to the young group who used neural regions specialised for face processing, namely the fusiform gyrus (bilaterally), older participants recruited only the right fusiform gyrus and the orbitofrontal cortex, which processes faces as well as other objects. The authors argued that this altered neural recruitment pattern indicates a compensatory action to maintain performance. This finding raises an interesting question concerning the mechanism of integration of neural networks and the subsequent impact ageing might have.

Gray and colleagues (1989) proposed that neurons from different anatomic regions are able to coordinate neural responses by lining up or

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white matter integrity and age-related differences in cognition. *Neuroscience, 276*, 187-205. https://doi.org/10.1016/j.neuroscience.2013.11.026 .

[7] General Slowing Hypothesis: "behavioral slowing is mediated by a generalized deficit in processing speed of the CNS, which might be at origin of performance decline in a large variety of tasks" Sleimen-Malkoun, R., Temprado, J. J., & Berton, E. (2013). Age-related dedifferentiation of cognitive and motor slowing: insight from the comparison of Hick-Hyman and Fitts' laws. *Front Aging Neurosci, 5*, 62. https://doi.org/10.3389/fnagi.2013.00062 .

syncing certain characteristics, namely: phase, spatial separation and preferred orientation of cells, which are influenced by global stimulus characteristics. Their study was conducted on the cat visual cortex and their data were derived from spike trains. The data showed that neural responses were oscillatory with no phase difference across spatially separated regions, receptive fields were non-overlapping and cells were homogenously orientated. Finally, global features of the stimuli, e.g. coherent motion, enhanced synchronisation.

A wide range of studies focusing on different brain frequencies have demonstrated that ageing directly affects these connectivity mechanisms by altering the oscillatory characteristics of brain frequencies, namely the power and phase, to varying degrees. These changes are mediated by neurotransmitters that determine the strength and timing of firing patterns of populations of neurons that enable functional connectivity (Barr et al., 2014; Cuypers et al., 2018; Kumar, 2015; Pinheiro & Mulle, 2006; Zahr et al., 2008; Zhou & Danbolt, 2014). For example, GABA, the main inhibitory transmitter, modulates the timing of pyramidal activation and has a role in generating gamma oscillations (Barr et al., 2014) but declines with age (Cuypers et al., 2018; Porges et al., 2017). Critically, a decrease in its levels within the PFC and hippocampus have been linked to memory decline (McQuail et al., 2015). Glutamate, the main excitatory transmitter, is the most abundant (Zhou & Danbolt, 2014) and projects throughout cortical and subcortical structures, playing an important role in learning and memory (Kumar, 2015). Altered glutamate levels have also been linked to ageing. Other neurotransmitters also affected by ageing are

dopamine, acetylcholine and norepinephrine. They play a role in executive processes like working memory, which is the focus of subsequent chapters in this thesis.

1.2.2 Brain oscillations and ageing

Berger (1929) was the first to show that the electrical activity generated by the brain could be monitored via an electroencephalogram (EEG). Since then, research has shown that specific cognitive tasks can be reliably mapped to particular patterns of neural activity using specific calculations (Babiloni et al., 2016; Cannon et al., 2014; Donner & Siegel, 2011; Ward, 2003). Klimesch (2012) argued that the alpha frequency band (8-12 Hz) is dominant in the brain and provides the anchor point for a global frequency structure with frequency bands, namely delta (2-3 Hz), theta (4-6 Hz), beta (16-25 Hz) and gamma (≥ 32 Hz) occurring in discrete bands around alpha.

Alpha power has been shown to play a role in cognitive functions such as attention (e.g. Benedek et al., 2014). Klimesch (2012) argued that event-related synchronisation of alpha is inhibitory and pivotal in suppressing task-irrelevant information, while event-related desynchronisation is disinhibiting and linked to task-relevant responses. Alpha frequency dynamics are known to change with age. For example, studies have shown that the frequency slows down, reduces power and shifts to a more anterior direction (ibid). Knyazeva and colleagues (2018) conducted an EEG study with young to older participants, measuring alpha rhythm. Their analyses revealed a multi-component structure in the alpha rhythm, comprising a high-frequency component originating from the

occipito-parietal cortex and a low-frequency component emanating from the occipito-temporal cortex. This distinction was particularly marked in the younger adults. However, Knyazeva and colleagues (2018) noted a slowing of both frequency components with age. They also observed that the peak for the high-frequency component became gradually and significantly attenuated with age, thereby degrading the differentiation between the two components. In addition, the weight of the peak of the higher component shifting from the dorsal midline occipital region towards occipito-temporal region and the lower frequency component's peak shifting anteriorly but remaining in the occipital region. Thus, with increasing age, the multiple-component characteristic of alpha faded to a single-component frequency.

Delta, which originates from the medial frontal cortex, plays an important role in both non-rapid-eye-movement sleep (N-REM) and cognition. For example, research shows that sleep, in particular N-REM sleep, facilitates memory processing, connectivity between the hippocampus and cortex and neural plasticity (Hill et al., 2007). Disrupted sleep has a serious pervasive effect on cognitive performance, quality of life and health (Maggio et al., 2013). Conversely, poor health, psychological distress and psychiatric illness contributes to poor sleep quality (Han et al., 2012; McEwen, Gray, et al., 2015). Thus, measuring sleep quality can provide a useful marker for health. An early study of healthy men showed that age affected delta activity during sleep and that these changes were non-linear (Ehlers & Kupfer, 1989). Importantly, older participants had less REM sleep, less sleep efficiency and sleep was more

fragmented. A more recent study found a similar impact of age on delta activity, but additionally, that this relationship was moderated by growth hormone production, which declines with age, along with rising evening cortisol levels, which they found to have a significant impact at >50 years of age (Van Cauter et al., 2000).

Vlahou and colleagues (2014) showed that the level of delta and theta resting power has a pronounced impact on cognitive performance. They found that delta and theta power linearly decreased with age, that this effect occurred over all regions of the brain and a decrease of power significantly impaired cognitive performance. Indeed, they found that older participants (≥ 55years) who did better on the task had higher levels of slow wave resting power. Additionally, Ishii and colleagues (2017) argued that, in the absence of alpha slowing, an increased slow wave resting-state power, especially in the theta frequency, is evidence of healthy cognitive function.

Theta power, as indicated above, is important in a range of higher processes such as adaptive cognitive control, working memory and cognitive effort (Cavanagh & Frank, 2014). Moreover, frontal midline theta, which originates from the medial PFC (Ishii et al., 1999), has been linked to a broad spectrum of higher cognitive functions, including attention, working memory and emotional regulation (Mitchell et al., 2008; Onoda et al., 2017). EEG evidence has shown that frontal-midline theta frequency may be observed as event-related potential (ERP) components, each representing a specific role, such as error detection. Each ERP signature represents a particular phase-angle, which reflects a particular firing

pattern of a population of neurons. This mechanism, in turn, is time-specific and provides the means by which neuronal populations are segregated. Cavanaugh and Frank (2014) argued that a stronger firing pattern would result in a more enhanced trough or a lower peak, because neurons in a population are oscillating in the same way, encouraging neurons to interact and collectively modulate synaptic plasticity. This phase-locking activity would facilitate decision-making. However, as mentioned in the previous section, ageing reduces the effectiveness of this activity, by dulling the strength and timing of these intricately balanced firing patterns.

Tóth and colleagues (2014) demonstrated in a study comparing young and older participants that frontal midline theta connectivity affected the efficiency of working memory maintenance and was modulated by ageing. They observed deficits in recognition accuracy in older adults, but not reaction time. In the young group, integrated neural activity was observed within the frontal cortex and between fronto-temporal and fronto-occipital areas. However, in older participants there was a lack of connectivity between mid-frontal and lateral frontal regions and between mid-frontal and temporal regions. Tóth and colleagues (2014) argued that grey matter loss in the hippocampus and lateral frontal cortex may explain the result.

Beta power changes have also been linked to ageing and research shows that reduced beta activity in older adults may be detected in EEG signals before impact becomes apparent in behavioural performance (Winterling, 2019). A recent review (2017) indicated that fluctuations in

beta power play an important role in top-down processing of tasks and are important in long-range network integration. For example, Kamiński et al. (2012) showed in an EEG study with young adults that increased alertness, indicated by increased reaction time during a delayed spatial discrimination task, elicited a strong beta frequency signal over the parietal area prior to both visual and auditory stimuli. In a subsequent visual attention task by the same research team (Gola et al., 2012) older and young participants were compared. They found that the older adult group could be partitioned into low or high scorers, though the sub-groups were comparable regarding age, education and Mini-mental state exam scores. Importantly, within the lower-performing group, the expected anticipatory increase in beta frequency occurred significantly later compared to the high-performing older participants. Moreover, they found it difficult to maintain an increased beta frequency during the interval between cue and target. Overall, scores indicated that the older participants were also slower and less accurate compared to the young participants.

The gamma frequency occurs across cortical and sub-cortical brain regions and is also pivotal to a range of cognitive processes such as memory, selective attention, motivation, behavioural control and perception (Barr et al., 2014; Bosman et al., 2014). This frequency band works within local circuits, such as the hippocampus, where gamma oscillation synchronisation reflects the integrated firing patterns of two different types of neurons: excitatory pyramidal neurons and inhibitory interneurons (Bosman et al., 2014). This balance between excitation and inhibition among neurons is typical within the brain and enables the

segregation of local neural circuits, which can then be communicated to other parts of the brain via long-range projection. Indeed, Başar and colleagues (2015) presented evidence of around 3 to 4 sub-ranges[8] within gamma and that sensory receptors directly transmitted information across three routes: thalamus, reticular formation and over the limbic system. In an *in vitro* study on the mouse hippocampus, Vreugdenhil and Toescu (2005) found that ageing led to reduced gamma power. This outcome was not caused by a change in cell density, reduced extracellular space or a loss of connectivity within CA3. It appeared that the issue arose through changes in CA3 excitatory circuitry, which affected the strength but not the frequency characteristics of gamma. More recently, Barr and colleagues (2014) demonstrated age-related differences in gamma oscillations in a working memory task with young and middle-aged adults. They argued that GABA may be a key factor because it decreases with age, affecting the activation of CA3 neurons. Thus, gamma oscillations may be a potential marker for healthy ageing (ibid).

Cross-coupling of different oscillatory frequencies allow for the integration of different neural populations to enable cognition and other behaviours (Ward, 2003). An example is high gamma amplitude coupled with theta phase where information 'packets' are processed within individual gamma cycles at different phases of theta frequency (Lisman & Jensen, 2013). Park and colleagues (2011) conducted a study with older

[8] 25-30 Hz, 30-35 Hz, 40-45 Hz Basar, E., Tulay, E., & Guntekin, B. (2015). Multiple gamma oscillations in the brain: a new strategy to differentiate functional correlates and P300 dynamics. *Int J Psychophysiol, 95*(3), 406-420. https://doi.org/10.1016/j.ijpsycho.2015.01.013
, ibid..

participants in which they recorded EEG whilst participants completed a spatial memory task. They found that theta-gamma coupling was positively associated with delayed figure recall in the right parietal cortex and topographic maps, an area known to be affected by dementia. Theta-gamma coupling is argued to be a sensitive marker for PFC functioning (Goodman et al., 2018).

1.2.3 Section 2 Summary

It is important to distinguish between pathological ageing and normal ageing as they have different trajectories. Pathological ageing is more commonly associated with oxidative damage whereas normal ageing is more typically associated with mitochondrial ageing. In normal ageing, such mitochondrial degradation causes inefficiencies in energy homeostasis and leads to changes in synapses and their circuits. Specifically, synapses become less malleable and responsive, secreting lower levels of neurotransmitters which, consequently, undermines the finely tuned functional neural networks that connect different anatomical regions. Critically, poorer synaptic function results in changes to the power, phase and phase angle of oscillatory activity, which typically becomes flatter, making phase-locking more difficult and thereby affecting the firing patterns of neurons. Behaviourally, this dysregulation manifests as more variable cognition performance, sleep and subjective well-being.

The following section discusses the more positive topic of cognitive resilience, which demonstrates the remarkable evolutionary adaptive capacity of the brain. In addition, the possibility of slowing down or halting cognitive decline caused by ageing will be considered.

1.3 Section 3: Cognitive Resilience and Ageing

1.3.1 Resilience and compensatory mechanisms in older adults

Advances in science have improved our understanding of how biological ageing processes impact cognition over time. Arenaza-Urquijo and colleagues (2019) conducted an MRI and FDG[9]-PET study with cognitively resilient adults ≥ 80 years to investigate markers that would predict cognitive performance in this group. Variables measured included demographics and ageing, dementia markers[10] and standardised cognitive tests measuring attention, memory, visuo-spatial ability and language. They found that greater glucose metabolism in grey matter, especially in the frontal lobes, was positively associated with cognitive performance. Interestingly, APOE4 status and amyloid levels had little impact, which may be associated with levels of specific beta-amyloid anti-bodies (Peters, 2002). Moreover, evidence indicates that both tau and Amyloid-beta are required to see rapid cognitive decline in preclinical AD (Sperling et al., 2019), thus differentiating the effects of pathological vs. normal ageing.

As the above paragraph suggests, the brain is functionally and biologically robust (Whitacre, 2012; Whitacre & Bender, 2010). The brain has evolved to cope with a certain amount of adversity through the partial and excessive overlap in function across many different modules (Sporns

[9] FDG = fluorodeoxyglucose. It is a sugar tagged with a radiopharmaceutical designed to show up in a PET scan.
[10] Markers were: amyloid burden, FDG (glucose metabolism) and cortical thickness from areas associated with Alzheimer's Disease, APOE4 status, cardiovascular and metabolic health.

& Betzel, 2016; Whitacre & Bender, 2010). This network buffering mechanism is not unique to the brain, but common to a range of highly evolved biological systems (Whitacre, 2012; Whitacre & Bender, 2010). The brain can spontaneously draw upon available resources rather than rely on a set of central scripts based on matching up one-to-one actions with context (e.g. Shah et al., 2018). Thus, the brain may be described as "self-organised", allowing performance to be maintained even if the structure originally assigned to a task has been damaged/disabled (Whitacre, 2012; Whitacre & Bender, 2010).

Within the brain there are three mechanisms that help maintain functional integrity: developmental variation and selection, experiential selection and re-entrant signalling (Edelman, 1993). In developmental variation and selection, structural diversity is developed through epigenetic regulation of cells such as whether cell division should/shouldn't occur, extend more dendrites and so on. Experiential selection is driven by experience and behaviour, allowing for neuronal groups to be dynamically selected through continuously changing synaptic activity perturbed by experience and behaviour. Re-entrant signalling is important for mapping the external environment onto neuronal populations. Edelman (1993) describes re-entry as "ongoing parallel signalling between separate neuronal groups occurring along large numbers of ordered anatomical connections in a bilateral and recursive fashion" (p 117). This mechanism is dynamic, inherently parallel and distributed within and between the cortex, basal ganglia and cerebellum (ibid). With the above in mind,

numerous theories have been proposed indicating how the brain compensates for age-related structural deterioration within the brain.

In the context of working memory performance, Salthouse (1994) demonstrated that ageing degrades the speed with which information is encoded or activated. Salthouse (1996) subsequently proposed his processing-speed theory of adult age differences which holds that a small number of common factors accounts for age-related variance in most reaction time measures. However he noted, in line with Edelman's aforementioned experiential mechanism, that age-related slowing is neither universal, uniform nor unitary. This is because working memory performance affected by several factors. For example, having a broader vocabulary would reduce processing burden in a word-related task. Importantly, evidence from path analysis following cognitive tests of adults aged 18 to 87 indicated a strong association between age and perceptual speed and perceptual speed and decision accuracy but a weak relationship between age and decision accuracy (Salthouse, 1996). Study time (solution time) was found not to be related to perceptual speed but was associated with age and decision accuracy. Thus, older participants spent longer on solution time and this was associated with better accuracy. Thus, older adults may use cognitive strategies or accumulated knowledge to compensate for slower processing speed. Social interactions may similarly offset the impact of ageing on cognition (Charles, 2010; Charles & Carstensen, 2010). Evidence indicates that older adults are better at regulating emotional experiences and using attentional strategies than middle-aged and young adults and, consequently, prioritise positive

over negative experiences (Charles, 2010). Importantly, Charles and Carstensen (2010) report that older adults who have well-established social networks and are very sociable perform relatively better than less socially engaged individuals in cognitive tasks.

Cabeza (2002a; 2002b) argued that bilateral activation increases with age and proposed the HAROLD model of ageing: “Hemispheric asymmetry reduction in older adults”. However, Berlingeri and colleagues (2013) argued that HAROLD represents a specialised compensatory mechanism whereas their evidence supports a more general compensatory approach i.e. that contralateral brain areas, not necessarily related to the ipsilateral specialised area, are also recruited. This finding is congruent with the argument that the brain comprises a system that competitively interacts through the application of a “concurrent stochastic process” to resolve dysfunction (Whitacre & Bender, 2010, p. 2).

Ghisletta and Lindenberger (2003) proposed the dedifferentiation hypothesis, which maintains that cognitive performance, assumed to comprise biologically driven fluid intelligence and environmentally driven crystallised intelligence, becomes increasingly weighted towards the effects of ageing on fluid intelligence. Their longitudinal study supports this hypothesis by demonstrating that perceptual speed (fluid intelligence), predicted knowledge (crystallised intelligence) both of which were predicted by the age-related impact on processing speed. Thus, fluid intelligence, which is argued to represent the efficiency of cognitive control mechanisms like speed, power and complexity (Craik & Bialystok, 2006), becomes increasingly tied to the fate of anatomical brain structures. Thus,

crystallised aspects of intelligence *per se* may remain stable with age (ibid). de Frias and colleagues' (2007) findings also support the dedifferentiation hypothesis. They demonstrated in their longitudinal study, that inter-individual variability in the rate of changes in different cognitive abilities increases in older age and that these changes in different cognitive abilities become increasingly more correlated, but only from about 65 years old. Again, these findings do not contradict what is known about the adaptive nature of neural systems, which develop, mature and age in the context of dynamic, epigenetically driven neural structures and functional connectivity (Edelman, 1993; Whitacre, 2012; Whitacre & Bender, 2010).

Park and Reuter-Lorenz's (2009) "scaffolding theory of cognitive ageing" (STAC) acknowledges the adaptive nature of the brain, stating that "It is not merely the brain's response to normal aging; it is the brain's normal response to challenge" (page 183). For example, Hoekzema and colleagues (2017) demonstrated significant and lasting changes in the cerebral cortex of pregnant women via the process of synaptic pruning. The purpose being the fine-tuning of functional networks to prepare for motherhood.

Scaffolding is a process that starts in early development (Petersen et al., 1998), where structural networks shift from being more dispersed to being more specialised: a skill is learned and practiced, creating over-learning. Once that specialised neural circuit has been formed and developed, the more disperse region from which it arose maintains its ability to undertake that skill/task (Park & Reuter-Lorenz, 2009). These

regions provide secondary neural networks/scaffolds which support and maintain cognitive function in the face of structural deterioration/dysfunction by supplementing, complementing or completely taking over a task or function that might otherwise fail. Importantly, this compensatory mechanism exploits the highly flexible nature of the PFC to ensure maximal efficiency of cognitive performance. Addressing the impact of external factors, they revised their “scaffolding theory of cognitive ageing” model (STAC-r) to include neural resource enrichment and depletion (Reuter-Lorenz & Park, 2014). Their review featured a wide range of studies supporting the key roles played by these variables. Examples of neural enrichment given were social activities and intellectual challenges like higher education, good cardiovascular fitness and leisure activities. According to Stern (2009), these activities are ways of shoring up cognitive reserve that would allow functionality to be maintained even in the face of neural pathology. Neural depletion examples include the presence of APOE-4, which has been associated with an increased risk of AD. Moreover, lifestyle factors such as smoking and diabetes reduce vascular health, increasing the risk of neural and heart damage through increased amyloid deposits and deteriorating white matter. Stress, already mentioned, causes the hippocampus to shrink, contributing to both cognitive and emotional difficulties (Reuter-Lorenz & Park, 2014).

In resilient ageing individuals, it appears that white and grey matter undergo a complex process of reorganisation to preserve connectivity, particularly within and between key areas such as the PFC, hippocampus and corpus callosum. Changes include adjustments in temporal dynamics

and topography (Gonzalez-Escamilla et al., 2018). In addition, neural plasticity is maintained across the lifespan (Skaper et al., 2017). These findings, together with the literature indicating that environmental factors may grant neural reserve[11], suggest that there is scope to maintain optimal cognition in older age.

1.3.2 Interventions to enhance cognition

As indicated by Reuter-Lorenz and Park's (2014) "scaffolding theory of cognitive ageing" model (STAC-r) in the previous section, various lifestyle activities such as intellectual/social engagement, new learning and exercise may benefit neural health and cognition in older age. Indeed, there is a wide range of possible interventions that may preserve brain health and, thereby, also subjective well-being in ageing individuals. For example, a broad literature shows that calorie restriction (Balasubramanian et al., 2017) and exercise (Vecchio et al., 2018) have potential to be highly efficacious. These activities maintain brain health through a range of mechanisms/pathways. Calorie restriction benefits have been linked to metabolic regulators, which play a role in metabolism and inflammation (Balasubramanian et al., 2017); research suggests that insulin plays a role in spatial learning, therefore must be carefully regulated (Skaper et al., 2017). Exercise studies indicate that brain-derived neurotrophic factor (BDNF), associated with cardio-vascular

[11] Neural reserve, a feature of cognitive reserve, is the ability to maintain task performance with brain pathology as compared to those completing the same task with healthy brains Stern, Y. (2009). Cognitive reserve. *Neuropsychologia, 47*(10), 2015-2028. https://doi.org/10.1016/j.neuropsychologia.2009.03.004 .

exercise, improves brain health (Vecchio et al., 2018). For example, BDNF improves neural differentiation and synaptic plasticity and aids in maintaining the health of astrocytes, thereby reducing inflammation and protecting the blood brain barrier. Long-term exercise was found to reduce the build-up of plaques in the hippocampus and cortex (Vecchio et al., 2018). Moreover, in a population-based study of women, regular exercise was associated with an anti-inflammatory effect, the largest contributing factor (32.6%) in lowering risk of cardio-vascular events (Mora et al., 2007). Thus, BDNF plays a key role in neuro-plasticity (Castren & Kojima, 2017; Thoenen, 1995). From a well-being point of view, BDNF offers a useful case-in-point of how brain health affects mood. Previous work has shown that levels of BDNF, through its mediatory effects on plasticity, may have an anti-depressant effect (Castren & Monteggia, 2021). These options all offer rich indirect benefits to a range of structures by enhancing the health of the neural substrate, discussed in section 2, thereby improving functional connectivity. However, for many, particularly older adults, some of these activities are not possible or would be difficult to maintain; Brand and Cheval (2019) provide an insightful discussion on exercise motivation and physical inactivity in this context. Exercise benefits require one to be able-bodied to obtain the cardio-vascular benefits. Moreover, there is still debate regarding the relationship between physical activity and cognitive functioning. For instance, a systematic review of 12 randomised controlled trials (n=754) investigated the benefits of aerobic exercise programmes for those aged > 55 (Young et al., 2015). They found no evidence that aerobic exercise or increased fitness

enhanced cognitive performance in this group. However, a more recent study that extracted data from two large-scale genome-wide association studies (UK Biobank and COGENT) (n=257,841) found evidence of a benefit of moderate and vigorous exercise on cognitive function and no reverse causal effect (that those with better cognitive performance are more likely to exercise) (Cheval et al., 2023). Regarding caloric restriction (CR), researchers do not see this as a viable option: "…the goal of CR research is to figure out how it works, not to promote it as a lifestyle." (Balasubramanian et al., 2017, p. 41). Two other, potentially more broadly achievable options, though not without limitations, are worthy of further consideration. Meditation and transcranial electrical stimulation. While these methods are very different, evidence suggests that both have the potential to improve functional connectivity and, consequently, cognitive performance.

1.3.3 Meditation as a method of maintaining cognitive performance

Meditation is a non-religious practice of quieting the mind by focusing inwardly, whilst remaining alert. The operational definition used by researchers is less straightforward. There are a wide variety of meditations and Nash and Newberg (2013) have recommended specifying the details of the meditation studied on the basis of certain key elements, including cognitive strategies used during meditation such as focused attention versus effortless awareness, as well as whether eyes are open or closed and so on. These details are pivotal, because they activate different brain areas with potentially differing effects. For example, Tomasino and colleagues (2014) found that Buddhist-based meditations,

which focus on mindfulness, activated the supramarginal gyrus cluster, an area in the parietal lobe associated with attention (Kashkouli Nejad et al., 2015). On the other hand, Hindu-based meditations, which focus more on pure consciousness, activated the left hippocampus, left superior temporal gyrus, left post-central gyrus, left superior parietal lobule and right middle cingulate gyrus (Tomasino et al., 2014). These areas are correlated with functions that include memory and spatial orientation (ibid). Ignoring these ontological and methodological differences for the moment, the benefits in terms of ageing will now be outlined.

As discussed earlier in the chapter, cumulative life stress appears to accelerate ageing. An over-activated HPA increases oxidative damage and inflammation leading to telomere shortening and cellular damage/loss. A related effect is that the dendrites and synapses in the hippocampus contract leading to shrinkage of this structure, while those in the amygdala expand. The negative mental and physical health consequences of this include anxiety, depression and cardiovascular disease as well as poorer cognitive performance (McEwen et al., 2016). However, meditation has the potential to reverse these effects.

Meditation was found to improve stress resilience[12], mediated by improved functional connectivity (Kwak et al., 2019). These authors also observed an enhanced activation of the default mode network, a functional network important to cognition, which can become less functionally

[12] "Resilience is defined as an individual's capacity for recover after significant adversity" Kwak, S., Lee, T. Y., Jung, W. H., Hur, J. W., Bae, D., Hwang, W. J., Cho, K. I. K., Lim, K. O., Kim, S. Y., Park, H. Y., & Kwon, J. S. (2019). The Immediate and Sustained Positive Effects of Meditation on Resilience Are Mediated by Changes in the Resting Brain. *Front Hum Neurosci, 13*, 101. https://doi.org/10.3389/fnhum.2019.00101 .

connected with advancing age (Avelar-Pereira et al., 2017; Vidal-Pineiro et al., 2014). Improved resilience scores were maintained at 3-month follow-up.

According to Kaliman (2019), epigenetic mechanisms may provide a pathway for meditation to reverse or mitigate the effects of cumulative life stress and exploratory research has shown neurophysiological differences comparing long-term meditators to non-meditators. For example, a study with long-term Buddhist-based meditators, compared to controls, showed significantly increased levels of grey matter density in the medulla oblongata, anterior cerebellum, left superior and inferior frontal gyrus and left fusiform gyrus (Vestergaard-Poulsen et al., 2009). They argued that these changes provide a route to protect against the impact of stress and enhance attention (ibid). Similarly, differences in cortical thickness were observed by Lazar (2005) in sub-regions, such as the PFC and right anterior insula when comparing long-term Insight meditators and controls. More recently, structural changes have also been reported by Posner and colleagues, who found that mindfulness-based stress reduction enhanced white matter density, possibly through enhanced frontal midline theta activity (Posner et al., 2014; Tang, Lu, et al., 2012). Midline theta, as previously mentioned, plays a central role in a range of cognitive functions.

Changes have also been reported in endocrine function of long-term meditators. For example, Ferrarelli and colleagues (2013) found, compared to meditation-naïve participants, that long-term meditators showed enhanced parietal-occipital gamma power during NREM sleep,

which was positively associated with daily meditation practice, rather than sleep architecture. In addition, meditation has been found to reduce blood pressure, cortisol levels, resting heart rate, lipids and inflammation (Creswell et al., 2012; Ooi et al., 2017; Pascoe et al., 2017; Rosenkranz et al., 2016).

Telomere length, affected by ageing and cumulative stress, is also improved through meditation. A small (n=4) meta-analysis of mindfulness meditation studies found a medium effect size (0.46) indicating that meditation increased telomerase activity (Schutte & Malouff, 2014). In another study (Conklin et al., 2019), telomere length (in leukocytes) in a group of long-term Zen meditators was found to be longer compared to controls. Conklin and colleagues' (2019) interpretation of the finding was that meditation may influence telomere biology by mediating stress reactivity and resilience capacity.

Meditation is also believed to benefit naïve participants. Fennell and colleagues (2016) demonstrated reduced anger after just one meditation session in a group of naïve meditators, as measured by respiration rate, blood pressure and pulse, compared to expert meditators. Similarly, Tang and colleagues (2007) showed that 5 days of mind body stress reduction was sufficient to enhance self-regulation and cognition compared to relaxation alone. For short and long-term meditators, evidence suggests improvements in cognition as well.

Research suggests that meditation may enhance attention, working memory capacity, executive function and self-regulation (Holzel et al.,

2011) (see Chiesa et al., 2011 for review). For example, Tsai and Chou (2016) compared experts in either open monitoring or focused attention meditation to controls. The study showed that both expert groups had more enhanced executive control, compared to non-meditators, as measured by the attention network test; the open monitoring experts also out-performed controls on orienting attention. In a second experiment, novices received 3 months of focused attention mediation[13] training and showed an improvement in executive attention compared to their baseline score. More recently, Basso and colleagues (2019) randomised naïve participants to either 13-minute daily podcast sessions (control) or 13-minute guided meditations. They found that, compared to controls, meditators showed reduced negative state mood and anxiety scores as well as enhanced attention, working memory and recognition memory performance after 8 weeks of practice.

In terms of ageing, Gard and colleagues' (2014) systematic review (n=12) of meditation studies with older adult participants suggested that meditation may offset cognitive decline caused by ageing, with benefits such as improved executive function, processing speed, memory and attention. In the only recent longitudinal study on the cognitive impact of meditation on ageing, Zanesco et al. (2018) recruited experienced meditators and randomly assigned them to a 3-month intensive Buddhist meditation training retreat condition or wait-list control condition in an earlier study (Sahdra et al., 2011), which showed increased response inhibition and attenuated vigilance decrement. At the 7-year follow-up

[13] Focused attention was chosen, because it can be learned quickly.

(Zanesco et al., 2018), performance in response inhibition accuracy and reaction time variability was moderated by dose (low, medium or high continued practice), indicating that, with ongoing practice, sustained attention and response inhibition can be maintained with increasing age. This finding is supported by the literature (see Ramirez-Barrantes et al., 2019 for review).

There are a few caveats to the promising results of meditation. The range of meditations reported in the literature is considerable. Some are mind-body practices, while others are purely mental activities. Of those that are purely mental activities, there are different types, which are believed to activate different regions (as previously mentioned). In addition, there are differences in dose, age and study design, which may seriously affect reported results. For example, a recent study showed that, when non-specific events are controlled for, 2 weeks of focused attention was not sufficient to enhance working memory capacity (Baranski & Was, 2018). Another study revealed that expectation has a marked impact on results and should be incorporated into study design (Pratzlich et al., 2016). In addition, meditation may not necessarily be better than exercise or other forms of intervention such as pharmaceuticals (de Bruin et al., 2016; Goyal et al., 2014; van der Zwan et al., 2015). Whilst this may be true, the weight of evidence suggests that meditation is a viable choice through its subtle but persistent impact on neural networks that are capable of harnessing processes like attention, memory and brain states (Tang et al., 2015; Tang, Rothbart, et al., 2012; Vago & Zeidan, 2016).

Another more direct option is electrical neurostimulation, which has been shown to enhance cognitive functions.

1.3.4 Transcranial electrical neuromodulation (tES)

Transcranial electrical stimulation is a potentially useful tool for understanding and enhancing cognition function (Parkin et al., 2015). The three types of tES typically used in clinical and research studies are: transcranial direct current stimulation (tDCS), transcranial random noise stimulation (tRNS) and transcranial alternating current stimulation (tACS). All three methods involve placing electrodes on the scalp and aim to manipulate neuronal activity by emitting a small amount of electrical current (typically 1 – 2.5 mA) for a set period of time (e.g. 20 min), which modulates firing rates of neurons, but remains sub-threshold (Antal & Herrmann, 2016; Bikson et al., 2018). More specifically, these electrodes introduce a change to the existing voltage gradient[14] in the extracellular space within the brain, which then polarises the neurons at the stimulation site (Rahman et al., 2015). Typically, a voltage gradient within the range of endogenously generated electric fields would be required to perturb neuronal networks (Bland & Sale, 2019) with at least 1 mV/mm as a minimum (Vöröslakos et al., 2018).

Transcranial direct current stimulation achieves this perturbation by emitting a constant current through anode (+ve) and cathode (-ve) electrodes which, respectively, enhance or depress the threshold of action

[14] Voltage gradient refers to a change in electrical potential over a given distance Rahman, A., Lafon, B., & Bikson, M. (2015). Multilevel computational models for predicting the cellular effects of noninvasive brain stimulation. *Prog Brain Res, 222*, 25-40. https://doi.org/10.1016/bs.pbr.2015.09.003 .

potentials (Paulus, 2011). This effect is achieved by the current flowing into the anode electrode and out of the cathode electrode, via the area being stimulated and the neurons under the anodal electrode become depolarised, or excitatory, while those under the cathode electrode become hyperpolarised, or inhibitory (Radman et al., 2009). Animal models, simulation studies and the extensive body of research on the human motor cortex offers the clearest picture of the efficacy of tDCS (Jackson et al., 2016; Stagg et al., 2018; Stagg et al., 2009; Stagg & Nitsche, 2011). Longer-term after-effects, such as long-term potentiation (LTP), may occur via chemically induced mechanisms including modulation of glutamate and GABA receptors (Cohen Kadosh et al., 2015; Nitsche et al., 2003) with synaptic plasticity considered as central to lasting tDCS effects (Jackson et al., 2016).

Transcranial alternative current stimulation involves the application of a frequency-specific sinusoidal waveform, giving it a discernible advantage over tDCS. Where tDCS relies solely on voltage-related membrane perturbation of neurons (Bikson et al., 2004), tACS' impact on endogenous neural networks is synergistic because it can harness the amplification effects of frequency resonance to further enhance synchronised network activity (Bikson et al., 2018; Francis et al., 2003; Radman et al., 2007; Reato et al., 2010). Though note that tACS cannot override endogenous frequencies (Schmidt et al., 2014). Indeed, while it seems unlikely that < 1V/m of externally applied current could have any impact on quiescent neurons, the physiological mechanism underlying neuronal action potential activation is linear and, thus, incrementally

adding energy can change the timing and/or the probability of neurons firing (Bland & Sale, 2019; Harris et al., 2002; Radman et al., 2007; Stagg et al., 2018). Thus, when an exogenously applied current and endogenous frequencies are similar, intensities in the range of 0.2 to 0.5 V/m have been effective in altering spike timing of neurons (Bland & Sale, 2019). Furthermore, evidence suggests that neural networks may be more sensitive than individual neurons (Deans et al., 2007). Consequently, as noted by Polanía and colleagues (2011), the effect of electrical stimulation may be site-specific but is not site limited. Thus, targeting a particular frequency may offer a more directed and therefore efficacious neuromodulation tool to evaluate/modulate neural networks and neural network connectivity.

Transcranial random noise stimulation, a variant of tACS (Antal & Hermann, 2016), applies a random amplitude and frequency pattern and is polarity-independent. Higher frequencies (100 – 640 Hz) elicit enhanced cortical excitability (ibid), possibly by increasing the signal-to-noise ratio through increasing sensitivity of neurons (Jaušovec & Pahor, 2017). Thus tRNS may work via a stochastic resonance mechanism where noise within the system is enhanced, raising its responsiveness to an input signal (Herrera-Murillo et al., 2022). Another possible hypothesis is that sub-threshold stimulations applied repeatedly disrupt homeostasis and enhance task-related neuronal activity (Fertonani et al., 2011 cited in Reed & Cohen Kadosh, 2018). A potential advantage of tRNS is that it produces excitatory changes at both electrode sites, which may afford more efficient

stimulation, depending on the objective of the research (Cohen Kadosh, 2015).

Evidence to date indicates that tDCS, tACS and tRNS can enhance executive processes including working memory, attention and decision-making (for reviews see Coffman et al., 2014; Frohlich et al., 2015; Polania et al., 2018; Schutter, 2016). Most recently, a systematic review showed that of 34 articles, 28 reported improved cognitive function in areas such as executive function, cognitive flexibility and attention (Feltman et al., 2020). Additionally, other work has shown that tDCS is a promising method of enhancing self-regulatory behaviour such as persistence and impulse control by stimulating regions within the PFC (Kelley et al., 2018). Klink and colleagues' (2020) review of 57 studies indicated that theta-tACS benefited functions such as working memory, executive function and declarative memory while gamma-tACS improved perception but were less consistent for higher cognitive tasks. In a review of studies using tRNS as a treatment for neurological disorders, the overall finding was that tRNS-based therapies worked best with concurrent neurological/psychological assessments that allowed for after-effects to be measured. The reviewed studies typically found evidence for a possible stochastic mechanism of action. Whilst there do not appear to be reviews of tRNS studies in healthy adults, tRNS does demonstrate cognitive benefits in numerous studies. Brevet-Aeby and colleagues (2017) found in a longitudinal double-blind sham-controlled study that 3 tRNS sessions relative to sham or a single tRNS session improved inhibitory control for at least a week. Another study showed that with 5 days of consecutive

stimulation, learning improved with stimulation over the left DLPFC, which was still detectable 6 months later (Snowball et al., 2013). This finding is congruent with a more recent finding that 4 days' parietal tRNS plus working memory training resulted in improved working memory and inhibition relative to sham which their EEG data suggested was driven by top-down theta oscillatory activity (Tatti et al., 2017). Transcranial random noise stimulation has also been used to study its effect on mood. However, the study found no evidence of elevated mood in the tRNS group relative to sham. They did find, though, that individual differences in age and trait mood may have played a role in their study's outcome.

Most research has focused on healthy young adults or clinical populations. Relatively few studies have been conducted with older healthy adults. However, findings seem to indicate two important outcomes: firstly, tACS and tDCS studies can elicit cognitive enhancement in healthy older participants (e.g. Antonenko et al., 2016; Berryhill & Jones, 2012; Holland et al., 2011; Meinzer et al., 2013; Reinhart & Nguyen, 2019); secondly, some studies have been able to demonstrate, through fMRI and/or EEG data, that functional network patterns do differ in older adults when they engage in cognitive tasks during tES. Such findings agree with previous research regarding the impact of ageing on functional connectivity and, from a methodological point of view, they should always be tested as a separate group in neurostimulation studies. For example, Reinhart and Nguyen (2019) used tACS at a theta-gamma coupled frequency to successfully enhance working memory in older participants, whose tACS-induced performance was comparable to the young group's

baseline performance. Crucially, performance accuracy improved with no change to reaction times, therefore older adults were not maintaining accuracy by slowing down. They were also able to show accuracy gains from 8 min into the 25-min stimulation, peaking at the first post-stimulation time bin, which continued throughout the post-stimulation period. Their study further provided evidence for the hypothesis that cognitive decline in older adults relates to deteriorating functional connectivity between frontal and other anatomical regions. Reinhart and Nguyen (2019) argued that the improvements elicited may have been a consequence of entrainment, with longer-lasting effects reflecting strengthening of synaptic connections, as previous researchers have argued (Stecher et al., 2017).

Emonson and colleagues (2019) conducted an EEG TMS study where healthy young and older adults as well as a small sample with mild cognitive impairment (MCI) were compared on tDCS cognitive performance. They found no change in cognitive performance across groups. The neurobiological results showed that cortical excitation was significantly enhanced in the younger group only, which correlated with performance on the n-back task; older adults and MCI did not show variation in their peak amplitudes following tDCS stimulation unlike previous studies that did show variations (Meinzer et al., 2013 and Antonenko et al., 2017). Emonson et al. (2019) argued that this may indicate that healthy and pathological ageing is distinguished by atypical amplitude peak activity, which could be measured at baseline. In general, their findings revealed a varied neurobiological response in the three groups, with younger participants being more neurobiologically responsive

to the stimulation; healthy older participants' data showed very limited responsiveness or atypical responsiveness. The reason may relate to a limited capacity to respond (ibid) and is suggestive of the compressed adaptive responsivity discussed early in this chapter. The MCI group were unresponsive to both tDCS and TMS, indicating that a single-session of tDCS may not be enough to enhance cognition in this group. As with many tES studies, the sample, especially the MCI group, was small, however.

In general, tES research findings should be interpreted with cautious optimism. Studies often differ with regards to parameters like current density and sample size and findings in one anatomical region, such as the motor cortex, cannot necessarily be extrapolated to other areas (Nitsche et al., 2008). Jacobson and colleagues' (2012) meta-analysis found that with the typical anodal-cathodal tDCS montage, effects were fairly consistent in motor studies but variable in cognition tasks. Similarly, Horvarth and colleagues (2015) conducted a meta-analysis of single-session tDCS studies with healthy adults covering a range of cognitive tasks and found no significant effect for these tasks. Moreover, Hoy and colleagues (2013) found that efficacy of tDCS is dose-dependent. Their results showed the most enhanced effect of working memory performance for 1 mA, as compared to 2 mA and sham. This finding mirrors the mechanism of endogenous neuromodulators such as dopamine, acetylcholine and serotonin where too much or too little ultimately leads to poor cognitive performance (Thiele & Bellgrove, 2018). In addition, montage placement is key. For example, in a recent tACS study Wolinski and colleagues (2018) used two montages differing in their

return electrodes to test the impact of tACS on working memory capacity: ipsilateral pairing (P4/right supraorbital) and standard pairing (P4/Cz). They found evidence of an effect in the case of the P4/right supraorbital montage, but not the montage employing the often-used referent electrode placement (Cz). They argued that tACS may have maximised highly lateralised functional networks within the right parietal area. In terms of evidence of long-term potentiation, Veniero and colleagues (2015) found that after-effects of tES, based on EEG evidence, indicated that oscillatory tDCS, tACS and tRNS were commonly found, though there was a lack of consistency across studies (Veniero et al., 2015).

Transcranial electrical stimulation is, nonetheless, a promising tool and replication and standardisation of protocols will ensure greater consistency of findings in the future, where the focus should be on producing effect sizes with potential clinical value (Parkin et al., 2015).

A general caveat is noted: MM and tES still require some motivation and monetary cost.

1.3.5 Section 3 Summary

The self-organised and malleable nature of the brain makes it resilient and robust in the face of challenges. Functional integrity is maintained via a range of mechanisms. Older brains likely compensate for biological ageing and environmental stressors discussed in sections 1 and 2 and a number of theories have been proposed to explain this. The literature suggests that good cognitive function can be maintained in later

years given the brain's ability to restructure alongside compensatory mechanisms.

A number of behavioural strategies can benefit cognitive performance, including calorie-restriction, exercise, meditation and tES. While all of these options are well-supported by evidence, each has advantages and disadvantages. Two of the more promising candidates are meditation and tES, because they are suitable for any age and rely less on internal levels of motivation than exercise and calorie-restricted eating.

This chapter provides an overview of the impact of ageing and cumulative stress on the brain and cognition. The first section showed that certain biological and environmental factors like cumulative life stress cause structural and biochemical changes that lead to deterioration of functional neural networks which can become less connected and unbalanced, adversely affecting cognition and, consequently, quality of life. However, the brain strives to maintain functionality and has evolved a range of compensatory mechanisms to maintain optimal functioning. It is possible to augment these processes by being proactive. Research suggests that interventions such as meditation and tES can reverse/mitigate some of the structural damage and chemical imbalance caused by ageing and stress to the extent that older participants are able to produce cognitive performance on a par with younger adults. The next step is to thoroughly investigate their potential, being mindful of the pitfalls and methodological issues that have been raised. To investigate the benefits of tES and meditation for optimal higher cognitive function and

subjective well-being, Chapter 2 aims to evaluate the efficacy of transcranial alternating current stimulation relative to mindfulness meditation regarding working memory and subjective well-being in adults. Chapter 3 aims to investigate the cognitive effects of tACS and of cumulative life stress on young and older adults. Due to mandatory lock-down enforced from 20th March 2020 to May 2021 with possibility of future lock-downs, I changed the direction of the planned research because in-person research was not allowed. All subsequent chapters (Chapters 4 to 6) comprise observational online studies as a direct consequence. Chapters 4 and Chapter 5 evaluate the impact of cumulative stress, ageing and the interaction of the two on working memory and subjective well-being. In Chapter 4, a Bayesian meta-analysis is used to robustly evaluate the effect size of ageing, cumulative stress and their interaction on working memory performance. In Chapter 5, cross-sectional and longitudinal studies are used to explore whether ageing, cumulative stress, subjective sleep quality, adverse childhood events and/or resilience are associated with working memory performance. Chapter 6 aims to update and improve the widely used Social Readjustment Rating Scale. Chapter 7 provides a discussion of the thesis as a whole, ending with final recommendations.

Chapter 2: What is the efficacy of mindfulness meditation compared to transcranial alternating current stimulation (tACS) in enhancing working memory performance and/or subjective well-being in adults? A systematic review comparing the effect sizes of meditation outcomes vs tACS outcomes in studies conducted from 1988 to 2020.

2.1. Introduction

The UK is likely to face significant challenges arising from an ageing population given the ongoing increase in life-expectancy year-on-year (Park, 2022). Ageing is associated with increased variability in cognitive function and a commonly observed research finding is that older adults perform worse in working memory and processing speed tasks compared to young adults (Vlahou et al., 2014). One underlying cause is structural deterioration of the brain (Fjell et al., 2014). Moreover, while cognitive decline is known to accompany ageing, for nearly a million people over 65 (~7% of ≥ 65 yrs UK population) it is accompanied by disability and early mortality because of dementia or Alzheimer's Disease (AD) (Wittenberg et al., 2019).

Biological processes associated with ageing are a known risk factor in developing dementia/AD, however there are also numerous environmental risk factors. Cumulative stress is one such factor and is arguably difficult to avoid. While it is beneficial to experience some acute stress, cumulative effects of chronic or repeated bouts of acute stress can be harmful. Both acute and accumulated stress effects are linked with structural remodelling in the brain (McEwen et al., 2012), however

cumulative stress is also associated with greater stress reactivity and potentially damage to the brain, the autonomic nervous system and other areas because of ongoing exposure to glucocorticoids via the stress response (McEwen, 2016). Congruently, Marshall et al. (2018; 2017; 2016; 2016b; 2015) found that older adults with high cumulative life stress showed impaired performance in working memory (WM), inhibitory control and spatial discrimination tasks compared to low cumulative life stress older and young participants. Additionally, their associated EEG data revealed changes in power and synchronisation of specific brain frequencies, which were associated with deficits in cognitive performance and may be associated with early signs of dementia. Living longer *and* having a good quality of life is not a given. It is therefore essential to find ways to mitigate the effects of ageing and cumulative stress, particularly given that ageing begins in early adulthood (Daugherty et al., 2016; Park & Reuter-Lorenz, 2009) and stressful events are likely to occur throughout the life span.

In Chapter 1, two treatment interventions were highlighted as potential candidates to improve cognition and subjective well-being in healthy adults: mindfulness meditation (MM) and transcranial alternating current stimulation (tACS). Both methods are commercially available, safe and practical. Their efficacy in improving cognitive function and well-being has been demonstrated scientifically (Gard, Taquet, et al., 2014; Tavakoli & Yun, 2017; Tsai & Chou, 2016) and both methods modulate neurological functioning relatively quickly in young and older adults (e.g. Antonenko et al., 2016; Brown et al., 2023; Colzato et al., 2016; McHugh et al., 2010).

Thus, benefits may begin from the first treatment. Importantly, MM and tACS are passive activities, making them suitable for disabled and/or frail individuals and are potentially easier to maintain than, for example, exercise, calorie-restricted eating or learning a new language. Within the meditation and tES literature, there are numerous approaches. The reasons for choosing MM and tACS will be explained in turn.

Mindfulness meditation was selected because it requires effortful cognitive control, but is also relatively straightforward to learn and can be done in-person or via smart phone/similar technologies. For example, mobile phone applications such as ‘Headspace’ (e.g. Zollars et al., 2019) and ‘Calm’ (e.g. Huberty et al., 2019), provide simple, step-by-step instructions to users. Mindfulness meditation has a focused attention component with eyes closed in a seated position. Typically, a mindful meditator directs their attention to an external focus, such as breathing, whilst maintaining a present state of mind. Whenever the mind wanders, the meditator returns their focus to the breath without judgement (Lutz et al., 2008). Mindfulness meditation may also aim to simply keep an open monitoring state following a period of focused attention (ibid). Importantly, focused attention and open monitoring mindfulness meditation approaches have been shown to benefit higher-order cognitive function as they require shifting and maintaining attention for a set length of time (Tang, Rothbart, et al., 2012). In particular, the anterior cingulate cortex, reciprocally connected to the dorsolateral prefrontal cortex (Haber et al., 2022), is the region most consistently associated with this modulation of attention (Tang et al., 2015). Congruently, evidence indicates that open monitoring and

focused attention expert meditators have better executive control than non-meditators (Tsai & Chou, 2016). Furthermore, an fMRI randomised control trial with stressed, job-seeking adults showed that, following a 3-day mindfulness training residential retreat, resting-state functional connectivity between the dorsolateral prefrontal cortex (DLPFC) and dorsal and ventral corticolimbic circuits was improved relative to matched controls in the relaxation condition (Taren et al., 2017). This finding, the authors argued, supports previous work that MM improves functional connectivity in neural networks important to executive function and self-regulation.

Transcranial alternating current stimulation was chosen because, of the available tES methods, it is uniquely able to synergistically entrain specific endogenous neural frequencies ‘online’ and can produce changes in plasticity ‘offline’ (Helfrich et al., 2014). Thus, the investigator can target specific pathways/neural networks by tapping into one or more ‘nodes’ of that network that might be critical to optimal cognitive functions including inhibition, attention and WM in both young and older healthy adults (Abellaneda-Pérez et al., 2022; de Boer et al., 2021; Goldthorpe et al., 2020). For example, in a review of 104 studies (from 34 articles) Booth and colleagues (2022) showed that, relative to sham stimulation, posterior theta-tACS modulates WM activity whilst anterior gamma-tACS modulates long-term memory activity in healthy adults.

Whilst both MM and tACS benefit cognitive performance and psychological well-being, their efficacy has not been directly compared in previous research. This is made somewhat more complicated by the fact

that neither method has shown consistent efficacy in cognition and subjective well-being, possibly reflecting methodological inconsistencies. Moreover, their mechanisms of action are still under investigation (see these reviews of tACS and MM, respecitvely: Al Qasem et al., 2022; Casedas et al., 2020).

The aim of this systematic review is therefore to evaluate the effectiveness of each method relative to the other, regarding higher order cognitive function and subjective well-being. Only the overall effects of treatment vs. no treatment within each approach (tACS, MM) will be evaluated. This will be followed by an evaluation of tACS vs. MM. The reason for this is that efficacy would need to be demonstrated through a clear pattern of effect in favour of improved WM and/or subjective well-being, leading to an enhanced quality of life. This is because a ‘one-size fits most’ method is needed in order to be viable for application to most adults across the lifespan, particularly older adults.

Working memory is a complex limited-capacity system, which allows one to temporarily store, maintain, monitor and manipulate information thereby enabling learning, problem-solving and comprehension (Baddeley, 2012; Baddeley & Hitch, 1974). Working memory is absolutely critical to decision-making and problem-solving (Miyake & Friedman, 2012; Miyake et al., 2000). Indeed, WM dysfunction is a significant characteristic of most psychological/psychiatric illnesses (Millan et al., 2012). Thus, WM has a direct bearing on quality of life. It draws on a broader anatomical network than declarative and non-declarative memory, including the prefrontal cortex (PFC), medial temporal

lobe (MTL), parietal cortex, basal ganglia and cerebellum (Laroche et al., 2000; Nadel & Hardt, 2011; Nee et al., 2013; Owens et al., 2018). The neural networks within the prefrontal cortex extend to and from distal regions, including the MTL, parietal cortex and other sub-cortical regions (Squire et al., 2004). These neural networks are particularly vulnerable to the effects of ageing (Bartzokis, 2004) and psychiatric illness (Buzsaki & Watson, 2012; Hare & Duman, 2020). Consequently, the PFC is an important and viable target for treatment. Mindfulness meditation (Mrazek et al., 2013; Zeidan et al., 2010) and tACS (Jausovec et al., 2014; Violante et al., 2017) have been shown to improve WM. Only studies that include WM task performance are reviewed given WM's key role in executive function (Wager & Smith, 2003) and subjective well-being (Banks et al., 2015).

To evaluate the impact of tACS and MM on emotional regulation/stress, subjective well-being outcomes are reviewed as a proxy variable. Subjective well-being may be defined as "…the extent to which a person believes or feels that his or her life is going well." (Diener et al., 2018, p. 1). Previous tACS (e.g. Hu et al., 2021; Onoda et al., 2017) and MM (Banks et al., 2015; Jha et al., 2010) studies have targeted emotional regulation and/or subjective well-being and have used a range of standard measures for this purpose. Some examples are the Positive and Negative Affective Schedule (PANAS) (Watson et al., 1988), a measure of affective state, and the Perceived Stress Questionnaire (PSQ) (Levenstein et al., 1993), a measure of stressful life events. In the present study, only standard, well-validated tasks are included to reduce heterogeneity

between studies caused by differences in tasks. Regarding both tACS and MM studies, the approach of the present review is to reduce methodological and design variations as much as possible to minimise statistical noise.

2.2. Methods

The present review identified published studies from January 1988 to December 2020[15] to ascertain the efficacy of mindfulness meditation compared to transcranial electrical stimulation methods in enhancing cognitive performance and/or subjective well-being in adults aged ≥18 years. Efficacy was operationalised as effect size, which was derived from cognitive and subjective well-being outcomes, respectively. Outcome data used included reaction time and accuracy data as well as self-reported subject well-being task scores. Preferred Reporting Items were followed for systematic review and meta-analysis protocols (PRISMA-P) 2020 guidelines in reporting results provided in Appendix 1 using a pre-registered protocol (PROSPERO registration: CRD42018117100).

2.2.1 Eligibility criteria

'Efficacy' was operationalised as improvement or enhancement as demonstrated by effect size, as noted earlier. To this end, eligible studies had to be published in peer-reviewed original research articles in English and comprised clinical studies, randomised control trials or time series

[15] The original time period was 1988 to 2018. This period was chosen to strike a balance between a large population of studies that does not ignore important work from previous decades (30 years' research in both fields) but reflects the important weight given to more recent work, which generally has improved rigour.

studies with ≥ 2 time-points of measurement (e.g. pre- and post-treatment designs). Given that the aim was to provide efficacy of treatment for healthy adults, only studies with healthy adult samples and healthy control groups in the case of clinical trials with clinical populations were eligible. Only studies using human participants aged ≥ 18 years were included; older aged samples (> 60 years) had to have been screened using the Mini-mental state exam (MMSE) (Folstein et al., 1975) with a score of ≥ 26 to rule out possible dementia. The MMSE maximum score is 30. Scores between 24 and 30 indicate the absence of dementia clinically. However, for research, it is prudent to exclude scores on/close this boundary to avoid capturing individuals with prodromal signs of cognitive impairment/dementia. Regarding meditation specifically, long-term, intermediate or naïve practitioners of meditation were accepted. In addition, meditation duration had to be ≥ 10 minutes, with eyes closed and seated for the duration of meditation delivered by a trained teacher, a smart phone application (“App”) or a CD/computer audio file. For tACS, participants could be naïve to non-invasive neurostimulation methods or not. Studies had to have used typical, safe protocols delivering current of 1 to 2.5 mA over a period of 10 to 30 minutes per stimulation period (Antal et al., 2017).

Studies were excluded if they: a) did not evaluate WM and/or subjective well-being outcomes; b) included children; c) did not have a comparison group (or in the case of tACS, a sham condition); d) were conducted prior to 1988; e) included sleep or any other treatment/intervention in conjunction with the intervention under review; f)

included a physical or therapeutic component (e.g. mind-body stress reduction (MBSR) or mindfulness-based cognitive therapy (MBCT).

The full protocol and inclusion and exclusion criteria applied are provided in Appendix 2.

2.2.2 Outcomes

The primary outcome measure was the overall effect size of each intervention type (MM, tACS). These overall effect sizes were calculated using means and standard deviations based on comparison between MM vs. a control group and between tACS active vs. sham stimulation. The relative difference of these effect sizes were then used to compare the impact of MM and tACS regarding cognitive performance and subjective well-being. Only studies using well-validated measures were included in the review to enhance comparability across studies of performance measured. Cognitive tasks included were: the digit span task including forward-only and backward-only versions, N-back task, Operation Span tasks, reading span tasks, delayed match-to-sample, letter-number sequencing, WAIS Working Memory Index and Sternberg. Subjective well-being tasks included were: STAI-S/-T (Spielberger, 1983), DASS (Lovibond & Lovibond, 1995), POMS (Mcnair et al., 1971), PANAS (Watson et al., 1988), GHQ (Goldberg et al., 1997), PSQI (Buysse et al., 1989). Other subjective well-being measures were also considered provided that their reliability and validity had been demonstrated in a peer-reviewed journal.

2.2.3 Search strategy and selection criteria

Scopus, Pubmed, Ebsco Host, Cochrane Library, Science Direct and Web of Science electronic databases were targeted using search terms as set out below in Tables 2.1 and 2.2, respectively. All references were downloaded and filtered within Endnote. This approach was taken because the electronic databases varied somewhat regarding classifications of articles/limiter options, therefore only the most basic, universal limiters (i.e. 'human' and 'articles and reviews' were applied). Using this approach allowed for review criteria to be applied systematically and consistently.

Table 2.1 Electronic Databases searched.

Database	Weblink
Scopus:	https://www.scopus.com/search/form.uri?display=basic
Pubmed (searched via NCBI):	https://account.ncbi.nlm.nih.gov/
Ebsco:	https://www.ebsco.com/
Cochrane Library:	https://www.cochranelibrary.com/advanced-search/search-manager
ScienceDirect:	https://www.sciencedirect.com
Web of Science:	http://apps.webofknowledge.com/

Table 2.2 Search strings used in each of the above databases along with filters, limiters and dates applied to each search.

	TERMS	Filter	Limiters	Dates
1	"mindfulness meditation"	Human	Articles and Reviews	
2	"mindfulness training"	Human	Articles and Reviews	
3	"Open monitoring meditation" OR "OMM"	Human	Articles and Reviews	
4	"Headspace App" OR "meditation app"	Human	Articles and Reviews	
5	"tACS" OR "transcranial alternating current stimulation"	Human	Articles and Reviews	
6	"tRNS" OR "transcranial random noise stimulation"	Human	Articles and Reviews	
7	"tDCS" OR "transcranial direct current stimulation"	Human	Articles and Reviews	≥1988 - 2020
8	"Non-invasive neur* stim*" OR "Non-invasive brain stim*" OR "transcranial electrical stimulation" OR "Electrical neural mod*"	Human		

2.2.4 Data extraction

Within Endnote, one reviewer, DW systematically filtered out irrelevant references, namely: studies < 1988; samples < 18 years; reviews, editorials, book chapters and all other non-original research articles; registered clinical trials; case studies; and studies patently unrelated to the intended search e.g. genetics, engineering, sports. Only research articles that clearly related to transcranial electrical stimulation and meditation were retained from this broad reference-capture.

This initial systematic filtering exercise was followed by a 2-stage screening process: 1) titles and abstracts were screened based on inclusion/exclusion criteria as previously described. At this stage, all transcranial electrical stimulation articles and articles that referred to MM were retained. All titles/abstracts were reviewed by DW, RR and AS independently for eligibility for each intervention type. All reviewers were blind to each other's 'accept/reject' judgements until reviews were complete. Discrepancies were resolved by discussion with a fourth reviewer, NC who made the final decision.

2) At the second stage, remaining articles were downloaded and read in full and screened based on the inclusion/exclusion criteria as in stage 1. Only tACS and MM studies, as per the eligibility criteria, were retained for meta-analysis. The full-article review was conducted by DW and RR. Discrepancies between reviewers were resolved by discussion

with a third reviewer (NC) who made the final decision. No automation tools were used at any stage of the review.

All other aspects of the systematic review and meta-analysis namely data processing and data analysis were undertaken by DW and reviewed by RR. The risk of bias (RoB) was conducted by DW and overseen by RR. The tables and values from eligible source studies provided the data used for the meta-analyses. Where data were insufficient to perform calculations (e.g. only a p-value was given) or methods were unclear (e.g. duration of meditation), the lead authors of source studies were emailed requesting these data/clarifications followed by one reminder email where relevant.

2.2.5 Risk-of-bias assessment

Risk of bias (RoB) was assessed using the Cochrane risk of bias tool called 'RoB2' (Higgins et al., 2022). The RoB2 excel tool was used to conduct the assessment and generate graphic summaries (see Results).

The RoB output forms part of the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) criteria (Guyatt et al., 2011). The GRADE system provides an overall rating of the quality of evidence meta-analysed. The benefit of using GRADE is that it summarises the evidence obtained, systematically enabling well-grounded recommendations. Whilst typically used in clinical settings, it was designed to be used in a wide range of applications (ibid).

2.2.6 Data synthesis and analysis

Standardised mean differences were calculated within a random effects model. A random effects model was chosen because the meta-analysed studies were quite varied. Statistical heterogeneity, which considers variance between studies, used tau² (τ^2), derived using a restricted maximum likelihood estimator (Viechtbauer, 2016). The Hartung-Knapp adjustment[16] (Hartung & Knapp, 2001; Knapp & Hartung, 2003) was used to calculate the 95% confidence interval around the pooled effect (Harrer et al., 2021).

Data were summarised in Excel and studies to be meta-analysed were then imported into SPSS v.25 where initial standardised effect sizes were calculated. They were then imported into R studio. Meta-analyses were conducted in R studio (RStudio Team, 2022) with packages: dmetar (Harrer et al., 2021) and meta (Viechtbauer, 2010). These packages also served to create the funnel plots and forest plots per meta-analysis.

GPower v.3.1.9.7 (Faul et al., 2007) and Cohen's (1992) effect sizes: 0.2, 0.5 and 0.8 for small, medium and large effect sizes, respectively, were used to evaluate precision of results as part of the GRADE evaluation.

Given that the purpose of this meta-analysis was to evaluate whether the treatment (tACS, MM) benefitted WM and/or subjective well-being, studies aiming to disrupt these outcomes were not included in the

[16] The Hartung-Knapp adjustment is based on a t-distribution and controls for uncertainty in estimated between-study heterogeneity (Harrer et al., 2021).

analysis. This is relevant to tACS, which has been shown to disrupt as well as enhance targeted neural networks (Alekseichuk et al., 2017; Chander et al., 2016; Marone & Rinaldi, 2023; Reinhart & Nguyen, 2019).

Each effect size represents an independent sample. Thus, there may be more than one effect size per study representing separate experiments each with its own independent sample. E.g. Jones and colleagues (2019) conducted two separate tACS experiments, each testing a specific montage manipulation using an individual sample therefore Jones' work contributed two effect sizes to the meta-analysis.

2.2.6.1 Standardised mean difference calculations

The aim was to make as few approximations as possible to maximise accuracy. Thus, in the first instance, Cohen's d(z) values were calculated based on reported F-values and total sample size (N):

$$\frac{\sqrt{F\ ratio}}{\sqrt{N}}$$

When F values were not available, reported means and standard deviations were used to calculate Glass's ∆:

$$\frac{\bar{x}_1 - \bar{x}_0}{s_0}$$

There are at least 5 distinct ways of calculating SMD (standard mean difference) (http://jakewestfall.org/blog/index.php/2016/03/25/five-different-cohens-d-statistics-for-within-subject-designs/) (Harrer et al., 2021). A solution proposed by Becker ((1988) cited in Harrer et al., 2021) was chosen because it is less likely to be affected by treatment effects.

From a between-subjects perspective, the control group represents a general population (Lin & Aloe, 2021).

2.2.6.2 Standard error calculations

For between-subjects study designs the standard error $(SEsmd)$ calculation used was:

$$SEsmd = \sqrt{\frac{n_1 + n_2}{n_1 n_2} + \frac{(smd\_btwn)^2}{2(n_1, +n_2)}}$$

For within-subjects study designs the standard error calculation used was:

$$SEsmd = \sqrt{\frac{2(1-r)}{n} + \frac{(smd\_within)^2}{2n}}$$

As recommended by Borenstein et al. (2009) the correlation coefficient (r) used in the formula is r = 0.5, because the groups being compared are assumed to be correlated (Harrer et al., 2021).

2.2.6.3 Aggregation

Some studies provided means/standard deviation (SD) tables of tasks that had more than one component. For example, the PANAS comprises a positive affect (PA) subscale and a negative affect (NA) subscale, producing 2 sets of means/SDs per group (MM, controls). Here a Hedge's g was derived by meta-analysing the two sub-scale standardised means and their standard errors to provide the effect size for that study. The Hedge's g confidence intervals were used to calculate the

associated standard errors. If a study measured more than one task (e.g. PANAS and PSQ) then the same approach was taken iteratively. An effect size was created per task, as needed, and the final effect size per task was then meta-analysed to create an aggregated effect size based on all eligible tasks. Thus, a Hedge's g value was obtained for the PANAS, then this Hedge's g and PSQ Cohen's d(z) was meta-analysed to provide an aggregated Hedge's g value for that study. The Hedge's g value is comparable to Cohen's d for samples where n > 20 (Lakens, 2013) and therefore appropriate to include with the non-aggregated Cohen's d values to be meta-analysed.

Note that for aggregated effect sizes, the value of N (total sample size) was adjusted to include only the groups (treatment vs. control) upon which the effect size would be based. These adjusted N values were also used in the final meta-analysis. Observed effects were visually presented using forest plots.

Funnel plots and Egger's regression test were used to evaluate publication and small study biases in each set of results meta-analysed. Egger's test measures asymmetry in the funnel plot by regressing the standardised effect size on precision, the reciprocal of the standard error (Egger et al., 1997). Precision is strongly linked to sample size (ibid).

2.3. Results

2.3.1 Mindfulness Meditation

Fig. 2.1 PRISMA flow diagram (Page et al., 2021) shows that a total of 15 studies were eligible for review, comprising a sample of 1210

participants. All were randomised control trials. Of these, only two studies (n=128) measured WM. Fourteen of the 15 studies evaluated subjective well-being as an outcome measure of which 3 could not be meta-analysed because they reported insufficient data. A further 2 studies were excluded because they demonstrated a high risk of bias. For all eligible studies, Table 2.3 gives the study ID, authors, population targeted and number of participants by study.

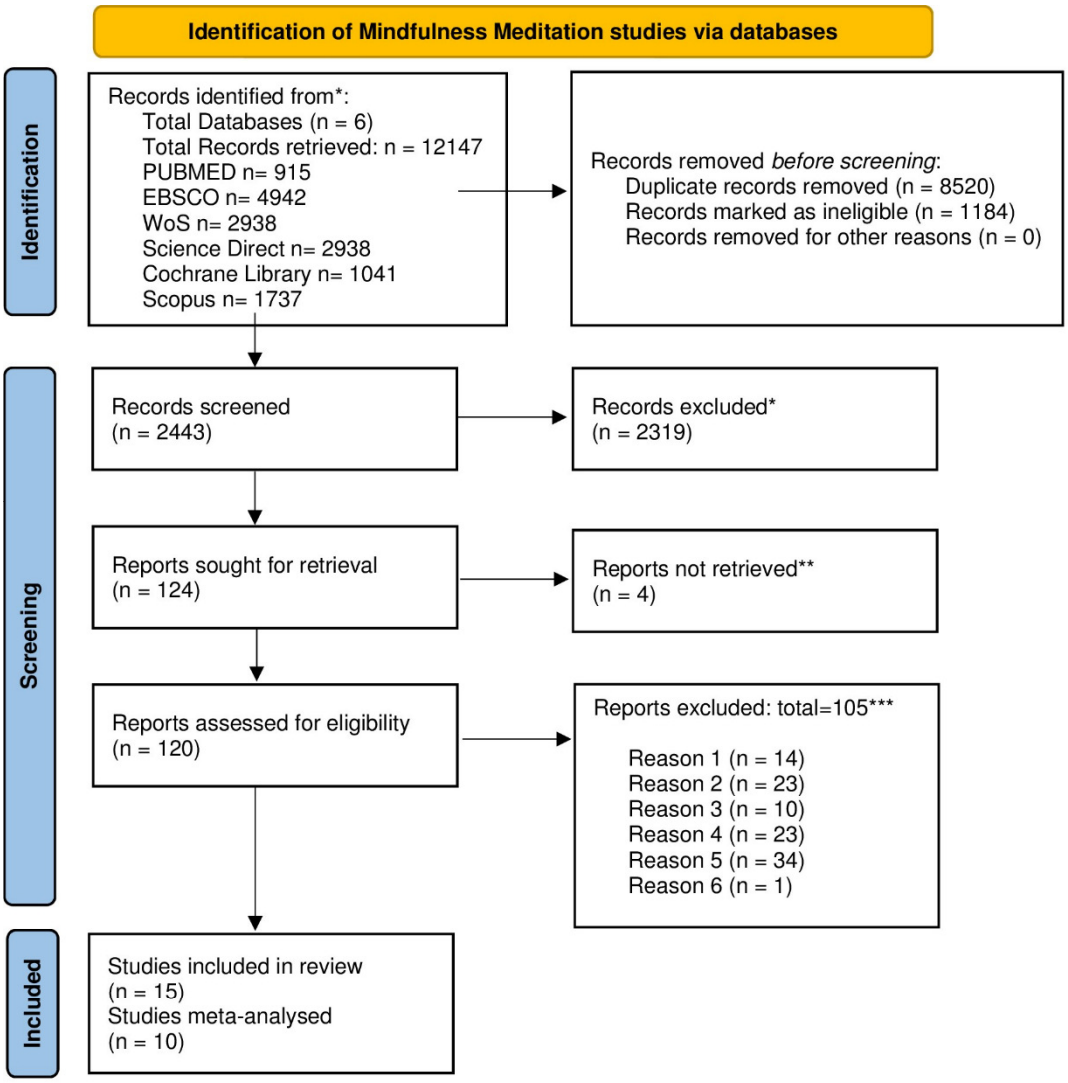

Fig. 2.1 Flowchart showing steps in the selection of eligible studies.

*Records were discarded if they were unrelated to the research question; did not include a subjective well-being or cognitive task; had no healthy control group; were published < 1988; not original research article; targeted population was children; used a physical and/or therapeutic component as part of the mindfulness meditation treatment condition such as mind-body stress reduction (MBSR), mindfulness-based cognitive behavioural therapy (MBCT), yoga, walking and the like; evaluated impact of more than one intervention within a hypothesis e.g. mindfulness meditation + induced stress.

**Reports not retrieved describes abstracts for which a full article could not be found or where the reference was for a correction of a full article.

***Reasons for exclusion were: 1) 2 treatment manipulations (mindfulness combined with, for example, an anxiety manipulation); 2) MM with a physical and/or therapeutic component; 3) no control group; 4) no working memory or subjective well-being measure or non-standard task; 5) eyes open meditation/non-standard MM practice; 6) not English.

Table 2.3 Study characteristics of Mindfulness Meditation studies retrieved for review and meta-analysis.

study ID	Study	Population	SWB* meta-analysis	Cognitive meta-analysis	Total Sample (N)	Analysed Sample (N)
2	Aspy et al. (2017)	students	1	0	115	115
5	Bell et al. (2015)	students	0	0	57	-
11	Chow et al. (2017)	students	0	0	61	-
20	Diaz-Silveira et al. (2020)	staff from one employer	1	0	94	94
24	Edwards et al. (2018)	students	1	0	66	44
33	Greenberg et al. (2018)	adults (top 25th percentile SAT/4 yrs of university educ)	0	1	79	79
47	Jislin-Goldberg et al. (2012)	students	1	0	51	51
51	Josefsson et al. (2014)	working adults	1	0	103	73
63	Lai et al. (2015)	students	1	0	70	44
88	Polizzi et al. (2019)	students	1	0	91	60
98	Sahdra et al. (2011)	adults	0	0	60	-
106	Stinson et al. (2020)	students	0	0	166	-
107	Strait et al. (2020)	students	0	0	93	-
122	Zeidan et al. (2010)	students	1	0	82	56
123	Zeidan et al. (2010)	students	1	1	49	49

*SWB = subjective well-being

For all 10 analysed studies, Table 2.4 provides age, sex and mindfulness meditation intervention details by study. None of the meta-analysed studies included long-term meditators; 4 studies comprised exclusively naïve meditators (studyIDs 47, 63, 122, 123), 3 included naïve meditators and those with limited experience e.g. once or twice per month (studyIDs 2,20,24), 1 study (studyID 51) reported that their study comprised a comparable mix of those with previous experience and naïve meditators across comparison groups, but did not explicitly state what the extent of previous meditation was, and 2 studies (studyIDs 33, 88) did not report previous meditation experience. Median total number of minutes meditated was 80 min (IQR 14.45 min to 457.30 min). Median total under supervision was 60 min (IQR 12.30 min to 100 min).

Table 2.4 Age, gender and Mindfulness Meditation intervention details of studies retrieved for review and meta-analysis.

study ID	Mean age (SD)	Females (N)	Control activity	duration (minutes/ meditation)	lab/tutorials /guided sessions (N)	total supervised minutes	total at-home/ unsupervised minutes	Total minutes meditated	delivery method (recording/in-person/app)	compliance outcome reported[a]
2	20.5 (4.3)	75	relaxation	14.3	1	14.5	0	14.5	online recording (mp3)	no
20	46.81 (6.37)	67	control	15-30	5	0	600	600	recording/in-person	no
24	21.66 (nr)	71	sitting quietly	10	1	10	0	10	in-person instruction	n/a
33	27.28 (nr)	70	creative writing	30	4	120	600	720	Zoom (with instructor); at-home practice using secure link to access recordings	no
47	25 (4.3)	65	no-intervention control	20 min (in-session); 15 min out-of-session	4	80	180	260	in-person and at home (using a CD)	no
51	48.13 (nr)	62	relaxation	45	8	315	0	315	in-person instruction	n/a
63	18.86 (2.67)	66	counting backwards	15	1	1	0	15	in-person instruction	n/a
88	18.55 (0.82)	77	sitting quietly	15	1	15	nr	15	in-person and at home (using script of in-person meditation practice)	no
122	20.7 (nr)	50	sham MM (breathing exercises)	20	3	20	0	60	in-person instruction	n/a
123	22.5 (nr)	29	listening to book reading	20	4	20	0	80	in-person instruction	n/a

nr = not reported

n/a = not applicable

[a]All included studies measured compliance but none reported these data.

The final meta-analysis for subjective well-being was based on 9 subjective well-being studies (n=586). The benefit of mindful meditation (MM) was evaluated relative to an active (k=5) or passive (k=4) control group measured with a range of self-report indices of anxiety, depression, mood and perceived health and psychological well-being. The median sample size was 56 (IQR 46.5-83.5). The median average age was 21.7 (IQR 19.7-35.9) and median proportion of females per study was 65.7%. Table 2.5 provides details regarding the tasks used to measure subjective well-being. Appendix 3 provides full details of the names, constructs measured, score ranges and interpretation of scores of all subjective well-being measures along with corresponding studies using each one.

Table 2.5 Subjective well-being task details and meditation duration by study.

study ID	Name of Subjective well-being task	Dependent Variable	Interpretation of score
2	PANAS	summed score for PA/NA (aggregated)	Higher score = greater negative affect; Higher score = greater positive affect*
20	PSQ GHQ-12	(raw score-30)/90; summed score	Higher score = greater levels of stress; Higher score = poorer perceived health
24	POMS	summed score (total mood disturbance score)	Higher score = greater mood disturbance
47	PANAS	summed score for PA/NA (aggregated)	Higher score = greater negative affect; Higher score = greater positive affect*
51	HAD; PWB	summed score per sub-scale (aggregated); summed score	Higher score = greater levels of stress/depression; Higher score = better psychological well-being*
63	POMS-SF	summed score (total mood disturbance score)	Higher score = greater mood disturbance
88	PANAS	summed score for PA/NA (aggregated)	Higher score = greater negative affect; Higher score = greater positive affect*
122	POMS; STAI-S	summed score (total mood disturbance score); summed score	Higher score = greater mood disturbance; Higher score = greater anxious state
123	POMS; STAI-S	summed score (total mood disturbance score); summed score	Higher score = greater mood disturbance; Higher score = greater anxious state

*For most scales, a positive score reflects greater levels of negative affect/mood/anxiety. However, in one subscale of the PANAS and for the PWB a positive score indicates positive affect therefore the sign was reversed in these cases for the meta-analysis.

Though there were only two WM studies (studyID 33, studyID 123), a meta-analysis was performed for accuracy. Both studies used an active control group as comparator. The median sample size was 64. The median average age was 24.9 and median proportion of females per study was 64.8%. Only one of the two studies provided sufficient RT data for analysis therefore no meta-analysis was performed for WM processing speed.

2.3.1.1 Risk of bias and GRADE evidence evaluation

Risk of bias was assessed for all eligible studies (k=15). There was a low risk of bias across most studies, as shown in Fig. 2.2. Two studies were excluded because of a high risk of bias. The rationale for this is based on the Cochrane Handbook (Schünemann et al., 2022) which states that evidence is more certain when most studies in the meta-analysis achieve a low risk of bias rating. Given the small number of eligible studies, no high-risk studies were included. Reasons for ratings are given in the RoB Report in Appendix 4. A further 3 studies were dropped prior to the GRADE evaluation and meta-analysis because there was insufficient data, leaving a final total of 10 studies of which 8 measured only subjective well-being, one measured only WM and one measured subjective well-being and WM. Overall, the GRADE evidence rating for subjective well-being was very low as shown in Table 2.6, which provides a summary of the certainty of evidence for RoB, consistency, directness, precision and publication bias. This is because, although RoB was low across the board for every study, 95% confidence intervals

around the pooled effect size included zero. In addition, the test for heterogeneity was not statistically significant. Most studies (7 of 9) evaluated student samples (mainly young adults) and thus may not generalise to older adults nor to non-student populations. Statistical power and the level of precision of each study is also an important consideration. Assuming a mixed factorial ANOVA design with time (pre-treatment, post-treatment) as within-subjects factor and group (MM vs. controls) as between-subjects factor, a medium-sized effect (0.5) would require a total sample size of 34 to achieve a power of .80. However, for a small effect size (0.2) a total sample of 200 would be needed to achieve a power of .80. Assuming that a small effect size is more likely, the number of participants per study was too small indicating that they were all underpowered. The risk of publication bias and small samples bias are typically measured with a funnel plot and an Egger's test. However, when the number of studies included in a meta-analysis is low ($k<10$), Egger's test is deemed unwise as it lacks sufficient power to detect a publication bias (Sterne et al., 2011). Fig. 2.3 provides a contour-enhanced funnel plot, which shows that studies' results were fairly evenly distributed around the null with no apparent publication bias. However, as with the Egger's test, the low number of studies means the funnel plot is of limited value in this case. The source studies were from a range of journals conducted by a variety of different academic institutions, which also mitigates the risk of publication bias.

Study ID	Study DOI	Experimental	Comparator	Outcome	Weight	D1	D2	D3	D4	D5	Overall
2	10.1177/0033294116685867	Mindfulness Meditation	active/passive control condition	PANAS-NA;PANAS-PA	1	+	+	+	+	+	+
5	10.1891/0889-8391.29.4.343	Mindfulness Meditation	active/passive control condition	STAI-STATE/TRAIT	0	!	!	+	+	-	-
11	10.1007/s12671-016-0631-8	Mindfulness Meditation	active/passive control condition	DASS, POMS	1	+	+	+	+	+	+
20	10.3390/ijerph17082839	Mindfulness Meditation	active/passive control condition	PSQ, GHQ-12	1	+	+	+	+	+	+
24	10.15171/hpp.2018.23	Mindfulness Meditation	active/passive control condition	POMS (3 of the subscales)	1	+	+	+	+	+	+
33	10.1007/s11682-018-9858-4	Mindfulness Meditation	active/passive control condition	Proactive interference error rates and RTs (of correct responses)	1	+	+	+	+	+	+
47	10.1080/17439760.2012.700724	Mindfulness Meditation	active/passive control condition	PANAS-PA	1	+	+	+	+	+	+
51	10.1007/s12671-012-0142-1	Mindfulness Meditation	active/passive control condition	PWB, HAD	1	+	+	+	+	+	+
63	10.1007/s12671-014-0347-6	Mindfulness Meditation	active/passive control condition	POMS-SF	1	+	+	+	+	+	+
88	10.1037/cns0000194	Mindfulness Meditation	active/passive control condition	PANAS-NA;PANAS-PA	1	+	!	+	+	+	!
98	10.1037/a0022764	Mindfulness Meditation	active/passive control condition	STAI-T	1	!	+	+	+	+	!
106	10.1097/01.NEP.0000000000000635	Mindfulness Meditation	active/passive control condition	STAI-STATE/TRAIT	0	-	-	-	+	-	-
107	10.1177/0098628320901386	Mindfulness Meditation	active/passive control condition	GAD-7, PSS-4	1	+	+	+	+	+	+
122	10.1089/acm.2009.0321	Mindfulness Meditation	active/passive control condition	POMS; STAI-S	1	+	+	+	+	+	+
123	10.1016/j.concog.2010.03.014	Mindfulness Meditation	active/passive control condition	n-back; digit span; POMS; STAI-S;CED-S	1	+	+	+	+	+	+

+ Low risk
! Some concerns
- High risk

D1 Randomisation process
D2 Deviations from the intended interventions
D3 Missing outcome data
D4 Measurement of the outcome
D5 Selection of the reported result

Fig. 2.2 Risk of Bias Summary: Mindfulness Meditation studies using a between-subjects design (subjective well-being and cognitive measures; n=15)

Table 2.6 GRADE evidence profile: mindfulness meditation benefit to subjective well-being.

		Certainty rating by category				No. of Participants (studies)	Effect Size	Quality Rating
Category	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**publication bias**	586 (9)	0.10 [0.06-0.15]	Very low
Evaluation	*No serious limitations*	*No serious inconsistencies*	*Serious indirectness*	*Very serious imprecision*	*Undetected*			
Mindfulness Meditation Group vs. Control Group	RoB assessment showed all 9 studies had a low risk of bias.	Zero is included within the confidence intervals for every study and the test for heterogeneity was not statistically significant indicating a consistent outcome.	Most studies tested student samples which may limit the generalisability of findings given that this review intended to include adults across the lifespan not just young and middle aged adults. The rating is downgraded to serious when generalised to adults across the lifespan but not serious when considering young adults.	Assuming a small effect is more likely, the number of participants per study was too small, indicating they are all underpowered. Thus, precision is poor and certainty in the evidence is therefore very low.	Funnel plot shows that results were distributed around the null with no apparent publication bias. However the number of studies included in the meta-analysis is small, therefore the funnel plot has limited value. Nevertheless, the plot is indicative of a low risk of publication bias. The sample included studies from a range of universities and journals which mitigates risk of publication bias.			

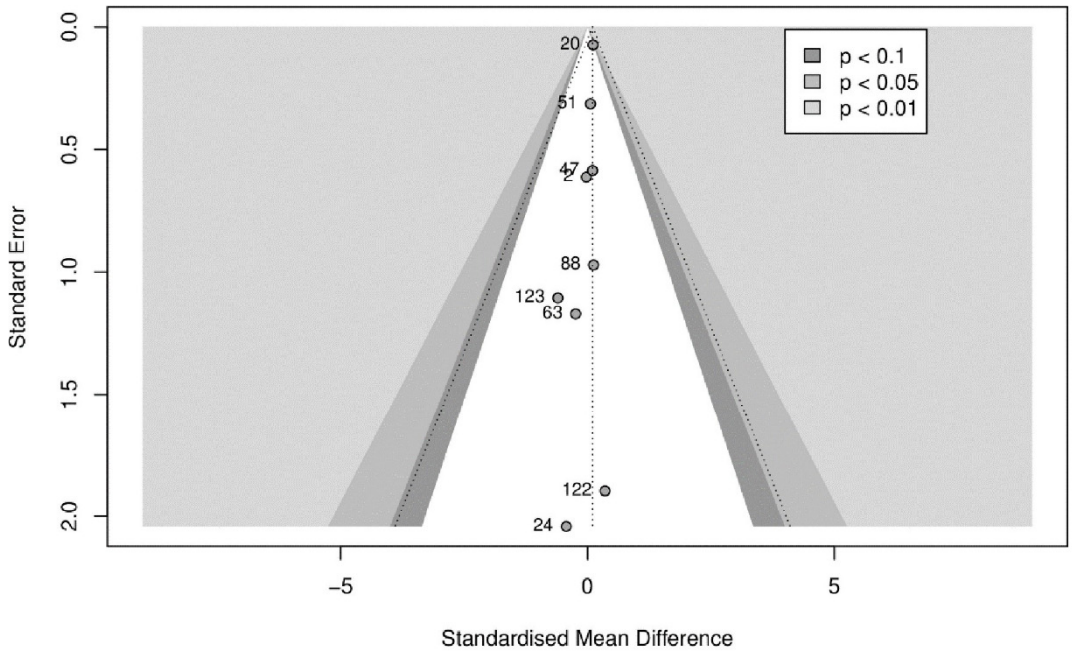

Fig. 2.3 Funnel Plot of studies included in the Mindfulness Meditation subjective well-being meta-analysis (k=9).
Values on the plot represent individual study IDs.

The GRADE evaluation was similarly very low for the WM accuracy meta-analysis (k=2) with the same short-comings regarding indirectness and imprecision. Details are given in Table 2.7. Fig. 2.4 provides the funnel plot of studyIDs 33 and 123, both of which were distributed around the null.

Table 2.7 GRADE evidence profile: mindfulness meditation benefit to working memory accuracy.

		Certainty rating by category				No. of Participants (studies)	Effect Size	Quality Rating
Category	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**publication bias**	128 (2)	0.19 [-0.04-0.42]	Very low
Evaluation	*No serious limitations*	*No serious inconsistencies*	*Serious indirectness*	*Very serious imprecision*	*Undetected*			
Mindfulness Meditation Group vs. Control Group	RoB assessment showed both studies had a low risk of bias.	Zero is included within the confidence intervals for both studies and the test for heterogeneity was not statistically significant indicating a consistent outcome.	StudyID tested adults who were fairly high functioning (top 25th percentile SATs/4 yrs of university education) aged 18 to 50; studyID 123 tested a student sample. Generalisability of findings is therefore limited to higher functioning, younger adults who either are currently students or were students and may therefore not be valid when considering adults who have not had a tertiary education nor those in the middle to older age range (both studies had an average age < 30 yrs). The rating for indirectness is downgraded to serious as the findings do not generalised reliably to adults across the lifespan but would be 'not serious' when considering young adults.	Assuming a small effect is more likely, the number of participants per study (studyID 33=79; studyID 123=49 vs. required n=200) was insufficient, indicating they were underpowered. Thus, precision is poor and certainty in the evidence is therefore very low.	Funnel plot shows that the studies were distributed around the null with no apparent publication bias. However with only two studies included in the meta-analysis, the funnel plot has limited value. Nevertheless, the plot is indicative of a low risk of publication bias. The sample included studies from different universities and journals which mitigates risk of publication bias.			

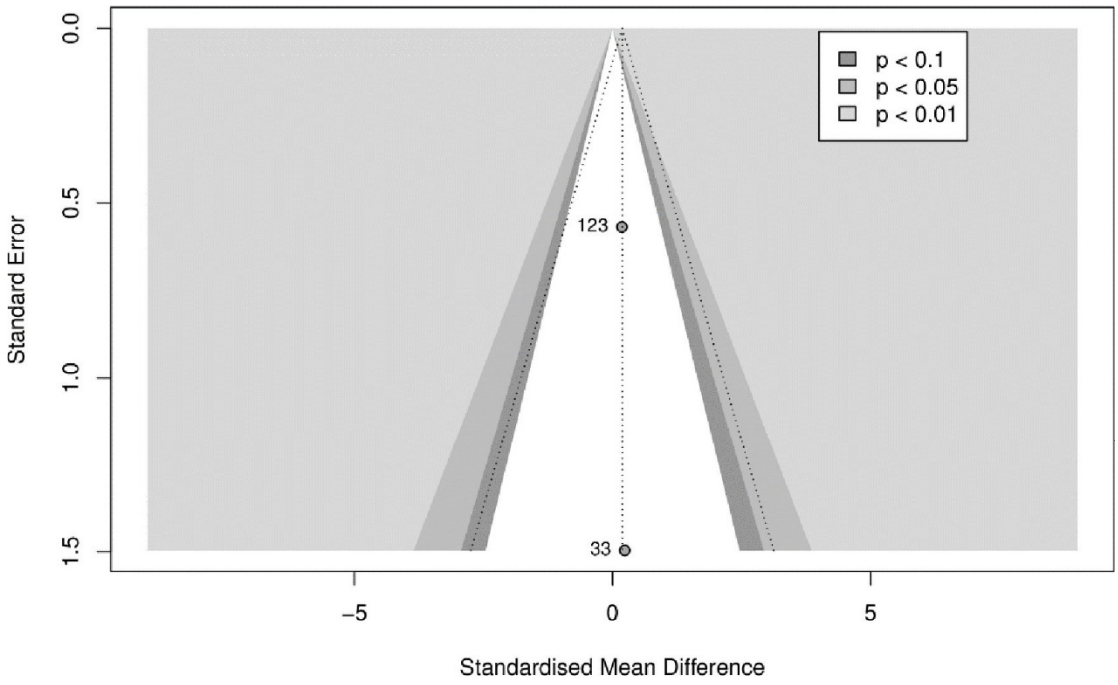

Fig. 2.4 Funnel Plot of studies included in the Mindfulness Meditation working memory accuracy meta-analysis (k=2).
Values on the plot represent individual study IDs.

2.3.1.2 Subjective well-being meta-analysis outcome

The meta-analysis (k=9) shows that MM participants' levels of subjective well-being improved more relative to participants who were randomised to a control condition (SMD = 0.10, 95% confidence intervals: 0.06 to 0.15, $p < .001$, $\tau^2 = 0$) as shown in Fig. 2.5. However, 91% of the pooled effect size was explained by a single study (studyID 20) which suggests that the outcome of this meta-analysis may not be reliable. By removing this study (n=94), the pooled effect size became statistically not significant, as shown in Fig. 2.6: SMD = 0.02, 95% confidence intervals: -0.13 to 0.16, $p = .802$, $\tau^2 = 0$).

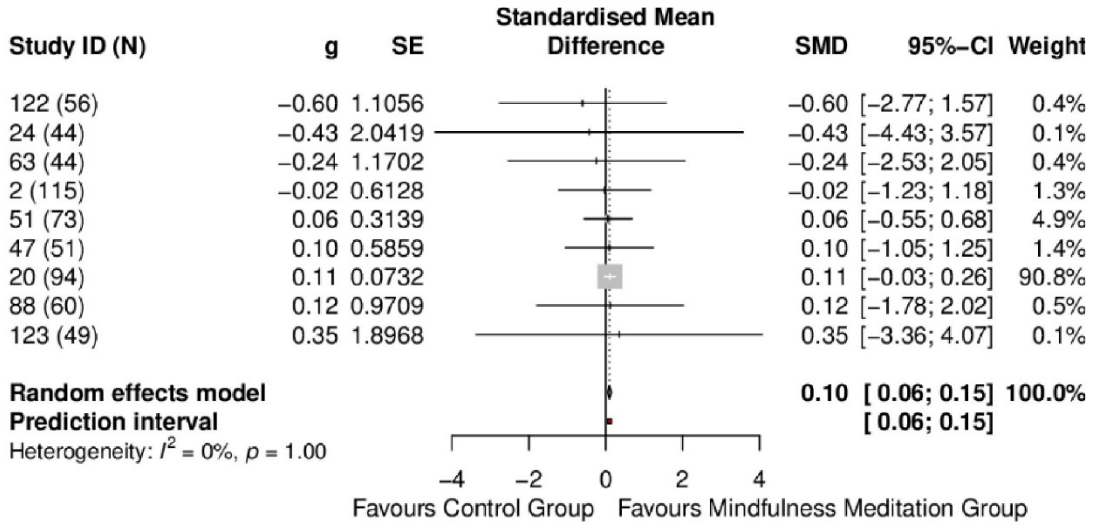

Fig. 2.5 Forest plot of the overall comparison of MM vs. control participants.
As shown, the overall effect size was small but statistically significant. Study ID 20 (n=94) contributed the most to the pooled effect size.

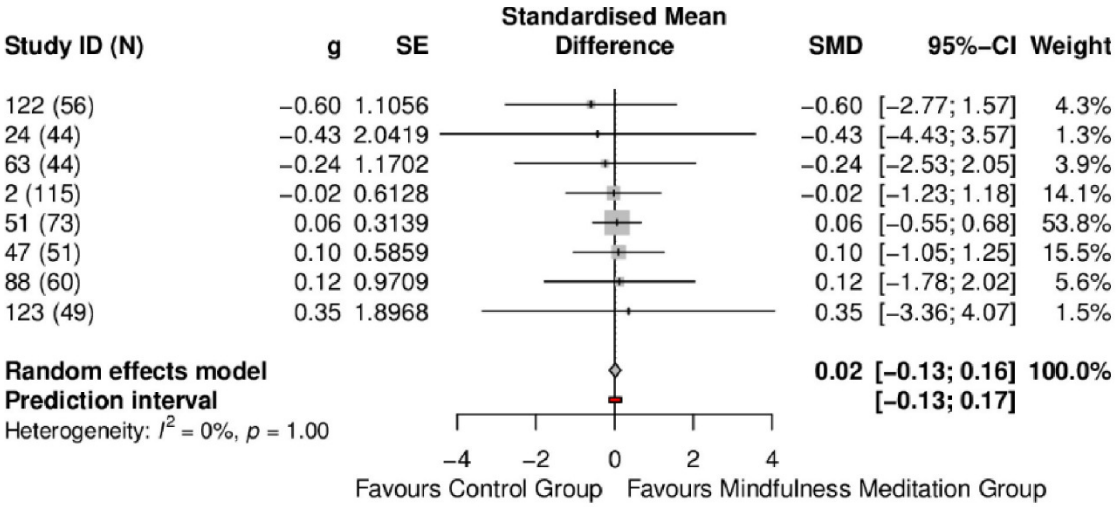

Fig. 2.6 Forest plot of the overall subjective well-being comparison of MM vs. control participants without studyID 20.
As shown, the overall effect size includes zero, indicating that it is not statistically significant.

Another factor to consider is that studies varied regarding the total duration meditated. Table 2.4 indicates that there are two potential sub-groups based on total minutes meditated with 3 studies (studyIDs 20, 47 and 51) reporting substantially longer overall durations (≥ 260 min) than the other studies (≤ 80 min). Assuming that any benefit is positively,

linearly associated with time meditated, one would expect these studies to have a greater effect size relative to the short-duration MM studies. To explore this possibility, the 3 long-duration studies were meta-analysed. The SMD = 0.11, 95% confidence intervals: 0.07 to 0.14, p = .005, $\tau^2 = 0$. For the following reasons this finding has limited value because the relative weight contributed to the effect size by each study was very uneven. As in the overall subjective well-being analysis, studyID 20 (n=94) contributed most of the weight (93.5%) followed by studyID 51 (n=73) (5.1%) and studyID 47 (n=51) (1.5%). Furthermore, each individual effect size included zero in its confidence interval and studyID 20 (n=94) had no supervised sessions and levels of compliance were not reported.

2.3.1.3 Working memory accuracy meta-analysis outcome

Based on 2 studies, MM participants' WM performance was not reliably better than that of active control participants (SMD = 0.19, 95% confidence intervals: -0.04 to 0.42, p = .062, $\tau^2 = 0$), as shown in Fig. 2.7. This finding indicates that MM is unlikely to benefit WM accuracy.

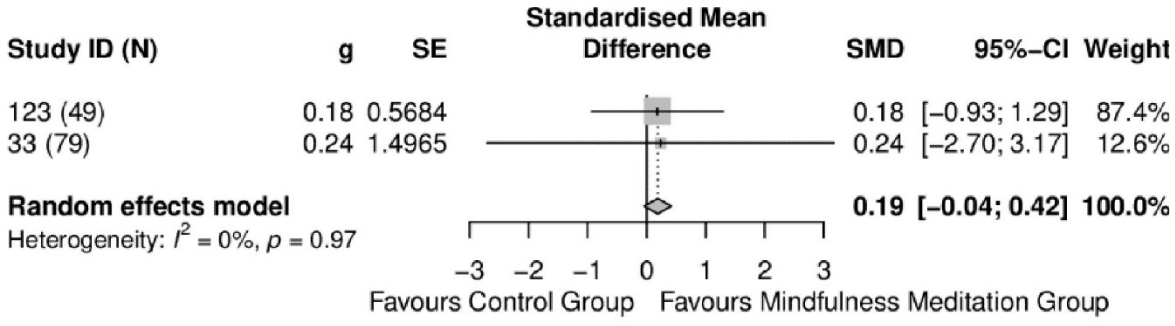

Fig. 2.7 Forest plot of the overall working memory accuracy comparison of MM vs. control participants.
In both studies, mindfulness meditation was reported to show improved performance, reduced error rates in the studyID 33 and greater accuracy in studyID 123. However, as shown, the overall effect size includes zero, indicating that the meta-analysed finding did not reach statistical significance.

2.3.2 Transcranial Alternating Current Stimulation (tACS)

A total of 17 studies (n=553) were eligible for review as the PRISMA flow diagram (Page et al., 2021) depicted by Fig. 2.8 indicates. Table 2.8 provides study ID, authors, experiment number, population targeted and number of participants by study. Table 2.9 provides age, sex and tACS intervention details by study. Of these studies, only one measured subjective well-being (n=24), the remaining studies measured WM performance. Two (n=39) of the 16 WM studies could not be meta-analysed because they did not report sufficient data and another (n=20) could only be meta-analysed for RT data because of limited information reported. The 17 studies contributed 20 experiments (studyIDs 10, 70, 114, 133 and 134 each measured 2 samples per research report). Median total stimulation time[17] was 20 min (IQR 15.45 min to 23.45 min).

[17] Based on the 20 experimental outcomes from 17 studies (1 subjective well-being study and 16 WM studies).

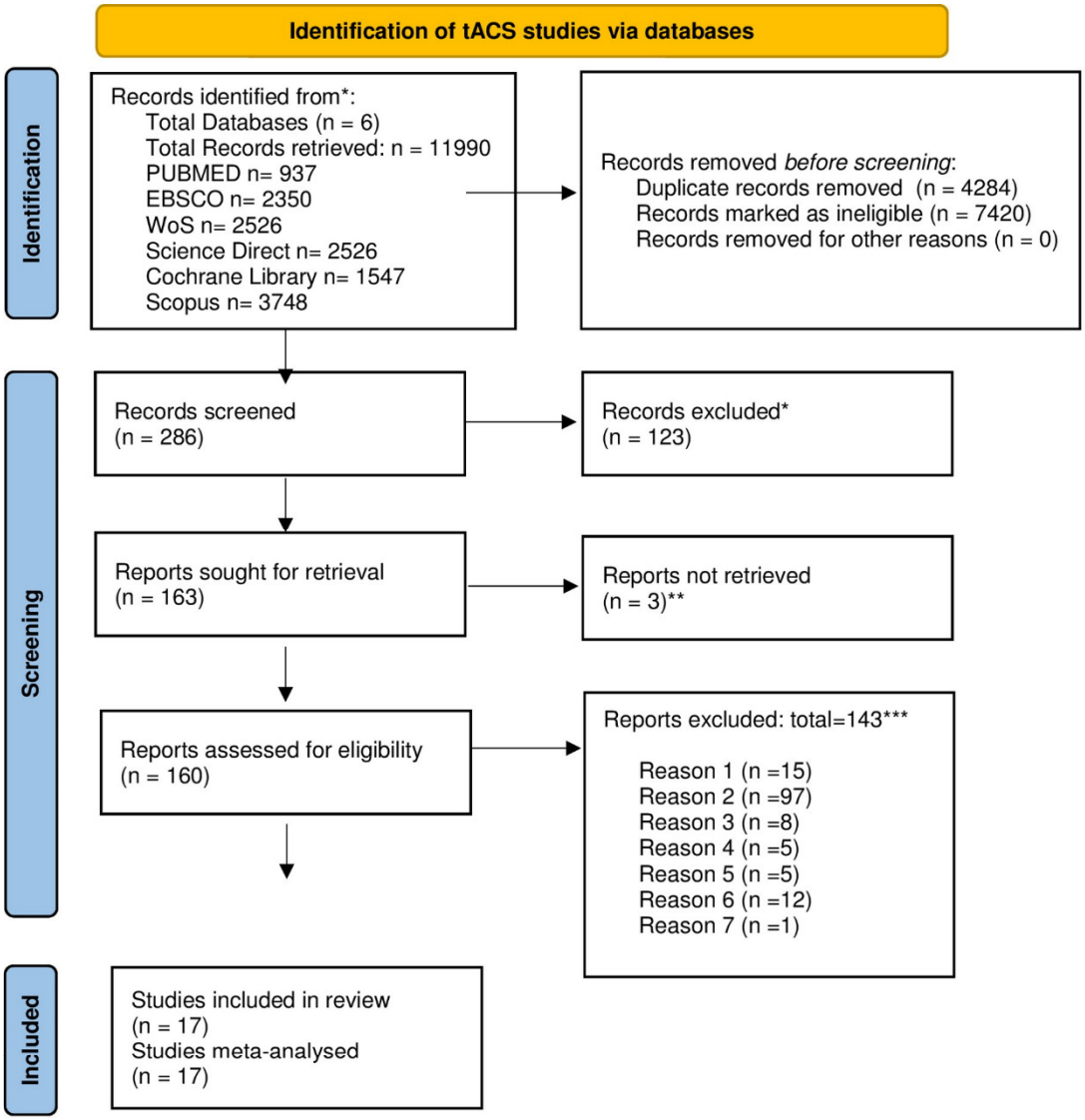

Fig. 2.8 Flowchart showing steps in the selection of eligible tACS studies.

*Records were discarded if they were unrelated to the research question; did not include a subjective well-being or cognitive task; had no healthy control group; were published < 1988; not original research article; targeted population was children; montage targeted M1 or an area not relevant to higher-order executive function; or evaluated impact of more than one intervention within a hypothesis e.g. tACS + sleep.

**Reports not retrieved describes abstracts for which a full article could not be found

***Reasons for exclusion were: 1) met exclusion criteria regarding tACS protocol e.g. stimulation < 10 min; 2) no working memory or subjective well-being measure or non-standard task; 3) montage did not target cognitive function 4) blinding not reported and insufficient information regarding sham protocol; 5) published abstracts that did not have sufficient information/for which a full article using the same dataset had already been counted ; 6) not original research/technical reports/protocol documents; 7) not English.

Table 2.8 Study characteristics of tACS studies retrieved for review and meta-analysis.

studyID	Study	Experiment	Population	SWB meta-analysis	Cognitive meta-analysis	Total Sample (N)	Analysed Sample (N)
1	Abellaneda-Perez et al. (2020)	1	adult volunteers	0	1	29	-
3	Alekseichuk et al., (2017)	1	adult volunteers	0	1	25	25
10	Antonenko et al., (2016)	1	young and older adult volunteers	1	0	24	-
16	Borghini et al., (2018)	2	older adult volunteers	0	1	25	25
61	Hoy et al., (2015)	1	adult volunteers	0	1	18	18
65	Hu et al., (2022)*	1	students	0	1	20	20
68	Jausovec et al., (2014)	1	students	0	1	36	36
70	Jones et al., (2019)	1	adult volunteers	0	1	30	30
70	Jones et al., (2019)	2	adult volunteers	0	1	38	38
80	Kleinert et al., (2017)	1	adult volunteers	0	1	18	18
90	Meiron et al., (2014)	1	female-only adults	0	1	24	24
105	Pahor et al., (2018)	1	female-only students	0	1	72	72
114	Reinhart et al., (2019)	1	older adult volunteers	0	1	42	42
114	Reinhart et al., (2019)	2	older adult volunteers	0	1	28	28
116	Rohner et al., (2018)	1	adult volunteers	0	1	30	-
133	Tseng et al., (2016)	1	students	0	1	20	20
133	Tseng et al., (2016)	2	students	0	1	20	20
134	Tseng et al., (2018)	1	students	0	1	24	24
134	Tseng et al., (2018)	2	students	0	1	24	24
144	Violante et al., (2017)	1	adult volunteers	0	1	10	10
155	Wolinski et al., (2018)	1	adult volunteers	0	1	16	16

*Only RTs could be analysed for this study.

Table 2.9 Study characteristics of tACS studies retrieved for review and meta-analysis.

studyID	Mean age (SD)	Females (N)	Frequency Band (Hz)	Montage (active/reference)	Current intensity (mA)	electrode size (cm^2)	Simulation (in minutes)	Sham (in seconds)	Stimulation blinding
1	25.25 (4.22)	20	6	F3/FP2	2.00	35	20	30	single[1,2]
3	23.5 (2.9)	13	6	AF3, P3, AF4, P4; AF3, AF4, P3, P4	2.00	3.14	18	10	double[1]
10	22.3 (1.5)	nr	6	CP5/contralat-supraorbital	1.00	35	20	30	single[1]
10	66.3 (3.9)	nr	6	CP5/contralat-supraorbital	1.00	35	20	30	single[1]
16	69.1 (4.5)	11	4; 10; 35	P3/P4	1.50	35	20	20	double[1]
61	29.3 (7.65)	9	40	F3/contralat-supraorbital	1.50	35	20	30	single[2]
65	22.55 (3.35)	11	5.45 (mean)	F3 & P3/return electrodes: AF3, F5, F1, FC3	1.00	nr	30	30	single[1,2]
68	20.42 (4.25)	27	ITF*	F3/contralat-supraorbital; P3/contralat-supraorb; P4/contralat-suptraorb	1.75	35	15	30	single[2]
70	24.6 (6.54)	23	7	F4/P4	1.00	25	15	0	double[1]
70	24.5 (5.48)	25	4.5	F4/P4, F3/F4	1.00	25	15	0	double[1]
80	25.2 (2.96)	9	5	F4 & P4/Cz (return electrode)	1.00	25	26	30	single[1]
90	21.5 (2.06)	24	4.5	F3/AF3; F4/AF4	1.00	16	20	20	single[1,2]
105	20.38 (1.48)	72	4.89-5.28 Hz; 31.81-33.22 Hz	P3/P4 (1.76 mA); F3/P3 (1.75 mA); F4/P4 (1.6 mA); F3/F4 (1.45 mA)	1.76	35	15	60	single[2]
114	68.8 (4.4)	22	ITF	E27/E12/E29/L4/G32/K5 [targeting left DLPFC & left temporal cortex]	1.60	1.13	25	30	double[3]
114	68.8 (4.4)	22	ITF	E27/E12/E29/L4/G32/K5 [left DLPFC & left temporal cortex] (1.6 mA); unifocal frontal theta-tuned stimulation (0.6 mA); unifocal temporal theta-tuned stimulation (1 mA); frontotemporal in-phase 8 Hz stimulation (1.6 mA)	various	1.13	25	30	double[3]
116	26.2 (3.0)	30	6	F3/P3	1.00	35	15	60	single[1,2]
133	21 (nr)	8	40	T5 & CP1/rightCheek	1.50	25;35	20	30	single[1,2]
133	21 (nr)	8	40	T5 & CP1/rightCheek	1.50	25;35	20	30	single[1,2]
134	23 (nr)	23	6	P3 & P4/left cheek	1.60	16;35	20 - 24	30	single[1]
134	23 (nr)	23	6	P3 & P4/left cheek	1.60	16;35	20 - 24	30	single[1]
144	28.6 (5)	6	6	F4 & P4/T8	1.00	20	26.5	30	single[1]
155	28.3 (7.6)	9	4;7	P4/supraorbital; P4/Cz	1.24	35	12	41s (4 Hz); 24s (7 Hz)	single[1]

ITF = individualised theta frequency; * ITF was based on individual peak alpha frequency minus 5.

[1]working memory task applied during online stimulation ; [2]working memory task applied during offline stimulation; [3]continuous task measurement through online then offline.

The benefit of tACS was evaluated relative to an equivalent sham condition. Meta-analysed studies measured WM accuracy and/or reaction time (RT) with a range of tasks, provided in Table 2.10, which also indicates load levels used and dependent measure/s by task.

Table 2.10 Working memory tasks their load levels and associated dependent variable(s).

studyID	Working Memory Task	Load levels	Dependent Variable (accuracy)	Dependent Variable (RT)
3	N-back	2	HR-FA (% correct)	accurate log-transformed RTs
16	Retro-cue WM task	n/a	p(T)	-
61	N-back	2,3	accuracy diff scores [(post-pre)/pre]	accurate RTs [(post-pre)/pre]
65	Sternberg	2,4,6	accuracy (% correct)	correct RTs
68	N-back	1,2,3	number of correct responses (corrected for wrong responses)	-
70	N-back	3	d' (discriminability index)	correct median RTs
80	Match-to-sample task	1,3	%correct	correct RTs
90	N-back	2	% correct (accuracy)	correct RTs
105	Change-detection task	4,6,8	K [N*(H-F)/(1-F)	correct RTs
105	N-back	2,3	number of correct responses (corrected for wrong responses)	correct RTs
114	Change-detection task	n/a	online then offline accuracy (% correct)	correct RTs
133	Change-detection task	n/a	d' (discriminability index)	-
134	Change-detection task	n/a	K [N*(H-F)/(1-F)	-
144	N-back	1,2	% correct/d'	correct RTs
155	Delayed match-to-sample	4,5,6	K (K=S*(H-F)	-

n/a = not applicable (load was not manipulated); for some tasks RTs were not measured (-).

The WM accuracy meta-analysis was based on 13 of the eligible studies. As shown in Table 2.9, some of these studies comprised 2 separate experiments with independent samples, therefore, each experiment with an independent sample was treated as a separate study for the meta-analysis giving a total of 17 experiments analysed (n = 470). The median sample size was 24 (IQR 19-33). The median age was 24.5 (IQR 22.3-29.0) and the median proportion of females per study was 60% (IQR 50%-87.2%).

The WM reaction time (RT) meta-analysis was based on 8 of the eligible studies contributing 9 experiments (n = 257). The median sample size was 24 (IQR 18-35). The median age was 25.2 (IQR 22.0-49.1) and the median proportion of females per study was 55% (IQR 51%-89.3%).

2.3.2.1 Risk of bias: accuracy and reaction time tACS

The RoB was low across all 17 eligible studies as shown in Figs. 2.9 and 2.10, which depict RoB for cross-over/repeated measures studies and randomised control trials, respectively. The respective RoB full reports are provided in Appendix 5 and 6.

Study ID	Study DOI	Experimental	Comparator	Outcome	Weight	D1	DS	D2	D3	D4	D5	Overall
3	10.3233/rnn-160714	tACS	sham	HR-FA (% correct);accurate log-transformed RTs	1	+	!	+	+	+	+	+
10*	10.1155/2016/4274127	tACS	sham	PANAS-NA;PANAS-PA	1	+	+	+	+	+	+	+
16	10.1523/JNEUROSCI.1285-17.2018	tACS	sham	p(T)	1	+	+	+	!	+	+	!
61	10.1016/j.bandc.2015.11.002	tACS	sham	accuracy diff scores [(post-pre)/pre]; accurate RTs	1	+	+	+	+	+	+	+
65*	10.1016/j.ibneur.2022.10.013	tACS	sham	accuracy (% correct); correct RTs	1	+	+	+	+	+	+	+
68	10.1016/j.actpsy.2013.11.011	tACS	sham	number of correct responses (corrected for wrong responses)	1	+	+	+	+	+	+	+
70	10.1016/j.brainres.2019.146324	tACS	sham	d' (discriminability index); correct median RTs	1	+	+	+	+	+	+	+
80	10.3389/fnhum.2017.00367	tACS	sham	%correct; correct RTs	1	+	+	+	+	+	+	+
105	10.3389/fnhum.2017.00651	tACS	sham	K [N*(H-F)/(1-F); correct trials; RTs	1	+	+	+	+	+	+	+
114	10.1038/s41593-019-0371-x	tACS	sham	online then offline accuracy (% correct); RTs	1	+	+	+	+	+	+	+
116**	10.3389/fnins.2018.00761	tACS	sham	d' (discriminability index); RT hits	1	+	+	+	+	+	+	+
133	10.1038/srep32138	tACS	sham	d' (discriminability index)	1	+	+	+	+	+	+	+
134	10.1038/s41598-017-18449-w	tACS	sham	K [N*(H-F)/(1-F)	1	+	+	+	+	+	+	+
144	10.7554/eLife.22001	tACS	sham	% correct/d'; correct RTs	1	+	+	+	+	+	+	+
155	10.1371/journal.pbio.2005348	tACS	sham	K (K=S*(H-F)	1	+	+	+	+	+	+	+

+ Low risk
! Some concerns
- High risk

D1 Randomisation process
DS Bias arising from period and carryover effects
D2 Deviations from the intended interventions
D3 Missing outcome data
D4 Measurement of the outcome
D5 Selection of the reported result

Fig. 2.9 Risk of Bias Summary: tACS Studies using a within-subjects design (subjective well-being and cognitive measures; n=15)

*Study only measured subjective well-being, therefore not included in any meta-analyses.

**Study included in RT meta-analysis only because there was insufficient information reported for accuracy.

***Study did not report sufficient information to be included any meta-analyses.

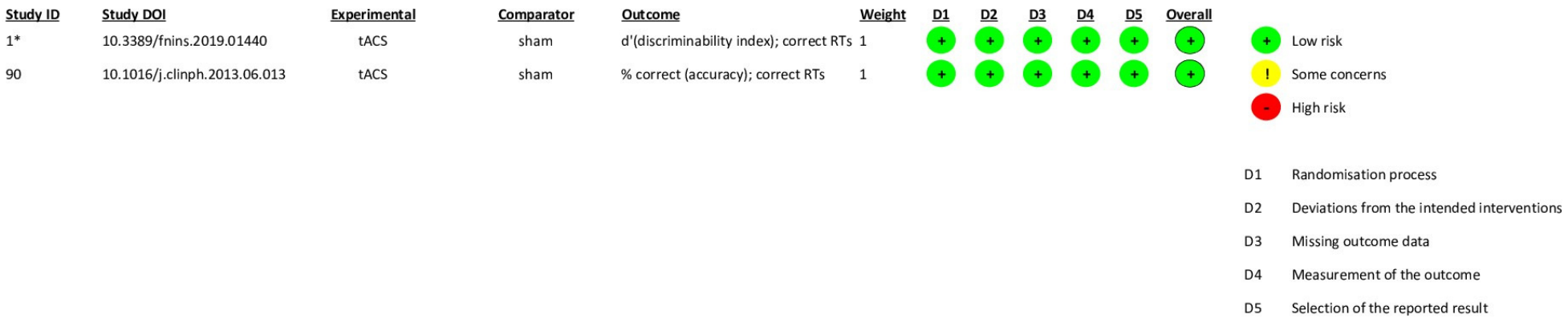

Fig. 2.10 Risk of Bias Summary: tACS Studies using a between-subjects design (RCTs; n=2)

*Study did not report sufficient information to be included in any meta-analyses.

2.3.2.2 GRADE evidence evaluation: accuracy tACS meta-analysis

The GRADE evaluation was conducted separately for the accuracy and RT meta-analyses as not all studies were present in both analyses.

The GRADE evidence rating for the WM accuracy meta-analysis was moderate. Table 2.11 provides a summary of the certainty of evidence. The GRADE evaluation showed that there were no serious limitations posed by RoB, inconsistency or publication bias. Fig. 2.11, a 'leave-one-out' forest plot that provides an analysis of the influence of individual studies, and Table 2.11 show that a considerable amount of the between-study heterogeneity was driven by 3 studies (4 experiments): studyIDs 68, 70 (exp.1) and 114 (exp. 1 and 2) (see 'Accuracy meta-analysis outcome' for the sensitivity analysis assessing their impact on the pooled effect size). The evidence profile was down-graded on the basis of serious limitations in indirectness and imprecision. For indirectness, the experiments' samples were typically drawn from young adults. Only 2 of 13 studies (contributing 3 experiments) tested older adults. Thus, the findings would be less generalizable to middle-aged and older adults but reasonably generalizable to young adults. For imprecision, sample sizes were underpowered, because, assuming a 2 x 2 fully within-subjects factorial ANOVA design and a small effect size (0.2), which is more likely, a total sample size of 36 would be needed to achieve a power of .80. By comparison, the median sample size here was 24, which would achieve a power of only .61.

Table 2.11 GRADE evidence profile: transcranial alternating current stimulation benefit to working memory accuracy.

	Certainty rating by category					No. of Participants (studies)	Effect Size	Quality Rating
Category	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**publication bias**	470 (13)*	0.24 [0.08-0.40]	Moderate
Evaluation	*No serious limitations*	*No serious inconsistencies*	*Serious indirectness*	*Serious imprecision*	*Undetected*			
tACS accuracy vs. Sham	RoB assessment shows all 17 studies had a low risk of bias.	Upon examining the funnel plot it can be observed that there are some differing estimates of effect indicating some heterogeneity. This can be explained by one experiment which is an outlier and 2 experiments (from one study) which used a much more sophisticated technique relative to the other experiments to maximise the benefits of tACS and therefore may be categorised as a sub-group.	A range of ages were included across the 13 meta-analysed studies. Two of the 13 studies (which contributed 3 experiments) tested elderly adults, while the remaining studies focused on young adults. In two studies only females were included. Given that this review intended to include adults across the lifespan generalisability of findings is limited for middle-aged and older adults but not limited when considering young adults.	Assuming a small effect is more likely, the number of participants per study was insufficient.	Funnel plot shows that results were distributed around the middle with one influencing outlier (studyID 68). Consequently the funnel plot is indicative of a low risk of publication bias. The sample included studies from a range of universities and journals which mitigates risk of publication bias.			

*13 studies contributing 17 experiments

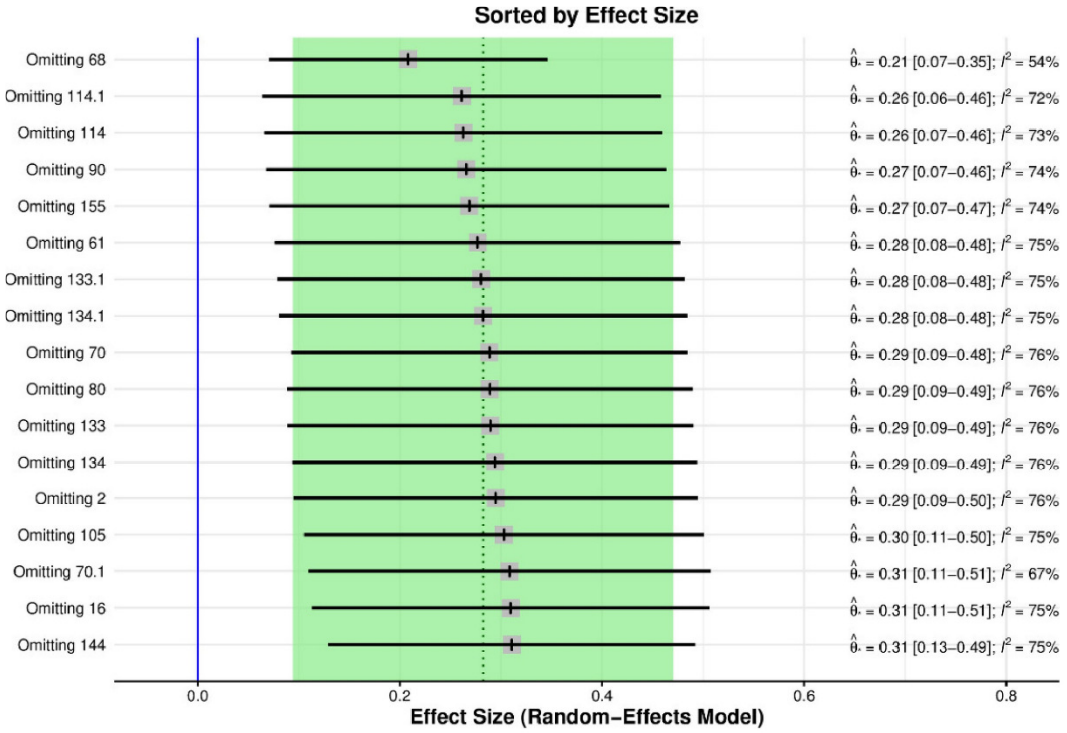

Fig. 2.11 tACS accuracy: Leave-one-out forest plot
The between-experiment heterogeneity was statistically significant (τ^2= 0.09 (95%CI: 0.03-0.27) with an I^2 value of 74% (95%CI: 58-83.9%). This heterogeneity may indicate some differences in true effect sizes between studies because I^2 > 50% (Harrer et al., 2021). The leave-in-out method shows that when studyID68 is removed, I^2 drops to 54% (from 74%), when removing studyID 70 (experiment 1) the I^2 value drops to 67% and when studyID 114 (experiments 1 and 2) are removed they reduce the I^2 value by a total of 3%.

The funnel plot below, Fig. 2.12, shows that studies were reasonably evenly distributed around the intercept with some outlying values. Egger's test of the intercept was statistically significant indicating an intercept bias of 1.54 (95%CI: 0.36 to 2.72), t = 2.564, p = .022. Ideally, the funnel plot should be symmetrical, indicated by an intercept value distributed around zero (Harrer et al., 2021). A statistically significant non-zero intercept, as indicated above, could be interpreted as publication bias as smaller studies' effect sizes distort the intercept value. The result may be most likely explained by the outlying experiment, studyID68 which found a large effect as indicated by Fig. 2.11, but has a small sample (n = 36).

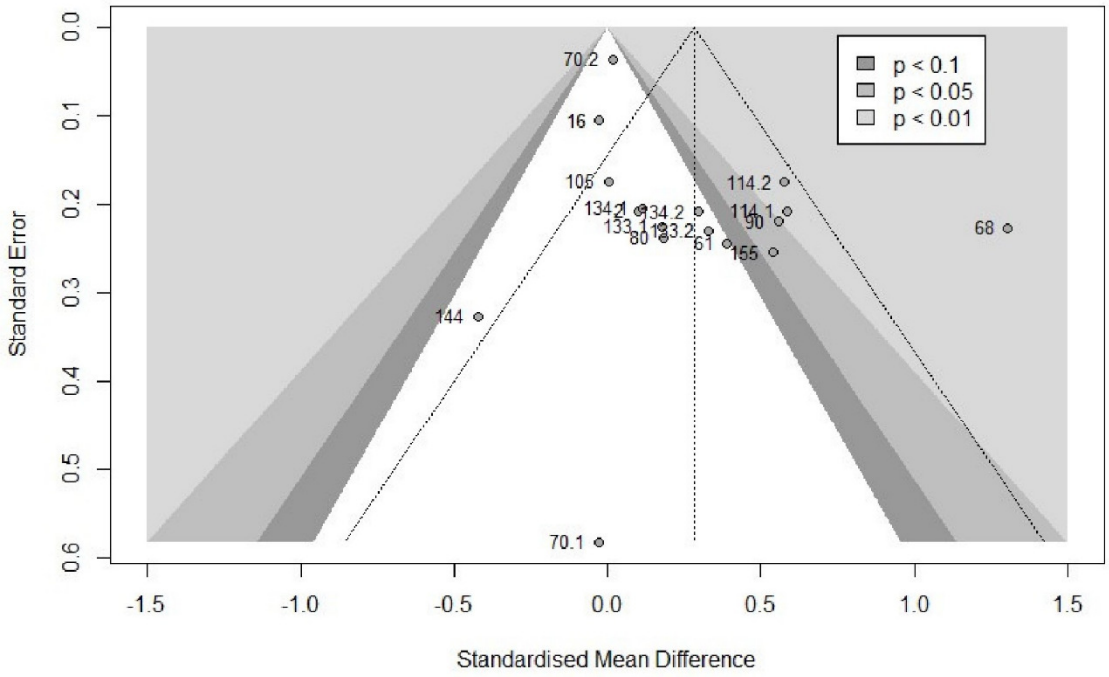

Fig. 2.12 Funnel Plot of studies included in the tACS accuracy meta-analysis (k=13 contributing 17 experiments).
Values on the plot represent individual study IDs.

2.3.2.3 GRADE evidence evaluation: reaction time tACS meta-analysis

The GRADE evidence rating for the WM reaction time meta-analysis was moderate. Table 2.12 provides a summary of the certainty of evidence. As with the accuracy meta-analysis, the GRADE evaluation revealed no serious limitations posed by risk of bias, inconsistency or publication bias. However, the studies were likely underpowered given that the median sample size (Mdn=24) fell below the estimated required sample size of 36 to achieve a power of .80. In addition, with fewer studies included, generalisability was seriously impacted given that only one research group (studyID 114 experiments 1 and 2) tested older adults and

two of the remaining 7 studies included only females. The funnel plot indicates no signs of publication bias as observed in Fig. 2.13.

Table 2.12 GRADE evidence profile: transcranial alternating current stimulation benefit to working memory reaction time.

			Certainty rating by category			No. of Participants (studies)	Effect Size	Quality Rating
Category	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**publication bias**	257(8)*	0.24 [0.08-0.40]	Moderate
Evaluation	*No serious limitations*	*No serious inconsistencies*	*Serious indirectness*	*Serious imprecision*	*Undetected*			
tACS RT vs. Sham	RoB assessment showed all studies had a low risk of bias.	Zero was included within the confidence intervals for all studies in this meta-analysis and the test for heterogeneity was not statistically significant indicating a consistent outcome.	Across the 8 meta-analysed studies only 1 (contributing 2 experiments) tested older adults, while the remaining studies' samples comprised young adults. In two studies only females were included. Given that this review intended to include adults across the lifespan generalisability of findings is limited for middle-aged and older adults but less so for young adult populations.	Assuming a small effect is more likely, the number of participants per study was insufficient.	Funnel plot shows that results were distributed around the intercept with one outlier (studyID 144). Consequently the funnel plot is indicative of a low risk of publication bias but is of limited value given the small set of studies. The sample included studies from a range of universities and journals which mitigates risk of publication bias.			

*8 studies contributing 9 experiments

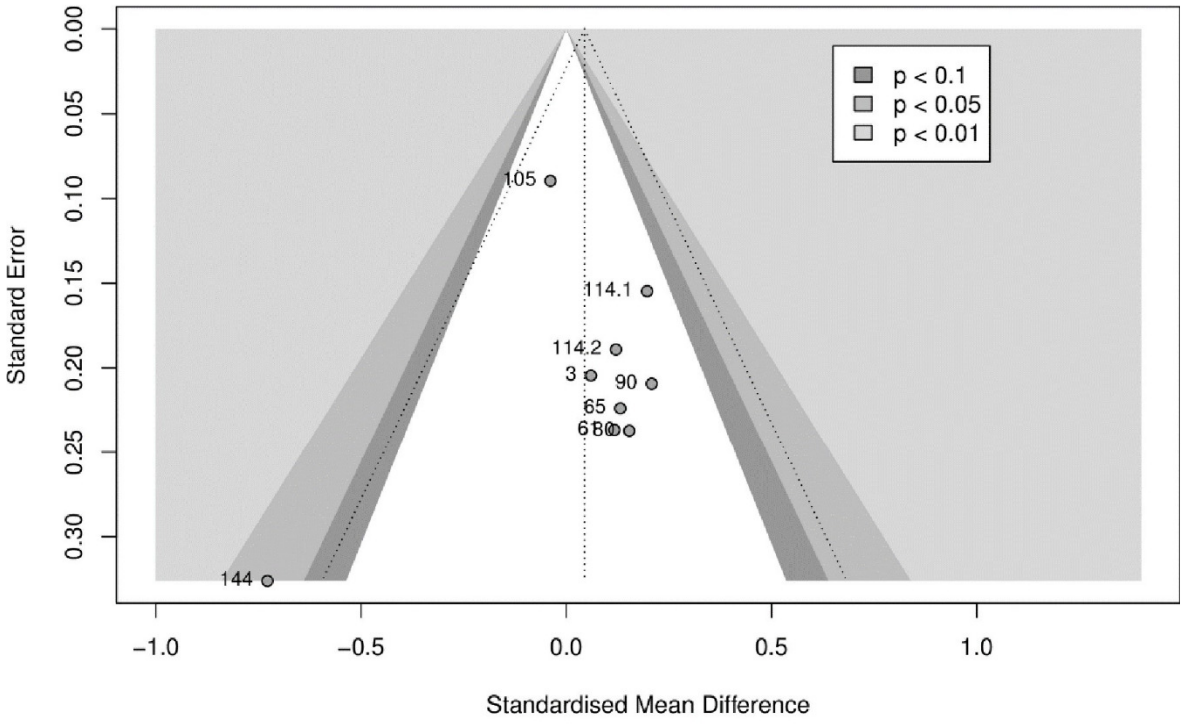

Fig. 2.13 Funnel Plot of studies included in the tACS reaction time (RT) meta-analysis (k=8 contributing 9 experiments).
Values on the plot represent individual study IDs.

2.3.2.4 Accuracy meta-analysis outcome

Referring to the forest plot depicted in Fig. 2.14 below, the meta-analysis revealed, based on 13 studies (17 experiments), that tACS participants' WM accuracy improved relative to sham (SMD = 0.28, 95%CI: 0.09 to 0.47). However, Fig. 2.11 shows that heterogeneity was statistically significant ($p < .01$) and that the predictive validity was poor ($g = -0.37$ to 0.93).

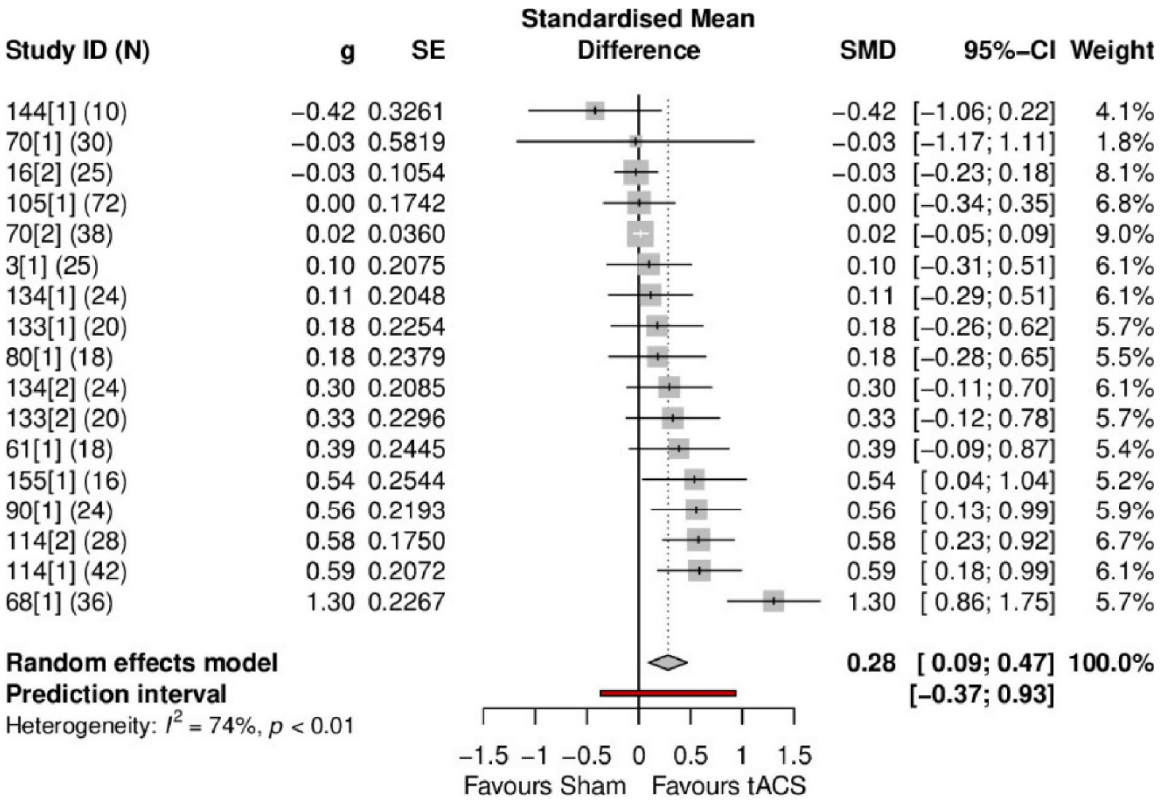

Fig. 2.14 Forest plot of the overall comparison of tACS vs. sham stimulation (17 experiments).
As shown, the overall effect size was statistically significant. Heterogeneity was also statistically significant.

A considerable proportion (30%) of the between-study heterogeneity was related to three studies: studyID 68, studyID 70 (experiment 1) and studyID 114 (experiments 1 and 2), as indicated in the leave-one-out forest plot, Fig. 2.11, and Table 2.11. Thus, a series of sensitivity analyses, presented in Table 2.13 below, was performed to ascertain whether removing one or more of these influencing studies had an impact on the level of heterogeneity. Initially, all 3 studies (4 experiments) were removed, then two of the most influential studies, studyIDs 68 and 70 (experiment 1), which, in combination contributed 27%, and then one study at a time.

Table 2.13. Sensitivity Analysis presenting Hedge's g, 95% confidence intervals and two measures of heterogeneity: I^2, its 95% confidence intervals and the 95% prediction intervals (PI).

Sensitivity Analysis	g	95%CI	p	95%PI	I^2	95%CI
Main Analysis	0.28	0.09-0.47	0.006	-0.37-0.93	74%	58-84%
Remove all influential studies	0.13	0.00-0.26	0.050	-0.54	33%	0-66%
Remove studyID 68 & 70 (exp 1)	0.21	0.07-0.36	0.007	-0.20-0.62	57%	24-76%
Remove studyID 70	0.29	0.09-0.48	0.007	-0.38-0.95	76%	60-85%
Remove studyID 68	0.21	0.07-0.35	0.006	-0.19-0.61	54%	20-74%
Remove studyID 114 (exps 1, 2)	0.24	0.03-0.44	0.0264	-0.43-0.91	71%	51-83%

The results of this sensitivity analysis suggests that the most valid representation of the effect of tACS relative to sham on WM accuracy was to remove studyID 68, which contributed the most to heterogeneity with a limited negative impact on the overall effect size when removed, as demonstrated in the forest plot below (Fig. 2.15).

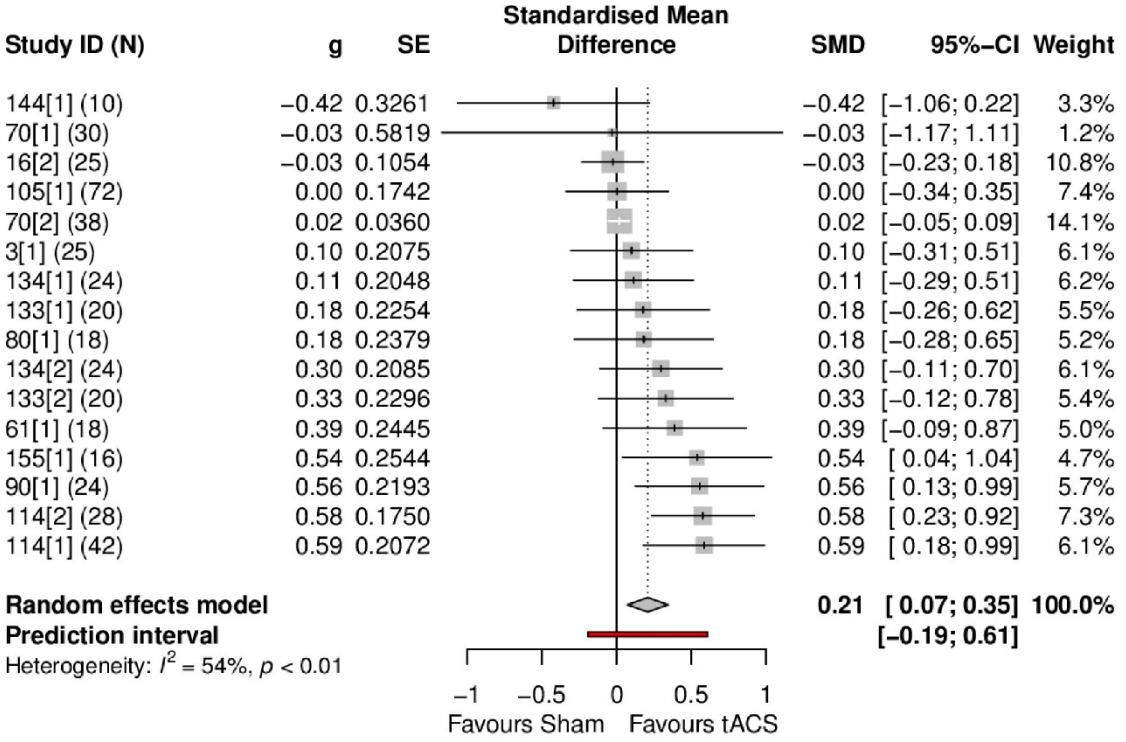

Fig. 2.15 Sensitivity Analysis: forest plot of the overall comparison of tACS vs. sham stimulation without studyID 68 (k=12 contributing 16 experiments).
As shown, the overall effect size remained statistically significant, as did heterogeneity (though 20% lower).

Referring back to the main analysis forest plot (Fig. 2.14), studyID 114's two experiments contributed a relatively large effect to the pooled result. This may be because studyID 114 used a much more sophisticated tACS protocol than did the other studies. Moreover, their target population comprised older adults. Thus, a further sensitivity analysis was conducted to evaluate whether studyID 114 represented a separate sub-group.

Following the removal of the outlier (studyID 68) the meta-analysis was performed once more this time without studyID 114 (experiments 1 and 2) to assess whether the pooled effect size remained statistically significant. Fig. 2.16 presents the forest plot, which shows that removing studyID 114 reduced the pooled effect size of the main group (SMD = 0.13, 95%CI: 0.0 to 0.25, p = .0425). Noteworthy is that the heterogeneity dropped from 54% (Fig. 2.15) to 28% (p = .16). Next, a fixed effects model was used to calculate the pooled effect of studyID 114's experiments 1 and 2. The result was statistically significant: SMD = 0.58 (95%CI: 0.32 to 0.84, p < .01).

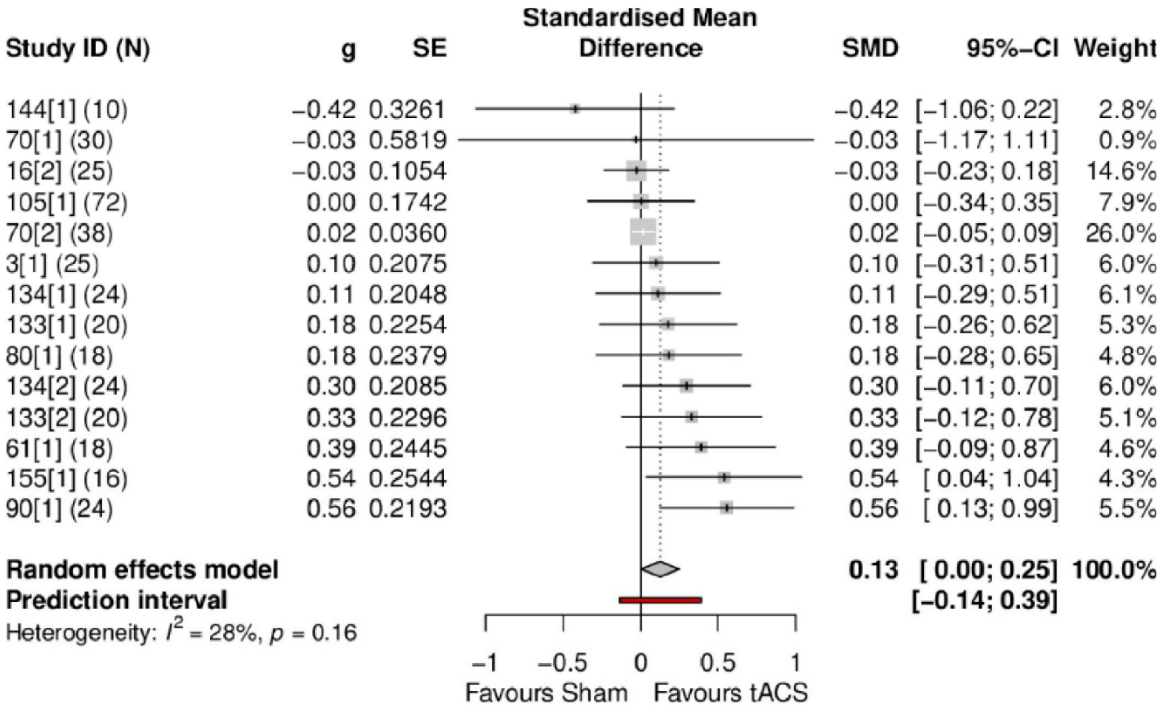

Fig. 2.16 Sensitivity Analysis: forest plot of the overall comparison of tACS vs. sham stimulation without studyID 68 and studyID 114 (k=11 contributing 14 experiments).
This forest plot shows that the overall effect size was no longer statistically significant. In addition, the value for I^2 was not statistically significant (p = .16) indicating a low level of between-study heterogeneity.

The finding presented in Fig. 2.16 and the pooled effect for studyID 114 suggest that the original meta-analysed set of studies are best considered separately: a sub-group of 11 studies (14 experiments) which indicated no statistically significant benefit of tACS on WM accuracy and a sub-group comprising two experiments from one research group that used a more sophisticated tACS protocol with an older sample that showed a moderate effect.

2.3.2.5 Reaction time meta-analysis outcome

Based on 8 studies (9 experiments) tACS participants' working memory RT did not show a significant change relative to sham (SMD = -

0.04, 95%CI: -18.0 to 0.9). Heterogeneity was not statistically significant (p = .37).

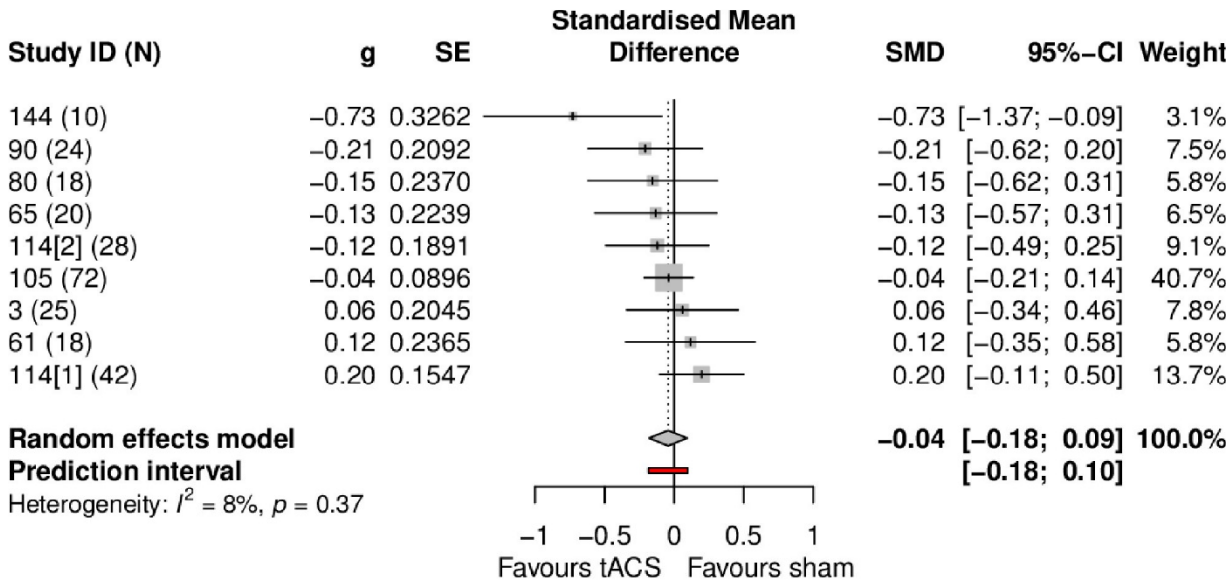

Fig. 2.17 Forest plot of the overall comparison of tACS RT vs. sham stimulation 8 studies (9 experiments).
The overall effect size was not statistically significant.

2.3.3 Comparing Mindfulness Meditation and tACS

There were 2 WM accuracy studies meta-analysed for MM studies compared to 13 for tACS and neither yielded a statistically significant benefit of treatment effect. Thus, no meaningful comparison could be conducted between MM and tACS for WM accuracy. No other comparisons (RT, subjective well-being) were possible because there was insufficient data.

2.4. Discussion

The present systematic review identified 15 eligible MM and 17 eligible tACS studies. For MM, a meta-analysis was performed for subjective well-being and WM accuracy. For tACS, WM studies were

meta-analysed. No effect size comparisons were performed because there was insufficient data. The MM subjective well-being meta-analysis of 8 studies (n=492) revealed no statistically significant evidence that MM enhanced levels of subjective well-being. The tACS accuracy meta-analysis of 13 studies (17 experiments) (n=470) revealed two findings: firstly, the analysed studies comprised two distinct sub-groups with different results: in the larger sub-group (k=11), there was no statistically significant evidence of improved WM accuracy relative to sham. In the smaller sub-group, based on two experiments from one study, there was a statistically significant moderate effect size in favour of tACS; secondly, it is possible to group together tACS studies that applied varied stimulation protocols. The tACS RT meta-analysis of 8 (n=257) studies revealed no statistically significant evidence that tACS improves working memory RTs.

2.4.1 Mindfulness Meditation

The present meta-analysis found no evidence to support the hypothesis that MM reduces stress or improves positive affect as represented by the tasks used by the reviewed studies. It may be that an effect exists, but there was insufficient statistical power to detect it as the source studies were underpowered. In addition, only a small number of studies were eligible for analysis relative to the initial number of studies included in the full review (10 vs. 124). This was due to restricting studies based on the type of MM (non-physical only) and level of detail reported. The lack of methodological rigour in meditation research has been highlighted in the literature (Chiesa et al., 2011; Fox et al., 2014; Schumer et al., 2018; Sedlmeier et al., 2012; Sedlmeier et al., 2018). Indeed, in the

present meta-analysis some typical examples noted were: inadequate control features in the study design such as a lack of control group, blinding and compliance checks, small sample sizes and insufficient details reported regarding the MM technique used. Many reviews acknowledged that their conclusions are also somewhat tenuous because they could only draw from the available pool of evidence, which in this case, has numerous methodological limitations. In addition, their conclusions are based on the outcomes from a mix of techniques ranging from entirely passive closed eyes, seated MM such as focused attention and those with a strong physical component like mindfulness-based stress reduction (MBSR) (e.g. Casedas et al., 2020; Chiesa et al., 2011; Keng et al., 2011; Schumer et al., 2018). Is it valid to analyse MM techniques with and without a physical component? Previous research points to enhanced expression of brain-derived neurotrophic factor (BDNF) through exercise (Vecchio et al., 2018). One may therefore speculate that MBSR presents such an opportunity for some practitioners thereby enhancing meditation benefits. Evidence appears to support this potential disparity in possible mechanisms to improved well-being when meditating. However, this evidence is unreliable and thereby provides a case in point for the fundamental difficulty in the field: Sedlmeier and colleagues (2018) found a larger benefit for non-physical MM vs. physical MM in studies with a passive control group in their review of healthy long-term MM practitioners. However, the opposite effect was found in studies with an active control group. In both results, the authors reported that confidence intervals were broad and unreliable. Carmody and Baer (2008) noted in their findings

with participants that included distressed adults that the yoga component of MBSR yielded particularly striking positive results. Meditations with a physical component would also require additional focus and greater motivation. Consequently, some people may be less likely to sign up for a randomised control trial where they may be required to undertake MM with a physical element vs. without. Thus, in addition to the introduction of an added mechanism of action is the increased potential for selection bias, which, even with a randomised control design, cannot be entirely mitigated. A further complication related specifically to measuring subjective well-being is that it is necessarily self-report. It might, therefore, be more instructive to evaluate subjective well-being benefits of MM indirectly by measuring the body's stress response to particular visual and auditory stimuli with indices such as EEG, fMRI or cortisol levels. Even then, further work is needed before firm conclusions may be drawn as indicated by Fox and colleagues (2014). Their systematic review and meta-analysis investigated the potential for meditation to alter brain structure. In their discussion they set out in detail a number of methodological limitations such as selection bias, pre-existing brain structure differences and measurement error within the field.

2.4.2 Transcranial alternating current stimulation

2.4.2.1 Working memory accuracy

The meta-analysis revealed no statistically significant effect of tACS relative to sham on WM though the pattern of findings observed in the forest plots suggests that there was a trend to an effect. By comparison, a recent systematic review of healthy adults reported a small-to-medium

effect of tACS on WM and long-term memory performance overall (Booth et al., 2022). Similarly, Klink and colleagues' (2020) systematic review of 57 studies indicated that theta-tACS benefits executive function, including WM performance. As with the MM meta-analysis, the source studies' sample sizes were small relative to the effect being sought. Most studies used within-subjects designs, however, which reduced error variance. Transcranial alternating current stimulation protocols can vary regarding phase, frequency, amplitude and inter-stimulation intervals (Herrmann et al., 2013; Hosseinian et al., 2021; Hsu et al., 2017). On this basis, collapsing studies across these design features may have diminished the true effect. Based on the studies here this seems unlikely. The advantage of tACS is that specific cognitive functions are targeted with appropriate frequencies. Given the established evidence that theta in particular is pivotal to optimal WM performance, almost all the studies used a theta frequency. Only 4 studies testing gamma frequencies in addition to or instead of theta. Only studyID 144 showed a negative result on the forest plot, however, this study did not differ fundamentally from the others regarding current density or frequency. Moreover, the sample size was small (n=10) therefore it may represent statistical variation. Where a distinction was apparent was regarding studyIDs 114(1) and (2). These two experiments tested older adults and utilised an individualised theta-gamma coupled frequency specifically selected based on peak WM performance in conjunction with a high definition montage of 6 electrodes simultaneously targeting two anatomical regions. Moreover, their change detection task involved no repeated stimuli pairs thereby reducing the

statistical noise introduced by practice effects. The likely driver of this clear evidence of improvement in performance was a combination of the superior tACS protocol and the age of the participants. In their experiment 3, Reinhart and Nguyen (2019) demonstrated that anti-phase stimulation reduced performance in a sample of young adult participants, thus, separating the impact of age and stimulation. However, age is also important; older adults are likely to benefit more than young adults from tACS stimulation because they have a broader scope for improvement. Congruently, previous work has shown that there is an upper limit to tACS-related perceptual (Castellano et al., 2017) and visual memory (Hsu et al., 2014; Tseng et al., 2012) performance. Further evidence for the effect of improvement potential was replicated by Reinhart and Nguyen (2019) in their 4th experiment. Using the individualised protocol, they applied stimulation to the subset of poorly-performing young participants who were baseline controls for the older participants in experiment 1 (studyID 114(1)) and found that this sub-group showed a significant benefit of tACS in WM performance.

2.4.2.2 Working memory reaction time

The RT meta-analysis revealed no statistically significant evidence of faster RTs. Klink et al.'s (2020) systematic review indicated that theta- and alpha-tACS reduced response times in higher cognitive tasks and that this effect interacted with load. In the current meta-analysis some studies used numerous load conditions which were averaged over to evaluate the overall effect of stimulation. Thus, any subtle benefit of RT would have been lost to statistical variation. The theta frequency has been described

as a carrier frequency and a pace-maker frequency, working across long-range networks (Alekseichuk et al., 2017). As such, extraneous stimulation may have a short-lived or restricted effect on overall response speed as energy dissipates across these longer ranges. For instance, Reinhart and Nguyen (2019) found that RT gains were reliably measurable only in the middle 3-min time bins in their older adult sample. In addition, the source studies varied regarding whether or not they reported the results of any speed-accuracy trade-off and, if they did, how they measured it. For instance, studyID 3 measured speed-accuracy trade-off using a diffusion drift modelling approach whereas studyID 80 added a control task to rule out simple motor effects on RTs.

2.4.3 Limitations

A meta-analysis is a powerful statistical technique that can be very informative; however they do have limitations. Two are of particular importance in the present work: the quality and the heterogeneity of source studies. The quality was controlled by omitting high risk of bias studies as well as those that did not provide important methodological details such as blinding or sham protocols and/or details regarding interventions like duration or how a treatment was applied. To control for heterogeneity, only standard, commonly used outcome measures and treatments were included. In the case of tACS, only montages specifically targeting cognitive function were eligible, as this would limit statistical noise introduced by confounds such as motor or perceptual effects. Regarding MM, the likewise restriction was to only include passive (non-physical) meditation protocols to rule out confounds such as enhanced

effects due to increased BDNF expression. The disadvantage of such restrictions was that it severely limited the number of eligible studies. Consequently, as the GRADE evaluations indicate, the evidence reported has limited interpretability due to poor generalisability and precision. A further caveat is that most source studies comprised small samples and eligible studies involving older adult participants were few with none targeting middle-aged adults. Furthermore, it must be acknowledged, as with most meta-analyses, that there was a range of study designs and treatment applications. Importantly, it is not known whether a duration of, say, 10 minutes' tACS stimulation would be equivalent to 10 minutes' MM. This is in and of itself important to investigate further if the relative benefits of these two interventions are to be understood. Note also that none of the RCTs included were registered. Whilst every effort was made to be accurate, standardised mean differences were derived from available statistical outputs, which varied, and in some cases, standard errors had to be estimated.

The systematic review was completed manually, which introduces the possibility of missed reports. Wherever possible, review articles were checked to reduce the risk of overlooking any eligible studies. In addition, the RoB assessment was conducted by only one reviewer, which may have resulted in (some) selection bias. This risk was mitigated by RR's review of the RoB decisions and applying strict selection criteria at the outset, agreed upon by the research team using a pre-registered protocol. Thus, almost all studies had a low RoB. In the few cases of high RoB, the Cochrane guidelines were followed.

2.4.4 Conclusion

This chapter aimed to compare the efficacy of tACS and MM to improve WM performance and/or subjective well-being. Effect sizes were derived from the meta-analysed results of good quality studies. Strict inclusion criteria were applied to capitalise on available statistical power. No direct comparisons of tACS vs. MM were possible because the number of studies for WM was insufficient and for subjective well-being there were no studies to compare. The MM meta-analyses did not show any evidence of a benefit to subjective well-being, contrary to previous findings. In addition, WM accuracy is unlikely to improve with MM. The tACS accuracy meta-analyses showed that there were two subgroups. In the main sub-group there was no statistically significant improved performance overall with active tACS though the forest plot indicated a trend to effect. In the smaller sub-group, the more sophisticated protocol and older adult sample showed a moderate effect. The RT meta-analysis revealed no statistical evidence of faster WM responses using active tACS. Importantly, the consistency across studies in the tACS forest plots suggests that one can analyse these studies together despite a broad range of stimulation protocols. The more sophisticated tACS protocol highlights that there is potential for a step-change in efficacy that future work should focus on. Measures of subjective well-being should be added to such studies. This chapter highlights the limited scientific rigour within mindfulness meditation research and future work should include registered controlled trials to raise the standard.

2.5 Supporting Information

Appendix 1	PRISMA table.
Appendix 2	Protocol document including inclusion and exclusion criteria.
Appendix 3	Indices, constructs measured, score ranges and interpretation of scores and the reviewed studies they were used in.
Appendix 4	Risk of Bias full report and studies ineligible for analysis for the Mindfulness Meditation meta-analysis.
Appendix 5	Risk of Bias full report and studies ineligible for analysis for the tACS working memory accuracy meta-analysis.
Appendix 6	Risk of Bias full report and studies ineligible for analysis for the tACS working memory RT meta-analysis.

A section containing all appendices can be found starting from page 395, at the end of this thesis.

Chapter 3: A pilot study investigating the cognitive effects of tACS and of cumulative life stress on young and older adults.

3.1 Introduction

Memory is a distinctive mental function that enables us to encode, store and retrieve information (Kandel, 2006; Squire, 2009). Memory may be divided into declarative memory, which refers to information that one can consciously recall including spatial, semantic[18] and episodic[19] memory, and non-declarative memory (Cohen & Squire, 1980), which is unconscious memory for movement, actions, priming, skills and habits (Roediger et al., 2017). Working memory is an additional system, which provides the ability to store, maintain, monitor and manipulate a limited amount of information over a brief time-period, thereby facilitating comprehension and learning (Baddeley, 2012; Baddeley & Hitch, 1974). Memory processes are underpinned by a wide range of anatomical structures, including the hippocampus, prefrontal, parietal and temporal regions (Faraco et al., 2011; Laroche et al., 2000; Nadel & Hardt, 2011; Nee et al., 2013; Owens et al., 2018; Yonelinas, 2013), which are connected via short- and long-range neural networks. These neural

[18] Semantic memory is a form of long-term memory that provides us with information about facts, objects and words and symbols Warrington, E. K. (2017). Semantic Memory☆. In *Reference Module in Neuroscience and Biobehavioral Psychology*. Elsevier. https://doi.org/10.1016/b978-0-12-809324-5.04565-x .

[19] Episodic memory is a form of long-term memory relating to "…particular events situated in space and time, as well as the underlying cognitive processes and neural mechanisms involved in remembering those events." Roediger, H. L., Zaromb, F. M., & Lin, W. (2017). A Typology of Memory Terms ☆. In J. H. Byrne (Ed.), *Learning and Memory: A Comprehensive Reference* (pp. 7-19). Academic Press. https://doi.org/10.1016/b978-0-12-809324-5.21003-1 .

networks are highly efficient in young adults but vulnerable to the effects of ageing (Ankudowich et al., 2019; Dickerson & Eichenbaum, 2010; Janowsky et al., 1989) and stress (McEwen, 1998, 2001; Sapolsky, 1993; Sapolsky et al., 1986).

A wide range of studies have demonstrated that younger adults typically outperform older adults in tasks measuring, *inter alia*, processing speed, working memory and episodic memory. For example, Head and colleagues (2008) conducted a behavioural-fMRI study comparing young and older adult participants' performance of 18 tasks measuring cognitive functions including working memory, processing speed, episodic memory and inhibition. Age-related differences were observed across cognitive functions. Structurally, age differences in prefrontal white and gray matter, caudate nucleus and hippocampal volume were also observed. Furthermore, Dennis and colleagues (2008) conducted an fMRI study on source memory, which relates to an event's context regarding time, place and the like. There were three key findings. Firstly, older adults had less activation in the hippocampus, fusiform region, PFC and parahippocampal 'place' area than young adults. Secondly, this finding was statistically significant for source memory performance, which relates to episodic memory (more vulnerable to ageing), but not item memory performance, which relates to semantic memory (less vulnerable to ageing). Third, they found stronger prefrontal activation in older adults than young adults.

These findings highlight that young and older adults process information differently. Young adults typically rely on specialised structures for information processing while older adults recruit structures more

generally. For example, research shows that young adults bilaterally activate the fusiform gyrus to process faces, while the older group activate the right fusiform gyrus and orbitofrontal cortex, which processes faces and other objects (Burianova et al., 2013). The findings also highlight that age-related structural changes like reductions in cortical volume and neurotransmitter levels and degraded white matter tracts (Tsapanou et al., 2019) can reduce efficiency and connectivity of neural networks (Fjell & Walhovd, 2010; Hedden & Gabrieli, 2004; Sala-Llonch et al., 2015). Importantly, research suggests that endocrine systems also act as a mechanism of ageing (Finch, 1976). In particular, stress hormones may accelerate brain ageing thereby further contributing to poorer memory function in older age (Landfield, 1978; Porter & Landfield, 1998; Sapolsky et al., 1985).

Glucocorticoids together with their corresponding high concentration of receptors in the hippocampus, prefrontal cortex (PFC) and amygdala play a central role in adaptation through memory and learning alongside the regulation of energy supply, cardiovascular responsiveness and immune function (Frodl & O'Keane, 2013). While this dynamic system is highly adaptive, allowing the targeted brain structures to expand and contract their dendrite arbours in response to environmental context, glucocorticoids have the potential to accelerate ageing if circulating levels are not appropriately regulated (McEwen, Gray, et al., 2015; Nichols et al., 2001; Sapolsky et al., 1986). Moreover, as a number of studies appear to show, the combined allostatic load of ageing and stress increases the likelihood of accelerated brain ageing. Souza-

Talarico and colleagues (2011) concluded in their review that chronic stress exposure in the context of ageing shows similar markers to Alzheimer's Disease regarding dendritic atrophy and oxidative stress. In a series of cross-sectional studies Marshall and colleagues compared young and older adults with high versus low levels of cumulative life stress, as measured by self-report life events questionnaires, on a range of cognitive tasks paired with EEG (Marshall et al., 2016; Marshall et al., 2016b; Marshall et al., 2015). Their key finding across all studies was that older adults who had experienced many stressful events over the course of their life performed less well in working memory, inhibitory control and spatial discrimination tasks than their lower stress counterparts and both high and low cumulative stress young adults. Additionally, Marshall et al.'s resting- and active-state EEG data revealed changes in oscillatory dynamics, such as power and synchronisation of theta (Marshall et al., 2016b) and alpha (Marshall et al., 2015) frequencies, which were associated with deficits in performance and early signs of cognitive decline (Marshall & Cooper, 2017).

Given the impact of ageing and stress on older adults' memory performance and given the malleability of the neural structures underpinning these functions this pilot study investigated whether perturbing the functional efficiency of neural networks via exogenous entrainment might be beneficial to memory performance. Non-invasive brain stimulation (NIBS) methods such as transcranial electrical stimulation (tES) provide extra impetus to neural processing by applying a potential difference (in volts) across the area of the brain which improves

the efficiency of encoding, processing and retrieval of information (Chakraborty et al., 2018; Lavidor, 2016; Pisoni, Mattavelli, et al., 2018; Pisoni, Vergallito, et al., 2018). In particular, transcranial alternating current (tACS) uses sinusoidal alternating current where the frequency can be “tuned” to resonate with specific brain frequencies potentially offering an efficacious outcome for cognitive performance (Frohlich & McCormick, 2010; Herrmann et al., 2013; Kasten et al., 2018; Schmidt et al., 2014). In addition, the reliability of the statistically significant interaction between age and cumulative stress found by Marshall and colleagues was assessed with the view to evaluate the extent to which stimulation might benefit high vs. low cumulative stress older individuals relative to young adults. Thus, the present study had two broad aims:

a) replicate Marshall and colleagues’ (2015) finding which showed that high cumulative stress older adults performed worse than low cumulative stress older adults and all young adults on the 2-back task. Replicating this effect would add weight to the theory that cumulative stress accelerates ageing. To target episodic memory a picture free recall task was added. Free recall has been empirically linked to prefrontal and MTL activity (e.g. Dickerson et al., 2007; Floel et al., 2012; Rimmele et al., 2010; Sperling et al., 2019). Given that episodic memory and working memory are interrelated, using two tasks would provide converging evidence of an effect of stress and/or ageing on accuracy.

b) test whether tACS stimulation can improve neural network efficiency during memory tasks in older and young adults. If

successful and assuming the successful replication of Marshall's work, it was further expected that performance of the high cumulative stress older adults would be more comparable with that of the low cumulative stress older adults during the active condition relative to sham. It is unclear to what extent low cumulative stress older adults and young adults would benefit from the stimulation. However, Reinhart and Nguyen (2019) demonstrated that poorly performing young adults improved with theta-gamma tACS stimulation, therefore some improvement in the low cumulative stress older and young adults was expected, driven by the poorer performers.

Given the aims of this study and the context of the aforementioned research, selecting a suitable frequency for entrainment was a key consideration in designing an appropriate tACS protocol. For these purposes, theta oscillations were considered a valid target. Theta frequency is central to cognition in general (Colgin, 2013; Klimesch, 1999; Klimesch et al., 2008; Zhang et al., 2018) and working memory in particular (Sauseng et al., 2010). The theta frequency oscillates in the range of 4 – 8 Hz and has been described as a 'carrier' wave, pivotal to information transmission across different neural networks throughout the brain (Canolty et al., 2006; Lisman & Idiart, 1995). Moreover, studies indicate that theta power is positively correlated with working memory load particularly in frontal regions (Boonstra et al., 2013; Gevins et al., 1997). Transcranial alternating current studies stimulating within the 4-8 Hz range have successfully modulated neural networks (e.g. Chander et al., 2016;

Klink, Peter, et al., 2020; Meiron & Lavidor, 2014; Santarnecchi et al., 2016), including the mid-point value of 6 Hz (e.g. Fusco et al., 2018; Polania et al., 2012; Rohner et al., 2018; Wolinski et al., 2018). Crucially, improvements in neural network activity and behavioural performance on working memory at the mid-point value 6 Hz have been achieved. Polanía and colleagues (2012), for example, demonstrated that a stimulation protocol with 6 Hz tACS in-phase resulted in reduced reaction times compared to sham while the 180° relative phase condition led to increased RTs compared to sham. Stimulation was applied to left DLPFC[20] (F3) and left parietal cortex (P3). This finding was replicated by Violante and colleagues (2017) who stimulated the right-hemisphere fronto-parietal network (F4 and P4) at 6 Hz, in combination with fMRI, whilst participants completed a verbal n-back task of increasing difficulty. They found that the 2-back, but not the 1-back, showed improved reaction time during in-phase tACS compared to out-of-phase tACS and sham. Episodic memory studies incorporating a tACS manipulation have demonstrated that the gamma frequency can be entrained to manipulate performance with both memory improvement (Javadi et al., 2017; Nomura et al., 2019) and impairments shown (Lara et al., 2018). In addition, Braun and colleagues (2017) showed that beta frequency does not have any impact on episodic memory performance. Thus, it appeared that the question of whether theta tACS can manipulate episodic memory performance had not been directly addressed.

[20] DLPFC = dorsolateral prefrontal cortex

The literature indicates a wide range of anatomical areas important to working and episodic memory, which warrants careful consideration of which anatomical site/s to target. Using a 2-electrode set-up two different sites were targeted to test which could best harness the exogenous stimulation to improve memory performance: bilateral stimulation of the DLPFC (Site 1) or the fronto-parietal network (Site 2). Site 1 was chosen because firstly, the DLPFC is central to executive control and working memory capacity and therefore mediates memory performance by enhancing processing specificity, speed and capacity (Barbey et al., 2013; Blumenfeld & Ranganath, 2019; Gratton et al., 2013; Long et al., 2010; McAndrews & Milner, 1991; Petrides & Pandya, 2002; Ren et al., 2019; Touzani et al., 2007). Secondly, frontal regions are geared to domain-general complex activity (Fedorenko et al., 2013). Thus, exogenous entrainment may synergistically enhance the existing processing efficiency, particularly in older adults given the changes in information processing mentioned earlier (Burke et al., 2019; Gonzalez-Aguilar & Grasso, 2018). Thirdly, ageing particularly affects frontal white matter microstructural integrity, which declines along an anterior to posterior gradient (Head et al., 2004). Fourthly, high cortisol levels, concomitant with chronic stress, are associated with reduced prefrontal network connectivity (Arnsten, 2009). Thus, bilateral DLPFC stimulation may facilitating memory performance by spreading synaptic activation across a frontal executive neural network.

Site 2, the fronto-parietal network, is critical to a wide range of high-level cognitive tasks, including episodic and working memory and

processing speed (Marek & Dosenbach, 2018). For example, Popov et al. (2018) found that an increase in frontal midline theta power alongside decreased posterior alpha was correlated with better n-back performance. Fusco and colleagues (2018) applied a range of frequencies including 6 Hz tACS at FCz and Pz to target the medial frontal cortex in conjunction with a Flanker task. The theta stimulation alone successfully improved reaction time for congruent stimuli compared to sham. This montage was also successfully employed by Vosskuhl and colleagues (2015) who showed that the theta frequency led to reduced post-error slowing in their theta tACS working memory study.

3.2 Method

3.2.1 Participants

Twenty-four older adult (M = 69.17[21], SD = 6.23, range = 60 to 84; 16 females) and 23 young adult volunteers (M = 21.13[22], SD = 4.13, range = 18 to 34; 18 females) participated in the study. Young and older samples were comparable regarding educational level ($\chi^2(1) < 1$ and gender ($\chi^2(1) < 1$. Young adults were recruited from the University of Essex student population and older adults from the Colchester area. Participants received a payment of £30 or course credits. The study was approved by the University of Essex Faculty of Science and Engineering Ethics

[21] Median age = 68.5 years.
[22] Median age = 19 years.

Committee (Ethics ID: DW1901). All participants gave written informed consent.

All participants completed two online screening questionnaires, prior to being included: a brief medical history [Appendix 1] and an adapted version of the Transcranial Magnetic Stimulation Adult Safety Screen (TASS) (Keel et al., 2001) [Appendix 2]. In addition to neurostimulation contraindications, diagnosed psychiatric disorders; medications affecting the central nervous system; history of substance abuse; and severe trauma in the past (e.g. physical/sexual abuse) were also excluded. The older adults also completed the Mini-Mental State Examination (MMSE) (Folstein et al., 1975). The MMSE is a reliable, 30-item measure of cognitive functioning. Scores > 23 indicate the absence of cognitive impairment (Tombaugh & McIntyre, 1992); participants scoring < 26 were excluded to enhance homogeneity of the sample's cognitive function. All participants were naïve to transcranial electrical stimulation apart from one younger and one older adult participant who had taken part in a tACS and tDCS study, respectively, in the past. Neither had experienced any adverse events.

3.2.2 Design

A block-randomised, single-blind, cross-over sham-controlled, mixed factorial design was used. Each participant received active and sham stimulation conditions over two sessions, at the same time of day, at least one week apart to prevent carry-over effects of stimulation and minimise practice effects. Stimulation order was counter-balanced across

participants, within each age group, and then block-randomised. Randomisation was done using computer-generated numbers (www.random.org). Block-size was 4 to ensure even assignment of stimulation conditions. Within the counter-balanced block-randomised matrix, participants were assigned to either montage 1 or montage 2. This pilot study was not pre-registered.

3.2.3 tACS Stimulation Protocol

A DC-Stimulator Plus (Neuroconn, Germany) was used. Stimulation was applied using two 25 cm^2 conductive rubber electrodes inside saline-soaked sponges (0.9% saline solution). The sponge electrodes were placed inside an EasyCap sized according to head-circumference measurements. To ensure good skin contact, rubber bands were used over the cap as needed. Current was applied to either montage 1: F3/F4 or montage 2: FCz/Pz sites, according to the 10-20 system, at 6 Hz (theta frequency). The FCz/Pz site intended to stimulate the medial frontal cortex. The F3/F4 site intended to stimulate the DLPFC.

In the active stimulation condition, 1500 μA peak-to-peak stimulation was administered over 20 minutes (including 20 s ramp-up and ramp–down), in-phase (0°), with no DC offset. Previous studies have demonstrated that 1500 μA current intensity is well-tolerated and is sufficient to elicit an effect (Fusco et al., 2018; Jausovec & Jausovec, 2014; Pahor & Jaušovec, 2017). To ensure comfort and control for presence/absence of phosphenes, current intensity was individually assessed. Stimulation intensity began at 1500 μA peak-to-peak and reduced intensity in 100 μA decrements with a duration of 30 s per

decrement, ramped up and down, until phosphenes were absent and discomfort was reduced. While almost all participants tolerated 1500 μA well with no phosphenes reported, one young adult participant (subject 11) received a current intensity of 1400 μA due to experiencing discomfort at 1500 μA. One older adult participant (subject 20) received a current intensity of 800 μA due to phosphenes. Comfort was monitored before, during and after stimulation.

The 'study mode' setting was used for both active and sham sessions as the intention was to replicate and extend this tACS study in the future under double-blind conditions. The sham set-up with a DC-Stimulator Plus provides a pre-set sham protocol based on the time of the stimulation period along with very brief increases in amplitude throughout the stimulation period aimed to mimic sensations experienced in the active stimulation condition. Sham comprised 39 seconds of stimulation (1180s/30=39.3 s) with the same 20-second ramp-up and -down. Participants were told that they would be administered active stimulation in this study as masking may enhance blinding efficacy (Berger, 2012).

To habituate to the stimulation, participants watched a nature video for the first ~5 min of each stimulation session.

3.2.4 Measures of demographics, cumulative stress and general well-being

To measure current and general health and subjective well-being, data were collected regarding age, gender, cigarette and alcohol

consumption, exercise and so on. Given the considerable inter-individual variability in behavioural performance associated with stress and ageing (Burke et al., 2019; Fischer et al., 2021; McEwen, Gray, et al., 2015; Scholten et al., 2020), a range of self-report measures were included namely: sleep quality, resilience, anxiety and perceived stress to ascertain whether high-stress older individuals differ significantly compared to their low-stress counter-parts. Marshall et al.'s (2015) study compared low and high cumulative stress samples within each age group on the included stress and anxiety measures. They found that low and high cumulative stress groups were statistically comparable on all measures, which reinforced their conclusions that the differences they observed between low and high cumulative stress older adults were related to the cumulative effects of stress and not trait or state anxiety and not psychological distress. The present study added sleep quality and resilience to broaden the range of factors compared between the groups prior to the main analysis. Other measures such as depression were not added because consideration had to be given to participant fatigue in completing the study and to focus the research on ageing and stress.

3.2.4.1 Cumulative experienced stress: the ability to adapt to life changes

Cumulative experienced stress was measured as the accumulated effect of life changes over the course of participants' lives. Age-specific self-report questionnaires were used in line with Marshall et al.'s (2015) study. The rationale for this, given that it may affect stress-related differences, is set out in detail in their study (pp. 2142-3). The Social

Readjustment Rating Scale (SRRS) (Holmes & Rahe, 1967) comprises 43 items and was used with the older participants (60-85 years), while the Life Events Scale for Students (LESS) (Clements & Turpin, 1996) comprises 36 items and was administered to the young adult group (18-35 years) and is based on the SRRS (Linden, 1984). The SRRS items were chosen based on empirical evidence linking them to illnesses such as cardiovascular and gastrointestinal disease (Holmes & Rahe, 1967). Both scales work in the same way: each item has an associated weight or 'life change units' (LCU) ranging from 1 to 100, given by independent samples of raters, which represents the amount of adjustment required for that event. For example, in the LESS 'death of a parent' carries the highest average weight, '100', whilst 'vacation alone/with friends' was rated an average of 16. In the SRRS, 'death of a spouse' was given the highest average weighting of '100' and 'minor violations of the law' received an average weight of '11'. Both the LESS and SRRS have provided predictive validity showing a positive association between the life events score and health consequences (Clements & Turpin, 2000; Linden, 1984; Nicholson et al., 2021).

The original SRRS asks participants to indicate events experienced over a year. Marshall et al. (2015) modified the time-frame to assess the cumulative effect of stress over one's life. Hence, the instructions for both the LESS and SRRS questionnaires read: '*Please indicate which of the following events have occurred in your life. If any event occurred more than once, provide the number of times the event occurred. If the event did not occur, choose zero*.' All responses were converted to binary units and

then multiplied by their given 'weight' or life change units (LCU) and summed to give a total life change score (LCS) per participant. The LESS score range is 0 to 1849. The SRRS scores range is 0 to 1466. In both questionnaires, a higher LCS indicates a higher level of accumulated stress. Linden (1984) who designed the original LESS speculated that students tended to assign higher values to events because many events would be novel and therefore require more intense adjustment. Given the difference in ratings, (and difference in number of items) LCS scores were converted to z-scores for between-groups comparisons.

3.2.4.2 Perceived Stress

Current perceived stress was measured with the Perceived Stress Scale-10 (PSS-10) (Cohen et al., 1983; Cohen & Williamson, 1988), which "…measures how unpredictable, uncontrollable and overloaded respondents find their lives" (Cohen et al., 1988, p. 34). The PSS-10 comprises 10 questions relating to how often certain thoughts and feelings had occurred in the last month, on a 5-point Likert Scale. It has good internal consistency (Cronbach $\alpha > .70$) and re-test reliability (> .70). Response choices range from 0 ('Never') to 4 ('Very Often'). Six questions are negative (1,2,3,6,9,10) and 4 are positive (4,5,7,8). The negative items represent the subscale, 'perceived distress/helplessness'. The positive items represent the 'perceived coping/self-efficacy' subscale. The PSS index is the obtained sum total of all items (positive items are reverse-scored first). The score range is 0 to 40. A higher score indicates a greater level of perceived stress. The PSS-10 has been validated in a wide range of populations including older adults (Ezzati et al., 2014).

3.2.4.3 Sub-clinical Anxiety

State and trait anxiety was measured with the Spielberger State-Trait Anxiety Inventory (STAI) Y Form (Spielberger, 1983; Spielberger et al., 1970), which has been validated across a wide range of populations (Kvaal et al., 2005; Rossi & Pourtois, 2012; Spielberger, 1983) with good internal consistency (Cronbach α ≥ .70) and test-retest reliability (≥.40 state; .86 trait) (Gros et al., 2007; Rule & Traver, 1983; Spielberger, 1983). The state and trait anxiety scales of the STAI comprise 20 statements per scale. All 40 items are rated on a 4-point Likert scale. For the STAI-S ratings are from 1 ('Not at all') to 4 ('Very much so'). For the STAI-T ratings are from 1 ('Almost never') to 4 ('Almost always'). Score range is 20 to 80 on each scale (STAI-S, STAI-T). A higher STAI-S score indicates increased reactivity to some situations. A higher STAI-T score indicates a propensity for emotional difficulties more generally (Bieling et al., 1998; Spielberger, 1983).

3.2.4.4 Brief Resilience Scale

To assess participants' ability to recover from stressful events, the Brief Resilience Scale (BRS) (Smith et al., 2008) was administered. The BRS performs well psychometrically with good internal consistency (Cronbach α <.95 > .70) and test-retest validity (interclass correlation coefficient .69 to .62) in a range of populations (e.g. Fung, 2020; Kunzler et al., 2018) and was found to be well-suited to stress-related contexts (Windle et al., 2011). Participants self-report the extent to which they agreed with 6 statements on a scale of 1 ('Strongly Disagree') to 5 ('Strongly Agree'). Three statements were worded positively (items 1,3,5)

and 3 negatively (items 2,4,6). Scores comprised the mean value (after reverse-scoring the negative items). A higher mean BRS indicates greater resilience; BRS is negatively associated with physical symptoms and negative affect (e.g. irritability and distress) (Smith et al., 2008).

3.2.4.5 Subjective Sleep Quality

Sleep quality was measured over the last month with the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989). Sleep quality has been consistently linked to variability in cognitive performance, stress, anxiety and illness (Becker et al., 2015; Buysse et al., 1989; Dzierzewski et al., 2018; Gaultney, 2010; Hershner & Chervin, 2014; Miyata et al., 2013). Individual items yielded a Cronbach α of 0.83, indicating a high degree of internal consistency. Test-retest reliability revealed coefficient of .85 and there was good discriminant validity between clinical (depressed, disorders initiating and maintaining sleep, disorders of excessive somnolence) and control groups ($p < .001$). Only questions 5 and 6, from the PSQI were used to reduce potential response fatigue. Both questions used a 4-point rating scale (range: 0 to 3). Question 5a, in this study, provided an index for ‘sleep latency’, rated as: ‘Not during the past month’ = 0 to ‘Three or more times a week’ = 3). Question 5 b-j comprises 10 questions assessing ‘sleep disturbances’ rated as per Q5a above. Question 5 b-j were summed providing a total ‘sleep disturbances’ score per participant. This score was then categorised within one of four categories: 0; 1-9; 10-18; or 19-27, recoded as 0; 1; 2; or 3, respectively. Question 6 is a single question used to measure ‘subjective sleep quality’ rated as ‘Very good’ = 0 to ‘Very bad’ = 3. A global PSQI score was then

computed as the sum of the final values for questions 5a, b and 6, respectively (range: 0 to 9). A higher score indicated poorer subjective sleep quality. Note that these methods were adapted from the original PSQI which yields a global score of 0 – 21, based on 7 components.

3.2.5 Cognitive tasks

Participants completed computerised memory tasks, each measuring a particular aspect of memory. Both were completed during stimulation.

3.2.5.1 Picture Free Recall Task with delayed recall

The picture free recall task was used as a measure of episodic memory and, given that recall was delayed, it also provided converging evidence for working memory. Participants memorised 20 black-and-white line drawings that were presented in randomised order (Snodgrass & Vanderwart, 1980). Stimuli were presented one at a time, for 4 seconds each, preceded by a 1-second inter-stimulus interval comprising a blank white screen with a black fixation cross at the centre.

During the encoding phase, participants were instructed to say the name of each item as it appeared on the screen and remember as many as they could, because they would be asked to recall them later. Participants then completed a working memory task[23] followed by the recall phase of this task. They were told that they had two minutes to recall

[23] 7 minutes allows 1 minute to read two instruction reminder slides plus 40 x 3000 x 3 = 6 minutes for the trials themselves.

as many items as they could remember, in any order. Free recall was measured as the number of correctly recalled items (possible range: 0 – 20) and then converted into percent correct. Recalled items named differently to the expected one were marked correct if they matched items spoken during encoding (e.g. ‘letter’ instead of ‘envelope’). Participants attended two sessions and were therefore given two parallel versions of the task, counter-balanced across participants, within age groups.

3.2.5.2 N-back task

Participants completed the 2-back task (Kirchner, 1958) (see Marshall et al., 2015 for full details) as a measure of working memory. They completed the practice prior to the tACS protocol and the actual task during tACS to ensure that a uniform amount of time was spent on the task during the stimulation period. The practice comprised a 20-trial 1-back task to habituate to the task, followed by a 20-trial 2-back version to practice the task under test.

In addition to clear verbal and on-screen instructions, participants were reminded that they would receive only the 2-back experimental trials during the stimulation period with no practice.

For the 1-back task, participants responded by pressing the spacebar if the current number was the same as the one presented before. For the 2-back task, participants matched the current number to the one presented 2 positions before. Each trial comprised a randomly selected stimulus (randomised numbers 1, 2, 3 or 4) presented for 500 ms. Participants had 3000 ms (500 ms +2500 ms) to respond. There were

39 targets and 81 non-targets in total, equally distributed in a randomised manner across 3 blocks of 40 trials, split by two self-paced breaks. Reaction time and accuracy were measured.

Each participant's reaction time (RT) means and standard deviations, measured in milliseconds, were calculated per block per session for correct hits. Only RTs within 2.5 standard deviations of the mean were analysed for each participant to reduce the impact of outliers.

N-back trials are comprised of hits, misses, correct rejections and false alarms. Correct responses (hits and correct rejections) were also recorded and converted to percentages per block (hits + correct rejections/total responses). To minimise the statistical impact of response bias, d' values were calculated by block for each subject as follows: The z transformations were derived using the statistical formula NORMSINV(Hit rate) – NORMSINV(False alarm rate) in Microsoft Excel. Perfect scores were adjusted using these formulae: 1 – 1/(2n) for perfect hit rate, and 1/(2n) for zero false alarm rate, where *n* was number of total hits and false alarms, respectively (Haatveit et al., 2010; Stanislaw & Todorov, 1999). Higher d' values represent better accuracy, while a negative d' represents response confusion and/or response bias (Stanislaw & Todorov, 1999). In this sample those with a negative d' value had either a high number of misses (11/13), indicating response confusion, or false alarms (16/27), indicating response bias, therefore only blocks with positive d' values were analysed.

3.2.6 Comfort and blinding assessment

Participants were asked to rate their comfort level on visual analogue scales from 0 (“Very uncomfortable”) to 100 (“Very comfortable”) measured to 2 dp. They could also provide a description of any sensations or discomfort experienced. These were administered prior to stimulation, 30 seconds after starting the stimulation, 30 seconds prior to the end of stimulation and after the stimulation period was complete.

At the end of session 2, all participants were asked: “Do you think that you received real stimulation during your participation in this study? YES_ NO_” for session 1 then 2. For each judgement they were also asked to rate how confident they were in their judgement (1 = ‘low confidence’, 2 = ‘moderate confidence’, 3 = ‘high confidence’).

3.2.7 Procedure

Participants were informed that they would be taking part in a tACS stimulation study where they would complete a number of computerised cognitive tasks before, during and after a 20-minute tACS stimulation period. All tasks were fully explained prior to stimulation. Participants confirmed that they understood the instructions and any questions were answered. For the stimulation period, participants were given a period of habituation prior to starting the cognitive tasks, which were given following a standard order (see Fig.3.1).

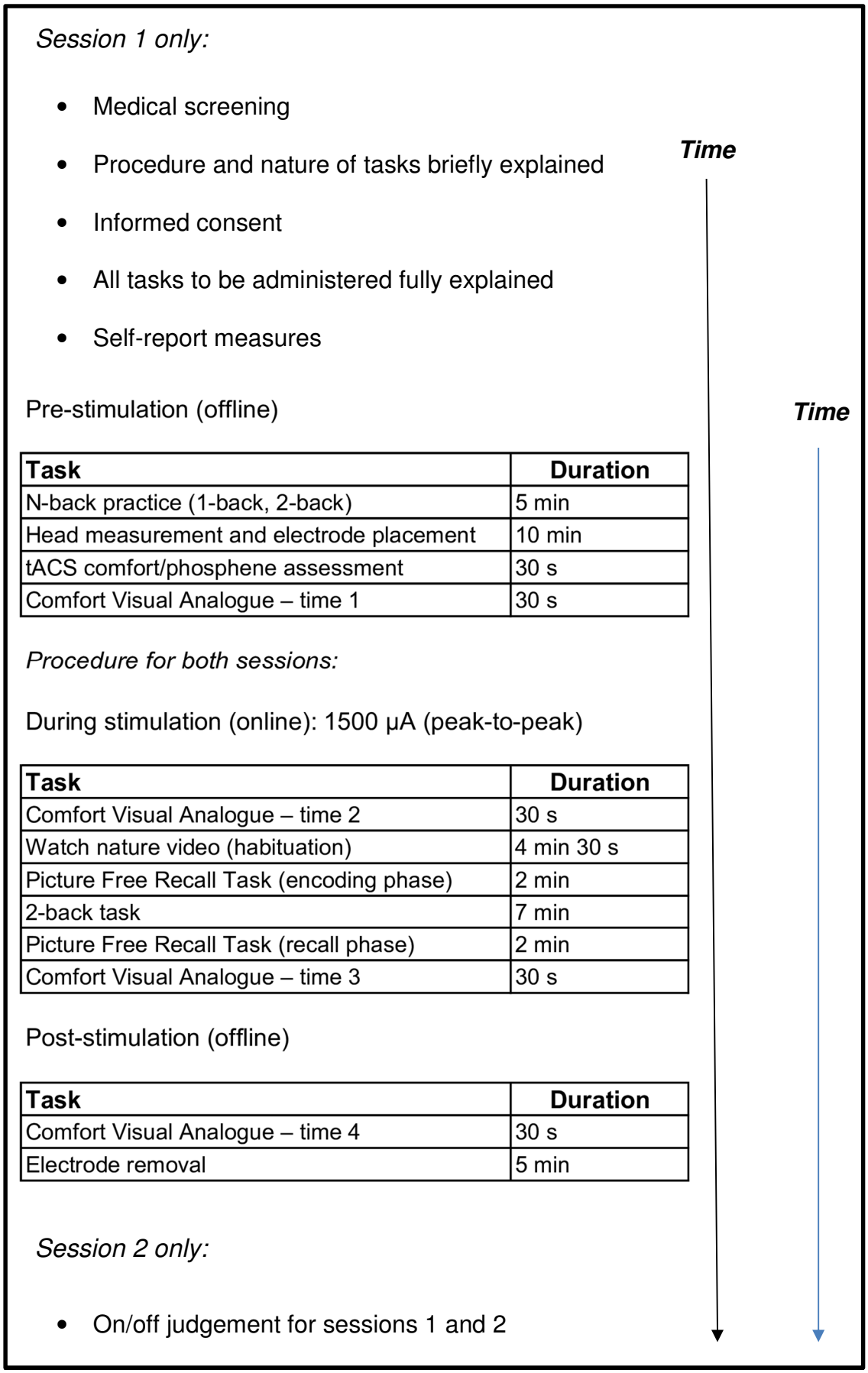

Fig. 3.1. Study Procedure for session 1 and 2

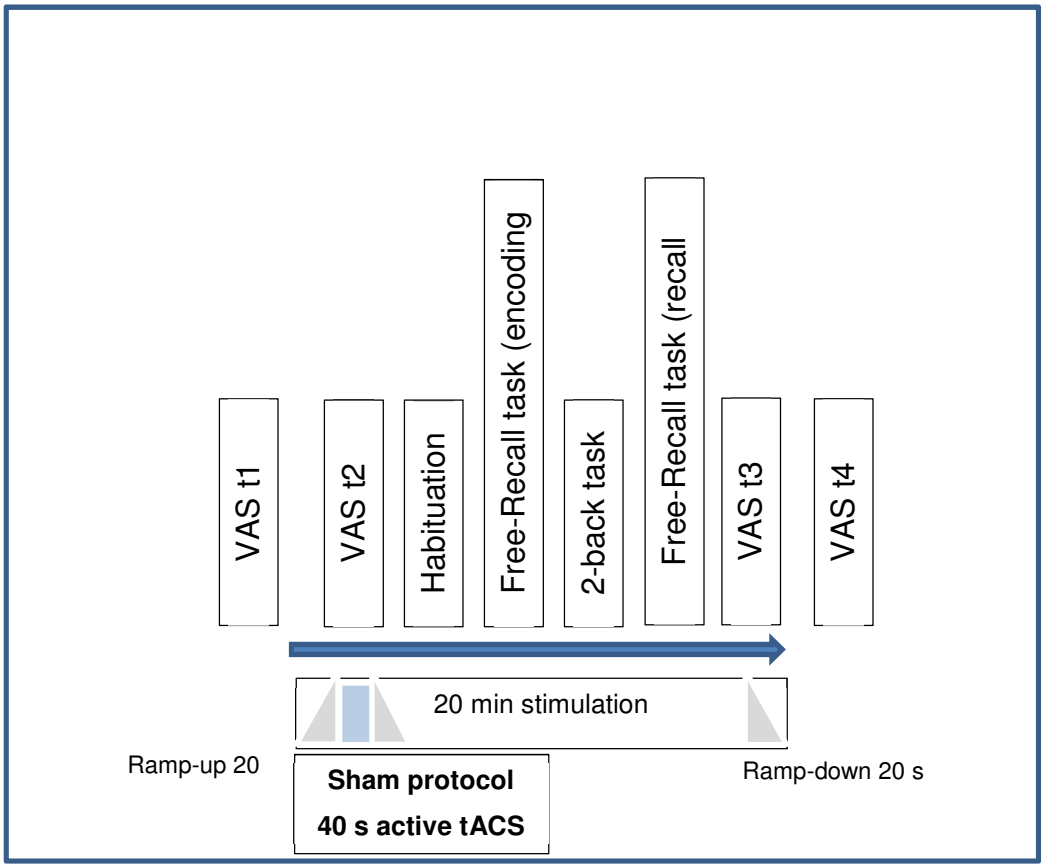

Fig. 3.2. Diagram showing time progression of stimulation with tasks

3.2.8 Statistical Analysis

Prior to any analyses, participants' cumulative stress scores were categorised into 'high stress' or 'low stress' groups based on a median split value derived from the respective age-appropriate life events questionnaires. Using a median split allowed for an ANOVA factorial design to be used to compare the impact of different levels of cumulative stress among young and older adults. Values are provided in 'Results'. Where a score fell on the median, that participant was assigned to the low stress group, which is more conservative given the hypothesis.

tACS analysis

For the tACS analysis, analysis of variance (ANOVA) and Bayes factors[24] (BF) were used to evaluate factors' effect sizes where the distributions were approximately normal. Where this was not the case, both parametric and non-parametric analyses were reported.

For the picture free-recall task, to assess the effect of stimulation condition by age group, stress group and stimulation montage, a 2 (stimulation condition: active, sham) x 2 (age group: YA, OA) x 2 (stress group: LS[25], HS[26]) x 2 (montage: F3/F4, FCz/Pz) mixed factorial ANOVA was conducted. The model excluded all 4-way interactions as these were not part of the planned investigation. The dependent variable was percent correct.

For the n-back task, to assess the effect of stimulation condition and block by age group, stress group and stimulation montage, a 2 (stimulation condition: active, sham) x 3 (block: 1,2,3) x 2 (age group: YA, OA) x 2 (stress group: LS, HS) x 2 (montage: F3/F4, FCz/Pz) mixed factorial ANOVA was conducted. The model excluded the 5-way interaction as this did not form part of the planned investigation. The model also excluded all 4-way interactions apart from one: stimulation condition*block*cumulative stress*age group. The dependent variables in

[24] In Bayesian statistics, a Bayes factor serves as an alternative to the frequentist p-value for hypothesis testing. A Bayes factor (BF) of > 3 provides evidence roughly equivalent to a p-value of 0.05 (Jeffreys, 1939) while a BF of < 1/3 favours the null. A Bayes factor of between 3 and 10 would provide "substantial" evidence in favour of active tACS having a genuine impact on behavioural outcomes and a BF of between 3 and 1/3 would suggest that the statistical evidence is inconclusive (Lee & Wagenmakers, 2013; Wetzels & Wagenmakers, 2012).

[25] LS = low cumulative stress group

[26] HS = high cumulative stress group

all working memory analyses were n-back accuracy (operationalised as percent correct and d-prime) and RT scores.

Replication analysis

Scores for sham-only session 1 participants were analysed to replicate Marshall and colleagues' (2015) hierarchical 3-step linear regression. Variables were entered in the order as set out in their report. The dependent variables were as specified in the tACS analysis above. In the first step of the hierarchical regression, participants' cumulative stress z-scores and age group (coded as -1 for young adults, 1 for older adults) were entered as predictive variables. In step 2, the interaction effect, cumulative stress z-score multiplied by age, was added. In the third step, gender, education, average weekly alcohol intake, average weekly exercise and perceived stress scores were added.

Sample size

The sample size rationale for this study was to replicate Marshall's significant interaction effect between age and cumulative stress with a sample of 60 participants. Marshall's effect size for the age x stress interaction, achieved with n=60, was 0.4.

This study is not powered for a 5-way ANOVA because it is a replication of a previous study combined with a pilot study for a potential fully powered future study.

Statistical methods

In the frequentist analyses, 95% bias-corrected accelerated (BCa) bootstrap results were provided were possible to enhance the robustness of results. Bootstrapping makes fewer assumptions about the underlying distributions and therefore results are based on a more accurate estimate of the standard error (Crawley, 2014; Wilcox & Rousselet, 2018). For ANOVA and regression analyses the original sample was resampled 2000 times (Efron & Tibshirani, 1993). For simple comparisons (e.g. follow-up t-tests), 1000 samples were taken. The alpha was set to < 0.05 for all analyses with Bonferroni corrections applied as needed.

Bayes factors were calculated alongside frequentist ANOVAs because they avoid confining the researcher to a "reject or fail-to-reject" decision-making process as with a frequentist statistical approach (Rouder et al., 2017, p. 304). Evidence is graded towards one of two competing hypotheses. In the present study these hypotheses are the null (active tACS does not affect performance) vs. the alternative hypothesis (active tACS changes performance). The grading in BFs provides evidence for data invariance or insensitivity), which avoids the statement of 'no evidence of an effect' required in frequentist statistics (Rouder et al., 2017).

Bayes factor ANOVAS in JASP 0.16.1 (The Jasp Team, 2022; Rouder et al., 2012; Rouder et al., 2017; Wetzels et al., 2012) were performed, which uses the 'BayesFactor' package (Morey & Rouder, 2010; Rouder et al., 2012; Rouder et al., 2017). The default prior model settings as computed by Rouder and colleagues (2012; 2017) were used.

Importantly, Rouder et al.'s approach prioritise consistency and scale invariance to ensure that their default priors are valid for factorial ANOVAs. Consistency is ensured through implementation of multiple g-priors where there is a separate g-parameter for each factor. This allows for orthogonality between factors' effects. Scale invariance is ensured by measuring the standardised effects. The default prior effect size is modelled on a Cauchy distribution scaled to $\frac{\sqrt{2}}{2}$ which captures small effects efficiently but has fatter tales than the normal distribution to also capture larger effects. Default priors are relatively less informative and therefore less efficient than informed priors at providing evidence of an effect but they are, consequently, also less risky and may ultimately be better at capturing the true effect size of the variables under test as indicated by recent simulation studies (Stefan et al., 2019).

In JASP, the 'matched models' option under 'Effects' was selected to exclude models with interactions and no corresponding main effects because they tend to be difficult to interpret.

JASP's default null hypothesis was used, which includes the grand mean, error and 'subject' as a random effect (i.e. the null model excludes all fixed factors).

Marshall's effect size for the age x stress interaction, achieved with n=60, was 0.4. Thus, I based my initial sample size on this estimate. Based on G-power, the estimated sample size for a 2 x 3 interaction was n=79. On this basis my initial sample size was perhaps too low. Note, however, that this was a pilot study, which was intended to be exploratory.

My preferred statistical approach was to use Bayesian statistics which is not subject to the stopping rule and therefore an *a priori* power calculation is not necessary. Thus, one may continue to increase one's sample size until the evidence presented by the data clearly supports either H1 or H0.

3.3 Results

3.3.1 Comfort and Blinding

During active stimulation, only one participant scored < 50.0 on the comfort VAS, at time 3 only. During sham, three participants scored < 50.0 at time 2 and 3. No participants asked to withdraw because of discomfort. Mild adverse effects, namely, tingling, itching and scratching sensations were reported. Comfort VAS data distributions were negatively skewed and did not lend themselves to transformation, therefore a non-parametric analysis only was performed. Median scores ranged from 83.57 to 85.53 (IQR = 24.19) for active stimulation[27] and 80.82 to 83.28 (IQR = 26.09) for sham[23]. A Wilcoxon signed rank test compared active and sham comfort per time interval VAS with no statistically significant differences (p's ≥ 0.278). Bayes Factors (BF) were either anecdotal ($BF_{time\ 3}$ = 0.42) or supported the null BFs ≤ 0.26. These results suggest that comfort was comparable during active and sham conditions at all time-intervals. For each stimulation condition, a Friedman test of differences was conducted to compare comfort reporting over the 4 time intervals. There were no statistically significant differences (p's ≥ 0.069). There was no equivalent BF test, however, Bayesian Wilcoxon signed rank test were conducted in

[27] Interquartile range (IQR) for the average of 4 VAS readings. VAS range: 0 – 100 (see 'Methods').

lieu. In the active stimulation condition, there was substantial evidence of a difference in comfort of time between time 1 and 2 (BF = 8.82) with time 1 being more comfortable (M = 86.58, SD = 13.58) than time 2 (M = 84.14, SD = 14.90). There was anecdotal evidence (BF = 0.46) between time 2 and 4 (M = 84.57, SD = 15.43) and evidence for the null for the remaining comparisons (BFs ≤ 0.32). In the sham condition, there was anecdotal evidence (BF = 0.48) comparing time 2 (M = 84.27, SD = 20.04) and 3 (M = 81.11, SD = 20.79) and time 3 and 4 (M = 83.84, SD = 19.78) (BF = 0.38). Evidence supported the null for the remaining comparisons (BFs ≤ 0.24). The difference between time 1 and 2 in the active condition is noteworthy, though, practically small. The remaining differences suggest that comfort levels were fairly consistent over time within each stimulation condition.

Participants were not able to discern the difference between stimulation conditions, as assessed by measuring proportion of successful judgements per session overall, nor by age and stress groups (p's ≥ 0.066). For both sessions, participants typically selected 'moderate' confidence for their on/off judgements.

3.3.2 Demographic details

Prior to any analyses, participants were categorised into either the low or high cumulative stress group within their age group. The median split value for young adults was 592, based on the LESS. For older adults, the value was 899, based on the SRRS. High and low stress groups were then compared. The means, standard deviations and inferential statistics for all biographical and self-report measures are presented in Table 3.1.

These indicated that, within each age group, high and low stress groups were comparable regarding age and education. Regarding gender, the YA chi square comparison reported in Table 3.1 was not statistically significant ($\chi^2(1)$ 3.663, p = 0.056) but the corresponding Bayes Factor (BF = 8.94) showed substantial evidence in favour of an association between stress group and proportions of gender. These results suggest that there were significantly more females in the high stress group than the low stress group (7 vs. 11 females). The likewise comparison for the OAs was not statistically significant and Bayesian evidence was anecdotal (p = 0.665; BF = 0.69). Health risk-taking behaviours, alcohol and cigarette consumption, were low and statistically comparable. Health enhancement behaviours, exercise and yoga were comparable. However, Table 3.1 indicates a statistically significant age group by stress group association for meditation. The finding shown was for YAs who had a significantly larger proportion of non-meditators in the low stress than high stress group (12 vs. 6) ($\chi^2(1)$ 4.554, p = 0.033). The corresponding BF shows strong evidence for this finding (BF = 16.14). The likewise comparison for OAs was not statistically significant and Bayesian evidence was anecdotal (p = 0.217; BF = 1.97). Within both age groups, all self-report measures yielded comparable results between high and low cumulative stress subsets.

Table 3.1 Descriptive statistics and p-values for demographics, lifestyle and stress responses of young and older adults by stress group.

	Young Adults		Older Adults			
	Low Stress (n=12)	High Stress (n = 11)	Low Stress (n=12)	High Stress (n=12)	p	BF
Age (years: mean (SD))	20.3 (2.5)	22 (5.4)	67.3 (5.9)	71.1 (6.2)	≥0.135[b]	≤0.88[d]
Gender (m:f)	5:7	0:11	5:7	3:9	≥0.056[c]	≤**8.94**†[e]
Education (years: mean (SD))	14.50 (0.45)	15.64 (0.47)	14.67 (0.54)	14.58 (0.68)	≥0.097[b]	≤1.09[d]
Cigarette consumption (typical daily n)	0	3	0	0	-	-
Alcohol consumption (weekly units in-take)[a]	5.73 (2.44)	1.48 (0.88)	3.65 (2.29)	2.60 (0.67)	≥0.123[b]	≤0.92[d]
Exercise (hours per week)[a]	2.83 (0.39)	2.91 (0.37)	2.42 (0.49)	3.25 (0.37)	≥0.194b[b]	≤ 0.79[d]
Yoga (yes:no)	2:10	4:7	0:12	1:11	≥0.549[c]	≤1.03[e]
Meditation (yes:no)	0:12	5:6	3:9	0:12	≥0.033*[c]	≤**16.14**†[e]
Physical disability (yes:no)	0	0	0	1	-	-
Brief Resilience Scale[a]	3.49 (0.21)	3.89 (0.25)	3.89 (0.19)	3.85 (0.19)	≥0.219[b]	≤0.84[d]
STAI - S[a]	33.83 (2.69)	33.64 (2.92)	28.42 (1.52)	29.92 (2.95)	≥0.656[b]	≤0.43[d]
STAI - T[a]	41.92 (3.17)	39.64 (2.77)	32.75 (2.65)	30.25 (2.71)	≥0.516[b]	≤0.47[d]
Perceived Stress Scale[a]	13.83 (1.51)	16.73 (1.56)	8.83 (1.66)	10.75 (1.99)	≥0.196[b]	≤0.71[d]
Sleep Quality (summed components range: 0 - 9)[a]	3.25 (0.39)	2.73 (0.36)	2.92 (0.45)	3.42 (0.42)	≥0.339[b]	≤0.54[d]

[a] Mean (SE). Standard error obtained via BCa Bootstrap with 1000 samples.

[b] Independent samples t-test (low vs high stress) were performed by age group (Mann-Whitney U test were also performed with similar outcomes).

[c] Chi-Square test for independence (low vs high stress) were performed by age group (p-value represents Yates' Continuity Correction).

[d] Bayes Factor (BF) Independent samples t-test (low vs high stress) were performed by age group (Bayesian M-W U test were also performed with similar outcomes). Robustness checks agreed with reported outputs.

[e] Bayesian contingency table analysis (stress group by age group).

* significant at < 0.05; ** significant at < 0.01.

† Bayes factor evidence favours H1 (> 3).

‡ Bayes factor evidence favours H0 (< ⅓).

3.3.3 Picture Free Recall Task

Two YA and 2 OA participants were excluded from the analysis, because they did not complete session 2. The final analysed sample comprised 21 young adults (age: M = 21.2, SD = 4.3; 16 females) and 22 older adults (age: M = 69.3, SD = 4.3; 15 females).

3.3.3.1 Practice effects analysis

A paired samples t-test demonstrated no statistically significant difference between session 1 (M = 43.72, SE = 2.12) and 2 (M = 44.77, SE = 2.25) ($p > 0.5$) performance, indicating comparable performance over time.

3.3.3.2 Memory List equivalence analysis

Prior to the main study, two picture free recall task versions were piloted with a separate sample of 10 student participants. Participants were randomly assigned to either List 1 (n = 5) or List 2 (n = 5). An independent samples t-test indicated that the two lists were comparable (t(8) -0.839, p = 0.426).

Prior to the planned analysis, a paired samples t-test was conducted to further assess list-equivalence. Participants had better accuracy in List 1 (M = 46.03, SE = 2.09) than List 2 (M = 42.68, SE = 1.95) with a mean difference of 3.4% (t(42) 2.377, p = 0.024, BCa 95% CI: 0.47, 6.05). The main analysis proceeded as planned, but the potential systematic bias this difference may have introduced was noted.

3.3.3.3 tACS stimulation analysis

Table 3.2 shows the means, standard errors and ANOVA results for active and sham performance split by age and stress groups.

There was a significant main effect of age ($F(1,38)$ 13.574, $p < 0.001$, $\eta^2_p = 0.263$). Young Adults ($M = 52.09$, $SE = 2.8$) were 38.6% more accurate than OAs ($M = 37.59$, $SE = 2.75$). There were no other statistically significant main effects nor interactions (p's ≥ 0.1).

Table 3.2 Picture Free Recall Task: Descriptive statistics for Percent Correct comparing Active vs. Sham by Age Group, Stress Group and Stimulation Montage.

	Age group		Stress Group		Stimulation Montage		Factorial ANOVA F-ratios				
	YA[a]	OA[b]	LS[c]	HS[d]	F3/F4	FCz/Pz	Active vs. Sham	YA vs. OA	LS vs. HS	Age x Stress	F3/F4 vs. FCz/Pz
Stimulation Condition	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	F	F	F	F	F
Active	53.26 (3.16)	37.84 (3.11)	54.15 (4.37)	52.37 (4.6)	44.92 (3.05)	46.19 (3.25)	0.793	13.574**	2.659	0.109	0.326
Sham	50.91 (2.88)	37.34 (2.83)	55.15 (3.97)	46.67 (4.18)	42.5 (2.77)	45.76 (2.96)					
Overall	52.09 (2.8)	37.59 (2.75)	48.05 (2.75)	41.63 (2.8)	43.71 (2.7)	45.97 (2.88)					

* $p < 0.05$; ** $p < 0.01$

[a] YA = Young Adult (n=21), [b] OA = Older Adult (n=22), [c] LS = low cumulative stress (n=22), [d] HS = high cumulative stress (n=21)

A BF ANOVA was conducted with stimulation condition as the within-subjects factor and age group and stress group as between-subjects factors. The BF ANOVA results agreed with the classic ANOVA, as there was very strong evidence for an age main effect (BF = 54.16) only. The analysis further found insensitive evidence for stress group (BF = 1.06), stimulation montage (BF = 0.51) and the interaction effect of interest: the two-way age by stress group interaction (BF = 0.57) and evidence for the null regarding stimulation condition (BF = 0.31).

In summary, the evidence presented consistently showed that picture recall accuracy did not vary because of active tACS, stress group or montage allocation. Moreover, there was no interaction between age and stress. There was an overall age effect, as expected.

3.3.3.4 Replication analysis

Table 3.3 provides all biographical descriptive and inferential statistics for the sham-only sub-sample used. There were no statistically significant differences between the low and high stress groups in either YA or OA samples.

Table 3.3 Session 1 sham-only sub-sample: Descriptive statistics and p-values for demographics, lifestyle and stress responses of young and older adults by stress group used for the replication of Marshall et al.'s (2015) study.

	Young Adults		Older Adults		
	Low Stress (n=6)	High Stress (n=5)	Low Stress (n=5)	High Stress (n=5)	p
Age (mean (SD))	20.5 (3.2)	19.8 (1.8)	72.60 (10.69)	69.40 (3.8)	≥0.556[b]
Gender (m:f)	03:03	00:05	03:02	00:05	≥0.168[c]
Education (number of years)[a]	14.50 (0.76)	15.20 (0.73)	15.20 (1.06)	14.20 (0.99)	≥0.508[d]
Alcohol consumption (weekly unit in-take)[a]	5.83 (3.02)	2.10 (1.05)	3.55 (2.88)	1.35 (0.50)	≥0.336[d]
Exercise (hours per week)[a]	3.00 (0.71)	2.60 (0.73)	1.80 (0.71)	2.40 (0.50)	≥0.521[b]
Perceived Stress Scale[a]	13.33 (1.30)	18.60 (1.91)	9.60 (2.53)	12.40 (2.62)	≥0.057[f]

[a] Mean (SE). Standard error obtained via BCa Bootstrap with 1000 samples.

[b] Independent samples t-test (low vs high stress) were performed by age group.

[c] Chi-Square test for independence (low vs high stress) were performed by age group (p-value represents Yates Continuity Correction).

[d] Independent samples t-test (low vs high stress) were performed by age group (M-W U test were also performed with similar outcomes).

[e] Mann Whitney-U comparison was statistically significant for both groups (p's = 0.004).

[f] Mann Whitney-U comparison was statistically significant for the young adult group only (p = 0.044).

[g] Univariate ANOVA based on BCa Boostrap with 2000 samples, confirmed the hierarchical regression result for between-groups high vs. low cumulative stress comparison.

* significant at $p < 0.05$ (based on BCa Bootstrap with 1000 samples).

** significant at $p < 0.01$ (based on BCa Bootstrap with 1000 samples).

A hierarchical 3-step regression analysis was performed with percent correct as dependent variable.

The first model was statistically significant ($F_{\Delta}(2,21)$ 5.591, p = 0.011), accounting for 29% of the adjusted variance[28], indicating that age and cumulative stress had a predictive effect on percent correct. Inspecting the individual contributions of each coefficient for model 1, increasing age (b = -6.22, SE = 2.87, p = 0.047, BCa 95% CI: -12.05, -0.60) and cumulative stress (b = -5.33, SE = 2.09, p = 0.009, BCa 95% CI: -8.97, -0.92) predicted poorer accuracy. Cumulative stress (b = -7.27, SE = 4.38, p = 0.036, BCa 95% CI: -13.29, -1.98) remained statistically significant in model 2. There were no statistically significant coefficients for model 3 (p's ≥ 0.150).

In summary, the replication analysis revealed that the age by cumulative stress interaction was not statistically significant. However, age and cumulative stress independently impaired performance. Specifically, increasing age and cumulative stress both predicted poorer recall performance.

3.3.4 N-Back Task

In addition to the 4 participants excluded due to attrition, a further 3 older participants were excluded who had not completed the n-back task correctly. The final analysed sample comprised 19 older (M = 69.1, SD =

[28] Variance explained was 35%, however, given the small sample size, the more conservative estimate of adjusted R^2 is more appropriate here.

6.4, range = 60 to 84; 12 females) and 21 young adults (M = 21.2, SD = 4.3, range = 19 to 34; 16 females).

For accuracy data, percent correct and d' were analysed as dependent variables. Only percent correct data are reported here to make the commentary more intuitive [d' analyses are provided in Appendix 3]. Both measures are broadly consistent.

3.3.4.1 Practice effects analysis

Table 3.4 shows means and standard errors for percent correct and reaction time by session by block. The 2 (session: 1,2) x 3 (block: 1,2,3) repeated ANOVA conducted for percent correct revealed a statistically significant main effect for session ($F(1, 39)$ 13.187, $p = 0.001$, $\eta^2_p = 0.253$), with 3.5% better accuracy, overall, in session 2 (M = 91.96, SE = 0.94) than session 1 (M = 88.73, SE = 1.24). Bonferroni-corrected comparisons for block revealed no statistically significant differences (p's > 0.9), indicating that performance was consistent over time. The session by block interaction was not statistically significant (p > 0.3), indicating consistency over time for each session. The identical ANOVA for RTs revealed no statistically significant effects.

Table 3.4 N-Back Accuracy and Reaction Time: Means and standard errors (SE) for sessions 1 and 2, by block.

	Percent Correct (N=40)			Reaction Time (N=40)		
	Block 1	*Block 2*	*Block 3*	*Block 1*	*Block 2*	*Block 3*
Session	*mean (SE)*	*mean (SE)*	*mean (SE)*	*mean (SE)*	*mean (SE)*	*mean (SE)*
Session 1	88.38 (1.35)	89.44 (1.54)	88.38 (1.34)	887.87 (45.92)	885.23 (40.85)	901.22 (37.47)
Session 2	91.63 (1.11)	91.69 (1.12)	92.56 (0.99)	844.44 (37.40)	866.57 (38.94)	845.68 (35.21)

3.3.4.2 Speed/accuracy trade-off analysis

Congruent with the above finding, Pearson correlation coefficients of percent correct hits[29] and RTs by session, split by block, revealed no statistically significant correlations (p's ≥ 0.081, BFs ≤ 0.86), suggesting that evidence of a speed/accuracy trade-off was anecdotal at best.

In summary, the accuracy results revealed a modest learning effect with no statistically detectable effect of learning on RTs and no evidence of a speed/accuracy trade-off.

3.3.4.3 tACS stimulation analysis

Table 3.5 shows the means and standard errors by stimulation condition, for block (test duration), age group, stress group and montage for percent correct and RTs. Table 3.6 provides the p-values and BFs for the comparisons of interest. The table shows a statistically significant main effect for stimulation condition (F(1,35) 6.382, p = 0.016, μ_p^2 = 0.154) with participants performing 2.8% better during active stimulation (M = 91.60, SE = 0.94) than sham (M = 89.13, SE = 1.14). Moreover, age and stress groups' main effects were statistically significant. For age group YAs (M = 92.44, SE = 1.28) were 4.71% more accurate than OAs (M = 88.28, SE = 1.34) (F(1,35) 5.043, p = 0.031, η^2_p = 0.126). For stress group LS (M = 92.43, SE = 1.28) were 4.68% more accurate than HS (M = 88.3, SE = 1.35) (F(1,35) 4.880, p = 0.034, η^2_p = 0.122). The age x stress interaction was not statistically significant, however (F(1,35) < 1). There was a

[29] Percent correct hits rather than the analysed percent correct variable (hits+correct rejections) were selected because RTs were only captured for correct hits. It would therefore be more precise to measure the trade-off between latency and accuracy of hits only.

statistically significant interaction of age group by block (F(2,70) 4.145, p = 0.020, η^2_p = 0.106). Simple main effects analyses were not statistically significant for either age groups (p's > 0.1). Post hoc independent samples t-tests comparing performance by age group for each block indicated that YA were statistically significantly more accurate than OA in the first (t(38) 2.958, p = 0.011, BCa 95% CI: 2.02, 9.98) and third (t(38) 2.375, p = 0.019, BCa 95% CI: 0.54, 8.49) blocks. Young adults outperformed OAs in block 1 (M_{YA} = 92.92, SE = 1.36 vs. M_{OA} = 86.78, SE = 1.54) and block 3 (M_{YA} = 92.68, SE = 1.16 vs. M_{OA} = 88.03, SE = 1.58). However, these findings were not significant at the Bonferroni corrected alpha (α = 0.05/5 = 0.01). Older and young participants were comparable in block 2 (p > 0.3). There were no other statistically significant main effects or interactions (p's ≥ 0.1). For the BF ANOVA analysis, BFs were derived from two separate models. One BF ANOVA was conducted with age group and stress group as between-subjects factors and then a separate BF ANOVA to evaluate montage. This was because entering 3 between-subjects variables into the model was too computationally demanding for JASP[30]. The corresponding BFs presented in Table 3.6 revealed very strong evidence for stimulation condition (BF = 45.70), which is congruent with the ANOVA result, whilst evidence of age group (BF = 2.88) and stress group (BF = 1.47) was anecdotal. These two findings do not agree with the classic ANOVA result. The age by stress interaction evidence was

[30] A 2 (stimulation condition: active, sham) x 3 (block: b1, b2, b3) x 2 (age group: YA, OA) x 2 (LS, HS) x 2 (F3/F4, FCz/Pz) would generate well over 7000 models to evaluate).

anecdotal but approaching the null (BF = 0.35). Evidence for the stimulation condition by stress (BF = 1.34) was anecdotal.

Table 3.5 N-back Task - Accuracy & RT: Descriptive statistics for Stimulation Condition by Duration (block), Age Group, Stress Group and Stimulation Montage.

	Task Duration			Age group		Stress Group		Stimulation Montage	
Stimulation Condition	Block 1	Block 2	Block 3	YA[a]	OA[b]	LS[c]	HS[d]	F3/F4[e]	FCz/Pz[f]
Percent Correct	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)
Active	90.88 (1.14)	92.68 (1.05)	91.23 (1.09)	93.77 (1.3)	89.42 (1.37)	93.01 (1.31)	90.18 (1.37)	90.08 (1.34)	93.11 (1.34)
Sham	89.14 (1.15)	88.53 (1.45)	89.72 (1.29)	91.12 (1.57)	87.15 (1.65)	91.85 (1.58)	86.41 (1.66)	88.02 (1.63)	90.24 (1.62)
Overall	90.01 (1.00)	90.60 (1.06)	90.48 (0.99)	92.44 (1.28)	88.28 (1.34)	92.43 (1.28)	88.3 (1.35)	89.05 (1.32)	91.67 (1.31)
RT	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)
Active	864.85 (37.64)	884.94 (42.97)	916.22 (39.00)	813.75 (49.64)	963.59 (52.18)	838.04 (49.88)	939.3 (52.46)	862.48 (51.28)	914.86 (51.02)
Sham	886.10 (37.11)	879.5 (34.23)	840.92 (30.56)	775.98 (43.45)	961.71 (45.68)	810.46 (43.66)	927.22 (45.92)	834.49 (44.89)	903.19 (44.66)
Overall	875.47 (33.01)	882.22 (36.02)	878.57 (31.64)	794.86 (44.11)	962.65 (46.37)	824.25 (44.32)	933.26 (46.62)	848.49 (45.57)	909.02 (45.34)

[a] YA = Young Adult (n=21), [b] OA = Older Adult (n=19), [c] LS = low cumulative stress (n=21), [d] HS = high cumulative stress (n=19), [e] F3/F4 = bifrontal montage (n=20), [f] Fcz/Pz = fronto-parietal montage (n=20).

Table 3.6 N-back Task Accuracy and RT: F-ratio p-values and Bayes Factors for all main effects and interactions of interest.

	Main Effects					Interaction Effects				
Percent Correct	active vs. sham	block 1:3	YA vs. OA	LS vs. HS	F3/F4 vs. FCz/Pz	Stimulation Condition x Block	Stimulation Condition x Age	Stimulation Condition x Stress	Stimulation Condition x Montage	Age x Stress
p-value	**0.016**	0.695	**0.031**	**0.034**	0.17	0.128	0.843	0.193	0.686	0.896
BF	**45.70**†	0.05‡	2.88	1.47	0.57	0.28‡	0.18‡	1.34	0.28‡	0.35
RT										
p-value	0.374	0.931	**0.013**	0.101	0.355	**0.045**	0.421	0.73	0.716	0.724
BF	0.29‡	0.05‡	**3.61**†	1.31	0.61	0.87	0.34	0.21‡	0.24‡	0.56

† Bayes factor evidence favours H1 (> 3)

‡ Bayes factor evidence favours H0 (< ⅓)

As Table 3.6 shows, the remaining main and interaction effects revealed evidence for the null.

Reaction time descriptive statistics, p-values and BFs are reported also in Tables 3.5 and 3.6. Table 3.5 shows that the main effect of age was statistically significant (F(1,35) 6.865, p = 0.013, η^2_p = 0.164), with YAs (M = 794.86, SE = 44.11) responding faster, overall, than OAs (M = 962.65, SE = 46.37). No other main effects were statistically significant.

The ANOVA revealed two statistically significant interaction effects: block by stress group (F(2,70) 5.818, p = 0.005, η^2_p = 0.143) and stimulation condition by block (F(2,70) 3.249, p = 0.045, η^2_p = 0.085).

The block by stress group result was evaluated with a repeated measures ANOVA for LS and HS groups, respectively. The model included a Bonferroni-adjusted alpha to control for multiple pairwise comparisons. The main effect for block was statistically significant (F(2,40) 3.822, p = 0.030, η^2_p = 0.160) for LS participants only and a post hoc pairwise t-test revealed a statistically significant difference between the first and third blocks (p = 0.024). Independent samples t-tests compared LS and HS groups for each block, revealing a statistically significant difference between groups for the first block only (t(38) -2.537, p 0.023, BCa 95% CI: -326.21, -20.75). This finding was not significant after applying multiple-comparison corrections (0.05/3=0.017). Blocks 2 and 3 comparisons revealed comparable performance between groups (p's > 0.1).

For the stimulation condition by block interaction, repeated measures simple main effects analyses revealed no statistically significant differences between block for either active or sham performance (p's > 0.1). Pairwise t-tests comparing active and sham for each block revealed a statistically significant difference for block 3 only (t(39) 2.542, p 0.015, BCa 95% CI: 17.55, 130.65), shown in Fig. 3.3. This finding was marginally significant after applying Bonferroni corrections (0.05/5 = 0.01). Active stimulation RTs (M = 911.47, SE = 37.33) were, on average, 76.05 ms slower than sham RTs (M = 835.43, SE = 31.43). Differences between active and sham performance for blocks 1 and 2 were statistically comparable (p's > 0.5). No other interactions were statistically significant.

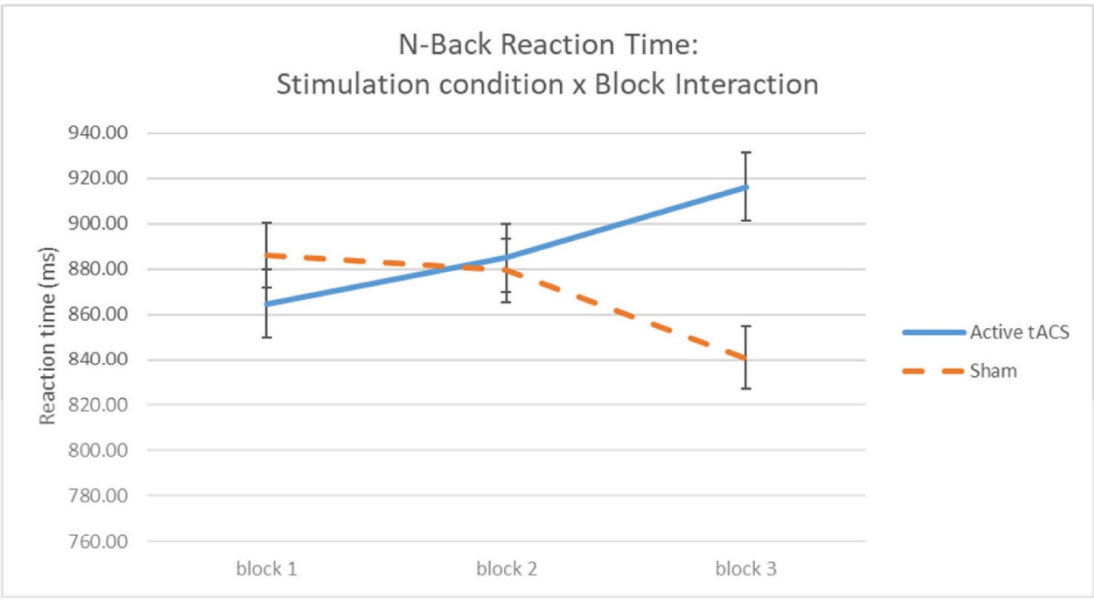

Fig. 3.3 Plot shows mean reaction times (ms) during active relative to sham stimulation by block. Error bars represent standard errors of the mean values.

The BF ANOVA with age group and stress group as between-groups factors revealed substantial evidence of age (BF = 3.61), which is

congruent with the frequentist analysis. The BF for stress (BF = 1.31) and montage (BF = 0.61) revealed insensitive evidence, while the two-way interactions of age by stress (BF = 0.56), stimulation condition by age (BF = 34) and stimulation condition by block (BF =0.87) were also insensitive. As shown in Table 3.6, the latter interaction effect's BF does not support the frequentist analysis finding. For the remaining main and interaction effects, the evidence supports the null.

3.3.4.4 Speed/accuracy trade-off analysis

Speed was measured using mean RTs (which were for correct hits only), therefore speed/accuracy trade-off compares the percentage of correct hits to these RTs. Pearson correlation coefficients for each stimulation condition by block by age, revealed that no correlations were statistically significant (p's ≥ 0.154), except for YA block 2 active condition ($r = -0.512$, $p = 0.018$, BCa 95% CI: -0.680,-0.458), which did not survive correction ($\alpha = 0.004$). These findings suggest that a speed/accuracy trade-off is unlikely to have biased the aforementioned tACS results.

In summary, relative to sham, active tACS led to improved accuracy overall but slowed RT performance in block 3. There was no statistical evidence to support an age by stress interaction. Low stress participants were more accurate than HS participants, but were comparable regarding RTs. Young adults were more accurate and faster in their RT than OAs. Finally, for both accuracy and RT, evidence supported the null for stimulation montage allocation.

3.3.4.5 Replication analysis

As with the picture free recall task, a hierarchical 3-step regression analysis was performed on sham-only session 1 data for both outcome measures: percent correct and reaction time, respectively.

The regression analysis for accuracy revealed a statistically significant result for the first model only ($F_{\Delta}(2,18)$ 5.203, p = 0.016), accounting for 30% of the adjusted variance[31]. Adding the interaction term (step 2) or life-style/biodemographic variables (step 3) did not improve the variance explained significantly. Regarding individual coefficients, cumulative stress alone showed a statistically significant predictive effect (b = -4.534, SE = 0.191, p = 0.025, BCa 95% CI: -8.49, -01.49) in model 1, suggesting that as cumulative stress increases, accuracy likely decreases. No other coefficients were statistically significant (p's > 0.2). Though, when the interaction term (model 2) and life-style and biodemographic factors (model 3) are taken into account, this finding does not hold true.

In the RT analysis, the first model (step 1) was statistically significant ($F_{\Delta}(2,18)$ 5.898, p = 0.011), accounting for 33% of the adjusted variance[32]. Adding the interaction effect and biodemographic/lifestyle variables did not improve the variance explained significantly (p's ≥ 0.149). Inspecting the individual coefficients' effects, age group had a slowing impact on RT in the first (b = 132.33, SE = 43.99, p = 0.008, BCa 95% CI: 47.24, 206.84) and second models (b = 114.54, SE = 42.18, p = 0.013, BCa 95% CI: 36.31, 182.45). No other individual coefficients were

[31] The standard R^2 value was 37%.
[32] The standard R^2 value was 40%.

statistically significant (p's ≥ 0.068). Hence, stress and ageing independently affected working memory performance but did not interact. Note that this finding does not persist when life-style/biodemographic variables are factored in. However, the sample size per condition was considerably smaller (n = 5) than Marshall's study (n = 15).

Taken together, the accuracy and RT replication analyses with sham session 1 participants revealed that stress and age were independently, negatively associated with performance; with advancing age and with greater levels of cumulative stress, accuracy and RT performance showed some preliminary evidence of deterioration. There was no evidence of an age by cumulative stress interaction.

3.4 Discussion

The present study had two broad aims, namely to ascertain whether tACS could improve memory performance and secondly to replicate a previous finding that showed an accelerating effect of ageing consequent to higher levels of cumulative life stress. The results relating to these aims are presented in terms of four main outcomes. Regarding the former aim, 1) Active theta tACS was successfully demonstrated to be able to improve accuracy in working memory, but not episodic memory, relative to sham. In addition, active stimulation had a slowing effect on 2-back reaction times towards the end of the task; 2) there was no detectible evidence of an effect of montage, indicating no advantage for either bilateral DLPFC stimulation or fronto-parietal stimulation. Relating to the latter aim, 3) No evidence was found of an accelerative effect of stress on ageing; 4) Overall, cumulative stress moderated reaction time

performance at the start of the task and, though not statistically significant, the low stress group RTs were consistently shorter on average than the high stress group's RTs. This is despite low stress individuals slowing down significantly over the duration of the task.

The finding that tACS at 6 Hz provided a 2.8% improvement in working memory performance contributes to existing evidence indicating that theta tACS has the potential to enhance working memory performance (e.g. Chander et al., 2016; Jausovec et al., 2014; Meiron & Lavidor, 2014; Pahor & Jaušovec, 2017; Polania et al., 2012; Violante et al., 2017; Wolinski et al., 2018). A similar improvement was not evident in the picture recall task, a reliable measure of episodic memory (Coynel et al., 2017). Optimal episodic memory performance is critically reliant on the ability of the hippocampus to integrate contextual information, an important component of episodic memory (Dickerson & Eichenbaum, 2010). Given that the hippocampus is a sub-cortical region acting in concert with other anatomical regions such as the PFC (Yeh & Rose, 2019), effective perturbation would rely on successfully stimulating a relevant network node, as attempted in this study. Whilst evidence is presented that the cortical regions were stimulated, given the overall improvement in accuracy during tACS, it could be argued that this was unsuccessful in sufficiently lowering the excitation threshold to depolarise hippocampal neurons. It may be that because two larger electrodes were used this delivered relatively defuse current to the cortex. Thus, the finding likely represents a general uplift of theta activity in superficial regions of the

targeted neural networks. This may also help explain why neither montage showed a particular advantage.

Unexpectedly, independent of age and stress, response latencies during active stimulation were longer relative to sham in the final block. There was no statistically significant correlation between speed and accuracy, which suggests that this result was unlikely to be due to a speed/accuracy trade-off. In contrast to this, some previous theta tACS studies found that tACS facilitated faster responding relative to sham. For example, Polanía and colleagues (2012) found, in their study using a delayed letter discrimination task, that RTs were faster consequent to tACS vs. sham. Similarly, Fusco et al. (2018) found reduced post-error slowing with no increase in error rate vs. sham in their flanker task. However, as in the present study, Holczer and colleagues (2020) found in their 6 Hz tACS study investigating cognitive conflict processing that RTs were slower for active than sham participants with no evidence of an effect on corresponding accuracy. Interestingly, and in contrast to Holczer et al., the present study revealed a benefit in accuracy, driven mainly by performance in the second block, where a 4% improvement was observed in the active vs. sham condition (compared to a 2% improvement in blocks 1 and 3). Moreover, the active and sham RT profiles were different: RTs in the active condition were 2% faster than sham in block 1, then slower than sham in blocks 2 (1% slower) and 3 (9% slower). This may be caused by processing fatigue with participants reaching maximal performance efficiency in block 2 followed by a significant drop-off in processing speed. This suggests that theta tACS can improve accuracy performance but

causes rapid fatigue. In addition, the literature indicates that theta oscillations support one's ability to maintain and recall working memory representations (Jensen & Tesche, 2002). Equally importantly alpha frequency works to stabilise visual attention (Clayton et al., 2018) therefore it's possible that targeting one frequency may have had a destabilising effect on the attentional component of working memory leading to a less predictability in effect over time.

The ANOVA results indicated that stimulation condition did not interact with age or stress groups; again this outcome seems at odds with previous research. Evidence suggests that there is an upper perceptual point of saturation, which constrains stimulation-based enhancement (Castellano et al., 2017). Indeed, research has shown that poorer performers appear to benefit more from stimulation than those at optimum (Krause et al., 2019; Reinhart & Nguyen, 2019; Tseng et al., 2012). Thus, given that most of the poorer performers in this study were older adults, greater stimulation-based improvements in the older adults relative to the stimulation-based improvements in the younger group were expected. A larger sample might provide clarity on this issue in a future study.

Contrary to expectations and contrary to existing evidence (Marshall et al., 2016; Marshall et al., 2016b; Marshall et al., 2015), these findings revealed no age by cumulative life stress interaction effect on accuracy. There is no clear reason for this suggesting that further replication would be needed. However, there was an overall age effect, which is in line with current ageing research (Drury et al., 2000; Henkel, 2008; Otani et al., 2008; Pliatsikas et al., 2019; Zarantonello et al., 2020).

Indeed, the ANOVA results showed that younger participants were consistently more accurate (and faster) than the older group across tasks. In particular, the age effect in accuracy was quite striking in the free recall task where young adults were 14.5% more accurate than older adults compared to a 4.2% advantage in the 2-back task. Coynel and colleagues (2017) conducted an fMRI study with young adults using a similar design where picture free-recall encoding and recall was intermitted by a 2-back task. They observed a positive correlation between global connectivity and accuracy in the free recall but not the 2-back task. This, they argued, implies that a decline in episodic memory performance in older adults may be attributable to the level of structural connectivity rather than grey matter volume. This evidence fits well with the age-effect finding in this study and is congruent with the aforementioned points that the hippocampus may have been beyond the reach of any stimulation benefit on recall performance. Additionally, refreshing opportunities have been shown to aid recall (Loaiza & McCabe, 2012). Such opportunities would have been maximally impaired in this study due to the long delay between encoding and recall in the protocol along with having to allocate processing resources to executing the 2-back task during that delay, compounding age-related decrements in recall ability (Kahana et al., 2002).

Regarding RT, Marshall and colleagues did not observe an age by stress interaction in reaction time performance, which is congruent with this study's findings. They observed a stress group difference in RTs for the Sternberg but not the 2-back task. In contrast, a stress-related difference in this sample's 2-back RTs was observed. High and low stress

participants, independent of age or stimulation condition, differed significantly in RTs for the first block of the n-back task. In addition, whilst not statistically significant, RT patterns over the duration of the task also differed between the groups: low stress participants were consistently faster than high stress participants. In particular, the low stress group's responses were 19% faster than those in the high stress group in the first block, which dropped off by 8% and 5% in blocks 2 and 3, respectively. In contrast, the high stress group gained momentum over time, progressively and consistently speeding up in each block (6% improvement by block 3). The low stress group's RT profile is congruent with current research. Vigilance (sustained attention) diminishes over time (Warm et al., 2008) and is influenced by a range of factors including cognitive load, motivation and time pressure (Al-Shargie et al., 2019). In addition, the task itself may also be viewed as a source of stress (Hancock & Warm, 1989). The high stress group's RT profile is harder to interpret. One possibility is that, given the greater number of stressful events, these individuals have learned to approach relatively novel situations more cautiously but also with a more adaptive coping style which allowed them to find their feet and settle into the task (Folkman & Moskowitz, 2004).

A strength of this study was the inclusion of Bayesian statistical methods, which confirmed the ANOVA results and enhanced interpretability of non-statistically significant results. A larger sample is recommended in a future study to replicate the tACS finding and elucidate the relative benefits of the respective montages employed here.

3.4.1 Conclusion

In terms of this study's aims, the same design as Marshall et al.'s study was used, however, these statistically more robust findings were incongruent with their results. Contrary to expectation, no interaction between age and cumulative stress was observed but RT performance varied with high vs. low levels of cumulative stress. This finding suggests that cumulative stress may play a role in modulating processing speed.

Secondly, the design used by Marshall et al. (2015) was extended to evaluate whether tACS stimulation can improve neural network efficiency during memory tasks in older and young adults. Accuracy in working memory was improved but not episodic memory with theta tACS. This finding implies that the theta tACS stimulation technique used was effective at activating cortical regions but not sub-cortical regions, which are crucial for episodic memory. Additionally, no variations in performance benefit between the two montages were found, possibly because diffuse rather than focused stimulation was used. Unexpectedly, relative to sham, tACS had a slowing effect on RTs.

A follow-up replication study is recommended to confirm these results regarding the effect of stress on ageing and to evaluate the practical/clinical significance of the tACS-induced improvement which was attained in working memory accuracy.

3.5 Supporting Information

Appendix 1 Medical questionnaire.

Appendix 2 Transcranial Neurostimulation Safety Questionnaire.

Appendix 3 Table with percent correct and dprime ANOVA results for the 2-back task.

A section containing all appendices can be found starting from page 395, at the end of this thesis.

Chapter 4: note to the examiners.

Chapter 4 has been submitted for publication with the following title and authors:

Do non-traumatic stressful life events and ageing negatively impact working memory performance and do they interact to further impair working memory performance?

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Chapter 4: Do non-traumatic stressful life events and ageing negatively impact working memory performance and do they interact to further impair working memory performance?

4.1 Introduction

Both stress and natural ageing independently produce allostatic load within the brain and body. Allostatic load is the accumulated wear and tear caused by the repeated attempts to adapt to change (McEwen & Stellar, 1993; Sterling & Eyer, 1988). Within the brain, allostatic load translates into structural changes over time which include retracted dendrites and spine density, spine loss (Morrison & Baxter, 2012) and reduced hippocampal neurogenesis (Ansell et al., 2012; Arnsten, 2010; Arnsten et al., 2012; Conrad, 2008, 2010; McKlveen et al., 2013; Wolf, 2003). Consequently, cognitive higher functioning can deteriorate resulting in difficulties with memory and attention. These executive functions drive decision-making and learning and, without their optimal function, quality of life suffers especially with advancing age.

Two areas of the brain that are particularly important to cognitive function and most vulnerable to the effects of allostatic load due to ageing and stress (McEwen, 2002; Shiels et al., 2019) are the hippocampus and the prefrontal cortex (PFC). For example, ageing has been linked to reduced white matter (Fotenos et al., 2005) and myelination integrity (Tsapanou et al., 2019). This deterioration starts in the neocortex (Bennett et al., 2010; Gunning-Dixon et al., 2009) along with generally lower levels of neurotransmitters (Anyanwu, 2007; and see Hedden & Gabrieli, 2004

for general review) and consequently fewer receptors, leading to less efficient neural connections (Fjell & Walhovd, 2010; Sala-Llonch et al., 2015). These structural and chemical changes then manifest in poorer behavioural outcomes. Studies of healthy ageing that compare young with older adults have shown that young adults outperform older adults on a range of tasks measuring processing speed, working memory and episodic memory in particular. For example, Vasquez and colleagues (2016) administered executive tasks for switching, inhibition, fluency, problem solving and working memory in young and older adults. They found that older adults' executive control was poorer than that of young adults as evidenced by longer, more variable reaction time, poorer accuracy and greater variability in performance across tasks within subjects; these effects were found to be linear with age with the most older participants (75-85 yrs) performing worst. Ageing is also associated with endocrine changes, such as increased diurnal cortisol levels, which have been associated with hippocampal volume atrophy. The hippocampus, PFC and amygdala contain naturally high concentrations of glucocorticoid receptors (Madalena & Lerch, 2017; McEwen, Bowles, et al., 2015; McEwen et al., 1968) which allows for enhanced malleability, facilitating dynamic and flexible responsivity to the environment. However, these receptors can be flooded by glucocorticoids in response to perceived stress. Both animal and human studies have demonstrated that perceived environmental stressors accelerate the ageing process within the brain, which can moderate how well one performs mental tasks (Goosens & Sapolsky, 2007; Lupien et al., 2009; Peters, 2002; Sapolsky, 1993). For

instance, in a population-based longitudinal study of adults aged 65 years and older (n=6207), increased levels of perceived stress predicted poorer cognitive performance and a faster rate of cognitive decline (Aggarwal et al., 2014). The ability of glucocorticoids to modulate memory function is well-documented (Lupien et al., 2007; Schwabe & Wolf, 2013) and, taken to the extreme, can be toxic to neurons causing permanent structural damage (Sapolsky et al., 1986).

To investigate the combined allostatic load of ageing and stress, previous research has focused on chronic stress. Souza-Talarico and colleagues (2011) concluded in their review that chronic stress exposure, in the context of ageing, shows similar markers to Alzheimer's Disease regarding dendritic atrophy and oxidative stress. Another approach has been to investigate the cumulative effect of life events stress. Holmes and Rahe (1967) found that the same cluster of life events typically preceded illness onset, which led them to develop and validate the Social Readjustment Rating Scale (SRRS). It was subsequently used to demonstrate predictive validity of illness onset in clinical settings (Wyler et al., 1971). Holmes and Rahe (1967) argued that these life events disrupted the status quo of day-to-day life and required a certain amount of adjustment, which they operationalised as a numerical weight ranging in value from 0 to 100 based on the averaged weightings assigned by a sample of male and female adult raters. The SRRS asks responders to indicate which of 43 events they have experienced over the last 12 months. The events comprise a variety of life stressors that can vary in severity and rely on how the individual appraises the event (e.g. 'change

to a different line of work', 'death of a close friend', 'outstanding personal achievement'). The sum of the selected (weighted) events produces a 'life events score', which can then index the burden of cumulative stress over 12 months. Marshall and colleagues extended the original SRRS by asking participants to report which events they had experienced over the course of their lives. The sum of the selected events produced a life events score representing cumulative stress experienced over their entire lives. For the young adult sample, Marshall et al. used the Life Events Stress Scale, which is based on the SRRS and was developed in the same way, using weighted scores derived from young adult raters. Using this approach in a series of cross-sectional studies, Marshall and colleagues compared young and older adults with varying levels of cumulative stress on a range of cognitive tasks paired with EEG (Marshall et al., 2016; Marshall et al., 2016b; Marshall et al., 2015). Their key finding was that older adults who reported higher levels of cumulative stress performed less well in working memory, inhibitory control and spatial discrimination tasks compared to their lower stress counterparts and the young-adult sample. Given the consistency of this finding across tasks, the deleterious impact of stress on cognition does indeed appear to be cumulative and impacts a broad spectrum of executive functions. Furthermore, the accompanying resting- and active-state EEG data revealed changes in oscillatory dynamics, such as power and synchronisation of theta (Marshall et al., 2016b) and alpha frequencies (Marshall et al., 2015), which were associated with deficits in performance and early signs of cognitive decline (Marshall & Cooper, 2017).

Capitalising on these findings, this study was conducted with the aim of replicating the interaction between age and cumulative life stress found by Marshall et al. (2015) and extending this research by developing a neurostimulation-based treatment protocol with the intention of mitigating the impact of stress and ageing on cognitive function.

The choice to replicate the working memory study was made because working memory is a reasonable proxy for higher cognitive function (Yaple & Vakhrushev, 2018). Working memory is a multi-functional system that allows one to hold in mind a small number of elements, for a few seconds, whilst simultaneously manipulating them for some goal-directed purpose such as comprehension, learning and problem-solving (Baddeley, 2000, 2012; Baddeley & Hitch, 1974). It is supported by a broad range of anatomical structures, including the PFC and medial temporal lobe (Faraco et al., 2011; Laroche et al., 2000; Nadel & Hardt, 2011; Nee et al., 2013; Owens et al., 2018; Yonelinas, 2013), which are connected via short- and long-range neural networks (Alekseichuk et al., 2017; Warren et al., 2019). These networks are highly vulnerable to the effects of ageing (Ankudowich et al., 2019; Dickerson & Eichenbaum, 2010; Janowsky et al., 1989) and stress (Goosens & Sapolsky, 2007; McEwen, 1998, 2001; Sapolsky, 1993). Indeed, working memory impairment is a central component in most neurological and neurodegenerative disorders (Baddeley et al., 1991; Gold et al., 2019; Kirova et al., 2015; Moran, 2016; Nikolin et al., 2021; Ramos et al., 2020).

Briefly, as presented in Chapter 3, a statistically significant ageing effect was found but there was no evidence of an interaction between age

and cumulative life stress. However, the initial sample size was considerably smaller than Marshall et al.'s (2015) (n=15 vs. n=60) due to the study design. Interestingly, the findings of a recent longitudinal study by Sussams and colleagues (2020) were also incongruent with the hypothesis that accelerated brain ageing follows from higher levels of cumulative stress. They found no evidence for a relationship between an objective life event measure, perceived stress, increased rate of cognitive decline or conversion to dementia by the end of their ≤ 5.5 year longitudinal study. Their older adult sample comprised control (n=68) and mild cognitive impaired (n=133) participants, assessed at baseline. They did find, however, that there was an impact of cortisol on cognitive performance, which was present at baseline.

Given the incongruence between these findings and those of Marshall et al. (2015) and given the implications for research into the impact of life events stress, further follow-up was conducted. This follow-up took the form of 3 studies: Study 1, Study 2A and Study 2B. Study 1 used the data from the first session of the study described in Chapter 3, which evaluated the impact of transcranial alternating current on working memory in older and younger participants. Study 2A and Study 2B were additional studies that extended the sample size and aimed to replicate Study 1's findings. Study 2A and Study 2B also found no evidence of an interaction effect. Study 1, Study 2A and Study 2B form a meta-analysed sample that are the subject of this chapter which aim to answer the question of whether repeated stress response activations from life events

(i.e. cumulative stress) can accelerate brain ageing, particularly in combination with normal ageing.

Note that the present study was conducted around the period of the Covid-19 pandemic, which was likely to have been particularly stressful given the level of disruption and uncertainty at the time. From this perspective, Marshall and colleagues' (2015) study was conducted well before the pandemic while the first study (Study 1) was conducted from September 2019 to March 2020, just before the first ever UK Covid-19 lockdown ("Timeline of UK Government Coronavirus Lockdowns and Restrictions," 2023). The subsequent 2 studies (Study 2A and Study 2B), which were run in sequence, followed in April 2021 just after the easing of full lockdown measures. It is reasonable to expect that stress would be greater in these three studies relative to Marshall's study and, consequently, finding an interaction between ageing and cumulative stress may arguably be more likely. However, given that these individual study results did not find evidence of any interaction these results are robust.

The aim of the present study, given the afore-mentioned inconsistencies in findings, was to assess all the data collected using an iterative Bayesian meta-analysis with Bayes factors as an alternative approach to standard null hypothesis significance testing. The advantage of the Bayes factor, defined as the ratio of the likelihood of the alternative hypothesis (H1) to the likelihood of the null hypothesis (H0), is that it provides a relative indicator of the strength (sensitivity) of evidence for two competing hypotheses irrespective of power (Dienes, 2014). Three conclusions may be drawn from a Bayes factor: evidence for the null

hypothesis (H0), evidence for the alternative hypothesis (H1) or evidence for neither hypothesis because the presented evidence is not sufficiently sensitive (Dienes, 2014). By also accounting for the potential lack of sensitivity in the data, a more comprehensive result is provided to inform future research in this field. Moreover, using a meta-analytic approach provides information about the overall size and consistency of any effect. Applied in the present case, the novel step of conducting a Bayesian meta-analysis on the effect sizes of all the individual studies (incorporating Marshall et al.'s study into the prior model) was taken to indicate whether there is a negative impact on working memory (H1) or no such effect (H0) or that there is insufficient evidence for either hypothesis for a) age, b) cumulative stress and c) the interaction of age and cumulative stress.

4.2 Method

All studies (Study 1, Study 2A and Study 2B) and their procedures were approved by the Science and Health Faculty Ethics Subcommittee 3 of the University of Essex (Ethics IDs: DW1901, ETH2021-0828). All procedures were carried out in accordance to the Declaration of Helsinki, excepting the requirement for pre-registration. All participants gave informed consent before participating. In Study 1 participants gave written informed consent. For Studies 2A and 2B, being online-only studies, participants had to select 'yes' or 'no' on-screen for each consent statement in lieu of providing written consent before being allowed to proceed to the study.

4.2.1 Participants

A total of 173 individuals took part across three replication studies. Within each study, some participants were excluded from analysis for various reasons including not completing the task properly (Appendix 1 provides participation details by study). The total number of participants excluded across the 3 studies was 17, leaving a total analysed sample of 156 individuals. In Study 1, the final analysed sample comprised 19 older (M = 69.1, SD = 6.4, range = 60 to 84; 12 females) and 21 young adults (M = 21.2, SD = 4.3, range = 19 to 34; 16 females). In Study 2A, the final sample comprised 31 young (M = 28.5, SD = 4.0, range = 21 to 34; 13 females) and 27 older participants (M = 64.1, SD = 4.0, range = 60 to 73; 18 females). In Study 2B the final sample comprised 29 young (M = 27.9, SD = 4.9, range = 18 to 35; 22 females) and 29 older participants (M = 64.7, SD = 5.0, range = 60 to 79; 17 females). Median values and interquartile ranges by age are also provided (Appendix 2). All participants were right-handed as assessed by the Edinburgh Handedness Inventory.

The first of the 3 studies, which is reported in Chapter 3, was conducted in person and the 2 remaining studies were conducted exclusively online. Participants for Study 1 were recruited from the local community in Colchester, UK and academic staff and students at the University of Essex (September 2019 to March 2020). All other participants were recruited via Prolific, an online participant recruitment platform (19th April to 1st May 2021).

Individuals with a history of substance/alcohol abuse were excluded as well as those who had: experienced a traumatic childhood event such

as sexual/physical abuse; Type 1 diabetes; a severe heart condition; any neurological (e.g. stroke, mild cognitive impairment, Parkinson's Disease, epilepsy) or psychiatric (e.g. depression, anxiety) conditions; a learning difficulty (e.g. dyslexia). Individuals taking psychoactive medications were also excluded. In Study 1, participants were screened for suitability prior to attending their first session. Participants who were eligible were then invited to attend the study. For the online Prolific studies, prospective participants were presented with these items as a list prior to signing up for the study and asked not to sign up if they met any of these specified exclusion criteria. For the online studies, the participant pool was selected based on the above criteria within the Prolific platform, where the options were available, to ensure that volunteers were suitable. Additional checks were embedded within the questionnaire aimed at retrospectively excluding participants who were unsuitable. For example, participants who consumed alcohol within 12 hours of participation were excluded, as were individuals taking prescription medications causing drowsiness. Participants were paid (£10/hr) or received student credits. All participants provided informed consent following a description of the tasks and procedures, which were included in an information sheet and again prior to each task.

4.2.2 Measures

4.2.2.1 Measures of demographics, cumulative stress and general well-being

Participants completed a range of self-report measures administered using Qualtrics software. All the same indices as Marshall

and colleagues (2015) for perceived stress and anxiety were used. In addition to these questionnaires, participants were asked to report their subjective sleep quality and resilience as part of the extension study (details of these statistical outputs are provided in Appendix 3).

Life events as a measure of cumulative stress: cumulative stress was measured as the accumulated effect of experienced stress, which accompanied adjustments, made to events/changes over the course of participants' lives as set out in Marshall et al. (2015). For example, death of a close friend, taking out a mortgage or changing schools. The Social Readjustment Rating Scale (SRRS) (Holmes & Rahe, 1967) comprises 43 items and was used for the older participants. The Life Events Scale for Students (LESS) (Clements & Turpin, 1996), comprising 36 items, was administered to the young participants.

For Study 1, the instructions given in both questionnaires were: 'Please indicate which of the following events have occurred in your life. If any event occurred more than once, provide the number of times the event occurred. If the event did not occur, choose zero.' All responses were converted to binary units and then multiplied by the given 'weight' or life change units (LCU) and summed to give a total life events score for each participant. For the LESS, scores ranged from 0 – 1849 and for the SRRS, scores ranged from 0 – 1466. For Study 2A and 2B, participants were asked to simply indicate whether each event had occurred, given that these were analysed as a binary variable in Study 1. Participants were therefore simply asked to indicate 'yes' or 'no' whether each item had occurred in their life.

Perceived Stress: Current perceived stress was measured with the Perceived Stress Scale-10 (PSS-10) (Cohen et al., 1983; Cohen & Williamson, 1988), which "…measures how unpredictable, uncontrollable and overloaded respondents find their lives." (p. 43) (Cohen et al., 1988, p. 34). The PSS-10 has good internal consistency (Cronbach α > .70) and re-test reliability (> .70). The PSS-10 comprises 10 questions relating to how often certain thoughts and feelings have occurred in the last month on a 5-point Likert Scale. Responses range from 0 ('Never') to 4 ('Very Often'). Six of the questions are negative (1,2,3,6,9,10), representing the subscale 'perceived distress/helplessness', while the positive items, represent the 'perceived coping/self-efficacy' subscale. Perceived stress is measured using the obtained sum total of all items (with positive items being reverse-scored first). Possible score range: 0 to 40 with higher scores indicating a greater level of perceived stress. The PSS-10 has been validated in a wide range of populations including older individuals (Ezzati et al., 2014).

Sub-clinical Anxiety: State and trait anxiety was measured with the Spielberger State-Trait Anxiety Inventory (STAI) Y Form (Spielberger, 1983; Spielberger et al., 1970), which has been validated across a wide range of populations (Kvaal et al., 2005; Rossi & Pourtois, 2012; Spielberger, 1983) showing good internal consistency (Cronbach α ≥ .70) and test-retest reliability (≥.40 state; .86 trait) (Gros et al., 2007; Rule & Traver, 1983; Spielberger, 1983). The state anxiety scale of the STAI comprises 20 statements focused on the intensity of feelings at the present moment. The STAI-S ratings range from 1 ('Not at all') to 4 ('Very much so'). The STAI trait scale comprises 20 statements focused on the

frequency of feelings generally. Ratings for the STAI-T range from 1 (‘Almost never’) to 4 (‘Almost always’). Possible scores range from 20 to 80 on each scale (STAI-S, STAI-T). A higher score indicates greater anxiety (Spielberger, 1983).

To assess working memory, participants completed the 2-back task (Kirchner, 1958) using the Inquisit platform (Millisecond Software) as in Marshall et al. (2015). In Study 1 and 2A, participants practiced the 1- and 2-back task followed by 2-back experimental trials. Practice sets comprised 20 trials each. In Study 2B, participants received 1-back practice trials followed by 1-back experimental trials and 2-back practice trials followed by 2-back experimental trials. In Study 1, the task was explained verbally in addition to on-screen instructions. Participants confirmed that they understood the task before starting the practice. For online participants (Study 2A and 2B), to compensate for the lack of in-person instruction, participants were shown a detailed demo with instructions and could replay this if they wished. In addition, those scoring below 65% in either 1-back or 2-back practice trials completed an additional set of 20 trials in the respective condition automatically prior to moving on to the experimental trials. The maximum number of practice trials per version was 40 (2 sets of 20). Across all studies, 10 participants repeated the practice trials.

The stimuli presented were Arabic numbers 1-4 (Helvetica) embedded within a 50% random noise grey background. For the 1-back task, participants responded by pressing the spacebar if the current item was the same as the one presented before. For the 2-back task,

participants were asked to do the same but matching the current item to the one presented 2 positions before. Each trial was preceded by a blank black screen presented for 200 ms, followed by a randomly selected stimulus slide (number 1, 2, 3 or 4) presented for 500 ms, with an inter-trial interval of 2500 ms. Participants had the full 3000 ms (500 ms +2500 ms) to respond. There were 39 targets and 81 non-targets in total, equally distributed across 3 blocks of 40 trials. Thus, 13 targets and 27 non-targets per block. The blocks were split by two self-paced breaks. There were two measurement indices: reaction time and accuracy.

N-back trials comprise hits, misses, correct rejections and false alarms. Percent correct (hits + correct rejections/120 trials *100) and d-prime values for accuracy and reaction time in milliseconds for correct hits were measured. To minimise the statistical impact of response bias, d' values were calculated by block for each subject as follows: The z transformations were derived using the statistical formula NORMSINV(Hit rate) – NORMSINV(False alarm rate) in Microsoft Excel. Perfect scores were adjusted using these formulae: 1 – 1/(2n) for perfect hit rate, and 1/(2n) for zero false alarm rate, where n was number of total hits and false alarms, respectively (Haatveit et al., 2010; Stanislaw & Todorov, 1999). Higher d' values represent better accuracy, while a negative d' represents response confusion and/or response bias (Stanislaw & Todorov, 1999). This was true for this sample, as those with a negative d' value had either a high number of misses (11/13 trials) indicating response confusion or false alarms (16/27 trials) indicating response bias. Only blocks with positive d' values were, therefore, analysed. Note that only percent correct

values for accuracy were reported, which were comparable to d-prime values for all analyses. Frequentist statistical outcomes by study for d-prime and percent correct values are given in Supporting Information (Appendix 4).

Each participant's reaction time (RT) means and standard deviations were calculated per block for hits. Only RTs within 2.5 standard deviations of the mean were analysed for each participant (details given in Results section) to reduce statistical bias.

4.2.3 Design and Statistical Analysis

Prior to any analyses, participants' cumulative stress scores were categorised into 'high' or 'low' cumulative stress groups based on a median split value derived from the respective age-specific experienced stress questionnaires. While this approach is controversial, it is a valid choice provided that the independent variables are uncorrelated (Iacobucci et al., 2014, 2015). Moreover, this method allowed the evaluation of performance differences between high and low levels of cumulative stress with two different life events scales and the intended analyses to be conducted. The 'low stress' group denoted those who had experienced a lower level of cumulative stress over the course of their lives thus far whilst the 'high stress' group denoted those who had experienced a higher level of cumulative stress over their lives thus far. In Study 1, the median split value for young adults, based on the LESS, was 592 (IQR: 492 to 639.5). For older adults, the value was 913 (IQR: 753 to 1009), based on the SRRS. In Study 2A, the median split LESS value for

young adults was 577 (IQR: 357 to 691) and for the older group, the SRRS value was 738 (IQR: 632 – 845). In Study 2B, the median split values were 516 (IQR: 348 - 692) and 766 (IQR: 684.5 to 849.5), respectively. Any LESS or SRRS values that fell on the median were allocated to the low stress group, the more conservative approach given the hypothesis. A supplemental table is also provided with each participant's total cumulative stress score for each study, which shows that participants varied in cumulative stress within and between age groups (Appendix 5).

Prior to the planned analysis, the N-back data were assessed for evidence of a speed-accuracy trade-off for hits using Pearson Product Moment Correlation Coefficients (Bruyer & Brysbaert, 2011). The variables used were percent correct hits and RTs therefore a speed-accuracy trade-off would be indicated by a positive correlation. Where a speed-accuracy trade-off was found, percent correct statistically significant results are still reported but conclusions in these cases are based on RT data only as RT data provides a relatively more sensitive representation of any evidence of effect caused by ageing and/or cumulative stress.

Bayes factors (BFs) were calculated by study, based on mean differences for percent correct and reaction time. These statistics were computed for the main effects of age group, stress level, their interaction and the effects of stress level within each age group. For the interaction effects analysis only mean differences were calculated for the harmonic rather than arithmetic mean, given uneven groups.

Following the method provided by Dienes and colleagues (2018) using Dienes' calculator http://www.lifesci.sussex.ac.uk/home/Zoltan_Dienes/inference/bayes_normalposterior.swf found at http://www.lifesci.sussex.ac.uk/home/Zoltan_Dienes/inference/Bayes.htm (web link, p. 118:) (2008), posterior means and standard deviations were used to meta-analyse the strength of the overall evidence for an effect for the three studies. This method is suitable where the series of studies to be meta-analysed are based on the same hypothesis with the same dependent variable (Dienes, 2008), as in the present report. A BF was also calculated for each iteration and for Marshall et al.'s (2015) reported effect sizes. For the prior model, a normal distribution was assumed given that most values were expected to be within 2 standard deviations of the mean.

The iterative meta-analysis started with Marshall et al.'s study (2015). The steps are set out in Table 4.1, which were as follows: in the first step, the mean difference and the standard error of the mean difference (SEM) for Marshall et al.'s study (2015) served as the prior for Study 1 while the likelihood comprised the mean difference and SEM for Study 1. In the second step, the posterior mean and standard deviation calculated from the preceding step served as the prior for Study 2A and the likelihood comprised the mean difference and SEM for Study 2A. In the third and final step, the resulting posterior mean and standard deviation from step 2 served as the prior for Study 2B. Study 2B's mean

difference and SEM was the likelihood which provided a posterior mean and standard deviation which provided the effect size for each effect.

Table 4.1 Order of steps for study effect sizes entered into the iterative Bayesian meta-analysis.

Iterations	prior values	likelihood values	posterior values
Step 1	Marshall et al. (2015) mean difference (SEM)[a]	Study 1 mean difference (SEM)	Marshall et al. (2015)*Study 1 mean, SD, 95% credible interval[c]
Step 2	Study 1 posterior mean and SD[b]	Study 2A mean difference (SEM)	Study 1*Study 2A mean, SD, 95% credible interval
Step 3	Study 2A posterior mean and SD	Study 2B mean difference (SEM)	Study 2A*Study 2B mean, SD, 95% credible interval

[a] SEM = standard error of the mean.

[b] SD = standard deviation.

[c] Upper and Lower values representing the range of credible effect size values. If this range includes zero, H0 is more likely.

To calculate the BF, Dienes' BF calculator (https://harry-tattan-birch.shinyapps.io/bayes-factor-calculator/) was used. The steps for BF calculations are set out in Table 4.2. To calculate a BF for Marshall et al.'s (2015) effect size an estimated expected effect size was used as prior for each of the 3 effects under test. This approach was used because aside from Marshall et al.'s work, no previous research has investigated the effects of cumulative life events stress nor how such effects interact with age in this way. Bayesian inference, unlike frequentist methods, views probability as subjective (Kruschke, 2015; Russo, 2020). Thus, one may start with a subjective (prior) belief about the credibility of probabilities, which can be mathematically described as a distribution with a probable point estimate. Bayesian inference then incrementally reallocates the credibility of probabilities (Kruschke, 2015) when new data are introduced. Thus, Bayesian inference provides a method to reach an increasingly more likely outcome (Stone, 2016).

Table 4.2 Bayes Factor input variables.

Iterations	prior value	likelihood values	BF
Step 0	estimated effect size[a]	Marshall et al. (2015) mean difference (SEM)[b]	Marshall et al., 2015
Step 1	Marshall et al. (2015) mean difference (SEM)	Study 1 mean difference (SEM)	Study 1
Step 2	Study 1 posterior 0.5*upper credible interval[c]	Study 2A mean difference (SEM)	Study 2A
Step 3	Study 2A posterior 0.5*upper credible interval	Study 2B mean difference (SEM)	Study 2B

[a] Based on a reasonable expected maximum difference between groups.

[b] SEM = standard error of the mean

[c] Upper values of the 95% credible interval represent the maximum likely effect size. Fifty percent of this value represents 1 standard deviation and serves as the prior.

To calculate the BFs for each step of the meta-analysis 0.5 of the upper credible interval of the posterior from the previous step was used as prior, where possible. As stated in Table 4.2, the upper credible interval of the posterior represents the maximum likely effect size and 0.5 represents

one standard deviation. For Step 1's BF Marshall et al.'s effect size was used as prior because there was no posterior. The BFs for Steps 2 and 3 were calculated with 0.5 of the upper credible interval of the previous step, as shown in Table 4.2. The likelihood values were the same as for the meta-analysis.

The final row in Tables 4.3 to 4.5 (see Results section) provides the meta-analytically derived evidence of effect of age group, stress level and within-age groups' performance differences due to high vs. low cumulative stress levels. Wetzels and Wagenmaker's (2012) classification indicated that BF values ranging from 3 to 10 represent "substantial evidence for H1", values ranging from 10 to 30 represent "strong evidence for H1" and values ranging from 30 to 100 represent "very strong evidence for H1". Values in the range of <3 to > ⅓ are regarded as "anecdotal (insensitive) evidence for H1" with '1' representing no evidence in either direction. Values ranging from ⅓ and smaller provide evidence of increasing strength for the null. For interest, a standard meta-analysis is provided for the 3 replications studies in the Supporting Information (Appendix 6). Robustness checks were calculated alongside the final BF. Briefly, a robust BF is indicated by the extent to which different prior distribution scale factors produce a consistent BF. Scale factors applied to test the robustness of the BF ranged from 3 (which represents the t-distribution at 2 degrees of freedom) to 7 (half-Cauchy distribution, which is equivalent to the t-distribution with 1 degree of freedom) (Dienes, 2015, 2019).

Note that sleep quality and resilience were not included in the analysis because these measures form part of a wider extension project, which includes the present replication of Marshall et al.'s (2015) study who did not test these variables in their work.

4.2.4 Procedure

In all studies, participants were told that they would be taking part in a study comprising questionnaires and one or more cognitive tasks, depending on the study, and provided with a comprehensive explanation prior to each measure. Fig. 4.1 provides the basic structure (Appendix 7 provides the full procedure and set of tasks for each study).

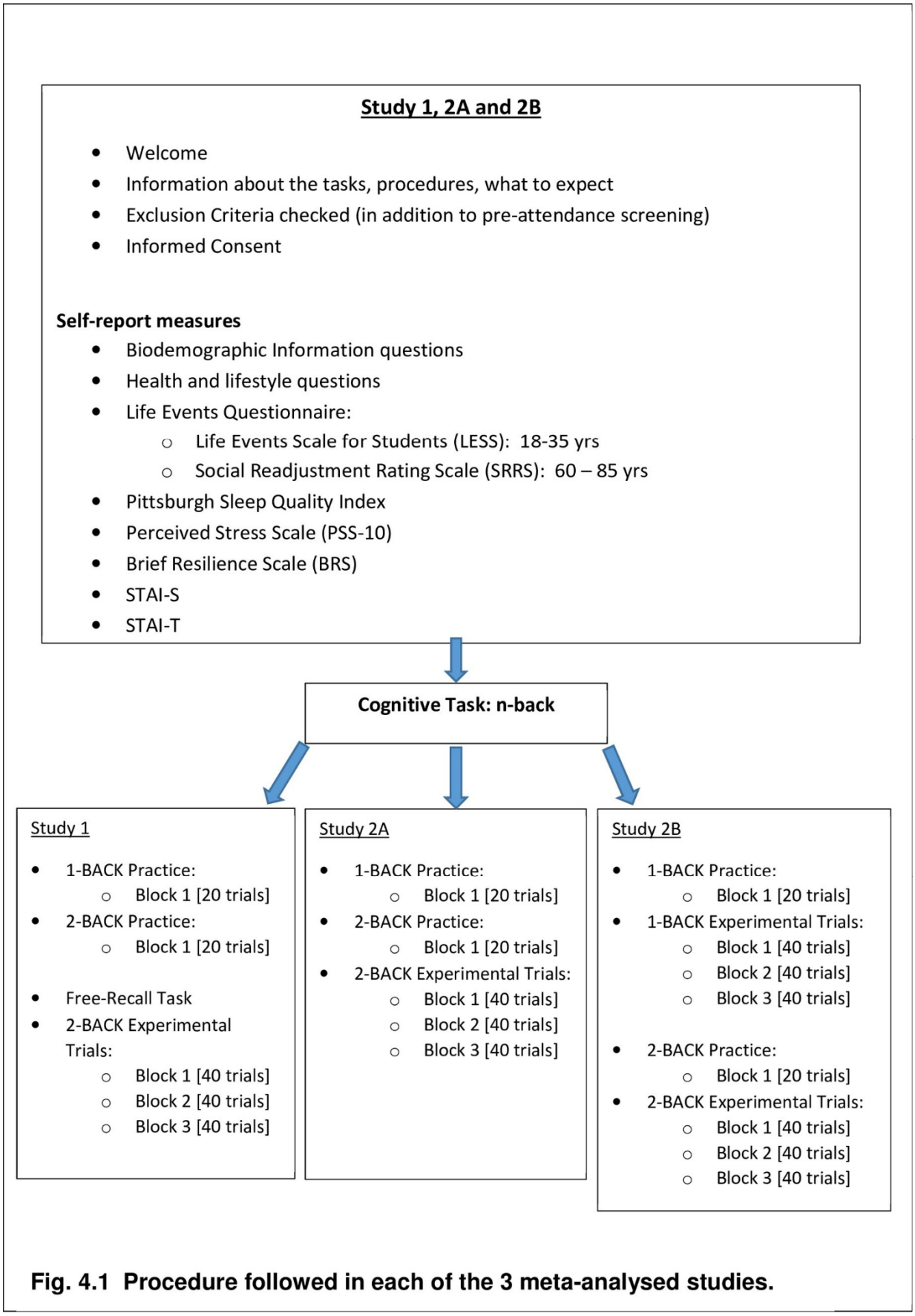

Fig. 4.1 Procedure followed in each of the 3 meta-analysed studies.

4.3 Results

4.3.1 Biodemographical and self-reported anxiety, stress and resilience outcomes

Tables 4.3a to c show biodemographic variables by study. For Study 2A, Table 4.3b shows a statistically significant difference in STAI-T scores in the older group with low stress (LS) older adults scoring on average -10.90 (SE = 4.15) points lower than high stress (HS) older adults: (t(18) -2.654, p = 0.025, bias-corrected and accelerated (BCa) 95% CI: -19.62 to -2.36. There were no other statistically significant differences. For Study 2B, Table 4.3c shows a statistically significant difference for exercise among older adults only, with a mean difference of -1.44 hrs (SE = 0.55) indicating that the HS group spent more time exercising on average than the LS group: t(27) -2.530, p = 0.012, BCa 95% CI: -2.45 to -0.29. No other comparisons were statistically significant. Table 4.3d provides means and standard errors by age group by stress group for each study and shows no overlap between high and low stress groups within age group for any studies.

Table 4.3a Descriptive statistics and p-values for biodemographics, lifestyle and self-reported stress and anxiety by age group, by stress group for Study 1.

	Young Adults			Older Adults		
Study 1 (n=40)	Low Stress (n=11)	High Stress (n=10)	p	Low Stress (n=10)	High Stress (n=9)	p
Age (years: mean (SD))	20.55 (2.54)	22.00 (5.66)	0.449[b]	69.30 (8.31)	68.89 (3.92)	0.894[b]
Gender (m:f)	05:06	00:10	0.054[d]	06:04	01:08	0.084[d]
Education (years: mean (SD))	14.55 (1.63)	15.50 (1.58)	0.191[b]	14.80 (2.04)	14.56 (2.65)	0.824[b]
Cigarette consumption (typical daily n)	0	3	-	0	0	-
Alcohol consumption (weekly units in-take)[a]	6.20 (2.54)	1.63 (0.88)	0.125[c]	4.48 (2.57)	2.56 (0.73)	0.509[c]
Exercise (hours per week)[a]	2.91 (0.44)	2.90 (0.44)	0.988[b]	2.20 (0.54)	3.11 (0.49)	0.237[b]
Yoga (yes:no)	02:09	03:07	0.903[d]	00:10	01:08	0.212[d]
Meditation (yes:no)	00:11	04:06	0.076[d]	02:08	00:09	0.503[d]
Physical disability (yes:no)	0	0	-	0	1	-
STAI - S[a]	32.45 (2.49)	34.30 (3.16)	0.650[b]	29.80 (2.25)	29.56 (3.51)	0.954[c]
STAI - T[a]	40.82 (3.19)	39.80 (3.06)	0.823[b]	31.80 (3.14)	32.89 (3.12)	0.814[b]
Perceived Stress Scale[a]	13.00 (1.33)	16.90 (1.69)	0.078[b]	9.00 (1.81)	12.22 (2.37)	0.298[b]

[a] Mean (SE). Standard error obtained via BCa Bootstrap with 1000 samples.

[b] p-value (two-tailed) calculated using an independent samples t-test.

[c] p-value (two-tailed) calculated using Welch's t-test.

[d] p-value (two-tailed) calculated using a chi-square test for independence (with Yates' Correction).

Table 4.3b Descriptive statistics and p-values for biodemographics, lifestyle, self-reported stress and anxiety comparisons by age group, by stress group for Study 2A.

		Young Adults			Older Adults		
Study 2A (n=58)		Low Stress (n=16)	High Stress (n=15)	p	Low Stress (n=14)	High Stress (n=13)	p
	Age (years: mean (SD))	27.44 (4.07)	29.67 (3.62)	0.119[b]	62.86 (2.88)	65.46 (4.59)	0.096[c]
	Gender (m:f)	09:07	09:06	0.833[d]	07:07	02:11	0.134[e]
	Education (years: mean (SD))	17.25 (2.05)	16.00 (2.07)	0.102[b]	15.93 (2.70)	16.46 (2.03)	0.570[b]
	Cigarette consumption (typical daily n)[a]	0.00 (0.00)	1.67 (1.11)	0.173[c]	2.64 (1.37)	1.23 (1.11)	0.464[b]
	Alcohol consumption (weekly units in-take)[a]	1.45 (0.48)	1.95 (0.92)	0.622[b]	4.63 (1.86)	1.25 (0.62)	0.099[c]
	Exercise (hours per week)[a]	3.56 (0.39)	3.67 (0.29)	0.835[b]	3.79 (0.34)	3.62 (0.40)	0.756[b]
	Yoga (yes:no)	02:14	01:14	1[e]	00:14	00:13	-
	Meditation (yes:no)	00:16	00:15	-	01:13	00:13	-
	Physical disability (yes:no)	00:16	00:15	-	01:13	01:12	1[e]
	STAI - S[a]	33.75 (2.20)	35.87 (2.89)	0.567[b]	27.00 (1.82)	34.85 (3.82)	0.084[c]
	STAI - T[a]	41.13 (2.34)	39.20 (3.24)	0.635[b]	32.64 (1.82)	43.54 (3.68)	0.025[c]
	Perceived Stress Scale (PSS-10)[a]	14.31 (1.31)	14.60 (2.02)	0.918[b]	11.36 (1.78)	17.00 (2.21)	0.064[b]

[a] Mean (SE). Standard error obtained via BCa Bootstrap with 1000 samples.

[b] p-value (two-tailed) calculated using an independent samples t-test.

[c] p-value (two-tailed) calculated using Welch's t-test.

[d] p-value (two-tailed) calculated using a chi-square test for independence.

[e] p-value (two-tailed) calculated using a chi-square test for independence (with Yates' Correction).

Table 4.3c Descriptive statistics and p-values for biodemographics, lifestyle, self-reported stress and anxiety comparisons by age group, by stress group for Study 2B.

		Young Adults			Older Adults		
Study 2B (n=58)		Low Stress (n=15)	High Stress (n=14)	p	Low Stress (n=15)	High Stress (n=14)	p
	Age (years: mean (SD))	27.33 (5.45)	28.50 (4.40)	0.533[b]	63.53 (3.85)	65.93 (5.81)	0.199[b]
	Gender (m:f)	05:10	02:12	0.445[e]	06:09	06:08	0.876[d]
	Education (years: mean (SD))	16.13 (2.26)	16.00 (1.96)	0.867[b]	15.13 (2.03)	15.64 (2.76)	0.574[b]
	Cigarette consumption (typical daily n)[a]	1.40 (1.03)	0.07 (0.07)	0.227[c]	1.00 (0.97)	0.00 (0)	0.334[c]
	Alcohol consumption (weekly units in-take)[a]	1.28 (0.99)	1.82 (0.76)	0.674[b]	4.75 (1.56)	10.38 (2.51)	0.077[c]
	Exercise (hours per week)[a]	2.27 (0.39)	2.50 (0.32)	0.656[b]	2.20 (0.37)	3.64 (0.42)	0.012[c]
	Yoga (yes:no)	01:14	01:13	1[e]	00:15	01:13	0.972[e]
	Meditation (yes:no)	03:12	02:12	1[e]	00:15	02:12	0.433[e]
	Physical disability (yes:no)	00:15	01:13	0.972[e]	01:14	02:12	0.950[e]
	STAI - S[a]	35.80 (3.77)	38.64 (2.35)	0.532[b]	25.40 (1.06)	26.21 (1.68)	0.692[b]
	STAI - T[a]	44.53 (2.90)	45.00 (2.91)	0.923[b]	30.93 (1.71)	33.14 (2.36)	0.466[b]
	Perceived Stress Scale (PSS-10)[a]	15.20 (1.89)	17.29 (1.65)	0.420[b]	9.33 (1.16)	8.86 (1.43)	0.805[b]

[a] Mean (SE). Standard ϵ

[b] p-value (two-tailed) calculated using an independent samples t-test.

[c] p-value (two-tailed) calculated using Welch's t-test.

[d] p-value (two-tailed) calculated using a chi-square test for independence.

[e] p-value (two-tailed) calculated using a chi-square test for independence (with Yates' Correction).

Table 4.3d. Means and standard errors of total cumulative stress scores for each study by age group by stress group.

	Young Adults		Older Adults	
	Low Stress	High Stress	Low Stress	High Stress
Study	mean (SE)	mean (SE)	mean (SE)	mean (SE)
Study 1 (n=40)	460.36 (44.02)	691.70 (31.88)	760.34 (40.79)	993.11 (20.09)
Study 2A (n=58)	391.56 (31.95)	703.53 (25.67)	602.36 (38.49)	846.46 (20.91)
Study 2B (n=58)	358.80 (19.49)	706.14 (33.65)	643.33 (32.78)	860.86 (17.69)

Young adults completed the Life Events Scale for Students (LESS). Score range: 0 – 1849.

Older adults completed the Social Readjustment Rating Scale (SRRS). Score range: 0 – 1466.

4.3.2 N-Back Task

Data removed following RT trimming (trials > 2.5 SD) resulted in a loss of ≤ 3% trials per study. Means and standard deviations for percent correct and reaction time were calculated as averaged performance over 120 trials. The correlation coefficient for RT hits and percent correct hits was consistently negative and not statistically significant (p's ≥ 0.179) for all studies indicating that a speed-accuracy trade-off would be unlikely to bias the planned statistical analyses.

A median split was used because age group and stress group were not significantly correlated (p > .9). Given that the median split between high and low stress groups by study led to an overlap in classification of high and low stress between the studies, a single median split was also derived by grouping all studies' observations. For the LESS the single median split was 577 and for the SRRS, 786. For ease of reference, a table with all the high vs. low median split values is provided in Supporting Information (Appendix 8). Using the single median split, the same statistical procedures were conducted as for the planned analyses, described in 'Design and Statistical Analysis', which used the median split

derived by study. The outcomes for both sets of analyses were found to be comparable, therefore the results were reported for the planned analysis here and results were provided for the identical analysis using the single median split in Supporting Information (Appendix 9).

Table 4.4 presents the meta-analysis showing the effect of age on accuracy and reaction time performance. An appendix provides a set of tables with all data entered into each analysis in the Supporting Information (Appendix 10). Table 4.4 shows that as each study's data was added and the sample size increased, the effect size decreased. The final credible interval ranged between .4% and 4.3%. Had there been robust evidence to show that young adults outperformed older adults, the effect size and corresponding BFs would have increased with each newly added dataset. Inspecting the BFs in the table, Marshall et al.'s reported effect size was supported by strong evidence (BF = 15.99) for a difference in accuracy between young and older adults with young adults out-performing older adults. However, with the additional data, BFs decreased, providing anecdotal evidence only (BFs ≤ 1.59). A likewise outcome was evident for reaction time: Marshall et al.'s reported result of a difference in response latencies between older and young adults was supported by substantial evidence (BF = 3.77) indicating that young adults were significantly faster than older adults. However, as with accuracy, each dataset added incrementally lead to a smaller rather than larger effect size. The final credible interval ranged from -186.5 ms to -63.42 ms with a corresponding BF supported by anecdotal evidence (BF = 1.33).

Table 4.4 Age group percent correct and RT mean differences, standard errors, credible intervals and Bayes factors for all studies.

		Young vs. Older Adults				
		Prior	***Likelihood***	***Posterior***		
Accuracy (% correct)	*N: Incremental Increase*	*mean Difference (SE)*	*mean Difference (SE)*	*mean Difference (SE)*	95% credible interval[a]	BF
Marshall et al. (N=60)	60	5.00[a]	4.83 (1.64)			15.99[†]
Study 1 (N=40)	100	4.83 (1.64)	4.35 (2.42)	4.68 (1.36)	2.02, 7.34	1.59
Study 2A (N=58)	158	4.68 (1.36)	1.29 (2.12)	3.70 (1.14)	1.46, 5.94	0.58
Study 2B (N=58)	216	3.70 (1.14)	-1.98 (2.06)	2.37 (1.00)	0.41, 4.33	0.78
Reaction Time (ms)	*N: Incremental Increase*	*mean Difference (SE)*	*mean Difference (SE)*	*mean Difference (SE)*	95% credible interval[a]	BF
Marshall et al. (N=46)	46	50.00[b]	-441.28 (109.07)			3.77[†]
Study 1 (N=40)	86	-241.43 (59.76)	-358.56, -124.30	-241.43 (59.76)	-358.56, -124.30	2.64
Study 2A (N=58)	144	-165.46 (42.35)	-248.47, -82.44	-165.46 (42.35)	-248.47, -82.44	1.22
Study 2B (N=58)	202	-124.96 (31.40)	-186.50, -63.42	-124.96 (31.40)	-186.50, -63.42	1.33

[a] In the first iteration, an estimated maximum performance difference of 10% was assumed. Half of this value (5%) was used as a vague prior. This prior was used to calculate the BF for Marshall et al. (2015)'s result.

[b] In the first iteration, an estimated maximum performance difference of 100 ms was assumed. Half of this value (50 ms) was used as a vague prior. This prior was used to calculate the BF for Marshall et al. (2015)'s result.

[†] evidence favours H1 (BF > 3).

[‡] evidence favours H0 (BF < ⅓).

Table 4.5 presents the results for the overall comparison of low vs. high cumulative life stress groups for accuracy and reaction time. Marshall et al.'s reported result provided anecdotal evidence for accuracy (BF = 2.54) and reaction time (BF = 0.96) indicating that it is unclear whether or not high levels of cumulative life stress affect performance outcomes. The table shows that by adding new data and additional power this outcome remained consistently within the anecdotal range (BFs ≤ 1.27). For accuracy, the final credible interval for accuracy ranged between 0.9% and 4.8%. For reaction time, the range was -70.7 ms to 57.3 ms.

Table 4.5 Cumulative stress percent correct and RT mean differences, standard errors, credible intervals and Bayes factors for all studies.

		Low Stress vs. High Stress				
		Prior	***Likelihood***	***Posterior***		
Accuracy (% correct)	*N: Incremental Increase*	*mean Difference (SE)*	*mean Difference (SE)*	*mean Difference (SE)*	95% credible interval[a]	BF
Marshall et al. (N=60)	60	5.00[a]	3.50 (1.62)			2.54
Study 1 (N=40)	100	3.50 (1.62)	5.77 (2.35)	4.23 (1.33)	1.62, 6.85	2.36
Study 2A (N=58)	158	4.23 (1.33)	3.79 (2.2)	4.11 (1.14)	1.88, 6.35	1.55
Study 2B (N=58)	216	4.11 (1.14)	-1.18 (2.07)	2.88 (1.00)	0.93, 4.84	0.61
Reaction Time (ms)		*mean Difference (SE)*	*mean Difference (SE)*	*mean Difference (SE)*	95% credible interval[a]	BF
Marshall et al. (N=46)	46	50.00[b]	62.33 (158.09)			0.96
Study 1 (N=40)	86	62.33 (158.09)	-146.53 (72.13)	-110.54 (65.62)	-239.16, 18.08	1.27
Study 2A (N=58)	144	-110.54 (65.62)	64.12 (59.29)	-14.38 (43.99)	-100.61, 71.85	1
Study 2B (N=58)	202	-14.38 (43.99)	2.63 (48.69)	-6.73 (32.64)	-70.72, 57.25	0.81

[a] In the first iteration, an estimated maximum performance difference of 10% was assumed. Half of this value (5%) was used as a vague prior. This prior was used to calculate the BF for Marshall et al. (2015)'s result.

[b] In the first iteration, an estimated maximum performance difference of 100 ms was assumed. Half of this value (50 ms) was used as a vague prior. This prior was used to calculate the BF for Marshall et al. (2015)'s result.

† evidence favours H1 (BF > 3).

‡ evidence favours H0 (BF < ⅓).

Table 4.6 presents the outcome for the interaction effect. Marshall et al. critically found a statistically significant interaction effect for accuracy, which was supported by strong evidence (BF = 50.86) as shown in the table. However, with each iteration, the effect size decreased and the BF provided anecdotal evidence only (BFs ≤ 1.06). The final credible interval for accuracy was .9% to 4.8% with a corresponding BF of 1.06. Marshall et al. did not find a statistically significant interaction for reaction time, which corresponded with the BF outcome (BFs ≤ 1.00). The final credible interval for RT was -89.7 ms to 162.9 ms with a corresponding BF of 0.62. Hence, the interaction effect between age and stress is not robust.

Table 4.6 Percent correct and RT mean differences, standard errors, credible intervals and Bayes factors for young low and high stress groups by older low and high stress groups interaction effect for all studies.

		Age by Stress Group Interaction				
		Prior	***Likelihood***	***Posterior***		
Accuracy (% correct)	*N: Incremental Increase*	*mean Difference (SE)*	*mean Difference (SE)*	*mean Difference (SE)*	95% credible interval[a]	BF
Marshall et al. (N=60)	60	2.50[a]	-12.55 (2.85)			50.86[†]
Study 1 (N=40)	100	-12.55 (2.85)	1.53 (4.65)	-8.70 (2.43)	-13.47, -3.94	0.62
Study 2A (N=58)	158	-8.70 (2.43)	-1.54 (4.23)	-6.92 (2.11)	-11.05, -2.79	0.92
Study 2B (N=58)	216	-6.92 (2.11)	6.39 (4.23)	-4.28 (1.89)	-7.98, -0.58	1.06
Reaction Time (ms)		*mean Difference (SE)*	*mean Difference (SE)*	*mean Difference (SE)*	95% credible interval[a]	BF
Marshall et al. (N=46)	46	25.50[b]	-47.75 (254.72)			1
Study 1 (N=40)	86	-47.75 (254.72)	104.80 (138.22)	70.10 (121.49)	-168.01, 308.22	0.99
Study 2A (N=58)	144	70.10 (121.49)	93.36 (123.58)	81.53 (86.64)	-88.27, 251.33	0.74
Study 2B (N=58)	202	81.53 (86.64)	-19.04 (96.41)	36.60 (64.44)	-89.70, 162.90	0.62

[a] In the first iteration, an estimated maximum performance difference of 5% was assumed. Half of this value (2.5%) was used as a vague prior. This prior was used to calculate the BF for Marshall et al. (2015)'s result.

[b] In the first iteration, an estimated maximum performance difference of 50 ms was assumed. Half of this value (25 ms) was used as a vague prior. This prior was used to calculate the BF for Marshall et al. (2015)'s result.

[†] evidence favours H1 (BF > 3).

[‡] evidence favours H0 (BF < ⅓).

Table 4.7a and 4.7b provide additional information for low vs. high stress groups within age group. In each table, regardless of the initial BF and effect size obtained for Marshall et al., the respective final outcomes indicate anecdotal evidence.

Table 4.7a YA percent correct and RT mean differences, standard errors, credible intervals and Bayes factors by stress group within age group for all studies.

		YA: Low vs. High Stress				
		Prior	***Likelihood***	***Posterior***		
Accuracy (% correct)	*N: Incremental Increase*	*mean Difference (SE)*	*mean Difference (SE)*	*mean Difference (SE)*	95% credible Interval[a]	BF
Marshall et al. (N=60)	60	5.00[a]	-2.39 (1.88)			0.71
Study 1 (N=40)	100	-2.39 (1.88)	6.13 (3.12)	-0.13 (1.61)	-3.28, 3.03	1.2
Study 2A (N=58)	158	-0.13 (1.61)	3.16 (3.06)	0.59 (1.42)	-2.21, 3.38	1
Study 2B (N=58)	216	0.59 (1.42)	1.79 (3.60)	0.75 (1.32)	-1.85, 3.34	0.93
Reaction Time (ms)		*mean Difference (SE)*	*mean Difference (SE)*	*mean Difference (SE)*	95% credible Interval[a]	BF
Marshall et al. (N=46)	46	12.50[b]	-87.32 (78.59)			1
Study 1 (N=40)	86	-87.32 (78.59)	-111.89 (109.76)	-95.65 (63.90)	-220.89, 29.60	1
Study 2A (N=58)	144	-95.65 (63.90)	121.94 (82.12)	-13.59 (50.43)	-112.44, 85.26	1.02
Study 2B (N=58)	202	-13.59 (50.43)	-25.33 (65.47)	-17.96 (39.95)	-96.27, 60.35	0.86

[a] In the first iteration, an estimated maximum performance difference of 10% was assumed. Half of this value (5%) was used as a vague prior. This prior was used to calculate the BF for Marshall et al. (2015)'s result.

[b] In the first iteration, an estimated maximum performance difference of 25 ms was assumed. Half of this value (12.5 ms) was used as a vague prior. This prior was used to calculate the BF for Marshall et al. (2015)'s result.

† evidence favours H1 (BF > 3).

‡ evidence favours H0 (BF < ⅓).

Table 4.7b OA percent correct and RT mean differences, standard errors, credible intervals and Bayes Factors by stress group within age group for all studies.

		OA: Low vs. High Stress				
		Prior	***Likelihood***	***Posterior***		
Accuracy (% correct)	*N: Incremental Increase*	*mean Difference (SE)*	*mean Difference (SE)*	*mean Difference (SE)*	95% credible Interval[a]	BF
Marshall et al. (N=60)	60	12.50[a]	9.39 (2.01)			>100[†]
Study 1 (N=40)	100	9.39 (2.01)	5.39 (3.26)	8.29 (1.71)	4.93, 11.64	1.43
Study 2A (N=58)	158	8.29 (1.71)	4.53 (2.83)	7.28 (1.47)	4.4, 10.15	1.23
Study 2B (N=58)	216	7.28 (1.47)	-4.15 (2.14)	3.62 (1.21)	1.25, 5.99	1.94
Reaction Time (ms)	*N: Incremental Increase*	*mean Difference (SE)*	*mean Difference (SE)*	*mean Difference (SE)*	95% credible Interval[a]	BF
Marshall et al. (N=46)	46	37.50[b]	102.87 (209.13)			0.99
Study 1 (N=40)	86	102.87 (209.13)	-185.66 (75.62)	-152.3 (71.11)	-291.68, -12.92	2.15
Study 2A (N=58)	144	-152.3 (71.11)	-2.73 (93.16)	-97.23 (56.53)	-208.03, 13.56	1
Study 2B (N=58)	202	-97.23 (56.53)	30.59 (69.27)	-46.14 (43.79)	-131.98, 39.7	0.98

[a] In the first iteration, an estimated maximum performance difference of 25% was assumed. Half of this value (12.5%) was used as a vague prior. This prior was used to calculate the BF for Marshall et al. (2015)'s result.

[b] In the first iteration, an estimated maximum performance difference of 75 ms was assumed. Half of this value (37.5 ms) was used as a vague prior. This prior was used to calculate the BF for Marshall et al. (2015)'s result.

[†] evidence favours H1 (> 3).

[‡] evidence favours H0 (< ⅓).

Sensitivity analyses revealed that all of the above reported BFs but one were consistent across a range of scale factors, which indicates that the obtained BF values are robust. The exception was the comparison of low vs. high stress groups (Step 1) where the BF was 2.36. Here the BF showed substantial evidence with the Student's t (BF = 3.08) and Cauchy (BF = 3.28) distributions but subsequently dropped back into the anecdotal range (BFs ≤ 1.55) as more data were added. On this basis, the BF for the overall comparison of low and high stress groups is still fairly robust.

Post hoc, WM performance was assessed to determine whether it varied as a consequence of study mode (in-person vs. online) given that Marshall et al.'s (2015) study and Study 1 were in-person studies whereas Studies 2A and 2B were conducted online. To evaluate whether accuracy (n-back percent correct, d-prime) and/or n-back RT varied as a function of study mode (in-person: Marshall, Study 1 vs. online: Study 2A, Study 2B) an independent samples t-test was conducted for each dependent variable. The result showed that accuracy scores were comparable (p's ≥ .099); however for RTs the result was statistically significant: t(118) 2.940, p = .004. Corresponding BFs for percent correct and d-prime indicated evidence for the null (BF = 0.21) and the insensitive range bordering on the null (BF = 0.34), respectively. For RTs there was strong evidence supporting an effect (BF = 17.53). Bayes Factors were calculated in JASP (2022). These results indicate that participants who took part in-person were slower (M = 853.48, SE = 44.99) on average than online participants (M = 709.84, SE = 19.51). Reasons may include that the online

participants were more computer literate, making them faster or they were less stressed. As such, this result suggests that it is only valid to compare Study 1's RT results with Marshall et al.'s work. However, all the statistical results and consequent conclusions are the same whether online (Study 2A, 2B) results are included or excluded. Tables 4.4 to 4.7a,b illustrate this.

4.4 Discussion

The aim of the present study was to assess the strength of the evidence supporting the hypothesis that higher cognitive function, as measured by working memory, is negatively affected by cumulative life stress, ageing and/or the interaction of the two. Marshall and colleagues (2015) conducted a study with 60 participants which showed a robust age by cumulative stress effect where only older participants with a higher cumulative stress score showed impaired performance on a 2-back (and Sternberg,(1966)) task. Their result was not replicated using an iterative Bayesian meta-analysis, comprising three replication studies (N_{total}=156) with the same 2-back task and cumulative stress measures. Indeed, for all 3 effects investigated, namely, ageing, cumulative stress and their interaction, the results fell within the anecdotal range (⅓<BF<3).

The analysis of the age by cumulative stress interaction revealed a finding within the anecdotal range for accuracy and RT. In particular, where Marshall et al.'s study shows a clear detriment in accuracy of older high stress participants compared to older low stress participants and no detectible effect of stress in the young low vs. high stress groups, no such interaction was found. For both accuracy and RT, older adults showed

inconclusive evidence of an effect of cumulative stress. Likewise for young adults. Thus, the present study does not support the hypothesis that high stress older adults show a particular impairment due to the cumulative impact of stress on higher cognitive function, as measured in working memory.

This inconclusive result for cumulative life stress is incongruent with Marshall et al.'s study, which found no evidence of an effect; from a Bayesian perspective the present results indicate that additional data is needed to provide evidence to confirm either the null or an effect of cumulative stress. One possible reason for these results is that ageing is a powerful mediator and may have masked the effect of cumulative stress on cognition. For example, in a meta-analysis investigating the impact of processing speed on cognition, Verhaeghen (2013) found that ageing mediated performance on a range of cognitive functions such as working memory, executive control and task shifting, explaining ≤ 58% of age-related variance. In light of such evidence, one may speculate that YA performance may better represent the impact of cumulative stress on cognition without the added variance contributed by ageing effects on performance. Indeed, studies of YAs that have investigated the effects of recent life events stress (4 to 6 months) found that high stress YAs showed blunted autonomic responsivity (Clements & Turpin, 2000) and had poorer academic performance, psychological and physical health (1984) than low stress YA. Low stress YAs were also better able to avoid risks when making decisions (2021). Given that a YA sample was evaluated and their results also fell within the insensitive range suggests

that how the impact of cumulative stress on working memory was measured may not have been sufficiently reliable relative to the sample size.

The overall comparison by age group was inconclusive for both accuracy and RT. The finding for RT in particular was unexpected given that processing speed in the context of higher cognitive function draws on a wide range of neural networks, which, as mentioned in the introduction, deteriorate with advancing age (Fotenos et al., 2005; Kerchner et al., 2012; Lu et al., 2011; Podell et al., 2012; Salthouse, 1994, 1996, 2012; Tsapanou et al., 2019). Indeed, Verhaeghen (2013) found processing speed explained 78% of the variance in cognitive functions. This finding was also at odds with Marshall et al.'s results, which showed that older adults were slower and less accurate than young adults. Using Bayesian methods, the results suggest that more data are needed.

All 3 of the replication studies produced consistently small effect sizes which is incongruent with the much larger effects that were expected based on Marshall et al.'s findings. There are a number of factors that may explain these outcomes. Older adults' stress responsivity appears to be less efficient and consequently may have relatively limited impact on memory performance (Pulopulos et al., 2015). Individual differences, too, play a role regarding both cognitive ability (Verhaeghen, 2013) and basal cortisol levels (Franz et al., 2011). Previous research found that working memory declines with age but interacts with sex and education (Pliatsikas et al., 2019) and that processing complexity is more vulnerable to ageing than the (passive) storage components of working memory (Baddeley et

al., 2005). The hierarchical linear regressions (unpublished data) conducted for each of the replication studies separately, with stress scores as a continuous variable, showed no impact of age group or education on performance, nor indeed other factors such as gender, exercise, perceived stress or alcohol consumption. Was there a speed-accuracy trade-off? The analyses suggest not. However note that, compared to the young adults, there was more variability in older adults' scores and they do tend to be more cautious when providing responses (Hofer & Alwin, 2008).

The present study's findings should be interpreted alongside some caveats. While a meta-analysis has advantages in providing better statistical power, the impact of confounding moderating/mediating factors cannot be ruled out. In particular, Study 1 and Marshall et al.'s study were conducted in-person whilst Studies 2A and 2B were performed online. In addition, the Covid-19 pandemic occurred around the time of these 3 studies. The iterative approach allows the effects of each study to be considered separately and no evidence was found to indicate that these factors had an impact on the conclusions. The data comprised retrospectively collected life events information, which are only an indicator of the accumulated stress impact that people have experienced. That conclusive evidence of an age by cumulative stress interaction effect was not found is unlikely to be because the study was underpowered. When Study 1 was designed, it was expected to be well-powered as Marshall's study demonstrated a robust interaction effect with a much smaller sample (60 vs. 156). Moreover, an iterative Bayesian meta-analysis was used, which displays the pattern of the effect over studies in

addition to providing a pooled effect size. Bayesian statistics are not subject to the stopping rule of frequentist methods and therefore the number of participants enrolled for a study can be incrementally increased until the data are sensitive enough to reveal sufficient evidence to confidently conclude an outcome in favour of either H1 or H0 (Dienes, 2014) or neither. Throughout, the effect sizes became progressively smaller with each incremental increase in sample size, which was comparatively large. Note that the meta-analysis assumed that there is one effect size being measured, however given the consistency of the effect sizes with three independent samples, this assumption appears valid here. The data was analysed using a common median split and median split by sample, with very similar results, which provides additional assurance as to the sensitivity of the analysis. This is in addition to sensitivity analysis conducted to confirm the robustness of BFs reported. Thus, these findings are robust.

In conclusion, the Bayesian meta-analysis suggests inconclusive evidence for the effect of ageing, cumulative stress and their interaction on working memory, as measured with a life events questionnaire. The design of the study at the outset was well-powered given the previous research. The results, however, indicate that this was not the case and it is argued that using a life events questionnaire to evaluate the impact of cumulative life stress on working memory with relatively small sample sizes will not reliably capture any effect that might exist because there are too many extraneous factors including individual differences, developmental factors and epigenetics (Marr et al., 2010; Sapolsky, 2015).

4.5 Supporting Information

Appendix 1	Participant details for all 3 studies.
Appendix 2	Age median IQR values for participants for all 3 studies.
Appendix 3	Additional tasks administered during the study (description and results).
Appendix 4	Analyses for percent correct and D-prime means, SEs and Univariate ANOVA results for all 3 studies.
Appendix 5	Frequency table of the total cumulative stress score for each participant in each study.
Appendix 6	An excel workbook containing a series of tables showing power analysis and traditional meta-analysis outcomes.
Appendix 7	Study design and procedure for all 3 studies.
Appendix 8	Reference table providing the median splits for all 3 studies.
Appendix 9	Sensitivity analysis: A comparison using a single median split.
Appendix 10	Data tables for all iterative analyses and Bayes factor calculations.

A section containing all appendices can be found starting from page 395, at the end of this thesis.

Chapter 5: An observational study investigating the impact of cumulative life stress, sleep quality, resilience and adverse childhood experiences on working memory in a cross-sectional and longitudinal sample of adults across the lifespan.

5.1 Introduction

Thus far, it has been demonstrated with the 2-back working memory task that ageing and cumulative life stress may independently impair working memory accuracy and RTs, but do not interact to accelerate cognitive ageing. If cumulative stress does have any accelerating effect on ageing it may be small and therefore mitigated/masked by individual differences, developmental factors and/or epigenetics. This chapter builds on these findings by expanding the investigation in three important ways. Firstly, while the previous work provides insights into effects on the accuracy and reaction time of working memory (WM), it did not touch on working memory capacity (WMC) *per se*. Adding WMC may enhance our understanding of the impact of cumulative stress and ageing on WM function, because evidence shows that WMC is particularly sensitive to ageing effects (Craik, 2016; Gick et al., 1988; Jaroslawska & Rhodes, 2019; Salthouse, 1994). Secondly, the investigation was expanded by adding factors identified as potentially significant through a review of the literature (indicated in Chapter 1). These are: resilience, sleep quality and adverse childhood experiences. The studies completed thus far and the wider literature indicate that the effects of life events stress and ageing on cognitive health (and health in general) are complexly interwoven with a broad range of endogenous and

exogenous variables. Expanding the investation to include these three factors is likely to explain more of the variance in performance outcomes, thereby filling in some gaps in existing knowledge. Thirdly, previous findings are based on cross-sectional and longitudinal studies. However, the number of variables measured in each study have, by necessity or design, been limited. For example, numerous studies have investigated stressful life events and/or sleep quality on outcomes while others have investigated sleep quality and resilience on outcomes. A broader set of concomitant variables both cross-sectionally and longitudinally is therefore applied here. The rationale is set out in detail below.

Working memory capacity refers to how much information one can actively maintain and process simultaneously, from moment-to-moment (Baddeley, 2012; Logie et al., 2020; Sweller, 1994). Age-related decline in WM performance has been attributed mainly to an age-related reduced WMC (Brockmole & Logie, 2013) which, in turn, has been shown to diminish in a linear manner (Bopp & Verhaeghen, 2005). Previous work indicates that age-related WMC changes may be explained by poorer executive attentional control and slower processing (Lustig et al., 2007; Reuter-Lorenz & Lustig, 2017; Salthouse, 1994, 1996). Moreover, factors such as sleep deprivation, stress and anxiety can deplete WMC by reducing the availability of processing resources (Caviola et al., 2017). Complicating matters further, WMC is known to differ considerably between individuals (Engle, 2002; Luck & Vogel, 2013). Neuroimaging research suggests that these differences are driven by developmental and epigenetic factors (Conway & Engle, 1996) and the subsequent impact on

both structural and functional connectivity creates variations in information processing efficiency (Rottschy et al., 2012). The consensus from extensive research seems to indicate that individual differences in WMC ultimately represent variations in general attentional resources. This can be assessed by measuring attentional task switching, which requires both effort and control (Conway & Engle, 1996). While the n-back task captures mental load well by allowing for a change of 'n' stimuli and tracking this manipulation in terms of accuracy and RT performance it does not involve nor measure attentional switching. Evaluating the impact of cumulative stress, ageing and sleep quality, resilience and adverse childhood experiences (ACEs) on WM using a task specifically designed to capture WMC, such as WM span task, would therefore broaden our understanding of these factors' association with WM function. A WM span task is a task which has two components: the number of items to recall alongside an equal number of, for example, sentences or mathematical operations. Thus, WM span tasks simultaneously tax processing capability e.g. verifying mathematical equations, whilst recall of digits or words is measured with the aim of engaging executive attentional processes (Conway et al., 2005; Turner & Engle, 1989).

As indicated above, the effects of sleep quality, resilience and ACEs have been shown to affect WMC and will be discussed in turn below.

Good sleep quality protects against age-related cognitive decline (Scullin & Bliwise, 2015). Conversely, ageing adults are vulnerable to the

effects of poor sleep (Carroll et al., 2016; Frohnhofen et al., 2017). Interestingly, these effects potentially start from middle age when sleep quality begins to diminish (Pace-Schott & Spencer, 2011). Indeed, there is evidence of a link between self-reported poor sleep in middle-aged individuals, neurodegeneration biomarkers such as amyloid deposition and cognitive decline (Scullin & Bliwise, 2015). This finding suggests that studying middle-aged adults may be important in understanding the relationship between ageing and cognitive health particularly given that healthy older adults do not show a consistent association between sleep and cognitive functioning (ibid). This inconsistency may be explained by age-related changes in homoeostatic factors, endocrine function and circadian regulation, which play a role in disrupting sleep and vary considerably between individuals (Maggio et al., 2013). For example, a longitudinal study by Song et al. (2015) revealed that increased N1 sleep time and reduced REM sleep time predicted poorer cognitive functioning with increasing age. Perceived stress also undermines healthy sleep. For example, being stressed can significantly impact sleep reactivity, defined as an individual's ability to maintain normal sleep (falling asleep and staying asleep) (Kalmbach et al., 2018). Moreover, in a longitudinal study with college students Yang and colleagues (2014) showed that stress-related sleep disturbances and maladaptive sleep beliefs were associated with insomnia, a clinical sleep disorder. Given that sleep is sensitive to both ageing and stress, an important further consideration is whether their negative impact on sleep quality translates to poorer cognitive performance. Regarding WM specifically, the literature is inconsistent.

deLafortune et al. (2014) found with a sample of 50 to 91 year-olds that higher spindle density during sleep was significantly correlated with better verbal learning, attention and verbal fluency while WM performance was not correlated with any sleep variables. Xie et al. (2019), in contrast, demonstrated an ageing effect in a broader sample (21 – 77 yrs). They showed that WM precision but not WMC showed an age-related deficit. In a study investigating the impact of sleep deprivation on recognition memory, Ratcliff and colleagues (2018) found that sleep deprivation degraded the quality of information stored in memory likely due to poorer attentional resources. Thus, WMC may vary based on sleep quality variability (Conway & Engle, 1996). While these cross-sectional studies show some inconsistencies, evidence from longitudinal and population-based studies indicate that there is a robust link between sleep and cognition. However, assessment is typically with a global cognitive measure such as mini-mental state exam or similar (e.g. Benito-León et al., 2009; Ferrie et al., 2011; Potvin et al., 2012). A more targeted approach to studying the impact of sleep on cognition longitudinally is therefore needed. Importantly, as with stress, poor sleep quality does not necessarily result in impaired cognitive performance and does not guarantee a diagnosis of dementia in later life (Loerbroks et al., 2010; Scullin & Bliwise, 2015). A possible reason could be the mitigating effects of protective factors such as psychological resilience which past stress-focused research did not typically control for.

Resilience, which may be defined as "…managing well in the face of stressors…" (Seery et al., 2013, p. 1181), has been shown to develop

through experiencing challenging life events requiring considerable adjustment (Fletcher & Sarkar, 2013). Resilience can therefore be seen as a manifestation of personal strength that develops over time (Scholten et al., 2020). Importantly, moderate amounts of challenging life events facilitate psychological resilience while experiencing no such stressors, or many, do not (Seery et al., 2010; Seery & Quinton, 2016). Resilience also protects against the effects of poor sleep, which is a common stress-related symptom. For example, a large-scale study of veterans without a current mental health condition showed that, within the poor sleeper group, higher levels of resilience predicted less psychological distress. Similarly, Li et al. (2019) found that stressful life events in a student sample predicted poorer sleep quality but that poor sleep quality and rumination were less impactful with higher levels of resilience. Congruent with these findings, in a study with older adults, the rate of sleep problems reported were inversely related to resilience (Grossman et al., 2021). Likewise, Harvanek and colleagues (2021) demonstrated that while cumulative stress is associated with epigenetic ageing in healthy younger to middle-aged adults (range 18 – 50 yrs) even after controlling for physiological, behavioural and demographic factors, resilience mitigated its impact. In particular, emotional regulation and self-control moderated the relationship between stress and ageing and between stress and insulin resistence, respectively. Resilience is also important in the context of traumatic experiences. For example, Cicchetti and colleagues (1993) found that most maltreated children strive for resilience in spite of adversity and, equally interestingly, 15% of non-maltreated and 22% of

maltreated children showed none of the 7 resilient adaptive indices measured which are derived from a wide range of tests[33].The adaptive indices comprised: 'Prosocial', 'Disruptive-Aggressive', 'Withdrawn', 'Child Depression Inventory', 'School risk index', 'Internalizing' and 'Externalizing'. Some of these were composite scores. This finding highlights that while developmental outcomes for many who experience adversity in childhood are known to increase allostatic load in later life, resilience may mitigate their effects in some individuals. Conversely, a proportion of individuals who have had no early trauma may find adjustments to life's typical ups and downs challenging. For this reason, investigating the impact of cumulative stress and ageing on cognition should also measure concomitant levels of resilience to provide a more comprehensive understanding of research outcomes.

Adverse childhood experiences (ACEs) are the final factor to discuss. The Crime Survey for England and Wales estimated that 20% of adults aged 18 to 74 experienced at least one form of adverse childhood experience before the age of 16. Adverse childhood experiences typically refer to physical, emotional or sexual abuse, neglect or witnessing violence/abuse. Evidence suggests a dose-response relationship between

[33] The indices were based on: Child Depression Inventory (CDI; Kovacs, 1982), Self-Esteem Inventory (SEI; Coopersmith, 1981), The Peabody Picture Vocabulary Test-Revised (PPVT-R; Dunn & Dunn, 1981), a peer measure called 'peer nomination method' (Coie & Dodge, 1983), counsellor measures included a variety of instruments including behaviour ratings, the Pupil Evaluation Inventory (PEI), the Teacher's Report Form (TRF) of the Child Behaviour Checklist (CBCL) and the California Child Q-set (CCQ), Behaviour ratings (Wright, 1983) involved counsellors rating each child on 9 items, using a 7-point scale, evaluating 3 interpersonal functioning aspects: prosocial behaviour, aggression and withdrawal. School measures which measured adaptation in school by indexing 5 possible risk indicators including attendance problems, achievement tests, suspensions, failing grades and being 2/more years below age-level.

the number of ACEs and the severity of ill-health in adulthood (Chartier et al., 2010). Indeed, ACEs have been linked to a number of physical health risks, including obesity, heart, lung and liver disease (Anda et al., 2006; Chartier et al., 2010; Dube et al., 2004; Felitti & Anda, 2010; Felitti et al., 1998). In addition, 148 healthy participants in a structural MRI study, which controlled for trait anxiety, depression, intelligence, age, education and recent stressful life events, showed significant functional and structural changes. These changes included decreased grey-matter volume in the insula, hippocampus, and anterior cingulate gyrus, *inter alia* (Dannlowski et al., 2012). In studies of ACE-afflicted children and adolescents, structural changes have been linked to poorer executive function in general and WM in particular (Cowell et al., 2015; Kavanaugh et al., 2017). However, whether such effects reach into adulthood is unclear. For example, Feeney et al. (2013) found, in a large-scale longitudinal study of older adults (> 50 yrs), that a history of ACEs was associated with improved memory, executive function and processing speed despite experiencing poorer psychological health. Dunn and colleagues, on the contrary, found no evidence of an effect on memory in their large-scale study of 24-32 year-olds when comparing participants who had experienced sexual or physical abuse in childhood with those who had had no such experiences. However, they did find that the age of sexual abuse significantly predicted memory performance within this group. Thus, it is not merely presence vs. absence of ACEs that should be considered but when the trauma occurred. Ji and colleagues (2018) investigated the effects of recent stressful life experiences and ACEs on response

inhibition, cognitive flexibility and WM in college students. Their results suggested that stressful life events and ACEs affected response times but not accuracy. However, they did not analyse the interaction effect of ACEs and recent life events on cognitive performance and therefore it is difficult to know how the combined effect of early experiences and recent life events might affect executive functions such as WM. Most recently, Roberts and colleagues' (2022) study with middle-aged women (n = 13,984) found, after controlling for socioeconomic status and head trauma, that those who had been exposed to physical, emotional and sexual abuse in childhood performed less well in the cognitive tests compared to those who had never experienced ACEs. In particular, there was a strong association between ACEs and their WM/learning composite score. Moreover, women who had experienced greater severity of abuse had poorer cognitive function compared to those who had experienced less severe ACEs. Thus, further clarity regarding the association between ACEs and WM in middle and older-aged adults, in the context of the aforementioned factors, would benefit the field.

There are no previous studies that have measured the impact of cumulative life stress, ageing, subjective sleep quality, ACEs and resilience on WMC using a complex span task. To this end, 3 studies, each with specific aims, were conducted.

In the present study, one sample of adults was recruited to evaluate the effects of the aforementioned independent measures on working memory performance (working memory capacity, working memory accuracy and reaction time) in 3 separate analyses. First, a cross-

sectional analysis on adults aged 18 to 85 yrs was conducted to leverage the statistical power from this sample. This analylsis sought to assess the relationship between cumulative life stress, ageing, subjective sleep quality and resilience alongside health, lifestyle and gender covariates, on three outcome measures of WM using the Automated Operation Span Task (A-Ospan) (Conway et al., 2005; Unsworth et al., 2009). The A-Ospan is a complex span task providing 3 indices of WM performance as follows: absolute span, a measure of WMC; letters correctly recalled, a measure of WM accuracy; and reaction time (the time taken to recall correct letters). The A-Ospan is a well-validated measure of WM which has been shown to activate brain regions associated with WM processes (Faraco et al., 2011). Moreover, it carries a high mental load which would be expected to put participants under considerable pressure. In doing so it was hoped to accentuate any cognitive differences between low and high cumulative stress participants. Based on the literature, the overall expectations for this cross-sectional analysis were that cognitive performance would be positively associated with subjective sleep quality and resilience but negatively associated with cumulative stress and age. Thus, older adults were expected to do less well on the A-Ospan task than younger adults and those with poorer sleep quality were expected to do less well than those with better sleep quality. Likewise, those with lower levels of resilience were expected to perform less well than those who reported higher levels of resilience. Those reporting higher levels of cumulative stress were expected to perform less well than those reporting lower levels. Moreover, re-assessing the previous finding that there was

no conclusive evidence of an interaction effect between cumulative stress and ageing, the results were expected to reveal differences in high and low levels of cumulative stress to be comparable between young and older participants. However, if there is an accelerative effect of cumulative stress on cognitive ageing, evidence of this would most likely be found in the cross-sectional study as the total accumulated adjustment to all reported life events experienced over the participants' lives up until the day of testing would be measured. This being true, it would be expected that older adults with higher levels of cumulative stress would perform less well on one or more of the WM measures than older adults with lower cumulative stress and all younger adults.

Second, a longitudinal analysis was conducted to explore the potentially accelerative effects of ageing and stress, targeting only the older two age groups (36 – 59 yrs and 60 – 85 yrs). Changes in WM performance over an 18-month period were investigated to determine whether they were associated with different levels of cumulative stress, age, resilience and/or subjective sleep quality. Evaluating performance over 18 months deviates from typical longitudinal designs because the focus is on the short to medium-term rather than over several years. This decision was driven by both practical and theoretical considerations. Practically, time to run this study was limited by PhD requirements. Theoretically, though numerous early studies measured the effects of recent life events on health within a 6 to 24 month time-frame more recently conducted longitudinal studies (>1990s) focused exclusively on longer time frames (≥2.5 yrs) (Bougea et al., 2022). While the literature

suggests that any effects of cumulative stress are more likely to present after a longer time period, any shorter-term effects should not be ignored. Particularly given that the earlier studies showed, in both prosepctive and retrospective designs, that life events stress were positively associated with illness reporting (Holmes & Rahe, 1967; Rahe & Arthur, 1978). Moreover, no studies thus far have investigated short to medium-term effects of all of these variables in one study. The choice to focus specifically on middle and older-aged adults was because both are potentially more 'at risk' to ageing effects than young adults. Ageing begins at approximately 30 years of age and any differences between 'middle' and 'older' age may provide important insights. Indeed, the aforementioned finding on sleep quality by Pace-Schott and Spencer (2011) is a case in point. It was expected that a percentage change over time in one or more of the WM measures would be associated with whether participants reported high or low levels of cumulative stress. Thus, those in the low stress group were expected to show a percentage change indicating some learning effect/gain over time, while participants with high levels of cumulative stress were expected to show no change, or poorer WM performance. This would be more likely if there is indeed an interaction between age and cumulative stress given that such a finding implies that stress accelerates ageing. Those with persistently poor sleep scores and/or resilience were similarly expected to show a deterioration in cognition over time. Age *per se* was not expected to have any effect on WM performance over time given that MA and OAs typically show learning gains.

Third, another longitudinal analysis was conducted with the specific aim of exploring the association between age, ACEs, cumulative stress, the interaction between cumulative stress and ACEs and WM performance over time. In this analysis, the change in all A-Ospan indices from time 1 to time 3 using difference scores (18 months minus baseline) in those with high vs. low levels of cumulative stress were compared within age groups (middle and older-aged adults). Regarding the interaction between ACEs and cumulative stress on the 3 WM outputs, the aim was to assess the extent to which their combined effect is associated with differences in performance and if so, whether this difference exists in one or both age groups. This would indicate whether more focus is needed on research within the middle-aged adult group, which has received less research attention relative to over 60's. A negative association between ACEs and/or cumulative stress and cognitive performance was expected. Moreover, the magnitude of this association was expected to be greater in the older relative to middle-aged group given that the older group would have experienced more life events and ageing research indicates poorer physiological resilience making adjustment more costly (Pomatto & Davies, 2017). A positive association was expected between participants who had experienced ACEs and those who scored high on cumulative stress. As with cumulative stress, poorer cognitive performance was expected from those who had experienced more ACEs compared to those who had experienced few/none.

5.2 Method

5.2.1 Participants

Four hundred and forty nine individuals applied to participate in the longitudinal study. Healthy adults aged 18 to 85 years were invited. This invitation was also extended to older participants who attended the neurostimulation study reported in Chapter 3 (referred to as 'Study 1' in Chapter 4). Participants with neurological conditions e.g. stroke or epilepsy, developmental conditions e.g. Autistic Spectrum Disorder or diagnosed mental health conditions e.g. depression were excluded. Those on psychoactive medications were also excluded. Further excluded were participants who withdrew prior to completing the cognitive task, could not complete the cognitive task due to technical difficulties with the software or who performed the task poorly/incorrectly. For the longitudinal analysis, participants' data were included only if they completed all 3 study iterations.

For this exclusively online study, young adults were recruited from the University of Essex student population via social media and word-of-mouth. Middle-aged and older adults were recruited from the Colchester area via local media, University of 3rd Age and word-of-mouth and Prolific, an online recruitment platform. Participants received a payment (£10/hr) and/or entered into a £50 voucher prize draw or received course credits. The study was approved by the University of Essex Faculty of Science and Engineering Ethics Committee (Ethics ID: ETH1920-1215, ETH2021-0828). All participants gave informed consent online after downloading the participant information sheet, which provided full details of the study.

Participants were categorised into age-groups: 18 to 35 years (young adults), 36 to 59 years (middle-aged adults) and 60 to 85 years (older adults). Young adults (YA) were included at time 1 only and served as a comparison group for middle-aged (MA) and older adults (OA) in the cross-sectional and longitudinal analysis. For the longitudinal analysis, participants were contacted twice more following time 1, approximately 9 months apart, to complete the study again.

5.2.2 Design

Using one sample, 3 separate designs were used to evaluate the effects of cumulative life stress, ageing, subjective sleep quality and resilience on working memory performance (working memory capacity, working memory accuracy and reaction time). Data was collected from the full age range (18 to 85 years) at time 1. These data were analysed cross-sectionally. Data from middle-aged and older adults (36 to 85 years) only were collected twice more, at time 2 and 3. To assess the impact of adverse childhood events (ACEs), those middle-aged and older adults who completed time 1 and time 3 were invited to participate in a follow-on study conducted 2 weeks following time 3. Fig. 5.1 provides full design details. This study was not pre-registered.

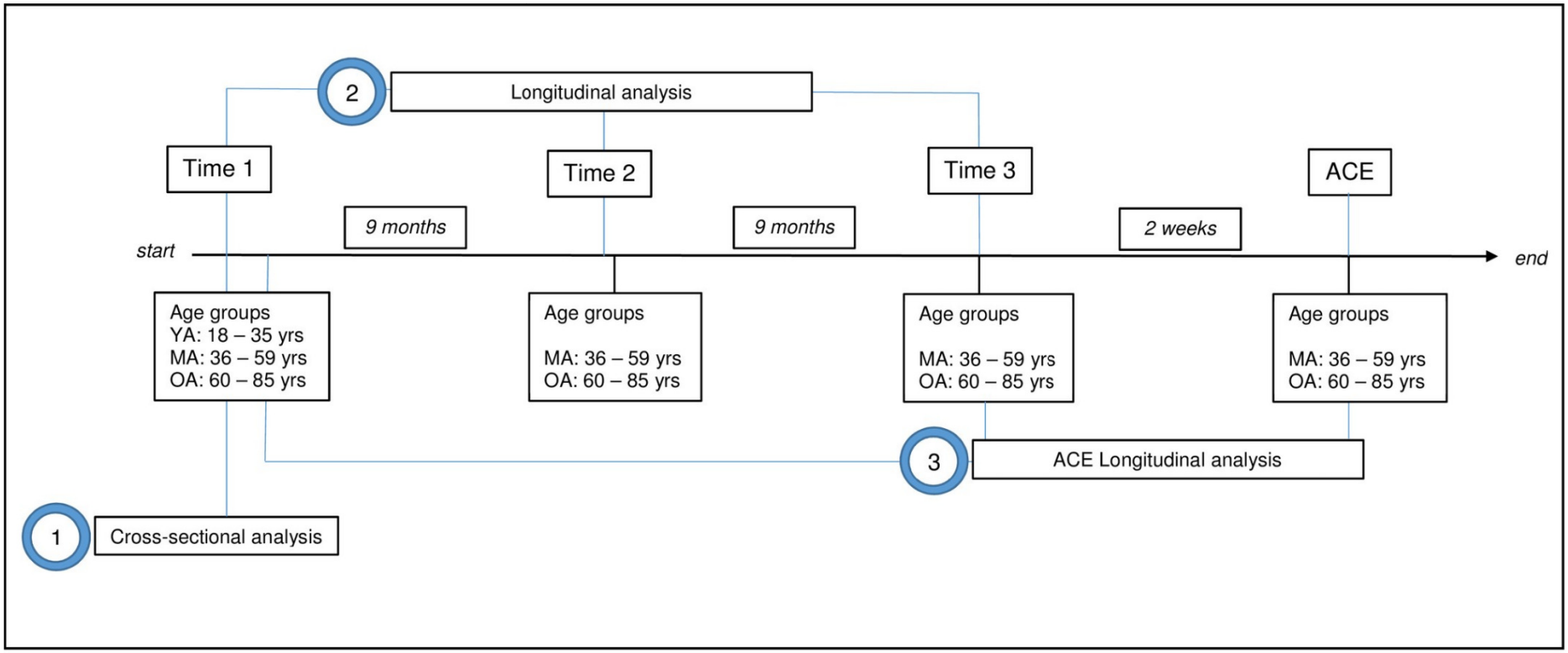

Fig. 5.1 Test Design: Using one sample, 3 separate analyses were conducted.

Analysis 1: Adults aged 18 to 85 years completed time 1. These data were subject to a cross-sectional analysis (n=351). See Fig. 2 for this study's procedure.

Analysis 2: Of the adults who completed time 1, participants aged 36 – 85 years were invited to continue with the study and complete time 2 and time 3, approximately 9 months apart. These data (time 1, time 2 and time3) were subject to a longitudinal analysis (n=53 of 351). On each occasion, participants completed a series of questionnaires administered via the Qualtrics online platform followed by the Automated Operation-span task administered via the Inquisit online platform. See Fig. 3 for procedure.

Analysis 3: Of the adults who completed the longitudinal study, those who completed time 1 AND time 3 were invited to participate in the Adverse Childhood Experiences (ACE) longitudinal study and completed a series of ACE questionnaires. These data (time 1 and time3) were subject to a longitudinal analysis (n=46 of 351). Their working memory performance (working memory capacity, working memory accuracy and reaction time) were measured in terms of age, cumulative stress and the interaction of cumulative stress and each ACE measure. See Fig. 4 for procedure.

5.2.3 Measures

5.2.3.1 Demographics, cumulative stress and general well-being

To reduce the risk of attrition, the overall length of the survey component at time 1 was minimised as much possible. Items were added at time 3 to provide additional information regarding the longitudinal sample. Study measures are provided in Fig. 5.2 for the cross-sectional analysis, Fig. 5.3 for the longitudinal analysis and Fig. 5.4 for the ACE longitudinal analysis. Note that each analysis used either the full sample (Analysis 1: cross-sectional analysis) or part of the full sample (Analysis 2: longitudinal analysis – t1, t2, t3; Analysis 3: t1, t3).

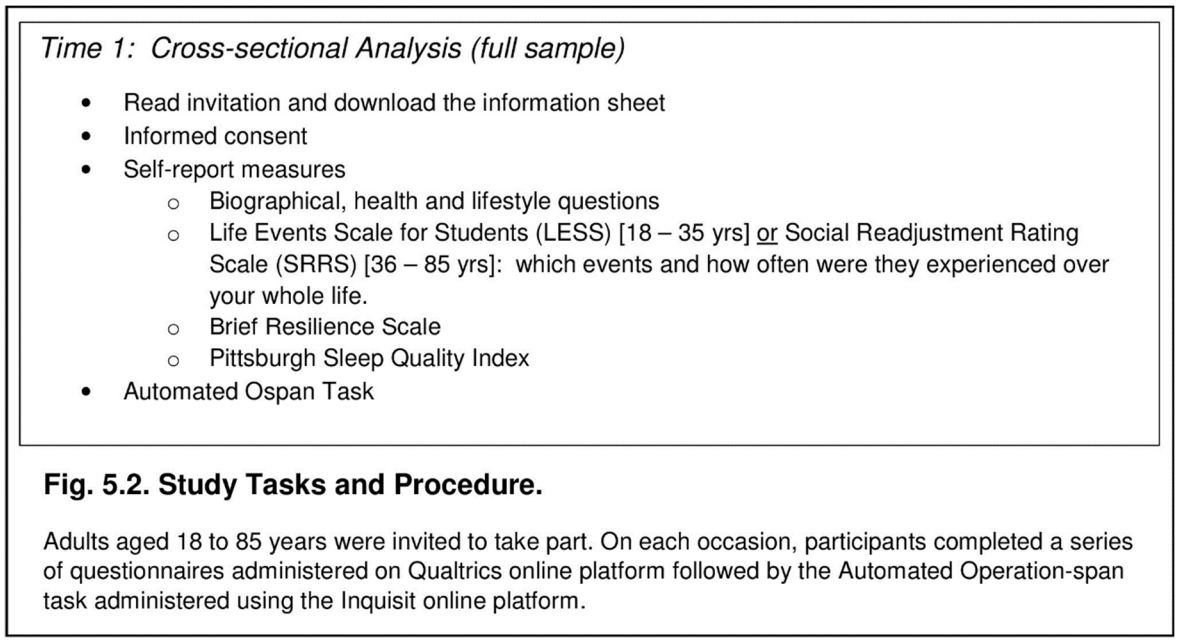

Fig. 5.2. Study Tasks and Procedure.

Adults aged 18 to 85 years were invited to take part. On each occasion, participants completed a series of questionnaires administered on Qualtrics online platform followed by the Automated Operation-span task administered using the Inquisit online platform.

Time 1: Longitudinal study [36 – 85 yrs]:

- Read invitation and download the information sheet
- Informed consent
- Self-report measures
  - Biographical, health and lifestyle questions
  - Life Events Scale for Students (LESS) [18 – 35 yrs] or Social Readjustment Rating Scale (SRRS) [36 – 85 yrs]: which events and how often were they experienced over your whole life.
  - Brief Resilience Scale
  - Pittsburgh Sleep Quality Index
- Automated Ospan Task

Time 2: Longitudinal study [36 – 85 yrs]: approximately 9 months after time 1

- Read invitation and download the information sheet
- Informed consent
- Self-report measures
  - Biographical, health and lifestyle questions
  - Social Readjustment Rating Scale (SRRS) experienced over the past 9 months.
  - Brief Resilience Scale
  - Pittsburgh Sleep Quality Index
- Automated Ospan Task

Time 3: Longitudinal study [36 – 85 yrs]: approximately 9 months after time 2

- Read invitation and download the information sheet
- Informed consent
- Self-report measures
  - Biographical, health and lifestyle questions
  - Social Readjustment Rating Scale (SRRS): experienced over the past 9 months.
  - Brief Resilience Scale
  - Pittsburgh Sleep Quality Index
  - PSS-10
  - STAI-STATE
  - STAI-TRAIT
- Automated Ospan Task

Fig. 5.3 Study Tasks and Procedure.

Adults aged 36 to 85 years completed time 1, time 2 and time 3, approximately 9 months apart.

Note: Although time 1 was completed by all participants (18 to 85 years), only data from those in the age range of 36 to 85 years were analysed longitudinally (t1 vs. t2 vs. t3).

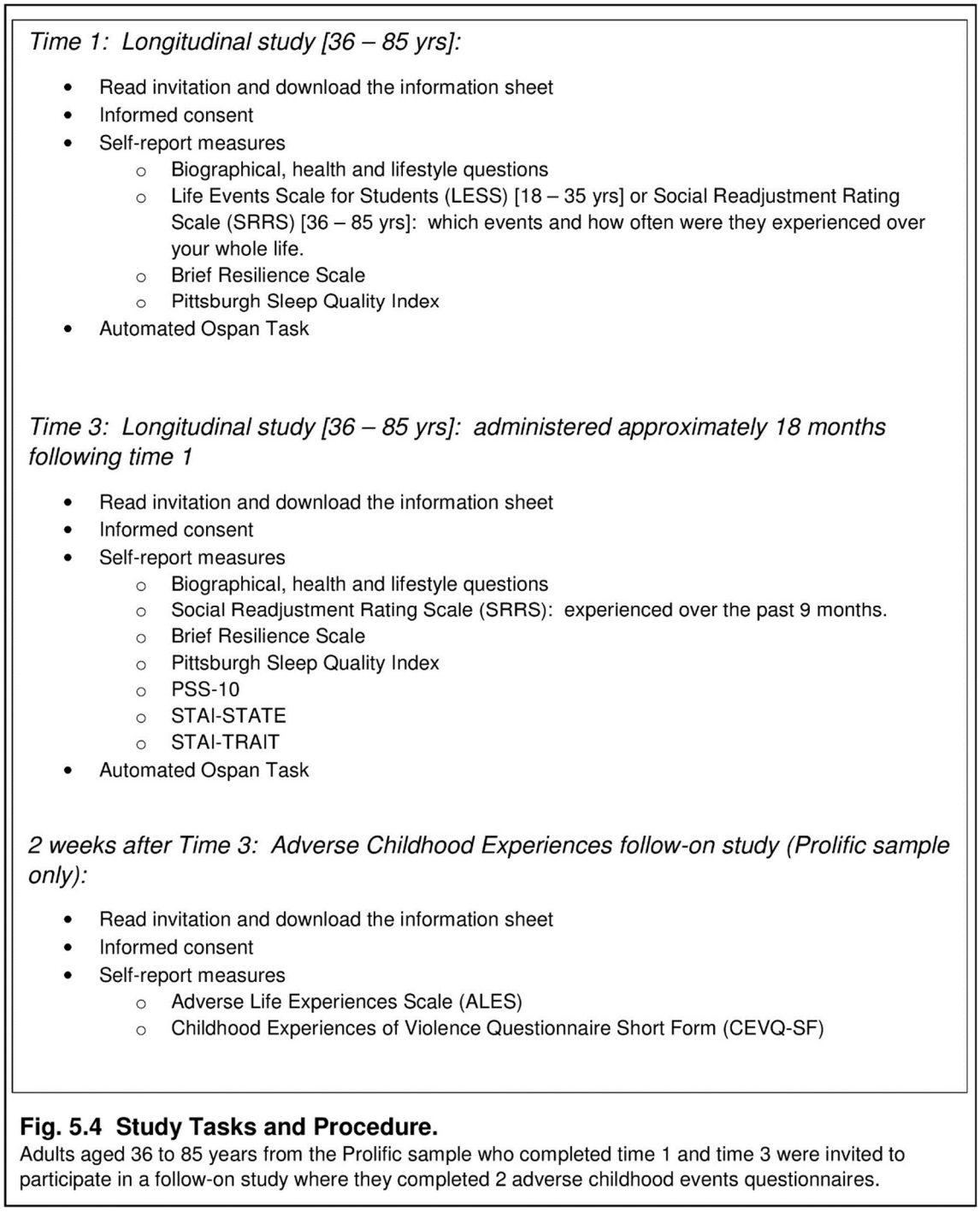

Fig. 5.4 Study Tasks and Procedure.
Adults aged 36 to 85 years from the Prolific sample who completed time 1 and time 3 were invited to participate in a follow-on study where they completed 2 adverse childhood events questionnaires.

5.2.4 Measures administered at Time 1, Time 2 and Time 3

5.2.4.1 Life events as a measure of cumulative stress

Cumulative stress was defined as the sum of the weighted life events experienced over a specified period of time. In this study, cumulative stress was measured over participants' whole lives and the

most recent 9 and 18 months. For YA the Life Events Scale for Students (LESS) (Clements & Turpin, 1996) was used, comprising 36 items. For the MA and OA the Social Readjustment Rating Scale (SRRS) (Holmes & Rahe, 1967) was used comprising 43 items (see Chapter 3 for full details).

For the whole life measure, the instructions given in both questionnaires were: '*Please indicate which of the following events have occurred in your life. If any event occurred more than once, provide the number of times the event occurred. If the event did not occur, choose zero*.' At time 2 and time 3, participants were asked to complete the respective life events questionnaire in relation to the last 9 months. All responses were converted to binary units and then multiplied by their given 'weight' or life change units (LCU) and summed to give a total LCU score for each participant for the respective period. Cumulative stress was measured over 3 time periods, therefore the measures were: life (LCU_{life}), 18 months ($LCU_{18mnths}$) and 9 months (LCU_{9mnths}).

For the LESS, scores ranged from 0 – 1849 and for the SRRS, scores ranged from 0 – 1466. Given the difference in ratings (and difference in number of items), LCU scores were converted to z-scores for between-groups comparisons.

5.2.4.2 Brief Resilience Scale

Participants' ability to recover from stressful events was measured with the Brief Resilience Scale (BRS) (Smith et al., 2008). Chapter 3 provides psychometric details. Participants self-reported the extent to which they agreed with 6 statements about their resilience on a scale of 1

('Strongly Disagree') to 5 ('Strongly Agree'). Better resilience is indicated by a higher mean score.

5.2.4.3 Subjective Sleep Quality

Self-reported sleep quality was measured with the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989). Chapter 3 provides psychometric details. The PSQI comprises 18 items asking participants about their overall sleep quality over the past month. There are 7 components: sleep quality, sleep latency, habitual sleep efficiency, sleep duration, sleep disturbances, day-time dysfunction and use of sleep medication. The PSQI yields a global score of 0 – 21, based on these components. Poorer sleepers are indicated by a score of > 5. Thus, a lower score indicates better sleep quality.

5.2.4.4 Cognitive Task: Automated Operation Span Task (A-Ospan)

The A-Ospan task (Unsworth et al., 2009) was used, downloaded from Millisecond and run with Inquisit software. The task requires participants to complete mathematical calculations whilst remembering a set of randomly presented letters (T, L, Q, N, F, H, Y, S, P, K, R, J) ranging in length or 'set size'. There are 5 set sizes, ranging from 3 to 7 letters. There were 3 trials per set, thus the test session comprised 15 trials giving a total of 75 letters and 75 maths problems. The order of set sizes was randomised. Each set was preceded by a maths calculation. Each A-Ospan trial therefore started with a maths calculation followed by a letter.

Prior to commencing the actual trials participants completed a comprehensive practice session. The practice introduced each of the components separately (letter recall and maths operations, respectively) and then combined them in a 3rd and final step to consolidate comprehension. The practice started with a simple letter span of up to 3 randomly chosen letters. Next, participants completed maths operations e.g. "(1*2)+1 =?". They were asked to solve each calculation as quickly as possible and use their mouse to click through to the next screen, which provided an answer e.g. '3' with 'True' or 'False' response options. Accuracy feedback followed each trial. The software calculated how long it took to complete these calculations. The average calculation time plus 2.5 SD then served as the time cap for completing the maths calculation per trial in the actual trials for each participant. The third set of the practice put the dual aspects of the task together. First, a maths operation was presented, the participant then clicked through to select True/False for the given answer, then the randomly selected to-be-remembered letter was presented. When a participant took longer than their mean time + 2.5 SD, the maths trial was recorded as a 'speed error' and the participant was automatically moved on to the letter component.

At the top right corner of the screen there was a running score in red with the participant's current accuracy, which had to be maintained at ≥ 85%. This value appeared in the final component of the practice session and throughout the actual trials. Participants received no feedback on errors during the task apart from this running accuracy value. See Unsworth et al. (2009) for a full description of the A-Ospan task.

Two accuracy measures were used: a) absolute span (A-Ospan: x/75) and b) letter recall percent correct (LR %correct: x/75*100). A-Ospan refers to the absolute span score, which measures WMC. It is an 'all-or-nothing' measure that includes recalled letters from fully correct sets only. Letter recall percent correct (LR %correct) refers to the partial-credit score measuring overall WM performance. Here, all letters correctly recalled in the correct position counted towards a summed total, regardless of whether the full set was correctly recalled. The partial-credit score was converted into a percentage.

To ensure validity of the dataset, as the data were collected online, participants were excluded who scored < 10% of the maximum A-Ospan score (7.5/75) or 100% (75/75) as both extremes reflect irregular performance. A very low score indicates that participants either did not understand the task or could not perform it. A perfect score is unlikely given the difficulty and time-pressured nature of the task. For example, in Đokić and colleagues's (2018) lab-based study < 1% of 497 participants obtained 75/75. To ensure that participants' processing capacity is maximised, the standard approach is to discard datasets where maths accuracy is < 85% (Conway et al., 2005). However, more recent studies demonstrated that participants' processing capacity is sufficiently engaged even when accuracy is lower or not controlled for at all (Đokić et al., 2018; Unsworth et al., 2009). The present results were assessed and data was excluded based on the approach used by the most recent studies.

Overall processing speed was measured as the time taken (in milliseconds) to select the correct letters from the 4 x 3 letter matrix. In

calculating participants' mean reaction time (RT) values only latencies for correctly chosen letters were included. Latencies assigned as 'exit', 'clear' and 'blank' were therefore removed as were incorrect letters.

To summarise, the dependent variable for WMC was A-Ospan while the dependent variable for overall WM accuracy was LR %correct. The dependent variable for processing speed was letter recall mean reaction time (RT).

5.2.5 Measures administered at Time 3 only

5.2.5.1 Perceived Stress

Stress perception was measured with the Perceived Stress Scale-10 (PSS-10) (Cohen et al., 1983; Cohen & Williamson, 1988). Chapter 3 provides psychometric details. The PSS-10 comprises 10 questions relating to how often certain thoughts and feelings had occurred in the last month on a 5-point Likert Scale. Responses ranged from 0 ('Never') to 4 ('Very Often'). Scores range from 0 to 40. A higher score indicates greater perceived stress.

5.2.5.2 Sub-clinical Anxiety

State and trait anxiety was measured with the Spielberger State-Trait Anxiety Inventory (STAI) Y Form (Spielberger, 1983; Spielberger et al., 1970). Chapter 3 provides psychometric details. The STAI-S comprises 20 statements focused on the intensity of feelings at the present moment. Item ratings range from 1 ('Not at all') to 4 ('Very much so'). The STAI-T comprises 20 statements focused on the frequency of feelings generally. Item ratings range from 1 ('Almost never') to 4 ('Almost

always'). Possible scores range from 20 to 80 on each scale (STAI-S, STAI-T). In either index, a higher score indicates greater anxiety (Spielberger, 1983).

5.2.6 Measures administered in the follow-on study

5.2.6.1 Adverse Childhood Experiences

Adverse Life Experiences Scale (ALES)

Hawes and colleagues (2021) constructed and validated the ALES, which extends the original 10 adverse childhood events derived by Felitti et al. (1998). The ALES indexes the developmental timing and occurrence of ACEs in parents and their children. This questionnaire was adapted by using only the 24-item portion of the ALES administered to parents in the ALES validation study and the time-frame was limited from birth to late adolescence (< 18 years). Appendix 1 provides a copy of this scale. Hawes et al. (2021) demonstrated good internal consistency ($\alpha = 0.86$) and test-retest reliability (ICC = 0.85) of the ALES caregiver scale and total ALES scores correlated significantly ($r = 0.38$, $p < .001$) with psychological distress (Hawes et al., 2021). Using this adapted version of the ALES allowed the timing and chronicity of a wide range of ACEs to be ascertained. The dependent variables were ACE chronicity and lifetime ACE. ACE chronicity was operationalised as the age-averaged sum of the number of age categories in which any risk factor item was reported to have occurred. Lifetime ACE was a cumulative measure accounting for the extent of ACEs experienced, operationalised as the sum of any ACEs reported (range: 0 – 23). This value achieved a Cronbach alpha of 0.64. The 24th item was 'other' and was not included in the validation process.

Childhood Experiences of Violence Questionnaire Short Form (CEVQ-SF)

Joshi et al. (2021) adapted 14 items from the Childhood Experiences of Violence Questionnaire Short Form (CEVQ-SF) (Tanaka et al., 2012; Walsh et al., 2008) to measure prevalence of ACEs. A copy is provided in Appendix 2. Test-retest reliability and validity were tested with adolescents aged 14 to 17 and demonstrated good internal consistency (α = .85) and moderate to good test-retest reliability (2-week test) (α ≥ 0.68) (see also Saini et al., 2019). The adapted version of CEVQ measured the frequency and severity of ACEs by asking participants to indicate how many times they had experienced items 1 to 11 on a 5-point Likert scale (never, 1-2 times, 3-5 times, 6-10 times, more than 10 times) and whether or not they had experienced items 12 – 14 (yes/no). These items were used to derive a severity index of 8 core ACEs: 'physical abuse', 'sexual abuse', 'emotional abuse', 'neglect', 'exposure to intimate partner violence', 'parental divorce/separation', 'death of a parent', 'living with family member/mental health problems'. The ACE severity index was derived by classifying a particular ACE as present or absent depending on the frequency or presence of certain events. For example, physical abuse was classified as present if participants reported ≥ 3 times for 'Did an adult slap you on the face, head or ears or hit or spank you with something hard to hurt you?', ≥ 3 times for 'Did an adult push, grab, shove or throw something at you to hurt you?' or ≥ 1 to 'Did an adult kick, bite, punch, choke, burn you, or physically attack you in some way?'. Appendix 3

provides the classification system for each core ACE as set out and applied by Joshi et al. (2021).

The variable for ACE severity, derived as described above, was operationalised as the sum of core ACEs experienced.

5.2.7 Procedure

At time 1, following informed consent, participants proceeded to the survey where they provided biographical details (age, sex) and answered questions regarding lifestyle and physical well-being. Next, they completed either the LESS (YA) or SRRS (MA, OA) and the resilience and sleep quality questionnaires. They were then notified that they would be transferred to “the cognitive task” (the A-Ospan) that would take approximately 20 minutes to complete. This process occurred automatically. In total, the study took approximately 50 – 60 minutes to complete. At time 3, participants additionally completed the PSS-10 and STAI-state and –trait questionnaires prior to the A-Ospan task. Completion time remained within 50 – 60 minute estimate as participants would be familiar with the study’s procedure and the life events questionnaires would take less time to complete.

5.2.8 Statistical Analysis

Descriptive statistics were calculated for all variables of interest. For Analysis 1, the cross-sectional study, a hierarchical regression analysis was performed to evaluate the relationships between the outcome variables (A-Ospan, LC %correct and RT) and the variables of interest (age, stress group, age x stress group interaction, BRS and PSQI). Sex

(male/female), average weekly alcohol in-take (units), average daily caffeine in-take (mg), average daily number of cigarettes smoked, BMI, chronic medical condition (yes/no) and physical disability (yes/no) were included as covariates. Preliminary analyses to test the assumptions of linearity, multicollinearity, normality and homoscedasticity were conducted prior to each hierarchical regression analysis.

In Analysis 2, the longitudinal analyses, McNemar tests were conducted on percentage change values to assess differences in WM performance over time between high and low stress participants, split by age. As with the cross-sectional analyses, the outcome measures were A-Ospan, LC %correct and RTs. Cumulative stress groups (high stress group vs. low stress group) were based on a median split derived from the mean SRRS scores, across time 1, 2 and 3, for the whole sample.

In Analysis 3, the longitudinal study investigated the association between ACEs, stress, ageing and changes in cognitive performance over 18 months with a hierarchical regression analysis. Difference scores (time 3 minus time 1) were used for all 3 outcome variables (A-Ospan; LR %correct; RT). In addition to age*cumulative stress, the impact of 3 ACE variables were measured: ACE chronicity, cumulative ACE and ACE severity along with their interactions with cumulative stress (chronicity*stress; lifetime*stress; severity*stress) on the 3 WM outcome measures. The aim of the latter was to assess whether the combined effect of cumulative stress and early adverse life experiences had a measurable association with cognitive performance. ACE chronicity represented the age-averaged sum of the number of age categories (≥ 0)

in which any risk factor item occurred. A higher value indicated that ACEs were experienced over a longer period of childhood (0 - 18 years) (Hawes et al., 2021). Cumulative ACE represented the sum of any ACEs reported (range: 0 – 23) (ibid). Adverse childhood events severity represented the sum of 0 to 8 types of ACEs experienced (range: 0 – 8) (Joshi et al., 2021). The latter represented how many different ACEs were experienced. As in Analysis 1, preliminary analyses to test the assumptions of linearity, multicollinearity, normality and homoscedasticity were conducted prior to each hierarchical regression analysis.

In all 3 analyses, parametric statistical methods were used where distributions were normal; otherwise the non-parametric alternative was used. Where possible, both frequentist and Bayesian outcomes were provided. Regarding the latter, Bayes factors (BFs) were reported when they differed from frequentist outcomes and subsequent conclusions were based on the BF outcome. Bayes factors provide an index of evidence on a continuous scale. They represent how many times more likely the data are under the alternative hypothesis (H1) than the null (H0). When this value is > 3.0, the evidence favours H1, values from 3.0 to 0.33 indicate inconclusive evidence and values < 0.33 favour H0. In the analysis, JASP 0.16.2 (2022) was used which has a default prior known as the Jeffreys–Zellner–Siow (JZS) Prior (Rouder et al., 2012; Rouder et al., 2017; Wetzels & Wagenmakers, 2012). The JZS has been empirically tested to be robust against the Jeffreys–Lindley–Bartlett paradox (see Wagenmakers & Ly, 2022 for definition and discussion). Taking this approach means applying a relatively weak prior model to the data, which

may be less sensitive to detecting possible effects. However, given that it was not known what was expected when including sleep quality, resilience and ACEs into the investigation, a broader approach was adopted to ensure any effects were detected. In interpreting the BF Wezels and Wagenmaker's (2012) BF classifications were applied, which offer a useful heuristic guideline (Wagenmakers et al., 2016; Wetzels & Wagenmakers, 2012).

5.3 Results

5.3.1 Analysis 1: Cross-sectional analysis

5.3.1.1 Preliminary A-Ospan Analyses

Initial inspection of the data revealed that 26 participants (YA 10, MA 12, OA 4) had to be excluded because their A-Ospan scores were <7.5, indicating that they either did not understand the task or could not perform it. A further 16 participants (YA 3, MA 8, OA 5) were excluded because they achieved a perfect A-Ospan score (75/75). One of these participants emailed to say that they had written down the letters as they proceeded through the task. Roughly 1% of the total sample (n=4) was expected to achieve a perfect score. Moreover, the A-Ospan distribution showed a spike at the upper tail, suggested an unexpectedly high number of perfect scores. For the avoidance of doubt, all participants scoring 100% were excluded.

The analysis revealed that recall performance positively co-varied with maths accuracy regardless of the cut-off. Refer to Fig. 5.5, which provides a scatter plot of percent correct for maths by recall, contrasting

those who achieved the 85% cut-off with those that did not. All datasets below the 85% cut-off were therefore retained.

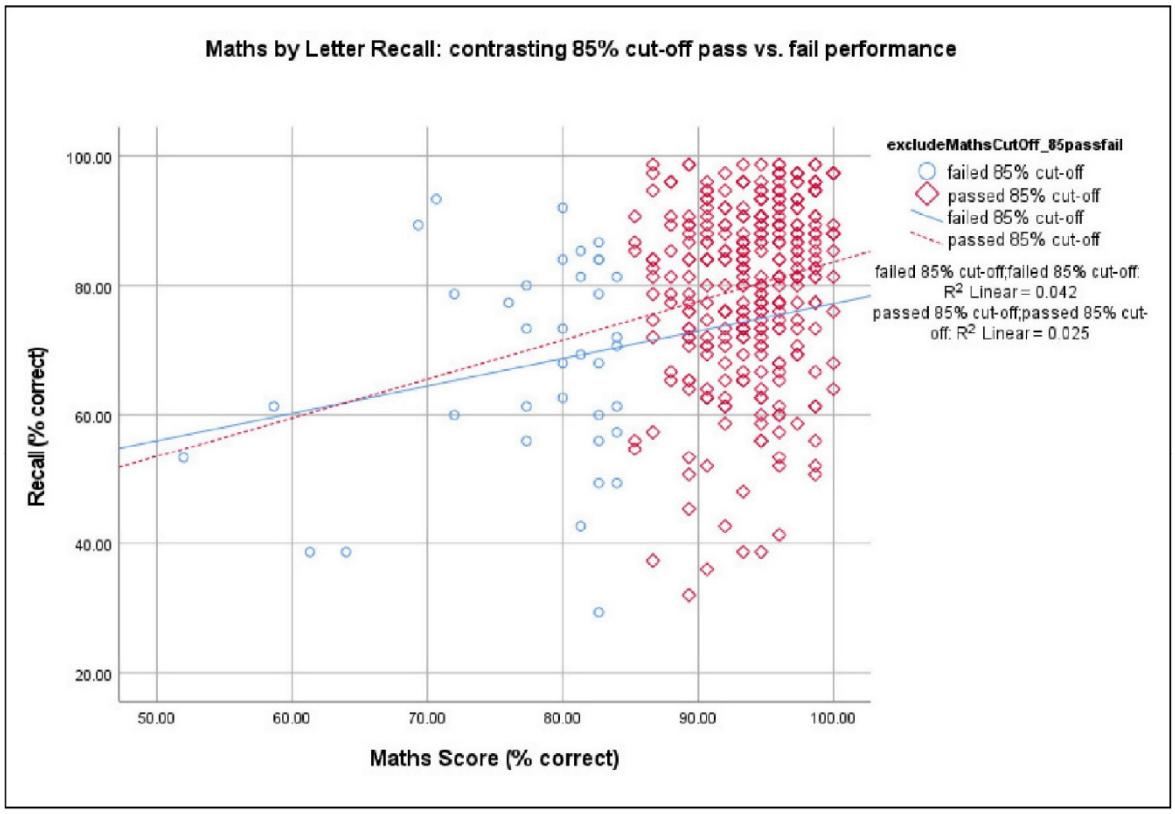

Fig. 5.5. Scatter plot showing a positive association between maths accuracy and recall accuracy independent of cut-off.

Prior to analysing the impact of cumulative stress, resilience and subjective sleep quality on WM, A-Ospan performance was tested for comparability across data sources (Prolific; members of the community; social media; online student recruitment platform) and study samples (longitudinal participants; single-session participants). A univariate ANOVA was conducted with A-Ospan and letter recall percent correct as respective dependent variables. Regarding data source there were no statistically significant main effects or interactions for either the A-Ospan or letter recall analyses (F's ≤ 1.550, p's > .1). Likewise, there were no

statistically significant main effects or interactions for either analysis (F's ≤ 1.466, p's > .2) comparing longitudinal and single-session groups. All samples were therefore combined and analysed as a single cross-sectional sample (N=351).

5.3.1.2 Biographical results by age group: resilience, sleep quality, lifestyle and health

The final cross-sectional (time 1) sample consisted of 351 participants, comprising 160 YA (M = 22.8, SD = 4.3, range = 18 to 35, 120 females), 103 MA (M = 47.1, SD = 6.8, range = 36 to 59, 67 females) and 88 OA (M = 67.4, SD = 4.9, range = 60 to 81, 51 females). Note that 10 of the OA participants also attended 'Study 1' (the Chapter 3 study).

Participants were compared based on age group. Table 5.1 provides descriptive and inferential statistical results.

Table 5.1 Time 1 sample's descriptive statistics and p-values for biographical, lifestyle, health and well-being, by age group.

	Time 1 Sample				
N = 351	**Young Adults**	**Middle-aged Adults**	**Older Adults**	**p-value**	**BF**
Age (years: mean (range))	22.8 (18 - 35)	47.2 (36 - 59)	67.4 (60 - 81)	-	-
Sex (m:f)	39:121	36:67	37:51	0.038[b]	9.04
Physical disability (yes:no)	7:153	6:97	11:77	0.047[b]	0.20
Chronic Illness (yes:no)	4:96**	17:83**	33:67**	<0.001[b]	>100
Body Mass Index (BMI: median (IQR))	22.9 (20.5-26.7)**	26.2 (22.7-31.8)	27.3 (23.5-30.2)	<0.001[c]	n/a[f]
Caffeine consumption, average daily (mg)[a]	117.7 (8.4)**	184 (12.42)	165.4 (14.15)	<0.001[c]	n/a[f]
Caffeine drinker vs. Non-drinker (yes:no)	114:46:00	88:15:00	69:19:00	0.026[b]	1.29
Smoker vs. Non-smoker (yes:no)	32:128	17:86	4:84	0.005[b]	11.28
Cigarette consumption, average daily (n: median (IQR))	2 (1 - 5)**	10 (4 - 15)	12.5 (8.5 - 18.8)	0.001[c]	n/a[f]
Alcohol drinker vs. Non-drinker (yes:no)	137:23:00	92:11:00	77:11:00	0.678[b]	0.03
Alcohol consumption, average weekly (units)[a]	3.4 (0.55)*	4.2 (0.73)	6 (1.01)*	0.332[c]	n/a[f]
Brief Resilience Scale[a]	3.08 (0.06)**	3.24 (0.09)	3.52 (0.09)**	<0.001[d]	n/a[f]
PSQI (global sleep score: md (IQR)	7 (5-9)**	6 (4-9)	5 (4-8)**	0.026[c]	n/a[f]
Cumulative Life Events Score (z Score)	0 (0.08)	-0.24 (0.1)	0.28 (0.1)	0.001[d]	n/a[f]
Life Events Scale for Students (LESS)[a]	694.14 (21.43)			-	-
Social Readjustment Rating Scale (SRRS)[a]		710.66 (19.2)	811.34 (18.59)	<0.001[d]	90.19

[a] Mean (SE).

[b] Pearson Chi-square.

[c] Kruskal-Wallis Test.

[d] One-way ANOVA (BCa Bootstrap with 2000 samples).

[e] Independent samples t-test (BCa Bootstrap with 1000 samples).

[f] A Bayesian equivalent test is not available in JASP.

Where statistically significant omnibus results were found, additional inferential tests were conducted. Follow-up equivalent-test BFs were also calculated and agreed with the frequentist results on most findings. Where this was not the case, details are given.

An independent samples t-test revealed that there were significantly more females (n=239) than males (n=112) overall (t(349) -3.508, p = .001). The equivalent Bayesian t-test similarly showed strong evidence (BF = 41.96). The significant chi square result reported for sex in Table 5.1 was followed up with additional tests. Comparing relative proportions of females/males by age-group, chi-square tests showed that the YA group had relatively more females than OAs (76% vs. 58%, respectively) ($\chi^2(1)$ 8.341, p = .004), but both these groups' proportion of females were comparable to those in the MA group (65%) (p's ≥ .07). Thus, there was a disproportionate number of female participants in the YA group (76% vs. 24%), whilst OAs showed the most comparable female/male split (58% vs. 42%). Bayes factors were fairly congruent, providing substantial evidence for a disproportionate number of females in the YA relative to the OA group (BF = 9.04), anecdotal evidence for a difference between YAs and MAs (BF = 0.78) and evidence supporting the null when comparing male/female proportions between MA and OAs was found.

Chi square tests revealed that the proportion of participants reporting a chronic illness/condition was significantly greater in OAs (33%) than MA (16.5%) and significantly greater in MAs than YAs (4.4%) with

results of (χ^2(1) 7.023, p = .008) (BF = 4.98) and (χ^2(1) 11.118, p = .001) (BF = 19.27), respectively. The difference was greatest for OAs relative to YA (χ^2(1) 37.370, p < .001) (BF > 100). Thus, reporting chronic illness is associated with age group with the greatest disparity between YA and OAs.

Table 5.1 shows significant differences for two continuous health and life-style indicators: BMI and caffeine consumption. Mann-Whitney U tests revealed that BMI was greater for MA (Mdn = 26.2) than for YA (Mdn = 22.9) (z = -3.686, p < .001) and greater for OA (Mdn = 27.3) than for YA (z = -4.824, p < .001). Likewise, Bayesian Mann-Whitney U tests revealed very strong evidence for both comparisons (BFs ≥ 56.29). There was no statistically significant difference between MA and OAs (p > .4) and the corresponding Bayesian test found anecdotal evidence (BF = 1.75). Regarding average daily caffeine consumption Table 5.1 shows a statistically significant difference between age groups (χ^2(2) n=351) 20.162, p < .001). Follow-up Mann-Whitney U tests revealed that caffeine consumption was greater among MAs (Mdn = 169 mg/day) than YAs (Mdn = 93 mg/day) (z = -4.326, p < .001) and greater among OAs (Mdn = 149 mg/day) than YAs (z = -2.784, p = .005). Bayesian Mann-Whitney U tests agreed with the MA vs. YA frequentist result (BF > 100) but showed anecdotal evidence for the YA vs. OA comparison (BF = 2.09). Consumption levels were comparable between MA and OAs (p = .257) (BF = 0.25). Though consumption was highest amongst MA individuals it was well within safe consumption limits of 400 mg/day as set out by the

European Food Standards Agency (2015). These sets of results showed that there was an age-related difference in BMI and caffeine consumption.

The highest proportion of caffeine consumers was the MA group (85.4%) followed by OAs (78.4%) and YAs (71.3%). Table 5.1 indicates significant differences comparing proportions of caffeine consumers per age group though the BF indicated anecdotal evidence. Follow-up chi square tests revealed a significant association between age and proportion of caffeine consumers for YA vs. MAs only, with fewer YA consumers relative to MAs ($X^2(1)$ 7.080, p = .008) (BF = 4.86). There were no significant associations between proportion of caffeine consumers and age group for YA vs. OA (p = .220; BF = 0.30), nor MA vs. OA (p = .206; BF = 0.30).

The highest proportion of smokers was among YAs (20%) followed by MAs (16.5%) and OAs (4.5%). Chi-square tests revealed a significant association between age group and proportion of smokers for MA vs. OAs and for YA vs. OAs. In the latter comparison, there were significantly more smokers in the YA relative to in the OA group ($X^2(1)$ 10.928, p = .001) (BF = 47.3). Likewise, there were significantly more smokers in the MA than OA group ($X^2(1)$ 6.936, p = .008) (BF = 3.86). There was no association for YA vs. MAs (p > .4; BF = 0.16). Only 15% of the whole sample were smokers and average number of cigarettes smoked per day across the sample was very low (M = 1.04, SE = 0.19). A Kruskal-Wallis test comparing number of cigarettes smoked per day among smokers only revealed a statistically significant difference between groups ($\chi^2(2,n=53)$ 15.106, p. = .001. Follow-up Mann-Whitney U tests revealed a statistically

significant difference between YAs and MAs ($z = -3.327$, $p = .001$) with higher consumption among MA individuals on average. However, the Bayesian Mann-Whitney U supported the null (BF = 0.17). Similarly, the YAs vs. OAs comparison was statistically significant ($z = -2.615$, $p = .009$), but the Bayesian test again supported the null (BF = 0.31). The MAs and OAs were comparable to ($p > .4$; BF = 0.35).

No evidence was found of differences between groups for average weekly alcohol consumption and number of alcohol drinkers vs. non-drinkers. Average alcohol consumption across groups was well below the recommended 14 units/week (M = 4.31, SE = 0.44). This was driven by females (n=239) who drank, on average, about half as much as males (n=112) (Mdn = 0.75, IQR: 0.25 – 3.5 vs. Mdn = 1.5, IQR: 0.25 – 6, respectively). Fig. 5.6 displays significant age group differences for the main variables of interest: BRS, PSQI and cumulative stress (z-scores derived from respective LESS and SRRS scores).

Fig. 5.6. Tukey tests following a statistically significant one-way ANOVA finding comparing BRS scores by age ($F(2,348)$ 8.137, $p < .001$) indicated that OA (M 3.52) were more resilient than YA (M 3.08)($p < .001$). The likewise BF supported this result with decisive evidence ($BF > 100$). There was a trend to significance for the MA (M 3.24) vs. OA (p .057) with anedotal evidence ($BF = 1.49$) reflected by the Bayesian analysis, but no significant difference between MA and YA ($p > .2$). The likewise BF indicated anecdotal evidence ($BF = 0.47$). These results suggest relatively better resilience with increasing age specifically when comparing YA and OA. A statistically significant Kruskal-Wallis Test comparing PSQI scores by age group, revealed a significant difference between groups (χ^2 (2, n =351) 7.322, p .025). Follow-up Mann-Whitney U tests revealed a statistically significant difference between YA and OA with YA reporting poorer sleep quality (Mdn = 7) than OA (Mdn = 5). Comparisons for YA vs. MA and OA vs. MA were not statistically significant (p's ≥ 0.066). Note that likewise BF Mann-Whitney U comparisons revealed anecdotal evidence at best for all comparisons, suggesting similar levels of sleep quality across groups ($2.02 \leq BF \geq .17$). A one-way ANOVA comparing cumulative stress levels across age using z-scores revealed a statistically significant difference ($F(2,348)$ 6.763, $p = .001$) with post hoc Tukey tests indicating that MA experienced significantly less stress compared to OA ($p = .001$), supported by very strong Bayesian evidence ($BF = 91.57$). Comparisons between YA and OA and between YA and MA were comparable (p's ≥ .078; BFs ≤ 1.40).

5.3.1.3 Main Analysis: Hierarchical Linear Regression

Following preliminary analyses ensuring that all assumptions regarding linearity, normality, collinearity and homoscedasticity were met, a sequence of hierarchical linear regressions was conducted, one for each WM outcome measure. Cigarette consumption was excluded from these analyses because few participants smoked resulting in mostly zero entries. In the first of three hierarchical linear regression analyses the effect of age, cumulative stress, the age by cumulative stress interaction was assessed as well as subjective sleep quality and self-reported

resilience on WMC (A-Ospan). Sex, lifestyle and health factors were entered as covariates. In the first step the original predictors were entered: age, stress group (LS 0; HS 1), which explained 1% of the variance and was not statistically significant ($F_{\Delta}(2,277) < 1$). In step 2 the age*stress interaction was added, which increased the variance explained to 2% and was not statistically significant ($F_{\Delta}(1,276) < 1$). For the interaction, age was centred on the group mean before being multiplied by either 0 (LS) or 1 (HS). In step 3 PSQI and BRS were entered, which increased the variance explained to 3% and was not statistically significant ($F_{\Delta}(2,274) < 1$). In step 4 all covariates were added: sex (females 1; males -1), average weekly alcohol consumption (units/week), caffeine consumption (mg/day), BMI (weight_kg /(height_cm * height_cm)*10000), physical disability (no 0; yes 1) and chronic medical condition (no 0; yes 1), which increased the variance explained to 4%. Thus, the full model explained only 4% of total variance and was not statistically significant ($F_{\Delta}(6,268) < 1$). The model therefore does not serve to explain WMC. In the likewise analysis with LC %correct the full model explained 6% of the variance ($F_{\Delta} < 1$). A Bayesian multiple linear regression was conducted including only continuous variables (i.e. stress group, sex, disability and CI were excluded), which presented the same outcome (BF < 3) with a null model indicated as the best fit for the data (BF = 0.95).

In the RT analysis, the first step (age, stress group) was statistically significant and explained 21% of the total variance ($F(2,277)$ 36.182, $p < 0.001$). There was no change with step 2 and adding the 3rd and 4th steps increased the total variance explained to 22% and 23%, respectively. No

steps after step 1 were statistically significant (p's ≥ .302). Thus, only the first model was statistically significant and positive, indicating that an increase in age was associated with slower RTs. Inspecting the individual beta values, age was statistically significant across all models (betas ≥ 0.432, p's < 0.001). In model 1 there was a slowing effect of 14.69 ms (SE = 1.73) per added year of age. For models 2 to 4 these values were 13.85 ms (SE = 1.91), 14.32 (SE = 1.95) and 14.16 (SE = 2.20), respectively.

In summary, these results indicate no linear association between WMC or accuracy with any of the predictive variables or covariates. There was clear evidence of a consistent, positive association between slower RTs and increasing age.

5.3.1.4 Discussion: Cross-sectional Analysis

The aim of the cross-sectional analysis (Analysis 1) was to investigate the impact of a range of psychological, life-style and health variables on WM performance. The main finding was that increasing age was associated with a slowing of reaction time. No other significant associations were found between WMC or accuracy and the variables of interest or covariates and no evidence of an interaction effect of age and cumulative stress on any aspect of WM performance measured. Thus, apart from an expected age-related slowing effect on processing speed, this large sample revealed no overall impact of health, lifestyle or psychological factors on WM performance.

That no significant age by cumulative stress interaction was found for any of the WM indices, with a larger sample (n=351), using a different

well-validated task, strongly suggests that cumulative stress, as measured with the Social Readjustment Rating Scale, does not accelerate cognitive ageing. If the effect of cumulative stress exists but is very small (as estimated in the previous chapter), then, one would require a sample ≥ ~220 with a power of .80 to show such an effect. The sample used here was therefore sufficient in size to have shown this effect. The finding that RTs were relatively slower for older participants replicates the findings from Chapter 3 and aligns with existing evidence that processing speed declines with age discussed in previous chapters (Salthouse, 1994, 1996; Verhaeghen, 2013). However, there was no corresponding reduction in accuracy or capacity, suggesting that functional connectivity was relatively unaffected by ageing and stress in the sample. Functional connectivity, has been found to be more predictive of executive function than structural connectivity (Dhamala et al., 2021). It is important to point out that there is overall evidence showing a small differential age-related effect on WMC as demonstrated in a recent meta-analysis, despite a wide range of conflicting dual-task and complex span task findings (Jaroslawska & Rhodes, 2019).

Both the Bayesian and frequentist analyses showed that neither subjective sleep quality nor resilience were associated with WM performance. The OAs reported slightly better sleep quality than MA and YA groups, however this difference was only significant relative to YAs. Based on Buysee's clinical distinction of 'good' vs. 'poor' sleepers, the YA group experienced clinically poor sleep over the past month, which can negatively affect executive function (e.g. Ratcliff & Van Dongen, 2018).

However, the literature is inconsistent as mentioned previously. A study by Ling and colleagues (2020) who investigated the effects of insomnia and short sleep duration on WM in young people (12 – 24 yrs), found no evidence of an effect of insomnia or short sleep duration on their dual n-back or episodic memory tasks. They did find, however, that insomnia reduced performance on both components of the digit span task. These findings suggest that whilst sleep quality is important, YA are able to cope sufficiently with reduced sleep duration and insomnia symptoms on more complex WM tasks. As with sleep quality, self-reported resilience was significantly higher in OAs than YAs. This result is congruent with previous work arguing that the capacity for resilience develops over time, based on person-environment interactions (Fletcher & Sarkar, 2013). This study, being observational in nature, is limited in the conclusions that can be drawn. Physiological measures of stress and sleep alongside an experimental study design would be needed to investigate whether the YAs' WM performance was moderated by poorer sleep and/or lower levels of resilience.

5.3.2 Analysis 2: Longitudinal analysis

5.3.2.1 Biographical results by age group:

Of the 351 participants in the cross-sectional analysis, 108 MA and OAs had accepted the invitation to participate in the longitudinal study. Of 108 participants, 83 completed time 2 and 84 completed time 3. Some participants missed time 2, but completed time 3 or vice versa. All participants who completed time 2 and/or time 3 completed time 1. Five

participants were excluded in each session who scored either < 7.5/75 or 75/75, leaving a final total of 78 time 2 and 79 time 3 participants. Given the high rate of attrition with many missing data-points, only full datasets were analysed, with a final sample of 53, comprising 25 MAs (M = 48.6, SD = 6.7, range = 38 to 59, 13 females) and 28 OAs (M = 68.3, SD = 5.5, range = 59 to 61, 14 females). The within-groups sample sizes were too small to provide a reliable result for any analysis by age group as initially planned (MA_n = 25, OA_n = 28), therefore all analyses were conducted with the total sample. Table 5.2 provides the descriptive statistics for the analysed sample.

Table 5.2 Longitudinal samples' descriptive statistics and p-values for biographical, lifestyle, health and well-being, by age group for time 1, time 2 and time 3.

	Time 1 (N=53)		Time 2 (N=53)		Time 3 (N = 53)	
	Middle-aged Adults	**Older Adults**	**Middle-aged Adults**	**Older Adults**	**Middle-aged Adults**	**Older Adults**
Age (years: mean (SD))	48.64 (1.36)	68.3 (1.06)	48.24 (1.34)	67.89 (1.02)	49.04 (1.3)	68.71 (0.99)
Sex (m:f)	12:13	14:14	12:13	14:14	12:13	14:14
Body Mass Index (BMI: median (IQR))	26.53 (22.28 - 30.11)	27.97 (23.51 - 30.12)	26.53 (21.84 - 31.14)	27.16 (23.51 - 31.02)	26.9 (22.39 - 30.52)	27.77 (23.46 - 30.32)
Smoker vs. Non-smoker (yes:no)	04:21	00:28	04:21	00:28	03:22	00:28
Cigarette consumption, average daily (n)[a]	1.5 (0.9)	0 (0)	1.4 (0.9)	0 (0)	0.6 (0.3)	0 (0)
Alcohol drinker vs. Non-drinker (yes:no)	24:01:00	28:00:00	22:03	28:00:00	23:02	27:01:00
Alcohol consumption (weekly units in-take)[a]	5.31 (1.48)	5.82 (1.8)	4.97 (1.75)	5.21 (2.04)	6.55 (2.36)	5.18 (1.86)
Caffeine drinker vs. Non-drinker (yes:no)	21:04	23:05	17:08	24:04:00	19:06	25:03:00
Caffeine (typical daily mg in-take)[a]	175.52 (24.25)	179.5 (24.3)	132.48 (22.42)	193.71 (25.85)	142.8 (22.7)	181.75 (23.35)
Physical disability (yes:no)	00:25	01:27	01:24	03:25	00:25	00:28
Chronic Illness (yes:no)	02:23	07:21	05:20	06:22	06:19	09:19
Brief Resilience Scale[a]	3.62 (0.14)	3.51 (0.13)	3.68 (0.13)	3.5 (0.1)	3.77 (0.13)	3.53 (0.12)
PSQI (global sleep score: md (IQR)	5 (3.5 - 7)	5 (4 - 8.5)	5 (4 - 5.5)	6 (4.25 - 8)	4 (2 - 5)	4 (3 - 6.75)
STAI- state[a]					31.88 (1.79)	34 (1.96)
STAI- trait[a]					36.6 (1.87)	36.61 (2.02)
PSS10[a]					15.84 (1.08)	15.93 (1.26)
Cumulative Life Events Score (Summed: Mdn (IQR)) by age by time	682 (621 - 790.5)	774.5 (627 - 893)	705 (631 - 795.5)	788 (693.75 - 893)	755 (631 - 811)	817.5 (709.3 - 907.3)

[a] Mean (SE). Standard error obtained via BCa Bootstrap with 1000 samples.

5.3.2.2 Main Analysis: McNemar Tests

McNemar tests were used to assess whether changes in participants' performance over time co-varied with being high or low in cumulative stress in the outcome variables: A-Ospan, LC %correct and RT. Frequency breakdowns are presented indicating the frequency of improved/deteriorated participants by time by age group in Table 5.3. Three sets of percentage change outcomes were measured per WM performance index applied to the whole sample (n=53) only: time 1 to time 2, time 2 to time 3 and time 1 to time 3, each test comprising a 2 x 2 matrix. Participants showing no change in score were included with those who had deteriorated because ≤ 2 participants per age group showed no change in performance. Cumulative stress groups (high stress group vs. low stress group) were based on a median split derived from the mean SRRS scores, across time 1, 2 and 3, for the whole sample (Mdn = 742, IQR 668 – 847). No differences were found in any of the frequentist (χ^2's ≤ 3, p's ≥ .167) or Bayesian comparisons (BF's ≤ 2.76), indicating that any change in WM performance over time was unrelated to high vs. low levels of cumulative stress.

Table 5.3 McNemar Contingency Table comparing proportion of high vs. low stress participants who improved vs. deteriorated over time.

		A-Ospan		Letters Correct		Letters Correct RT	
	Percentage change	high stress group	low stress group	high stress group	low stress group	high stress group	low stress group
time 1 to time 2	deteriorated	12	13	12	13	14	16
	improved	14	14	14	14	12	11
time 2 to time 3	deteriorated	18	17	17	17	12	15
	improved	8	10	9	10	14	12
time 1 to time 3	deteriorated	16	14	15	13	13	21
	improved	10	13	11	14	13	6

5.3.2.3 Discussion: Longitudinal Analysis

The aim of the longitudinal study was to explore, over an 18-month period, whether any changes in WM performance in middle-aged and older-aged adults were associated with different levels of cumulative stress, age, their interaction, resilience and/or sleep quality. Only 35% and 36% of the longitudinal sample were eligible for time 2 and time 3 analysis, respectively, limiting the analysis to conducting simple McNemar comparisons for each outcome measure. The results showed that percentage changes in WM performance over time were not associated with high vs. low cumulative stress levels. However it is noted that even for a simple McNemar analysis, this sample was very small because of attrition.

5.3.3 Analysis 3: Adverse Childhood Experiences (ACEs) follow-on study

The sample size was small (n=46) relative to the number of comparisons planned, therefore the age*cumulative stress interaction was

not analysed nor any covariate associations. Consequently, a high vs. low cumulative stress median split was calculated based on the total sample (Mdn = 744,50, IQR: 629.6 – 828.5).

5.3.3.1 Biographical results by age group:

Table 5.4 shows the biographical details of the analysed sample. Descriptive statistics by age by stress group using the total sample median split are provided in Appendix 4.

Table 5.4. Longitudinal Adverse Childhood Experiences samples' descriptive statistics for biographical, lifestyle, health and well-being, by age group.

ACE participants who completed time 1 and time 3 (N=46)

	Low Stress (n=23)	High Stress (n=23)
Age (years: mean (SD))	58.3 (11.3)	62.8 (8.6)
Sex (m:f)	11:12	13:10
Body Mass Index (BMI: mdn (IQR))[b]	25.1 (21.6 - 32.4)	28 (24.2 - 32.6)
Smoker vs. Non-smoker (yes:no)	21:2	22:1
Cigarette consumption, average daily (n)[a]	0.89(0.54)	0.24(0.24)
Alcohol drinker vs. Non-drinker (yes:no)	2:21	4:19
Alcohol consumption (weekly units in-take)[a]	7.59(2.1)	5.22(2.06)
Caffeine drinker vs. Non-drinker (yes:no)	6:17	4:19
Caffeine (typical daily mg in-take)[a]	155.28(24.61)	164.87(19.35)
Physical disability (yes:no)	0:23	1:22
Chronic Illness (yes:no)	17:6	18:5
Brief Resilience Scale[a]	3.76 (0.14)	3.55 (0.15)
PSQI (global sleep score: mdn (IQR)[b]	4.5 (2.5 - 6.5)	5.5 (4 - 8.5)
STAI- state[c]	33.65 (2.35)	33.87 (2.46)
STAI- trait[c]	36.22 (2.33)	37.78 (2.35)
PSS10[c]	15.78 (1.39)	16.35 (1.45)
Cumulative Life Events Score (mdn (IQR))[d]	610.51 (23.93)	863.34 (23.48)
Cumulative ACEs (0 - 8: mdn (IQR))	2 (1 - 3)	2 (1 - 3)
Lifetime ACE score (0 - 23)	2.96 (0.46)	4.17 (0.6)
Age-corrected Chronicity Index (higher value = increased chronicity)	0.09 (0.01)	0.12 (0.02)

.All dichotomous variables represent time 3

[a] Mean of time 1 and time 3 (SE). Standard error obtained via BCa Bootstrap with 1000 samples.

[b] Median and interquartile range based on Mean(time1,time3).

[c] Values collected at time 3 only. Mean (SE). Standard error obtained via BCa Bootstrap with 1000 samples.

[d] Total life change units value comprising the sum of time 3 value and time 1 value.

5.3.3.2 Main Analysis: Hierarchical Linear Regression

The association between age, cumulative stress, ACEs (cumulative ACE, ACE chronicity and ACE severity), ACE by stress interactions (cumulative ACE *stress; ACE chronicity*stress; ACE severity*stress) and WM performance was measured using hierarchical linear regressions. Recall that WM was measured using difference scores (time 3 minus time 1) for each of the 3 outcome indices. For the interactions, ACE variables were centred on their grand means while the sample's cumulative stress

scores were centred on their median before being multiplied. The preliminary analyses showed that all regression assumptions were met for the A-Ospan and LC %correct variables but the mean RT variable violated the linearity assumption, therefore median RTs were analysed instead.

For the A-Ospan analysis, in the first step the predictors were entered: age (mean [time 1,time 3]), SRRS score (mean[time 1, time 3]), cumulative ACE, ACE chronicity and ACE severity which explained 2% of the variance. In step 2, the interactions were added to evaluate their contribution to the overall model: cumulative ACE score*stress; ACE chronicity*stress; ACE severity*stress, which increased variance explained to 6%. The full model was not statistically significant ($F(7,38) < 1$), suggesting that there was no significant association between WM capacity, cumulative stress, age, ACEs nor any interactions between ACEs and stress. The Bayesian multiple linear regression analysis, with the same variables as above entered together, indicated that the null model was the most appropriate (BF = 11.26), though there was anecdotal evidence for the stress by cumulative ACE interaction model (BF = 0.53). All other models yielded evidence for the null (BFs ≤ 0.32). The LC percent correct analysis, the final model explained 7% of the total variance and was not statistically significant ($F(7, 38) < 1$). The Bayesian multiple linear regression analysis supported the null model (BF = 11.27) with anecdotal evidence for the stress by cumulative ACE interaction (BF = 0.46) and age (BF = 0.34) models, though these are bordering on the null. The median RT HLR final model explained 11% of the total variance and was not statistically significant ($F(7,38) < 1$). The Bayesian linear regression

revealed support for the null model (BF = 8.71). There was anecdotal evidence for the age (BF = 0.42), ACE chronicity (BF = 0.42) and ACE severity models (BF 0.40). Taken together, neither WM capacity, accuracy nor RT performances were significantly associated with ACEs, age or cumulative stress. Bayesian outputs produced broadly comparable findings with most BFs supporting the null or anecdotal, bordering on the null.

5.3.3.3 Discussion: ACE Study

The study showed no evidence of an association between age, ACEs, cumulative stress or their interactions over an 18 month period with any aspect of WM performance. Covariates were not included, given the small size of the sample and given that these had not had an impact on the initial larger cross-sectional sample.

5.4 General Discussion

This chapter aimed to assess whether ageing, cumulative stress, subjective sleep quality, ACEs and/or resilience were associated with WM accuracy, capacity and/or processing speed. To this end, a complex span task was used to deepen the understanding of different aspects of WM function that might be affected, particularly in light of the findings in the previous chapters relating to the effects of cumulative stress. The investigation included both cross-sectional and longitudinal analyses of the variables of interest. Overall, these studies indicated that RT slowed with increasing age, which is congruent with current evidence (Salthouse,

1996; Verhaeghen, 2013). No detectible evidence was found of an effect of cumulative stress, ageing nor their interaction on any aspect of WM. Similarly, no indication was found that sleep quality or resilience were related to WM performance, but it is noted that levels of resilience improved with age. Interestingly, no association was found between ACEs and WM. No evidence was found of an association between the combined effect of ACEs and cumulative stress, and WM.

This study has shown that there were no detectable associations between the variables of interest and WM over an 18-month period with the sample sizes used. This finding was consistent using both frequentist and Bayesian statistical analyses. This study provides evidence that, if there is an effect, it is likely to be small or apparent only over a longer time period. In addition, this study was the first in many respects and consequently used a weak Bayesian prior model, which may require a larger sample to compensate for a lack of sensitivity. Future studies will be able to use an informed prior based on this study, which would improve their statistical power.

5.5 Supporting Information

Appendix 1	Adverse Life Experiences Scale (ALES).
Appendix 2	Childhood Experiences of Violence Questionnaire short form (CEVQ-SF).
Appendix 3	Core ACE classifications.
Appendix 4	Longitudinal Adverse Childhood Experiences samples' descriptive statistics for biographical, lifestyle, health and well-being, by age group.

A section containing all appendices can be found starting from page 395, at the end of this thesis.

Chapter 6: note to the examiners.

Chapter 6 has been submitted for publication with the following title and authors:

The Social Readjustment Rating Scale: updated and modernised

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Chapter 6: The Social Readjustment Rating Scale: updated and modernised.

6.1 Introduction

The Social Readjustment Rating Scale (Holmes & Rahe, 1967) was used throughout this thesis. It was introduced in 1967 and contains some out-dated elements. However, despite numerous updates the original version is still in use. This thesis also used the original version to be consistent with Marshall et al.'s (2015) study and other literature. An updated version that is compatible with the original version would have been used if it were available. This chapter therefore seeks to address this limitation by providing a modernised version and allows for comparisons with the original, referred to hence-forth as 'backwards-compatible'.

The Social Readjustment Rating Scale (SRRS) is a 43-item list of typically experienced life change events commonly used by researchers interested in the impact of stress on health and well-being. It was designed to predict the allostatic load (physiological cost) of the transient social adjustment required when certain life events occur (e.g. marriage, traffic ticket or a loan). It is well-validated and is cited in over 6000, widely varied, scientific publications. For example, it has been used to measure the association between experienced stress and accelerated cognitive ageing (Marshall & Cooper, 2017; Marshall et al., 2016; Marshall et al., 2016b; Marshall et al., 2015), to measure suicide risk (Blasco-Fontecilla et al., 2012) and to evaluate the impact of stress severity on dermatitis (Wardhana et al., 2020). The life events were chosen based on sound

empirical evidence (see references 1-12 cited in Holmes & Rahe, 1967) that is arguably still relevant today (e.g. Hulbert-Williams & Hastings, 2008; Jiang et al., 2020; Salleh, 2008; Scully et al., 2016). Numerous updates to the rating norms and modifications to the scale items have been undertaken (Hobson & Delunas, 2001; Hobson et al., 1998; Miller & Rahe, 1997; Muhlenkamp et al., 1975; Scully et al., 2016) to address validity and reliability concerns (e.g. Cleary, 1981; Cooper et al., 2006; Murphy & Brown, 1980) yet many researchers still use the original version (e.g. Dong et al., 2020; Marshall et al., 2015; Sesar et al., 2021). A brief history of the SRRS' development is provided, highlighting reasons for updates and modifications and why these may have failed to persuade researchers to deviate from the original. The proposed updates are then outlined.

The SRRS evolved from the Schedule of Recent Life Events (SRE) (Hawkins et al., 1957; Rahe, 1978) which captures a broad spectrum of 42 positively and negatively valenced items which require some level of social readjustment, desirable or undesirable, life-changing or minor (Amundson et al., 1989). Social readjustment refers to the amount and duration of change in one's usual routine resulting from various life events. Holmes and Rahe's SRRS comprised the 42 SRE items plus "Christmas". Holmes and Rahe's (1967) SRRS study revealed marked similarity between sub-groups in terms of the relative significance of the life events (e.g. 'marriage' vs. 'death of a spouse'), indicating some level of universal agreement for certain experiences. The primary aim of the SRRS was to improve the precision with which the impact of life events on illness onset

was measured. Each item has an averaged weighting based on the estimated magnitude of change assigned by a convenience sample of 394 males (179) and females (215) who varied in age, class, education, marital status, religion and race. The raters were asked to rate the magnitude of social readjustment required for each life event irrespective of the desirability of the event, using all their experience as well as what they had learned to be the case for others, *relative* to the social readjustment needed after marriage. Marriage served as the anchor item with an arbitrary value of 500. The weight for each item was then derived by taking the raters' average weight and dividing by 10. These weights represent 'Life Change Units' (LCU). This set of 43 LCUs provide a set of norms that accompany the SRRS. Social Readjustment Rating Scale respondents would indicate which of the 43 items they have experienced over a certain time-frame (e.g. the previous 12 months). All the LCUs corresponding to the respective items are then summed to produce a total LCU value, which may be used to predict physiological and/or psychological impact for each respondent. For example, a respondent might tick "Death of Spouse" which is 100 LCUs, "Troubles with the boss" (30 LCUs) and "Change in residence" (32 LCUs) giving a total of 162 LCUs. Based on empirical work, Rahe (1972) found that a score of about 150 suggested that the respondent would remain healthy over the next 12 months while those falling ill over the same period were typically found to score > 300.

The SRRS and SRE were applauded for adding an objective element to the study of life stress and its impact on health. However it was also argued that it was inherently flawed because the event items were not

equally well-comprehended by less educated samples (e.g. Komaroff et al., 1968) and the accuracy of event-reporting varied (Cooper et al., 2006). Furthermore, operationalising “illness” and “life events” are difficult (Sarason et al., 1975). One review indicated life events likely explained no more than 9% of illness variance (Rabkin & Struening, 1976) and Rahe and colleagues themselves stated that precipitating stressful life events were a necessary but not sufficient antecedent to illness onset (Rahe et al., 1964). Researchers have sought to address some of these and other concerns as described below.

Muhlenkamp and colleagues (1975) noted that the SRRS normative sample did not include those over age 70. They published an extension, providing independent ratings from a sample (N=41) of 65 to 84 year olds and modified the instructions by assigning a value of 50 for marriage, rather than 500, to provide a more meaningful and familiar anchor for participants. Raters gave higher ratings for most items relative to the original but there was significant agreement regarding the rank ordering of items. However, these weights were never used in conjunction with any subsequent application of the SRRS by researchers including Miller and Rahe’s (1997) update, which replicated the characteristics of the original sample. Moreover, no further validation was undertaken of Miller and Rahe’s (1997) update, which may have hindered its adoption in future studies. To my knowledge, researchers have sought only to apply the original weights though modifications to the scale items were undertaken on an ad hoc basis. For example Komaroff et al. (1968) substituted

“marital reconciliation with spouse” with “getting back together” as it was more meaningful to the target population.

Hobson and colleagues (2001, 1998) addressed sample and content criticisms of the original SRRS with an extended, modified “Social Readjustment Rating Scale Revised” (SRRS-R). To address the SRRS’ outdated and insufficiently representative sample the SRRS-R was based on norms derived from a larger sample (n=3122), representative of a cross-section of Americans regarding age, race, gender, ethnicity, income and geographical location. To address criticisms around content, Hobson and colleagues asked a 30-member expert panel to add, amend or remove existing items, which produced a 51-item scale. Other criticisms were that some SRRS items can be interpreted as symptoms/outcomes rather than precipitating events - the ‘contamination hypothesis’ - e.g. “Change in sleeping habits” could indicate that a new job, like shift work, (precipitating event) has occurred or it could indicate the symptom/outcome of a stressful experience. Some items lack representativeness in modern, multi-cultural societies (e.g. “Christmas”) and some items’ wording is ambiguous, biased or out-dated (e.g. “Mortgage or loan greater than $10,000”). Using their extended, modified scale, Hobson et al. (1998) found that there were significant differences in the way individuals evaluated the stressfulness of different events. On this basis they concluded that using simple unitary weights (occurred vs. not occurred) risked masking these differences and that further work needs to assess the impact of using group-based weights vs. individually derived weights vs. unit weights. Whilst they found that results were statistically

significant, effect sizes were very small and ratings were remarkably similar across age, gender and income categories. Their approach validly addressed concerns however the SRRS-R departed notably from the original SRRS negating any opportunity for cross-comparability and, consequently, the SRRS-R has not been incorporated into any subsequent publications to the best of my knowledge.

Around the same time, Scully and colleagues (2016) published updated SRRS ratings and addressed 3 content-related criticisms of the SRRS. They assessed the validity of the contamination hypothesis, mentioned previously. In addition, some evidence suggested that undesirable life events would have a stronger stress response than desirable ones (Mueller et al., 1977; Ross & Mirowsky, 1979) though not all findings agree (Stallings et al., 2016). Similarly, uncontrollable life events would have a more potent stress impact than controllable ones (ibid). In phase 1 of Scully and colleagues' study (Scully et al., 2016), the original SRRS instructions were administered to a random sample of Florida residents (n=200) whose ratings were used to derive updated weights (LCUs) for all items. In phase 2, another sample completed the SRRS, reporting experienced events a) within the last 12 months and b) ever. They also completed a modified version of the Symptom Checklist-90 which measured stress-related symptoms. A group of university staff and PhD student raters (n=7) categorised all the SRRS items as desirable, undesirable or neutral. A separate group of PhD student raters (n=7) categorised the items as either controllable or uncontrollable. Comparisons of symptom reporting were conducted based on these

categorisations. Regression analyses revealed that the SRRS in its original form was predictive of stress symptoms. In addition, consistently more variance was explained when regression models included all items than when only respective undesirable/uncontrollable items were included. Thus, including only negative items was found to limit the utility of the SRRS. They also found that symptoms associated with events reported over the last 12 months had greater predictive power, suggesting that the stress impact of life events diminished with passing time. They concluded that “the SRRS is a robust instrument for identifying the potential for stress-related outcomes” (Scully et al., 2016, p. 875).

Twenty years on from the last attempts to modernise the SRRS, the primary aim of the current study was to update and improve the SRRS without fundamentally changing the scale to allow for cross-comparison of studies, which may have played a role in previous updates not being incorporated into subsequent versions. Six areas of focus were identified: First, the original weightings are 5 decades old and required updating. Second, biases in item wording were removed. Third, the complete and accurate wording from the raters’ version was re-instated. As Holmes and David pointed out: “We regret the decision to save space on the Social Readjustment Rating Scale, because the complete wording is the accurate and more helpful form.” (Holmes & David, 1989, p. 30). The SRRS ‘rating’ questionnaire comprised detailed statements, along with examples in some cases. The actual scale’s wording is much simplified. For example:

- Raters assessed: “Major change in usual type and/or amount of recreation”. The final SRRS use to evaluate illness onset was simplified to: “Change in recreation”.
- Raters assessed: “Minor violations of the law e.g. traffic tickets, jay walking, disturbing the peace”. The final version was simplified to: “Minor violations of the law”.

Thus, the final version leaves the reader to make assumptions about what ‘counts’ and what does not, resulting in increased inter-individual differences in responding. This portion of inter-individual variability was reduced by reinstating the ‘rater’ version of items.

Fourth, information was collected regarding the potential for systematic bias that may have affected the magnitude of weight that raters assigned to each item. Raters were asked to indicate the extent to which their rating was based on their own personal experiences of events. They were also asked how lonely they were and how frequently they felt lonely. Loneliness as chosen for two reasons, firstly as part of the evaluation of a new item, “Single person, living alone”, that was added to the end of the scale and secondly, as a proxy for depression which is associated with loneliness and stress (Brown et al., 2018; Eres et al., 2023; Lasgaard et al., 2016; Lee et al., 2021). Thus, loneliness allowed the evaluation of whether ratings varied based on emotional state at the time of rating.

Fifth, the rater sample was made more representative, proportionality reflecting the demographics within the UK regarding age, gender and ethnicity.

Sixth, the need for new items was considered. A rating was added to the norms set for being single and living alone, with its inclusion as optional at the end of the SRRS. In addition, an opportunity was provided for raters to add an item and its weight, which they believed could improve future work regarding what people find difficult to adjust to at the current time.

In this cross-sectional survey study, an assessment was made of the extent to which the sample's ratings deviated from those of the original, replicating earlier similar analyses. Previous work indicates that this is likely. For example, Miller and Rahe (1997) in their update found ratings differed when comparing males and females and married with unmarried individuals. Women's ratings were, on average, 17% higher than those of men. Muhlenkamp et al. (1975) measured differences between their older adult sample and the original raters with items categorised into 'family', 'personal', 'work' and 'finance'. A replication of this analysis was undertaken. The extent to which the rank order of items from the updated SRRS agreed with that of the original was also evaluated.

6.2 Method

6.2.1 Study design

A survey method was used comprising a series of online questionnaires via Qualtrics. Data were collected from a convenience sample in a single, online-only session. The present study broadly replicates that of Holmes and Rahe (1967) who recruited a convenience sample of adults aged ≥ 18 years to rate a list of 42 life events, using a

proportional scaling method. This study was pre-registered (https://osf.io/3wmsj).

6.2.2 Participants

Six hundred and thirty adults aged 18 to 85 accepted the invitation to participate. The sample selection criteria were based on the UK's current age distribution and gender breakdown and England and Wales' ethnicity breakdown published by the ONS (2022). Based on ONS estimates for England and Wales, 84.8% of the population is white. Roughly that proportion of Caucasians was recruited with the remaining proportion comprising non-Caucasian ethnic groups. Regarding sex, a 50/50 split was targeted, reflecting a similar split within the UK population. Ethnic and sex breakdowns were nested within age bands proportioned as per ONS statistics.

Participants were recruited via social media, word-of-mouth, SONA (local university student recruiting platform) and Prolific, an online participant recruitment platform. Participants had to be ≥ 18 years to be included in this study. Within the Prolific platform participants currently located in the UK were selected and anyone who had taken part in any of the previous studies were excluded. No other exclusion criteria were applied. Participants were recruited and data collected from February 2021 to May 2021. Respondents were anonymous; no personally identifiable information was collected. Thus, participants could not be identified during or after data collection. Participants volunteered either without payment, received a £4.50 payment or course credits. The study was approved by the University of Essex Faculty of Science and

Engineering Ethics Committee (Ethics ID: ETH2021-0829). All participants gave written informed consent using an online form, which had to be read and agreed to before they could gain access to the study.

6.2.3 Measures

6.2.3.1 Social Readjustment Rating Questionnaire (SRRQ)

The updated SRRQ with instructions administered to the rater sample is provided in Appendix 1. For comparison, the original SRRQ instructions are provided in Appendix 2. To reduce potential variations in interpretation, the SRRQ was administered with modified instructions based on those of Muhlenkamp et al. (1975) who changed the weight for marriage from 500 to 50 and simplified the instructions themselves. Using marriage (50) as the anchor point, participants were instructed to rate each item from 0 to 100. Some wording was simplified but kept as close to the original as possible, asking participants to draw on their experience and those of others when giving their ratings, as in the original version. Note that in the original SRRQ participants rated 42 items (relative to marriage). The updated SRRQ includes a 43rd item to be rated: 'Single person, living alone'[34]. The outcome variables for the SRRQ were the mean weights assigned to each of 43 items (range: 0 – 100). The mean ratings were derived by averaging the ratings given across participants for each respective item.

[34] Please note that the SRRQ shows 'Single person, living alone' as item 44, this is because 'marriage' is included at the top of the form as item 1 with the assigned value of 50.

6.2.3.2 Social Readjustment Rating Scale 2022 updated

The updated SRRS, used in conjunction with the SRRQ ratings, is provided in Appendix 3. In accordance with the SRRQ, the updated SRRS also contains the new item at the end of the scale, 'Single person, living alone'. Consequently, the total number of life change units for a given participant is based on 44 items rather than the original 43. Participants were asked to respond 'yes' or 'no' with the instruction: "Please indicate which of the following events have occurred in your whole life". The order of items were randomised and then presented in the same order across participants. Some subtle updates or clarifications to wording were applied e.g. 'spouse' became 'spouse/life partner'. Due to inflation the monetary value used for loans was removed, as recommended by Holmes and David (1989). The outcome variable was the binary value for each of the items multiplied by the corresponding item 'weight' (life change units). The products were then summed to provide a total life change units score which represents one's life change intensity (Rahe, 1975). A higher value indicates greater intensity (i.e. a greater level of adaptation to change was needed).

6.2.3.3 Invitation to add own item

In this single-item questionnaire respondents were asked: "If you could add one more item to the list, what would it be?". Participants used the text box to provide a response or they could leave it blank and continue. In the follow-up question, participants were asked to provide a rating for this item relative to marriage. Valid responses therefore required

2 components: a life event (given in their own words) and a corresponding rating.

6.2.3.4 Experiential basis for SRRS ratings

An instruction was given to measure the extent to which the participants' ratings were based on their own experience: "At the start of this survey you were asked to rate a range of life events by comparing them to marriage. To what extent was your chosen rating based on your own personal experience? Please slide the scale to indicate as best you can how much your rating was based on your own experience from 'not at all based on my own experience' (0) to 'completely based on my own experience' (100)." Appendix 4 provides a copy of this questionnaire. The outcome variable was the value given for each item (range: 0 to 100).

6.2.3.5 Loneliness questionnaire

The ONS recommends the following 4 questions to measure loneliness: "How often do you feel that you lack companionship?", "How often do you feel left out?" and "How often do you feel isolated from others?" with response options of 'hardly ever or never = 1', 'some of the time = 2' and 'often = 3'. Scores for these 3 items are summed (range: 3 to 9). A higher score indicates a greater degree of loneliness. The 4th question asked: "How often do you feel lonely?" with 6 response options ranging from 'often/always' = 1 to 'never' = 5 and 'prefer not to say' = 6 (Robards, 2022). A lower score indicates a greater level of loneliness. The first 3 questions were taken from the University of California, Los Angeles loneliness scale (UCLA v3) (Russell, 1996) which was adapted to a 3-item scale: R-UCLA (Hughes et al., 2004) as used in English Longitudinal

Study of Ageing (Lee et al., 2021). The UCLA scale has good reliability (coefficient α range: 0.89 to 0.94) and test re-test reliability (r = 0.73). The scale's reliability and validity was tested on students, teachers, nurses and older participants (> 65 years). The R-UCLA has an alpha coefficient of 0.72 with good internal consistency (Hughes et al., 2004). The final question forms part of the Community Life Survey (Department for Culture, Media and Sport, 2020). Appendix 5 provides a copy of these survey items. Thus, loneliness was measured with two outcome measures: loneliness level as a summed value (range: 3 to 9); loneliness frequency as a single-item value (range: 1 to 5).

6.2.4 Procedure

Participants read the information sheet, accepted the invitation to take part, gave online informed consent by completing a check-list then provided biographical details, namely age, ethnicity, gender, religion, relationship status and employment status (see Results). They were presented with the following in sequential order: the SRRS rating questionnaire, updated SRRS, new item with corresponding rating, personal experience questionnaire, 4-item loneliness questionnaire.

6.2.5 Statistical Analysis

Descriptive statistics are provided for all items. Data were analysed using parametric and/or non-parametric analyses alongside equivalent Bayesian comparisons, depending on whether distributions were normal or skewed. Where any disparity existed between frequentist and Bayesian results, conclusions were based on the Bayes factors (BF) to reduce Type 1 error. Bayesian analyses were conducted in JASP 0.16.2.0 (2022).

Sensitivity analyses for BFs for between-groups comparisons were also conducted to ensure that expected effect sizes were scaled appropriately.

Numerous previous SRRS studies used geometric means. However, the original SRRS weights were derived using arithmetic weights therefore these were used (the Results provides full details). For frequentist analyses, alpha levels at < .05 were applied to control for type 1 error. To be comparable to Miller and Rahe (1997), 99% confidence intervals were used.

The open-ended item (see 'Invitation to add own item') was analysed by a simple frequency method where the number of times a particular event was given was counted as '1'. Only events with an accompanying rating were counted.

6.3 Results

Six hundred and thirty respondents were recruited and consented to take part in the study. Ninety of 630 participants logged off from the study part-way and their data could not be used. Of the remaining 540 respondents, all completed the study in full apart from 5 who completed most of the study (≥ 90%). As part of the informed consent, all participants had agreed that any data collected up to the point of withdrawal may be used. These 5 respondents' data were therefore retained. None provided data for the loneliness questionnaire, which was the last item of the study. Four of the 5 respondents rated the SRRQ and gave responses to the SRRS but logged off without completing the remaining items (personal experience, selecting own item, loneliness). Analyses were conducted with

all available data using list-wise or pair-wise deletion, as appropriate. Sample sizes are given for each table.

Descriptive statistics for demographic details are given in Table 6.1. There were 453 Prolific participants (84%), SONA (8%) and social media/word-of-mouth (8%). Eighty-seven percent of the sample were British, 4% were EU nationals, 2% were USA nationals and 7% were from other countries. Most (95%) reported English as their first language.

Table 6.1 Descriptive statistics for biodemographic details of the total sample.

		mean (min-max)	median (IQR)	n* (%)
Age	< 30 years	23.08 (18 - 29)	22 (20 - 27)	116 (21.5)
	30 to 60 years	45.18 (30 - 60)	45 (37 - 53)	291 (53.9)
	> 60 years	69.81 (61 - 84)	70 (65 - 75)	133 (24.6)
Gender	female			308 (57)
	male			230 (42.6)
	gender-fluid			2 (0.4)
Education	years	15.31 (12 - 21)	15 (14 - 17)	540 (100)
Relationship status	married			236 (43.7)
	long-term relationship			107 (19.8)
	in a relationship			30 (5.6)
	separated			5 (0.9)
	divorced			21 (3.9)
	widowed			11 (2)
	life partner died			5 (0.9)
	single			125 (23.2)
Ethnicity	white			455 (84.3)
	mixed race (all)			23 (4.3)
	asian (southern/southeastern asia)			24 (4.4)
	chinese (east asian)			7 (1.3)
	black (any region)			31 (5.7)
Religion	no religion			266 (49.3)
	Christian			234 (43.3)
	Buddhist			4 (0.7)
	Hindu			5 (0.9)
	Jewish			6 (1.1)
	Muslim			17 (3.2)
	Sikh			5 (0.9)
	any other religion			3 (0.6)
Employment status	full-time or part-time employed			348 (64.4)
	currently unemployed, looking for work			14 (2.6)
	long-term sick or disabled			11 (2)
	looking after home or family			28 (5.2)
	retired			97 (18)
	have never worked			2 (0.4)
	student (p/t or f/t) and currently unemployed			39 (7.2)
	other			1 (0.2)

*N=540

Wording was adjusted/modernised on 12 items of the rating questionnaire (Table 6.2). To assess whether this may have caused those weights to change by more than the unchanged items a Mann-Whitney U test was conducted on the difference scores (new minus original weight) by wording-changed vs. wording-unchanged items. The difference was not statistically significant ($p > .685$) ($Mdn_{changed}$ 10.2 vs. $Mdn_{unchanged}$ 8.8)

though the equivalent BF of 0.35 was within the anecdotal range, suggesting that participants' ratings were unlikely to vary with the wording changes.

Table 6.2. Changed Items

	Original item wording	**New item wording**
1.	Death of spouse	Death of a spouse or life partner
2.	Minor violations of the law (e.g. traffic ticket, jay walking, disturbing the peace)	Minor violations of the law (e.g. traffic ticket, disturbing the peace)
3.	Pregnancy	Pregnancy (either yourself or being the father or life partner)
4.	Gaining a new family member (e.g. through birth, adoption, oldster moving in, etc.)	Gaining a new family member (e.g. through birth, adoption, grandparent moving in, etc.)
5.	Marital separation from mate	Marital separation
6.	Major change in church activities (e.g. a lot more or a lot less than usual)	Major change in religious activities (e.g. a lot more or a lot less than usual)
7.	Marital reconciliation with mate	Marital reconciliation
8.	Being fired from work	Losing your job (redundancy, dismissal, etc.)
9.	Major change in the number of arguments with spouse (e.g. either a lot more or a lot less than usual regarding child-rearing, personal habits, etc.)	Major change in the number of arguments with spouse or life partner (e.g. either a lot more or a lot less than usual regarding child-rearing, personal habits, etc.)
10.	Spouse begins or stops working outside the home	Spouse or life partner begins or stops working
11.	Taking on a mortgage greater than $10,000 (e.g. purchasing a home, business, etc.)	Taking on a mortgage or loan for a major purchase (e.g. purchasing a home, business, etc.)
12.	Taking on a mortgage or loan less than $10,000 (e.g. purchasing a car or furniture, paying for college fees, etc.)	Taking on a loan for a lesser purchase (e.g. purchasing a car or furniture, paying for college fees, etc.)

6.3.1 SRRS ratings then and now: a comparison with Holmes & Rahe (1967)

The original scale had a score-range of 0 to 1466, while the newly weighted version's range extended to 1871, increasing the total by 405 life change units (LCUs). Of the original 42 event items rated, 39 increased and 4 decreased. Of the items that increased, 3 items increased by ≥ 25 LCUs relative to the original scale: 'Foreclosure/repossession on mortgage or loan' (62_{new} vs. $30_{original}$), 'Death of a close friend' (64_{new} vs. $37_{original}$) and 'Pregnancy' (65_{new} vs. $40_{original}$). When including the 44^{th} item, 'Single person, living alone', the range increased to 1909 (1871+38). A Mann-Whitney U test found that total LCUs were, on average, higher in the current (Mdn = 40.1, n=43) relative to the original scale (Mdn = 29, n=43) ($z = -2.807$, $p = .005$, $r = .3$). The Bayesian Mann-Whitney U test supported this finding with substantial evidence (BF = 6.22). Sensitivity analyses are provided in Appendix 6 and indicate that applying different Bayesian priors did not affect the outcome, therefore the reported BFs are reliable. A Kendall's tau correlation coefficient was conducted to evaluate the level of agreement between the two scales. This revealed that the original weights were strongly, positively associated with the new weights ($r = .751$, $p < .001$). The corresponding Bayesian Kendall's tau provided decisive evidence for this finding (BF > 100), suggesting that the respondents in the new scale and the original rating sample were comparable in the hierarchy of change for their evaluations. Table 6.3 presents the descriptive statistics and rank order of the SRRS items for the original and new scale weights. The table provides the arithmetic

means with their standard errors and 99% confidence intervals, plus the geometric means and median values. The events are ordered by the rank of absolute change in number of LCUs, from highest to lowest (1 to 43) to provide a visual comparison of change between original and new weights. Regarding how consistent participants' ratings were for each item, it was observed that the range of ratings spanned the full range of 0 to 100 on most items (38/43). The magnitude of IQRs and 99% BCa confidence intervals for each of the 43 items were therefore inspected to better ascertain consensus of ratings. Table 6.3 shows that the largest IQR magnitude was 40, which was for 'Outstanding personal achievement' and 'Retirement from work'. Next largest were 'Gaining a new family member' (39), 'Death of a close family member' (35), 'Son or daughter leaving home' (35), 'Losing your job' (35), 'Taking on a mortgage or loan for a major purchase' (35), 'Major business readjustment' (35) and 'Single person, living alone' (35). The smallest IQR was for 'Major change in social activities' (20). Table 6.3 shows the largest BCa confidence interval was for 'Detention in jail or other institution' (73.79 - 79.66) and the smallest was for 'Revision of personal habits' (20.95 - 24.85). Of the largest BCa confidence intervals, 3 coincided with some of the largest IQR items: 'gaining a new family member' (49.05 - 54.65), 'Retirement from work' (46.73 - 52.45) and 'Single person, living alone' (35.41 - 41.16). These results suggest that for 79% of items (33/42) participants were consistent in their ratings across items but for the remaining 21% (9/42) respondents were relatively less consistent.

Table 6.3 Present study vs. original weights and rank order of SRRS events*.

Event	Holmes & Rahe			Present Study				Difference Score	
	original rank	weight	present rank	Mean (SE)[a]	99 % CI[b]	Geometric Mean[c]	Median (IQR)	present - original weight	rank: absolute change[d]
Foreclosure/repossession on mortgage or loan	21	30	9	62.39 (1.07)	59.65, 65.09	32.71	40 (25 - 60)	32.4	1
Death of a close friend	17	37	8	64.05 (1.12)	61.08, 66.8	44.9	50 (40 - 70)	27.1	2
Pregnancy	12	40	6	64.66 (1.06)	62.03, 67.27	47.63	60 (40 - 70)	24.7	3
Change in residence	32	20	19	42.69 (0.95)	40.33, 44.99	34.54	40 (30 - 59.8)	22.7	4
Major change in work hours or conditions	31	20	27	37.09 (0.84)	34.76, 39.32	20.44	25 (10 - 40)	17.1	5
Major change in sleeping habits	38	16	30	31.92 (0.84)	29.83, 34.3	24.85	30 (20 - 40)	15.9	6
Changing to a new school	33	20	28	34.6 (0.93)	32.29, 36.95	29.5	35 (20 - 50)	14.6	7
Major change in living conditions	28	25	24	39.36 (0.9)	37.01, 41.75	23.76	30 (20 - 50)	14.4	8
Spouse/life partner begins or stops working	26	26	22	40.06 (0.9)	37.72, 42.36	21.22	30 (10 - 50)	14.1	9
Major change in financial state	16	38	12	52.02 (0.94)	49.68, 54.68	35.47	50 (30 - 65)	14	10
Losing your job	8	47	10	60.97 (1.03)	58.2, 63.5	24.33	30 (20 - 50)	14	11
Detention in jail or other institution	4	63	2	76.88 (1.14)	73.79, 79.66	61.65	80 (70 - 99)	13.9	12
Death of a spouse or life partner	1	100	1	86.83 (0.98)	84.16, 89.21	73.78	95 (80 - 100)	-13.2	13
Death of a close family member	5	63	3	75.84 (1.02)	73.13, 78.46	67.57	80 (60.5 - 95)	12.8	14
Gaining a new family member	14	39	13	51.81 (1.11)	49.05, 54.65	29.09	40 (20 - 50)	12.8	15
Son or daughter leaving home	23	29	21	41.66 (0.99)	39.2, 44.19	21.75	30 (15 - 40)	12.7	16
Major change in eating habits	40	15	35	27.39 (0.77)	25.2, 29.47	15.72	20 (10 - 30)	12.4	17
Major change in the health or behaviour of a family member	11	44	11	55.73 (0.98)	53.06, 58.24	38.01	50 (30 - 70)	11.7	18
Major personal injury or illness	6	53	7	64.36 (0.98)	61.9, 66.91	55.98	70 (50 - 80)	11.4	19
Taking on a mortgage or loan for a major purchase	20	31	20	42.22 (0.99)	39.78, 44.79	34.98	45 (30 - 60)	11.2	20
Minor violations of the law	43	11	40	22.14 (0.76)	20.12, 24.19	14.99	20 (10 - 30)	11.1	21
Major change in usual type and/or amount of recreation	34	19	34	29.08 (0.78)	27.01, 31.04	11.43	15 (5 - 30)	10.1	22
Major change in the number of arguments with spouse-life pa	19	35	18	44.21 (0.92)	41.75, 46.56	31.1	40 (25.5 - 50)	9.2	23
Major change in responsibilities at work	22	29	26	37.8 (0.83)	35.54, 39.94	50.24	70 (50 - 80)	8.8	24

Table 3 cont'd overleaf.

Table 6.3 Present study vs. original weights and rank order of SRRS events*.

Event	Holmes & Rahe			Present Study				Difference Score	
	original rank	weight	present rank	Mean (SE)[a]	99 % CI[b]	Geometric Mean[c]	Median (IQR)	present - original weight	rank: absolute change[d]
Taking on a loan for a lesser purchase	37	17	36	25.12 (0.84)	22.97, 27.6	17.36	20 (10 - 35)	8.1	25
Beginning or ceasing formal schooling	27	26	29	33.88 (0.91)	31.57, 36.14	31.07	40 (25 - 55)	7.9	26
Major change in number of family get-togethers	39	15	38	22.88 (0.76)	20.9, 24.92	20.74	25 (10 - 40)	7.9	27
Christmas	42	12	43	19.78 (0.84)	17.79, 21.93	11.8	10 (5 - 30)	7.8	28
Major business readjustment	15	39	16	46.73 (1.06)	43.96, 49.49	40.18	50 (30.8 - 70)	7.7	29
Vacation	41	13	42	20.09 (0.81)	18.03, 22.25	12.64	10 (6 - 30)	7.1	30
Major change in social activities	36	18	37	24.39 (0.8)	22.31, 26.45	17.35	20 (10 - 30)	6.4	31
Troubles with the boss	30	23	33	29.15 (0.9)	26.72, 31.74	15.66	20 (10 - 30)	6.2	32
Divorce	2	73	4	67.86 (1.03)	65.2, 70.41	56.03	70 (52.8 - 85)	-5.1	33
Retirement from work	10	45	15	49.64 (1.08)	46.73, 52.45	35.58	50 (30 - 60)	4.6	34
Changing to a different line of work	18	36	23	39.48 (0.85)	37.3, 41.68	52.64	70 (45.8 - 80)	3.5	35
Outstanding personal achievement	25	28	32	30.94 (0.96)	28.49, 33.55	30.56	38.5 (21.3 - 50)	2.9	36
In-law troubles	24	29	31	30.94 (0.91)	28.62, 33.26	31.31	40 (25 - 60)	1.9	37
Marital separation	3	65	5	66.9 (1.01)	64.28, 69.33	55.98	70 (50 - 80)	1.9	38
Marital reconciliation	9	45	17	46.24 (0.97)	43.77, 48.59	51.32	65 (45 - 80)	1.2	39
Revision of personal habits	29	24	39	22.8 (0.77)	20.95, 24.85	30.96	40 (25 - 53.8)	-1.2	40
Major change in religious activities	35	19	41	20.09 (0.8)	18.01, 22.2	22.07	30 (15 - 40)	1.1	41
Sexual difficulties	13	39	25	38.07 (0.92)	35.74, 40.61	53.44	70 (50 - 80)	-0.9	42
Marriage (pre-set weight)	7	50	14	50				0	43
Single person, living alone				38.16 (1.13)	35.41, 41.16	24.14	40 (15 - 50)		

* Table's values are ordered by absolute change in weights.

[a] Mean (SE). Standard error obtained via BCa Bootstrap with 1000 samples.

[b] 99% confidence intervals obtained via BCa Bootstrap with 1000 samples.

[c] Where participants responded with a zero value, these were replaced with '1' to allow this value to be calculated.

[d] Rank is based on absolute change (difference score: 2022 weight - original weight). Negative signs were ignored in creating the rank order. Rank values in red indicate that the weight upon which it is based was higher in the original version.

6.3.2 The SRRS categorised as 'family', 'personal', 'financial' or 'work' life events

Rahe and colleagues delineated their 43 SRRS items in terms of 'family', 'personal', 'work' and 'financial' life events (Rahe, 1972, 1975). A copy is provided in Appendix 7. The correlations between the original and new weightings were evaluated by these categories, using Kendall's tau. The result revealed strong, positive associations between original and new weights for family ($r = 0.818$, $p < .001$), personal (0.638, $p < .001$) and work (0.905, $p = .004$) events. However, original and new weights showed no statistically significant association for financial items ($p > .4$). Bayesian Kendall's tau correlations confirmed these findings with decisive evidence for family and personal categories ($BF > 100$) and strong evidence for work-related events ($BF = 12.24$). For financial items, the Bayesian Kendall's tau revealed anecdotal evidence ($BF = 0.68$). Thus, original and new samples co-varied on all categories except financial events for which evidence was inconclusive.

Demographic differences were examined within each of the 4 categories. Table 6.4 provides medians with interquartile (IQR) ranges for all variables analysed. Appendix 8 provides medians and interquartile ranges for all broad categories for demographical variables.

Table 6.4 Descriptive statistics for SRRS events categorised by family, financial, personal and work, per demographic f

			Mean SRRS weights			
			family items	financial items	personal items	work items
demographic factor	sub-groups	overall weight	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
age						
	< 30 years (n=116)	40.3 (30.3 - 54.3)	53.6 (44.8 - 61)	50 (33.8 - 55.8)	35.5 (28.6 - 45.3)	42.1 (31.6 - 54.3)
	30 to 60 years (n=291)	39.7 (29.7 - 57.8)	54.6 (45.7 - 64.3)	45 (35 - 52.5)	34.7 (28.9 - 43.3)	43.6 (32.1 - 52.9)
	> 60 years (n=133)	39.4 (28.7 - 57.1)	53.9 (46.1 - 61.1)	46.5 (35.6 - 58.8)	33.4 (26.4 - 46.6)	42.9 (33.2 - 54.7)
sex						
	female (n=308)	43.9 (32.4 - 58.9)	57.1 (48.9 - 64.9)	47.5 (37.5 - 56.2)	36.9 (30.6 - 46.5)	45.7 (35.7 - 55.7)
	male(n=230)	35.4 (25.3 - 50.8)	50.4 (42.4 - 58.8)	42.5 (30 - 55)	32.3 (24.7 - 40.5)	40 (29.3 - 50)
ethnicity						
	white (n=455)	39.3 (28.7 - 56.3)	54.3 (46.4 - 61.8)	46.3 (35 - 55)	34.2 (27.9 - 43.7)	42.9 (32.9 - 52.9)
	non-white[a] (n=85)	40.7 (32.5 - 53)	55.4 (44.8 - 63.8)	50 (37.4 - 59.4)	37.9 (27.4 - 47.9)	45.7 (31.8 - 55.7)
religion						
	no religion (n=274)	39 (28.1 - 55.4)	55.5 (46.4 - 64.3)	47.5 (35 - 57.5)	35.7 (27.7 - 46.6)	44.3 (33.4 - 54.4)
	religion[b] (n=266)	40.9 (30.1 - 56)	53.6 (45.6 - 60.7)	45 (35 - 54.1)	33.9 (28 - 41.1)	42.1 (32.1 - 52.1)
relationship status						
	married[c] (n=343)	40.7 (30.6 - 57.6)	55 (46.8 - 64.5)	46.5 (35 - 55)	34.7 (28.4 - 45.3)	42.9 (32.9 - 54.3)
	unmarried (n=197)	37.7 (29.8 - 53.2)	53.6 (44.6 - 60.7)	45.8 (34.8 - 55.6)	34.7 (27.1 - 44.2)	43.6 (32.5 - 52.9)
employment status						
	employed (n=348)	39.8 (28.3 - 55.9)	54.3 (46.1 - 63)	46 (35 - 55)	34.7 (28.2 - 44.5)	42.9 (32.9 - 55)
	unemployed[e] (n=192)	39.2 (30.7 - 55.4)	54.3 (45.8 - 61.1)	47 (35 - 57.5)	34.7 (27.3 - 44.7)	43.2 (31.6 - 52.6)

[a] 'Non-white' includes all ethnicities: mixed race, Asian (southern/southeastern Asia), Chinese (east Asian), black (any region).

[b] 'Religious' includes all religions: Christian, Buddhist, Hindu, Jewish, Muslim, Sikh, any other religion.

[c] 'married' includes married and long-term partners.

[d] 'unmarried' includes those who don't qualify as 'c': divorced, in a relationship, life partner died, separated, single, widowed.

[e] currently unemployed and looking for work, have never worked, long-term sick/disabled, looking after home or family, retired, student (p/t or f/t) and currently unemployed, other.

For age, ratings of young, middle-aged and older-aged groups were compared for each of the 4 categories with Kruskal-Wallis tests, which revealed no statistically significant differences between groups (p's > .2). Bayesian Mann-Whitney U tests were used to compare the respective groups as there is no corresponding Bayesian non-parametric one-way ANOVA equivalent. The outcomes were congruent with the frequentist findings and consistently supported the null (BFs ≤ 0.26). Sensitivity analyses are provided in Appendix 6 and support these BF results. Comparing female and male average ratings, in contrast, revealed a statistically significant difference using Mann-Whitney U tests for family events (Mdn = 57.1 vs. 50.4), personal events (Mdn = 36.9 vs. 32.3), financial events (Mdn = 47.5 vs. 42.5) and work events (Mdn = 45.7 vs. 40) (p's < .001) with females' ratings being consistently higher than males', respectively. Bayesian Mann-Whitney U tests revealed strong evidence for financial items (BF = 27.22) and decisive evidence for all other categories (BF > 100). Sensitivity analyses are provided in Appendix 6 and support these BFs. These results are shown in Fig. 6.1. Ethnicity, religion, relationship status and employment variables were collapsed into dichotomised variables to simplify comparison. Details are given in Table 6.4. Appendix 8 provides full comparisons. For ethnicity, a Mann-Whitney U test of white vs. (combined) non-white sub-sets indicated no statistically significant between-groups differences for any of the 4 categories (p's > .1). Likewise, the Bayesian analyses revealed evidence for the null for all comparisons (BFs ≤ 0.20). For religion, a Mann-Whitney U test comparing non-religious vs. (combined) religious groups revealed a statistically

significant difference for personal events ($Z = -2.006$, $p = .047$) with the non-religious group assigning a higher average weight to this category of events than the religious group (Mdn = 35.7 vs. 33.9, respectively). However, the Bayesian Mann-Whitney U test revealed anecdotal evidence ($BF = 0.59$). Comparisons for family, work and financial categories were not statistically significant (p's $> .1$) which was confirmed by the Bayesian results which supported the null ($BFs \leq 0.28$). For relationship status, a Mann-Whitney U test comparing (combined) married vs. (combined) unmarried groups showed a statistically significant difference for family events ($Z = -2.144$, $p = .032$) only with the married group giving higher ratings than the unmarried group (Mdn = 55 vs. 53.6, respectively). However, the Bayesian Mann-Whitney U test revealed anecdotal evidence ($BF = 1.74$). The comparisons for personal, financial and work were not statistically significant (p's $> .3$), confirmed by Bayesian evidence for the null ($BFs \leq 0.16$). For employment status, a Mann-Whitney U test comparing employed vs. (combined) unemployed groups revealed no statistically significant differences (p's $> .2$) for any of the categories. Congruent with this outcome, Bayesian Mann-Whitney U tests revealed evidence for the null for all comparisons ($BFs \leq 0.20$). Sensitivity analyses are provided in Appendix 6 for all the above-mentioned Bayesian Mann-Whitney U comparisons and support the reported BFs.

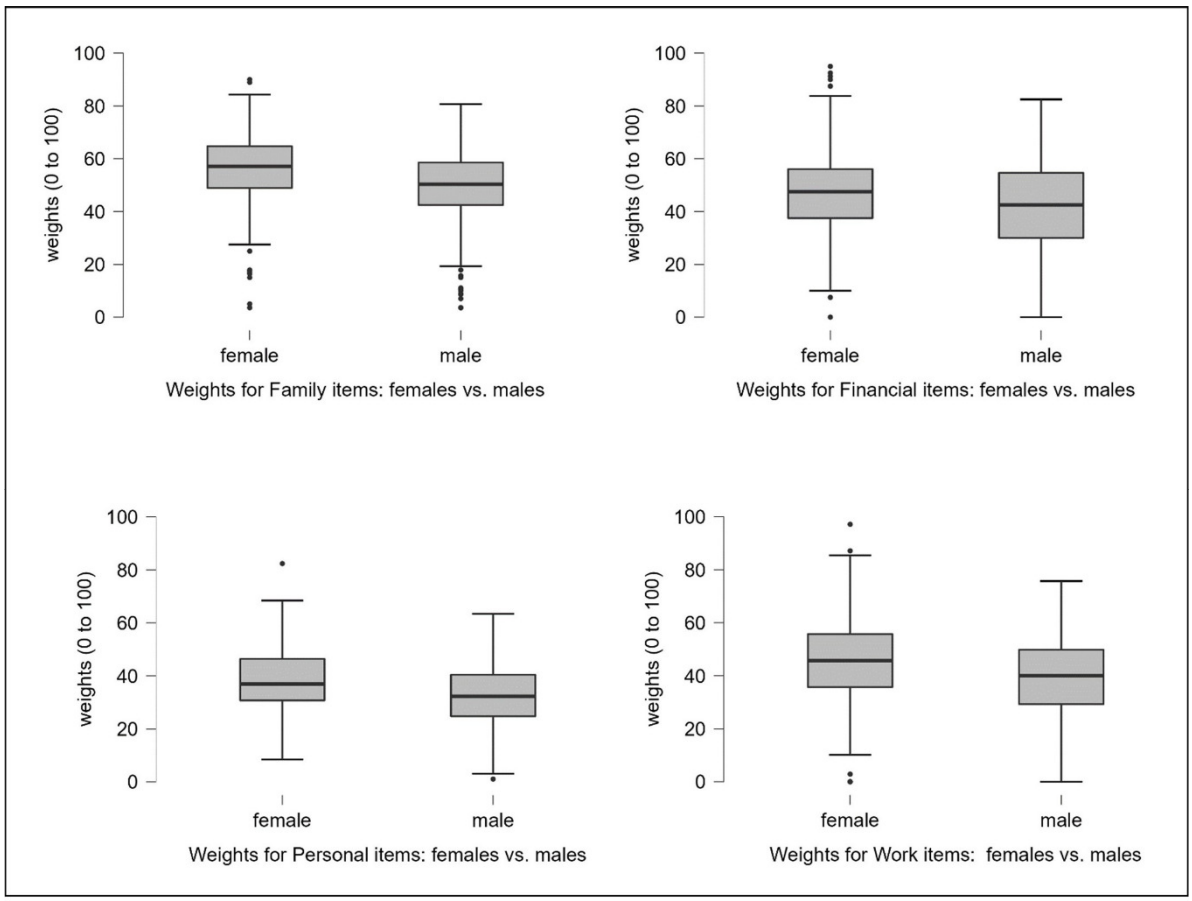

Fig. 6.1. Box plots showing differences between males and females based on event categories. From top-left to bottom-right these are, 'Family', 'Financial', 'Personal' and 'Work'.

6.3.3 SRRS weights: comparing normative and 70+ sub-samples

Muhlenkamp and colleagues (1975) who extended the original SRRS by adding weights to represent those aged ≥ 65 to 84 years compared the original normative sample's ratings (<30 years to > 60 years, n=394) with those from their new, older group (65 to 84 yrs, n=41). A similar approach was followed here, however the older group was 70 to 84 years to minimise overlap with previously represented older age groups (e.g. 65 to 69 year-olds). The original study stated that there were 51 raters > 60 years (i.e. no maximum age reported) while Muhlenkamp et al. (1975) stated in their report that the original SRRS did not include adults over 70 years. Thus, the sample was grouped as those aged 18 to 69

years (‘normative sample’, n=473) vs. 70+ years (‘70+ sample’, n=67). Between-groups differences were evaluated overall as well as within the previously mentioned 4 life events categories: ‘family’, ‘personal’, ‘work’ and ‘financial’.

In the overall assessment the normative sample’s summed total LCUs was higher (LCU_{total} 1829) than that of the 70+ group (LCU_{total} 1759), however a Mann-Whitney U test found no statistically significant difference between the two groups, on average ($p > .7$). Likewise, the Bayesian equivalent supported the null ($BF = 0.24$). Sensitivity analyses (Appendix 6) are congruent with this outcome. Further, the Kendall’s tau indicated that the lists were strongly, positively correlated ($r = .884$, $p < .001$). The corresponding Bayesian Kendall’s tau provided decisive evidence for this finding ($BF > 100$). Of the 42 items rated, only 12 were higher for the 70+ group. Thus, the normative and older samples co-varied strongly regarding the ratings, though the normative sample’s ratings were consistently higher for most items. To assess whether there were any systematic differences in ratings between the normative group and 70+ group based on the 4 categories, a chi-square was conducted with event category (family, personal, financial, work) and proportion of change (> adjustment required in 70+ participants vs. > adjustment required in normative participants). The association was not statistically significant ($p = .648$). Likewise, the Bayesian contingency tables test supported the null ($BF = 0.17$). These findings suggest that there were no significant age-based differences in ratings across the different categories of events.

6.3.4 SRRS weights: comparing young, middle-aged and older adults

A set of SRRS weights and ranks for each age group were created and are provided in Table 6.5. Summing the weights by age group, it was found that YAs' summed weights value or total life change units (LCU_{total}) was 1866, for MAs the LCU_{total} was 1875 and for OAs it was 1867. A Kruskal-Wallis test revealed no statistically significant differences ($p > .997$). Bayesian non-parametric Mann-Whitney U comparisons agreed with these findings, showing evidence for the null ($BFs = 0.23$). Bayes factor sensitivity analyses (Appendix 6) were comparable. These results indicated comparable overall weights across the life span. In assessing the strength of association across all items between the pairs of age groups (YA vs. MA; MA vs. OA; YA vs. OA), Kendall's tau correlation coefficients indicated very strong, positive correlations ($r's \geq .835$, $p's < .001$). Bayesian Kendall's tau coefficients agreed with these findings ($BFs > 100$).

Table 6.5 SRRS events by young, middle-aged and older adults' weights and ranks.

	Holmes & Rahe	Present study								
		Young adults			Middle-aged adults			Older adults		
Event	*original rank*	rank	Mean (SE)[a]	99 % CI[b]	rank	Mean (SE)[a]	99 % CI[b]	rank	Mean (SE)[a]	99 % CI[b]
Death of a spouse or life partner	1	1	85.65 (2.1)	79.53, 90.65	1	87.72 (1.24)	84.24, 90.8	1	85.92 (2.07)	80.27, 91.08
Divorce	2	6	65.13 (2.15)	59.34, 70.87	4	68.28 (1.39)	64.66, 71.64	4	69.34 (2.05)	63.45, 74.43
Marital separation	3	7	62.17 (2.15)	56.95, 67.54	5	68.09 (1.33)	64.49, 71.59	5	68.44 (1.92)	63.1, 73.18
Detention in jail or other institution	4	3	70.65 (2.53)	63.62, 76.69	2	79.74 (1.38)	76.4, 83.08	2	76.08 (2.4)	69.22, 81.99
Death of a close family member	5	2	75.26 (2.44)	68, 80.98	3	76.92 (1.38)	73.26, 80.32	3	74 (2.02)	68.54, 79.04
Major personal injury or illness	6	8	59.84 (2.14)	53.53, 65.63	6	65.72 (1.31)	62.46, 68.98	7	65.33 (1.89)	60.53, 70.24
Marriage (pre-set weight)	7	14	50		14	50		13	50	
Losing your job	8	9	59.05 (2.22)	52.93, 64.54	10	61.7 (1.37)	57.99, 65.51	9	61.06 (2.2)	55.08, 67.03
Marital reconciliation	9	18	44.11 (1.95)	38.77, 49.37	16	47.01 (1.36)	43.26, 50.26	17	46.41 (1.9)	41.07, 51.2
Retirement from work	10	13	50.16 (2.38)	44.24, 56.17	15	49.9 (1.47)	46.34, 53.55	16	48.63 (2.18)	42.8, 53.99
Major change in the health or behaviour of a family member	11	15	49.13 (2.08)	43.87, 54.63	11	57.75 (1.31)	54.44, 61.2	11	57.06 (1.9)	51.71, 62.19
Pregnancy	12	5	66.61 (2.45)	60.49, 72.75	8	64.19 (1.36)	60.74, 67.54	8	63.97 (1.99)	58.47, 68.63
Sexual difficulties	13	30	34.47 (1.9)	29.8, 39.8	25	38.94 (1.28)	35.54, 42.3	24	39.29 (1.91)	33.98, 44.56
Gaining a new family member	14	12	52.8 (2.38)	47.02, 59.34	12	52.52 (1.55)	48.36, 56.6	15	49.41 (2.02)	44.34, 54.25
Major business readjustment	15	17	44.69 (2.27)	37.94, 50.73	17	46.19 (1.43)	42.65, 49.8	14	49.68 (2.24)	44.15, 55.21
Major change in financial state	16	11	54.3 (2.04)	49.06, 59.65	13	51.59 (1.24)	48.35, 54.94	12	50.96 (1.95)	45.2, 56.64
Death of a close friend	17	4	69.68 (2.37)	63.06, 75.74	7	64.99 (1.54)	60.83, 68.64	10	57.09 (2.17)	51.23, 62.53
Changing to a different line of work	18	22	40.88 (2)	35.67, 45.97	23	39.66 (1.14)	36.82, 42.83	26	37.86 (1.83)	33.26, 42.16
Major change in the number of arguments with spouse/life partner	19	19	42.55 (1.91)	37.52, 47.67	18	44.42 (1.27)	41.01, 47.6	19	45.22 (2.01)	39.13, 50.98
Taking on a mortgage or loan for a major purchase	20	16	46.09 (2.25)	40.23, 52.17	22	40 (1.28)	37.09, 44.12	20	43.71 (2)	38.3, 48.95
Foreclosure/repossession on mortgage or loan	21	10	55.22 (2.23)	49.49, 61.59	9	63.09 (1.41)	59.57, 66.72	6	67.11 (2.27)	60.81, 72.56
Major change in responsibilities at work	22	26	38.16 (1.79)	33.27, 42.88	28	37.09 (1.1)	34.21, 40.3	25	39.02 (1.73)	34.25, 43.78
Son or daughter leaving home	23	21	40.92 (1.97)	35.67, 45.87	19	41.98 (1.38)	38.62, 45.75	22	41.61 (1.99)	36.39, 46.26

Table 5 cont'd overleaf.

Table 6.5 SRRS events by young, middle-aged and older adults' weights and ranks.

	Holmes & Rahe	Present study								
		Young adults			Middle-aged adults			Older adults		
Event	***original rank***	**rank**	**Mean (SE)[a]**	**99 % CI[b]**	**rank**	**Mean (SE)[a]**	**99 % CI[b]**	**rank**	**Mean (SE)[a]**	**99 % CI[b]**
In-law troubles	24	34	30.3 (1.99)	25.21, 35.09	32	30.25 (1.18)	27.05, 33.34	31	33.02 (1.85)	28.48, 38.37
Outstanding personal achievement	25	36	29.21 (2.07)	24.57, 34.16	34	29.66 (1.23)	26.45, 33.05	28	35.26 (1.98)	30.36, 40.52
Spouse/life partner begins or stops working	26	23	40.34 (1.89)	35.55, 45.12	20	41.88 (1.25)	38.85, 45.73	27	35.84 (1.85)	31.21, 40.86
Beginning or ceasing formal schooling	27	28	36.34 (2)	30.93, 41.56	31	33.07 (1.18)	30.26, 36.41	30	33.51 (2.02)	28.31, 39.14
Major change in living conditions	28	24	39.28 (2.03)	34.28, 45.03	24	39.38 (1.24)	36.05, 42.25	23	39.38 (1.87)	34.36, 44.22
Revision of personal habits	29	38	27.25 (1.93)	22.7, 32.39	41	21.56 (1)	19.19, 24.34	42	21.65 (1.39)	17.89, 25.55
Troubles with the boss	30	40	24.69 (1.84)	20.51, 29.09	33	30.03 (1.25)	26.94, 33.46	33	31.12 (2.01)	25.7, 36.14
Major change in work hours or conditions	31	25	38.64 (1.8)	33.95, 43.11	26	38.41 (1.15)	35.22, 42.12	32	32.85 (1.69)	28.43, 37.43
Change in residence	32	20	41.01 (2.04)	36.02, 46.2	21	41.75 (1.29)	38.69, 44.92	18	46.23 (1.81)	41.48, 50.53
Changing to a new school	33	27	37.5 (2.02)	32.94, 42.68	29	33.51 (1.25)	30.37, 36.51	29	34.44 (2.12)	28.5, 40.14
Major change in usual type and/or amount of recreation	34	31	33.24 (1.86)	28.83, 38.04	35	28.65 (1.02)	26.2, 31.28	35	26.38 (1.5)	22.8, 30.77
Major change in religious activities	35	39	26.08 (1.7)	22.08, 30.2	44	18.05 (1.02)	15.55, 20.85	44	19.33 (1.7)	14.88, 24.21
Major change in social activities	36	37	28.78 (1.9)	24.2, 33.82	38	23.3 (1.06)	20.31, 26.5	39	22.95 (1.4)	19.4, 26.91
Taking on a loan for a lesser purchase	37	35	29.83 (1.95)	25.3, 35.2	37	23.51 (1.1)	20.85, 26.6	36	24.55 (1.66)	20.33, 28.88
Major change in sleeping habits	38	32	32.26 (2.13)	27.13, 37.73	30	33.25 (1.12)	30.21, 36.13	34	28.74 (1.49)	25.24, 32.57
Major change in number of family get-togethers	39	41	24.53 (1.88)	20.13, 29.1	40	21.73 (0.94)	19.44, 24.4	38	23.97 (1.56)	20.28, 28.06
Major change in eating habits	40	33	30.68 (1.94)	26.24, 36.11	36	27.63 (1.06)	24.81, 30.71	37	24 (1.36)	20.63, 28.16
Vacation	41	42	21.45 (2.05)	16.28, 26.5	43	19.13 (1.07)	16.33, 22.04	43	21 (1.51)	17.29, 25.52
Christmas	42	44	16.95 (1.7)	12.65, 21.35	42	19.79 (1.09)	16.76, 22.86	41	22.23 (1.93)	17.62, 27.65
Minor violations of the law	43	43	19.85 (1.47)	16.66, 24.09	39	22.72 (1.04)	20, 25.45	40	22.87 (1.64)	18.4, 27.3
Single person, living alone		29	34.96 (2.59)	28.55, 41.39	27	37.84 (1.49)	33.92, 41.51	21	41.66 (2.28)	35.82, 48.26

[a] SE = Standard Error.

[b] CI = Confidence Intervals.

6.3.5 SRRS weights: comparing males and females

Miller and Rahe (1997) found that females' ratings were 17% higher on average than that of males. Table 6.6 provides the descriptive statistics for the present samples' weights and ranking by sex. Females' summed weights (LCU_{total} 1992) were found to be 14% higher than those for males (LCU_{total} 1708). The corresponding Mann-Whitney U test was not statistically significant ($z = -1.840$, $p = .066$, $r = .2$), suggesting that the average difference between males' (Mdn = 35.3, n=43) and females' (Mdn = 45.1, n=43) LCU_{total} was statistically comparable. The corresponding Bayesian test revealed anecdotal evidence for this finding (BF = 1.42). Bayes factor sensitivity analyses (Appendix 6) were comparable. A Kendall's tau correlation coefficient indicated a very strong, positive correlation between males' and females' ratings ($r = .892$, $p < .001$), as indicated by Fig. 6.2. The corresponding Bayesian Kendall's tau correlation revealed decisive evidence for this finding (BF > 100). These results suggest that whilst females' ratings were higher than males' on all items, there was strong covariance between them. The 3 items with the greatest difference in ratings, with males' ratings being lower in each case, were 'Death of a close friend' (-15 LCU), 'Spouse/life partner begins or stops working' (-13 LCU) and 'Son or daughter leaving home' (-12 LCU). A likewise comparison regarding the 3 items with the smallest difference were 'Gaining a new family member' (-1 LCU), 'Retirement from work' (-2 LCU) and 'Marital reconciliation' (-3 LCU).

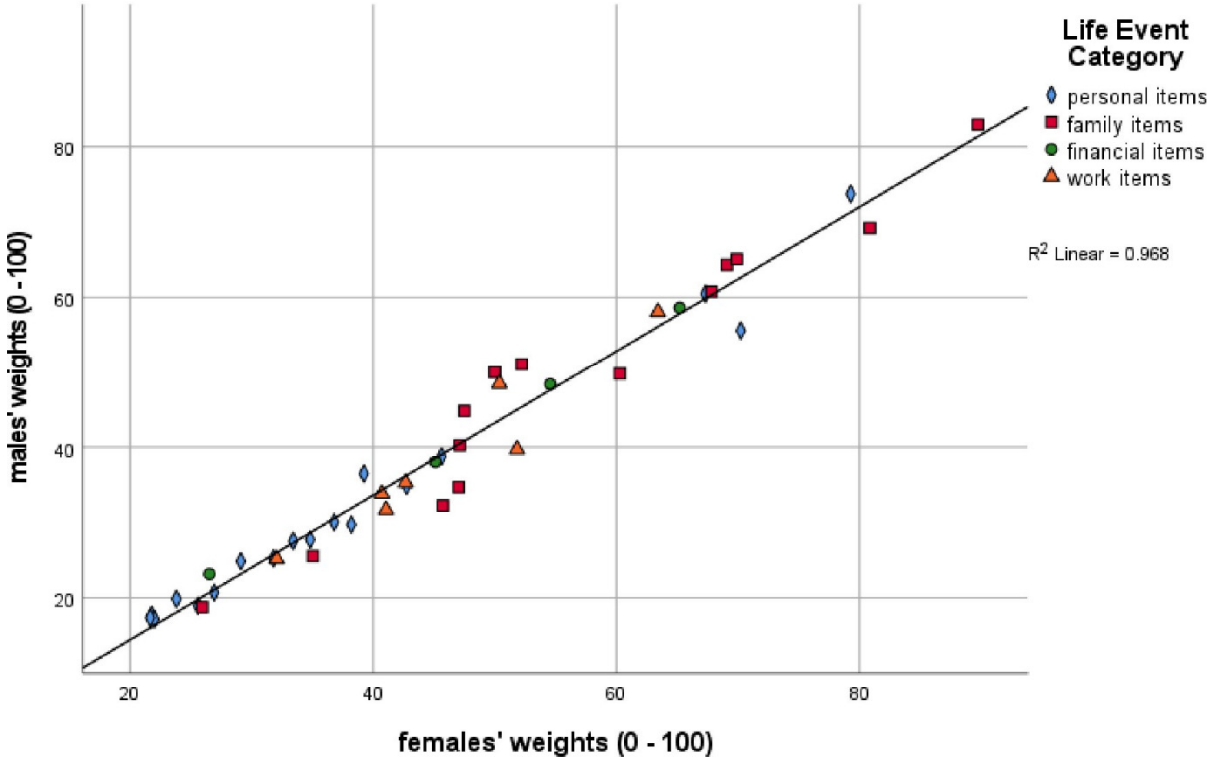

Fig.6.2. Scatter plot showing the covariance of females' and males' weights by items with weights (life change units) ranging from 0 to 100, grouped by category: 'Personal', 'Family', 'Financial' and 'Work'.

Table 6.6 SRRS events by females' and males' weights and ranks.

	Female			Male		
Event	rank	M (SE)	99% CI	rank	M (SE)	99% CI
Death of a spouse or life partner	1	89.73 (1.03)	86.48, 92.62	1	82.96 (1.75)	78.09, 87.37
Divorce	5	69.91 (1.31)	66.38, 73.15	4	65.1 (1.68)	61.02, 69.41
Marital separation	6	69.09 (1.23)	65.79, 72.11	5	64.34 (1.68)	59.93, 68.35
Detention in jail or other institution	3	79.28 (1.38)	75.21, 83.25	2	73.78 (1.77)	69.04, 78.63
Death of a close family member	2	80.85 (1.22)	77.52, 84.07	3	69.23 (1.76)	64.72, 74.2
Major personal injury or illness	8	67.33 (1.21)	64.07, 70.62	7	60.52 (1.57)	56.38, 64.28
Marriage (arbitrary weight)	16	50		15	50	
Losing your job	10	63.43 (1.3)	60.34, 66.66	9	58.09 (1.66)	53.8, 61.99
Marital reconciliation	17	47.5 (1.16)	44.07, 51.14	16	44.83 (1.52)	41.11, 48.59
Retirement from work	15	50.39 (1.37)	46.91, 54.32	14	48.51 (1.7)	44.07, 52.58
Major change in the health or behaviour of a family mer	11	60.28 (1.15)	56.98, 63.32	10	49.82 (1.64)	45.73, 53.98
Pregnancy	7	67.81 (1.35)	64.44, 71.52	6	60.78 (1.73)	56.34, 65.43
Sexual difficulties	27	39.24 (1.17)	35.88, 42.18	26	36.52 (1.47)	32.68, 40
Gaining a new family member	13	52.21 (1.44)	48.95, 55.73	12	51.09 (1.8)	45.9, 55.72
Major business readjustment	14	51.84 (1.33)	48.6, 55.11	13	39.73 (1.61)	35.45, 44.14
Major change in financial state	12	54.58 (1.21)	51.52, 57.64	11	48.44 (1.49)	44.56, 52.34
Death of a close friend	4	70.24 (1.36)	66.8, 73.76	10	55.62 (1.88)	51.5, 60.37
Changing to a different line of work	24	42.67 (1.16)	39.52, 45.87	23	35.33 (1.26)	32.05, 38.56
Major change in the number of arguments with spouse-	18	47.12 (1.23)	43.79, 50.4	17	40.27 (1.42)	36.54, 43.59
Taking on a mortgage or loan for a major purchase	22	45.12 (1.25)	42.06, 48.23	21	38.09 (1.49)	33.95, 41.64
Foreclosure/repossession on mortgage or loan	9	65.23 (1.44)	61.56, 68.54	8	58.65 (1.75)	54.29, 63.21
Major change in responsibilities at work	26	40.72 (1.13)	37.81, 43.77	25	33.86 (1.23)	30.51, 37.15
Son or daughter leaving home	19	47.02 (1.27)	44.07, 50.45	18	34.71 (1.45)	30.96, 38.58

Table 6 cont'd overleaf.

Table 6.6 SRRS events by females' and males' weights and ranks.

	Female			Male		
Event	rank	M (SE)	99% CI	rank	M (SE)	99% CI
In-law troubles	30	35.04 (1.18)	32.08, 38.33	29	25.56 (1.27)	22.25, 28.63
Outstanding personal achievement	32	33.43 (1.35)	30.1, 36.98	31	27.58 (1.31)	23.73, 31.23
Spouse/life partner begins or stops working	20	45.73 (1.17)	42.81, 48.54	19	32.25 (1.24)	29.04, 35.63
Beginning or ceasing formal schooling	29	36.79 (1.2)	33.98, 40.25	28	30.07 (1.38)	26.45, 33.54
Major change in living conditions	23	42.76 (1.2)	39.5, 46.39	22	34.89 (1.4)	31, 38.96
Revision of personal habits	39	25.59 (1.11)	22.56, 28.84	38	18.97 (1.03)	16.52, 21.82
Troubles with the boss	33	32.07 (1.26)	28.61, 35.55	32	25.19 (1.3)	21.83, 28.38
Major change in work hours or conditions	25	41.06 (1.11)	37.97, 44.21	24	31.7 (1.23)	28.6, 34.82
Change in residence	21	45.63 (1.22)	42.38, 48.8	20	38.79 (1.5)	34.66, 42.62
Changing to a new school	28	38.2 (1.29)	34.82, 41.54	27	29.76 (1.34)	26.23, 33.14
Major change in usual type and/or amount of recreation	34	31.81 (1.03)	29.2, 34.92	33	25.28 (1.11)	22.33, 28.14
Major change in religious activities	42	21.8 (1.08)	19.25, 24.56	41	17.77 (1.2)	14.86, 21.02
Major change in social activities	36	26.93 (1.03)	24.45, 29.45	35	20.73 (1.12)	17.94, 23.51
Taking on a loan for a lesser purchase	37	26.53 (1.12)	23.56, 29.65	36	23.19 (1.24)	19.64, 26.52
Major change in sleeping habits	31	34.81 (1.15)	31.64, 37.69	30	27.77 (1.22)	24.9, 31.18
Major change in number of family get-togethers	38	25.93 (1.08)	23.17, 28.91	37	18.78 (1)	16.27, 21.23
Major change in eating habits	35	29.11 (1.03)	26.46, 31.62	34	24.89 (1.15)	22.09, 27.91
Vacation	41	22.01 (1.12)	19.34, 24.97	40	17.21 (1.1)	14.33, 20.1
Christmas	43	21.66 (1.16)	18.87, 24.53	42	17.38 (1.18)	14.5, 20.74
Minor violations of the law	40	23.82 (1.06)	21.32, 26.44	39	19.87 (1.14)	17.18, 22.73
Single person, living alone*		40.10 (1.55)	35.91, 44.52		35.37 (1.76)	30.48, 39.73

*'Single person, living alone' was not included in the ranking as it was not part of the original rating of the SRRS.

6.3.6 Impact of personal experience on SRRS ratings

To ascertain whether there was a link between ratings for each life event and personal experience of that item a series of correlations using Kendall's tau were conducted. Descriptive statistics for personal experience in Table 6.7 are provided. Of 42 items, 18 showed a statistically significant correlation (p's ≤ .042). However, all coefficients were very small (r ≤ .146). The Bayesian Kendall's tau similarly found evidence ranging from substantial to decisive (BFs ≥ 3.0) for 15 items. Of these, 6 items were supported by ≥ very strong evidence but correlation coefficients remained small with magnitudes ranging from 0.108 to 0.146 as shown in Appendix 9. These results suggest that there may have been some events for which personal experience were weakly, positively associated with event ratings. Overall, however, participants' personal experiences did not appear to systematically bias their ratings.

Table 6.7 Descriptive statistics showing the extent to which ratings were based on personal experience.

Life event	Mean % (SE)*	Median % (IQR)
Christmas	83.39 (1.14)	99 (76 - 100)
Vacation	81.35 (1.1)	93 (68 - 100)
Death of a close family member	73.11 (1.55)	90.5 (60 - 100)
Change in residence	72.96 (1.42)	85 (59 - 100)
Beginning or ceasing formal schooling	68.05 (1.56)	80 (45.5 - 100)
Pregnancy	56.17 (1.95)	77.5 (0 - 100)
Major change in the health or behaviour of a family member	65.4 (1.53)	75 (41 - 100)
Taking on a mortgage or loan for a major purchase	58.39 (1.81)	74 (2 - 100)
Gaining a new family member	58.74 (1.78)	70.5 (7.5 - 100)
Major change in sleeping habits	62.54 (1.53)	70 (29 - 100)
Changing to a new school	58.56 (1.7)	70 (13 - 100)
Troubles with the boss	58.63 (1.63)	70 (19.5 - 99)
Major change in financial state	62.59 (1.43)	70 (39 - 94.5)
Taking on a loan for a lesser purchase	54.91 (1.8)	68 (1.5 - 100)
Changing to a different line of work	56.08 (1.6)	66 (17 - 89.5)
Major change in number of family get-togethers	57.12 (1.49)	63.5 (26 - 86)
Major change in eating habits	56.3 (1.55)	63 (20.5 - 90)
Single person, living alone	51.99 (1.89)	61.5 (0 - 100)
Major change in responsibilities at work	53.77 (1.55)	61 (18 - 86)
Major change in work hours or conditions	54.15 (1.5)	61 (21 - 81)
Outstanding personal achievement	51.31 (1.62)	56 (13 - 85)
Major change in usual type and/or amount of recreation	49.05 (1.51)	55 (12 - 77)
Major personal injury or illness	49.93 (1.73)	54.5 (4 - 95.5)
Major change in social activities	48.51 (1.5)	53 (13.5 - 76)
Major change in living conditions	47.19 (1.66)	51 (1 - 82)
Losing your job	46.81 (1.81)	50.5 (0 - 93)
Major change in the number of arguments with spouse/life partner	43.12 (1.58)	44 (1 - 74)
Revision of personal habits	42.1 (1.56)	41.5 (3 - 72)
Minor violations of the law	43.8 (1.8)	35 (0 - 89)
Spouse/life partner begins or stops working	42.17 (1.81)	26.5 (0 - 90)
Death of a close friend	40.33 (1.84)	17 (0 - 90)
Sexual difficulties	33.85 (1.64)	15 (0 - 69)
In-law troubles	32.57 (1.67)	11 (0 - 66)
Major change in religious activities	25.72 (1.51)	2.5 (0 - 51)
Son or daughter leaving home	34.66 (1.86)	1 (0 - 87)
Marital separation	26.48 (1.7)	0 (0 - 55.5)
Death of a spouse or life partner	17.71 (1.48)	0 (0 - 11)
Divorce	25.52 (1.71)	0 (0 - 53)
Marital reconciliation	15.4 (1.33)	0 (0 - 10)
Major business readjustment	20.75 (1.37)	0 (0 - 31)
Retirement from work	28.6 (1.75)	0 (0 - 61)
Foreclosure/repossession on mortgage or loan	11.04 (1.11)	0 (0 - 3)
Detention in jail or other institution	10.58 (1.18)	0 (0 - 0)

*Ordered from highest to lowest mean % personal experience.

A value of 100 indicates that the rating for an item was completely based on personal experience.

A value of 0 indicates that the rating for an item was not at all based on personal experience.

N = 536

6.3.7 Impact of loneliness on SRRS ratings

Overall, participants' average loneliness score (loneliness level), as measured by the R-UCLA (higher value = higher level of loneliness), was M = 5.1 (SE = .08), ranging from 3 to 9. In response to how often respondents felt lonely (loneliness frequency), with a lower value indicating feeling lonely more often, 9.8% (n=53) were lonely 'often/always', 24.1% (n=130) 'some of the time, 24.3% (n=131) 'occasionally', 27.6% (n=149) 'hardly ever' while 13% (n=70) indicated 'never'.

To explore whether loneliness affected SRRS ratings, Kendall's tau correlational analyses were conducted to test the association between the R-UCLA and loneliness frequency measures and each of the 43 SRRS rating items. The frequentist analyses for both level and frequency of loneliness revealed statistically significant correlations for 7 items (p's ≤ .039), however the correlation coefficients were very small (r ≤ .128). For both level and frequency, 5 items were 'Revision of personal habits'; 'Foreclosure/repossession on mortgage or loan'; 'Detention in jail or other institution'; 'Major change in usual type and/or amount of recreation'; 'Major change in work hours or conditions' and 'Major change in religious activities'. For loneliness level only 'Major change in sleeping habits' was significant. For loneliness frequency only 'Major change in social activities' was significant. Bayesian analysis was only conducted for loneliness level as there was no equivalent non-parametric Bayesian analysis for loneliness frequency in JASP. The Bayesian Kendall's tau conducted between R-UCLA scores and ratings revealed only two noteworthy results:

decisive evidence for a small positive correlation (r = 0.128, BF > 100) between ‘Revision of personal habits’ and R-UCLA scores and substantial evidence, likewise, for 'Single person, living alone' and R-UCLA scores (r = 0.082, BF = 3.18). These outcomes indicated that an increase in the respective ratings was associated with an increase in level of loneliness experienced. All other associations either supported the null ($ratings_n$ = 32; BF ≤ 0.30) or evidence was anecdotal ($ratings_n$ = 9; ≤ 0.35 BF ≤ 2.42).

6.3.8 Extending the SRRS: new items

6.3.8.1 Proposed new item: ‘Single person, living alone’

A 44th item: ‘Single person, living alone’ was added. Table 6.8 provides descriptive statistics and rank for this item relative to the existing 43 life events. As the table shows, the overall averaged weight based on the arithmetic mean was 38 (SE = 1.13), which places its rank as lower than marriage. Non-parametric frequentist and Bayesian statistics were used to evaluate whether ratings for this event differed depending on age, sex, ethnicity, relationship status, employment status or religion. Table 6.9 presents their descriptive statistics. A Kruskal Wallis test revealed no statistically significant differences between age groups (p > .07). Bayesian Mann-Whitney U tests compared all 2-way age group combinations and similarly found evidence supporting the null regarding YA vs. MA and MA vs. OA (BFs ≤ 0.17). Evidence comparing YA and OA was anecdotal (BF = 0.43). Comparing males and females, a Mann-Whitney U test revealed a statistically significant difference (z = -2.086, p = .034) with females (Mdn = 40) rating this item higher than males (Mdn = 30). The Bayesian Mann-Whitney U revealed anecdotal evidence (BF = 0.52), however. For

ethnicity (white vs. non-white) and employment (employed vs. unemployed) ratings between groups were comparable for both frequentist ($p > .3$) and Bayesian ($BF \leq 0.14$) tests. In contrast, both relationship status (married vs. unmarried) and religion (religious vs. non-religious) frequentist Mann Whitney tests revealed statistically significant outcomes. The married group (Mdn = 40) assigned a higher rating than the unmarried group (Mdn = 35) ($z = -2.578$, $p = .01$) and for the religion comparison, the religion group (Mdn = 40) ($z = -2.615$, $p = .009$) rated this item higher than the no religion group (Mdn = 30). However, the corresponding Bayesian Mann-Whitney U results revealed anecdotal evidence for both relationship status ($BF = 1.77$) and religion ($BF = 1.68$). Thus, it remains unclear if participants from these respective sub-groups differ systematically regarding this item.

These results indicate that ratings for ‘Single person, living alone’ were comparable across age groups, ethnicity and employment status. However, for sex, religion and relationship status evidence was inconclusive. Bayes factor sensitivity analyses (Appendix 6) were comparable for all Mann-Whitney U comparisons reported above.

Table 6.8 New vs. original weights and rank order of SRRS events, including new item: 'Single person, living alone'.

	Holmes & Rahe		Present Study				
Event	**rank**	**weight**	**rank**	**Mean (SE)[a]**	**99 % CI[b]**	**Geometric Mean[c]**	**Mdn (IQR)[d]**
Death of a spouse or life partner	1	100	1	86.83 (0.98)	84.16, 89.21	73.78	95 (80 - 100)
Detention in jail or other institution	4	63	2	76.88 (1.14)	73.79, 79.66	61.65	80 (70 - 99)
Death of a close family member	5	63	3	75.84 (1.02)	73.13, 78.46	67.57	80 (60.5 - 95)
Divorce	2	73	4	67.86 (1.03)	65.2, 70.41	56.03	70 (52.8 - 85)
Marital separation	3	65	5	66.9 (1.01)	64.28, 69.33	55.98	70 (50 - 80)
Pregnancy	12	40	6	64.66 (1.06)	62.03, 67.27	47.63	60 (40 - 70)
Major personal injury or illness	6	53	7	64.36 (0.98)	61.9, 66.91	55.98	70 (50 - 80)
Death of a close friend	17	37	8	64.05 (1.12)	61.08, 66.8	44.9	50 (40 - 70)
Foreclosure/repossession on mortgage or loan	21	30	9	62.39 (1.07)	59.65, 65.09	32.71	40 (25 - 60)
Losing your job	8	47	10	60.97 (1.03)	58.2, 63.5	24.33	30 (20 - 50)
Major change in the health or behaviour of a family member	11	44	11	55.73 (0.98)	53.06, 58.24	38.01	50 (30 - 70)
Major change in financial state	16	38	12	52.02 (0.94)	49.68, 54.68	35.47	50 (30 - 65)
Gaining a new family member	14	39	13	51.81 (1.11)	49.05, 54.65	29.09	40 (20 - 50)
Marriage (pre-set weight)	7	50	14	50			
Retirement from work	10	45	15	49.64 (1.08)	46.73, 52.45	35.58	50 (30 - 60)
Major business readjustment	15	39	16	46.73 (1.06)	43.96, 49.49	40.18	50 (30.8 - 70)
Marital reconciliation	9	45	17	46.24 (0.97)	43.77, 48.59	51.32	65 (45 - 80)
Major change in the number of arguments with spouse-life partner	19	35	18	44.21 (0.92)	41.75, 46.56	31.1	40 (25.5 - 50)
Change in residence	32	20	19	42.69 (0.95)	40.33, 44.99	34.54	40 (30 - 59.8)
Taking on a mortgage or loan for a major purchase	20	31	20	42.22 (0.99)	39.78, 44.79	34.98	45 (30 - 60)
Son or daughter leaving home	23	29	21	41.66 (0.99)	39.2, 44.19	21.75	30 (15 - 40)
Spouse/life partner begins or stops working	26	26	22	40.06 (0.9)	37.72, 42.36	21.22	30 (10 - 50)
Changing to a different line of work	18	36	23	39.48 (0.85)	37.3, 41.68	52.64	70 (45.8 - 80)

Table 8 cont'd overleaf.

Table 6.8 New vs. original weights and rank order of SRRS events, including new item: 'Single person, living alone'.

	Holmes & Rahe		Present Study				
Event	**rank**	**weight**	**rank**	**Mean (SE)[a]**	**99 % CI[b]**	**Geometric Mean[c]**	**Mdn (IQR)[d]**
Major change in living conditions	28	25	24	39.36 (0.9)	37.01, 41.75	23.76	30 (20 - 50)
Single person, living alone			25	38.16 (1.13)	35.41, 41.16	24.14	40 (15 - 50)
Sexual difficulties	13	39	26	38.07 (0.92)	35.74, 40.61	53.44	70 (50 - 80)
Major change in responsibilities at work	22	29	27	37.8 (0.83)	35.54, 39.94	50.24	70 (50 - 80)
Major change in work hours or conditions	31	20	28	37.09 (0.84)	34.76, 39.32	20.44	25 (10 - 40)
Changing to a new school	33	20	29	34.6 (0.93)	32.29, 36.95	29.5	35 (20 - 50)
Beginning or ceasing formal schooling	27	26	30	33.88 (0.91)	31.57, 36.14	31.07	40 (25 - 55)
Major change in sleeping habits	38	16	31	31.92 (0.84)	29.83, 34.3	24.85	30 (20 - 40)
Outstanding personal achievement	25	28	32	30.94 (0.96)	28.49, 33.55	30.56	38.5 (21.3 - 50)
In-law troubles	24	29	33	30.94 (0.91)	28.62, 33.26	31.31	40 (25 - 60)
Troubles with the boss	30	23	34	29.15 (0.9)	26.72, 31.74	15.66	20 (10 - 30)
Major change in usual type and/or amount of recreation	34	19	35	29.08 (0.78)	27.01, 31.04	11.43	15 (5 - 30)
Major change in eating habits	40	15	36	27.39 (0.77)	25.2, 29.47	15.72	20 (10 - 30)
Taking on a loan for a lesser purchase	37	17	37	25.12 (0.84)	22.97, 27.6	17.36	20 (10 - 35)
Major change in social activities	36	18	38	24.39 (0.8)	22.31, 26.45	17.35	20 (10 - 30)
Major change in number of family get-togethers	39	15	39	22.88 (0.76)	20.9, 24.92	20.74	25 (10 - 40)
Revision of personal habits	29	24	40	22.8 (0.77)	20.95, 24.85	30.96	40 (25 - 53.8)
Minor violations of the law	43	11	41	22.14 (0.76)	20.12, 24.19	14.99	20 (10 - 30)
Major change in religious activities	35	19	42	20.09 (0.8)	18.01, 22.2	22.07	30 (15 - 40)
Vacation	41	13	43	20.09 (0.81)	18.03, 22.25	12.64	10 (6 - 30)
Christmas	42	12	44	19.78 (0.84)	17.79, 21.93	11.8	10 (5 - 30)

Table ordered by Present Study's ranks, including 'Single person, living alone'.

[a] Mean (SE). Standard error obtained via BCa Bootstrap with 1000 samples.

[b] 99% confidence intervals obtained via BCa Bootstrap with 1000 samples.

[c] Where participants responded with a zero value, these were replaced with '1' to allow this value to be calculated.

[d] Mdn (IQR) = Median and inter-quartile range in brackets.

Table 6.9 Descriptive statistics for 'Single person, living alone' per demographic factor.

demographic factor	sub-groups	Mean (SE)	Median (IQR)
age			
	< 30 years	34.96 (2.61)	30 (10 - 50)
	30 to 60 years	37.84 (1.52)	35 (18 - 50)
	> 60 years	41.66 (2.31)	45 (20 - 65)
sex			
	female	40.1 (1.51)	40 (20 - 60)
	male	35.37 (1.73)	30 (10 - 50)
ethnicity			
	white	38.62 (1.25)	40 (15 - 52)
	non-white[a]	35.72 (2.81)	30 (15.5 - 50)
religion			
	no religion	35.35 (1.67)	30 (10 - 50)
	religious[b]	40.88 (1.56)	40 (20 - 60)
relationship status			
	married[c]	40.22 (1.41)	40 (20 - 60)
	unmarried[d]	34.57 (1.93)	35 (10 - 50)
employment status			
	employed	37.26 (1.42)	35 (15 - 50)
	unemployed[e]	39.79 (1.93)	40 (15.3 - 60)

[a] 'non-white' included all ethnicities: mixed race, Asian (southern/southeastern Asia), Chinese (east Asian), black (any region).

[b] 'religious' includes all religions: Christian, Buddhist, Hindu, Jewish, Muslim, Sikh, any other religion.

[c] 'married' includes married and long-term partners.

[d] 'unmarried' includes those who don't qualify as 'c': divorced, in a relationship, life partner died, separated, single, widowed.

[e] 'unemployed' includes those currently unemployed and looking for work, have never worked, long-term sick/disabled, looking after home or family, retired, student (p/t or f/t) and currently unemployed, other.

6.3.8.2 Items proposed by respondents

Participants were asked to provide a new item along with a corresponding rating for the amount of adjustment it required. Of 540

participants 259 (48%) gave no response, 50 (9.3%) suggested an item that was already in the SRRS. Further, one respondent gave a comment rather than an item, leaving 230 (42.6%) responses. Of 230 responses 43 items were ‘one-off’ suggestions (e.g. ‘Brexit’), which were grouped as ‘other’ and a further 11 participants offered more than one item but with only one rating. These 54 responses were excluded from consideration because their respective ratings were either unclear or could not be averaged. The final list comprised 176 respondents’ proposed new items along with their weightings, given in Table 6.10. Items were given in participants’ own words therefore item wording was chosen as appropriate. For example, the item: ‘Death of a pet’ was based on statements including ‘loss of a pet’, ‘losing a pet’, ‘death of a family pet’ and ‘death of a pet’. The top 3 items were ‘Mental health issue’ (17%), ‘Death of a pet’ (14.8%) and ‘Emigration’ (8.5%). The averaged weights were 77, 72 and 69, respectively, as the table shows.

Table 6.10. Mean and standard errors (SE) for own items and frequency of raters per item.

Suggested additional items for SRRS	Number of raters (n=176)	Mean (SE)
Mental health difficulties	30	77.2 (3.56)
Death of pet	26	72.31 (4.43)
Emigration	15	69.27 (4.93)
Relationship break-up	12	71.25 (6.8)
Covid (having the illness/unspecified)	10	76.5 (7.15)
Covid restrictions (e.g. lock-down)	7	70 (7.94)
Accident (e.g. car accident)	6	57.17 (10.59)
Becoming a carer (e.g. elderly relative)	6	81.67 (5.43)
Getting a pet	6	38.33 (4.94)
Infidelity (having affair)	6	78.67 (7.23)
Relocation	5	62 (3.39)
War/conflict	5	95 (5)
Addiction	4	62.5 (8.54)
Change in state policy/regime (e.g. Brexit)	4	60.75 (14.08)
Natural disaster	4	80 (4.08)
Sexuality/gender-identity (e.g. identifying as gay)	4	57.5 (12.5)
Trouble with neighbours	4	48.75 (14.35)
Victim of crime	4	48.75 (14.78)
Abuse	3	88.33 (4.41)
Adjusting to older age	3	60 (5.77)
Bullying	3	75 (2.89)
Domestic violence	3	91.67 (4.41)
Assault	2	47.5 (17.5)
Terminal illness	2	82.5 (7.5)
Wedding	2	80 (20)

6.4 Discussion

The SRRS weights were successfully updated using the ratings of 540 predominantly UK respondents aged 18 to 84. In addition, item wording was modernised, one optional extra item was added to the end of the scale and 3 potential new items proposed by raters were identified, namely: ‘Mental health issue’, ‘Death of a pet’ and ‘Emigration’. Changes/modernisations made did not affect the meaning of any of the

original items. No items were removed. By doing so, the SRRS was improved and backwards-compatibility with the original scale, that continues to be widely used, was maintained.

The main findings were that the updated SRRS yielded a significantly higher total score on average than the original scale. However, the new weights were broadly consistent with the original weights. Comparing all life events in the original and new scales using Rahe's (1972) 4 categories, 'personal', 'family', 'work' and 'finance' it was found, as with the overall correlation, that there was a strong covariance for all categories except finance. Focusing on the present study's sample, young, middle-aged and older adults were comparable in their total LCU scores. Females assigned, on average, 14% higher weight to life events than males but the statistical evidence for this gender-based variation in life change units was inconclusive. Similarly, while the sample's +70s group assigned, on average, a 4% lower weight to life events than the normative-aged sample, this difference was statistically negligible. Regarding the possible influence of personal experience on ratings, some significant associations were found, though coefficient sizes were very small. The new additional item, 'Single person, living alone' required less adjustment relative to marriage. Most commonly, participants felt lonely occasionally and average level of loneliness was rated towards the lower end of the range. Loneliness was, at best, weakly associated with the SRRS ratings given. Thus, participants' ratings, particularly for 'Single person, living alone' were unlikely to have been influenced by their experience of loneliness.

6.4.1 SRRS life events require more adjustment now than in 1967

A comparison with the original SRRS weights indicated an overall average increase in rating values of 28%, which suggests that, on average, adults find SRRS events more taxing now than in 1967. Consistent with this increase, Miller and Rahe (1997)'s update (n=426) revealed a 45% overall increase. However, as in their update, a strong covariance pattern across ratings was found, but with some exceptions. Three of the items increased by ≥ 25 life change units (LCUs) relative to the original scale. They were also among the 6 items that had increased by ≥ 25 LCUs in the Miller and Rahe (1997) update. Taken together, the aforementioned outcomes suggest that since the original weights were derived there has been considerable change in perceived adjustment needed regarding certain key life events such as pregnancy and foreclosure on a loan, but on the whole, there is overall consensus regarding relative importance of the life events in the scale. The exception being financial items. The new sample's weights for the 4 financial life events did not correlate with the original sample and, as a category, showed the largest average increase in weights while family items showed the smallest increase. By comparison, the Miller and Rahe (1997) update also showed the largest average increase in weights for financial items but the smallest increase was for personal items. Interestingly, the Scully et al. (2016) update relative to the original indicated that, across categories, weights consistently decreased but the smallest decrease was for financial items. Scully's sample comprised 200 Florida residents, however, which makes their result less generalisable. The relative volatility of the financial

items may be because there are only 4 items included in this sub-set. In addition, one could argue that economic factors are generally more volatile than social factors though a thorough examination of this would be required.

6.4.2 Females' ratings for SRRS life events were slightly higher

Females' total LCUs were 14% higher on average relative to males' LCUs, though this difference was inconclusive. However, an in-depth Bayesian analysis for each of the 4 categories revealed substantial to very strong evidence that females' weights were consistently higher than males' weights. This pattern of higher weights among females is in line with Miller and Rahe (1997)'s update reporting that their females' weights were 17% higher. They did not report whether this difference was statistically significant. This pattern indicating that females typically assign a greater level of adjustment to change relative to males, warrants more detailed investigation in future work. Research investigating the gender-specific profiles of psychiatric disorders indicate that stressed women become hyper-aroused, which is a common feature of depression (Bangasser et al., 2018). However, stressed men's cognitive function can be differentially disrupted (Bangasser et al., 2018; Shields et al., 2016) and evidence shows that these differences associated with stress may be consequent to sex-based differences within the locus coeruleus-norepinephrine arousal system (Bangasser et al., 2019; Bangasser et al., 2018). These results show that there are numerous underlying psychological, physiological and environmental factors to consider

regarding gender-based differences in stress-reactivity and, by implication, perceived adjustment to different life events.

6.4.3 Adults aged 70+ rate SRRS items similarly to adults aged 18 to 69

The normative and 70+ groups gave comparable ratings on average. In contrast, Muhlenkamp et al. (1975)'s study (n=41) found that older participants assigned higher weights relative to the original 1967 sample. However, in line with the present study's results, they concluded that there was agreement regarding relative importance of some life events. They argued that their older group's higher ratings for 'personal' life events were consistent with literature indicating that adults become more self-orientated (egocentric) with age (Muhlenkamp et al., 1975). By comparison, the present results are congruent with the consistent finding in the literature that social and emotional functioning does not change significantly across the lifespan and that self-regulation, including coping with stressors, improves with age (Charles & Carstensen, 2010). Further support of this is that the young, middle-aged and older adults were comparable in their ratings, which yielded very similar averages and age did not reveal any systematic differences when considering items as categories. However, this does not mean that age should be ignored. While older age is associated with improved emotional well-being, they respond less well compared to the young in some situations. For example, older adults show more pronounced psychological and physiological reactions relative to younger adults when stressful events are complex, affecting multiple life domains, (Wrzus et al., 2013). It is also worth noting

that middle adulthood is associated with increased roles and responsibilities such as career progression and having a family. Moreover, they are pivotal to the younger and older members of their family (Lachman et al., 2015) which can be very stressful particularly for those caring for children and older parents/relatives (Gillett & Crisp, 2017). These points highlight the complexity of measuring the impact of life events at different points across the lifespan.

6.4.4 Adding ratings for a new item: 'Single person, living alone'

'Single person, living alone', the new item, yielded some differences in ratings between age groups with the greatest disparity between young and older adults (OA>YA). However, the result was inconclusive. The same was true for comparisons by relationship status, religion and sex. For ethnicity and employment status evidence supported the null. Particularly regarding the age-related finding, this life event is important to monitor in future work. The ONS (2019) data indicate a continuing upward trend in the number of one-person households. Moreover, the ONS data agrees with the findings of a recent study showing that among those in western countries, such as Europe and North America, more males than females live alone among young (25 to 29) and middle-aged adults (50 to 54) while more females live alone among older adults (75 to 79) (Esteve et al., 2020). Their review of global patterns further revealed that family-based living is most common, except in older age. Indeed, among ageing populations around the world, the number of older adults living alone is likely to increase (ibid). It is important to distinguish between sub-populations of older adults who live alone, as those with a diverse social

network (e.g. adult children, siblings, friends and neighbours to socialise with and ask for support) have been shown to have better well-being than those with a restricted network (few family and friends/neighbours to reach out to) (Djundeva et al., 2019).

6.4.5 Raters' 3 new items: 'Mental health issue', 'Death of a pet', 'Emigration'

Roughly half the respondents added an additional item to the given list of events to rate. The 3 most common items are indicated in the sub-title above. The full table of items provides further opportunities for future investigation.

6.4.6 The impact of personal experience and loneliness on ratings

No clear pattern of association was found between ratings and personal experience of the life events nor between ratings and loneliness scores. Regarding personal experiences, 35% of items were significantly correlated but coefficient sizes were of no practical significance, suggesting that respondents were not unduly influenced by their own personal experiences (i.e. they adhered to the instructions to consider their own experiences and those of others). The results for loneliness revealed that for the 2 items, 'Revision of personal habits' and 'Single person, living alone', there was a significant association with loneliness. Again, however, the coefficients were very small, providing confidence that ratings were not biased by loneliness scores suggesting that ratings did not vary systematically with emotional state.

6.4.7 Conclusion

This study's aim was to update and improve the SRRS weights without fundamentally changing the scale to allow for backwards-compatibility of studies. This was achieved by providing new weights for all original items. The updated weights were higher but broadly consistent with those of the original study except for financial items, which may vary considerably over time. Cross-comparability with the original version was allowed for by retaining all original items, making helpful changes to the wording of some items without changing their meaning and adding a new item to the end, which can be excluded for comparisons. This sample's ratings were not unduly by personal experiences of events nor loneliness. Such factors are important indicators of consistency across ratings but were not considered in the original scale nor subsequent versions.

The present study provides updated weights derived from a predominantly UK sample which is broadly proportionately representative regarding age, gender and ethnicity. Moreover, the age-range was broader and sample size slightly larger than the original. A new item was added to the end of the scale, 'Single person, living alone', which will benefit future work given that single-person households have increased in recent years. Three potential new items submitted by respondents have been identified: 'Mental health issue', 'Death of a pet' and 'Emigration'. Further work may be undertaken in future studies to determine whether these items would be beneficial to add. In addition, what is known about the impact of demographics, such as gender and age, on the rating of life events was updated and extended, providing additional scope for future work.

6.5 Supporting Information

Appendix 1 SRRQ (updated version).

Appendix 2 Original Instructions for SRRS.

Appendix 3 SRRS updated version.

Appendix 4 Personal experience of SRRS life events.

Appendix 5 Loneliness questionnaire.

Appendix 6 Bayes Factor sensitivity analysis for all Mann-Whitney U comparisons.

Appendix 7 Social Readjustment Rating Scale by demographic category (unabridged categories).

Appendix 8 Descriptive statistics for SRRS events by unabridged sub-group demographics.

Appendix 9 Bayesian Kendall's tau correlation between event ratings and degree to which these were based on personal experience.

A section containing all appendices can be found starting from page 395, at the end of this thesis.

Chapter 7: General Discussion

The research questions addressed by this thesis asked if cumulative life stress, as measured by a life events questionnaire, has an accelerative effect on ageing and whether practical, broadly available treatment methods such as neuro-electrical stimulation and mindfulness meditation could improve or mitigate executive function and subjective well-being.

Chapter 1 provided a literature review with a focus on two important factors known to moderate brain ageing, namely cumulative stress and ageing. The literature review indicated that both of these factors independently impair cognitive performance, particularly in older adults, via specific biological mechanisms of action, *inter alia*, oxidative stress, immune dysfunction and hormonal dysregulation. Biological dysregulation causes degradation of synapses, which ultimately results in degraded neural networks where changes in phase, phase angle and amplitude in brain oscillations lead to a weaker response to the environment. The consequences of such dysregulation are experienced as poorer cognitive competence and potentially lowered mood and perceived well-being (Castren & Kojima, 2017; Castren & Monteggia, 2021). When considering the effects of stress, particularly in parallel with those of ageing, the potential interaction of these two factors may change overall ageing trajectories. Consider that chronically circulating non-baseline levels of glucocorticoids have been shown to modulate brain structure including changes to dendrite number, length and density - particularly in the

hippocampus and amygdala – areas where glucocorticoid receptors are abundant. Consider also that ageing is known to blunt diurnal cortisol fluctuations. This in turn may be associated with dysfunction of the suprachiasmatic nucleus, which regulates the hypothalamic-pituitary-adrenocortical axis (HPA). Thus, it seems plausible that the two effects could combine in such a way as to accelerate ageing. This is what Marshall and colleagues found in their work on executive task performance comparing older and young adults who reported high vs. low levels of cumulative life stress. They showed (2015) that older adults who had experienced high levels of cumulative stress did less well in working memory accuracy relative to older adults who had experienced low levels of cumulative life stress and young adults, irrespective of cumulative stress experienced. Their EEG results were congruent with these outcomes and pointed to early cognitive decline in this sub-group. Not all research at the time was congruent with their findings, however. In a longitudinal study, Sussams and colleagues (2020) showed that neither stressful life events nor perceived stress were associated with early cognitive decline. Ultimately, whether through ageing, stress or the combined effect of the two, behavioural changes become apparent through reduced processing speed, a marker for fluid intelligence and decision-making.

Chapter 1 then went on to discuss how brain health can be maintained or stave off the effects of ageing and/or stress-related perturbations. Two alternatives, mindfulness meditation (MM) and transcranial electrical neuromodulation (tES), were chosen as viable

solutions because they are non-physical, simple, cost-effective and can potentially be done in any setting. Importantly, both have shown promising results in older and young adults but no previous studies have considered which is the better option and the state-of-the-art regarding both have considerable gaps in knowledge. The next step was to conduct a systematic review of these two interventions to ascertain the efficacy of each relative to the other.

Chapter 2 comprised a systematic review and meta-analysis of MM and transcranial alternative current stimulation (tACS) studies conducted from January 1988 to December 2020. Transcranial alternative current stimulation is a type of tES. The purpose was to ascertain the efficacy of tACS vs. MM to improve working memory (WM) performance and/or subjective well-being as demonstrated by a comparison of their overall effect sizes. Working memory performance was chosen as a proxy measure of executive function. Subjective well-being was operationalised and measured as levels of self-reported stress, anxiety, sleep quality and/or mood.

Original peer-reviewed articles were selected and systematically reviewed based on pre-set parameters. The target population was healthy adults ≥ 18 years. For tACS, included studies were sham-controlled with current intensity between 1 – 2 mA, for the continuous duration of ≥10 min, targeting anatomic areas relevant to executive function under single or double-blind conditions. Executive function is also important for emotional regulation and, by implication, subjective well-being, therefore no specific neural sites pertaining to subjective well-being were specified. Tasks were

performed online or post-stimulation. For MM, meditation protocols had to be seated with eyes closed for a continuous duration of ≥ 10 min per meditation session. Instruction had to have been received from a qualified instructor/recording and compliance measures reported for any unsupervised meditation practice. All studies had to use a between-subjects, pre-post design. All tasks had to be well-validated, measuring either working memory performance e.g. n-back task and/or self-reported subjective well-being e.g. Positive and Negative Affect Schedule (PANAS).

Fifteen eligible MM and 17 eligible tACS studies were identified by the systematic review. For MM, a meta-analysis was performed for subjective well-being and WM accuracy. For tACS, only WM studies were meta-analysed. No effect size comparisons between tACS and MM were possible due to insufficient data. For MM, 9 subjective well-being studies (n=586) were meta-analysed revealing no statistically significant evidence that MM improved subjective well-being. The tACS accuracy meta-analysis of 17 studies (n=553) revealed, through sensitivity analyses, that these studies could be separated into two distinct sub-groups. The larger sub-group (k=11) revealed no statistically significant evidence of improved WM accuracy relative to sham. The smaller sub-group, based on two experiments from one study, revealed a statistically significant moderate effect size in favour of tACS. Importantly, these sub-groups differed regarding two critical methodological factors: stimulation protocol and age group sampled. The larger sub-group tested only student/young-adult samples, whereas the smaller sub-group targeted older adults. The literature indicates that electrical stimulation yields a limited ‘improvement

range' in cognitive performance (Hsu et al., 2014; Tseng et al., 2012), which suggests that those with the worst performance are likely to improve the most. The smaller sub-group's findings were consistent with this hypothesis. Additionally, the smaller sub-group's stimulation protocol was substantially different to those used by the studies in the larger group. They applied 6 very small electrodes that targeted individually optimised theta-gamma coupled frequencies; the effect of stimulation was measured continuously across online then offline task performance. Their change detection task included no repeat sequences of stimuli, thereby reducing statistical noise from practice effects. In contrast, all the studies in the larger sub-group targeted one frequency range (theta or gamma) with ≤ 5 typically less focal electrodes with performance measured either online or offline. Moreover, while target stimuli were randomised, they were repeated in most tasks (e.g. n-back task where a limited range of numbers (1-9) were used).

There was no statistically significant evidence that tACS improved working memory RTs based on 8 (n=257) eligible meta-analysed studies.

While previous evidence has shown that tACS and MM can improve cognitive function and well-being (Gard, Taquet, et al., 2014; Tavakoli & Yun, 2017; Tsai & Chou, 2016) in young and older adults (e.g. Antonenko et al., 2016; Brown et al., 2021; Colzato et al., 2016; McHugh et al., 2010), the present work has shown that there are substantial caveats to the available evidence. In particular, MM studies lack scientific rigour – for example the level of detail of the MM implemented varies from study to study and the published meta-analyses of these studies adopt a

very broad interpretation of MM by including practices with both physical and non-physical components, which may differ qualitatively in their mechanisms of action. Along similar lines, tACS studies, while typically rigorous (e.g. single- or double-blind design), appear to differ based on target population (e.g. young vs. older adults), stimulation protocols (e.g. current density) and their level of sophistication (e.g. theta-gamma coupled vs. theta or gamma).

Chapter 3 aimed to replicate Marshall et al.'s (2015) working memory study that found a statistically significant interaction between age and cumulative stress, thus indicating that high cumulative stress older adults performed worse than low stress older adults and young adults. Their design was extended by adding a picture free recall task which aimed to target episodic memory, an important component of working memory. Note that both episodic and working memory are underpinned by the hippocampus and prefrontal cortex, which are malleable structures affected by both stress and ageing. In addition, Marshall et al.'s (2015) findings were extended by adding a neurostimulation protocol to assess whether tES could be used to enhance working memory performance. Transcranial alternating current stimulation (tACS) was chosen because it has the capacity to harness existing endogenous neural oscillations and therefore seemed more likely to succeed than tDCS. Methodologically, the aims were to test two different montages within this protocol to assess the best anatomical areas to target and the precise frequency to use, as there were theoretical reasons supporting multiple options described in detail in Chapter 3 (Barbey et al., 2013; Blumenfeld & Ranganath, 2019;

Fedorenko et al., 2013; Fusco et al., 2018; Marek & Dosenbach, 2018; Petrides & Pandya, 2002). It was also important to ensure that all the tasks were suitable and that the older adult sample could tolerate the full study protocols respecting comfort/fatigue as they would have to complete numerous tasks whilst also being stimulated. Importantly, frequentist and Bayesian statistics were used to ensure that the findings were robust. The study was a block-randomised single-blind cross-over sham-controlled design where a number of psychological measures were administered to assess sub-clinical trait and state anxiety, current levels of stress, sleep quality, resilience and cumulative stress levels. This was followed by a neurostimulation session where 6 Hz frequency tACS at 1 mA (peak-to-peak) was administered for 20 minutes. During the stimulation, participants completed a picture recall task followed by a 2-back task identical to that used by Marshall et al. (2015). Participants attended 2 sessions, 1 week apart at the same time of day. They were monitored for comfort before, during and after stimulation and blinding efficacy was assessed at the end of session 2. No participants withdrew due to adverse effects from the stimulation. A key finding of this study was that tACS was able to elicit a 2.8% statistically significant improvement in performance. This result contributes to existing evidence indicating that theta tACS has the potential to enhance working memory performance (e.g. Chander et al., 2016; Jausovec et al., 2014; Meiron & Lavidor, 2014; Pahor & Jaušovec, 2017; Polania et al., 2012; Violante et al., 2017; Wolinski et al., 2018). Interestingly, tACS caused a slowing in RTs in the final block of the 2-back task, with participants' responses being 9% slower during active

stimulation relative to sham trials. This finding accords with Holczer and colleagues' (2020) results. Their 6 Hz tACS study investigating cognitive conflict processing revealed that RTs were slower for active than sham participants with no evidence of an effect on corresponding accuracy. In the present study, it is speculated that participants reached maximal performance efficiency in block 2 (when accuracy was greatest) followed by processing fatigue and a consequent significant drop-off in processing speed. This suggests that theta tACS can improve accuracy performance but causes rapid processing fatigue. No detectable effect of montage was found. Moreover, no differences in performance were detected between active and sham stimulation for the picture free recall task. These outcomes may be explained by the stimulation protocol which used 2 large electrodes, which may have created a general depolarising effect making it difficult to discern any network-specific effects. In addition, stimulating effects, being diffuse, would have been limited to cortical regions (Ruffini et al., 2013). Regarding cumulative life stress, those high in cumulative life stress responded more slowly than their low-stress counterparts. Noteworthy is that high stress participants made RT gains as the task progressed. The literature has demonstrated robustly that working memory performance is affected by stress through the interaction between stress signalling and PFC circuits (Arnsten, 2009; Arnsten et al., 2012). It is therefore possible that high levels of cumulative stress results in limited resources being diverted away from the WM task because of this. Importantly, the age by cumulative stress interaction effect for accuracy was not replicated. This may be explained by a lack of statistical power as

only session 1 sham participants were entered into this analysis. The aforementioned results were consistent across Bayesian and frequentist analyses.

Chapter 3 demonstrated an effect of tACS on working memory performance using a 2-back task. No conclusive evidence was found of an accelerative effect of cumulative stress on ageing, thus the robust effects shown by Marshall and colleagues (2015) were not replicated, highlighting the importance of challenging the reliability of findings in research. Note that this pilot study was cut short because the University of Essex went into lock-down due to the Covid-19 pandemic. Consequently, it was not possible to complete data collection resulting in a slightly smaller sample than that used by Marshall et al. (2015) (n=40 vs. n=60).

In Chapter 4, two follow-up studies were conducted. In the first (Study 2A), the aim was to replicate the pilot study's findings with a new sample of participants to ascertain these results' robustness. Specifically, the intention was to confirm the previous findings which showed a) no statistically significant interaction between ageing and cumulative stress; b) poorer WM performance in high relative to low cumulative stress individuals; and c) slower RTs in high relative to low-stress individuals, particularly at the start of the 2-back task.

The second follow-up study (Study 2B) sought to ascertain whether the pilot study's RT results might be explained by mental load, as was pointed out by the authors of an acute stress study (Schoofs et al., 2008)

which obtained a similar result. In Study 2B, exactly the same protocol was used as in Study 2A but a 1-back task was added so that low and high mental load performance could be compared. Specifically, if the interaction found in the pilot study related to load (performance under high mental load conditions), one would expect that only the initial finding for the 2-back version of the n-back (in both follow-up tests) would be replicated. If the interaction related to timing (performance in the first block), one would expect that the same pattern in performance would be demonstrated for the first block of Study 2A (2-back) and the first block of Study 2B (1-back) in the respective studies. Methodologically, the aim of this work was to increase the sample size to better match that of Marshall et al. (2015). Consistent with Chapter 3, frequentist and Bayesian analyses were employed to ensure that the statistical outputs were reliable.

Given that only online studies were possible, the tACS condition and picture free recall task were dropped, the latter because it was not suited to an online format. Both studies employed the same n-back task as before. Independent samples of young adults (YA) and older adults (OA) were recruited for each study using Prolific, an online recruitment platform.

Studies 2A and 2B revealed no statistically significant overall effect for accuracy or RT performance in YA vs. OA participants or low cumulative stress (LS) vs. high cumulative stress (HS) participants. Critically, there was also no statistically significant interaction effect between age and cumulative stress.

Consequent to studies 2A and 2B, iterative Bayesian meta-analyses were conducted, respectively, for accuracy and RTs with the 3 sets of results from Study 1 (Chapter 3), Study 2A and Study 2B. Marshall et al.'s (2015) effect sizes served as prior models given that there were no studies available from the literature. The purpose was to assess the strength of the evidence supporting the hypothesis that working memory is detrimentally affected by cumulative stress, ageing and/or the interaction of the two. Importantly, better statistical power was harnessed by using a combined sample (N=156) with a powerful statistical technique (Bayesian statistics) that could demonstrate robustly whether there was evidence of an interaction between ageing and cumulative stress, evidence of no such effect or evidence that the outcome was inconclusive (i.e. further testing may be needed). The results of the meta-analyses revealed inconclusive evidence for an effect of ageing, cumulative stress and their interaction for WM accuracy and RTs.

Chapter 4 demonstrated no agreement between the present finding and Marshall et al.'s (2015) study. While their n-back results showed poorer performance in older than young adults, this study found an inconclusive result. Likewise, their key finding that there was a clear interaction between cumulative stress and ageing was not supported. It is possible that cumulative stress does degrade performance in older adults, but is masked by ageing effects. A previous meta-analysis by Verhaeghen (2013), in line with theoretical work by Salthouse (1994, 1996) demonstrating age-related slowing in processing speed, showed that ageing strongly mediates performance in higher cognitive function such as

WM and executive control. Interestingly, previous studies using the same/similar life stress measures as used here have shown that high cumulative stress YA were detrimentally affected academically, psychologically and physiologically relative to their low-stress counterparts (e.g. Clements & Turpin, 2000). Thus, it may be methodologically preferable to measure cumulative stress effects in a younger sample. A much larger sample may facilitate a clearer result in a future study.

In Chapter 5, a bigger sample was used given the findings in the previous chapter. Moreover, to address the retrospective nature of the study design, time was included as a factor by adding a longitudinal component. Within these considerations was the additional issue of target population. Many studies to-date have focused on comparing young and older adults. This approach was improved upon here by including a middle-aged sample given that, relative to young adults, they are high risk regarding ageing, cumulative stress, health and life-style choices. As reflected in Chapter 1, the range of factors that affect brain health are vast and highly complex. The investigation was therefore expanded to include subjective sleep quality, psychological resilience and adverse childhood events. These factors were identified in the review of the literature as potentially significant to executive functions, such as working memory in one's later years. In the same way that working memory weaves a common thread through a wide range of neurological and neurodegenerative disorders, sleep quality may act as an indicator of health. Indeed, most chronic conditions, whether physiological or psychological, include poor sleep as a symptom. Similarly, early trauma

has been linked to a wide range of health and psychological complaints in later life. Resilience, by contrast, appears to play a pivotal protective role that mitigates the negative effects of poor sleep, adverse childhood events as well as the effects of environmental stressors. Regarding working memory *per se*, the investigation was expanded to include working memory capacity. A well-validated complex span task, the Automated Operation Span Task (A-Ospan) was chosen, allowing for the measurement of working memory capacity in addition to accuracy and reaction time. Importantly, the A-Ospan is time-pressured with variable mental load, thereby potentially increasing any opportunity to accentuate differences in performance potentially associated with higher levels of cumulative stress, poor sleep/resilience and/or early trauma. A complement of these enhancements to the investigation was the continued use of Bayesian analyses alongside frequentist statistical tests to ensure the reliability of findings.

The results for the cross-sectional and longitudinal studies showed that age was positively associated with response speed as expected. As noted in Chapter 1, slower processing is likely to relate to deteriorating white matter integrity (Bennett & Madden, 2014; Gold et al., 2010; Liu et al., 2017; Ziegler et al., 2010), which in turn, reduces network connectivity, particularly long-range connectivity which is critical for WM that relies on a broad range of anatomical areas (Sullivan et al., 2019). Age was also positively associated with reported levels of resilience; older adults' resilience was significantly higher than that of young adults. This result is congruent with the previous finding that resilience is a skill that develops

over time, based on person-environment interactions (Fletcher & Sarkar, 2013). No statistically significant associations were found between any aspect of working memory performance, sleep quality, resilience or adverse childhood events. In addition, 18 months may not be a sufficient time interval to detect an association between the present study's variables of interest and working memory performance. The lack of evidence for any effects in the cross-sectional and longitudinal analyses presented in Chapter 5 is likely to be because of small sample size. Due to attrition only about a third of middle-aged and older participants completed all 3 iterations of the study.

Chapter 5 took the novel step of examining the effects of a wide range of factors on a complex span task in the context of healthy cognitive ageing: cumulative stress, psychological resilience, subjective sleep quality as well as severity, chronicity and frequency of adverse childhood events. The evidence supported the null, indicating no detectable association between any of these factors and ageing trajectories. This work provides an important initial step in examining complex factors such as ageing and cumulative stress in the context of a wider network of factors than previously undertaken in the literature. A population-based study is recommended to fully explore these relationships. This data lays the groundwork for future studies in this area by providing an estimated effect size that can be used as a starting point to develop an informed Bayesian prior in order to improve the power of future studies.

Chapter 6 focused on enhancing the quality of research relating to the Social Readjustment Rating Scale (SRRS). To achieve this, the SRRS

was updated and improved whilst allowing backwards compatibility. This approach was taken, because, although numerous updates have been performed over some 50 years, researchers continue to use the SRRS in its original 1967 form. One possible reason may be that revisions deviated considerably from the original. For example, Hobson and colleagues (1998) published the Revised Social Readjustment Rating Scale (R-SRRS), which added, removed and/or substantially modified some items (e.g. 'Marital separation' and 'Marital reconciliation' which are two separate items in the original SRRS and are ranked differently by raters, were modified to one item 'Separation or reconciliation with spouse/mate'). By ensuring that this update was backwards-compatible, a suitable alternative to the original SRRS was provided for future studies.

To improve and update the SRRS, it was re-rated with a new, larger sample of raters from a broader age range (18 – 85). The original SRRS norms were based on a US sample, therefore raters were selected from the UK population who were proportionately representative of the UK population regarding age, gender and ethnicity. Some items were reworded to be more inclusive/relevant without changing the meaning of the item. The wording used in the original rating version (which is called the 'Social Readjustment Rating Questionnaire') was reinstated, because it is clearer and includes examples in some cases. The present study's ratings were assessed for the presence of systematic bias in ratings regarding personal experience and loneliness, which served as a proxy for depression/emotional state. One optional extra item was added to the end of the SRRS: 'Single person, living alone'. For some this is a positive

experience, but for many it may be a risk factor for social isolation. In addition, raters were asked what they would add as an additional item, given the choice and the rating they would give it. Providing this open-ended question sought to evaluate what event/s the SRRS might be enhanced by in a future update.

To see how congruent the updated weights were with the original version and how different demographic aspects such as age and sex might affect raters' evaluations of how much adjustment was required for each item, 3 investigations were conducted. Firstly, analyses from the literature were replicated. In particular, the summed life change units score (total LCUs) of the original SRRS vs. the update, males' vs. females' average ratings and average ratings by age-group (Miller & Rahe, 1997) were compared. Additionally, average ratings of older adults (70+ yrs) vs. 'normative-age' adults (18 – 69 yrs) (Muhlenkamp et al., 1975) were compared. Secondly, Rahe (1972) categorised the SRRS into 4 sub-sets: 'personal', 'family', 'work' and 'financial'. The present ratings were compared with the original ratings, based on these category subtotals. Thirdly, the association of demographic variables (age, sex, ethnicity, relationship status, religion, employment status) within each of the 4 categories was examined.

The re-rating exercise produced a larger group of raters (540 vs. 394) from a broader age range (18 to 84 yrs vs. 18 to 70 yrs) relative to the original study. Moreover, the sample comprised mainly UK nationals (87%), broadly proportionately representative of the UK population regarding age, sex and ethnicity. Twelve items were re-worded/modernised in the rating

version of the Social Readjustment Rating Scale: the Social Readjustment Rating Questionnaire (SRRQ). The SRRQ wording reinstatement in the updated SRRS, resulted in 26 amended items which importantly did not affect participants' interpretation of the items. The optional extra item added to the end of the SRRS, 'Single person, living alone', yielded an average weight of 38, indicating that it required less adjustment than marriage. The ONS data shows that being single and living alone is on the rise. This event can be a positive experience but may also represent a risk factor for social isolation, depression and suicide (Motillon-Toudic et al., 2022; Stolz et al., 2016). Ratings for 'Single person, living alone' did not co-vary systematically with age, sex, ethnicity, religion, relationship status or employment status. Raters (response rate: 42.6%) proposed 3 new potential items: 'Mental health issue', 'Death of a pet' and 'Emigration' which may be explored in future work.

Ratings, on average, were higher than in the original 1967 study. However, the rankings were broadly similar indicating that, over the past 5 decades, these events' relative adjustment has remained quite consistent. Interestingly, there was no interaction between age group and total life change unit averages suggesting consistency across the life-span. In contrast, females, as a group, gave consistently higher ratings on average for each item relative to males, without exception. Comparing the updated with original ratings regarding the 4 categories, the studies were congruent regarding 'personal', 'work' and 'family', but not 'financial' events. This may be because economic factors are generally more volatile than social factors. Comparing demographic groups within the 4 categories, females

rated all items higher than males, as before. Religious and non-religious individuals were comparable, although for 'personal' events evidence was inconclusive rather than in the null range. Similarly, for relationship status (married vs. unmarried), evidence was inconclusive for 'family' events, but supported the null for 'personal', 'work' and 'financial' events. There were no noteworthy associations of age (YA/MA/OA[35]), ethnicity (white vs. non-white) or employment status (employed vs. unemployed), with evidence supporting the null.

In Chapter 6, a more technically robust version of a widely used life events measure, the Social Readjustment Rating Scale, was provided whilst maintaining backwards-compatibility. Unlike the original study, the present sample was proportionately demographically representative regarding age, sex and ethnicity. Using predominantly UK participants validates the SRRS norms for use with the UK population. Moreover, given the overall similarities with the original US-based norms, the results add to the converging evidence in the literature that the rank order of these 43 items is broadly universal (Hobson & Delunas, 2001; Hobson et al., 1998; Muhlenkamp et al., 1975; Woon et al., 2016). Though care should be taken when using the updated weights with non-Western cultures. It was demonstrated that these updated ratings were not biased by the extent to which raters had experienced the events personally or by emotional state, as measured by loneliness level and frequency. Note that using the present study's updated weights are likely suitable for the general population but if researchers intend to use these with specific sub-

[35] YA/MA/OA = young adults/middle-aged adults/older adults.

populations such as trauma survivors or those living in severe poverty, additional validation is advised.

A possible limitation is noted regarding participant payments. Across all studies in this thesis, student participants typically received course credits whereas all non-student participants were either paid a nominal fee and/or entered into a gift voucher draw or volunteered without payment. However, no analyses were conducted to evaluate whether responses were associated with differences in payment incentive as there was no reason to believe that this would introduce a bias and the most important factors that might affect outcomes were the *a priori* independent variables such as age and cumulative life stress.

7.1 Conclusion and recommendations

The accelerative impact of cumulative stress on cognitive ageing is either very small or there is no impact. This outcome was consistent across a range of differently designed studies, larger sample sizes, two different well-validated working memory tasks and several well-validated subjective well-being measures. Moreover, both Bayesian and frequentist methods produced consistent statistical results.

This work showed that ageing has a slowing effect on processing speed, but not on accuracy or working memory capacity. Cumulative stress, as measured with a life events scale, showed inconsistent effects on working memory performance.

It is also important to highlight that this work showed that self-reported resilience increased with age. This adds to previous work which

demonstrated that psychological resilience is protective and is a skill/ability that can be developed over the course of one's life.

It is recommended that future research uses the considerable bank of data collected as part of this thesis. In particular, the data would serve as an informed prior for future Bayesian studies. In addition, future research should adopt the methodological improvements highlighted such as taking heed of the small effect size that was found consistently pertaining to both cumulative stress and its interaction with age and ensuring that sample sizes are appropriately large. It is further recommended that more focus should be placed on middle-aged adults in future ageing-related research. Middle-aged adults are important because, as indicated in Chapter 5, sleep quality begins to diminish in the middle years (Pace-Schott & Spencer, 2011) which has been linked to neurodegeneration (Scullin & Bliwise, 2015). Moreover, others have shown that changes in hippocampal subfield activation provide an important marker for normal and pathological ageing with changes observed in 40 to 50 year-olds (Riphagen et al., 2020).

The findings in this thesis regarding cumulative life stress should provide reassurance to the public because they do not support the previous research which indicated that people who experience chronic stress or who have experienced many stressful life events may age faster than their lower stress counterparts. This is particularly the case now because the recent pandemic, war in Ukraine and cost of living crisis have increased levels of stress and the likelihood of a mental health crisis.

The pandemic meant this thesis had to be adapted to include online-only studies, which involved moving from an experimental approach to an observational one. This was an opportunity to challenge and improve upon some pre-existing research regarding the accelerative effects of cumulative stress on ageing in working memory using more robust statistical methods and larger, independent samples. Moreover it provided an improved and updated life events stress measure, the Social Readjustment Rating Scale, which can be used in future research and is backwards-compatible.

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Supporting information (Appendices) for all chapters

Chapter 2 **Supporting Information**

Appendix 1	PRISMA table.
Appendix 2	Protocol document including inclusion and exclusion criteria.
Appendix 3	Indices, constructs measured, score ranges and interpretation of scores and the reviewed studies they were used in.
Appendix 4	Risk of Bias full report and studies ineligible for analysis for the Mindfulness Meditation meta-analysis.
Appendix 5	Risk of Bias full report and studies ineligible for analysis for the tACS working memory accuracy meta-analysis.
Appendix 6	Risk of Bias full report and studies ineligible for analysis for the tACS working memory RT meta-analysis.

Chapter 2, Appendix 1

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	p 32
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	n/a
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	p 36
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	p 36
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	pp 39-40 & Appendix 2
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	p 39, Table 1 Appendix 2 page 7
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	pp 41-2, Tables 1, 2 & 3
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	pp 43-6
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	pp 46-7 Table 3
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	p 41 & Appendix 2 pp 4-5
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Appendix 2 pp 6,9,10
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	p 46, 47, Appendix 2 p 10
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	pp 47-49
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	pp 47, 48 Appendix 4, 6, 7

Chapter 2, Appendix 1

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	p 48
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	p 51
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	pp 47-8
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Appendix 2, p 10
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	pp 64, 82-5
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Not reported
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	pp 47
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	pp 53 (Fig 1), 68 (Fig 8)
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	pp 53 (Fig 1), 68 (Fig 8), Appendix 4, Appendix 5.
Study characteristics	17	Cite each included study and present its characteristics.	Table 4 Table 5 Table 6 Table 9 Table 10 Table 11
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Fig. 2, Fig. 9 & 10
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Figs. 5-7 Figs. 14 - 17

Chapter 2, Appendix 1

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	pp 52, 54-9, pp 67, 71-2, 75-6
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Figs. 5-7 Figs. 14 - 17
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Figs. 5-7 Figs. 14 - 17
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Figs. 5-7 Figs. 14 - 17
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Not conducted
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Figs. 5-7 Figs. 14 - 17
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	pp 87 - 94
	23b	Discuss any limitations of the evidence included in the review.	p 94
	23c	Discuss any limitations of the review processes used.	p 95
	23d	Discuss implications of the results for practice, policy, and future research.	P 96
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	PROSPERO 2018 CRD42018117100 Note that the original protocol document was registered and this registered protocol was used in the present work. However, only part of the larger registered protocol has

Chapter 2, Appendix 1

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
			been investigated and reported here.
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Appendix 2
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	n/a
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	n/a
Competing interests	26	Declare any competing interests of review authors.	n/a
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Available upon request

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

Chapter 2, Appendix 2: SYSTEMATIC REVIEW & META-ANALYSIS PROTOCOL

Contents

Chapter 2, Appendix 2: SYSTEMATIC REVIEW & META-ANALYSIS PROTOCOL

Research question:

What is the efficacy of mindfulness meditation compared to transcranial electrical stimulation methods in enhancing cognitive performance and/or well-being in adults?

A systematic review comparing the effect sizes of meditation outcomes vs tACS outcomes in RCTs and Controlled Clinical Trials conducted from 1988 until 2020.

Mindfulness Meditation: Seated, with eyes closed. Open monitoring technique, which is based on Buddhist meditation.

Dose: Duration of meditation or stimulation. In this review, participants should receive at least one session of ≥10 min duration of treatment condition (stimulation or meditation).

Specific types of tES being investigated: tACS

Operational definition of "efficacy": Improvement or enhancement as demonstrated by effect size. Measurement of at least a pre- and post-intervention should be reported.

Areas to be improved:

1. *cognitive functioning*, specifically working memory as a proxy for executive function.
2. *subjective well-being*, particularly self-reported levels of depression, sleep disturbance, anxiety and/or stress levels.

Operational definition of "improving cognitive performance": statistically significant finding for measures of executive function as measured by working memory tasks in favour of the intervention (mindfulness meditation, tACS).

Operational definition of "improving subjective well-being": statistically significant reduction in self-report outcomes of stress, depression, anxiety, sleep disturbance or negative mood (or conversely significant improvement in positive mood; sleep quality).

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Eligibility (inclusion) criteria:

Study designs

- Original research articles
- Clinical Study or Trial
- Controlled Clinical Trial
- RCT
- Time series studies with at least two points of measurement (before and after intervention)

Participants

- Human adults, ≥18 years of age.
- If study includes a healthy elderly group > 60 years, MMSE scores must be ≥ 26
- Must include a control group of healthy adults ≥ 18 yrs who are not currently suffering from any neurological conditions, receiving treatment for any psychological disorder including taking medication for same or have a history of substance abuse.
- Long-term, intermediate or naïve practitioners of any form of meditation

Interventions

Mindfulness Meditation

The efficacy of Mindfulness Meditation as a method to enhance cognitive function and perceived well-being would be ascertained by calculating the overall effect size of any improvements reported in the reviewed studies.

The specific meditation of interest is Mindfulness Mediation (MM), which may be delivered by a trained teacher, a smart phone application ("App") or a professionally approved/endorsed audio CD. Of particular interest is MM that is suitable for physically abled and disabled individuals, therefore only MM offered as a purely mental exercise will be reviewed (i.e. does not include yoga or physical activity). In addition, I aim to evaluate the impact of standard mindfulness meditation only, rather than mindfulness-based therapeutic interventions.

To be eligible for inclusion, MM studies must comply with these criteria:

- Test the impact of mindfulness meditation on cognitive functioning, particularly working memory and/or subjective well-being, particularly self-reported levels of depression, anxiety and stress levels.
- Mindfulness meditation with no physical or therapeutic component.
- Dose: 10 min or longer at least once.

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tES

The aim here is to consider the efficacy of tES regarding any cognitive and/or subjective well-being improvements reported.

To be eligible for inclusion, the tES studies must comply with these criteria:

- Transcranial alternating current stimulation (tACS), delivering current of 1 to 2.5 mA over a period of 10 to 30 minutes per stimulation period.
- tACS may be applied using any montages that activates areas important for cognitive/executive/emotional function such as, but not limited to, the dorsolateral prefrontal cortex; tACS studies of the motor cortex (M1) will therefore be excluded.

Control condition

Mindfulness Meditation

- MM studies must have a control group.
- Active control condition: relaxation, brain games/exercises, cognitive tasks.
- Passive control condition: waitlist-control, educational session about mindfulness/meditation/health/neutral topic.
- As with the active condition (Mindfulness meditation), the control condition (active/passive) should be matched for duration, attention and method of delivery e.g. via App, audio or by qualified teacher and should not include a physical or therapeutic component.

tES

- Studies administering tACS must have a sham condition.
- Studies must report how the sham condition was administered and what steps were taken to ensure participant blinding.
- Studies not using a sham condition or where sham is patently different from the active condition will be excluded.

Outcomes

To be considered for inclusion in the review, studies must report on cognitive performance and/or subjective well-being.

Cognitive measures may be one or more of the following (SEE APPENDIX A FOR LIST OF TASKS):

- Working Memory
- Executive function (in relation to working memory tasks only)
- Processing speed (in relation to working memory task measure e.g. reaction time/latency)

Subjective measures may be one or more of the following:

- Stress
- **Sub-clinical** Anxiety
- **Sub-clinical** Depression
- **Sub-clinical** Worry/Rumination
- Sleep

Review eligibility criteria:

- Peer-reviewed publications
- Methods of analyses must include accepted parametric or non-parametric method resulting in a test statistic and p-value or similar with mean and/or median values so that differences between groups can be assessed and an effect size derived.
- No neurological conditions or psycho-tropic meds or mental illness in the control group
- No neurological conditions or psycho-tropic meds or mental illness in the healthy adult test group if the RCT is comparing treatment intervention in two healthy adult samples.

Time period:

- January 1988 – December 2020

Language:

- English-only

Exclusion criteria (see Appendix C for full list)

1. Studies do not evaluate cognitive performance or subjective well-being outcome variables.
2. Studies where participants are <18 years.
3. No comparison/control group.
4. MBCT (mindfulness-based cognitive therapy).
5. MBSR (mindfulness-based stress reduction).
6. Any mindfulness meditation practice incorporating a physical element or therapeutic adaptation.
7. Studies < 1988.
8. Sleep studies

Chapter 2, Appendix 2: SYSTEMATIC REVIEW & META-ANALYSIS PROTOCOL

Reasons for using these exclusion criteria:
1: As I want to ascertain the extent to which mindfulness meditation benefits adults with respect to cognitive function and subjective well-being only studies covering at least one of these areas can be reviewed.

2: My research focuses on adults across the lifespan (not children or adolescents).

3: Studies without a comparison group lack the required scientific rigour to be reliable.

4,5,6: MBCT and MBSR are specific adaptations of mindfulness which are different in nature to 'standard' mindfulness practice. My research will focus on non-physical mindfulness therefore mindfulness adapted for therapeutic purposes and mindfulness with a physical component may bias the outcome of this review.

7: Not many RCTs were conducted on mindfulness prior to 1988 and some are unlikely to meet current standards required for RCT. There are many more good quality studies published in the last 2 decades.

8: Studies that include sleep as part of the intervention strategy will be excluded because it may be difficult to ascertain how much of the manipulation is caused by the stimulation/meditation and how much is due to sleep. For this reason, studies where tasks are performed and then a sleep intervention is given along with e.g. tACS overnight will not be considered

PICO

Participants: Adults 18 and over

Interventions: Mindfulness meditation and tACS

Comparators: Sham (in case of tACS) or relaxation/wait-list control/similar for mindfulness meditation.

Outcomes: Improved cognitive performance; reduced stress/improved subjective well-being. Cognition (working memory) and subjective well-being (stress, sub-clinical anxiety, sub-clinical depression, sleep quality).

Chapter 2, Appendix 2: SYSTEMATIC REVIEW & META-ANALYSIS PROTOCOL

.Search sites:

Electronic databases:

Scopus

https://www.scopus.com/search/form.uri?display=basic

Pubmed (searched via NCBI)

https://www.ncbi.nlm.nih.gov/myncbi/

Ebsco host database

Cochrane Library:

https://www.cochranelibrary.com/advanced-search/search-manager

ScienceDirect:

https://www.sciencedirect.com/user/login?returnURL=%2F

Web of Science:

http://apps.webofknowledge.com/

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Planned manual searches:

- Reference sections of articles selected from databases
- Original research articles featured in review articles, commentaries and letters

Search engine:

Google

Referencing Software:

Endnote

All references will be imported into separate Endnote libraries and then added one by one to a single Endnote library for each method of intervention:

1. Mindfulness meditation studies
2. tACS studies

Duplicate articles will be deleted and the amount of overlap in the records (number of duplicates) will be recorded.

Refined search

Databases searched tend to have non-uniform approaches, therefore a broad search was conducted of online databases. These will then be imported into Endnote and refined search will be carried out within endnote to ensure uniform approach to selection.

See extensive exclusion criteria: APPENDIX C

Refined criteria for overall relevance:

The title/abstract of each article will be screened to ensure that it includes at least one of the interventions being evaluated: Mindfulness meditation or one or more forms of tACS (as per original keywords and inclusion criteria).

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Excluded items

References excluded will be kept in an excluded folder for record purposes. As per the initial search, these comprised studies of:

- MBSR (this has a physical component)
- MBCT (this is a therapy application)
- Studies with children/adolescents (i.e. <18 years of age)
- Any mindfulness training adapted for therapeutic purposes
- Any Mindfulness meditation combined with any physical component e.g. yoga.
- **See extended list APPENDIX C**

Study selection for review:

Full texts of the remaining studies will then be screened for relevance.

Data extraction

A standardised form was created using Microsoft Excel to extract the following information:

- Study design
- Country
- Aims
- Ethical information
- Studied outcomes
- Sample size
- Participant characteristics
- Intervention characteristics
- Means
- Standard deviations
- Sample size

For meditation these specific items, where present, will be recorded:

- Dose
- Maximal hours meditated
- Recommended amt of home practice
- Description of instructor qualifications
- Participant adherence
- Participant drop-out rates

- Any adverse effects related to mindfulness

For tACS these specific items, where present, will be recorded:

- Dose
- Ramp-up/down
- Current density
- Number of sessions
- Stimulation mode (sham/active stimulation mode)
- Details about participants' confidence that they thought they received active stimulation
- Participant drop-out rates
- Adverse effects related to tACS

Quality and Risk of Bias assessment:

G.R.A.D.E (Grades of recommendation, assessment, development and evaluation) would serve to evaluate the evidence.

A risk of bias assessment will be made with regards to the following items for each study:

- Sequence generation
- Allocation concealment
- Blinding
- Incomplete outcome data
- Selective outcome reporting
- Other sources of bias

In addition, funnel plots and Egger's test will be used to evaluate publication bias.

Statistical outcomes

Effect sizes where possible, derived from means and standard deviations or non-parametric equivalent.

Effect sizes for:

- Mindfulness meditation (MM):
  - MM w/active control
  - MM w/inactive control
  - overall effect of MM
- tACS:
  - relative effect size of active vs sham stimulation condition for:

Chapter 2, Appendix 2: SYSTEMATIC REVIEW & META-ANALYSIS PROTOCOL

Table of search terms

	TERMS	filter	Limiters
1	“mindfulness meditation”	Human	Articles and Reviews
2	“mindfulness training”	Human	Articles and Reviews
3	“Open monitoring meditation” OR “OMM”	Human	Articles and Reviews
4	“Headspace App” OR “meditation app”	Human	Articles and Reviews
5	“tACS” OR “transcranial alternating current stimulation”	Human	Articles and Reviews
6	“tRNS” OR “transcranial random noise stimulation”	Human	Articles and Reviews
7	“tDCS” OR “transcranial direct current stimulation”	Human	Articles and Reviews
8	“Non-invasive neur* stim*” OR “Non-invasive brain stim*” OR “transcranial electrical stimulation” OR “Electrical neural mod*”	Human	

- tACS
  - overall effect size of tACS

Chapter 2, Appendix 2: SYSTEMATIC REVIEW & META-ANALYSIS PROTOCOL

APPENDIX A: Cognitive measures of executive function (working memory)

WORKING MEMORY

As measured with:

- Digits span: forward and backward; digit span forward only; digit span backward only
- N-back task
- Sternberg
- Operation Span
- Reading span
- Sternberg Task
- Delayed match-to-sample
- Letter-number sequencing
- WAIS Working Memory Index

There are many possible tasks. Authors must provide some validity/reliability stats with the task. I.e. they must demonstrate that the task is well-validated (or it must be conventionally used within the literature to be considered valid e.g. n-back)

APPENDIX B: Subjective well-being comparators

As measured with:

- Stress (state and/or trait) e.g. DASS
- Anxiety e.g. GAD7
- Depression e.g. BDI
- Sleep disturbance e.g. PSQI
- Mood e.g. PANAS, POMS
- Perceived well-being e.g. GHQ

There are many possible tasks. Authors must provide some validity/reliability stats with the task. I.e. they must demonstrate that the task is well-validated (or it must be conventionally used within the literature to be considered valid e.g. STAI).

APPENDIX C: Exclusion criteria

1. Headaches (not in context of tACS or mindfulness) *(No relevant to research question)*
2. Tilt angle research *(No relevant to research question)*
3. Speech including:
    a. phonological processing; *(No relevant to research question)*
    b. phoneme categorisation tasks *(No relevant to research question)*
4. Somatosensory system *(No relevant to research question)*
5. Technical: *(No relevant to research question)*
    a. Studies of a purely physiological nature e.g. only EEG or fMRI data (without cognitive tasks);
    b. Studies on head models;
    c. Studies with a theoretical purpose with no cognitive/well-being tasks;
    d. Safety studies also fall under this category;
    e. Computational modelling studies;
    f. Technical papers.
6. Non-standard tasks (e.g. verbal insight task) i.e. tasks designed for particular experiment or not used beyond one study *Methodological issue*
7. Sleep-related studies e.g. impact of tACS on sleep-memory consolidation relationship/sleep studies. Also exclude studies on sleep because this is considered a treatment/intervention. I'm only focusing on meditation and neurostimulation (formerly point 25) *Methodological issue*
8. Pain research *(No relevant to research question)*
9. Auditory *Methodological issue*
    a. Auditory attention
    b. Auditory perception
    c. tinnitus
10. Creativity studies *Methodological issue*
11. Verbal intelligence tasks (e.g. anagrams) **(NOTE: do not exclude ANY working memory tasks even if verbal)** *Methodological issue*
12. Remote association task *Methodological issue*
13. No control group (i.e. clinical patients assigned to different conditions but no controls). *Methodological issue*
14. Essential tremor *(No relevant to research question)*
15. Case study *Methodological issue*
16. Motor (MI stimulation studies). If the stimulation site is M1, it is not relevant to this systematic review because it does not provide direct

evidence of cognitive function in terms of working memory and attention with relevant tasks. *(No relevant to research question)*

17. Tactile *(No relevant to research question)*
18. Clinical trial registrations *Methodological issue*
19. Studies that do not evaluate cognitive performance or subjective well-being e.g. 'at rest'/'resting-state' connectivity (and/or objective well-being outcome variables). *(No relevant to research question)*
20. Studies where participants are <18 years *(No relevant to research question)*
21. MBCT (mindfulness-based cognitive therapy) *(No relevant to research question)*
22. MBSR (mindfulness-based stress reduction) *(No relevant to research question)*
23. Any mindfulness meditation practice incorporating a physical element or therapeutic adaptation *(No relevant to research question)*
24. Studies < 1988 *Methodological issue*
25. See point 7
26. Studies where < 10 min of treatment has been given per session. *(No relevant to research question)*
27. TMS *(No relevant to research question)*
28. Perception-only experiments e.g. visual search, perceptual learning, perceptual processing *(No relevant to research question)*
29. Review/Commentary/Primer/Discussion/Letter (i.e. any article that is not original research).
30. The study of aggression and/or violent behaviour.
31. Books and book chapters *(methodological issue – not original research)*
32. Exclude non-standard tACS devices (e.g. Halo wearable device used by athletes). The devices included in this review are limited to those typically used in peer-reviewed research by the majority of research teams rather than commercial devices available to consumers (methodological issue – comparability across studies; efficacy and safety of device).

Reasons for exclusion:

No relevant to research question: e.g. where the M1 region has been stimulated, this would not be relevant, because my objective would not be to stimulate this region specifically therefore any effect size derived from this region may not provide accurate information about effect size that might be achieved when

stimulating PFC or other areas related to higher cognitive functions such as conflict monitoring, etc.

Methodological issue Study design incompatible with a priori objectives

I will not be assessing studies that have only clinical populations/where studies have failed to test a control condition.

I will not be including case studies.

I will not be including studies prior to 1988 because few relevant studies were conducted prior to this date and quality of more recent studies is arguably better.

LIST OF REVIEW ARTICLES CHECKED FOR REFERENCES THAT MAY HAVE BEEN MISSED IN THE INITIAL SEARCH:

tACS

Abd Hamid, A. I., Gall, C., Speck, O., Antal, A., & Sabel, B. A. (2015). Effects of alternating current stimulation on the healthy and diseased brain. *Frontiers in Neuroscience, 9*(391).

Antal, A., & Paulus, W. (2013). Transcranial alternating current stimulation (tACS). *Front Hum Neurosci, 7*, 317. doi:10.3389/fnhum.2013.00317.

Brunyé, T. T. (2018). Modulating spatial processes and navigation via transcranial electrical stimulation: A mini review. *Frontiers in Human Neuroscience, 11*.

Cohen Kadosh, R. (2015). Modulating and enhancing cognition using brain stimulation: Science and fiction. *Journal of Cognitive Psychology, 27*(2), 141-163. Retrieved from https://doi.org/10.1080/20445911.2014.996569.

Elmasry, J., Loo, C., & Martin, D. (2015). A systematic review of transcranial electrical stimulation combined with cognitive training.

Herrmann, C. S., Rach, S., Neuling, T., & Struber, D. (2013). Transcranial alternating current stimulation: a review of the underlying mechanisms and modulation of cognitive processes. *Front Hum Neurosci, 7*, 279. doi:10.3389/fnhum.2013.00279

Huang, Y. Z., Sommer, M., Thickbroom, G., Hamada, M., Pascual-Leonne, A., Paulus, W., . . . Ugawa, Y. (2009). Consensus: New methodologies for brain stimulation. *Brain Stimul, 2*(1), 2-13. doi:10.1016/j.brs.2008.09.007

Chapter 2, Appendix 2: SYSTEMATIC REVIEW & META-ANALYSIS PROTOCOL

Karabanov, A. N., Saturnino, G. B., Thielscher, A., & Siebner, H. R. (2019). Can Transcranial Electrical Stimulation Localize Brain Function? *Frontiers in Psychology, 10*(213).

Kuo, M.-F., & Nitsche, M. A. (2015). Exploring prefrontal cortex functions in healthy humans by transcranial electrical stimulation. *Neuroscience Bulletin, 31*(2), 198-206.

Moreno-Duarte, I., Gebodh, N., Schestatsky, P., Guleyupoglu, B., Reato, D., Bikson, M., & Fregni, F. (2014). Chapter 2 - Transcranial Electrical Stimulation: Transcranial Direct Current Stimulation (tDCS), Transcranial Alternating Current Stimulation (tACS), Transcranial Pulsed Current Stimulation (tPCS), and Transcranial Random Noise Stimulation (tRNS). In R. Cohen Kadosh (Ed.), *The Stimulated Brain* (pp. 35-59). San Diego: Academic Press.

Schutter, D. J. (2016). Cutaneous retinal activation and neural entrainment in transcranial alternating current stimulation: A systematic review. *NeuroImage, 140*, 83-88. doi:10.1016/j.neuroimage.2015.09.067

Veniero, D., Vossen, A., Gross, J., & Thut, G. (2015). Lasting EEG/MEG Aftereffects of Rhythmic Transcranial Brain Stimulation: Level of Control Over Oscillatory Network Activity. *Frontiers in Cellular Neuroscience, 9*, 17.

Vosskuhl, J., Struber, D., & Herrmann, C. S. (2018). Non-invasive Brain Stimulation: A Paradigm Shift in Understanding Brain Oscillations. *Front Hum Neurosci, 12*, 211. doi:10.3389/fnhum.2018.00211

Zaghi, S., Acar, M., Hultgren, B., Boggio, P. S., & Fregni, F. (2010). Noninvasive Brain Stimulation with Low-Intensity Electrical Currents: Putative Mechanisms of Action for Direct and Alternating Current Stimulation. *Neuroscientist, 16*(3), 285-307.

Mindfulness Meditation

Casedas, L., Pirruccio, V., Vadillo, M. A., & Lupianez, J. (2020). Does Mindfulness Meditation Training Enhance Executive Control? A Systematic Review and Meta-Analysis of Randomized Controlled Trials in Adults. Mindfulness, 11(2), 411-424. doi:10.1007/s12671-019-01279-4

No additional original research reports were found consequent to reviewing the above review articles.

Appendix 3: Table of subjective well-being measures details and in which meta-analysed studies they were used

studyID	Name of the task	Construct measured	Score range	Interpretation
20	GHQ-12	General Health Questionnaire (GHQ-12) contains 6 positive and 6 negative items (rated on 4-point system from 'better/healthier than normal to 'much worse/more than usual at extreme end) and yields an overall score. There are 4 possible scoring methods (all use 4-point scoring).	Likert score yields a max score of 36; GHQ scoring yields a max score of 12	A higher score indicates greater severity
51	HAD	Hospital Anxiety and Depression Scale (HAD) consists of 2 subscales each comprising 7 items: HAD-A: anxiety (rated 0-3) , HAD-D: depression (rated 0-3) => summed score of 0-21 for each sub-scale. There are 3 cut-points: 0-6 (no anxiety/depression problems); 7-10 mild-moderate anxiety/depressed mood or gloominess; > 10 potential anxiety disorder/potential risk for clinical depression.	0-21 (per sub-scale)	A higher score indicates greater distress (anxiety/depression).

studyID	Name of the task	Construct measured	Score range	Interpretation
2,47,88	PANAS	*Positive and Negative Affect Schedule* (PANAS) consists of 20 self-rated items comprising 2 broadly independent subscales believed to measure positive/negative affect (10 items per sub-scale). Each subscale measures intensity (rated 1 to 5). Mean score for positive affect (PA) (range:10-50) = 33.3 (SD ± 7.2). Mean score for negative affect (NA) (range:10-50) = 17.4 (SD ± 6.2)	10-50	PA: Higher scores represent higher levels of positive affect. NA: Lower scores represent lower levels of negative affect.
24,63	POMS	*The Profile of Mood States* (POMS) consists of 65 items scored on a 5-point scale (0 to 4) from which a composite scale, a 'total mood disturbance score (TMDS) may be derived. TMDS = Tension-Anxiety + Depression-Dejection + Anger-Hostility + Fatigue-Inertia minus Vigour-Activity. The POMS-SF consists of 37 adjectives (e.g., Friendly, Tense) of possible moods/ feelings (rated 0 to 4), each to be scored on a 5-point scale. TMD = (Tension + Depression + Anger + Fatigue + Confusion) – Vigour.	0-260 0-148	Higher score indicates greater mood disturbance

studyID	Name of the task	Construct measured	Score range	Interpretation
20	PSQ	Perceived Stress Questionnaire (PSQ) consists of 30 items (rated 1 to 4). Scoring: (raw score-30)/90.	0-1	Higher scores indicate greater levels of stress.
51	PWB	Psychological Well-being (PWB) measures 6 sub-scales: self-acceptance, environmental mastery, positive relations, purpose in life, personal growth, autonomy (rated: 1 – 6). Short-form has18 items (score range: 3-18).		A higher score indicates better psychological well-being
122,123	STAI-S	State-Trait Anxiety Inventory (State)	20-80	

See over the page for studyID reference (study title, authors and year of publication)

studyID	TITLE	AUTHORS	YEAR
2	Mindfulness and Loving-Kindness Meditation	Aspy, Denholm J. and Proeve, Michael	2017
20	Mindfulness versus Physical Exercise: Effects of Two Recovery Strategies on Mental Health, Stress and Immunoglobulin A during Lunch Breaks. A Randomized Controlled Trial	Diaz-Silveira, C., Alcover, C. M., Burgos, F., Marcos, A. and Santed, M. A.	2020
24	Experimental effects of brief, single bouts of walking and meditation on mood profile in young adults	Edwards, M. K. and Loprinzi, P. D.	2018
47	Mindfulness and positive affect: Cross-sectional, prospective intervention, and real-time relations	Jislin-Goldberg, Tamar, Tanay, Galia and Bernstein, Amit	2012
51	The Effects of a Short-term Mindfulness Based Intervention on Self-reported Mindfulness, Decentering, Executive Attention, Psychological Health, and Coping Style: Examining Unique Mindfulness Effects and Mediators	Josefsson, Torbjörn, Lindwall, Magnus and Broberg, Anders	2014
63	A Comparison of the Attentional Effects of Single-Session Mindfulness Meditation and Fp-HEG Neurofeedback in Novices	Lai, Constantine, MacNeil, Benjamin and Frewen, Paul	2015
88	Brief meditation interventions: Mindfulness, implementation instructions, and loving kindness	Polizzi, Craig P., Baltman, Jessica and Lynn, Steven Jay	2019
122	Effects of Brief and Sham Mindfulness Meditation on Mood and Cardiovascular Variables	Zeidan, F., Johnson, S., Gordon, N., & Goolkasian, P.	2010b
123	Mindfulness meditation improves cognition: Evidence of brief mental training	Zeidan, F., Johnson, S. K., Diamond, B. J., David, Z., & Goolkasian, P.	2010a

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Curran, S., Andrykowski, M., & Studts, J. (1995). Short form of the Profile of Mood States (POMS-SF): Psychometric information. Psychological Assessment, 7, 80-83. doi:10.1037/1040-3590.7.1.80

Goldberg, D. P., Gater, R., Sartorius, N., Ustun, T. B., Piccinelli, M., Gureje, O., & Rutter, C. (1997). The validity of two versions of the GHQ in the WHO study of mental illness in general health care. Psychol Med, 27(1), 191-197. doi:10.1017/s0033291796004242

Levenstein, S., Prantera, C., Varvo, V., Scribano, M. L., Berto, E., Luzi, C., & Andreoli, A. (1993). Development of the Perceived Stress Questionnaire: a new tool for psychosomatic research. J Psychosom Res, 37(1), 19-32. doi:10.1016/0022-3999(93)90120-5

Mcnair, D. M., Lorr, M., & Droppleman, L. F. (1971). Manual for the Profile of Mood States.

Ryff, C. D. (1989). Happiness is everything, or is it? Explorations on the meaning of psychological well-being. Journal of personality and social psychology, 57(6), 1069-1081. doi:10.1037/0022-3514.57.6.1069

Ryff, C. D., & Keyes, C. L. M. (1995). The structure of psychological well-being revisited. Journal of personality and social psychology, 69(4), 719-727. doi:10.1037/0022-3514.69.4.719

Spielberger, C. D. (1983). Manual for the State-Trait-Anxiety Inventory: STAI (form Y). Palo Alto, CA: Consulting Psychologists Press.

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: the PANAS scales. Journal of personality and social psychology, 54(6), 1063.

Zigmond, A. S., & Snaith, R. P. (1983). The hospital anxiety and depression scale. Acta Psychiatr Scand, 67(6), 361-370. doi:10.1111/j.1600-0447.1983.tb09716.x

Unique ID	2	**Study ID**	10.1177/0033294116685867	**Assessor**	dw
Ref or Label	Aspy, Denholm J. and Proeve, Michael	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	Mindfulness Meditation	**Comparator**	active/passive control condition	**Source**	Journal article
Outcome	PANAS-NA;PANAS-PA	**Results**		**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the randomization process	1.1 Was the allocation sequence random?	PY	1.1 Randomisation occurred but the method of randomisation was not reported. ss were randomly allocated to one of 3 groups (p.106). 1.2 A random allocation does not allow for prior allocation sequences to be determined.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	1.3 Results indicate that groups were comparable across measurement indices at baseline. Authors reported comparable results for baseline PANAS PA/NA across groups (p. 108-9)

	Risk of bias judgement	**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	2.1 Participants were aware that they were either meditating or in the control group. Participants a) completed computerised baseline measures online, b) randomly assigned to an intervention/no intervention condition online. 2.2 Researchers were aware of the intervention.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	2.3 Nothing reported to indicate any deviations.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	2.6 All exclusions had a valid reason and all of the remainging participants were included in the comparison of baseline results and the analysis was appropriate. A one-way ANOVA confirmed comparable levels of pre-test
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	

	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PY	3. 1 Degrees of freedom were reported in results (p. 108-9)
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	

Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	PN	4.1 Outcomes were measured with standard scoring and entirely computer-based.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	4.2 The task was computer-based and administered in a standardised manner.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	4.3 Assessors were aware of the intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	4.4 The intervention was entirely online therefore limited interaction with the reearchers.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	

Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	5.1 There was no pre-specified statistical analysis plan in the methods section.
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	5.2 The standard summary scores were calculated.
	5.3 ... multiple eligible analyses of the data?	PN	5.3 A standard analysis was used that does not appear unreasonable.
	Risk of bias judgement	**Low**	5.1 There was no pre-specified statistical analysis plan in the methods section.
Overall bias	**Risk of bias judgement**	**Low**	5.1 There was no pre-specified statistical

Unique ID	5	**Study ID**	10.1891/0889-8391.29.4.343	**Assessor**	dw
Ref or Label	Bell, T. P.	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	Mindfulness Meditation	**Comparator**	active/passive control condition	**Source**	Journal article
Outcome	STAI-STATE/TRAIT	**Results**	NA	**Weight**	0

Domain	Signalling question	Response	Comments
Bias arising from the randomizatio n process	1.1 Was the allocation sequence random?	Y	1.1 Randomisation occurred and randomisation was done via computer-generated algorithm. 1.2 A random allocation does not allow for prior allocation sequences to be determined.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	NI	1.3 Baseline comparisons were not reported.
	Risk of bias judgement	**ome concern**	1.3 Baseline comparisons were not reported.

	2.1.Were participants aware of their assigned intervention during the trial?	Y	2.1 Participants were aware that they were either meditating or in the control group. 2.2 Researchers were aware of the intervention.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	2.3 Nothing reported to indicate any deviations.

Bias due to deviations from intended interventions	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PN	2.6 All exclusions had a valid reason and all of the remainging participants were included in the comparisons. ANOVAs and MANOVAs were used to evaluate significant outcomes. Within-ss comparisons were analysed fully
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	PN	No reported deviations to intended protocol and degrees of freedom reported indicate all 57 ss were included in the analyses.
	Risk of bias judgement	**ome concern**	2.6 Significant between-groups ANOVA outcomes (comparing 3 groups) were not followed up.
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PY	3.1 Degrees of freedom were reported in results (p. 349)
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	

	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measuremen	4.1 Was the method of measuring the outcome inappropriate?	PN	4.1 Outcomes were measured with standard scoring.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	4.2 Tasks were administered in a standardised manner across participants
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	4.3 Assessors were aware of the intervention.

t of the outcome	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	4.4 Outcomes were based on standard scoring method.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	5.1 Statistical analysis section sets out the intended evaluations (p. 348).
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	NI	5.2 No table of summary statistics were provided for demographics, baseline measures or outcome measures.
	5.3 ... multiple eligible analyses of the data?	NI	5.3 Groups comparisons were not fully analysed.
	Risk of bias judgement	**High**	5.2 No table of summary statistics were provided for demographics, baseline measures or outcome measures. 5.3 Groups comparisons were not fully analysed.
Overall bias	**Risk of bias judgement**	**High**	1.3 Baseline comparisons were not reported. 2.6 Significant between-groups ANOVA outcomes (comparing 3 groups) were not followed up. 5.2 No table of summary statistics were

Unique ID	11	**Study ID**	10.1007/s12671-016-0631-8	**Assessor**	dw
Ref or Label	Chow, Theodore, Javan, Tanaz, Ros, Tomas and Frewen, Paul	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	Mindfulness Meditation	**Comparator**	active/passive control condition	**Source**	Journal article
Outcome	DASS, POMS	**Results**	NA	**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the	1.1 Was the allocation sequence random?	PY	1.1 Randomisation occurred but the method of randomisation was not reported.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	1.2 A random allocation does not allow for prior allocation sequences to be determined.

randomization process	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	1.3 Results indicate that groups were comparable across measurement indices at baseline. Table 1 indicates that groups were comparable regarding pre-intervention outcome measures.
	Risk of bias judgement	**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	2.1 Participants were aware that they were either meditating or in the control group. Participants were a) randomised, b) assigned to an intervention, c)completed computerised baseline measures. 2.2 Researchers were aware of the intervention.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	2.3 Nothing reported to indicate any deviations.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	2.6 All exclusions had a valid reason and all of the remainging participants were included in the comparison of baseline results and the analysis was appropriate. MANOVAs were used to measure between-groups

	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PY	3. 1 Degrees of freedom were reported in results (p. 577-580)
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
	4.1 Was the method of measuring the outcome inappropriate?	PN	4.1 Outcomes were measured with standard scoring.

Bias in measurement of the outcome	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	4.2 Tasks were administered in a standardised manner across participants.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	4.3 Assessors were aware of the intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	4.4 Outcomes were based on standard scoring method.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	5.1 Statistical analysis section sets out the intended evaluations (p. 576).
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	5.2 The standard summary scores were calculated for each questionnaire.
	5.3 ... multiple eligible analyses of the data?	PN	5.3 The most robust analysis was used (parametric e.g. ANOVAs). Measured in accordance with their plan.

	Risk of bias judgement	**Low**	
Overall bias	**Risk of bias judgement**	**Low**	

Unique ID	20	**Study ID**	10.3390/ijerph17082839	**Assessor**	dw
Ref or Label	Diaz-Silveira, C., Alcover, C. M., Burgos, F., Marcos, A. and Santed, M. A.	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	Mindfulness Meditation	**Comparator**	active/passive control condition	**Source**	Journal article
Outcome	PSQ, GHQ-12	**Results**		**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**

Bias arising from the randomizatio n process	1.1 Was the allocation sequence random?	PY	1.1 Randomisation occurred but the method of randomisation was not reported. 1.2 "Potential participants were given participant numbers upon enrolment with Stata software by independent research assistants who had no access to the randomization form." (p.4)
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	1.3 Results indicate that groups were comparable across measurement indices at baseline.Table 1: groups were comparable across baseline measures (p.7)
	Risk of bias judgement	**Low**	
	2.1.Were participants aware of their assigned intervention during the trial?	Y	2.1 Participants were given detailed information regarding their intervention after completing computerised baseline measures. 2.2 Researchers were aware of the intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	2.3 Nothing reported to indicate any deviations.

Bias due to deviations from intended interventions	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	2.6 All exclusions had a valid reason and all of the remainging participants were included in the comparison of baseline results and the analysis was appropriate. Table 1.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PY	3. 1 Degrees of freedom were reported in results (pp.7-8).
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	

Bias due to missing outcome data	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	PN	4.1 Outcomes were measured with standard scoring.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	4.2 Tasks were administered in a standardised manner across participants.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	4.3 Assessors were aware of the intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	4.4 Outcomes were based on standard scoring method.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	

	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	5.1 Statistical analysis section sets out the intended evaluations (p.7)
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	5.2 The standard summary scores were calculated for each questionnaire.
	5.3 ... multiple eligible analyses of the data?	PN	5.3 A standard analysis was used that does not appear unreasonable.
	Risk of bias judgement	**Low**	
Overall bias	**Risk of bias judgement**	**Low**	

Unique ID	24	**Study ID**	10.15171/hpp.2018.23	**Assessor**	dw

Ref or Label	Edwards, M. K. and Loprinzi, P. D.	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	Mindfulness Meditation	**Comparator**	active/passive control condition	**Source**	Journal article
Outcome	POMS (3 of the subscales)	**Results**		**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	1.1 Randomisation occurred and randomisation was done via computer-generated algorithm. (p.172).
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	1.2 Randomised assignment to groups occurred after baseline measures were completed.
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	1.3 Results indicate that groups were comparable across measurement indices at baseline.
	Risk of bias judgement	**Low**	

Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	2.1 Participants were aware that they were either meditating or in the control group. Participants were a) completed computerised baseline measures, b) randomly assigned to an intervention. 2.2 Researchers were aware of the intervention.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	2.3 Nothing reported to indicate any deviations.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	All exclusions had a valid reason and all of the remainging participants were included in the comparison of baseline results and the analysis was appropriate. Table 1 (plus see p. 173)
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	

Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PY	3. 1 Degrees of freedom were reported in results; n values reported in Table 1.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measuremen	4.1 Was the method of measuring the outcome inappropriate?	PN	4.1 Outcomes were measured with standard scoring.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	4.2 Tasks were administered via computer in a standardised manner across participants.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	4.3 Assessors were aware of the intervention.

t of the outcome	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	4.4 Outcomes were all computer-based outputs
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	5.1 Statistical analysis section sets out the intended evaluations (p.173)
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	5.2 The standard summary scores were calculated for each questionnaire. Measured in accordance with their plan.
	5.3 ... multiple eligible analyses of the data?	PN	5.3 A standard analysis was used that does not appear unreasonable.
	Risk of bias judgement	**Low**	
Overall bias	**Risk of bias judgement**	**Low**	

Unique ID	33	**Study ID**	10.1007/s11682-018-9858-4	**Assessor**	dw
Ref or Label	Greenberg, Jonathan, Romero, Victoria, Elkin-Frankston, Seth, Bezdek, Matthew, Schumacher, Eric and Lazar, Sara	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	Mindfulness Meditation	**Comparator**	active/passive control condition	**Source**	Journal article
Outcome	Proactive interference error rates and RTs (of correct responses)	**Results**		**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the	1.1 Was the allocation sequence random?	PY	1.1 Randomisation occurred but the method of randomisation was not reported. Randomisation was 2:1 in favour of medtiation intervention. Intervention method was randomised (9 4-week programmes: 6 mindfulness and 3 creative writing courses). Participants were assigned to the currently available course until each was full. 1.2 Authors confirmed that ss only found out
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	

randomization process	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	1.3 Results indicate that groups were comparable across measurement indices at baseline. (Table 1).
	Risk of bias judgement	**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	2.1 Participants were a) randomised, b) assigned to an intervention, c)completed computerised baseline measures using an online link. 2.2 Researchers were aware of the intervention.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	Y	2.3 Trial participants did not all receive an MRI scan for valid reason (lack of funds).
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	PN	Authors confirmed that those who did not receive the MRI did not differ from the rest of the sample in the examined variables (p. 368)
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	2.6 All exclusions had a valid reason and all of the remainging participants were included in the comparison of baseline results and the analysis was appropriate (ANCOVA adjusted for baseline rates).

	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PY	3. 1 Degrees of freedom were reported in results and n values reported (Table 1).
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
	4.1 Was the method of measuring the outcome inappropriate?	PN	4.1 Outcomes were measured with standard scoring.

Bias in measurement of the outcome	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	4.2 Tasks were administered in a standardised manner across participants.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	4.3 Assessors were aware of the intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	4.4 Outcomes were based on standard scoring method.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	5.1 Statistical analysis section sets out the intended evaluations (p.370)
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	5.2 The standard summary scores were calculated for each questionnaire. Measured in accordance with their plan.
	5.3 ... multiple eligible analyses of the data?	PN	5.3 A standard analysis was used that does not appear unreasonable.

	Risk of bias judgement	**Low**	
Overall bias	**Risk of bias judgement**	**Low**	

Unique ID	47	**Study ID**	10.1080/17439760.2012.700724	**Assessor**	dw
Ref or Label	Jislin-Goldberg, Tamar, Tanay, Galia and Bernstein, Amit	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	Mindfulness Meditation	**Comparator**	active/passive control condition	**Source**	Journal article
Outcome	PANAS-PA	**Results**		**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**

Bias arising from the randomization process	1.1 Was the allocation sequence random?	PY	1.1 Randomisation occurred but the method of randomisation was not reported. 1.2 A random allocation does not allow for prior allocation sequences to be determined. Nothing reported regarding allocation sequence concealment.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	1.3 Results indicate that groups were comparable across measurement indices at baseline.
	Risk of bias judgement	**Low**	
Bias due to deviations from	2.1.Were participants aware of their assigned intervention during the trial?	Y	2.1 Participants were aware that they were either meditating or in the control group. Participants were a) randomised to an intervention, c)completed computerised baseline measures. 2.2 Researchers were aware of the intervention.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	2.3 Nothing reported to indicate any deviations.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	

from intended interventions	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	2.6 All exclusions had a valid reason and all of the remainging participants were included in the comparison of baseline results and the analysis was appropriate.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PY	3. 1 Degrees of freedom were reported in results and n values reported (Table 1).
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	

	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	PN	4.1 Outcomes were measured with standard scoring.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	4.2 Tasks were administered in a standardised manner across participants.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	4.3 Assessors were aware of the intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	4.4 Outcomes were based on standard scoring method.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PN	5.1 Study 1 and 2 both followed a very similar analysis plan but statistical analysis plan not reported in the methods section in either study.

Bias in selection of the reported result	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	5.2 The standard summary scores were calculated for each questionnaire.
	5.3 ... multiple eligible analyses of the data?	PN	5.3 A standard analysis was used that does not appear unreasonable.
	Risk of bias judgement	**Low**	5.1 Study 1 and 2 both followed a very similar analysis plan but statistical analysis plan not reported in the methods section in either study.
Overall bias	**Risk of bias judgement**	**Low**	

Unique ID	51	**Study ID**	10.1007/s12671-012-0142-1	**Assessor**	dw
Ref or Label	Josefsson, Torbjörn, Lindwall, Magnus and Broberg, Anders	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	Mindfulness Meditation	**Comparator**	active/passive control condition	**Source**	Journal article

Outcome	PWB, HAD	**Results**		**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	1.1 Randomisation occurred using a shuffle approach to random allocation rule (Schutz and Grimes, 2002) p.24 1.2 A random allocation does not allow for prior allocation sequences to be determined. Nothing reported regarding allocation sequence concealment.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	Y	1.3 Results indicate that groups were comparable across measurement indices at baseline. Authors reported that groups were comparable regarding age, gender, prior meditation experience but relaxation group
	Risk of bias judgement	**Low**	1.3 Results indicate that groups were comparable across measurement indices at baseline. Authors reported that groups were comparable regarding age, gender, prior meditation experience but relaxation group
	2.1.Were participants aware of their assigned intervention during the trial?	Y	2.1 Participants were aware that they were either meditating or in the control group. Participants were given a detailed explanation of the study, gave consent and were then randomised to a treatment/no treatment condition 2.2 Researchers were aware of the intervention.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	

Bias due to deviations from intended interventions	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	2.3 Nothing reported to indicate any deviations.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	2.6 All exclusions had a valid reason and all of the remainging participants were included in the comparison of baseline results and the analysis was appropriate.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PY	3. 1 Degrees of freedom were reported in results (p.26).
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	

Bias due to missing outcome data	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	PN	4.1 Outcomes were measured with standard scoring.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	4.2 Tasks were administered in a standardised manner across participants.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	4.3 Assessors were aware of the intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	4.4 Outcomes were based on standard scoring method.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	

	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	5.1 Statistical analysis section sets out the intended evaluations (p.25)
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	5.2 The standard summary scores were calculated for each questionnaire. Measured in accordance with their plan.
	5.3 ... multiple eligible analyses of the data?	PN	5.3 A standard analysis was used that does not appear unreasonable.
	Risk of bias judgement	**Low**	
Overall bias	**Risk of bias judgement**	**Low**	

Unique ID	63	**Study ID**	10.1007/s12671-014-0347-6	**Assessor**	dw

Ref or Label	Lai, Constantine, MacNeil, Benjamin and Frewen, Paul	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	Mindfulness Meditation	**Comparator**	active/passive control condition	**Source**	Journal article
Outcome	POMS-SF	**Results**		**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the randomization process	1.1 Was the allocation sequence random?	PY	1.1 Randomisation occurred but the method of randomisation was not reported.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	1.2 A random allocation does not allow for prior allocation sequences to be determined.
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	1.3 Results indicate that groups were comparable across measurement indices at baseline (Table 2).
	Risk of bias judgement	**Low**	

Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	2.1 Participants were aware that they were either meditating or in the other treatment/control group. Participants a) completed all baseline measures, b) randomly assigned to MM, NFB or counting control condition. 2.2 Researchers were aware of the intervention.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	2.3 Nothing reported to indicate any deviations.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	2.6 All exclusions had a valid reason and all of the remainging participants were included in the comparison of baseline results and the analysis was appropriate.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	

Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PY	3. 1 Degrees of freedom were reported in results (P. 1017).
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measuremen	4.1 Was the method of measuring the outcome inappropriate?	PN	4.1 Outcomes were measured with standard scoring.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	4.2 Tasks were administered in a standardised manner across participants.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	4.3 Assessors were aware of the intervention.

t of the outcome	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	4.4 Outcomes were based on standard scoring method.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	5.1 Statistical analysis methods section sets out the intended evaluations. (p.1016)
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	5.2 The standard summary scores were calculated for each questionnaire. Measured in accordance with their plan.
	5.3 ... multiple eligible analyses of the data?	PN	5.3 A standard analysis was used that does not appear unreasonable.
	Risk of bias judgement	**Low**	
Overall bias	**Risk of bias judgement**	**Low**	

Unique ID	88	**Study ID**	10.1037/cns0000194	**Assessor**	dw
Ref or Label	Polizzi, Craig P., Baltman, Jessica and Lynn, Steven Jay	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	Mindfulness Meditation	**Comparator**	active/passive control condition	**Source**	Journal article
Outcome	PANAS-NA;PANAS-PA	**Results**		**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the	1.1 Was the allocation sequence random?	Y	1.1 Randomisation occurred using a computer algorithm; randomization was conducted by generating a sequence of random numbers between 1 and 3. These random numbers corresponded to each treatment condition. When a participant signed up for the study, a number from the sequence was assigned to them indicating which instructions they would receive. (confirmed via email w/author)
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	

randomization process	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	1.3 Results indicate that groups were comparable across measurement indices at baseline.
	Risk of bias judgement	**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	2.1 Participants were aware that they were either meditating or in the control group. 2.2 Researchers were aware of the intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	2.3 Nothing reported to indicate any deviations.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	NI	None were reported.

	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	PN	
	Risk of bias judgement	**ome concerns**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PY	3. 1 Degrees of freedom were reported in results (pp. 369-70,373-4).
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
	4.1 Was the method of measuring the outcome inappropriate?	PN	4.1 Outcomes were measured with standard scoring.

Bias in measurement of the outcome	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	4.2 The questionnaires administered were given in randomised order at each assessment (p. 372).
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	4.3 Assessors were aware of the intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	4.4 Outcomes were based on standard scoring methods.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	5.1 Statistical analysis section sets out the intended evaluations; there is nothing in the paper to indicate any change in analysis plan. (p.369)
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	5.2 The standard summary scores were calculated for each questionnaire. Measured in accordance with their plan. The standard summary scores were calculated for each questionnaire.
	5.3 ... multiple eligible analyses of the data?	PN	5.3 Acceptable analysis was used (parametric e.g. ANOVAs). Measured in accordance with their plan. p.369

	Risk of bias judgement	**Low**	
Overall bias	**Risk of bias judgement**	**ome concern**	

Unique ID	98	**Study ID**	10.1037/a0022764	**Assessor**	dw
Ref or Label	Sahdra, B. K., MacLean, K. A., Ferrer, E., Shaver, P. R., Rosenberg, E. L., Jacobs, T. L., Zanesco, A. P., King, B. G., Aichele, S. R., Bridwell, D. A., Mangun, G. R., Lavy, S., Wallace, B. A. and Saron, C. D.	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	Mindfulness Meditation	**Comparator**	active/passive control condition	**Source**	Journal article
Outcome	STAI-T	**Results**	NA	**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**

Bias arising from the randomizatio n process	1.1 Was the allocation sequence random?	N	1.1 Stratified matched assigment was used (age, sex, years of meditation experience). 1.2 Concealment was not possible because participants were recruited for a retreat and had to comply with certain criteria e.g. not smoking/taking recreational drugs 3 months prior to the retreat.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	N	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PY	1.3 Results indicate that groups were comparable across the cognitive index at baseline but there is no information for the affective measures. Authors reported that waitlist control and MM groups were
	Risk of bias judgement	**ome concern**	1.3 Results indicate that groups were comparable across the cognitive index at baseline but there is no information for the affective measures. Authors reported that waitlist control and MM groups were
Bias due to deviations from	2.1.Were participants aware of their assigned intervention during the trial?	Y	2.1 Participants were aware that they were either meditating or in the wait-list control group. Participants in the experimental condition (MM) were given a detailed explanation; waitlist controls attended the 2nd retreat. 2.2 Researchers were aware of the intervention.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	2.3 Nothing reported to indicate any deviations.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	

from intended interventions	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	2.6 All exclusions had a valid reason and all of the remainging participants were included in the comparison of baseline results and the analysis was appropriate. Authors reported that groups were matched and comparable
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	3. 1 Degrees of freedom were reported in results (pp. 304-5).
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	

	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	PN	4.1 Outcomes were measured with standard scoring.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	4.2 Tasks were administered in a standardised manner across participants.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	4.3 Assessors were aware of the intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	4.4 Outcomes were based on standard scoring method.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	5.1 There was no pre-specified statistical analysis plan in the methods section.

Bias in selection of the reported result	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	5.2 The standard summary scores were calculated for each questionnaire.
	5.3 ... multiple eligible analyses of the data?	PN	5.3 A standard analysis was used that does not appear unreasonable. All measures were included in their model (Table 3)
	Risk of bias judgement	**Low**	5.1 There was no pre-specified statistical analysis plan in the methods section.
Overall bias	**Risk of bias judgement**	**ome concerns**	

Unique ID	106	**Study ID**	10.1097/01.NEP.0000000000000635	**Assessor**	dw
Ref or Label	Stinson, C., Curl, E. D., Hale, G., Knight, S., Pipkins, C., Hall, I., White, K., Thompson, N. and Wright, C.	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	Mindfulness Meditation	**Comparator**	active/passive control condition	**Source**	Journal article

Outcome	STAI-STATE/TRAIT	**Results**	NA	**Weight**	0

Domain	Signalling question	Response	Comments
Bias arising from the randomization process	1.1 Was the allocation sequence random?	N	Convenience sample (p.244)
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	N	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	NI	1.3 Authors reported participants in both groups were comparable regarding academic performance but a baseline comparison regarding STAI scores were not reported.
	Risk of bias judgement	**High**	Convenience sample (p.244) 1.3 Authors reported participants in both groups were comparable regarding academic performance but a baseline comparison regarding STAI scores were not reported.
	2.1.Were participants aware of their assigned intervention during the trial?	PY	2.1 Participants were aware that they were either meditating or in the control group. 2.2 Researchers were aware of the intervention.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	

Bias due to deviations from intended interventions	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	NI	The methods section did not included an analysis plan.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	NI	
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	Y	
	Risk of bias judgement	**High**	
	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	NI	3. 1 Degrees of freedom were reported in results but no information was given regarding number of ss who attended 6-8 sessions.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	N	

Bias due to missing outcome data	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NI	3.3 There is no documented reasons/explanations given for any withdrawals from the study which were very significant. 3.4 Nursing students (the population that was sampled) may have dropped out due to stress.
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	Y	
	Risk of bias judgement	**High**	3. 1 Degrees of freedom were reported in results but no information was given regarding number of ss who attended 6-8 sessions.
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	PN	4.1 Outcomes were measured with standard scoring.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	4.2 Tasks were administered in a standardised manner across participants.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	4.3 Assessors were aware of the intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	4.4 Outcomes were based on standard scoring method.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	

	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	5.1 There was no pre-specified statistical analysis plan in the methods section.
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	5.2 The standard summary scores were calculated for each sub-scale of the questionnaire.
	5.3 ... multiple eligible analyses of the data?	PY	5.3 A standard analysis was used for pre-post analysis but between groups comparisons were not analysed.
	Risk of bias judgement	**High**	5.1 There was no pre-specified statistical analysis plan in the methods section. 5.3 A standard analysis was used for pre-post analysis but between groups comparisons were not analysed.
Overall bias	**Risk of bias judgement**	**High**	

Unique ID	107	**Study ID**	10.1177/0098628320901386	**Assessor**	dw

Ref or Label	Strait, Julia Englund, Strait, Gerald Gill, McClain, Maryellen Brunson, Casillas, Laurel, Streich, Kristin, Harper, Kristina and Gomez, Jocelyn	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	Mindfulness Meditation	**Comparator**	active/passive control condition	**Source**	Journal article
Outcome	GAD-7, PSS-4	**Results**	N/A	**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the randomization process	1.1 Was the allocation sequence random?	PY	1.1 "Each student who completed the preintervention questionnaire was randomly assigned to either the intervention or the control group (irrespective of their class)." (p.164) No method of randomisation reported. 1.2 Course instructors were blind to group assignments. Nature of intervention (that it was a mindfulness practice) was not revealed until participants were in their assigned
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	1.3 Results indicate that groups were comparable across measurement indices at baseline.Table 1 confirmed groups were comparable regarding demographics and outcome measures.
	Risk of bias judgement	**Low**	

Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	2.1 Participants were aware that they were either meditating or in the control group. Participants in the experimental condition (MM) were given a detailed explanation of the intervention procedure. (p.164) 2.2 Researchers were aware of the intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	2.3 Nothing reported to indicate any deviations.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	2.6 All exclusions had a valid reason and all of the remainging participants were included in the comparison of baseline results and the analysis was appropriate. Poisson regression examined the effect of group assignment on
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	

Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PN	3. 1 Degrees of freedom were reported in results. Authors reported 10.75% missing data due to attrition.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	Y	Analyses were conducted using a method that factored in missing values (p.165).
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measuremen	4.1 Was the method of measuring the outcome inappropriate?	PN	4.1 Tasks were administered via computer; outcomes were measured with standard scoring.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	4.2 Tasks were administered in a standardised manner across participants.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	4.3 Assessors were aware of the intervention.

t of the outcome	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	4.4 Outcomes were based on standard scoring method. Outcomes were all computer-based.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	5.1 There was no pre-specified statistical analysis plan in the methods section.
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	5.2 The standard summary scores were calculated for each questionnaire.
	5.3 ... multiple eligible analyses of the data?	PN	5.3 A standard analysis was used that does not appear unreasonable (though no descriptive statistics are provided)
	Risk of bias judgement	**Low**	5.1 There was no pre-specified statistical analysis plan in the methods section.
Overall bias	**Risk of bias judgement**	**Low**	

Unique ID	122	**Study ID**	10.1089/acm.2009.0321	**Assessor**	dw
Ref or Label	Zeidan, F., Johnson, S., Gordon, N., & Goolkasian, P.	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	Mindfulness Meditation	**Comparator**	active/passive control condition	**Source**	Journal article(s)
Outcome	POMS; STAI-S	**Results**		**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the	1.1 Was the allocation sequence random?	PY	1.1 Randomisation occurred by assigning participant to next available intervention condition. 1.2 A random allocation does not allow for prior allocation sequences to be determined.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	

randomization process	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	1.3 Results indicate that groups were comparable across measurement indices at baseline.
	Risk of bias judgement	**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	PN	Participants in the sham group were told they were meditating as were participants in the active meditation group; controls signed up expecting to meditate but were then asked to simply sit on a chair (at the end of the study they were offered meditation). (p.2-3) 2.2 Researchers were aware of the intervention.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	PY	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	2.3 Nothing reported to indicate any deviations.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	2.6 All exclusions had a valid reason and all of the remainging participants were included in the comparison of baseline results.

	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PY	3.1 Degrees of freedom were reported in results.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
	4.1 Was the method of measuring the outcome inappropriate?	PN	4.1 Outcomes were measured with standard scoring.

Bias in measurement of the outcome	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	4.2 Tasks were administered in a standardised manner across participants.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	4.3 Assessors were aware of the intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	4.4 Outcomes were all computer-based outputs.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	5.1 Statistical analysis methods section sets out the intended evaluations.
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	5.2 The standard summary scores were calculated for each questionnaire. Measured in accordance with their methods section specification. p.2
	5.3 ... multiple eligible analyses of the data?	PY	5.3 The most robust analysis was used (parametric e.g. ANOVAs). Measured in accordance with their plan. However, they did not correctly follow up interaction effects.

	Risk of bias judgement	**Low**	5.3 The most robust analysis was used (parametric e.g. ANOVAs). Measured in accordance with their plan. However, they did not correctly follow up interaction effects.
Overall bias	**Risk of bias judgement**	**Low**	

Unique ID	123	**Study ID**	10.1016/j.concog.2010.03.014	**Assessor**	dw
Ref or Label	Zeidan, F., Johnson, S. K., Diamond, B. J., David, Z., & Goolkasian, P.	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	Mindfulness Meditation	**Comparator**	active/passive control condition	**Source**	Journal article
Outcome	n-back; digit span; POMS; STAI-S;CED-S	**Results**		**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**

Bias arising from the randomization process	1.1 Was the allocation sequence random?	PY	1.1 Randomisation occurred by assigning participant to next available intervention condition. 1.2 A random allocation does not allow for prior allocation sequences to be determined.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	1.3 Results indicate that groups were comparable across measurement indices at baseline (see Table 1).
	Risk of bias judgement	**Low**	
Bias due to deviations from	2.1.Were participants aware of their assigned intervention during the trial?	Y	2.1 Participants were aware that they were either meditating or in the control group. 2.2 Researchers were aware of the intervention.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	2.3 Nothing reported to indicate any deviations.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	

from intended interventions	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	2.6 All exclusions had a valid reason and all of the remainging participants were included in the comparison of baseline results. ANOVAs were used to measure between-groups differences. Table 1 indicates that groups
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	

	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PY	3.1 Degrees of freedom and n values were reported in results section.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	

Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	4.1 Outcomes were measured with standard scoring.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	4.2 Tasks were administered in a standardised manner across participants.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	4.3 Assessors were aware of the intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	4.4 Outcomes were all computer-based outputs.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	

	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	5.1 No published protocol referred to in the article; statistical analysis plan not reported in the methods section.
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	5.2 The standard summary scores were calculated for each questionnaire.
	5.3 ... multiple eligible analyses of the data?	PN	5.3 The most robust analysis was used (parametric e.g. ANOVAs).
	Risk of bias judgement	**Low**	5.1 No published protocol referred to in the article; statistical analysis plan not reported in the methods section.
Overall bias	**Risk of bias judgement**	**Low**	

index	cept / reje	count	notes	AUTHORS	TITLE	YEAR
1	reject	3	no contro group	Abdoun, O., Zorn, J., Poletti, S., Fucci, E. and Lutz, A.	Training novice practitioners to reliably report their meditation experience using shared phenomenological dimensions	2019
3	reject	3	no contro group	Bailey, N., Opie, J. L., Hassed, C. S. and Chambers, R.	Meditation practice, dispositional mindfulness, personality and program outcomes in mindfulness training for medical students	2019
4	reject	1	2 treatments (in	Banks, Jonathan B., Jha, Amishi P., Hood, Audrey V. B., Goller, Haley G. and Craig, Lindsay L.	Reducing the TUTs that hurt: the impact of a brief mindfulness induction on emotionally valenced mind wandering	2019
6	reject	4	no working men	Bennike, Ida, Wieghorst, Anders and Kirk, Ulrich	Online-based Mindfulness Training Reduces Behavioral Markers of Mind Wandering	2017
7	reject	1	2 treatments (m	Boe, Ole and Hagen, Kjetil	Using Mindfulness to Reduce the Perception of Stress During an Acute Stressful Situation	2015

index	cept / reje	count	notes	AUTHORS	TITLE	YEAR
8	reject	5	meditations wer	Burgstahler, Matthew S. and Stenson, Mary C.	Effects of guided mindfulness meditation on anxiety and stress in a pre-healthcare college student population: A pilot study	2019
9	reject	3	no control grou	Campillo, E., Ricarte, J., Ros, L., Nieto, M. and Latorre, J.	Effects of the Visual and Auditory Components of a Brief Mindfulness Intervention on Mood State and on Visual and Auditory Attention and Memory Task Performance	2018
10	reject	5	non-standard qu	Chittaro, L. and Vianello, A.	Evaluation of a mobile mindfulness app distributed through on-line stores: A 4-week study	2016
12	reject	5	only included pa	Chowdhury, Suchitra Roy	Impact of mindfulness on anxiety and well-being	2017
13	reject	0	ARTICLE RETRAC	Colzato, L. S., Sellaro, R., Samara, I., Baas, M. and Hommel, B.	Meditation-induced states predict attentional control over time (ARTICLE RETRACTED)	2015
14	reject	1	2 treatments (in	Conley, Sara, Faleer, Hannah, Raza, Gina, Bailey, Brenda and Wu, Kevin	The Moderating Effects of Rumination Facets on the Relationship Between Mindfulness and Distress Reduction	2018
15	reject	1	2 treatments (ts	Cruess, D. G., Finitsis, D. J., Smith, A. L., Goshe, B. M., Burnham, K., Burbridge, C. and O'Leary, K.	Brief Stress Management Reduces Acute Distress and Buffers Physiological Response to a Social Stress Test	2015

index	cept / reje	count	notes	AUTHORS	TITLE	YEAR
16	reject	2	includes physica	Damião Neto, Afonso, Lucchetti, Alessandra Lamas Granero, da Silva Ezequiel, Oscarina and Lucchetti, Giancarlo	Effects of a Required Large-Group Mindfulness Meditation Course on First-Year Medical Students' Mental Health and Quality of Life: a Randomized Controlled Trial	2020
17	reject	1	2 treatments (e	Daugherty, A. M., Sutton, B. P., Hillman, C. H., Kramer, A. F., Cohen, N. J. and Barbey, A. K.	Individual differences in the neurobiology of fluid intelligence predict responsiveness to training: Evidence from a comprehensive cognitive, mindfulness meditation, and aerobic exercise intervention	2020
18	reject	4	not working me	Delgado-Pastor, Luis Carlos, Perakakis, Pandelis, Subramanya, Pailoor, Telles, Shirley and Vila, Jaime	Mindfulness (Vipassana) meditation: Effects on P3b event-related potential and heart rate variability	2013
19	reject	1	2 treatments (ar	DeSteno, David, Lim, Daniel, Duong, Fred and Condon, Paul	Meditation inhibits aggressive responses to provocations	2017
21	reject	4	no working men	Draper-Clarke, Lucy J. and Edwards, David J. A.	Stress and coping among student teachers at a South African university: An exploratory study	2016
22	reject	0	not enough info	Durocher, John J., Marti, Hannah, Morin, Brigitte and Wakeham, Travis R.	Single Session Mindfulness Meditation Reduces Aortic Pulsatile Load and Anxiety in Mild to Moderately Anxious Adults	2018

index	cept / reje	count	notes	AUTHORS	TITLE	YEAR
23	reject	5	physical compor	Dvorakova, K., Kishida, M., Li, J., Elavsky, S., Broderick, P. C., Agrusti, M. R. and Greenberg, M. T.	Promoting healthy transition to college through mindfulness training with first-year college students: Pilot randomized controlled trial	2017
25	reject	4	no working men	Farrar, S. and Tapper, D. K.	The effect of mindfulness on rational thinking	2018
26	reject	5	meditation time	Flett, J. A. M., Conner, T. S., Riordan, B. C., Patterson, T. and Hayne, H.	App-based mindfulness meditation for psychological distress and adjustment to college in incoming university students: a pragmatic, randomised, waitlist-controlled trial	2020
27	reject	1	2 treatments (M	Galante, J., Dufour, G., Vainre, M., Wagner, A. P., Stochl, J., Benton, A., Howarth, E. and Jones, P. B.	Effectiveness of providing university students with a mindfulness-based intervention to increase resilience to stress: a pragmatic randomised controlled trial	2018
28	reject	5	observational st	Galla, B. M., O'Reilly, G. A., Kitil, M. J., Smalley, S. L. and Black, D. S.	Community-Based Mindfulness Program for Disease Prevention and Health Promotion: Targeting Stress Reduction	2015

index	cept / reje	count	notes	AUTHORS	TITLE	YEAR
29	reject	5	REVIEW PAPER	Garland, Eric L.	Restructuring reward processing with Mindfulness-Oriented Recovery Enhancement: novel therapeutic mechanisms to remediate hedonic dysregulation in addiction, stress, and pain	2016
30	reject	5	eyes open and n	Gluck, T. M. and Maercker, A.	A randomized controlled pilot study of a brief web-based mindfulness training	2011
31	reject	4	no working men	Grecucci, A., De Pisapia, N., Kusalagnana Thero, D., Paladino, M. P., Venuti, P. and Job, R.	Baseline and strategic effects behind mindful emotion regulation: behavioral and physiological investigation	2015
32	reject	2	meditation varie	Greenberg, J., Reiner, K. and Meiran, N.	Off with the old: mindfulness practice improves backward inhibition	2012
34	reject	0	CORRECTION NO	Greenberg, J., Romero, V. L., Elkin-Frankston, S., Bezdek, M. A., Schumacher, E. H. and Lazar, S. W.	Correction to: Reduced interference in working memory following mindfulness training is associated with increases in hippocampal volume	2019
35	reject	1	2 treatments (ts	Groesbeck, G., Bach, D., Stapleton, P., Blickheuser, K., Church, D. and Sims, R.	The Interrelated Physiological and Psychological Effects of EcoMeditation	2018
36	reject	5	total sample size	Harmony, Colin and Woodard, Cooper R.	Mindfulness Training for Staff in a School for Children with Autism and Other Developmental Disabilities: Effects on Staff Mindfulness and Student Behavior	2020

index	cept / reje	count	notes	AUTHORS	TITLE	YEAR
37	reject	5	eyes open medi	Hauswald, A., Ubelacker, T., Leske, S. and Weisz, N.	What it means to be Zen: Marked modulations of local and interareal synchronization during open monitoring meditation	2015
38	reject	4	no working men	Hinterberger, Thilo, Baierlein, Felicitas and Breitenbach, Natalie	Skin Conductance Feedback Meditation: Evaluation of a Novel Physiology-Assisted Meditation Style	2018
39	reject	5	not enough info	Horner, Janice K., Piercy, Brigit S., Eure, Lois and Woodard, Elizabeth K.	A pilot study to evaluate mindfulness as a strategy to improve inpatient nurse and patient experiences	2014
40	reject	2	MBCT, MBSR wi	Hulsheger, U. R., Alberts, H. J., Feinholdt, A. and Lang, J. W.	Benefits of mindfulness at work: the role of mindfulness in emotion regulation, emotional exhaustion, and job satisfaction	2013
41	reject	4	no working men	Immink, Maarten, Colzato, Lorenza, Stolte, Marije and Hommel, Bernhard	Sequence Learning Enhancement Following Single-Session Meditation Is Dependent on Metacontrol Mode and Experienced Effort	2017

index	cept / reje	count	notes	AUTHORS	TITLE	YEAR
42	reject	4	no working men	Isbel, Ben, Lagopoulos, Jim, Hermens, Daniel, Stefanidis, Kayla and Summers, Mathew J.	Mindfulness Improves Attention Resource Allocation During Response Inhibition in Older Adults	2020
43	reject	4	no working men	Isbel, Ben, Lagopoulos, Jim, Hermens, Daniel F. and Summers, Mathew J.	Mindfulness induces changes in anterior alpha asymmetry in healthy older adults	2019
44	reject	2	MBSR	Jain, Shamini, Shapiro, Shauna, Swanick, Summer, Roesch, Scott, Mills, Paul, Bell, Iris and Schwartz, Gary	A randomized controlled trial of mindfulness meditation versus relaxation training: Effects on distress, positive states of mind, rumination, and distraction	2007
45	reject	1	2 treatments (ar	Jankowski, Tomasz and Holas, Pawel	Effects of Brief Mindfulness Meditation on Attention Switching	2020
46	reject	3	no control grou	Jensen, C. G., Lansner, J., Petersen, A., Vangkilde, S. A., Ringkobing, S. P., Frokjaer, V. G., Adamsen, D., Knudsen, G. M., Denninger, J. W. and Hasselbalch, S. G.	Open and Calm - A randomized controlled trial evaluating a public stress reduction program in Denmark	2015
48	reject	4	no working men	Jo, H. G., Schmidt, S., Inacker, E., Markowiak, M. and Hinterberger, T.	Meditation and attention: A controlled study on long-term meditators in behavioral performance and event-related potentials of attentional control	2016

index	cept / reje	count	notes	AUTHORS	TITLE	YEAR
49	reject	5	Only recruited tl	John Lothes, II, Mochrie, Kirk, Wilson, Morgan and Hakan, Robert	The effect of dbt-informed mindfulness skills (what and how skills) and mindfulness-based stress reduction practices on test anxiety in college students: A mixed design study	2019
50	reject	5	body scan medit	Jones, Dusti R., Graham-Engeland, Jennifer E., Smyth, Joshua M. and Lehman, Barbara J.	Clarifying the Associations between Mindfulness Meditation and Emotion: Daily High- and Low-arousal Emotions and Emotional Variability	2018
52	reject	2	meditation inclu	Kang, Y. S., Choi, S. Y. and Ryu, E.	The effectiveness of a stress coping program based on mindfulness meditation on the stress, anxiety, and depression experienced by nursing students in Korea	2009
53	reject	5	meditation not (	Kar, S.	Resolution of academic stress by mindfulness meditation	2016
54	reject	4	no working men	Kass, Steven, VanWormer, Lisa, Mikulas, William, Legan, Shauna and Bumgarner, David	Effects of Mindfulness Training on Simulated Driving: Preliminary Results	2011
55	reject	4	no working men	Kemper, K. J., Powell, D., Helms, C. C. and Kim-Shapiro, D. B.	LOVING-KINDNESS MEDITATION'S EFFECTS ON NITRIC OXIDE AND PERCEIVED WELL-BEING: A PILOT STUDY IN EXPERIENCED AND INEXPERIENCED MEDITATORS	2015

index	cept / reje	count	notes	AUTHORS	TITLE	YEAR
56	reject	5	mindfulness trai	Kerr, Sandra L., Lucas, Lisa J., DiDomenico, Grace E., Mishra, Vipanchi, Stanton, Brian J., Shivde, Geeta, Pero, Alexandra N., Runyen, Madeline E. and Terry, Gabriella M.	Is mindfulness training useful for pre-service teachers? An exploratory investigation	2017
57	reject	4	no working men	Kirk, Ulrich, Wieghorst, Anders, Nielsen, Christian and Staiano, Walter	On-the-Spot Binaural Beats and Mindfulness Reduces Behavioral Markers of Mind Wandering	2019
58	reject	5	sample exclusiv	Kober, H., Brewer, J. A., Height, K. L. and Sinha, R.	Neural stress reactivity relates to smoking outcomes and differentiates between mindfulness and cognitive-behavioral treatments	2017
59	reject	4	no working men	Kozasa, E. H., Balardin, J. B., Sato, J. R., Chaim, K. T., Lacerda, S. S., Radvany, J., Mello, Leam and Amaro, E., Jr.	Effects of a 7-Day Meditation Retreat on the Brain Function of Meditators and Non-Meditators During an Attention Task	2018
60	reject	4	no working men	Kurmi, N., Bhagyalakshmi, K. and Kini, R.	Effect of mindfulness meditation on attention and visual scanning in elderly people - A randomized control trial	2019

index	cept / reje	count	notes	AUTHORS	TITLE	YEAR
61	reject	2	MBSR	Kvillemo, P., Brandberg, Y. and Branstrom, R.	Feasibility and Outcomes of an Internet-Based Mindfulness Training Program: A Pilot Randomized Controlled Trial	2016
62	reject	2	physical activitie	Kwak, S., Lee, T. Y., Jung, W. H., Hur, J. W., Bae, D., Hwang, W. J., Cho, K. I. K., Lim, K. O., Kim, S. Y., Park, H. Y. and Kwon, J. S.	The Immediate and Sustained Positive Effects of Meditation on Resilience Are Mediated by Changes in the Resting Brain	2019
64	reject	3	no control grou	Lane, J. D., Seskevich, J. E. and Pieper, C. F.	Brief meditation training can improve perceived stress and negative mood	2007
65	reject	5	validation of ser	Levinson, D. B., Stoll, E. L., Kindy, S. D., Merry, H. L. and Davidson, R. J.	A mind you can count on: Validating breath counting as a behavioral measure of mindfulness	2014
66	reject	2	MM included yo	Li, Y., Liu, F., Zhang, Q., Liu, X. and Wei, P.	The effect of mindfulness training on proactive and reactive cognitive control	2018
67	reject	4	no working men	Lin, Jian Wei and Mai, Li Jung	Impact of mindfulness meditation intervention on academic performance	2018

index	cept / reje	count	notes	AUTHORS	TITLE	YEAR
68	reject	3	no control grou	Linares, Leticia, Herrero-Fernández, David, Gorbeña, Susana and Estévez, Ana	Effectiveness of a mindfulness-based intervention on groups with presence/absence of clinically significant depressive symptoms	2019
69	reject	5	stressed adults;	Lindsay, Emily K., Chin, Brian, Greco, Carol M., Young, Shinzen, Brown, Kirk W., Wright, Aidan G. C., Smyth, Joshua M., Burkett, Deanna and Creswell, J. David	How mindfulness training promotes positive emotions: Dismantling acceptance skills training in two randomized controlled trials	2018
70	reject	4	no working men	Lindsay, Emily K., Young, Shinzen, Brown, Kirk Warren, Smyth, Joshua M. and Creswell, J. David	Mindfulness training reduces loneliness and increases social contact in a randomized controlled trial	2019
71	reject	2	MM included yo	Liu, X., Xu, W., Wang, Y., Williams, J. M., Geng, Y., Zhang, Q. and Liu, X.	Can Inner Peace be Improved by Mindfulness Training: A Randomized Controlled Trial	2015
72	reject	5	subjective meas	Logie, Kyle and Frewen, Paul	Self/Other Referential Processing Following Mindfulness and Loving-Kindness Meditation	2015
73	reject	2	MBSR	Lymeus, Freddie, Lundgren, Tobias and Hartig, Terry	Attentional Effort of Beginning Mindfulness Training Is Offset With Practice Directed Toward Images of Natural Scenery	2017
74	reject	3	no control grou	Mahlo, L. and Windsor, T. D.	Feasibility, Acceptability, and Preliminary Efficacy of an App-Based Mindfulness-Meditation Program Among Older Adults	2020
75	reject	3	no control grou	Mak, W. W., Chio, F. H., Chan, A. T., Lui, W. W. and Wu, E. K.	The Efficacy of Internet-Based Mindfulness Training and Cognitive-Behavioral Training With Telephone Support in the Enhancement of Mental Health Among College Students and Young Working Adults: Randomized Controlled Trial	2017
76	reject	4	no working men	McHugh, L., Simpson, A. and Reed, P.	Mindfulness as a potential intervention for stimulus over-selectivity in older adults	2010

index	cept / reje	count	notes	AUTHORS	TITLE	YEAR
77	reject	6	non-english	Möltner, H., Leve, J. and Esch, T.	Burnout Prevention and Mobile Mindfulness: Evaluation of an App-Based Health Training Program for Employees	2018
78	reject	5	observational st	Montero-Marin, J., Perez-Yus, M. C., Cebolla, A., Soler, J., Demarzo, M. and Garcia-Campayo, J.	Religiosity and Meditation Practice: Exploring Their Explanatory Power on Psychological Adjustment	2019
79	reject	2	MBSR	Munoz, Ricky T., Hoppes, Steve, Hellman, Chan M., Brunk, Kara L., Bragg, Jedidiah E. and Cummins, Carissa	The Effects of Mindfulness Meditation on Hope and Stress	2018
80	reject	1	2 treatments (e	Myint, K., Choy, K. L., Su, T. T. and Lam, S. K.	The effect of short-term practice of mindfulness meditation in alleviating stress in university students	2011
81	reject	2	MBSR	Nyhus, E., Engel, W. A., Pitfield, T. D. and Vakkur, I. M. W.	Combining Behavior and EEG to Study the Effects of Mindfulness Meditation on Episodic Memory	2020
82	reject	5	ss were all abov	Oken, B., Miller, M., Goodrich, E. and Wahbeh, H.	Effects of mindfulness meditation on self-rated stressrelated measures: improvements in neuroticism and ecological momentary assessment of stress	2014
83	reject	5	ss were all abov	Oken, Barry, Wahbeh, Helané, Goodrich, Elena, Klee, Daniel, Memmott, Tabatha, Miller, Meghan and Fu, Rongwei	Meditation in Stressed Older Adults: Improvements in Self-Rated Mental Health Not Paralleled by Improvements in Cognitive Function or Physiological Measures	2017

index	cept / reje	count	notes	AUTHORS	TITLE	YEAR
84	reject	5	ss were all abov	Oken, B., Wahbeh, H., Goodrich, E., Miller, M., Klee, D., Memmott, T. and Fu, R.	Mindfulness meditation in older adults: effects on stress, affect, cognition, and physiology	2016
85	reject	2	MBSR	Ong, J. C., Manber, R., Segal, Z., Xia, Y., Shapiro, S. and Wyatt, J.	A randomized controlled trial of mindfulness meditation for chronic insomnia: long-term outcomes	2014
86	reject	1	2 treatments (e	Orzech, Kevin, Shapiro, Shauna, Brown, Kirk Warren and McKay, Matthew	Intensive mindfulness training-related changes in cognitive and emotional experience	2009
87	reject	0	no paper and nc	Park, Janet	Randomized controlled trial for stress and anxiety management: biofeedback and mindfulness meditation	2014
89	reject	1	2 treatments (p	Pratzlich, M., Kossowsky, J., Gaab, J. and Krummenacher, P.	Impact of short-term meditation and expectation on executive brain functions	2016
90	reject	5	appears to requ	Quintana, M. and Rivera, O.	Mindfulness training online for stress reduction, a global measure	2012
91	reject	4	no working men	Rahl, Hayley A., Lindsay, Emily K., Pacilio, Laura E., Brown, Kirk W. and Creswell, J. David	Brief mindfulness meditation training reduces mind wandering: The critical role of acceptance	2017

index	cept / reje	count	notes	AUTHORS	TITLE	YEAR
92	reject	5	minimum of mo	Ribeiro, Letícia, Atchley, Rachel and Oken, Barry	Adherence to Practice of Mindfulness in Novice Meditators: Practices Chosen, Amount of Time Practiced, and Long-Term Effects Following a Mindfulness-Based Intervention	2018
93	reject	3	no control grou	Rojiani, Rahil, Santoyo, Juan F., Rahrig, Hadley, Roth, Harold D. and Britton, Willoughby B.	Women benefit more than men in response to college-based meditation training	2017
94	reject	2	mindfulness incl	Rönnlund, Michael, Koudriavtseva, Antonina, Germundsjö, Linnea, Eriksson, Terese, Åström, Elisabeth and Carelli, Maria Grazia	Mindfulness promotes a more balanced time perspective: Correlational and intervention-based evidence	2019
95	reject	5	military populat	Rothschild, Sarit, Kaplan, Gilat, Golan, Tomer and Barak, Yoram	Mindfulness meditation in the Israel Defense Forces: Effect on cognition and satisfaction with life–A randomized controlled trial	2017
96	reject	5	eyes probably cl	Rowland, Zarah, Wenzel, Mario and Kubiak, Thomas	A mind full of happiness: How mindfulness shapes affect dynamics in daily life	2018
97	reject	5	sample recruite	Rung, A. L., Oral, E., Berghammer, L. and Peters, E. S.	Feasibility and Acceptability of a Mobile Mindfulness Meditation Intervention Among Women: Intervention Study	2020

index	cept / reje	count	notes	AUTHORS	TITLE	YEAR
99	reject	4	no working men	Saunders, B., Rodrigo, A. H. and Inzlicht, M.	Mindful awareness of feelings increases neural performance monitoring	2016
100	reject	2	modified MBCT	Schanche, Elisabeth, Vøllestad, Jon, Binder, Per Einar, Osnes, Berge, Visted, Endre, Svendsen, Julie Lillebostad and Sørensen, Lin	Can clinical psychology students benefit from brief and intensive mindfulness training?	2020
101	reject	2	MBSR	Sevinc, G., Greenberg, J., Holzel, B. K., Gard, T., Calahan, T., Brunsch, V., Hashmi, J. A., Vangel, M., Orr, S. P., Milad, M. R. and Lazar, S. W.	Hippocampal circuits underlie improvements in self-reported anxiety following mindfulness training	2020
102	reject	2	MBSR	Sevinc, Gunes, Hölzel, Britta K., Greenberg, Jonathan, Gard, Tim, Brunsch, Vincent, Hashmi, Javaria A., Vangel, Mark, Orr, Scott P., Milad, Mohammed R. and Lazar, Sara W.	Strengthened Hippocampal Circuits Underlie Enhanced Retrieval of Extinguished Fear Memories Following Mindfulness Training	2019
103	reject	2	includes mindfu	Shankland, Rebecca, Favre, Pauline, Kotsou, Ilios and Mermillod, Martial	Mindfulness and De-automatization: Effect of Mindfulness-Based Interventions on Emotional Facial Expressions Processing	2020
104	reject	4	no working men	Smart, C. M., Segalowitz, S. J., Mulligan, B. P., Koudys, J. and Gawryluk, J. R.	Mindfulness Training for Older Adults with Subjective Cognitive Decline: Results from a Pilot Randomized Controlled Trial	2016
105	reject	2	MBSR	Spadaro, Kathleen C. and Hunker, Diane F.	Exploring The effects Of An online asynchronous mindfulness meditation intervention with nursing students On Stress, mood, And Cognition: A descriptive study	2016
108	reject	5	could not obtair	Sundin, E. C., Shonin, E., Van Gordon, W. and Horgan, L.	Mindfulness meditation, psychological wellbeing and resilience to stress: development and pilot study of the newly designed meditation based awareness training	2020

index	cept / reje	count	notes	AUTHORS	TITLE	YEAR
109	reject	5	observation stu	Teper, Rimma and Inzlicht, Michael	Meditation, mindfulness and executive control: the importance of emotional acceptance and brain-based performance monitoring	2013
110	reject	4	no working men	Tsai, M. H. and Chou, W. L.	Attentional orienting and executive control are affected by different types of meditation practice	2016
111	reject	4	no working men	Tsai, S. Y., Jaiswal, S., Chang, C. F., Liang, W. K., Muggleton, N. G. and Juan, C. H.	Meditation Effects on the Control of Involuntary Contingent Reorienting Revealed With Electroencephalographic and Behavioral Evidence	2018
112	reject	2	MBSR (they refe	Turner, Kielty	Mindfulness Skills Training: A Pilot Study of Changes in Mindfulness, Emotion Regulation, and Self-Perception of Aging in Older Participants	2014
113	reject	1	2 treatments (m	Turner, Lorinda, Galante, Julieta, Vainre, Maris, Stochl, Jan, Dufour, Géraldine and Jones, Peter B.	Immune dysregulation among students exposed to exam stress and its mitigation by mindfulness training: findings from an exploratory randomised trial	2020
114	reject	5	observational st	van den Hurk, Paul A. M., Giommi, Fabio, Gielen, Stan C., Speckens, Anne E. M. and Barendregt, Henk P.	Greater efficiency in attentional processing related to mindfulness meditation	2010
115	reject	2	meditation inclu	van der Zwan, Judith Esi, de Vente, Wieke, Huizink, Anja C., Bögels, Susan M. and de Bruin, Esther I.	Physical activity, mindfulness meditation, or heart rate variability biofeedback for stress reduction: a randomized controlled trial	2015
116	reject	2	meditation inclu	Vella, Elizabeth and McIver, Shane	Reducing stress and burnout in the public-sector work environment: A mindfulness meditation pilot study	2019

index	cept / reje	count	notes	AUTHORS	TITLE	YEAR
117	reject	5	selected based c	Versluis, A., Verkuil, B., Spinhoven, P. and Brosschot, J. F.	Effectiveness of a smartphone-based worry-reduction training for stress reduction: A randomized-controlled trial	2018
118	reject	5	ss were all abov	Wahbeh, Helané, Lane, James, Goodrich, Elena, Miller, Meghan and Oken, Barry	One-on-One Mindfulness Meditation Trainings in a Research Setting	2014
119	reject	5	non-neutral MM	Wahbeh, H. and Oken, B. S.	Internet Mindfulness Meditation Intervention for the General Public: Pilot Randomized Controlled Trial	2016
120	reject	2	MBSR which inc	Wimmer, L., von Stockhausen, L. and Bellingrath, S.	Improving emotion regulation and mood in teacher trainees: Effectiveness of two mindfulness trainings	2019
121	reject	3	no control grou	Wongtongkam, Nualnong, Krivokapic-Skoko, Branka, Duncan, Roderick and Bellio, Mariagrazia	The influence of a mindfulness-based intervention on job satisfaction and work-related stress and anxiety	2017
124	reject	1	2 treatments (n	Zeidan, F., Martucci, K. T., Kraft, R. A., McHaffie, J. G. and Coghill, R. C.	Neural correlates of mindfulness meditation-related anxiety relief	2014

Unique ID	3	**Study ID**	10.3233/rnn-160714	**Assessor**	DW
Ref or Label	Alekseichuk, I., Pabel, S. C., Antal, A. and Paulus, W., (2017)	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	tACS	**Comparator**	sham	**Source**	Journal article
Outcome	HR-FA (% correct)/accurate log-transformed RTs	**Results**	0.1	**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the randomization process	1.1 Was the allocation sequence random?	PY	No information was given regarding randomisation process.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	Within-ss design.
	Risk of bias judgement	**Low**	
Domain S: Risk of bias arising from period and carryover effects	S.1 Was the number of participants allocated to each of the two sequences equal or nearly equal?	Y	Fig 3 indicates n=25
	S.2 If N/PN/NI to S.1: Were period effects accounted for in the analysis?	NA	
	S.3 Was there sufficient time for any carryover effects to have disappeared before outcome assessment in the second period?	NI	Not reported
	Risk of bias judgement	**Some concerns**	

Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	N	"Control intervention was delivered with the same intensity and via the same electrode montage (AF3, AF4, P3, and P4) as for the real stimulation conditions, but only for 10 s at the beginning and end of the session, according to fadein/fade-out placebo protocol (Ambrus et al., 2012). The phase relationships between the
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	N	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	NA	
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	2.6 within-ss design so not applicable as ss received both sham and active stimulation.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	Fig 3 shows behavioural results which indicates n = 25.

Bias due to missing outcome data	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	d' measured accuracy
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	Conditions were administered in a standardised manner and steps were taken to control for experimenter bias: "the double-blind nature of the experimental procedure ensured that
	4.3 Were outcome assessors aware of the intervention received by study participants?	N	
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	NA	
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	

	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	Y	An analysis plan was reported in the methods section (p. 152) and reported results corresponded to this plan.
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	N	Results regarding all conditions were provided. See Fig 3, p. 153.
	5.3 ... multiple eligible analyses of the data?	N	Results regarding all conditions were provided. See Fig 3, p. 153.
	5.4 Is a result based on data from both periods sought, but unavailable on the basis of carryover having been identified?	N	"learning and session order had no significant impact on the group level statistics."
	Risk of bias judgement	**Low**	
Overall bias	**Risk of bias judgement**	**Low**	

Unique ID	10	**Study ID**	10.1155/2016/4274127	**Assessor**	DW

Ref or Label	Antonenko, D., Faxel, M., Grittner, U., Lavidor, M. and Floel, A., (2016)	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	tACS	**Comparator**	sham	**Source**	Journal article
Outcome	summed scores (PA, NA)	**Results**	NA	**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	Allocation to order was randomised and ordering was counter-balanced. Efforts were made to ensure equal treatment of participants (see p.8)
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	see Table 3
	Risk of bias judgement	**Low**	
	S.1 Was the number of participants allocated to each of the two sequences equal or nearly equal?	Y	within-ss design (regarding stimulation treatment).

Domain S: Risk of bias arising from period and carryover effects	S.2 If N/PN/NI to S.1: Were period effects accounted for in the analysis?	NA	
	S.3 Was there sufficient time for any carryover effects to have disappeared before outcome assessment in the second period?	Y	"Sessions were separated by seven days to avoid carryover effects and were administered at the same time of the day."
	Risk of bias judgement	**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	N	confirmed by blinding assessment, p. 9. Single-blind study.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	2.3 Nothing reported to indicate any deviations, though low risk in this type of trial as there is no benefit to receiving a particular trial protocol e.g. beneficial drug vs. placebo.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	2.6 within-ss design so not applicable as ss received both sham and active stimulation.

	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	NI	
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	Y	Reported results indicate that all/most participants' data were included with no missing values
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
	4.1 Was the method of measuring the outcome inappropriate?	N	Well-validated PANAS questionnaire was used which measures pos/neg affect comprising suitable number of items measured on a Likert Scale (p.8)
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	All ss treated the same.

Bias in measurement of the outcome	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	Single blind study
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	Blinding was successful therefore no influence on participant-outcome reports. No information to indicate that researcher's knowledge of treatments might affect ss responses. Outcomes were all computer-based outputs.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	Y	Reported results are congruent with the 'Statistical Analysis' section (p.8)
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	N	All outcomes associated with the scale were reported.
	5.3 ... multiple eligible analyses of the data?	N	Reported results are congruent with the 'Statistical Analysis' section (p.8)
	5.4 Is a result based on data from both periods sought, but unavailable on the basis of carryover having been identified?	N	5.4 No-one dropped out.
	Risk of bias judgement	**Low**	

Overall bias	**Risk of bias judgement**	**Low**	not included in meta-analysis

Unique ID	16	**Study ID**	10.1523/JNEUROSCI.1285-17.2018	**Assessor**	DW
Ref or Label	Borghini, Giulia, Candini, Michela, Filannino, Cristina, Hussain, Masud, Walsh, Vincent, Romei, Vincenzo, Zokaei, Nahid and Cappelletti,	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	tACS	**Comparator**	sham	**Source**	Journal article
Outcome	p(T)	**Results**	NA	**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**
Bias arising from the	1.1 Was the allocation sequence random?	N	The order of the stimulation conditions was counterbalanced and pseudorandomized across participants (p.3).
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	The same equipment is used for all ss therefore they cannot know their treatment allocation in advance: "To allow successful blinding of participants, during Sham stimulation the same setting was maintained

randomization process	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	No issues reported.
	Risk of bias judgement	**Low**	Pseudo-randomised order with counter-balancing with a 2-day wash-out indicates acceptable due diligence.
Domain S: Risk of bias arising from period and carryover effects	S.1 Was the number of participants allocated to each of the two sequences equal or nearly equal?	Y	One df value for a correlation analysis was reported which indicates n value (p. 4424)
	S.2 If N/PN/NI to S.1: Were period effects accounted for in the analysis?	NA	
	S.3 Was there sufficient time for any carryover effects to have disappeared before outcome assessment in the second period?	Y	2 day wash-out is sufficient (p. 4420)
	Risk of bias judgement	**Low**	Apart from df given for regression analyses, no other indicates were given regarding N values in the results section that confirms number of ss's data analysed.
	2.1.Were participants aware of their assigned intervention during the trial?	N	Double-blind design (p. 4419)
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	N	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	NA	

Bias due to deviations from intended interventions	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	2.6 within-ss design so not applicable as ss received both sham and active stimulation.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	Participants received both treatment conditions.
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PY	While there is no reason to doubt that information was available for all ss, very little information was given regarding n values in the results section and no information was provided regarding
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	

	Risk of bias judgement	**Some concerns**	While there is no reason to doubt that information was available for all ss, very little information was given regarding n values in the results section and no information was provided regarding
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	Recall precision (P) was used as an overall measure of performance, obtained by calculating the angular deviation between the orientation reported by the subject
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	4.2 The task was computer-based and administered in a standardised manner with appropriate randomisation of stimuli
	4.3 Were outcome assessors aware of the intervention received by study participants?	N	double-blind study
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	NA	
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	Y	Statistical analysis section sets out the intended evaluations (p. 4420)
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	Table 1 and 2 provides all outcomes associated with the measure, which is standard outcome for a retro-cueing task (probability of reporting correct target item (pT), p.4420-1

Bias in selection of the reported result	5.3 ... multiple eligible analyses of the data?	PN	5.3 The most robust analysis was used (parametric e.g. repeated measures regression analysis). Measured in accordance with their plan. p.4420-1
	5.4 Is a result based on data from both periods sought, but unavailable on the basis of carryover having been identified?	N	5.4 No-one dropped out.
	Risk of bias judgement	**Low**	
Overall bias	**Risk of bias judgement**	**Some concerns**	

Unique ID	61	**Study ID**	10.1016/j.bandc.2015.11.002	**Assessor**	DW
Ref or Label	Hoy, K. E., Bailey, N., Arnold, S., Windsor, K., John, J., Daskalakis, Z. J. and Fitzgerald, P. B., (2015)	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	tACS	**Comparator**	sham	**Source**	Journal article
Outcome	accuracy diff scores [(post-pre)/pre]; accurate RTs	**Results**	0.388873016	**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	"The three repeated sessions were randomised and counterbalanced across participants." (p.52) The same equipment is used for all ss therefore they cannot know their treatment allocation in advance
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	Within-ss design.
	Risk of bias judgement	**Low**	
Domain S: Risk of bias arising from period and carryover effects	S.1 Was the number of participants allocated to each of the two sequences equal or nearly equal?	Y	N values and df values indicate no missing ss (p.54)
	S.2 If N/PN/NI to S.1: Were period effects accounted for in the analysis?	NA	
	S.3 Was there sufficient time for any carryover effects to have disappeared before outcome assessment in the second period?	Y	72 hrs' wash-out (p.52)
	Risk of bias judgement	**Low**	

Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	N	"Blinding questionnaires were conducted at the end of each session." (p.52); "Sham stimulation began with a fade into a peak of 2 mA over 120 s, immediately followed by 30 s of constant current stimulation and a 15 s fade out." (p.53). Blinding reported as successful (p.54). Single-blind.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	N	Nothing reported to indicate any deviations.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	2.6 within-ss design so not applicable as ss received both sham and active stimulation.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	As reported in Results (p.54).

Bias due to missing outcome data	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	d prime is a discriminability index which takes into account the ability to correctly dependent variables were difference scores (post-pre)/pre
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	The task was administered in a standardised manner with appropriate randomisation of stimuli (p.53).
	4.3 Were outcome assessors aware of the intervention received by study participants?	N	Outcomes were computer-based outputs.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	NA	
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	

	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	Statistical analysis section sets out the intended evaluations (p.53)
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	All outcome measures were reported.
	5.3 ... multiple eligible analyses of the data?	PN	Appropriate summary statistics were reported.
	5.4 Is a result based on data from both periods sought, but unavailable on the basis of carryover having been identified?	N	5.4 No-one dropped out.
	Risk of bias judgement	**Low**	
Overall bias	**Risk of bias judgement**	**Low**	

Unique ID	65	**Study ID**	10.1016/j.ibneur.2022.10.013	**Assessor**	DW

Ref or Label	Hu, Zhenhong, Woods, Adam J., Samuel, Immanuel B. H., Meyyappan, Sreenivasan and Ding, Mingzhou, (2019)	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	tACS	**Comparator**	sham	**Source**	Journal article
Outcome	accuracy (% correct); correct RTs	**Results**	NA	**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	Randomisation procedure not specified. The same equipment is used for all ss therefore they cannot know their treatment allocation in advance.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	Within-ss design; nothing reported to indicate a problem with randomisation.
	Risk of bias judgement	**Low**	
	S.1 Was the number of participants allocated to each of the two sequences equal or nearly equal?	Y	Reported in Fig 3 (p.473)

Domain S: Risk of bias arising from period and carryover effects	S.2 If N/PN/NI to S.1: Were period effects accounted for in the analysis?	NA	
	S.3 Was there sufficient time for any carryover effects to have disappeared before outcome assessment in the second period?	Y	1 week (p.470)
	Risk of bias judgement	**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	PN	Single-blind design, but success of blinding not reported. 2.2 Researchers were aware of the intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	2.3 Nothing reported to indicate any deviations, though low risk in this type of trial as there is no benefit to receiving a particular trial protocol e.g. beneficial drug vs. placebo.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	2.6 within-ss design so not applicable as ss received both sham and active stimulation.

	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	Fig 3 indicates all participants' data were analysed (p.473).
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
	4.1 Was the method of measuring the outcome inappropriate?	N	computer-generated accuracy and RT as indicated in Fig 3 (p.473)
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	The task was administered in a standardised manner with appropriate randomisation of stimuli (p.471)

Bias in measurement of the outcome	4.3 Were outcome assessors aware of the intervention received by study participants?	PN	Outcomes were computer-based outputs.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	NA	
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	Statistical analysis section sets out the intended evaluations (p.472).
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	All outcome measures were reported (and author supplied the raw data).
	5.3 ... multiple eligible analyses of the data?	PN	Appropriate summary statistics were reported (and author supplied the raw data).
	5.4 Is a result based on data from both periods sought, but unavailable on the basis of carryover having been identified?	PN	5.4 Five participants did not complete all sessions (no reasons given)
	Risk of bias judgement	**Low**	

Overall bias	**Risk of bias judgement**	**Low**	

Unique ID	68	**Study ID**	10.1016/j.actpsy.2013.11.011	**Assessor**	DW
Ref or Label	Jausovec, N., Jausovec, K. and Pahor, A., (2014)	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	tACS	**Comparator**	sham	**Source**	Journal article
Outcome	number of correct responses (corrected for wrong responses)	**Results**	1.304160011	**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the	1.1 Was the allocation sequence random?	N	Counter-balanced (p.2) Participants were given the same test protocol with exception of difference in treatment allocation.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	

randomization process	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	Within-between design; WM measured at baseline indicating groups were comparable: "The respondents of the three groups were equalized with respect to sex and performance on
	Risk of bias judgement	**Low**	Counter-balanced and within-ss design, thus low risk of bias due to not being randomised.
Domain S: Risk of bias arising from period and carryover effects	S.1 Was the number of participants allocated to each of the two sequences equal or nearly equal?	Y	Df values reported in results and tables (see Tables 1 and 2) (p.4)
	S.2 If N/PN/NI to S.1: Were period effects accounted for in the analysis?	NA	
	S.3 Was there sufficient time for any carryover effects to have disappeared before outcome assessment in the second period?	Y	28 days (p.2)
	Risk of bias judgement	**Low**	
	2.1.Were participants aware of their assigned intervention during the trial?	N	Steps were taken to minimise skin sensations: "Themagnitude of the stimulating current was based on individually determined thresholds for skin sensations induced by tACS." (p.3). Single-blind study.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	N	2.3 Nothing reported to indicate any deviations, though low risk in this type of trial as there is no benefit to receiving a particular trial protocol e.g. beneficial drug vs. placebo.

Bias due to deviations from intended interventions	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	2.6 within-ss design so not applicable as ss received both sham and active stimulation.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	Tables and results report df values (p.3-4)
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	

	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	accuracy: number of correct responses (corrected for wrong responses) (p.3)
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	The task was administered in a standardised manner with appropriate randomisation of stimuli (p.3)
	4.3 Were outcome assessors aware of the intervention received by study participants?	N	Outcomes were computer-based outputs.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	NA	
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	5.1 Statistical analysis section sets out the intended evaluations (p.2-3)
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	5.2 The number of correct responses (corrected for wrong responses) used for accuracy. Measured in accordance with their plan. p.3

Bias in selection of the reported result	5.3 ... multiple eligible analyses of the data?	PN	5.3 The most robust analysis was used (parametric e.g. ANOVAs). Measured in accordance with their plan. p.2
	5.4 Is a result based on data from both periods sought, but unavailable on the basis of carryover having been identified?	N	5.4 No-one dropped out.
	Risk of bias judgement	**Low**	
Overall bias	**Risk of bias judgement**	**Low**	

Unique ID	70	**Study ID**	10.1016/j.brainres.2019.146324	**Assessor**	DW
Ref or Label	Jones, K. T., Arciniega, H. and Berryhill, M. E., (2019)	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	tACS	**Comparator**	sham	**Source**	Journal article
Outcome	d' (discriminability index); correct median RTs	**Results**	-0.12	**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the randomization process	1.1 Was the allocation sequence random?	N	counter-balanced (p.4). The same equipment is used for all ss therefore they cannot know their treatment allocation in advance; design was double-blind. Within-ss, double-blind design; nothing reported to indicate a problem with randomisation.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	Reported in results (p.2)
	Risk of bias judgement	**Low**	
Domain S: Risk of bias arising from period and carryover effects	S.1 Was the number of participants allocated to each of the two sequences equal or nearly equal?	Y	Degrees of freedom reported in Results (p.2)
	S.2 If N/PN/NI to S.1: Were period effects accounted for in the analysis?	NA	
	S.3 Was there sufficient time for any carryover effects to have disappeared before outcome assessment in the second period?	Y	At least one day apart (author confirmed).
	Risk of bias judgement	**Low**	

Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	N	Double-blind design (p.4)
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	N	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	NA	
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	2.6 within-ss design so not applicable as ss received both sham and active stimulation.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	Df values reported in Results (p.2)

Bias due to missing outcome data	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	Outcomes were computer-measured outputs based on correct response.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	The task was administered in a standardised manner with appropriate randomisation of stimuli (p.4)
	4.3 Were outcome assessors aware of the intervention received by study participants?	N	Double-blind design.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	NA	
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	

	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	The analysis is congruent with their previously published studies; there is nothing in the paper to indicate any change in analysis plan.
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	The most robust measure was used for accuracy (d') and RTs (median RTs in ms). Measured in accordance with their plan. p.2
	5.3 ... multiple eligible analyses of the data?	PN	The most robust analysis was used (parametric e.g. ANOVAs). Measured in accordance with their plan. p.2
	5.4 Is a result based on data from both periods sought, but unavailable on the basis of carryover having been identified?	PN	5.4 There was 1 drop-out in experiment 1 (did not complete all sessions).
	Risk of bias judgement	**Low**	
Overall bias	**Risk of bias judgement**	**Low**	

Unique ID	80	**Study ID**	10.3389/fnhum.2017.00367	**Assessor**	DW

Ref or Label	Kleinert, M. L., Szymanski, C. and Muller, V., (2017)	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	tACS	**Comparator**	sham	**Source**	Journal article
Outcome	%correct; correct RTs	**Results**	0.181564372	**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the randomization process	1.1 Was the allocation sequence random?	N	Pseudo-randomised allocation to group (all groups received all treatments); a Latin square repeated measures design.(p.4)
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	Participants were allocated to ensure balance across groups. See Experimental Procedure (p.3) WM was measured prior to stimulation (pre-during-post) (p.4)
	Risk of bias judgement	**Low**	Participants were allocated to groups in a balanced manner and according to baseline measures to ensure groups were comparable.)
	S.1 Was the number of participants allocated to each of the two sequences equal or nearly equal?	Y	Degrees of freedom reported in Results (p.8)

Domain S: Risk of bias arising from period and carryover effects	S.2 If N/PN/NI to S.1: Were period effects accounted for in the analysis?	NA	
	S.3 Was there sufficient time for any carryover effects to have disappeared before outcome assessment in the second period?	Y	5 days (p.3)
	Risk of bias judgement	**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	N	Single-blind design (p.4)
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	N	2.3 Nothing reported to indicate any deviations.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	2.6 within-ss design so not applicable as ss received both sham and active stimulation.

	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	3.1 Degrees of freedom reported in Results (p.8-9)
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
	4.1 Was the method of measuring the outcome inappropriate?	N	Outcomes were computer-measured outputs based on correct response.(p.4)
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	4.2 The task was computer-based and administered in a standardised manner with appropriate randomisation of stimuli (p.4)

Bias in measurement of the outcome	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	4.3 Assessors were aware of the intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	N	4.4 Outcomes were all computer-based outputs.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	The analysis is congruent with a previously published studies which they were intending to replicate; there is nothing in the paper to indicate any change in analysis plan.
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	Replicated previous study.
	5.3 ... multiple eligible analyses of the data?	PN	Replicated previous study.
	5.4 Is a result based on data from both periods sought, but unavailable on the basis of carryover having been identified?	N	5.4 No-one dropped out.
	Risk of bias judgement	**Low**	

Overall bias	**Risk of bias judgement**	**Low**	

Unique ID	105	**Study ID**	10.3389/fnhum.2017.00651	**Assessor**	DW
Ref or Label	Pahor, Anja and Jaušovec, Norbert, (2018)	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	tACS	**Comparator**	sham	**Source**	Journal article
Outcome	K [N*(H-F)/(1-F); RTs	**Results**	NA	**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**
Bias arising from the	1.1 Was the allocation sequence random?	PY	Randomisation occurred but the method of randomisation was not reported.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	1.2 The same equipment is used for all ss therefore they do not know their treatment allocation in advance.

randomization process	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	Baseline characteristics were compared and found to be comparable (p.4)
	Risk of bias judgement	**Low**	
Domain S: Risk of bias arising from period and carryover effects	S.1 Was the number of participants allocated to each of the two sequences equal or nearly equal?	Y	Conditions were counter-balanced; degrees of freedom reported in Results (p.8)
	S.2 If N/PN/NI to S.1: Were period effects accounted for in the analysis?	NA	
	S.3 Was there sufficient time for any carryover effects to have disappeared before outcome assessment in the second period?	Y	24 hrs (Procedure, p.4)
	Risk of bias judgement	**Low**	
	2.1.Were participants aware of their assigned intervention during the trial?	N	Single-blind; analyses indicated ss sensations during tACS and sham were comparable therefore blinding likely to have been successful (p.5). 2.2 Researchers were aware of the intervention (single-blind study).
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	2.3 Nothing reported to indicate any deviations, though low risk in this type of trial as there is no benefit to receiving a particular trial protocol e.g. beneficial drug vs. placebo.

Bias due to deviations from intended interventions	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	2.6 within-ss design so not applicable as ss received both sham and active stimulation.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	3.1 Degrees of freedom reported in Results (p.8-9).
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	

	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	4.1 Outcomes were computer-measured outputs based on correct response.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	4.2 The task was computer-based and administered in a standardised manner with appropriate randomisation of stimuli (p.4)
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	Assessors were aware of the intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	N	Outcomes were all computer-based outputs.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	5.1 Statistical analysis section sets out the intended evaluations (p.6)
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	5.2 The most robust measure was used for accuracy (K [N*(H-F)/(1-F)) and RTs (in ms). Measured in accordance with their plan (p.4,6)

Bias in selection of the reported result	5.3 ... multiple eligible analyses of the data?	PN	5.3 The most robust analysis was used (parametric e.g. ANOVAs). Measured in accordance with their plan. p.6
	5.4 Is a result based on data from both periods sought, but unavailable on the basis of carryover having been identified?	N	5.4 No-one dropped out.
	Risk of bias judgement	**Low**	
Overall bias	**Risk of bias judgement**	**Low**	

Unique ID	114	**Study ID**	10.1038/s41593-019-0371-x	**Assessor**	DW
Ref or Label	Reinhart, R. M. G. and Nguyen, J. A., (2019)	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	tACS	**Comparator**	sham	**Source**	Journal article
Outcome	online then offline accuracy (% correct); RTs	**Results**	0.586	**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the randomization process	1.1 Was the allocation sequence random?	PY	The order of stimulation was counterbalanced across subjects in Experiments 1 and 3, randomized across subjects in Experiment 2. 1.2 The same equipment is used for all ss therefore they do not know their treatment allocation in advance.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	1.3 Within-ss design; nothing reported to indicate a problem with randomisation.
	Risk of bias judgement	**Low**	
Domain S: Risk of bias arising from period and carryover effects	S.1 Was the number of participants allocated to each of the two sequences equal or nearly equal?	Y	Conditions were counter-balanced; degrees of freedom reported in Results (Fig2, Fig6)
	S.2 If N/PN/NI to S.1: Were period effects accounted for in the analysis?	NA	
	S.3 Was there sufficient time for any carryover effects to have disappeared before outcome assessment in the second period?	Y	at least one week
	Risk of bias judgement	**Low**	

Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	N	Confirmed by analyses undertaken which demonstated that participants were comfortable and VAS and safety ratings of symptoms/adverse effects were comparable. 2.2 Researchers were not aware of the intervention (double-blind study).
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	N	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	NA	
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	2.6 within-ss design so not applicable as ss received both sham and active stimulation.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	3.1 Degrees of freedom reported in Results (Fig2, Fig6)

Bias due to missing outcome data	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	4.1 Outcomes were computer-measured outputs based on correct response.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	4.2 The task was computer-based and administered in a standardised manner with appropriate randomisation of stimuli.
	4.3 Were outcome assessors aware of the intervention received by study participants?	N	double-blind study design
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	NA	
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	

	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	Statistical analysis section sets out the intended evaluations; there is nothing in the paper to indicate any change in analysis plan.
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	Used time bins of 4 minutes, which is subjective with no explanation otherwise standard outcome measurement definitions.
	5.3 ... multiple eligible analyses of the data?	PN	5.3 The most robust analysis was used (parametric e.g. t-tests). Measured in accordance with their plan. p.2
	5.4 Is a result based on data from both periods sought, but unavailable on the basis of carryover having been identified?	N	5.4 No-one dropped out.
	Risk of bias judgement	**Low**	
Overall bias	**Risk of bias judgement**	**Low**	

Unique ID	116	**Study ID**	10.3389/fnins.2018.00761	**Assessor**	DW

Ref or Label	Rohner, F., Breitling, C., Rufener, K. S., Heinze, H. J., Hinrichs, H., Krauel, K. and Sweeney-Reed, C. M., (2018)	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	tACS	**Comparator**	sham	**Source**	Journal article
Outcome	d' (discriminability index); RT hits	**Results**	NA	**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**
Bias arising from the randomization process	1.1 Was the allocation sequence random?	N	"The sequence of stimulation types was counter-balanced pseudo-randomly at the beginning of the study, and gender was balanced between the groups receiving stimulation in each particular order."(p.3) 1.2 The same equipment is used for all ss therefore they cannot know their treatment allocation in advance.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	"The pre-stimulation baseline did not differ according to stimulation type" (p.4). Within-ss design; nothing reported to indicate a problem with randomisation.
	Risk of bias judgement	**Low**	Counter-balanced and pseudo-randomised and balanced regarding gender and within-ss design, thus low risk of bias due to not being randomised.
	S.1 Was the number of participants allocated to each of the two sequences equal or nearly equal?	Y	Conditions were counter-balanced; degrees of freedom reported in Results (p.4-6)

Domain S: Risk of bias arising from period and carryover effects	S.2 If N/PN/NI to S.1: Were period effects accounted for in the analysis?	NA	
	S.3 Was there sufficient time for any carryover effects to have disappeared before outcome assessment in the second period?	Y	7 days (Study Design and Task, p.3)
	Risk of bias judgement	**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	N	Single-blind; authors reported that ss could not distinguish between stimulation type (p.6). 2.2 Researchers were aware of the intervention (single-blind study).
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	2.3 Nothing reported to indicate any deviations, though low risk in this type of trial as there is no benefit to receiving a particular trial protocol e.g. beneficial drug vs. placebo.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	2.6 within-ss design so not applicable as ss received both sham and active stimulation.

	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	Degrees of freedom were reported in results (pp. 4-5).
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
	4.1 Was the method of measuring the outcome inappropriate?	N	4.1 Outcomes were computer-measured outputs based on correct response.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	4.2 The task was computer-based and administered in a standardised manner with appropriate randomisation of stimuli (p.3)

Bias in measurement of the outcome	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	Assessors were aware of the intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	Outcomes were all computer-based outputs.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	Statistical analysis section sets out the intended evaluations (p. 3).
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	The most robust measure was used for accuracy (d') and RTs (median RTs in ms). Measured in accordance with their plan. p.3
	5.3 ... multiple eligible analyses of the data?	PN	The most robust analysis was used (parametric e.g. ANOVAs). Measured in accordance with their plan.
	5.4 Is a result based on data from both periods sought, but unavailable on the basis of carryover having been identified?	N	5.4 No-one dropped out.
	Risk of bias judgement	**Low**	

Overall bias	**Risk of bias judgement**	**Low**	not included in meta-analysis

Unique ID	133	**Study ID**	10.1038/srep32138	**Assessor**	DW
Ref or Label	Tseng, P., Chang, Y. T., Chang, C. F., Liang, W. K. and Juan, C. H., (2016)	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	tACS	**Comparator**	sham	**Source**	Journal article
Outcome	d' (discriminability index)	**Results**	0.177904469	**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**
Bias arising from the	1.1 Was the allocation sequence random?	N	Counter-balanced order of stimulation condition (Fig 1, p.2). 1.2 The same equipment is used for all ss therefore they cannot know their treatment allocation in advance.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	

randomization process	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	Within-ss design; nothing reported to indicate a problem with randomisation.
	Risk of bias judgement	**Low**	Counter-balanced and within-ss design, thus low risk of bias due to not being randomised.
Domain S: Risk of bias arising from period and carryover effects	S.1 Was the number of participants allocated to each of the two sequences equal or nearly equal?	Y	Conditions were counter-balanced; degrees of freedom reported in Results (p.4,7)
	S.2 If N/PN/NI to S.1: Were period effects accounted for in the analysis?	NA	
	S.3 Was there sufficient time for any carryover effects to have disappeared before outcome assessment in the second period?	Y	1 week (Fig1, p.2; Fig 4, p.7)
	Risk of bias judgement	**Low**	
	2.1.Were participants aware of their assigned intervention during the trial?	N	2.1 Single-blind; analyses indicated ss sensations during tACS and sham were comparable therefore blinding likely to have been successful (p.4). 2.2 Researchers were aware of the intervention (single-blind study).
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	2.3 Nothing reported to indicate any deviations, though low risk in this type of trial as there is no benefit to receiving a particular trial protocol e.g. beneficial drug vs. placebo.

Bias due to deviations from intended interventions	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	2.6 within-ss design so not applicable as ss received both sham and active stimulation.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	Degrees of freedom reported in Results (p.4,7)
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	

	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	4.1 Outcomes were computer-measured outputs based on correct response.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	4.2 The task was computer-based and administered in a standardised manner with appropriate randomisation of stimuli (p.3-4)
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	Assessors were aware of the intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	4.4 Outcomes were all computer-based outputs.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	5.1 Statistical analysis section sets out the intended evaluations (p.4)
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	N	5.2 The most robust measure was used for accuracy (d') and RTs (median RTs in ms). Measured in accordance with their plan. p.2

Bias in selection of the reported result	5.3 ... multiple eligible analyses of the data?	PN	5.3 The most robust analysis was used (parametric e.g. ANOVAs). Measured in accordance with their plan. p.3-4 (PY)
	5.4 Is a result based on data from both periods sought, but unavailable on the basis of carryover having been identified?	N	5.4 No-one dropped out.
	Risk of bias judgement	**Low**	
Overall bias	**Risk of bias judgement**	**Low**	

Unique ID	134	**Study ID**	10.1038/s41598-017-18449-w	**Assessor**	DW
Ref or Label	Tseng, P., Iu, K. C. and Juan, C. H., (2018)	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	tACS	**Comparator**	sham	**Source**	Journal article
Outcome	K [N*(H-F)/(1-F)	**Results**	0.113100251	**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the randomization process	1.1 Was the allocation sequence random?	N	Counter-balanced order of stimulation (p.3). 1.2 The same equipment is used for all ss therefore they cannot know their treatment allocation in advance.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	No baseline task for WM.
	Risk of bias judgement	**Low**	Counter-balanced and within-ss design, thus low risk of bias due to not being randomised.
Domain S: Risk of bias arising from period and carryover effects	S.1 Was the number of participants allocated to each of the two sequences equal or nearly equal?	Y	Degrees of freedom reported in Results (p.4)
	S.2 If N/PN/NI to S.1: Were period effects accounted for in the analysis?	NA	
	S.3 Was there sufficient time for any carryover effects to have disappeared before outcome assessment in the second period?	Y	1 week (p.3)
	Risk of bias judgement	**Low**	

Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	PN	2.1 Single-blind; analyses indicated ss sensations were not reported, however though it was in their previous paper and their methods section indicates that they took steps to minimise the differences in sensation between active and sham conditions (p.3). 2.2 Researchers were aware of the intervention (single-blind study).
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	2.3 Nothing reported to indicate any deviations, though low risk in this type of trial as there is no benefit to receiving a particular trial protocol
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	2.6 within-ss design so not applicable as ss received both sham and active stimulation.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	Degrees of freedom reported in Results (p.4)

Bias due to missing outcome data	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	4.1 Outcomes were computer-measured outputs based on correct response.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	4.2 The task was computer-based and administered in a standardised manner with appropriate randomisation of stimuli (p.3-4)
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	Assessors were aware of the intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	4.4 Outcomes were all computer-based outputs.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	

	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	Statistical analysis section sets out the intended evaluations (p.3,4)
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	N	5.2 The most robust measure was used for accuracy (K [N*(H-F)/(1-F)) and RTs (ms). Measured in accordance with their plan. p.3-4
	5.3 ... multiple eligible analyses of the data?	PN	5.3 The most robust analysis was used (parametric e.g. ANOVAs). Measured in accordance with their plan. p.2
	5.4 Is a result based on data from both periods sought, but unavailable on the basis of carryover having been identified?	N	5.4 No-one dropped out.
	Risk of bias judgement	**Low**	
Overall bias	**Risk of bias judgement**	**Low**	

Unique ID	144	**Study ID**	10.7554/eLife.22001	**Assessor**	DW

Ref or Label	Violante, I. R., Li, L. M., Carmichael, D. W., Lorenz, R., Leech, R., Hampshire, A., Rothwell, J. C. and Sharp, D. J., (2017)	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	tACS	**Comparator**	sham	**Source**	Journal article
Outcome	% correct/d'; correct RTs	**Results**	-0.421862083	**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the randomization process	1.1 Was the allocation sequence random?	N	Stimulation ordering was pseudo-randomised. 1.2 The same equipment is used for all ss therefore they cannot know their treatment allocation in advance.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	No baseline task was used to measure WM.
	Risk of bias judgement	**Low**	Counter-balanced and pseudo-randomised and within-ss design, thus low risk of bias due to not being randomised.
	S.1 Was the number of participants allocated to each of the two sequences equal or nearly equal?	Y	Degrees of freedom and n-values reported in Results (p.3,4).

Domain S: Risk of bias arising from period and carryover effects	S.2 If N/PN/NI to S.1: Were period effects accounted for in the analysis?	NA	
	S.3 Was there sufficient time for any carryover effects to have disappeared before outcome assessment in the second period?	Y	At least one day apart (p.15).
	Risk of bias judgement	**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	N	2.1 Single-blind; analyses indicated ss sensations during tACS and sham were comparable therefore blinding likely to have been successful (p.11) 2.2 Researchers were aware of the intervention (single-blind study).
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	2.3 Nothing reported to indicate any deviations, though low risk in this type of trial as there is no benefit to receiving a particular trial protocol e.g. beneficial drug vs. placebo.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	2.6 within-ss design so not applicable as ss received both sham and active stimulation.

	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	Degrees of freedom and n-values reported in Results (p.3,4).
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
	4.1 Was the method of measuring the outcome inappropriate?	N	4.1 Outcomes were computer-measured outputs based on correct response.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	4.2 The task was computer-based and administered in a standardised manner with appropriate randomisation of stimuli (p.14)

Bias in measurement of the outcome	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	4.3 Assessors were aware of the intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	Outcomes were all computer-based outputs.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	5.1 Statistical analysis section sets out the intended evaluations (p.18)
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	N	5.2 The most robust measure was used for accuracy (d' and % correct) and RTs (meanRT ms). Measured in accordance with their plan. p.14, 18
	5.3 ... multiple eligible analyses of the data?	PN	5.3 The most robust analysis was used (parametric e.g. ANOVAs). Measured in accordance with their plan. p.18
	5.4 Is a result based on data from both periods sought, but unavailable on the basis of carryover having been identified?	N	5.4 No-one dropped out.
	Risk of bias judgement	**Low**	

Overall bias	**Risk of bias judgement**	**Low**	

Unique ID	155	**Study ID**	10.1371/journal.pbio.2005348	**Assessor**	DW
Ref or Label	Wolinski, N., Cooper, N. R., Sauseng, P. and Romei, V., (2018)	**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	tACS	**Comparator**	sham	**Source**	Journal article
Outcome	K (K=S*(H-F)	**Results**		**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**
Bias arising from the	1.1 Was the allocation sequence random?	N	Counter-balanced (Design, p.11). 1.2 The same equipment is used for all ss therefore they cannot know their treatment allocation in advance.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	

randomization process	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	1.3 Within-ss design; nothing reported to indicate a problem with randomisation.
	Risk of bias judgement	**Low**	Counter-balanced order and within-ss design, thus low risk of bias due to not being randomised.
Domain S: Risk of bias arising from period and carryover effects	S.1 Was the number of participants allocated to each of the two sequences equal or nearly equal?	Y	Degrees of freedom reported in Results (p.4,5)
	S.2 If N/PN/NI to S.1: Were period effects accounted for in the analysis?	NA	
	S.3 Was there sufficient time for any carryover effects to have disappeared before outcome assessment in the second period?	Y	At least 24 hours (p.11)
	Risk of bias judgement	**Low**	
	2.1.Were participants aware of their assigned intervention during the trial?	N	2.1 Single-blind; analyses indicated ss sensations during tACS and sham were comparable therefore blinding likely to have been successful. 2.2 Researchers were aware of the intervention (single-blind study).
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	2.3 Nothing reported to indicate any deviations, though low risk in this type of trial as there is no benefit to receiving a particular trial protocol e.g. beneficial drug vs. placebo.

Bias due to deviations from intended interventions	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	2.6 within-ss design so not applicable as ss received both sham and active stimulation.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	3.1 Degrees of freedom reported in Results (p.4,5)
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	

	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	4.1 Outcomes were computer-measured outputs based on correct response.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	4.2 The task was computer-based and administered in a standardised manner with appropriate randomisation of stimuli (p.12)
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	4.3 Assessors were aware of the intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	4.4 Outcomes were all computer-based outputs.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
Bias in selection of the	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	5.1 Statistical analysis section sets out the intended evaluations (p.12-13)
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	N	5.2 The most robust measure was used for accuracy (K (K=S*(H-F)). Measured in accordance with their plan. p.12-13

reported result	5.3 ... multiple eligible analyses of the data?	PN	5.3 The most robust analysis was used (parametric e.g. ANOVAs). Measured in accordance with their plan. p.2
	5.4 Is a result based on data from both periods sought, but unavailable on the basis of carryover having been identified?	N	5.4 No-one dropped out.
	Risk of bias judgement	**Low**	
Overall bias	**Risk of bias judgement**	**Low**	

index	tACS	accept / reject	count	notes	AUTHORS	TITLE	YEAR
2	tACS	reject	1	Direct Cortical Stimulation	Alagapan, Sankaraleengam, Riddle, Justin, Huang, Wei Angel, Hadar, Eldad, Shin, Hae Won and Fröhlich, Flavio	Network-Targeted, Multi-site Direct Cortical Stimulation Enhances Working Memory by Modulating Phase Lag of Low-Frequency Oscillations	2019
4	tACS	reject	0	published abstract - not enough information reported	Alekseichuk, I., Pabel, S. C., Antal, A. and Paulus, W.	P206 Cross-hemispheric frontoparietal desynchronization impairs the visual-spatial working memory in humans	2017
5	tACS	reject	4	blinding/details about blinding not reported	Alekseichuk, I., Turi, Z., Amador de Lara, G., Antal, A. and Paulus, W.	Spatial Working Memory in Humans Depends on Theta and High Gamma Synchronization in the Prefrontal Cortex	2016
6	tACS	reject	4	published abstract - blinding not reported	Alekseichuk, I., Turi, Z., Antal, A. and Paulus, W.	ID 164 – TACS over the left dorsolateral prefrontal cortex improves hit rate, but not false alarm rate, in a spatial working memory task	2016
7	tACS	reject	2	not WM task/subjective well-being task	Alekseichuk, Ivan, Diers, Kersten, Paulus, Walter and Antal, Andrea	Transcranial electrical stimulation of the occipital cortex during visual perception modifies the magnitude of BOLD activity: A combined tES–fMRI approach	2016
8	tACS	reject	2	not WM task/subjective well-being task	Alekseichuk, Ivan, Turi, Zsolt, Veit, Sibel and Paulus, Walter	Model-driven neuromodulation of the right posterior region promotes encoding of long-term memories	2020
9	tACS	reject	6	Discussion/Review article	Antal, A. and Paulus, W.	Investigating neuroplastic changes in the human brain induced by transcranial direct (tDCS) and alternating current (tACS) stimulation methods	2012
11	tACS	reject	2	not WM task/subjective well-being task	Baltus, A., Wagner, S., Wolters, C. H. and Herrmann, C. S.	Optimized auditory transcranial alternating current stimulation improves individual auditory temporal resolution	2018
12	tACS	reject	2	not WM task/subjective well-being task	Baltus, Alina and Herrmann, Christoph S.	Individual gap detection ability can be enhanced with transcranial alternating current stimulation	2016

index	tACS	accept / reject	count	notes	AUTHORS	TITLE	YEAR
13	tACS	reject	2	not WM task/subjective well-being task	Baltus, Alina, Vosskuhl, Johannes, Boetzel, Cindy and Herrmann, Christoph Siegfried	Transcranial alternating current stimulation modulates auditory temporal resolution in elderly people	2018
14	tACS	reject	4	no mention of duration of stim or blinding	Bender, Monika, Romei, Vincenzo and Sauseng, Paul	Slow theta tACS of the right parietal cortex enhances contralateral visual working memory capacity	2019
15	HD-tACS	reject	2	not WM task/subjective well-being task	Bland, N. S., Mattingley, J. B. and Sale, M. V.	No Evidence for Phase-Specific Effects of 40 Hz HD-tACS on Multiple Object Tracking	2018
17	tACS	reject	2	not WM task/subjective well-being task	Brauer, Hannah, Ester Kadish, Navah, Pedersen, Anya, Siniatchkin, Michael and Moliadze, Vera	No Modulatory Effects when Stimulating the Right Inferior Frontal Gyrus with Continuous 6 Hz tACS and tRNS on Response Inhibition: A Behavioral Study	2018
18	tACS	reject	1	very short stim	Braun, V., Sokoliuk, R. and Hanslmayr, S.	On the effectiveness of event-related beta tACS on episodic memory formation and motor cortex excitability	2017
19	tACS	reject	1	5-min stim sessions w/short breaks	Brignani, D., Ruzzoli, M., Mauri, P. and Miniussi, C.	Is transcranial alternating current stimulation effective in modulating brain oscillations?	2013
20	tACS	reject	2	not WM task/subjective well-being task; ambiguous perception task	Cabral-Calderin, Y., Schmidt-Samoa, C. and Wilke, M.	Rhythmic gamma stimulation affects bistable perception	2015
21	tACS	reject	2	not WM task/subjective well-being task	Cappon, D., D' Ostilio, K., Garraux, G., Rothwell, J. C. and Bisiacchi, P.	Cortical modulation of automatic facilitation and inhibition by 10hz and 20hz transcranial alternating current stimulation (tACS)	2015
22	tACS	reject	3	montage targets M1 (i.e. not focused on executive function per se)	Cappon, Davide, Goljahani, Anahita, Laera, Gianvito and Bisiacchi, Patrizia	Interactions between non invasive transcranial brain stimulation (tACS) and brain oscillations: a quantitative EEG study	2016

index	tACS	accept / reject	count	notes	AUTHORS	TITLE	YEAR
23	burst-tACS	reject	1	5 second bursts	Castellano, M., Ibanez-Soria, D., Acedo, J., Kroupi, E., Martinez, X., Soria-Frisch, A., Dunne, S., Valls-Sole, J., Verma, A. and Ruffini, G.	Influence of burst tACS on the neural oscillations and detection of change in visual task	2017
24	burst-tACS	reject	1	5 second bursts	Castellano, M., Ibanez-Soria, D., Acedo, J., Kroupi, E., Martinez, X., Soria-Frisch, A., Valls-Sole, J., Verma, A. and Ruffini, G.	Tacs bursts slows your perception: increased RT in a speed of change detection task	2017
25	intermittent-	reject	1	5 second bursts	Castellano, Marta, Ibañez-Soria, David, Kroupi, Eleni, Acedo, Javier, Campolo, Michela, Soria-Frisch, Aureli, Valls-Sole, Josep, Verma, Ajay and Ruffini, Giulio	Intermittent tACS during a visual task impacts neural oscillations and LZW complexity	2020
26	tACS	reject	2	not WM task/subjective well-being task	Cecere, R., Rees, G. and Romei, V.	Individual differences in alpha frequency drive crossmodal illusory perception	2015
27	tACS	reject	2	not WM task/subjective well-being task	Chai, Yuhui, Sheng, Jingwei, Bandettini, Peter A. and Gao, Jia-Hong	Frequency-dependent tACS modulation of BOLD signal during rhythmic visual stimulation	2018
28	tACS	reject	1	stim period 4 min each	Chander, B. S., Witkowski, M., Braun, C., Robinson, S. E., Born, J., Cohen, L. G., Birbaumer, N. and Soekadar, S. R.	tACS Phase Locking of Frontal Midline Theta Oscillations Disrupts Working Memory Performance	2016
29	HD-tACS	reject	2	anxious group; no healthy control	Clancy, K., Kartvelishvili, N. and Li, W.	Individual differences and test-retest reliability in neural and mood effects of tACS	2019
30	tACS	reject	2	not WM task/subjective well-being task	Clayton, M. S., Yeung, N. and Cohen Kadosh, R.	Electrical stimulation of alpha oscillations stabilizes performance on visual attention tasks	2019
31	tACS	reject	2	not WM task/subjective well-being task	Clayton, M. S., Yeung, N. and Kadosh, R. C.	The Effects of 10Hz Transcranial Alternating Current Stimulation on Audiovisual Task Switching	2018
32	tACS	reject	6	study protcol, not report	Clayton, Michael S., Yeung, Nick and Kadosh, Roi Cohen	The Influence of Transcranial Alternating Current Stimulation at 10 Hz on Sustained Visual Attention	2017

index	tACS	accept / reject	count	notes	AUTHORS	TITLE	YEAR
33	tACS	reject	2	not WM task/subjective well-being task	de Lara, G., Alekseichuk, I., Turi, Z., Antal, A. and Paulus, W.	P207 Affecting declarative long-term memory with transcranial alternating current stimulation (tACS)	2017
34	tACS	reject	2	not WM task/subjective well-being task	de Lara, Gabriel Amador, Alekseichuk, Ivan, Turi, Zsolt, Lehr, Albert, Antal, Andrea and Paulus, Walter	Perturbation of theta-gamma coupling at the temporal lobe hinders verbal declarative memory	2018
35	tACS	reject	7	non-English	Dong, G., Shi, J., Yang, H., Liu, Y., Wu, Z. and Chen, X.	The influence of transcranial alternating current stimulation on mental rotation	2017
36	tACS	reject	5	not enough reported detail (no blinding, no time, mA)	Ermolova, Maria, Belyaeva, Valeria, Novikov, Nikita, Gutkin, Boris, Feurra, Matteo and Fedele, Tommaso	Changes in neuronal oscillations account for working memory dynamics: EEG-tACS study	2019
37	tACS	reject	1	stim period 3-4 min	Feurra, M., Galli, G., Pavone, E. F., Rossi, A. and Rossi, S.	Frequency-specific insight into short-term memory capacity	2016
38	tACS	reject	2	not WM task/subjective well-being task	Feurra, Matteo, Galli, Giulia and Rossi, Simone	Transcranial alternating current stimulation affects decision making	2012
39	tACS	reject	3	montage targets M1 (i.e. not focused on executive function per se)	Fresnoza, S.	Age-dependent effect of transcranial alternating current stimulation (tACS) on motor skill consolidation	2019
40	tACS	reject	1	5 min stim	Frohlich, F., Sellers, K., Boyle, M., Ali, M., Cordle, A., Vaughn, B. and Gilmore, J.	OP 9. Tailoring transcranial current stimulation to modulate cortical oscillations in computer simulations, ferrets, and humans	2013
41	tACS	reject	1	4 min stim; cognitive conflict	Fusco, Gabriele, Scandola, Michele, Feurra, Matteo, Pavone, Enea F., Rossi, Simone and Aglioti, Salvatore M.	Midfrontal theta transcranial alternating current stimulation modulates behavioural adjustment after error execution	2018
42	tACS	reject	2	not WM task/subjective well-being task	Gennaro, L. De, Simoni, E. De, Gorgoni, M., Moroni, F., Marzano, C., Ferrara, M., Ferlazzo, F. and Rossini, P. M.	24. Effect of transcranial alternating stimulation (tACS) on the spontaneous EEG	2013

index	tACS	accept / reject	count	notes	AUTHORS	TITLE	YEAR
43	tACS	reject	2	not WM task/subjective well-being task	Giller, Franziska, Bensmann, Wiebke, Mückschel, Moritz, Stock, Ann-Kathrin and Beste, Christian	Evidence for a causal role of superior frontal cortex theta oscillations during the processing of joint subliminal and conscious conflicts	2020
44	tACS	reject	2	not WM task/subjective well-being task	Grabner, Roland H., Krenn, Julia, Fink, Andreas, Arendasy, Martin and Benedek, Mathias	Effects of alpha and gamma transcranial alternating current stimulation (tACS) on verbal creativity and intelligence test performance	2018
45	tACS	reject	0	published abstract - not enough information reported	Grande, G., Golemme, M., Tatti, E., Chiesa, S., Velzen, J. Van, Bernardi Luft, C. Di and Cappelletti, M.	P127 A combined EEG and alpha tACS study on visual working memory in healthy ageing	2017
46	tACS	reject	3	montage targets M1 (i.e. not focused on executive function per se)	Guerra, A., Bologna, M., Paparella, G., Suppa, A., Colella, D., Di Lazzaro, V., Brown, P. and Berardelli, A.	Effects of Transcranial Alternating Current Stimulation on Repetitive Finger Movements in Healthy Humans	2018
47	tACS	reject	5	not enough info reported	Hashimoto, R. H. and Karima, A. K.	Improvement in auditory verbal memory induced by theta tACS to bilateral dorsal prefrontal cortex	2017
48	tACS	reject	3	montage targets M1 (i.e. not focused on executive function per se)	Heise, Kirstin-Friederike, Monteiro, Thiago, Leunissen, Inge, Mantini, Dante and Swinnen, Stephan	Distinct online and offline effects of alpha and beta transcranial alternating current stimulation (tACS) on continuous bimanual performance and task-set switching	2019
49	tACS	reject	6	Summary of findings - not original research article	Helfrich, R. F. and Schneider, T. R.	Modulation of cortical network activity by transcranial alternating current stimulation	2013
50	HD-tACS	reject	2	not WM task/subjective well-being task	Helfrich, R. F., Knepper, H., Nolte, G., Struber, D., Rach, S., Herrmann, C. S., Schneider, T. R. and Engel, A. K.	Selective modulation of interhemispheric functional connectivity by HD-tACS shapes perception	2014

index	tACS	accept / reject	count	notes	AUTHORS	TITLE	YEAR
51	tACS	reject	2	not WM task/subjective well-being task	Helfrich, R. F., Schneider, T. R., Rach, S., Trautmann-Lengsfeld, S. A., Engel, A. K. and Herrmann, C. S.	Entrainment of brain oscillations by transcranial alternating current stimulation	2014
52	tACS	reject	2	not WM task/subjective well-being task	Hermann, G., Rothkirch, I., Laufs, H. and Witt, K.	P105. Does transcranial alternating current stimulation entrain posterior alpha rhythm?	2018
53	tACS	reject	2	not WM task/subjective well-being task	Herring, J. D., Esterer, S., Marshall, T. R., Jensen, O. and Bergmann, T. O.	P189 Transcranial modulation of visually induced gamma power: a concurrent TACS-MEG study	2017
54	tACS	reject	2	not WM task/subjective well-being task	Herring, Jim D., Esterer, Sophie, Marshall, Tom R., Jensen, Ole and Bergmann, Til O.	Low-frequency alternating current stimulation rhythmically suppresses gamma-band oscillations and impairs perceptual performance	2019
55	tACS	reject	2	not WM task/subjective well-being task	Herrmann, C.	T012 Transcranial alternating current stimulation: Models, EEG/MEG, and cognition	2017
56	tACS	reject	6	technical - PROTOCOL	Herrmann, C. S.	Modeling-informed tACS allows shaping oscillatory activity in specific brain networks	2017
57	tACS	reject	2	not WM task/subjective well-being task	Herrmann, C. S., Murray, M. M., Ionta, S., Hutt, A. and Lefebvre, J.	Shaping Intrinsic Neural Oscillations with Periodic Stimulation	2016
58	tACS	reject	5	not enough information	Herrmann, C. S., Neuling, T., Rach, S. and Strüber, D.	Modulation of EEG oscillations via transcranial alternating current stimulation	2012
59	tACS	reject	0	published abstract - no paper available	Holczer, A., Vékony, T., Vécsei, L., Klivényi, P. and Must, A.	P.401 Online theta-range transcranial alternating current stimulation results in slower conflict processing	2020
60	tACS	reject	2	not WM task/subjective well-being task	Hopfinger, J. B., Parsons, J. and Frohlich, F.	Differential effects of 10-Hz and 40-Hz transcranial alternating current stimulation (tACS) on endogenous versus exogenous attention	2017

index	tACS	accept / reject	count	notes	AUTHORS	TITLE	YEAR
62	tACS	reject	1	tDCS (wrong stimulation type for this review)	Hsu, Tzu-Yu, Juan, Chi-Hung and Tseng, Philip	Individual differences and state-dependent responses in transcranial direct current stimulation	2016
63	tACS	reject	2	non-standard cog task	Hsu, W. Y., Zanto, T. P. and Gazzaley, A.	Parametric effects of transcranial alternating current stimulation on multitasking performance	2019
64	tACS	reject	2	non-standard cog task	Hsu, W. Y., Zanto, T. P., van Schouwenburg, M. R. and Gazzaley, A.	Enhancement of multitasking performance and neural oscillations by transcranial alternating current stimulation	2017
66	tACS	reject	2	not WM task/subjective well-being task; anger perception	Janik, A. B., Rezlescu, C. and Banissy, M. J.	Enhancing Anger Perception With Transcranial Alternating Current Stimulation Induced Gamma Oscillations	2015
67	tACS	reject	2	not WM task/subjective well-being task	Jausovec, N. and Jausovec, K.	Increasing working memory capacity with theta transcranial alternating current stimulation (tACS)	2014
69	tACS	reject	2	not WM task/subjective well-being task	Javadi, A. H., Glen, J. C., Halkiopoulos, S., Schulz, M. and Spiers, H. J.	Oscillatory Reinstatement Enhances Declarative Memory	2017
71	tACS	reject	5	not enough info reported	Juan, Chi-Hung, Liang, Wei-Kuang, Muggleton, Neil G., Tseng, Philip and Hsu, Tzu-Yu	Elucidating the interactions between individual differences and noninvasive brain stimulation effects in visual working memory by using tDCS, tACS and EEG	2017
72	tACS	reject	2	not WM task/subjective well-being task	Kanai, R., Paulus, W. and Walsh, V.	Transcranial alternating current stimulation (tACS) modulates cortical excitability as assessed by TMS-induced phosphene thresholds	2010
73	tACS	reject	2	not WM task/subjective well-being task	Kar, K. and Krekelberg, B.	Transcranial alternating current stimulation attenuates visual motion adaptation	2014

index	tACS	accept / reject	count	notes	AUTHORS	TITLE	YEAR
74	tACS	reject	2	not WM task/subjective well-being task	Kar, Kohitij, Duijnhouwer, Jacob and Krekelberg, Bart	tACS- What goes on inside? The neural consequences of transcranial alternating current stimulation	2014
75	tACS	reject	2	not WM task/subjective well-being task	Kasten, F. H., Dowsett, J. and Herrmann, C. S.	P202 Outlasting effect of transcranial alternating current stimulation (tACS) on individual alpha power decays within 90min after stimulation	2017
76	tACS	reject	2	not WM task/subjective well-being task	Kasten, F. H., Maess, B. and Herrmann, C. S.	Facilitated Event-Related Power Modulations during Transcranial Alternating Current Stimulation (tACS) Revealed by Concurrent tACS-MEG	2018
77	tACS	reject	2	not WM task/subjective well-being task	Kasten, F. H., Wendeln, T., Stecher, H. I. and Herrmann, C. S.	Hemisphere-specific, differential effects of lateralized, occipital-parietal alpha- versus gamma-tACS on endogenous but not exogenous visual-spatial attention	2020
78	tACS	reject	2	not WM task/subjective well-being task	Kasten, Florian H. and Herrmann, Christoph S.	Transcranial alternating current stimulation (tACS) enhances mental rotation performance during and after stimulation	2017
79	tACS	reject	2	not WM task/subjective well-being task	Kasten, Florian H., Dowsett, James and Herrmann, Christoph S.	Sustained aftereffect of α-tACS lasts up to 70 min after stimulation	2016
81	tACS	reject	2	not WM task/subjective well-being task	Klink, Katharina, Peter, Jessica, Wyss, Patric and Klöppel, Stefan	Transcranial electric current stimulation during associative memory encoding: Comparing tACS and tDCS effects in healthy aging	2020
82	tACS	reject	6	review article	Kuo, M. F. and Nitsche, M. A.	Effects of transcranial electrical stimulation on cognition	2012
83	tACS	reject	2	not WM task/subjective well-being task	Laczo, B., Antal, A., Niebergall, R., Treue, S. and Paulus, W.	Transcranial alternating stimulation in a high gamma frequency range applied over V1 improves contrast perception but does not modulate spatial attention	2012

index	tACS	accept / reject	count	notes	AUTHORS	TITLE	YEAR
84	HD-tACS	reject	2	not WM task/subjective well-being task	Lang, S., Gan, L., Alrazi, T. and Monchi, O.	High definition transcranial alternating current stimulation of the right fusiform cortex improves visual associative memory	2019
85	HD-tACS	reject	2	not WM task/subjective well-being task	Lang, Stefan, Gan, Liu, Alrazi, Tazrina and Monchi, Oury	Theta band high definition transcranial alternating current stimulation, but not transcranial direct current stimulation, improves associative memory performance	2019
86	HD-tACS	reject	2	not WM task/subjective well-being task	Lehr, Albert, Henneberg, Niklas, Nigam, Tarana, Paulus, Walter and Antal, Andrea	Modulation of Conflict Processing by Theta-Range tACS over the Dorsolateral Prefrontal Cortex	2019
87	tACS	reject	2	not WM task/subjective well-being task	Löffler, B. S., Stecher, H. I., Fudickar, S., De Sordi, D., Otto-Sobotka, F., Hein, A. and Herrmann, C. S.	Counteracting the Slowdown of Reaction Times in a Vigilance Experiment with 40-Hz Transcranial Alternating Current Stimulation	2018
88	tACS	reject	2	not WM task/subjective well-being task	Mansouri, F., Shanbour, A., Mazza, F., Fettes, P., Zariffa, J. and Downar, J.	Effect of Theta Transcranial Alternating Current Stimulation and Phase-Locked Transcranial Pulsed Current Stimulation on Learning and Cognitive Control	2019
89	tACS	reject	2	not WM task/subjective well-being task	Marko, Martin, Cimrová, Barbora and Riečanský, Igor	Neural theta oscillations support semantic memory retrieval	2019
91	tACS	reject	3	montage targets M1 (i.e. not focused on executive function per se)	Minami, S. and Amano, K.	Illusory Jitter Perceived at the Frequency of Alpha Oscillations	2017
92	tACS	reject	6	OPINION PIECE	Miniussi, C., Brignani, D. and Pellicciari, M. C.	Combining Transcranial Electrical Stimulation With Electroencephalography: A Multimodal Approach	2012

index	tACS	accept / reject	count	notes	AUTHORS	TITLE	YEAR
93	tACS	reject	2	not WM task/subjective well-being task	Moliadze, V., Sierau, L., Lyzhko, E., Stenner, T., Werchowski, M., Siniatchkin, M. and Hartwigsen, G.	10 Hz tACS over the prefrontal cortex facilitates phonological word decisions	2019
94	tACS	reject	2	not WM task/subjective well-being task	Mondino, Marine, Lenglos, Christophe, Cinti, Alessandra, Renauld, Emmanuelle and Fecteau, Shirley	Eye tracking of smoking-related stimuli in tobacco use disorder: A proof-of-concept study combining attention bias modification with alpha-transcranial alternating current stimulation	2020
95	tACS	reject	2	not WM task/subjective well-being task	Muller, N. G., Vellage, A. K., Heinze, H. J. and Zaehle, T.	Entrainment of Human Alpha Oscillations Selectively Enhances Visual Conjunction Search	2015
96	tACS	reject	2	not WM task/subjective well-being task	Naro, A., Corallo, F., De Salvo, S., Marra, A., Di Lorenzo, G., Muscara, N., Russo, M., Marino, S., De Luca, R., Bramanti, P. and Calabro, R. S.	Promising Role of Neuromodulation in Predicting the Progression of Mild Cognitive Impairment to Dementia	2016
97	tACS	reject	2	not WM task/subjective well-being task	Neubauer, A. C., Wammerl, M., Benedek, M., Jauk, E. and Jaušovec, N.	The influence of transcranial alternating current stimulation (tACS) on fluid intelligence: An fMRI study	2017
98	tACS	reject	3	montage targets occipital region (not executive function per se)	Neuling, T., Rach, S. and Herrmann, C.	P 12. Transcranial alternating current stimulation enhances endogenous alpha for 30min only for moderate alpha levels	2013
99	oscillating alp	reject	1	not tACS or tDCS	Neuling, T., Rach, S., Wagner, S., Wolters, C. H. and Herrmann, C. S.	Good vibrations: Oscillatory phase shapes perception	2012
100	tACS	reject	2	not WM task/subjective well-being task	Neuling, T., Ruhnau, P., Fusca, M., Demarchi, G., Herrmann, C. S. and Weisz, N.	Friends, not foes: Magnetoencephalography as a tool to uncover brain dynamics during transcranial alternating current stimulation	2015

index	tACS	accept / reject	count	notes	AUTHORS	TITLE	YEAR
101	HD-tACS	reject	2	not WM task/subjective well-being task	Nguyen, John, Deng, Yuqi and Reinhart, Robert M. G.	Brain-state determines learning improvements after transcranial alternating-current stimulation to frontal cortex	2018
102	tACS	reject	2	not WM task/subjective well-being task	Nomura, Tomonori, Asao, Akihiko and Kumasaka, Ayumi	Transcranial alternating current stimulation over the prefrontal cortex enhances episodic memory recognition	2019
103	tACS	reject	2	not WM task/subjective well-being task	Pahor, A. and Jausovec, N.	The effects of theta transcranial alternating current stimulation (tACS) on fluid intelligence	2014
104	tACS	reject	2	not WM task/subjective well-being task	Pahor, A. and Jausovec, N.	Making Brains run Faster: are they Becoming Smarter?	2016
106	tACS	reject	4	published abstract - blinding not reported	Paulus, W., Alekseichuk, I. and Antal, A.	Tacs in theta range improves the hit rate and general accuracy in a spatial working memory task	2015
107	tACS	reject	2	not WM task/subjective well-being task	Peter, S. E., Mederer, D., Habboush, N., Lyzhko, E., Siniatchkin, M. and Moliadze, V.	EP 135. Boosting cognitive control with transcranial alternating current stimulation	2016
108	tACS	reject	2	not WM task/subjective well-being task	Peter, S. E., Mederer, D., Habboush, N., Lyzhko, E., Siniatchkin, M. and Moliadze, V.	The effect of transcranial alternating current stimulation (tACS) on inhibitory control and error monitoring in healthy adults	2017
109	tACS	reject	2	not WM task/subjective well-being task	Polania, R., Nitsche, M. A., Korman, C., Batsikadze, G. and Paulus, W.	The importance of timing in segregated theta phase-coupling for cognitive performance	2012
110	tACS	reject	2	not WM task/subjective well-being task	Popp, F., Dallmer-Zerbe, I., Philipsen, A. and Herrmann, C. S.	Challenges of P300 Modulation Using Transcranial Alternating Current Stimulation (tACS)	2019
111	tACS	reject	2	not WM task/subjective well-being task	Popp, Fabian, Dallmer-Zerbe, Isa M. and Herrmann, Christoph S.	Transcranial Alternating current stimulation (tACS) as a tool to modulate P300 amplitude and latency	2016

index	tACS	accept / reject	count	notes	AUTHORS	TITLE	YEAR
112	tACS	reject	6	COMMENTARY	Quentin, R. and Cohen, L. G.	Reversing working memory decline in the elderly	2019
113	tACS	reject	2	not WM task/subjective well-being task	Radecke, J. O., Engel, A. K. and Schneider, T. R.	P151 Personalized transcranial alternating current stimulation for the modulation of lateralized visuo-spatial attention	2020
115	HD-tACS	reject	6	published abstract of full article already included	Reinhart, R., Grover, S., Wang, C. and Nguyen, J.	Improving working memory in older adults by synchronizing cortical interactions with alternating current	2019
117	tACS	reject	6	published abstract of full article already included	Romei, V., Cooper, N., Sauseng, P. and Wolinski, N.	P187 Individual differences in parietal theta frequency drive spatial working memory capacity	2017
118	tACS	reject	2	not WM task/subjective well-being task	Rostami, Reza, Kazemi, Reza, Mozaffarinejad, Farzaneh, Nasiri, Zahra, Rostami, Maryam, L.Hadipour, Abed and Sadeghihassanabadi, Fatemeh	6 hz transcranial alternating current stimulation of mpfc improves sustained attention and modulates alpha phase synchronization and power in dorsal attention network	2020
119	tACS	reject	2	not WM task/subjective well-being task	Ruhnau, Philipp, Keitel, Christian, Lithari, Chrysa, Weisz, Nathan and Neuling, Toralf	Flicker-driven responses in visual cortex change during matched-frequency transcranial alternating current stimulation	2016
120	tACS	reject	2	not WM task/subjective well-being task; ACS (treatment not related to mood/subjective well-being)	Sabel, B. A., Wang, J., Fähse, S., Cárdenas-Morales, L. and Antal, A.	Personality and stress influence vision restoration and recovery in glaucoma and optic neuropathy following alternating current stimulation: implications for personalized neuromodulation and rehabilitation	2020
121	tACS	reject	1	stim intensity too low (< 1 mA)	Santarnecchi, E., Muller, T., Rossi, S., Sarkar, A., Polizzotto, N. R., Rossi, A. and Cohen Kadosh, R.	Individual differences and specificity of prefrontal gamma frequency-tACS on fluid intelligence capabilities	2016

index	tACS	accept / reject	count	notes	AUTHORS	TITLE	YEAR
122	tACS	reject	2	not WM task/subjective well-being task	Santarnecchi, E., Polizzotto, N. R., Godone, M., Giovannelli, F., Feurra, M., Matzen, L., Rossi, A. and Rossi, S.	Frequency-dependent enhancement of fluid intelligence induced by transcranial oscillatory potentials	2013
123	tACS	reject	2	not WM task/subjective well-being task	Schaal, N. K., Pfeifer, J., Krause, V. and Pollok, B.	From amusic to musical?--Improving pitch memory in congenital amusia with transcranial alternating current stimulation	2015
124	tACS	reject	2	not WM task/subjective well-being task	Schuhmann, T., Kemmerer, S. K., Duecker, F., de Graaf, T. A., Oever, S. T., de Weerd, P. and Sack, A. T.	Left parietal tACS at alpha frequency induces a shift of visuospatial attention	2019
125	tACS	reject	2	not WM task/subjective well-being task	Sela, T., Kilim, A. and Lavidor, M.	Transcranial alternating current stimulation increases risk-taking behavior in the Balloon Analog Risk Task	2012
126	tACS	reject	2	used HC at baseline only	Shanbhag, V., Sreeraj S, V., Bose, A., Narayanswamy, J., Rao, N., Kesavan, M. and Venkatasubramanian, G.	Effect of tACS on Working Memory and Processing speed in Schizophrenia: An Open Label Study	2019
127	tACS	reject	2	not WM task/subjective well-being task	Somer, Elif, Allen, John, Brooks, Joseph L., Buttrill, Vaughan and Javadi, Amir-Homayoun	Theta phase-dependent modulation of perception by concurrent transcranial alternating current stimulation and periodic visual stimulation	2020
128	tACS	reject	3	montage targets M1 (i.e. not focused on executive function per se)	Splittgerber, M., Suwelack, J. H., Kadish, N. E. and Moliadze, V.	The Effects of 1 mA tACS and tRNS on Children/Adolescents and Adults: Investigating Age and Sensitivity to Sham Stimulation	2020
129	tACS	reject	2	not WM task/subjective well-being task	Stecher, H. I. and Herrmann, C. S.	Absence of Alpha-tACS Aftereffects in Darkness Reveals Importance of Taking Derivations of Stimulation Frequency and Individual Alpha Variability Into Account	2018

index	tACS	accept / reject	count	notes	AUTHORS	TITLE	YEAR
130	tACS	reject	3	montage targets M1 (i.e. not focused on executive function per se)	Sugata, H., Yagi, K., Yazawa, S., Nagase, Y., Tsuruta, K., Ikeda, T., Matsushita, K., Hara, M., Kawakami, K. and Kawakami, K.	Modulation of Motor Learning Capacity by Transcranial Alternating Current Stimulation	2018
131	tACS	reject	2	not WM task/subjective well-being task	Tesche, C. and Houck, J.	P126 Spatiotemporal and task dependence of broadband aftereffects observed following parietal 10-Hz tACS: A MEG study	2017
132	tACS	reject	2	not WM task/subjective well-being task	Tesche, C. and Houck, J.	Persistent changes in cortical, subcortical and network-level dynamics induced by 10-Hz tACS applied over bilateral parietal cortex: a MEG study	2019
135	tACS	reject	2	not WM task/subjective well-being task	Turi, Z., Mittner, M., Lehr, A., Burger, H., Antal, A. and Paulus, W.	theta - gamma Cross-Frequency Transcranial Alternating Current Stimulation over the Trough Impairs Cognitive Control	2020
136	tACS	reject	6	duplicate	Turi, Z., Mittner, M., Lehr, A., Bürger, H., Antal, A. and Paulus, W.	Θ-γ Cross-Frequency Transcranial Alternating Current Stimulation over the Trough Impairs Cognitive Control	2020
137	tACS	reject	2	not WM task/subjective well-being task	van der Plas, Mircea, Wang, Danying, Brittain, John-Stuart and Hanslmayr, Simon	Investigating the role of phase-synchrony during encoding of episodic memories using electrical stimulation	2020
138	tACS	reject	2	not WM task/subjective well-being task	van Driel, J., Sligte, I. G., Linders, J., Elport, D. and Cohen, M. X.	Frequency Band-Specific Electrical Brain Stimulation Modulates Cognitive Control Processes	2015
139	tACS	reject	2	not WM task/subjective well-being task	van Schouwenburg, M. R., Sorensen, L. K. A., de Klerk, R., Reteig, L. C. and Slagter, H. A.	No Differential Effects of Two Different Alpha-Band Electrical Stimulation Protocols Over Fronto-Parietal Regions on Spatial Attention	2018
140	tACS	reject	2	not WM task/subjective well-being task	van Schouwenburg, Martine R., Zanto, Theodore P. and Gazzaley, Adam	Spatial attention and the effects of frontoparietal alpha band stimulation	2017

index	tACS	accept / reject	count	notes	AUTHORS	TITLE	YEAR
141	tACS	reject	4	no blinding reported; no details regarding sham protocol given	Vaque-Alcazar, L., Abellaneda-Perez, K., Sala-Llonch, R., Bargallo, N., Pascual-Leone, A. and Bartres-Faz, D.	Transcranial direct and alternating currentstimulation exert differential expression of brain networks during a working memory task	2017
142	tACS	reject	2	not WM task/subjective well-being task	Veniero, Domenica, Benwell, Christopher S. Y., Ahrens, Merle M. and Thut, Gregor	Inconsistent effects of parietal α-tacs on pseudoneglect across two experiments: A failed internal replication	2017
143	tACS	reject	5	not enough information	Violante, I.	Exploring tACS effects on physiology and cognitive function through simultaneous imaging and Bayesian optimization approaches	2019
145	tACS	reject	6	published abstract of full article already included	Violante, I., Li, L., Carmichael, D., Hampshire, A., Rothwell, J. and Sharp, D.	P131 Phase-dependent modulations of brain activity and connectivity are dependent on cognitive state	2017
146	tACS	reject	2	not WM task/subjective well-being task	Vossen, Alexandra, Gross, Joachim and Thut, Gregor	Alpha Power Increase After Transcranial Alternating Current Stimulation at Alpha Frequency (α-tACS) Reflects Plastic Changes Rather Than Entrainment	2015
147	tACS	reject	2	not WM task/subjective well-being task	Vosskuhl, J., Huster, R. J. and Herrmann, C. S.	BOLD signal effects of transcranial alternating current stimulation (tACS) in the alpha range: A concurrent tACS-fMRI study	2016
148	tACS	reject	1	3 blocks of stimulation (~4 min per block)	Vosskuhl, Johannes, Huster, René J. and Herrmann, Christoph S.	Increase in short-term memory capacity induced by down-regulating individual theta frequency via transcranial alternating current stimulation	2015
149	tACS	reject	2	not WM task/subjective well-being task	Weiss, S. and Müller, H. M.	Facilitating word memorizing: frequency specificity of transcranial alternating current stimulation (tACS)?	2017

index	tACS	accept / reject	count	notes	AUTHORS	TITLE	YEAR
150	tACS	reject	6	case study	Weiss, S., Balduin, L. S. and Müller, H. M.	P184 Individual transcranial alternating current stimulation (tACS) within the beta range during verbal working memory	2017
151	tACS	reject	2	not WM task/subjective well-being task	Wiener, M., Parikh, A., Krakow, A. and Coslett, H. B.	An Intrinsic Role of Beta Oscillations in Memory for Time Estimation	2018
152	tACS	reject	2	not WM task/subjective well-being task	Wischnewski, M. and Schutter, Djlg	After-effects of transcranial alternating current stimulation on evoked delta and theta power	2017
153	tACS	reject	2	not WM task/subjective well-being task	Wischnewski, M., Zerr, P. and Schutter, Djlg	Effects of Theta Transcranial Alternating Current Stimulation Over the Frontal Cortex on Reversal Learning	2016
154	tACS	reject	2	not WM task/subjective well-being task	Wischnewski, Miles, Joergensen, Mie L., Compen, Boukje and Schutter, Dennis J. L. G.	Frontal Beta Transcranial Alternating Current Stimulation Improves Reversal Learning	2020
156	tACS	reject	2	not WM task/subjective well-being task	Wöstmann, Malte, Vosskuhl, Johannes, Obleser, Jonas and Herrmann, Christoph S.	Opposite effects of lateralised transcranial alpha versus gamma stimulation on auditory spatial attention	2018
157	tACS	reject	2	not WM task/subjective well-being task	Wynn, S., Kessels, R. and Schutter, D.	P259 Effects of parietal tACS on subjective and objective memory measures	2020
158	tACS	reject	1	<10 min stimulation	Wynn, Syanah C., Kessels, Roy P. C. and Schutter, Dennis J. L. G.	Effects of parietal exogenous oscillatory field potentials on subjectively perceived memory confidence	2020
159	tACS	reject	2	not WM task/subjective well-being task	Yaple, Z. and Vakhrushev, R.	Modulation of the frontal-parietal network by low intensity anti-phase 20Hz transcranial electrical stimulation boosts performance in the attentional blink task	2018

index	tACS	accept / reject	count	notes	AUTHORS	TITLE	YEAR
160	tACS	reject	2	not WM task/subjective well-being task	Yaple, Z., Martinez-Saito, M., Feurra, M., Shestakova, A. and Klucharev, V.	Transcranial Alternating Current Stimulation Modulates Risky Decision Making in a Frequency-Controlled Experiment	2017
161	tACS	reject	2	not WM task/subjective well-being task	Zaehle, T., Rach, S. and Herrmann, C. S.	Transcranial alternating current stimulation enhances individual alpha activity in human EEG	2010
162	tACS	reject	2	not WM task/subjective well-being task	Zavecz, Zsófia, Horváth, Kata, Solymosi, Péter, Janacsek, Karolina and Nemeth, Dezso	Frontal-midline theta frequency and probabilistic learning: A transcranial alternating current stimulation study	2020
163	tACS	reject	2	not WM task/subjective well-being task	Zizlsperger, L., Kummel, F. and Haarmeier, T.	Metacognitive Confidence Increases with, but Does Not Determine, Visual Perceptual Learning	2016

Unique ID	1	**Study ID**	10.3389/fnins.2019.01440	**Assessor**	dw
Ref or Label	Abellaneda-Perez, K., Vaque-Alcazar, L., Perellon-Alfonso, R., Bargallo, N., Kuo, M. F., Pascual-Leone, A., . . . Bartres-Faz, D. (2020)	**Aim**	assignment to intervention (the 'intention-to-treat'		
Experimental	theta-tACS	**Comparator**	sham	**Source**	Journal article(s)
Outcome	d'(discriminability index); correct RT	**Results**		**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	"A simple randomization procedure was used (Altman and Bland, 1999; Kang et al., 2008)". Quote from Altman study: "In the simplest procedure, simple randomisation, we determine each patient's treatment at random independently with no constraints. With equal allocation to two treatment groups this is equivalent to tossing a coin, although in practice coins are rarely used. Instead we use computer generated random numbers." 1.2 Quote from paper:"tES was applied inside an
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	Table 2 shows no differences between groups for age, gender, years of education, laterality and premorbid intelligence.
	Risk of bias judgement	**Low**	
	2.1.Were participants aware of their assigned intervention during the trial?	N	tES was applied inside an MRI scanner. In the sham condition, the current delivery was terminated after 30 s of stimulation with no further blinding

	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	processes. 2.2 Researchers were aware of the intervention (single-blind study).
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	2.3 Nothing reported to indicate any deviations, though low risk in this type of trial as there is no benefit to receiving a particular trial protocol e.g. beneficial drug vs. placebo.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
Bias due to deviations from intended interventions	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Supplementary Marterial provides a table of tES-related adverse events by treatment group: An interaction between experimental groups was found as regards tingling (H = 6.982, p = 0.030). Pairwise post hoc analyses revealed more tingling
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	Table 2 indicates the number of subjects per treatment condition analysed which matches the number of subjects recruited for the study under 'Participants'.

Bias due to missing outcome data	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	4.1 Outcomes were computer-measured outputs based on correct response.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	4.2 The task was computer-based and administered in a standardised manner with appropriate randomisation of stimuli.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	4.3 Assessors were aware of the intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	4.4 Outcomes were all computer-based outputs

	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	4.4 Outcomes were all computer-based outputs.
	Risk of bias judgement	**Low**	Normal distribution was reported; parametric methods were used.
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	Y	5.1 Statistical analysis section sets out the intended evaluations (p.80) which is also congruent with their previously published work and there is nothing in their results section to indicate a change in plan.
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	N	5.2 measure was used for accuracy (d') and RTs (median RTs in ms). Measured in accordance with their plan. p.5
	5.3 ... multiple eligible analyses of the data?	PN	5.3 The most robust analysis was used (parametric e.g. ANOVAs). Measured in accordance with their plan.p.5
	Risk of bias judgement	**Low**	
Overall bias	**Risk of bias judgement**	**Low**	

Unique ID	90	**Study ID**	10.1016/j.clinph.2013.06.013	**Assessor**	dw
Ref or Label	Meiron, O., & Lavidor, M. (2014).	**Aim**	assignment to intervention (the 'intention-to-treat'		
Experimental	active	**Comparator**	sham	**Source**	Journal article(s); Personal communication with triali
Outcome	% correct (accuracy); correct RTs	**Results**	0.25	**Weight**	1

Domain	Signalling question	Response	Comments
	1.1 Was the allocation sequence random?	Y	"Following scalp measurements, participants were randomly assigned to two different ‘‘online’’ (stimulation during working memory activity) tACS conditions." An email from the author confirmed that they used a simple randomization procedure using a randomized table.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	

Bias arising from the randomization process	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	"Prior to the tACS manipulation all participants completed a short-version standard handedness questionnaire (Oldfield, 1971) validating them as consistent right-handers. Age and education were matched across stimulation conditions. In the active tACS condition mean age and education were 21.5 (SD = 1.73) and 12.67 (SD = 1.07), respectively. In the sham-stimulation condition mean age and education were 21.5 (SD = 2.43) and 12.47 (SD = 1), respectively."
	Risk of bias judgement	**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	N	"The stimulation was well tolerated, there were no side effects, and participants' reports indicated they could not discriminate between the active versus the sham stimulation condition
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	PY	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	Nothing reported to suggest any deviation.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	A section on statistical analysis was given in the methods section justifying chosen analysis, which were parametric for the main analysis
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	

	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	As evidenced by degrees of freedom reported.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	PN	4.1 Outcomes were computer-measured outputs based on correct response.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	4.2 The task was computer-based and administered in a standardised manner with appropriate randomisation of stimuli.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	4.3 Assessors were aware of the intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	4.4 Outcomes were all computer-based outputs.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	

	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	Y	Analyses provided correspond to those outlined in the methods section under 'Statistical analysis'.
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	N	One cognitive task was used with 2 outcome measures which are both reported in results. Measured in accordance with their plan.
	5.3 ... multiple eligible analyses of the data?	PN	5.3 The most robust analysis was used (parametric e.g. ANOVAs). Measured in accordance with their plan.
	Risk of bias judgement	**Low**	
Overall bias	**Risk of bias judgement**	**Low**	

Chapter 3 Supporting Information

Appendix 1 Medical questionnaire.
Appendix 2 Transcranial Neurostimulation Safety Questionnaire.
Appendix 3 Table with percent correct and dprime ANOVA results for the 2-back task.

APPENDIX 1

Please read each question carefully and answer as honestly as you can. Where you are given options such as "Y / N", you may circle, underline or highlight the one you feel is most relevant to you.

ID: _____

Background Questionnaire

1. Age: _____

2. Sex: Female / Male

3. Are you right-handed?: Y / N (circle one)

    3.1 In your formative years, were you re-trained to be right-handed? Y / N

4. Have you ever experienced traumatic physical, sexual or emotional abuse?
   Yes / No / Would rather not say

5. Do you have diabetes? Y / N
   5.1. If yes, which type (tick one): Type 1 diabetes_____ OR Type 2 diabetes_____

6. Have you been diagnosed with any mental health issues (e.g. depression, anxiety) in the last 4 months? Y / N

    6.1 If yes, are you currently taking any medication? Y / N
    If yes, please specify:

_____

7. Do you have a history of substance or alcohol dependency?
   Yes / No / Would rather not say

Please read each question carefully and answer as honestly as you can. Where you are given options such as "Y / N", you may circle, underline or highlight the one you feel is most relevant to you.

8. Are you currently taking any psychoactive medication? e.g. fluoxetine, citalopram, venlafaxine, sertraline, citalopram, lithium

   Yes / No / Would rather not say

9. Have you taken any of the following drugs in the last 4 months? Tick all that apply or circle 'None' or 'Would rather not say' (examples are listed together with the conditions they would typically be used to treat):

   - ☐ Medications to treat/manage serious heart/lung conditions such as Theophylline, Sympathomimetics
   - ☐ Non-standard/recreational drugs such as Cocaine, MDMA (ecstasy), Marijuana, Ketamine
   - ☐ Antibiotics such as Penicillin, Metronidazole, Levofloxacin, Isoniazid, Imipenem, Ganciclovir
   - ☐ Anti-psychotic medications such as Olanzapine, Ziprasidone, Risperidone
   - ☐ Chemotherapy/cancer treatment medications such as Vincristine, Methotrexate
   - ☐ HIV/AIDS medications such as Ritonavir

   None / Would rather not say

10. Have you been diagnosed with developmental or learning special needs such as dyslexia, dyscalculia or Asperger's Syndrome? Y / N

Please read each question carefully and answer as honestly as you can. Where you are given options such as "Y / N", you may circle, underline or highlight the one you feel is most relevant to you.

11. What language(s) do(did) you speak from birth?

- ☐ English
- ☐ French
- ☐ German
- ☐ Spanish
- ☐ Other

12. Current Occupation (if retired, what was your occupation before retiring?):

- ☐ Student
- ☐ Administrative or secretarial role
- ☐ Professional role
- ☐ Caring, Leisure or service role
- ☐ Sales or customer services role
- ☐ Skilled trades role
- ☐ Process, plant or machine operative
- ☐ Other:_____

13. Level of Education:

- ☐ GCSE
- ☐ A-LEVEL
- ☐ Bachelor's degree
- ☐ Diploma
- ☐ NVQ or any vocational training
- ☐ Professional Qualification/s
- ☐ Master's degree
- ☐ PhD

Please read each question carefully and answer as honestly as you can. Where you are given options such as "Y / N", you may circle, underline or highlight the one you feel is most relevant to you.

14. Country of birth: _____

15. Do you smoke? Y / N

    If yes, how many cigarettes per day?

_____

16. How often do you have a drink containing alcohol?

- □ Never
- □ Monthly or less
- □ 2 – 4 times per MONTH
- □ 2 – 3 times per WEEK
- □ +4 times per WEEK

17. How many units of alcohol do you drink on a typical day when you are drinking?

- □ 1 – 2 units
- □ 3 – 4 units
- □ 5 – 6 units
- □ 7 – 9 units
- □ 10+

Please read each question carefully and answer as honestly as you can. Where you are given options such as "Y / N", you may circle, underline or highlight the one you feel is most relevant to you.

18. Do you have any physical disability? Y / N

If yes, please specify?

_____

18.1 If yes, do you currently feel that your disability affects your well-being? Y / N

- Strongly agree
- Somewhat agree
- Neither agree nor disagree
- Somewhat disagree
- Strongly disagree

19. Have you had any major surgery in the last five years? Y / N

If yes, please specify:

_____

20. Do you have any problems with your vision? Y / N

If yes, please specify:

_____

20.1. Do you wear glasses or contact lenses to correct your vision? Y / N

21. Do you have any problems with your hearing? Y / N

If yes, please specify:

_____

21.1. Do you wear a hearing aid? Y / N

Please read each question carefully and answer as honestly as you can. Where you are given options such as "Y / N", you may circle, underline or highlight the one you feel is most relevant to you.

22. Are you currently taking any PRESCRIPTION medication for chronic or acute pain? Y / N

    If yes, please specify:_____

23. Do you exercise? Y / N

    23.1. If yes, on average how many hours per week? (any activity as long as you are intending it as exercise)

- None
- 30 min
- 1 – 2 hours
- 3 – 4 hours
- 5 – 6 hours
- More than 6 hours

24. Do you practice yoga? Y / N

    24.1. Have you practiced yoga in the last 4 months? Y / N

        24.1.1. If yes, roughly how often did you practice?

- Once per week
- 2 – 3 times per week
- Every day
- Once fortnightly
- Once per month
- Every once in a while

Please read each question carefully and answer as honestly as you can. Where you are given options such as "Y / N", you may circle, underline or highlight the one you feel is most relevant to you.

25. Do you meditate? Y / N

25.1. Have you meditated in the last 4 months? Y / N

25.2. Please specify which meditation you practice and for how many months/years you have practiced:

_____

25.2.1. Roughly how often do you meditate?

- □ Twice per day, everyday
- □ Once per day, everyday
- □ 2 – 3 times per week
- □ A few times per month
- □ Every once in a while
- □ Other (please give details):_____

25.2.2. Roughly how long is each meditation session?

- □ Less than 10 minutes
- □ 10 – 15 minutes
- □ 20 minutes
- □ +25 minutes

APPENDIX 2

Transcranial Magnetic Stimulation† (TMS) Adult Safety Screen

Name:	
Age:	
Date:	

*Read carefully the following questions and at the end tick **YES** if one or more than one applies to you, otherwise tick **NO***

Did you ever undergo Transcranial Magnetic Stimulation in the past? If so, were there any problems?

_____

Did you ever undergo Transcranial Direct Current Stimulation in the past? If so, were there any problems?

_____

Did you ever undergo Transcranial Alternating Current Stimulation in the past? If so, were there any problems?

_____

Did you ever undergo Magnetic Resonance Imaging (MRI) in the past? If so, were there any problems?

_____

Do you suffer from frequent or severe headaches?

Do you have epilepsy or have you ever had a convulsion or a seizure?

Have you ever had a stroke?

Have you ever had a head trauma that was diagnosed as a concussion or was associated with loss of consciousness?

Have you ever had any illness that caused brain injury?

Do you have metal in the brain, skull or elsewhere in your body (e.g., splinters, fragments, clips, etc.)? If so, specify the type of metal.

Have you ever had any other brain-related condition?

Do you have a medication infusion device?

Have you ever had a fainting spell or syncope? If yes, please describe on which occasion(s)?

Do you have a cardiac pacemaker or intracardiac lines?

Do you have an implanted neurostimulator (e.g., DBS, epidural/subdural, VNS)?

Do you have any hearing problems or ringing in your ears?

Do you have cochlear implants?

Are you pregnant or is there any chance that you might be?

Do you suffer from or have you in the past suffered from any skin condition (e.g. eczema)?

Are you taking any medications? (please list)

YES _____ NO_____

*If you answered **yes** you may, if you wish, provide further details (use reverse if necessary):*

_____
_____
_____
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_____

† *For use with single-pulse TMS, paired-pulse TMS, or repetitive TMS.*

Chapter 3, Appendix 3

Table. Percent correct and d-prime means, standard errors and univariate ANOVA F values by age group and stress group for the 3 replication studies.

				Univariate ANOVA F-values		
		Young Adults	**Older Adults**	**YA vs. OA**	**Low Stress vs. High Stress**	**Age Grp x Stress Grp**
	Accuracy (% correct)	mean (SE)	mean (SE)	F	F	F
Study 1	*Low Stress (n=21)*	93.71 (0.81)	89.00 (1.98)	3.579	6.295**	0.026
	High Stress (n=19)	87.58 (3.21)	83.61 (2.79)			
Study 2A	*Low Stress (n=30)*	91.77 (1.78)	91.13 (1.37)	0.393	3.309	0.105
	High Stress (n=28)	88.61 (2.53)	86.60 (2.60)			
Study 2B	*Low Stress (n=30)*	90.72 (2.50)	89.83 (2.01)	0.963	0.309	1.960
	High Stress (n=28)	88.93 (2.52)	93.99 (0.88)			
	Accuracy (d-prime)	mean (SE)	mean (SE)	F	F	F
Study 1	*Low Stress (n=21)*	3.06 (0.11)	2.56 (0.2)	5.514*	4.990*	0.000
	High Stress (n=19)	2.58 (0.27)	2.07 (0.28)			
Study 2A	*Low Stress (n=30)*	2.96 (0.17)	2.79 (0.16)	1.290	2.790	0.102
	High Stress (n=28)	2.68 (0.23)	2.38 (0.26)			
Study 2B	*Low Stress (n=30)*	2.89 (0.21)	2.69 (0.19)	0.467	0.252	2.980
	High Stress (n=28)	2.66 (0.23)	3.11 (0.11)			

* significant at < 0.05 (two-tailed).

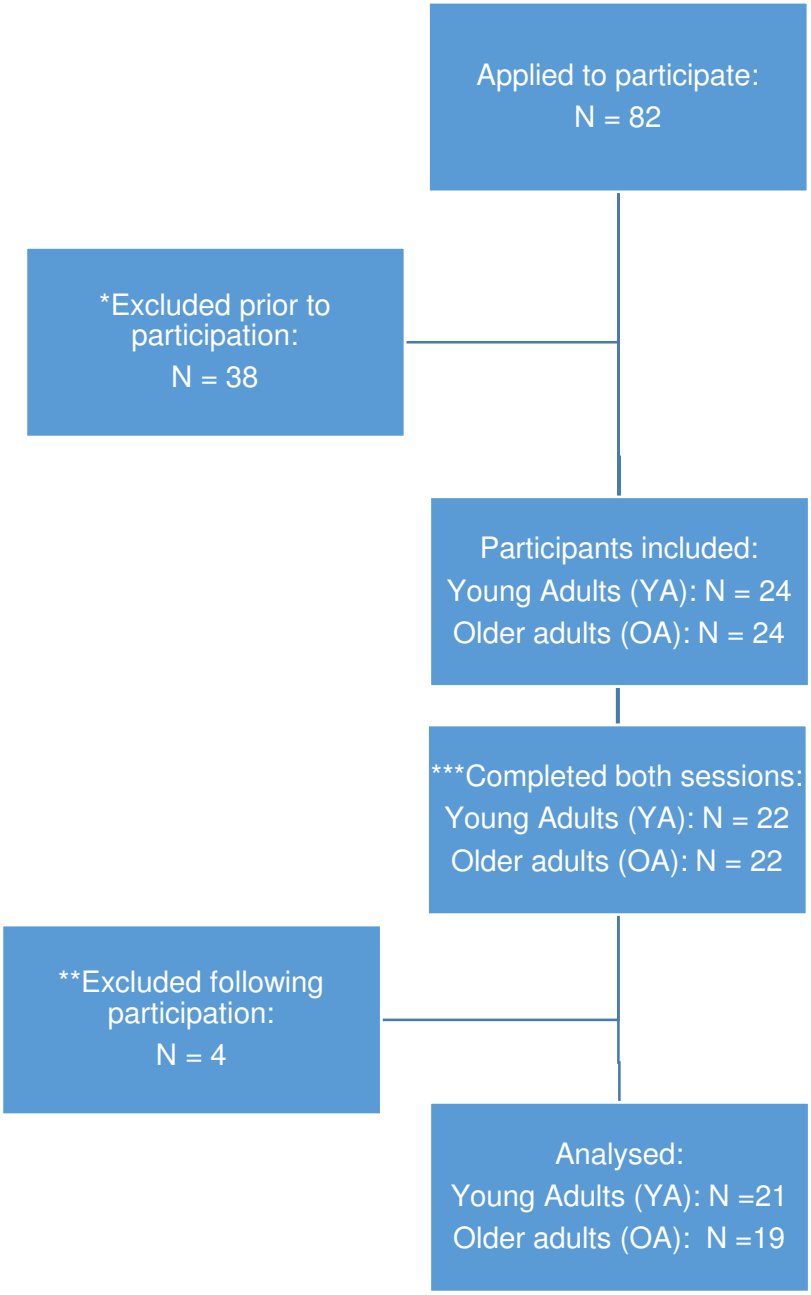
** significant at < 0.01 (two-tailed).

Chapter 4 Supporting Information

Appendix 1 Participant details for all 3 studies.
Appendix 2 Age median IQR values for participants for all 3 studies.
Appendix 3 Additional tasks administered during the study (description and results).
Appendix 4 Analyses for percent correct and D-prime means, SEs and Univariate ANOVA results for all 3 studies.
Appendix 5 Frequency table of the total cumulative stress score for each participant in each study.
Appendix 6 An excel workbook containing a series of tables showing power analysis and traditional meta-analysis outcomes.
Appendix 7 Study design and procedure for all 3 studies.
Appendix 8 Reference table providing the median splits for all 3 studies.
Appendix 9 Sensitivity analysis: A comparison using a single median split.
Appendix 10 Data tables for all iterative analyses and Bayes factor calculations.

Chapter 4, Appendix 1

Study 1 Participant record (in-person study)



*REASONS FOR EXCLUSION:

Left-handed(n=1), retrained to be right-handed (n=2), adverse childhood experience (e.g. abuse) (n=7), mental health diagnosis (n=7), taking medications that affect central nervous system (n=11), neurological condition (n=9), medical condition (n=1).

**REASONS FOR EXCLUSION:

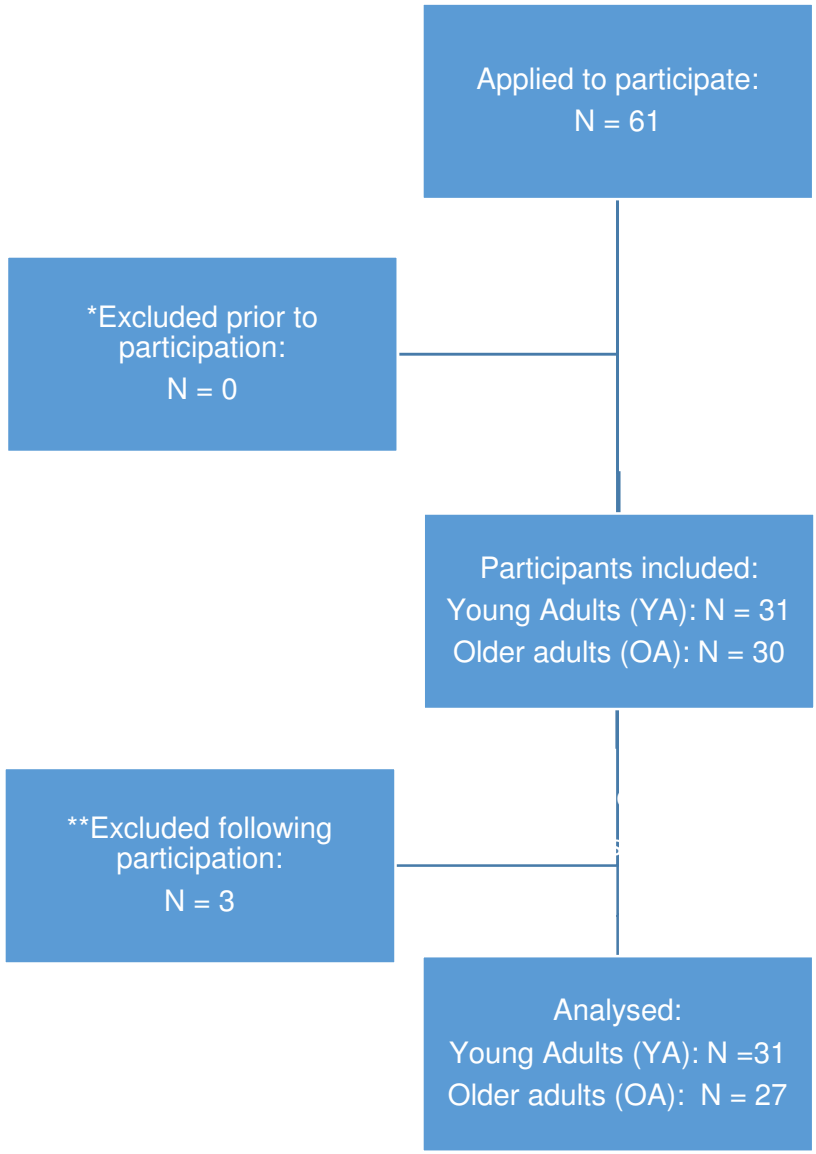
Poor cognitive task performance due to response confusion (e.g. pressed spacebar continuously) (n=4).

***ATTRITION:

4 participants did not attend session 2 because of enforced Covid19 lock-down (March 2020).

Chapter 4, Appendix 1

Study 2A Participant record (online only study)

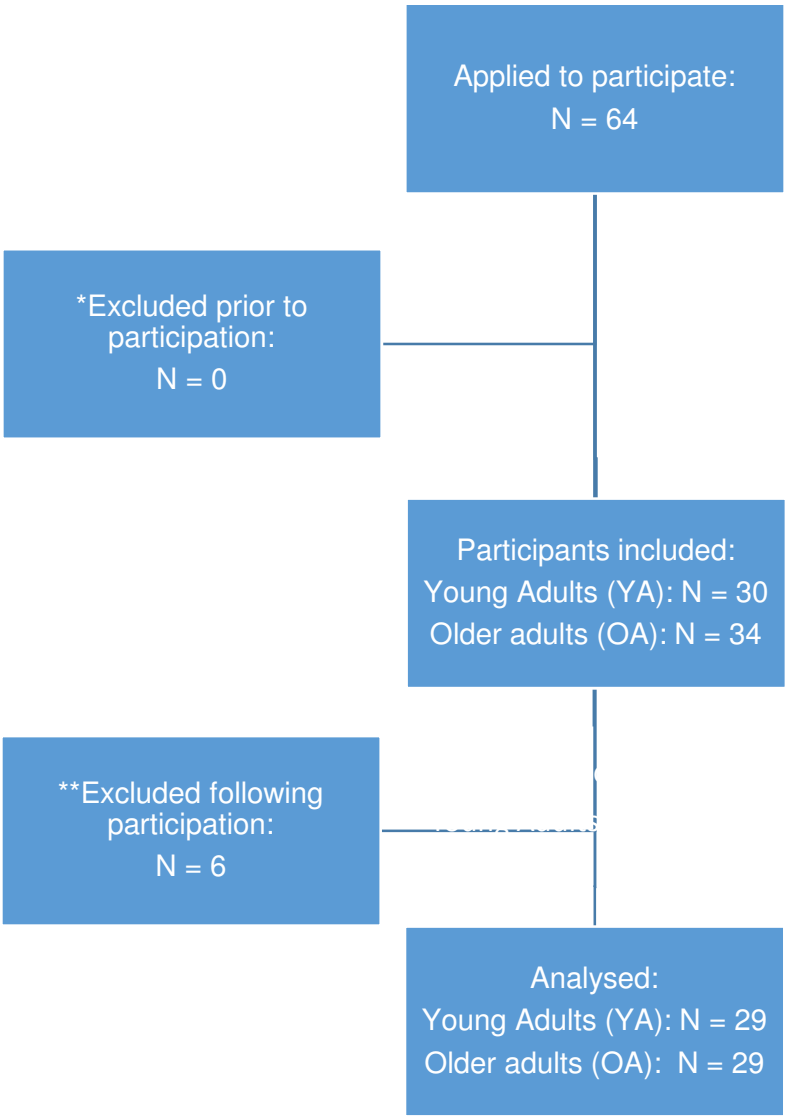


**<u>REASONS FOR EXCLUSION</u>:

Consumed alcohol within 12 hours of taking part in study (n=2); medications that cause drowsiness (n=1).

Chapter 4, Appendix 1

Study 2B Participant record (online only study)



**<u>REASONS FOR EXCLUSION</u>:

Consumed alcohol within 12 hours of taking part in study (n=3); poor cognitive performance due to response confusion (n=3).

Chapter 4, Appendix 2

Table. Age Median and IQR values for Young and Older Adult participants by study

	Median (IQR)	
Studies	Young Adults	Older Adults
Study 1	19 (19-22)	69 (64-73)
Study 2A	29 (25-32)	63 (61-67)
Study 2B	29 (24-31.5)	64 (61-65)

Chapter 4, Appendix 3

Additional tasks administered during the study (description and results)

Brief Resilience Scale

We wanted to extend Marshall's study protocol by adding resilience as a factor to enhance our understanding of how cumulative stress might affect cognition, given participants' ability to recover from stressful events. To this end, we administered the Brief Resilience Scale (BRS) [65]. The BRS has good internal consistency (Cronbach α <.95 > .70) and test-retest validity (interclass correlation coefficient .69 to .62) with a range of populations [e.g. 66, 67] and was found to be well-suited to stress-related contexts [68]. Participants were asked to self-report the extent to which they agreed with 6 statements on a scale of 1 ('Strongly Disagree') to 5 ('Strongly Agree'). Three of the statements were worded positively (items 1,3,5) and 3 negatively (items 2,4,6). Scores were derived by reverse-scoring items 2, 4 and 6 and then calculating the mean of all items. A higher mean score indicates greater resilience; previous research has shown that the BRS is negatively associated with physical symptoms and negative affect (e.g. irritability and distress) [65].

Subjective Sleep Quality

We also added the Pittsburgh Sleep Quality Index (PSQI) [69] to the study protocol to assess sleep quality, asking participants to report their sleep quality over the past month. Sleep quality has been consistently linked to variability in cognitive performance, stress, anxiety and illness [69-74]. Individual items in the PSQI yielded a Cronbach α of 0.83, indicating a high degree of internal consistency. Test-retest reliability

revealed coefficient of .85 and there was good discriminant validity between clinical (depressed, disorders initiating and maintaining sleep, disorders of excessive somnolence) and control groups ($p < .001$). We used only questions 5 and 6 to keep the experiment short to reduce fatigue. Both questions were rated on a 4-point scale (score range: 0 to 3). Question 5a, in this study, provided an index for 'sleep latency' and was rated as: 'Not during the past month' = 0 to 'Three or more times a week' = 3. Question 5 b-j comprises 10 questions assessing 'sleep disturbances' rated as per Q5a above. These values were summed for each participant. Summed totals were grouped into one of 4 brackets: 0; 1-9; 10-18; or 19-27, then recoded as a score of 0, 1, 2 or 3, respectively. Question 6 is a single question measuring 'subjective sleep quality' rated from 'Very good' = 0 to 'Very bad' = 3.

A global score, which had a score range of 0 – 9, was computed by summing the 3 aforementioned components, namely 'sleep latency', 'sleep disturbances' and 'subjective sleep quality'. Note that these methods are adapted from the original PSQI which yields a global score of 0 – 21, based on 7 components.

Results

Appendix 3, Table 1. Descriptive statistics and p-values for self-reported resilience and sleep quality by age, by stress group for each study.

Brief Resilience Scale

	Young Adults		Older Adults		
	Low Stress[a] (n=11)	High Stress[a] (n=10)	Low Stress[a] (n=10)	High Stress[a] (n=9)	p
Study 1 (N=40)	3.58 (0.20)	3.87 (0.28)	3.90 (0.20)	3.80 (0.25)	≥0.401[b,c]
Study 2A (N=58)	3.33 (0.22)	3.61 (0.26)	3.76 (0.26)	3.27 (0.29)	≥0.242[b,c]
Study 2B (N=58)	2.99 (0.26)	3.18 (0.23)	3.87 (0.16)	3.76 (0.16)	≥0.562[b,c]

Sleep Quality (summed components range: 0 - 9)

	Young Adults		Older Adults		
	Low Stress[a] (n=11)	High Stress[a] (n=10)	Low Stress[a] (n=10)	High Stress[a] (n=9)	p
Study 1 (N=40)	3.18 (0.41)	2.6 (0.37)	2.4 (0.39)*	3.89 (0.46)*	≥0.025[b,c]
Study 2A (N=58)	2.25 (0.31)	2.87 (0.34)	2.5 (0.33)	3.54 (0.5)	≥0.091[b,c]
Study 2B (N=58)	2.60 (0.51)	3.14 (0.43)	2.53 (0.44)	3.50 (0.38)	≥0.116[b,c]

[a] Mean (SE). Standard error obtained via BCa Bootstrap with 1000 samples.

[b] Independent samples t-test (low vs high stress) were performed by age group.

[c] Additional Mann-Whitney U test were performed with similar outcomes.

* significant at < 0.05

** significant at < 0.01

Chapter 4, Appendix 4

Table. Percent correct and d-prime means, standard errors and univariate ANOVA F values by age group and stress group for the 3 replication studies.

				Univariate ANOVA F-values		
	Accuracy (% correct)	**Young Adults**	**Older Adults**	YA vs. OA	Low Stress vs. High Stress	Age Grp x Stress Grp
Study 1	*Low Stress (n=21)*	93.71 (0.81)	89.00 (1.98)	3.579	6.295**	0.026
	High Stress (n=19)	87.58 (3.21)	83.61 (2.79)			
Study 2A	*Low Stress (n=30)*	91.77 (1.78)	91.13 (1.37)	0.393	3.309	0.105
	High Stress (n=28)	88.61 (2.53)	86.60 (2.60)			
Study 2B	*Low Stress (n=30)*	90.72 (2.50)	89.83 (2.01)	0.963	0.309	1.960
	High Stress (n=28)	88.93 (2.52)	93.99 (0.88)			
	Accuracy (d-prime)	mean (SE)	mean (SE)	F	F	F
Study 1	*Low Stress (n=21)*	3.06 (0.11)	2.56 (0.2)	5.514*	4.990*	0.000
	High Stress (n=19)	2.58 (0.27)	2.07 (0.28)			
Study 2A	*Low Stress (n=30)*	2.96 (0.17)	2.79 (0.16)	1.290	2.790	0.102
	High Stress (n=28)	2.68 (0.23)	2.38 (0.26)			
Study 2B	*Low Stress (n=30)*	2.89 (0.21)	2.69 (0.19)	0.467	0.252	2.980
	High Stress (n=28)	2.66 (0.23)	3.11 (0.11)			

* significant at < 0.05 (two-tailed).

** significant at < 0.01 (two-tailed).

Chapter 4, Appendix 5

Table. Frequency table of the total cumulative stress score for each participant in each study.

STUDY 1

LESS total score (whole life)				*SRRS total score (whole life)*			
Total LESS score	Frequency	Percent	Cumulative Percent	Total SRRS score	Frequency	Percent	Cumulative Percent
120	1	4.8	4.8	489	1	5.3	5.3
345	1	4.8	9.5	628	1	5.3	10.5
363	1	4.8	14.3	697	1	5.3	15.8
389	1	4.8	19.0	751	1	5.3	21.1
477	1	4.8	23.8	753	1	5.3	26.3
507	1	4.8	28.6	809	1	5.3	31.6
518	1	4.8	33.3	817	1	5.3	36.8
574	1	4.8	38.1	861	1	5.3	42.1
587	1	4.8	42.9	885	1	5.3	47.4
592	2	9.5	52.4	913	1	5.3	52.6
606	1	4.8	57.1	919	1	5.3	57.9
616	1	4.8	61.9	925	2	10.5	68.4
631	1	4.8	66.7	977	1	5.3	73.7
633	1	4.8	71.4	1009	1	5.3	78.9
638	1	4.8	76.2	1014	1	5.3	84.2
641	1	4.8	81.0	1028	1	5.3	89.5
682	1	4.8	85.7	1062	1	5.3	94.7
729	1	4.8	90.5	1079	1	5.3	100.0
857	1	4.8	95.2	Total	19	100.0	
884	1	4.8	100.0				
Total	21	100.0					

STUDY 2A

LESS total score (whole life)				*SRRS total score (whole life)*			
Total LESS score	Frequency	Percent	Cumulative Percent	Total SRRS score	Frequency	Percent	Cumulative Percent
161	1	3.2	3.2	193	1	3.7	3.7
229	1	3.2	6.5	446	1	3.7	7.4
265	1	3.2	9.7	512	1	3.7	11.1
307	1	3.2	12.9	558	1	3.7	14.8
323	1	3.2	16.1	589	1	3.7	18.5
327	1	3.2	19.4	631	1	3.7	22.2
357	2	6.5	25.8	632	1	3.7	25.9
385	1	3.2	29.0	659	1	3.7	29.6
392	1	3.2	32.3	682	1	3.7	33.3
411	1	3.2	35.5	685	1	3.7	37.0
493	1	3.2	38.7	690	1	3.7	40.7
545	1	3.2	41.9	696	1	3.7	44.4
563	1	3.2	45.2	722	1	3.7	48.1
573	1	3.2	48.4	738	1	3.7	51.9
577	1	3.2	51.6	748	1	3.7	55.6
584	1	3.2	54.8	755	1	3.7	59.3
608	1	3.2	58.1	786	1	3.7	63.0
633	1	3.2	61.3	794	1	3.7	66.7
636	1	3.2	64.5	803	1	3.7	70.4
641	1	3.2	67.7	828	1	3.7	74.1
658	1	3.2	71.0	845	1	3.7	77.8
662	1	3.2	74.2	850	1	3.7	81.5
691	1	3.2	77.4	859	1	3.7	85.2
702	1	3.2	80.6	867	1	3.7	88.9
704	1	3.2	83.9	901	1	3.7	92.6
710	1	3.2	87.1	976	1	3.7	96.3
711	1	3.2	90.3	992	1	3.7	100.0
788	1	3.2	93.5	Total	27	100.0	
874	1	3.2	96.8				
951	1	3.2	100.0				
Total	31	100.0					

STUDY 2B

LESS total score (whole life)				*SRRS total score (whole life)*			
Total LESS score	Frequency	Percent	Cumulative Percent	Total SRRS score	Frequency	Percent	Cumulative Percent
223	1	3.4	3.4	308	1	3.4	3.4
273	1	3.4	6.9	473	1	3.4	6.9
289	1	3.4	10.3	553	1	3.4	10.3
291	1	3.4	13.8	576	1	3.4	13.8
318	1	3.4	17.2	590	1	3.4	17.2
327	1	3.4	20.7	627	1	3.4	20.7
334	1	3.4	24.1	683	1	3.4	24.1
362	1	3.4	27.6	686	1	3.4	27.6
382	1	3.4	31.0	700	1	3.4	31.0
392	1	3.4	34.5	712	1	3.4	34.5
408	1	3.4	37.9	715	1	3.4	37.9
409	1	3.4	41.4	738	1	3.4	41.4
423	1	3.4	44.8	760	1	3.4	44.8
435	1	3.4	48.3	763	1	3.4	48.3
516	1	3.4	51.7	766	1	3.4	51.7
540	1	3.4	55.2	771	1	3.4	55.2
547	1	3.4	58.6	796	1	3.4	58.6
585	1	3.4	62.1	798	1	3.4	62.1
595	1	3.4	65.5	801	1	3.4	65.5
614	1	3.4	69.0	806	1	3.4	69.0
623	1	3.4	72.4	845	1	3.4	72.4
651	1	3.4	75.9	849	1	3.4	75.9
733	1	3.4	79.3	850	1	3.4	79.3
768	1	3.4	82.8	861	1	3.4	82.8
795	1	3.4	86.2	873	1	3.4	86.2
833	1	3.4	89.7	922	1	3.4	89.7
847	1	3.4	93.1	952	1	3.4	93.1
861	1	3.4	96.6	956	1	3.4	96.6
894	1	3.4	100.0	972	1	3.4	100.0
Total	29	100.0		Total	29	100.0	

Chapter 4, Appendix 6

Workbook contains traditional meta-analysis for 3 replication studies.
Forest Plots provide a visual representation.
Draper Plots are a useful complimentary visual representation.

meta-analysis conducted with these R libraries:

```
library(dmetar)
library(meta)
```

Power Calculation based on Marshall et al. (2015) age x stress group interaction effect.

G-power http://www.mormonsandscience.com/gpower-guide.html

Sample Parameters

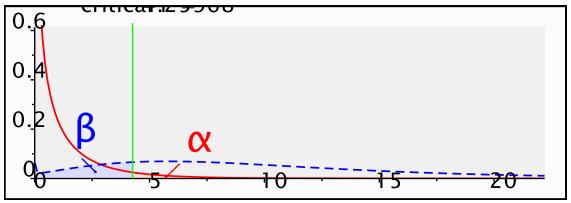
age group	stress group	n
Young adults	Low Stress	15
Young adults	High Stres	15
Older adults	Low Stress	15
Older adults	High Stres	15
N		**60**

$(YA_{LS}-YA_{HS})-(OA_{LS}-OA_{HS})$

	MeanDiff	seMeanDiff
Marshall Study	-12.55	2.85

Calculation input values:

Partial eta squared	0.234
Effect size:	0.55
Alpha:	0.05
Requested power:	0.80
Numerator df	1.00
Number of groups (cells)	4.00



Output given

power	0.99

Demoninator DF	24
Total Sample Size	28

Total sample required to detect an interaction effect at a power set to .80 = 28

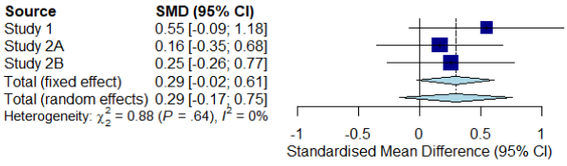
nBack 3 Studies overall age difference Percent Correct

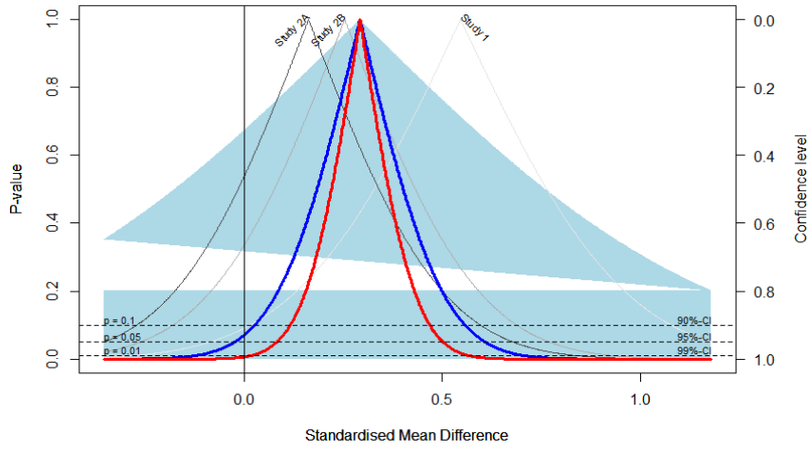
Number of studies combined	**k**	3
Number of observations	**N**	156

	SMD	95%-CI lower	95%-CI upper	z|t	p-value
Common effect model	0.29	-0.02	0.61	1.81	0.070
Random effects model	0.29	-0.17	0.75	2.73	0.112

Quantifying heterogeneity:	value	95%-CI lower	95%-CI upper	Q	df	p-value
tau^2	0	0.00	1.4933	0.88	2	0.644
tau	0	0.00	1.222			
I^2	0.00%	0.00%	89.60%			
H	1	1.00	3.10			

Details on meta-analytical method:
- Inverse variance method
- Restricted maximum-likelihood estimator for tau^2
- Q-profile method for confidence interval of tau^2 and tau
- Hartung-Knapp adjustment for random effects model
- Hedges' g (bias corrected standardised mean difference; using exact



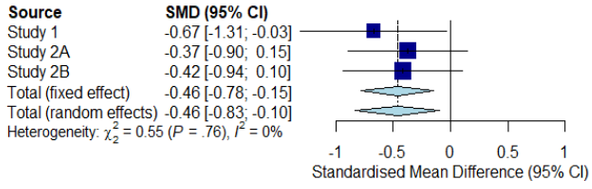


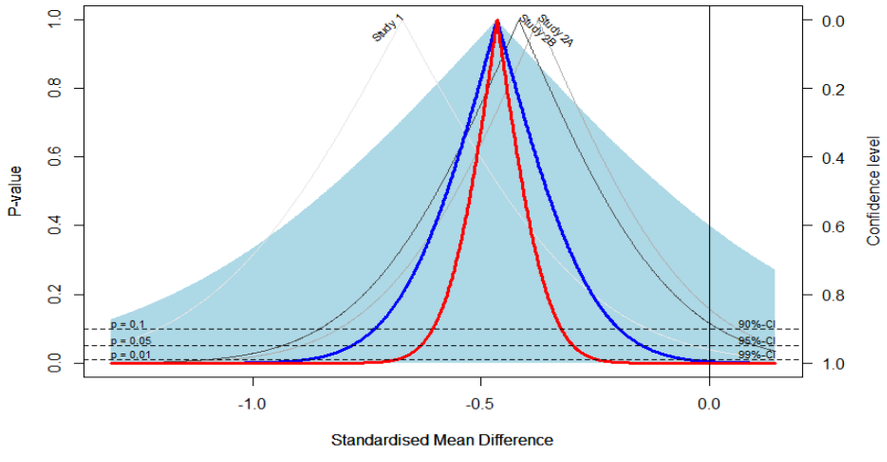
nBack 3 Studies overall age difference REACTION TIME

Number of studies combined	**k**	3
Number of observations	**N**	156

	SMD	95%-CI lower	95%-CI upper	z|t	p-value
Common effect model	-0.46	-0.78	-0.15	-2.86	0.004
Random effects model	-0.46	-0.83	-0.10	-5.43	0.032

Quantifying heterogeneity:	value	95%-CI lower	95%-CI upper	Q	df	p-value
tau^2	0.00	0.00	0.93	0.55	2	0.759
tau	0.00	0.00	0.96			
I^2	0.00%	0.00%	89.60%			
H	1.00	1.00	3.10			





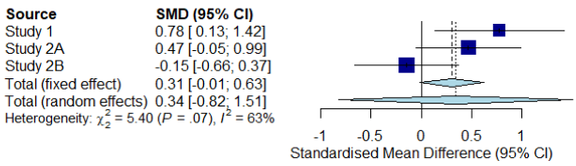
nBack 3 Studies overall stress difference Percent Correct

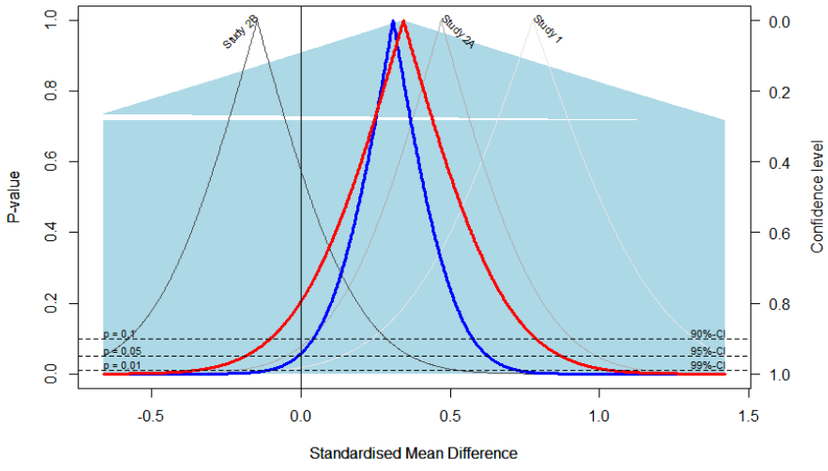
Number of studies combined	**k**	3
Number of observations	**N**	156

	SMD	95%-CI lower	95%-CI upper	z|t	p-value
Common effect model	0.31	-0.01	0.63	1.90	0.058
Random effects model	0.34	-0.82	1.51	1.27	0.333

Quantifying heterogeneity:	value	95%-CI lower	95%-CI upper	Q	df	p-value
tau^2	0.14	0.00	8.68	5.40	2	0.067
tau	0.37	0.00	2.95			
I^2	62.9%	0.0%	89.4%			
H	1.64	1.00	3.07			

Details on meta-analytical method:
- Inverse variance method
- Restricted maximum-likelihood estimator for tau^2
- Q-profile method for confidence interval of tau^2 and tau
- Hartung-Knapp adjustment for random effects model
- Hedges' g (bias corrected standardised mean difference; using exact



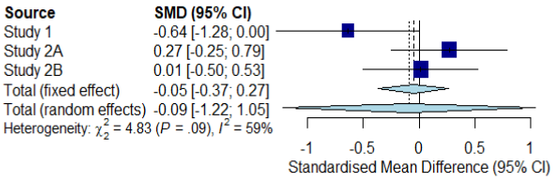


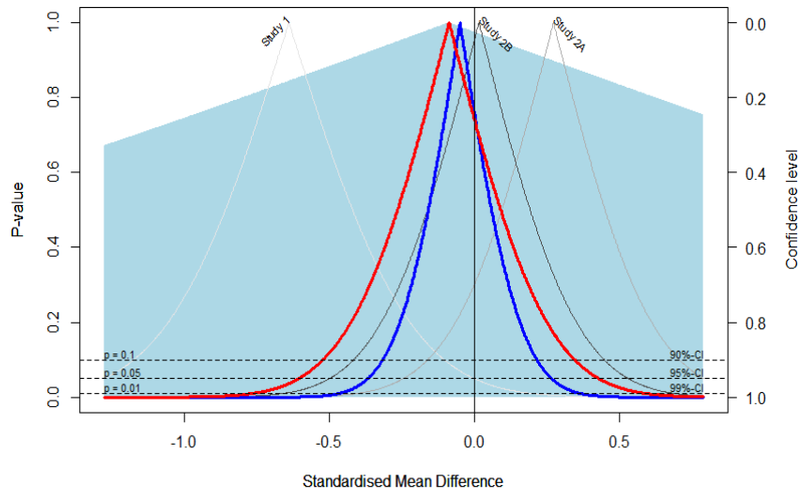
nBack 3 Studies overall stress difference REACTION TIME

Number of studies combined	**k**	3
Number of observations	**N**	156

	SMD	95%-CI lower	95%-CI upper	z|t	p-value
Common effect model	-0.05	-0.37	0.27	-0.32	0.753
Random effects model	-0.09	-1.22	1.05	-0.34	0.769

Quantifying heterogeneity:	value	95%-CI lower	95%-CI upper	Q	df	p-value
tau^2	0.12	0.00	8.64	4.83	2	0.089
tau	0.34	0.00	2.94			
I^2	58.6%	0.0%	88.2%			
H	1.55	1.00	2.91			





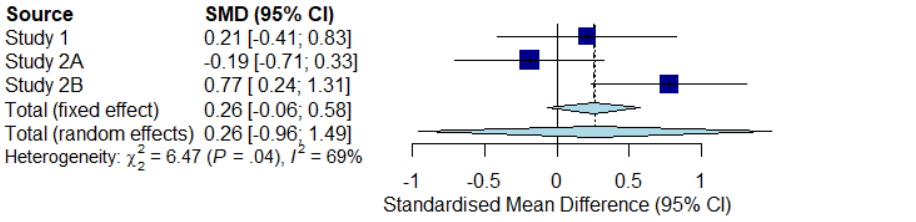
nBack 3 Studies ageXstress interaction Percent Correct

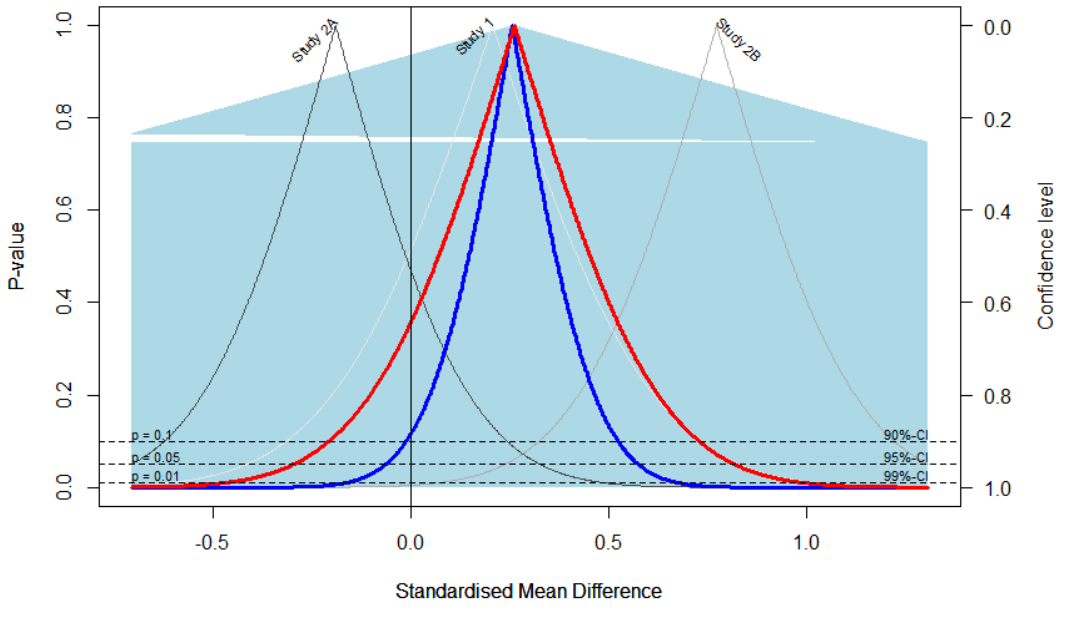
Number of studies combined	**k**	3
Number of observations	**N**	156

	SMD	95%-CI lower	95%-CI upper	z|t	p-value
Common effect model	0.26	-0.06	0.58	1.58	0.114
Random effects model	0.26	-0.96	1.49	0.92	0.453

Quantifying heterogeneity:	value	95%-CI lower	95%-CI upper	Q	df	p-value
tau^2	0.17	0.00	9.18	6.47	2	0.039
tau	0.41	0.00	3.03			
I^2	69.1%	0.0%	91.0%			
H	1.80	1.00	3.33			

Details on meta-analytical method:
- Inverse variance method
- Restricted maximum-likelihood estimator for tau^2
- Q-profile method for confidence interval of tau^2 and tau
- Hartung-Knapp adjustment for random effects model
- Hedges' g (bias corrected standardised mean difference; using exact



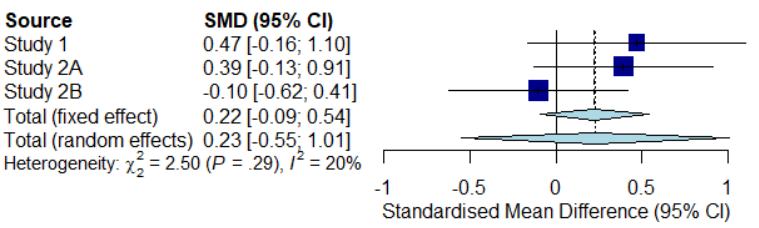


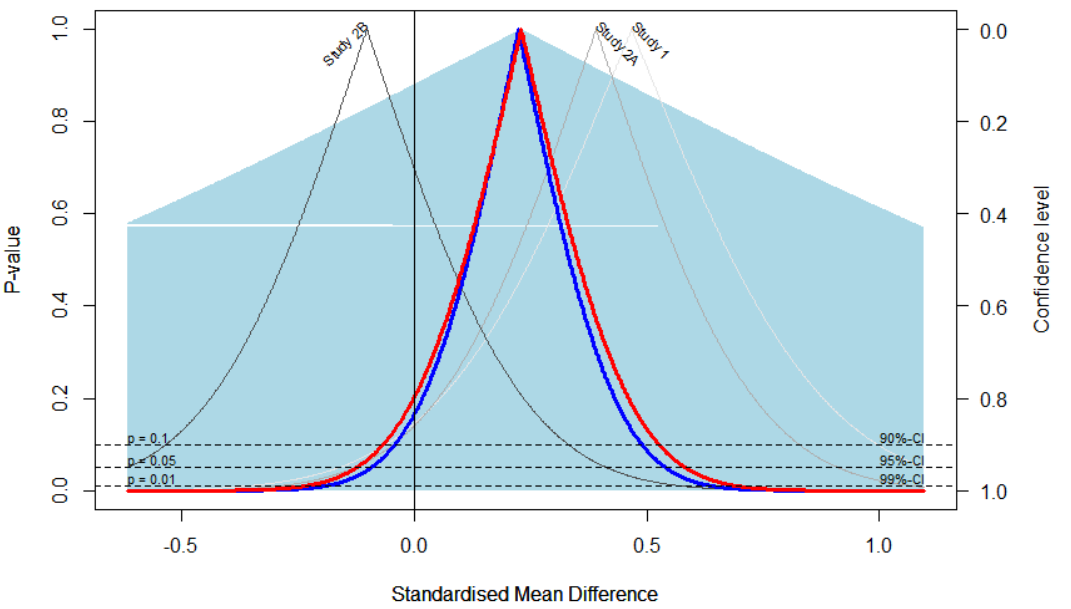
nBack 3 Studies ageXstress interaction REACTION TIME

Number of studies combined	**k**	3
Number of observations	**N**	156

	SMD	95%-CI lower	95%-CI upper	z|t	p-value
Common effect model	0.22	-0.09	0.54	1.39	0.165
Random effects model	0.23	-0.55	1.01	1.27	0.331

Quantifying heterogeneity:	value	95%-CI lower	95%-CI upper	Q	df	p-value
tau^2	0.02	0.00	3.69	2.50	2	0.286
tau	0.15	0.00	1.92			
I^2	20.2%	0.0%	91.7%			
H	1.12	1.00	3.47			





PERCENT CORRECT DATA

AGE

Studies	**es**	**weight**	**sample.size**	**se**	**var**	**ci.lo**	**ci.hi**	**measure**	**pooled_effect**
Study 1	0.55	9.60	40	0.32	0.10	-0.09	1.18	g	
Study 2A	0.16	14.38	58	0.26	0.07	-0.35	0.68	g	
Study 2B	0.25	14.38	58	0.26	0.07	-0.26	0.77	g	
All studies									0.29

STRESS

Studies	**es**	**weight**	**sample.size**	**se**	**var**	**ci.lo**	**ci.hi**	**measure**	**pooled_effect**
Study 1	0.78	9.25	40	0.33	0.11	0.13	1.42	g	
Study 2A	0.47	14.08	58	0.27	0.07	-0.05	0.99	g	
Study 2B	-0.15	14.44	58	0.26	0.07	-0.66	0.37	g	
All studies									0.31

INTERACTION

Studies	**es**	**weight**	**sample.size**	**se**	**var**	**ci.lo**	**ci.hi**	**measure**	**pooled_effect**
Study 1	0.21	9.92	40	0.32	0.10	-0.41	0.83	g	
Study 2A	-0.19	14.42	58	0.26	0.07	-0.71	0.33	g	
Study 2B	0.77	13.45	58	0.27	0.07	0.24	1.31	g	
All studies									0.26

REACTION TIME DATA

AGE

Studies	**es**	**weight**	**sample.size**	**se**	**var**	**ci.lo**	**ci.hi**	**measure**	**pooled_effect**
Study 1	-0.67	9.42	40	0.33	0.11	-1.31	-0.03	g	
Study 2A	-0.37	14.18	58	0.27	0.07	-0.90	0.15	g	
Study 2B	-0.42	14.18	58	0.27	0.07	-0.94	0.10	g	
All studies									-0.46

STRESS

Studies	**es**	**weight**	**sample.size**	**se**	**var**	**ci.lo**	**ci.hi**	**measure**	**pooled_effect**
Study 1	-0.64	9.47	40	0.32	0.11	-1.28	0.00	g	
Study 2A	0.27	14.35	58	0.26	0.07	-0.25	0.79	g	
Study 2B	0.01	14.48	58	0.26	0.07	-0.50	0.53	g	
All studies									-0.05

INTERACTION

Studies	**es**	**weight**	**sample.size**	**se**	**var**	**ci.lo**	**ci.hi**	**measure**	**pooled_effect**
Study 1	0.47	9.70	40	0.32	0.10	-0.16	1.10	g	
Study 2A	0.39	14.20	58	0.27	0.07	-0.13	0.91	g	
Study 2B	-0.10	14.46	58	0.26	0.07	-0.62	0.41	g	
All studies									0.22

Chapter 4, Appendix 7

Study 1 Test Design and Procedure

Participants attended 2 sessions at least a week apart, at the same time of day. Participants received both sham and active stimulation. Order of treatment and task version was counter-balanced and randomised within age group. The Bayesian meta-analysis included session 1 data only. A univariate analysis of variance (ANOVA) was conducted on these data with age group, stress group and stimulation order as factors to evaluate the impact of the transcranial alternating current stimulation treatment on cognitive performance given that half of the participants received active stimulation in session 1 (YA_n=10;OA_n=9). The ANOVA results revealed a main effect for stress group only ($F(1, 32)$ 6.789, $p = 0.014$). All other main effects and interaction effects were not statistically significant (p's ≥ 0.106), indicating that stimulation did not have a significant impact on performance overall nor did it affect age or stress groups in a systematic way.

Session 1 only:

- Medical screening
- Procedure and nature of tasks briefly explained
- Informed consent
- All tasks to be administered fully explained
- Self-report measures (as detailed for Studies 2A and 2B overleaf)

Procedure for <u>both</u> sessions:

Pre-stimulation (offline)

Task	Duration
N-back practice (1-back, 2-back)	5 min
Head measurement and electrode placement	10 min
tACS comfort/phosphene assessment	30 s
Comfort Visual Analogue – time 1	30 s

During 20 min transcranial alternating current stimulation (online): 1500 μA (peak-to-peak)

Task	Duration
Comfort Visual Analogue – time 2	30 s
Watch nature video (habituation)	4 min 30 s
Picture Free Recall Task (encoding phase)	2 min
2-back task	7 min
Picture Free Recall Task (recall phase)	2 min
Comfort Visual Analogue – time 3	30 s

Post-stimulation (offline)

Task	Duration
Comfort Visual Analogue – time 4	30 s
Electrode removal	5 min

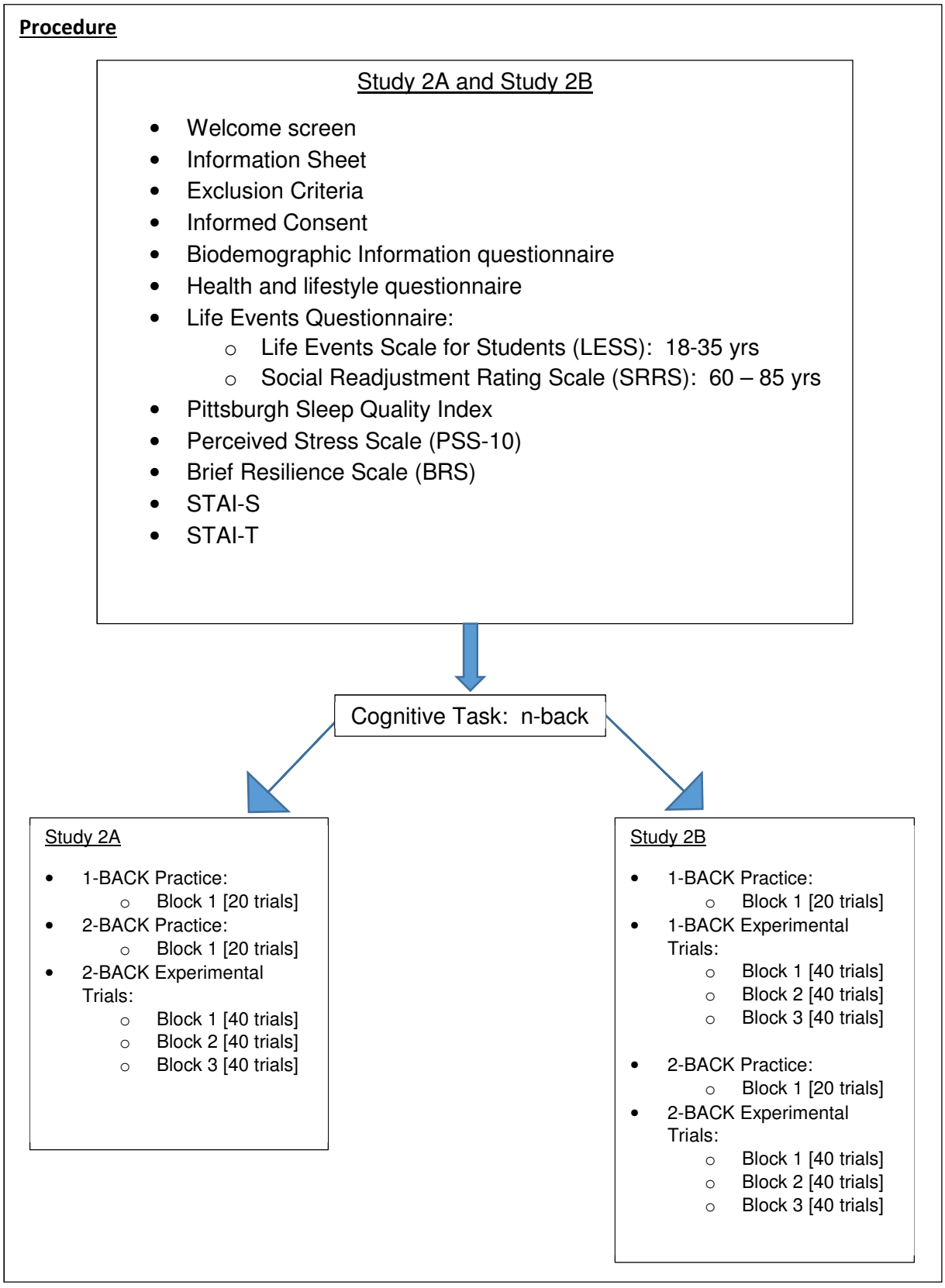
Session 2 only:

- On/off judgement for sessions 1 and 2

Chapter 4, Appendix 7

Study 2A & 2B Test Design and Procedure

Participants signed up via the Prolific participant recruitment platform. Following self-assessment for eligibility they completed one test session, which was held in the morning for older participants and in the afternoon for young participants, which was roughly in line with time of day Study 1 participants participated. We also excluded for handedness and most of the same exclusion criteria to be consistent with the sample for Study 1.



Chapter 4, Appendix 8

Table. Median split value with inter-quartile range by study and combined.

Study	n	LESS (n=81) median (IQR)	SRRS (n=75) median (IQR)
Study 1	40	592 (492.00 - 639.50)	913 (753.00 - 1009.00)
Study 2A	58	577 (357.00 - 691.00)	738 (632.00 - 845.00)
Study 2B	58	516 (348.00 - 692.00)	766 (684.50 - 849.50)
Study 1, 2A, 2B combined	**156**	**577 (383.50 - 660.00)**	**786 (685.00 - 873.00)**

Chapter 4, Appendix 9

Table. Sensitivity analysis: A comparison using a single median split.

Table 1. Means, standard errors and Univariate ANOVA F values by age group and stress group for the 3 replication studies, with single median split.

				Univariate ANOVA F-values		
		Young Adults	**Older Adults**	YA vs. OA	Low Stress vs. High Stress	Age Grp x Stress Grp
	Accuracy (% correct)	*mean (SE)*	*mean (SE)*	F	F	F
Study 1	*Low Stress (n=13)*	93.96 (0.98)	87.83 (4.06)	2.976	1.789	0.382
	High Stress (n = 27)	88.85 (2.53)	85.95 (1.98)			
Study 2A	*Low Stress (n=33)*	91.77 (1.77)	90.44 (1.55)	0.663	2.756	0.040
	High Stress (n = 25)	88.61 (2.41)	86.42 (3.04)			
Study 2B	*Low Stress (n=33)*	91.27 (2.26)	90.42 (1.91)	1.299	0.004	2.371
	High Stress (n = 25)	87.85 (2.89)	93.59 (0.84)			
	Reaction time (ms)					
Study 1	*Low Stress (n=13)*	698.43 (46.00)	804.99 (45.19)	2.953	8.423**	0.061
	High Stress (n = 27)	890.76 (83.57)	1033.24 (46.72)			
Study 2A	*Low Stress (n=33)*	698.19 (67.02)	726.37 (52.30)	2.088	0.866	0.998
	High Stress (n = 25)	576.26 (48.36)	730.71 (87.81)			
Study 2B	*Low Stress (n=33)*	712.57 (43.71)	780.15 (52.79)	2.510	0.122	0.041
	High Stress (n = 25)	685.55 (51.98)	772.97 (43.96)			

* significant at < 0.05

** significant at < 0.01

Chapter 4, Appendix 9

Table 2. Means, standard errors and Univariate ANOVA F values by age group and stress group for the 3 replication studies.

				Univariate ANOVA F-values		
		Young Adults	**Older Adults**	YA vs. OA	Low Stress vs. High Stress	Age Grp x Stress Grp
	Accuracy (% correct)	*mean (SE)*	*mean (SE)*	F	F	F
Study 1	*Low Stress (n=13)*	93.96 (0.98)	87.83 (4.06)	2.976	1.789	0.382
	High Stress (n = 27)	88.85 (2.53)	85.95 (1.98)			
Study 2A	*Low Stress (n=33)*	91.77 (1.77)	90.44 (1.55)	0.663	2.756	0.040
	High Stress (n = 25)	88.61 (2.41)	86.42 (3.04)			
Study 2B	*Low Stress (n=33)*	91.27 (2.26)	90.42 (1.91)	1.299	0.004	2.371
	High Stress (n = 25)	87.85 (2.89)	93.59 (0.84)			
	Reaction time (ms)					
Study 1	*Low Stress (n=13)*	698.43 (46.00)	804.99 (45.19)	2.953	8.423**	0.061
	High Stress (n = 27)	890.76 (83.57)	1033.24 (46.72)			
Study 2A	*Low Stress (n=33)*	698.19 (67.02)	726.37 (52.30)	2.088	0.866	0.998
	High Stress (n = 25)	576.26 (48.36)	730.71 (87.81)			
Study 2B	*Low Stress (n=33)*	712.57 (43.71)	780.15 (52.79)	2.510	0.122	0.041
	High Stress (n = 25)	685.55 (51.98)	772.97 (43.96)			

* significant at < 0.05

** significant at < 0.01

Chapter 4, Appendix 9

Table 3. Mean differences, standard errors and Bayes Factors for comparisons by age group and by stress level for the 3 replication studies, using single median split.

	Young vs. Older Adults			Low vs High Stress Adults		
Accuracy (% correct)	*Mean Difference (SE)*	$BF_{H(0,4.83)}$	95% CI[a]	*Mean Difference (SE)*	$BF_{H(0,3.50)}$	95% CI[a]
Study 1 (N=40)	4.35 (2.42)	3.09†		4.26 (2.35)	3.23†	
Study 2A (N=58)	1.29 (2.12)	0.67		3.35 (2.24)	2.14	
Study 2B (N=58)	-1.98 (2.06)	0.22		0.03 (2.16)	0.53	
All Data (N=156)	0.90 (1.26)	**0.48**	-1.57, 3.37	2.43 (1.30)	**3.12†**	-0.11, 4.97
Reaction Time (ms)	*Mean Difference (SE)*	$BF_{H(0,441.28)}$	95% CI[a]	*Mean Difference (SE)*	$BF_{H(0,62.33)}$	95% CI[a]
Study 1 (N=40)	-155.69 (71.44)*	3.18†		-225.23 (62.27)**	0.20‡	
Study 2A (N=58)	-88.79 (60.04)	0.73		74.67 (63.98)	1.58	
Study 2B (N=58)	-75.54 (46.79)	0.72		14.32 (46.76)	0.74	
All Data (N=156)	-96.37 (32.79)	**10.84†**	-160.64, -32.11	-34.69 (32.28)	**0.25‡**	-97.96, 28.58

[a] 95% credibility intervals are associated with the relevant "All Data" posterior mean (SE) value provided in the "Mean Difference (SE)" column.

* significant at < 0.05

** significant at < 0.01

† evidence favours H1

‡ evidence favours H0

Table 4. Mean differences, standard errors and Bayes Factors for comparisons for young low and high stress groups by older low and high stress groups for the 3 replication studies, using single median split.

	Age x Stress		
Accuracy (% correct)	*mean Difference (SE)*	$BF_{H(0,-12.55)}$	95% CI[a]
Study 1 (N=40)	4.23 (4.73)	0.80	
Study 2A (N=58)	-0.93 (4.36)	0.28	
Study 2B (N=58)	7.26 (4.22)	2.28	
All Data (N=156)	3.57 (2.55)	**0.93**	-1.43, 8.57
Reaction Time (ms)	*mean Difference (SE)*	$BF_{H(0,65.44)}$	95% CI[a]
Study 1 (N=40)	83.49 (119.97)	1.17	
Study 2A (N=58)	64.79 (125.86)	1.08	
Study 2B (N=58)	48.72 (95.88)	1.05	
All Data (N=156)	62.93 (64.36)	**1.35**	-63.23, 189.08

[a] 95% credibility intervals are associated with the relevant "All Data" posterior mean (SE) value provided in the "Mean Difference (SE)" column.

* significant at < 0.05

** significant at < 0.01

† evidence favours H1

‡ evidence favours H0

Chapter 4, Appendix 9

Table 5. Mean differences, standard errors and Bayes Factors for comparisons by stress group within age groups for the 3 replication studies, with single median split.

	YA: Low vs. High Stress			OA: Low vs. High Stress		
Accuracy (% correct)	*mean Difference (SE)*	$BF_{H(0,-2.39)}$	95% CI[a]	*mean Difference (SE)*	$BF_{H(0,9.39)}$	95% CI[a]
Study 1 (N=40)	5.11 (2.7)	2.94		1.88 (4.49)	0.60	
Study 2A (N=58)	3.16 (2.93)	1.47		4.02 (3.34)	1.11	
Study 2B (N=58)	3.43 (3.58)	1.35		-3.17 (2.09)	0.09‡	
All Data (N=156)	4.03 (1.74)	**6.64†**	0.63, 7.43	-0.74 (1.65)	**0.12‡**	-3.97, 2.49
Reaction Time (ms)	*mean Difference (SE)*	$BF_{H(0,-87.32)}$	95% CI[a]	*mean Difference (SE)*	$BF_{H(0,102.87)}$	95% CI[a]
Study 1 (N=40)	-192.33 (93.47)	3.61		-228.25 (64.86)**	0.13‡	
Study 2A (N=58)	121.94 (81.12)	2.16		-4.33 (100.57)	0.68	
Study 2B (N=58)	27.01 (68.67)	0.81		7.18 (66.46)	0.59	
All Data (N=156)	4.69 (45.72)	**0.50**	-84.91, 94.3	-94.26 (42.15)	**0.13‡**	-176.86, -11.65

[a] 95% credibility intervals are associated with the relevant "All Data" posterior mean (SE) value provided in the "Mean Difference (SE)" column.

* significant at < 0.05

** significant at < 0.01

† evidence favours H1

‡ evidence favours H0

Chapter 4, Appendix 10

These sheets calculate Bayesian meta analysis for percent correct data and reaction time data.

Prior distribution	normal (which represents a scale factor of 2 SD)
Prior estimated effect size	A subjective estimate of maximum expected difference between groups. To calculate the prior, this maximum value was divided by 2 to provide one standard deviation (with mean set to zero) e.g. a maximum difference between groups of 10% yields a prior of 5%.

Likelihood data

Marshall et al. (2015)	These data were fed into the meta analysis iteratively to obtain a final effect size which is the posterior of Study 2B.
Study 1	
Study 2A	
Study 2B	

All means and standard errors used are given in the tables.

PERCENT CORRECT: YA vs. OA	N	YA_n	OA_n	MeanDiff	seMeanDiff	YAmean	YAse	OAmean	OAse
Marshall Study(prior)	60	30	30	**4.83**	**1.64**	92.19	0.94	87.36	1.34
Study 1	40	21	19	**4.35**	**2.42**	90.79	1.66	86.45	1.73
Study 2A	58	31	27	**1.29**	**2.12**	90.24	1.48	88.95	1.47
Study 2B	58	29	29	**-1.98**	**2.06**	89.86	1.73	91.84	1.12

PERCENT CORRECT: LS vs. HS	N	LS_n	HS_n	MeanDiff	seMeanDiff	LSmean	LSse	HSmean	HSse
Marshall Study (prior)	60	30	30	**3.50**	**1.62**	91.53	0.93	88.03	1.37
Study 1	40	21	19	**5.77**	**2.35**	91.47	1.15	85.70	2.06
Study 2A	58	31	27	**3.79**	**2.20**	91.47	1.13	87.68	1.80
Study 2B	58	29	29	**-1.18**	**2.07**	90.28	1.52	91.46	1.40

PERCENT CORRECT: Age*Stress interacti	N	LS_n	HS_n	MeanDiff	seMeanDiff	$(YA_{LS}-YA_{HS})(OA_{LS}-OA_{HS})$	$(YA_{LS}-YA_{HS})-(OA_{LS}-OA_{HS})$	SE$_{diff}$	YA_LSmean	YA_LSse	YA_HSmean	YA_HSse	OA_LSmean	OA_LSse	OA_HSmean	OA_HSse
Marshall Study (prior)	60	30	30	**-12.55**	**2.85**	-2.70	-12.55	2.85	90.55	1.64	93.25	0.95	91.89	1.04	82.03	1.85
Study 1	40	21	19	**1.53**	**4.65**	7.18	1.53	4.65	93.64	0.81	86.47	3.17	88.54	2.05	82.90	2.72
Study 2A	58	30	28	**-1.54**	**4.23**	3.66	-1.54	4.23	91.24	1.75	87.57	2.50	90.84	1.40	85.64	2.61
Study 2B	58	30	28	**6.39**	**4.23**	1.69	6.39	4.23	89.47	2.56	87.77	2.58	89.18	1.94	93.88	0.88

PERCENT CORRECT: Young Adults (LS v	N	LS_n	HS_n	MeanDiff	seMeanDiff	LSmean	LSse	HSmean	HSse
Marshall Study (prior)	30	15	15	**-2.39**	**1.88**	91.00	1.61	93.39	0.93
Study 1	21	11	10	**6.13**	**3.12**	93.71	0.81	87.58	3.06
Study 2A	31	16	15	**3.16**	**3.06**	91.77	1.78	88.61	2.38
Study 2B	29	15	14	**1.79**	**3.60**	90.72	2.53	88.93	1.99

PERCENT CORRECT: Older Adults (LS vs	N	LS_n	HS_n	MeanDiff	seMeanDiff	LSmean	LSse	HSmean	HSse
Marshall Study (prior)	30	15	15	**9.39**	**2.01**	92.06	1.00	82.67	1.80
Study 1	19	10	9	**5.39**	**3.26**	89.00	1.94	83.61	2.71
Study 2A	27	14	13	**4.53**	**2.83**	91.13	1.40	86.60	2.51
Study 2B	29	15	14	**-4.15**	**2.14**	89.83	1.99	93.99	0.91

TABLE 2: Percent Correct Bayesian Meta Analysis values for all priors, likelihoods and posterior outputs.

	Prior		Likelihood		Posterior			
	mean	SE	mean	SE	*mean*	*SD*	*CI - lower*	*CI - upper*
Study 1	4.83	1.64	4.35	2.42	*4.68*	*1.36*	*2.02*	*7.34*
Study 2A	4.68	1.36	1.29	2.12	*3.70*	*1.14*	*1.46*	*5.94*
Study 2B	3.70	1.14	-1.98	2.06	*2.37*	*1.00*	*0.41*	*4.33*

	Prior		Likelihood		Posterior			
	mean	SE	mean	SE	*mean*	*SD*	*CI - lower*	*CI - upper*
Study 1	3.50	1.62	5.77	2.35	*4.23*	*1.33*	*1.62*	*6.85*
Study 2A	4.23	1.33	3.79	2.20	*4.11*	*1.14*	*1.88*	*6.35*
Study 2B	4.11	1.14	-1.18	2.07	*2.88*	*1.00*	*0.93*	*4.84*

	Prior		Likelihood		Posterior			
	mean	SE	mean	SE	*mean*	*SD*	*CI - lower*	*CI - upper*
Study 1	-12.55	2.85	1.53	4.65	*-8.70*	*2.43*	*-13.47*	*-3.94*
Study 2A	-8.70	2.43	-1.54	4.23	*-6.92*	*2.11*	*-11.05*	*-2.79*
Study 2B	-6.92	2.11	6.39	4.23	*-4.28*	*1.89*	*-7.98*	*-0.58*

	Prior		Likelihood		Posterior			
	mean	SE	mean	SE	*mean*	*SD*	*CI - lower*	*CI - upper*
Study 1	-2.39	1.88	6.13	3.12	-0.13	1.61	-3.28	3.03
Study 2A	-0.13	1.61	3.16	3.06	0.59	1.42	-2.21	3.38
Study 2B	0.59	1.42	1.79	3.60	0.75	1.32	-1.85	3.34

	Prior		Likelihood		Posterior			
	mean	SE	mean	SE	mean	SD	CI - lower	CI - upper
Study 1	9.39	2.01	5.39	3.26	8.29	1.71	4.93	11.64
Study 2A	8.29	1.71	4.53	2.83	7.28	1.47	4.40	10.15
Study 2B	7.28	1.47	-4.15	2.14	3.62	1.21	1.25	5.99

These values were entered into the calculator provided by Dienes (http://www.lifesci.sussex.ac.uk/home/Zoltan_Dienes/inference/bayes_normalposterior.swf) found in http://www.lifesci.sussex.ac.uk/home/Zoltan_Dienes/inference/Bayes.htm which gave a posterior mean and standard deviation plus 95% credible intervals.

Values were entered to 4 d.p.

Values in yellow represent the first effect sizes entered into the iterative meta analysis.

REACTION TIME: YA vs. OA	N	YA_n	OA_n	MeanDiff	seMeanDiff	YAmean	YAse	OAmean	OAse
Marshall Study(prior)	46	16	30	-441.28	109.07	532.69	42.13	973.97	102.69
Study 1	40	21	19	-155.69	71.44	817.49	56.44	973.18	42.50
Study 2A	58	31	27	-88.79	60.04	639.19	41.73	727.98	45.24
Study 2B	58	29	29	-75.54	46.79	701.39	31.89	776.93	34.44

REACTION TIME: LS vs. HS	N	LS_n	HS_n	MeanDiff	seMeanDiff	LSmean	LSse	HSmean	HSse
Marshall Study (prior)	46	22	24	62.33	158.09	853.00	124.70	790.67	94.15
Study 1	40	21	19	-146.53	72.13	821.84	43.30	968.37	57.31
Study 2A	58	30	28	64.12	59.29	711.48	43.40	647.35	43.06
Study 2B	58	30	28	2.63	48.69	740.43	36.37	737.80	31.78

REACTION TIME: Age*Stress interaction	N	LS_n	HS_n	MeanDiff	seMeanDiff	YALS-YAHS	OALS-OAHS′AHS)-(OALS	DiffSE	YA_LSmean	YA_LSse	YA_HSmean	YA_HSse	OA_LSmean	OA_LSse	OA_HSmean	OA_HSse
Marshall Study (prior)	46	22	24	-47.75	254.72	-59.87	-12.12	-47.75	254.72	459.00	46.76	518.87	63.45	719.06	166.15	731.19	136.76
Study 1	40	21	19	104.80	138.22	-75.54	-180.34	104.80	138.22	715.64	71.10	791.19	88.97	862.91	49.83	1043.25	59.12
Study 2A	58	30	28	93.36	123.58	91.27	-2.09	93.36	123.58	622.32	65.66	531.06	48.97	655.17	64.56	657.26	66.87
Study 2B	58	30	28	-19.04	96.41	-20.10	-1.05	-19.04	96.41	648.85	46.77	668.95	48.71	733.09	54.49	734.15	41.60

REACTION TIME: Young Adults (LS vs.	N	LS_n	HS_n	MeanDiff	seMeanDiff	LSmean	LSse	HSmean	HSse
Marshall Study (prior)	16	7	9	-87.32	78.59	483.57	46.81	570.89	63.67
Study 1	21	11	10	-111.89	109.76	764.21	68.79	876.10	88.14
Study 2A	31	16	15	121.94	82.12	698.19	66.76	576.26	48.46
Study 2B	29	15	14	-25.33	65.47	689.16	45.05	714.49	48.00

REACTION TIME: Older Adults (LS vs. H	N	LS_n	HS_n	MeanDiff	seMeanDiff	LSmean	LSse	HSmean	HSse
Marshall Study (prior)	30	15	15	102.87	209.13	1025.40	159.84	922.53	133.36
Study 1	19	10	9	-185.66	75.62	885.23	48.47	1070.89	59.15
Study 2A	27	14	13	-2.73	93.16	726.66	64.14	729.39	65.24
Study 2B	29	15	14	30.59	69.27	791.70	55.59	761.11	39.97

TABLE 4: Reaction Time Bayesian Meta Analysis values for all priors, likelihoods and posterior outputs.

	Prior		Likelihood		Posterior			
	mean	SE	mean	SE	*mean*	*SD*	*CI - lower*	*CI - upper*
Study 1	-441.28	109.07	-155.69	71.44	*-241.43*	*59.76*	*-358.56*	*-124.30*
Study 2A	-241.43	59.76	-88.79	60.04	*-165.46*	*42.35*	*-248.47*	*-82.44*
Study 2B	-165.46	42.35	-75.54	46.79	*-124.96*	*31.40*	*-186.50*	*-63.42*

	Prior		Likelihood		Posterior			
	mean	SE	mean	SE	*mean*	*SD*	*CI - lower*	*CI - upper*
Study 1	62.33	158.09	-146.53	72.13	*-110.54*	*65.62*	*-239.16*	*18.08*
Study 2A	-110.54	65.62	64.12	59.29	*-14.38*	*43.99*	*-100.61*	*71.85*
Study 2B	-14.38	43.99	2.63	48.69	*-6.73*	*32.64*	*-70.72*	*57.25*

	Prior		Likelihood		Posterior			
	mean	SE	mean	SE	*mean*	*SD*	*CI - lower*	*CI - upper*
Study 1	-47.75	254.72	104.80	138.22	*70.10*	*121.49*	*-168.01*	*308.22*
Study 2A	70.10	121.49	93.36	123.58	*81.53*	*86.64*	*-88.27*	*251.33*
Study 2B	81.53	86.64	-19.04	96.41	*36.60*	*64.44*	*-89.70*	*162.90*

	Prior		Likelihood		Posterior			
	mean	SE	mean	SE	*mean*	*SD*	*CI - lower*	*CI - upper*
Study 1	-87.32	78.59	-111.89	109.76	*-95.65*	*63.90*	*-220.89*	*29.60*
Study 2A	-95.65	63.90	121.94	82.12	*-13.59*	*50.43*	*-112.44*	*85.26*
Study 2B	-13.59	50.43	-25.33	65.47	*-17.96*	*39.95*	*-96.27*	*60.35*

	Prior		Likelihood		Posterior			
	mean	SE	mean	SE	*mean*	*SD*	*CI - lower*	*CI - upper*
Study 1	102.87	209.13	-185.66	75.62	*-152.30*	*71.11*	*-291.68*	*-12.92*
Study 2A	-152.30	71.11	-2.73	93.16	*-97.23*	*56.53*	*-208.03*	*13.56*
Study 2B	-97.23	56.53	30.59	69.27	*-46.14*	*43.79*	*-131.98*	*39.70*

These values were entered into the calculator provided by Dienes (http://www.lifesci.sussex.ac.uk/home/Zoltan_Dienes/inference/bayes_normalposterior.swf) found in http://www.lifesci.sussex.ac.uk/home/Zoltan_Dienes/inference/Bayes.htm which gave a posterior mean and standard deviation plus 95% credible intervals.

Values were entered to 4 d.p.

Values in yellow represent the first effect sizes entered into the iterative meta analysis.

Prior values		Age		Cumulative stress		Age * Stress		YA		OA	
		ACCURACY	REACTION TIME	ACCURACY	REACTION TIME	ACCURACY	REACTION TIME	ACCURACY	REACTION TIME	ACCURACY	REACTION TIME
		meanDiff	meanDiff	meanDiff	meanDiff	meanDiff	meanDiff	meanDiff	meanDiff	meanDiff	meanDiff
Estimated maximum difference		10.00	100.00	10.00	100.00	5.00	50.00	10.00	25.00	25.00	75.00
	SD	5	50	5	50	2.5	25	5	12.5	12.5	37.5

PERCENT CORRECT: YA vs. OA

		Prior			Likelihood		BF	Robustness checks		
		Max Difference	1 SD		meanDiff	meanDiffSE		Normal Dist	Student's t (2df)	Cauchy
Marshall BF	Estimated max effect size	10.00	5.00		4.83	1.64	15.99	15.99	13.30	11.96
BF1	Marshall meanDiff	4.83	2.42	Study 1	4.35	2.42	1.59	1.59	1.51	1.43
BF2	Study 1 posterior upper CI	7.34	3.67	Study 2A	1.29	2.12	0.58	0.58	0.50	0.46
BF3	Study 2A posterior upper CI	5.94	2.97	Study 2B	-1.98	2.06	0.78	0.78	0.67	0.62

PERCENT CORRECT: LS vs. HS

		Prior			Likelihood		BF	Robustness checks		
		Max Difference	1 SD		meanDiff	meanDiffSE		Normal Dist	Student's t (2df)	Cauchy
Marshall BF	Estimated max effect size	10.00	5.00		3.50	1.62	2.54	2.54	2.14	1.95
BF1	Marshall meanDiff	3.50	1.75	Study 1	5.77	2.35	2.36	2.36	3.08	3.28
BF2	Study 1 posterior upper CI	6.85	3.42	Study 2A	3.79	2.20	1.55	1.55	1.35	1.24
BF3	Study 2A posterior upper CI	6.35	3.17	Study 2B	-1.18	2.07	0.61	0.61	0.53	0.49

PERCENT CORRECT: Age*Stress interaction

		Prior			Likelihood		BF	Robustness checks		
		Max Difference	1 SD		meanDiff	meanDiffSE		Normal Dist	Student's t (2df)	Cauchy
Marshall BF	Estimated max effect size	5.00	2.50		-12.55	2.85	50.86	50.86	455.25	724.11
BF1	Marshall meanDiff	-12.55	-6.28	Study 1	1.53	4.65	0.62	0.62	0.53	0.49
BF2	Study 1 posterior upper CI	-3.94	-1.97	Study 2A	-1.54	4.23	0.92	0.92	0.84	0.79
BF3	Study 2A posterior upper CI	-2.79	-1.40	Study 2B	6.39	4.23	1.06	1.06	1.11	1.13

PERCENT CORRECT: Young Adults (LS vs. HS)

		Prior			Likelihood		BF	Robustness checks		
		Max Difference	1 SD		meanDiff	meanDiffSE		Normal Dist	Student's t (2df)	Cauchy
Marshall BF	Estimated max effect size	10.00	5.00		-2.39	1.88	0.71	0.71	0.62	0.57
BF1	Marshall meanDiff	-2.39	-1.19	Study 1	6.13	3.12	1.20	1.20	1.39	1.50
BF2	Study 1 posterior upper CI	3.03	1.51	Study 2A	3.16	3.06	1.00	1.00	0.95	0.91
BF3	Study 2A posterior upper CI	3.38	1.69	Study 2B	1.79	3.60	0.93	0.93	0.85	0.81

PERCENT CORRECT: Older Adults (LS vs. HS)

		Prior			Likelihood		BF	Robustness checks		
		Max Difference	1 SD		meanDiff	meanDiffSE		Normal Dist	Student's t (2df)	Cauchy
Marshall BF	Estimated max effect size	25.00	12.50		9.39	2.01	6374.86	6374.86	5274.71	4738.60
BF1	Marshall meanDiff	9.39	4.69	Study 1	5.39	3.26	1.43	1.43	1.25	1.15
BF2	Study 1 posterior upper CI	11.64	5.82	Study 2A	4.53	2.83	1.23	1.23	1.05	0.96
BF3	Study 2A posterior upper CI	10.15	5.07	Study 2B	-4.15	2.14	1.94	1.94	1.64	1.49

Prior values		Age		Cumulative stress		Age * Stress		YA		OA	
		ACCURACY	REACTION TIME	ACCURACY	REACTION TIME	ACCURACY	REACTION TIME	ACCURACY	REACTION TIME	ACCURACY	REACTION TIME
		meanDiff	meanDiff	meanDiff	meanDiff	meanDiff	meanDiff	meanDiff	meanDiff	meanDiff	meanDiff
Estimated maximum difference		10.00	100.00	10.00	100.00	5.00	50.00	10.00	25.00	25.00	75.00
	SD	5	50	5	50	2.5	25	5	12.5	12.5	37.5

PERCENT CORRECT: YA vs. OA

		Prior			Likelihood		BF	Robustness checks		
		Max Difference	1 SD		meanDiff	meanDiffSE		Normal Dist	Student's t (2df)	Cauchy
Marshall BF	Estimated max effect size	100.00	50.00		-441.28	109.07	3.77	3.77	32.89	64.15
BF1	Marshall meanDiff	-441.2792	-220.6396	Study 1	-155.69	71.44	2.64	2.64	2.23	2.03
BF2	Study 1 posterior upper CI	-124.2960	-62.1480	Study 2A	-88.79	60.04	1.22	1.22	1.11	1.04
BF3	Study 2A posterior upper CI	-82.4428	-41.2214	Study 2B	-75.54	46.79	1.33	1.33	1.26	1.20

PERCENT CORRECT: LS vs. HS

		Prior			Likelihood		BF	Robustness checks		
		Max Difference	1 SD		meanDiff	meanDiffSE		Normal Dist	Student's t (2df)	Cauchy
Marshall BF	Estimated max effect size	100.00	50.00		62.33	158.09	0.96	0.96	0.91	0.87
BF1	Marshall meanDiff	62.3333	31.1667	Study 1	-146.53	72.13	1.27	1.27	3.08	3.28
BF2	Study 1 posterior upper CI	18.0817	9.0409	Study 2A	64.12	59.29	1.00	1.00	1.00	1.00
BF3	Study 2A posterior upper CI	71.8503	35.9252	Study 2B	2.63	48.69	0.81	0.81	0.71	0.66

PERCENT CORRECT: Age*Stress interaction

		Prior			Likelihood		BF	Robustness checks		
		Max Difference	1 SD		meanDiff	meanDiffSE		Normal Dist	Student's t (2df)	Cauchy
Marshall BF	Estimated max effect size	50.00	25.00		-47.75	254.72	1.00	1.00	0.99	0.98
BF1	Marshall meanDiff	-47.7479	-23.8739	Study 1	104.80	138.22	0.99	0.99	0.98	0.97
BF2	Study 1 posterior upper CI	308.2152	154.1076	Study 2A	93.36	123.58	0.74	0.74	0.64	0.60
BF3	Study 2A posterior upper CI	251.3348	125.6674	Study 2B	-19.04	96.41	0.62	0.62	1.11	1.13

PERCENT CORRECT: Young Adults (LS vs. HS)

		Prior			Likelihood		BF	Robustness checks		
		Max Difference	1 SD		meanDiff	meanDiffSE		Normal Dist	Student's t (2df)	Cauchy
Marshall BF	Estimated max effect size	25.00	12.50		-87.32	78.59	1.00	1.00	1.01	1.01
BF1	Marshall meanDiff	-87.3175	-43.6587	Study 1	-111.89	109.76	1.00	1.00	0.97	0.94
BF2	Study 1 posterior upper CI	29.5998	14.7999	Study 2A	121.94	82.12	1.02	1.02	1.05	1.07
BF3	Study 2A posterior upper CI	85.2554	42.6277	Study 2B	-25.33	65.47	0.86	0.86	0.76	0.71

PERCENT CORRECT: Older Adults (LS vs. HS)

		Prior			Likelihood		BF	Robustness checks		
		Max Difference	1 SD		meanDiff	meanDiffSE		Normal Dist	Student's t (2df)	Cauchy
Marshall BF	Estimated max effect size	75.00	37.50		102.87	209.13	0.99	0.99	0.97	0.95
BF1	Marshall meanDiff	102.8667	51.4333	Study 1	-185.66	75.62	2.15	2.15	2.89	3.16
BF2	Study 1 posterior upper CI	-12.9210	-6.4605	Study 2A	-2.73	93.16	1.00	1.00	0.99	0.99
BF3	Study 2A posterior upper CI	13.5557	6.7779	Study 2B	30.59	69.27	0.98	0.98	1.64	1.49

Chapter 5 **Supporting Information**

Appendix 1 Adverse Life Experiences Scale (ALES).
Appendix 2 Childhood Experiences of Violence Questionnaire short form (CEVQ-SF).
Appendix 3 Core ACE classifications.
Appendix 4 Longitudinal Adverse Childhood Experiences samples' descriptive statistics for biographical, lifestyle, health and well-being, by age group.

Chapter 5, Appendix 1

ADVERSE LIFE EXPERIENCES SCALE: SELF-REPORT

	Challenging things sometimes happen in our lives. Have you experienced any of the following?		What was your age when this occurred? Select all that apply:					
1	**Have you been seriously ill or injured or been in a serious accident?**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)
2	**Have you missed out on an important part of your education? (e.g., lengthy time/s away from school, didn't receive necessary learning support)**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)
3	**Have you felt lonely, or been rejected or excluded by peers?**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)
4	**Have you been hurt, threatened, picked on, or insulted by peers?**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)
5	**Have you been affected by a natural disaster? (e.g., flood, bushfire, cyclone, or earthquake)**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)
6	**Has there been a time when your family was very poor, or experienced serious financial problems?**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)
7	**Have you lived in a neighborhood that was dangerous or where you saw people being hurt?**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)
8	**As a child or young person, did you ever not have enough to eat, have to wear dirty clothes, were not taken to a doctor when needed, or were left alone without someone to look after you?**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)
9	**Has an adult repeatedly sworn at, insulted, put down, humiliated, or threatened to hurt you?**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)
10	**Have you felt that no one in your family loved you or that no one thought you were important?**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)
12	**Have you seen a family member get pushed, slapped, hit, punched, kicked, or threatened by another family or household member?**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)

13	**Have you lived with someone who misused drugs or alcohol?**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)
14	**Have you lived with someone who was depressed, had a mental illness, or who attempted suicide?**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)
15	**Has a family member been arrested, jailed, or taken away by authorities?**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)
16	**Have you had to leave a country due to war, violence, and/or persecution?**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)
17	**Have you been discriminated against or felt like an outsider? (e.g., due to your race, gender, sexuality birthplace, culture or religion)**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)
18	**Have you been isolated or removed from a community, cultural group, or land?**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)
19	**Have you been pushed, grabbed, slapped, or injured by an adult?**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)
20	**Have you been forced into sexual acts, or forced to look at sexual things?**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)
21	**Have you seen another person seriously injured or killed, or have you repeatedly heard about others getting hurt or killed?**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)
22	**Have you been in combat or exposed to war?**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)
23	**Have you had a sibling, close extended family member or close friend die?**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)
24	**Have you been exposed to any other very stressful event or experience?** **If so, please specify_____**	**YES NO**	0-1 years	2-3 years	4-5 years	6-8 years	9-12 years	Adolescence (13-17yrs)

Chapter 5, Appendix 2

Items adapted from the Childhood Experiences of Violence Questionnaire (CEVQ) by Joshi et al. (2021)

Item 1 Before age 18, how many times did any one of your parents, step-parents or guardians swear at you, or say hurtful, insulting things that made you feel like you were not wanted or loved?

Item 2 Before age 18, how many times did you see or hear any one of your parents, step-parents or guardians hit each other or another adult in your home? By adult, I mean anyone 18 years and over.

Item 3 Before age 18, how many times did a parent or caregiver spank you with their hand on your bottom (bum), or slap you on your hand?

Item 4 Before age 18, how many times did an adult slap you on the face, head or ears or hit or spank you with something hard to hurt you?

Item 5 Before age 18, how many times did an adult push, grab, shove or throw something at you to hurt you?

Item 6 Before age 18, how many times did an adult kick, bite, punch, choke, burn you, or physically attack you in some way?

Item 7 Before age 18, how many times did your parents, step-parents or guardians not take care of your basic needs, such as keeping you clean or providing food or clothing?

Item 8 Before age 18, how many times did an adult force you or attempt to force you into any unwanted sexual activity, by threatening you, holding you down or hurting you in some way?

Item 9 Before age 18, how many times did an adult touch you against your will in any sexual way? By this, I mean anything from unwanted touching or grabbing, to kissing or fondling.

Item 10 Before age 18, did you ever see or talk to the police or anyone from child protective services about any of the things you mentioned?

Item 11 Before age 18, how many times did you see or hear any one of your parents, step-parents or guardians say hurtful or mean things to each other or to another adult in your home?

Item 12 Did you ever experience the death or serious illness of a parent or a primary caretaker?

Item 13 Did you experience the divorce or separation of your parents?

Item 14 Did anyone in your family ever suffer from mental or psychiatric illness or have a “breakdown”?

Chapter 5, Appendix 3

ACE classification	Frequency[a]	Items adapted from the Childhood Experiences of Violence Questionnaire
Divorce/Separation of parent	1	Did you experience the divorce or separation of your parents
Death of parent	1	Did you ever experience the death or serious illness of a parent or a primary caretaker
Family Mental illness	1	Did anyone in your family ever suffer from mental or psychiatric illness or have a "breakdown"
Emotional abuse	≥3	Did any one of your parents/step-parents/guardians swear at you/say hurtful/insulting things-made you feel not wanted/loved?
Exposure to intimate partner violence	≥6	Did you see or hear any one of your parents, step-parents or guardians say hurtful or mean things to each other or to another adult in your home?
Exposure to intimate partner violence	≥3	Did you see or hear any one of your parents, step-parents or guardians hit each other or another adult in your home? By adult, I mean anyone 18 years and over.
Physical abuse	≥3	Did an adult slap you on the face, head or ears or hit or spank you with something hard to hurt you?
Physical abuse	≥3	Did an adult push, grab, shove or throw something at you to hurt you?
Physical abuse	≥1	Did an adult kick, bite, punch, choke, burn you, or physically attack you in some way?
Neglect	≥1	Did your parents, step-parents or guardians not take care of your basic needs, such as keeping you clean or providing food or clothing?
Sexual abuse	≥1	Did an adult force you or attempt to force you into any unwanted sexual activity, by threatening you, holding you down or hurting you in some way?
Sexual abuse	≥1	Did an adult touch you against your will in any sexual way? By this, I mean anything from unwanted touching or grabbing, to kissing or fondling.
not assigned		Did you ever see or talk to the police or anyone from child protective services about any of the things you mentioned?
not assigned		Did a parent or caregiver spank you with their hand on your bottom (bum), or slap you on your hand?

[a] Frequency refers to the number of times an item was experienced e.g. ≥3 means the item was experienced 3 or more times. For the first 3 items (divorce/separation; death of a parent; family mental illness), the variable was dichotomous (yes/no).

Reference:
Joshi, D., Raina, P., Tonmyr, L., MacMillan, H. L., & Gonzalez, A. (2021). Prevalence of adverse childhood experiences among individuals aged 45 to 85 years: a cross-sectional analysis of the Canadian Longitudinal Study on Aging. *CMAJ open, 9*(1), E158-E166. doi:10.9778/cmajo.20200064

Chapter 5, Appendix 4

Table. Longitudinal Adverse Childhood Experiences samples' descriptive statistics for biographical, lifestyle, health and well-being, by age group.

	Middle-Aged Adults		Older Adults	
	Low Stress (n=12)	**High Stress (n=5)**	**Low Stress (n=11)**	**High Stress (n=18)**
Age (years: mean (SD))	49.58 (2.21)	50 (3.67)	67.82 (1.52)	66.39 (1.02)
Sex (m:f)	7:5	3:2	5:6	7:11
Body Mass Index (BMI: mdn (IQR))[b]	24.9 (1.93)	32.39 (1.43)	30.08 (2.02)	27.39 (1.18)
Smoker vs. Non-smoker (yes:no)	2:10	1:4	0:11	0:18
Cigarette consumption, average daily (n)[a]	1.71 (0.99)	1.1 (1.1)	0 (0)	0 (0)
Alcohol drinker vs. Non-drinker (yes:no)	11:1	3:2	10:1	16:2
Alcohol consumption (weekly units in-take)[a]	9.55 (3.34)	0.23 (0.08)	5.45 (2.44)	6.61 (2.55)
Caffeine drinker vs. Non-drinker (yes:no)	8:4	4:1	9:2	15:3
Caffeine (typical daily mg in-take)[a]	129.38 (28.99)	185.8 (16.06)	183.55 (40.3)	159.06 (24.36)
Physical disability (yes:no)	0:12	0:5	0:11	1:17
Chronic Illness (yes:no)	3:9	1:4	3:8	4:14
Brief Resilience Scale[a]	3.97 (0.13)	3.73 (0.23)	3.54 (0.26)	3.5 (0.19)
PSQI (global sleep score: mdn (IQR)[b]	4 (2.3 - 4.8)	6 (4.5 - 9.5)	6.5 (3.5 - 8.5)	5.3 (4 - 7)
STAI- state[c]	30.83 (3.05)	39 (5.86)	36.73 (3.53)	32.44 (2.69)
STAI- trait[c]	32.83 (2.32)	44 (4.48)	39.91 (3.98)	36.06 (2.65)
PSS10[c]	13.67 (1.22)	21.6 (3.06)	18.09 (2.47)	14.89 (1.51)
Cumulative Life Events Score (Summed: mdn (IQR)) by age by time	619.75 (530.3 - 672.5)	807.5 (799 - 822.5)	672.5 (611 - 696)	833.5 (794 - 909)
Cumulative ACEs (0 - 8: mdn (IQR))	1.5 (1 - 3)	2 (0.5 - 3.5)	2 (1 - 3)	2 (1 - 3.3)
Lifetime ACE score (0 - 23)	2.58 (0.62)	5.2 (1.76)	3.36 (0.72)	3.89 (0.59)
Age-corrected Chronicity Index	0.09 (0.02)	0.18 (0.07)	0.09 (0.02)	0.11 (0.02)

This table provides data for ACE participants who completed time 1 and time 3 (N=46). All dichotomous variables represent time 3.

[a] Mean of time 1 and time 3 (SE). Standard error obtained via BCa Bootstrap with 1000 samples.

[b] Median and interquartile range based on Mean(time1,time3).

[c] Values collected at time 3 only. Mean (SE). Standard error obtained via BCa Bootstrap with 1000 samples.

Chapter 6	**Supporting Information**
Appendix 1	SRRQ (updated version).
Appendix 2	Original Instructions for SRRS.
Appendix 3	SRRS updated version.
Appendix 4	Personal experience of SRRS life events.
Appendix 5	Loneliness questionnaire.
Appendix 6	Bayes Factor sensitivity analysis for all Mann-Whitney U comparisons.
Appendix 7	Social Readjustment Rating Scale by demographic category (unabridged categories).
Appendix 8	Descriptive statistics for SRRS events by unabridged sub-group demographics.
Appendix 9	Bayesian Kendall's tau correlation between event ratings and degree to which these were based on personal experience.

Chapter 6, Appendix 1

Social Readjustment Rating Questionnaire

The Social Readjustment Rating Scale

1. Social readjustment includes the amount and duration of change in one's accustomed pattern of life resulting from various life events. Social readjustment measures the intensity and length of time necessary for you to adapt, *regardless of the desirability of this event*.

2. *Use all of your own experience*, as well as what you have learned to be the case for others, in judging the amount of adjustment required. You need not have experienced something yourself to have an opinion about the amount of adjustment it would take.

3. Suppose that marriage takes 50 units of adjustment. Compare each of the events below to marriage and think to yourself, "Would this event require more or less adjustment than marriage?", "Would the readjustment take longer or shorter to accomplish?" If you decide the readjustment is more intense and protracted, enter a *proportionately larger* number than 50 for the event. If you decide the event represents less and shorter readjustment than marriage then indicate how much less by providing a *proportionately smaller* number next to the event. If it is equal to marriage, enter the number 50 next to the event.

Kindly use the above criteria to provide your chosen value for each of the events below relative to marriage, which is defined as 50.

Use any number between 0 - 100.

Chapter 6, Appendix 1

	Life Event	Rating
1	Troubles with the boss	
2	Detention in jail or other institution	
3	Death of a spouse or life partner	
4	Major change in sleeping habits (a lot more or a lot less, or change in part of day when asleep)	
5	Death of a close family member	
6	Major change in eating habits (a lot more or a lot less food intake, or very different meal hours or surroundings)	
7	Foreclosure/repossession on mortgage or loan	
8	Revision of personal habits (dress, manners, associations, etc.)	
9	Death of a close friend	
10	Minor violations of the law (e.g. traffic ticket, disturbing the peace)	
11	Outstanding personal achievement	
12	Pregnancy (either yourself or being the father)	
13	Major change in the health or behaviour of a family member	
14	Sexual difficulties	
15	In-law troubles	
16	Major change in number of family get-togethers (e.g. a lot more or a lot less than usual)	
17	Major change in financial state (e.g. a lot worse off or a lot better off than usual)	
18	Gaining a new family member (e.g. through birth, adoption, grandparent moving in, etc.)	
19	Change in residence	
20	Son or daughter leaving home (e.g. marriage, attending college, etc.)	
21	Marital separation	
22	Major change in religious activities (e.g. a lot more or a lot less than usual)	
23	Marital reconciliation	
24	Losing your job (redundancy, dismissal, etc.)	
25	Divorce	
26	Changing to a different line of work	
27	Major change in the number of arguments with spouse or life partner (e.g. either a lot more or a lot less than usual regarding child-rearing, personal habits, etc.)	
28	Major change in responsibilities at work (e.g. promotion, demotion, lateral transfer)	
29	Spouse or life partner begins or stops working	
30	Major change in work hours or conditions	
31	Major change in usual type and/or amount of recreation	
32	Taking on a mortgage or loan for a major purchase (e.g. purchasing a home, business, etc.)	
33	Taking on a loan for a lesser purchase (e.g. purchasing a car or furniture, paying for college fees, etc.)	
34	Major personal injury or illness	

	Life Event (cont'd.)	Rating
35	Major business readjustment (e.g. merger, reorganization, bankruptcy, etc.)	
36	Major change in social activities (e.g. clubs, dancing, movies, visiting, etc.)	
37	Major change in living conditions (e.g. building a new home, remodelling, deteriorating of home or neighbourhood)	
38	Retirement from work	
39	Vacation	
40	Christmas	
41	Changing to a new school	
42	Beginning or ceasing formal schooling	
43	Single person, living alone	

REFERENCE:

Holmes, T. H., & David, E. M. (Eds.). (1989). *Life change, life events, and illness: selected papers*: Praeger Publishers.

SRRS item wording changes.

Original item wording	New item wording
Death of spouse	Death of a spouse or life partner
Pregnancy	Pregnancy (either yourself or being the father)
Marital separation from mate	Marital separation
Major change in church activities (e.g. a lot more or a lot less than usual)	Major change in religious activities (e.g. a lot more or a lot less than usual)
Marital reconciliation with mate	Marital reconciliation
Being fired from work	Losing your job (redundancy, dismissal, etc.)
Major change in the number of arguments with spouse (e.g. either a lot more or a lot less than usual regarding child-rearing, personal habits, etc.)	Major change in the number of arguments with spouse or life partner (e.g. either a lot more or a lot less than usual regarding child-rearing, personal habits, etc.)
Spouse begins or stops working outside the home	Spouse or life partner begins or stops working
Taking on a mortgage greater than $10,000 (e.g. purchasing a home, business, etc.)	Taking on a mortgage or loan for a major purchase (e.g. purchasing a home, business, etc.)
Taking on a mortgage or loan less than $10,000 (e.g. purchasing a car or furniture, paying for college fees, etc.)	Taking on a loan for a lesser purchase (e.g. purchasing a car or furniture, paying for college fees, etc.)

Chapter 6, Appendix 2

Social Readjustment Rating Questionnaire original instructions

The Social Readjustment Rating Scale instructions only (Holmes & Rahe, 1967, p. 213)

A. Social readjustment includes the amount and duration of change in one's accustomed pattern of life resulting from various life events. As defined, social readjustment measures the intensity and length of time necessary to accommodate to a life event, *regardless of the desirability of this event.*

B. You are asked to rate a series of life events as to their relative degrees of necessary readjustment. In scoring*, use all of your experience* in arriving at your answer. This means personal experience where it applies as well as what you have learned to be the case for others. Some persons accommodate to change more readily than others; some persons adjust with particular ease or difficulty to only certain events. Therefore, strive to give your opinion of the average degree of readjustment necessary for each event rather than the extreme.

C. The mechanics of rating are these : Event 1, Marriage, has been given an arbitrary value of 500. As you complete each of the remaining events think to yourself, "Is this event indicative of more -or less readjustment than marriage?" "Would the readjustment take longer or shorter to accomplish?" If you decide the readjustment is more intense and protracted, then choose a *proportionately larger* number and place it in the blank directly opposite the event in the column marked "VALUES." If you decide the event represents less and shorter readjustment than marriage then indicate how much less by placing a proportionately smaller number in the opposite blank. (If an event requires intense readjustment over a short time span, it may approximate in value an event requiring less intense readjustment over a long period of time.) If the event is equal in social readjustment to marriage, record the number 500 opposite the event.

REFERENCE:

Holmes, T. H., & Rahe, R. H. (1967). The social readjustment rating scale. *Journal of psychosomatic research*.

Chapter 6, Appendix 3

Updated SRRS and table showing changes to items

Social Readjustment Rating Scale 2022

Life Event	Yes	No
Marriage	O	O
Losing your job (e.g. redundancy, dismissal, etc.)	O	O
Change in religious activities (e.g. a lot more or a lot less than usual)	O	O
Revision of personal habits (e.g. dress, manners, associations)	O	O
Sexual difficulties	O	O
Trouble with in-laws	O	O
Major change in health or behaviour of family member	O	O
Taking on a mortgage or loan for a major purchase (e.g. home, business)	O	O
Taking on a loan for a lesser purchase (e.g. car, furniture)	O	O
Change in eating habits (e.g. a lot more or a lot less food intake, or very different meal hours or surroundings)	O	O
Pregnancy either yourself or being the father	O	O
Troubles with boss	O	O
Change in financial state (e.g. a lot worse off or a lot better off than usual)	O	O
Change to a different line of work	O	O
Marital reconciliation	O	O
Change in number of arguments with spouse/life partner (e.g. either a lot more or a lot less than usual regarding child-rearing, personal habits, etc.)	O	O
Change in living conditions (e.g. building new home, remodelling, deterioration of neighbourhood or home)	O	O

Outstanding personal achievement	O	O
Retirement	O	O
Business readjustment (e.g. merger, reorganisation, bankruptcy)	O	O
Spouse/life partner begins or stops work	O	O
Change in residence	O	O
Change in sleeping habits (e.g. a lot more or a lot less, or change in part of day when asleep)	O	O
Gain of new family member (e.g. through birth, adoption, grandparent moving in)	O	O
Change in work hours or conditions	O	O
Son or daughter leaving home (e.g. attend college, marriage)	O	O
Change in responsibilities at work (e.g. promotion, demotion, lateral transfer)	O	O
Change in social activities (e.g. clubs, dancing, movies, visiting)	O	O
Divorce	O	O
Personal injury or illness	O	O
Death of close family member	O	O
Change in recreation type/amount	O	O
Death of spouse/life partner	O	O
Change in number of family get-togethers (e.g. a lot more or a lot less than usual)	O	O
Detention in jail or other institution	O	O
Marital separation	O	O
Vacation	O	O

Foreclosure/repossession on mortgage or loan	O	O
Death of close friend	O	O
Changing to a new school	O	O
Begin or end formal schooling	O	O
Christmas	O	O
Minor violations of the law (e.g. traffic/parking tickets)	O	O
Single person, living alone	O	O

Chapter 6, Appendix 3

Changed items:

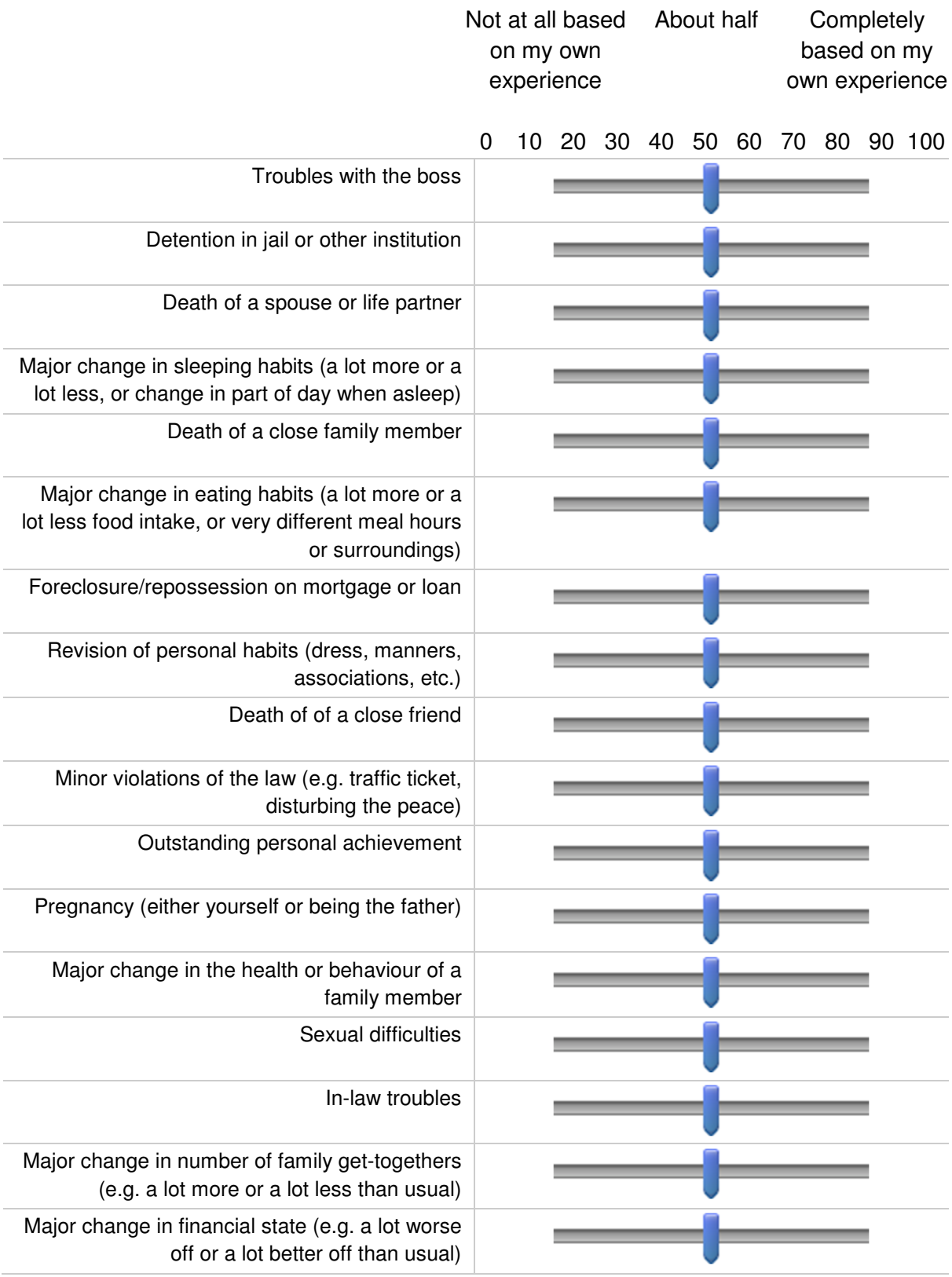
Original item rank	Original Item wording	New item wording
1	Death of spouse	Death of spouse/life partner
4	Jail term	Detention in jail or other institution
8	Fired at work	Losing your job (e.g. redundancy, dismissal, etc.)
11	Change in health of family member	Major change in health or behaviour of family member
12	Pregnancy	Pregnancy either yourself or being the father
13	Sex difficulties	Sexual difficulties
14	Gain of new family member	Gain of new family member (e.g. through birth, adoption, grandparent moving in)
15	Business readjustment	Business readjustment (e.g. merger, reorganisation, bankruptcy)
16	Change in financial state	Change in financial state (e.g. a lot worse off or a lot better off than usual)
19	Change in number of arguments with spouse	Change in number of arguments with spouse/life partner (e.g. either a lot more or a lot less than usual regarding child-rearing, personal habits, etc.)
20	Mortgage over $10,000	Taking on a mortgage or loan for a major purchase (e.g. home, business)
21	Foreclosure of mortgage or loan	Foreclosure/repossession on mortgage or loan
22	Change in responsibilities at work	Change in responsibilities at work (e.g. promotion, demotion, lateral transfer)
23	Son or daughter leaving home	Son or daughter leaving home (e.g. attend college, marriage)
26	Wife begin or stop work	Spouse/life partner begins or stops work
27	Begin or end schooling	Begin or end formal schooling
28	Change in living conditions	Change in living conditions (e.g. building new home, remodelling, deterioration of neighbourhood or home)
29	Revision of personal habits	Revision of personal habits (e.g. dress, manners, associations)
33	Change in schools	Changing to a new school
34	Change in recreation	Change in recreation type/amount
35	Change in church activities	Change in religious activities (e.g. a lot more or a lot less than usual)
36	Change in social activities	Change in social activities (e.g. clubs, dancing, movies, visiting)
37	Mortgage of loan less than $10,000	Taking on a loan for a lesser purchase (e.g. car, furniture)
38	Change in sleeping habits	Change in sleeping habits (e.g. a lot more or a lot less, or change in part of day when asleep)
39	Change in number of family get-togethers	Change in number of family get-togethers (e.g. a lot more or a lot less than usual)
40	Change in eating habits	Change in eating habits (e.g. a lot more or a lot less food intake, or very different meal hours or surroundings)
43	Minor violations of the law	Minor violations of the law (e.g. traffic/parking tickets)

Chapter 6, Appendix 4

Personal experience of SRRS life events

At the start of this survey you were asked to rate a range of life events by comparing them to marriage. To what extent was your chosen rating based on your own personal experience?

Please slide the scale to indicate as best you can how much your rating was based on your own experience from '***not at all based on my own experience***' **(0)** to '***completely based on my own experience***' **(100)**.


Not at all based on my own experience
About half
Completely based on my own experience
0 10 20 30 40 50 60 70 80 90 100
Troubles with the boss
Detention in jail or other institution
Death of a spouse or life partner
Major change in sleeping habits (a lot more or a lot less, or change in part of day when asleep)
Death of a close family member
Major change in eating habits (a lot more or a lot less food intake, or very different meal hours or surroundings)
Foreclosure/repossession on mortgage or loan
Revision of personal habits (dress, manners, associations, etc.)
Death of of a close friend
Minor violations of the law (e.g. traffic ticket, disturbing the peace)
Outstanding personal achievement
Pregnancy (either yourself or being the father)
Major change in the health or behaviour of a family member
Sexual difficulties
In-law troubles
Major change in number of family get-togethers (e.g. a lot more or a lot less than usual)
Major change in financial state (e.g. a lot worse off or a lot better off than usual)

Chapter 6, Appendix 4

Gaining a new family member (e.g. through birth, adoption, grandparent moving in, etc.)	
Change in residence	
Son or daughter leaving home (e.g. marriage, attending college, etc.)	
Marital separation	
Major change in religious activities (e.g. a lot more or a lot less than usual)	
Marital reconciliation	
Losing your job (made redundant, dismissed, etc.)	
Divorce	
Changing to a different line of work	
Major change in the number of arguments with spouse/life partner (e.g. either a lot more or a lot less than usual regarding child-rearing, personal habits, etc.)	
Major change in responsibilities at work (e.g. promotion, demotion, lateral transfer)	
Spouse/life partner begins or stops working	
Major change in work hours or conditions	
Major change in usual type and/or amount of recreation	
Taking on a mortgage or loan for a major purchase (e.g. purchasing a home, business, etc.)	
Taking on a loan for a lesser purchase (e.g. car, furniture)	
Major personal injury or illness	
Major business readjustment (e.g. merger, reorganization, bankruptcy,etc.)	
Major change in social activities (e.g. clubs, dancing, movies, visiting, etc.)	
Major change in living conditions (e.g. building a new home, remodelling, deteriorating of home or neighbourhood)	
Retirement from work	

Chapter 6, Appendix 4

Vacation	
Christmas	
Changing to a new school	
Beginning or ceasing formal schooling	
Single person, living alone	

Chapter 6, Appendix 5

Loneliness questionnaire

ONS Website contents *verbatim (Robards, 2022)*:

"Specifically, we recommend four questions to capture different aspects of loneliness. The first three questions are from the University of California, Los Angeles (UCLA) (Russell, 1996) three-item loneliness scale (Hughes, Waite, Hawkley, & Cacioppo, 2004). The wording of the UCLA questions and response options are taken from the English Longitudinal Study of Ageing (Lee et al., 2021). The last is a direct question about how often the respondent feels lonely, currently used on the Community Life Survey. For those aged 16 years and over, the loneliness measures should be as in Table 1."

Table 1: Recommended measures of loneliness for adults

Measures	Items	Response categories
The three-item UCLA Loneliness scale	1. How often do you feel that you lack companionship?	Hardly ever or never, Some of the time, Often
	2. How often do you feel left out?	Hardly ever or never, Some of the time, Often
	3. How often do you feel isolated from others?	Hardly ever or never, Some of the time, Often
The direct measure of loneliness	How often do you feel lonely?	Often/always, Some of the time, Occasionally, Hardly ever, Never

Source: Office for National Statistics (Robards, 2022)
[https://www.ons.gov.uk/peoplepopulationandcommunity/wellbeing/methodologies/measuringlonelinessguidanceforuseofthenationalindicatorsonsurveys]

R-UCLA Scoring:

Items 1 – 3: Hardly ever or never = 1, Some of the time = 2, Often = 3

A higher score indicates a greater degree of loneliness.

REFERENCES:

Hughes, M. E., Waite, L. J., Hawkley, L. C., & Cacioppo, J. T. (2004). A Short Scale for Measuring Loneliness in Large Surveys: Results From Two Population-Based Studies. *Res Aging, 26*(6), 655-672. doi:10.1177/0164027504268574

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Chapter 6, Appendix 6

Table. Robustness Checks for all Mann-Whitney U Bayesian Analyses

		Cauchy value			
		userPrior (medium)	wide prior	ultrawide prior	
Variable of interest	**Comparison**	**0.707**	**1.000**	**1.414**	**N**
	overall SRRS weights original sample vs. new sample	6.22	5.08	3.64	86
	Wording change weight difference (new - original)	0.35	0.29	0.21	43
	Normative sample vs. 'old-older' adults	0.24	0.17	0.12	86
age group	YA vs. MA	0.23	0.16	0.12	86
	YA vs. OA	0.22	0.16	0.12	86
	MA vs. OA	0.23	0.16	0.12	86
sex	Males vs. Females	1.42	1.22	0.90	86
age group (YA vs. MA)	family	0.21	0.11	0.08	407
	financial	0.26	0.14	0.10	407
	personal	0.13	0.09	0.06	407
	work	0.13	0.09	0.06	407
age group (YA vs. OA)	family	0.16	0.11	0.08	249
	financial	0.14	0.10	0.07	249
	personal	0.15	0.11	0.08	249
	work	0.14	0.11	0.08	249
age group (MA vs. OA)	family	0.11	0.08	0.06	424
	financial	0.19	0.16	0.11	424
	personal	0.12	0.08	0.06	424
	work	0.11	0.08	0.06	424
sex (m vs. f)	family	73382.37	57806.85	3206.45	538
	financial	27.22	30.46	18.36	538
	personal	4039.19	3507.24	3606.85	538
	work	367.71	2189.98	3213.54	538
ethnicity (white vs. non-white)	family	0.13	0.08	0.06	540
	financial	0.20	0.08	0.06	540
	personal	0.13	0.08	0.06	540
	work	0.12	0.07	0.05	540
religion (no religion vs. religion)	family	0.24	0.16	0.12	540
	financial	0.27	0.19	0.15	540
	personal	0.59	0.51	0.38	540
	work	0.28	0.22	0.16	540
relationship status (married vs. unmarried)	family	1.74	1.61	1.14	540
	financial	0.11	0.08	0.06	540
	personal	0.16	0.15	0.11	540
	work	0.13	0.12	0.09	540
employment status (employed vs. unemployed)	family	0.20	0.12	0.09	540
	financial	0.11	0.08	0.06	540
	personal	0.10	0.07	0.05	540
	work	0.15	0.12	0.09	540
single person, living alone	age group (YA vs. MA)	0.17	0.11	0.08	407
	age group (YA vs. OA)	0.43	0.34	0.26	249
	age group (MA vs. OA)	0.16	0.10	0.13	424
	sex (males vs. females)	0.52	0.34	0.25	538
	ethnicity (white vs. non-white)	0.14	0.10	0.07	540
	religion (religion vs. no religion)	1.68	0.99	0.71	540
	relationship status (married vs. not married)	1.89	1.39	1.01	540
	employment status (employed vs. unemployed)	0.12	0.09	0.06	540

This table provides sensitivity anayses for all between-subjects comparisons and the respective sample size used in each case. Sensitivity analyses were performed by adjusting the the Cauchy distribution which changes the likelihood of capturing evidence of an effect.

Chapter 6, Appendix 7

Social Readjustment Rating Scale by category (Rahe, 1975, p. 251)

Family

1. Death of a spouse
2. Divorce
3. Marital separation
4. Death of close family member
5. Marriage
6. Marital reconciliation
7. Major change in health of family
8. Pregnancy
9. Major change in arguments w/wife
10. Son/daughter leaving home
11. In-law troubles
12. Wife starting or ending work
13. Major change in family get-togethers
14. Addition of new family member

Personal

15. Detention in jail
16. Major personal injury or illness
17. Sexual difficulties
18. Death of a close friend
19. Outstanding personal achievement
20. Start or end of formal schooling
21. Major change in living conditions
22. Major revision of personal habits
23. Changing to a new school
24. Change in residence
25. Major change in recreation
26. Major change in church activities
27. Major change in sleeping habits
28. Major change in eating habits
29. Vacation
30. Christmas
31. Minor violations of the law

Work

32. Being fired from work
33. Retirement from work
34. Major business adjustment
35. Changing to a different line of work
36. Major change in work responsibilities
37. Trouble with the boss
38. Major change in working conditions

Financial

39. Major change in financial state
40. Mortgage or loan over 10,000
41. Mortgage foreclosure
42. Mortgage or loan less than 10,000

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Chapter 6, Appendix 8

Table. Descriptive statistics for SRRS events by unabridged sub-group demographics, categorised as family, financial, personal or work items.

		Mean SRRS weights			
		family items	financial items	personal items items	work items
Age	sub-groups	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
	< 30 years	53.6 (44.8 - 61)	50 (33.8 - 55.8)	35.5 (28.6 - 45.3)	42.1 (31.6 - 54.3)
	30 to 60 years	54.6 (45.7 - 64.3)	45 (35 - 52.5)	34.7 (28.9 - 43.3)	43.6 (32.1 - 52.9)
	> 60 years	53.9 (46.1 - 61.1)	46.5 (35.6 - 58.8)	33.4 (26.4 - 46.6)	42.9 (33.2 - 54.7)
Sex					
	female	57.1 (48.9 - 64.9)	47.5 (37.5 - 56.2)	36.9 (30.6 - 46.5)	45.7 (35.7 - 55.7)
	male	50.4 (42.4 - 58.8)	42.5 (30 - 55)	32.3 (24.7 - 40.5)	40 (29.3 - 50)
ethnicity					
	white	54.3 (46.4 - 61.8)	46.3 (35 - 55)	34.2 (27.9 - 43.7)	42.9 (32.9 - 52.9)
	mixed race	50.4 (39.8 - 59.6)	41.3 (33.8 - 60)	38.2 (30.8 - 44.5)	43.9 (30.7 - 50)
	asian (southern/southeastern asia)	50.7 (37 - 60.6)	42.5 (23 - 58.4)	30.6 (19 - 44.8)	43.6 (23.5 - 54.3)
	chinese (east asian)	58.6 (55.4 - 67.1)	50 (35 - 52.5)	35.3 (32.1 - 44.5)	48.6 (35.7 - 57.1)
	black (any region)	60.4 (46.8 - 67.9)	52.5 (42.5 - 65)	44.7 (32.6 - 49.8)	51.4 (40 - 60.1)
religion					
	no religion	53.6 (45.6 - 60.7)	45 (35 - 54.1)	33.9 (28 - 41.1)	42.1 (32.1 - 52.1)
	Christian	63 (43.7 - 73.3)	52.5 (26.9 - 77.2)	43.7 (27.1 - 48.2)	47.1 (32 - 53.2)
	Buddhist	55.7 (46.4 - 64.4)	47.5 (35 - 57.5)	36.1 (28.3 - 47.1)	44.3 (34.3 - 55.3)
	Hindu	49.6 (31.8 - 59.1)	58.8 (27.5 - 83.1)	32.8 (19.6 - 47.2)	45.7 (25.4 - 60.1)
	Jewish	48.7 (36.2 - 56.9)	38.1 (30.6 - 42.5)	28.1 (20.9 - 36.4)	37.5 (28.1 - 45.7)
	Muslim	50.4 (31.5 - 62.2)	42.5 (20.3 - 55)	33.7 (16.6 - 45.5)	32.9 (18.8 - 45.4)
	Sikh	51.8 (44.9 - 72)	58.8 (36.9 - 66.3)	28.7 (25.1 - 62.2)	53.6 (32.9 - 75.7)
	any other religion	55 (46.4 - .)	52.5 (42.5 - .)	31.6 (26.9 - .)	48.6 (35.7 - .)
relationship status					
	divorced	55 (45.9 - 58.9)	47.5 (35.6 - 56.3)	33.9 (31 - 41.7)	47.9 (34.3 - 52.5)
	in a relationship	50.5 (43.1 - 57.1)	41.3 (32.8 - 51.8)	34.3 (25.9 - 40.7)	38.2 (28.4 - 47)
	married/LTR	55 (46.8 - 64.5)	46.5 (35 - 55)	34.7 (28.4 - 45.3)	42.9 (32.9 - 54.3)
	separated	40.8 (16.9 - 54.4)	65 (10.6 - 69.8)	28 (17.4 - 40.3)	31.4 (14.3 - 51.4)
	single	54.3 (44.3 - 61.8)	46.3 (34.4 - 55.6)	35.8 (27.1 - 44.7)	44.3 (32.9 - 53.9)
	widowed/LP died	50.4 (45 - 58.8)	46.3 (35.3 - 59.7)	29.9 (28.2 - 48.8)	44.6 (29.5 - 52.5)
employment status					
	currently unemployed, looking for work	53.9 (43.9 - 63.5)	49.4 (41.3 - 56.9)	31.4 (26.2 - 38.2)	42.1 (31.4 - 54.1)
	full-time or part-time employed	54.3 (46.1 - 63)	46 (35 - 55)	34.7 (28.2 - 44.5)	42.9 (32.9 - 55)
	long-term sick or disabled	61.1 (57.9 - 67.4)	52.5 (47.5 - 65)	41.6 (36.9 - 49.5)	49.3 (45.7 - 61.4)
	looking after home or family	58.3 (50.8 - 64.4)	47.5 (37.8 - 52.5)	36.1 (32.1 - 42.9)	43.6 (32.3 - 50.5)
	other*	47.1 (40 - 55.7)	35 (28.1 - 50.6)	34.5 (22.1 - 38.7)	32.9 (27.9 - 54.6)
	retired	51.6 (44.1 - 59.3)	45 (33.8 - 58.1)	32.2 (25.3 - 46.1)	41.4 (29.6 - 52.4)
	student (p/t or f/t) and currently unemployed	51.1 (44.7 - 60.4)	48.8 (33.8 - 57.5)	37.4 (31.3 - 47.6)	44.3 (35 - 54.3)

*other combines 'have never worked' (n=2) and the entry where 1 person gave no specific details.

Chapter 6, Appendix 9

Table. Bayesian Kendall's tau correlation between event ratings and degree to which these were based on personal experience.

Rating vs. Personal experience of event	Kendall tau B	Lower 95% CI[a]	Upper 95% CI[a]	BF_{10}
Death of a close family member	0.146	0.09	0.20	19900.33
Detention in jail or other institution	-0.137	-0.19	-0.08	4564.74
Major change in the health or behaviour of a family member	0.135	0.08	0.19	3109.20
Major change in social activities	0.128	0.07	0.18	951.76
Major change in religious activities	0.125	0.07	0.18	672.81
Foreclosure/repossession on mortgage or loan	-0.108	-0.16	-0.05	62.30
Major change in sleeping habits	0.091	0.03	0.15	7.84
Major change in eating habits	0.089	0.03	0.15	6.53
Retirement from work	-0.088	-0.15	-0.03	6.00
Major change in usual type and/or amount of recreation	0.088	0.03	0.14	5.71
Major business readjustment	-0.084	-0.14	-0.03	4.00
Gaining a new family member	0.084	0.03	0.14	3.73
Revision of personal habits	0.083	0.03	0.14	3.33
Major change in number of family get-togethers	0.082	0.03	0.14	3.19
Sexual difficulties	0.081	0.03	0.14	3.00
Changing to a new school	0.077	0.02	0.13	1.98
Beginning or ceasing formal schooling	0.077	0.02	0.13	1.90
Change in residence	0.065	0.01	0.12	0.68
In-law troubles	0.063	0.01	0.12	0.61
Major change in the number of arguments with spouse-life partner	0.054	0.00	0.11	0.32
Troubles with the boss	0.053	0.00	0.11	0.31
Minor violations of the law	-0.05	-0.11	0.01	0.25
Vacation	-0.048	-0.11	0.01	0.22
Son or daughter leaving home	-0.047	-0.10	0.01	0.21
Spouse/life partner begins or stops working	-0.045	-0.10	0.01	0.19
Major change in financial state	0.042	-0.02	0.10	0.16
Outstanding personal achievement	0.037	-0.02	0.09	0.13
Marital reconciliation	-0.037	-0.09	0.02	0.13
Losing your job	-0.036	-0.09	0.02	0.12
Death of a close friend	-0.034	-0.09	0.02	0.11
Pregnancy	-0.03	-0.09	0.03	0.10
Changing to a different line of work	-0.029	-0.09	0.03	0.09
Christmas	-0.029	-0.09	0.03	0.09
Marital separation	0.025	-0.03	0.08	0.08
Major change in living conditions	0.023	-0.03	0.08	0.08
Major personal injury or illness	0.021	-0.04	0.08	0.08
Major change in responsibilities at work	0.019	-0.04	0.08	0.07
Death of a spouse or life partner	0.014	-0.04	0.07	0.06
Divorce	0.014	-0.04	0.07	0.06
Taking on a loan for a lesser purchase	-0.012	-0.07	0.05	0.06
Single person, living alone	-0.008	-0.07	0.05	0.06
Taking on a mortgage or loan for a major purchase	-0.003	-0.06	0.05	0.06
Major change in work hours or conditions	-0.004	-0.06	0.05	0.06

Bayes Factors (BFs) above the upper dotted line support H1 (that ratings correlate with personal experience).

BFs below the lower dotted line support H0 (that ratings do not correlate with personal experience).

BFs between the dotted lines support neither H1 nor H0 (i.e. evidence is inconclusive).

[a] CI = Credible Interval

N = 536