Staying gutsy during aging: the cost of stress on attention

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Acknowledgements

Three years does not seem like a long time but looking back to the start of this PhD a lot has happened, both good and bad. Starting a PhD during the tail end of a global pandemic is unsurprisingly, rather disruptive. The original plan for the thesis had to change dramatically because in person testing at the time was still restrictive. I could not collect saliva samples or measure brain activity. The first few months into the PhD seemed like a scramble to fit something new into something old to maintain some through line between proposal and actual outcome. That seems so long ago now because once the work starts proper everything else can fade into the background and it is easy to lose track of time, or at least the passage of time. However, there are some major people and events I would like to acknowledge.

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General Abstract

This thesis was carried out with two overall aims. The first was to test a possible interaction between cumulative stress and age on attentional processing. The second was to investigate the validity of a new theory of stress - the generalised unsafety theory of stress (GUTS; Brosschot, *et al.,* 2016). Over the course of this project, 1074 individuals took part in four experiments to help address these aims.

Previous work has reported an interaction effect where older high stress participants perform worse than older low stress participants and worse than younger high or low stress participants. This interaction, reported for various cognitive tasks such as inhibition and working memory, has not yet been tested on attention. In chapters 2 and 3, we therefore expanded on previous work by measuring attentional performance (using the attentional blink task) and life time exposure to stress using self-report measures. We report mixed evidence for the stress/age interaction effect on attention. We suggest two reasons for the mixed results. The first being the difference in task design deployed between chapters leading to compensatory strategies reducing the effect of stress. The second is that increased age is largely associated with worse attentional performance in rapid attentional tasks such as the attentional blink task and so little scope is left to find the subtler effects of stress and this is linked to task load. Previous work also reported a stress/age interaction effect for resting state Delta power as measured by electroencephalogram. We do not report an increase in delta power for older, high stress participants as predicted or an association between delta power and task performance.

Our other main aim was based on the proposition that the current understanding of stress fails to provide an explanation for the maintenance of chronic stress. GUTS attempts to address this suggesting a perception of generalised unsafety (GU) is the mechanism for chronic stress maintenance and that when important life domains are compromised they contribute to GU perception. We tested two of these domains: the social network and the body domain, in chapters 4 and 5. We measured participants self-report loneliness, social

fear, as well as perceived social support and self-esteem for the social network domain. We measured height, weight, BMI and overall physical activity for the body domain and used measured perceived stress as a proxy for GU. We found strong self-report evidence for the social network domain but not the body domain. However, we found no behavioural evidence for GUTS when using a valence discrimination task. We suggested this could be due to the problems of trying to operationalise GU. We also suggested GUTS might predict the perception of stress but not the behaviour associated with stress.

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Chapter 1 – General Introduction

1.1 Stress

1.1.1 Introducing Stress

Stress is a word synonymous with negative emotion. This is not surprising as stress often induces negative affect and is frequently provoked by negative or even life-threatening situations. Classically, stress was seen as a response to a perceived threat to internal homeostasis, where threat is the cognitive appraisal that one may not have the necessary resources to deal with the current demands placed on them (Denson, *et al*, 2009). Upon detecting a stressor, a threat to homeostasis, stress hormones are released throughout the body to induce short- and long-term physiological changes to promote adaptation. This process is referred to as the stress response (or allostasis) and the body is now in a state of stress (or an allostatic state). Once homeostasis is restored, the stress response is halted or 'turned off' (McEwen, 2004). In short, upon the perception of threat, the stress response is triggered, which puts the body in a state of action-preparedness, whereby the individual is physiologically able to deal with the threat. However, theories of stress are continuously evolving. Recently, a new theory suggested that upon the perception of unsafety and not threat, the stress response is uninhibited instead of triggered. This theory, called the Generalised Unsafety Theory of Stress (GUTS). It differs from classic theories on stress in that it is not the perception of threat that leads to a response but the perception of generalised unsafety (GU) and that the stress response is the default state of a biological system instead of being triggered by threat (Brosschot, *et al.*, 2016).

Physiologically, during the stress response the amygdala and brainstem causes the eventual release of cortisol and nor/adrenaline which in turn causes a cascade of changes within a biological system to deal with threat, or unsafety (Joëls & Baram, 2009; Romero & Butler, 2007; Sapolsky, *et al.,* 2000). Its evolutionary benefits cannot be understated when we consider that stress was a powerful enough influence on survival that its physiological mechanics were inherited through genes. In some, stress even increases performance and

acts as a motivator (Aronson, *et al.,* 2002; Norem & Cantor, 1986; Crum, *et al.,* 2013). Stress, however, is not sustainable long-term and prolonged over-activation can lead to a myriad of physiological diseases and psychopathologies. The strain placed on the body from this leads to general wear and tear of the body and is referred to as allostatic load in the allostasis account of stress (McEwen and Stellar, 1993).

There is a clear distinction between short-term stress, referred to as acute stress and prolonged stress, known as chronic stress. As acute stress is short lived and helps deal with immediate perceived homeostatic disruption (real or imagined) it is often adaptive. On the other hand, chronic stress lasts for a minimum of 3 months; sometimes it lasts for years, and leaves an organism constantly exposed to stress mediators. It is consequently maladaptive. A third measure of stress, cumulative stress, is the sum total experiences of stress over a lifetime that are not necessarily traumatic or long lasting. However, the repeated exposure to stress mediators in this fashion can also have maladaptive consequences (Pesonen, *et al.,* 2013). Regardless of the category of stress, stress mediators act to change physiological factors so that an organism can efficiently deal with the current stressor. The long-term exposure to these stress mediators leaves one susceptible to disease and cognitive disruption. However, while the detrimental physiological effects of stress are well-documented, cognitive disruption resulting from over exposure to stress has far more mixed results.

A series of studies attempted to reconcile these discrepant results and found cognitive disruption resulted from the interaction of age and chronic stress (Peavy, 2009) and accumulative stress in relation to memory and response inhibition (Marshall, *et al.,* 2015; Marshall, *et al.,* 2016a; Marshall, *et al.,* 2016b; Marshall, *et al.,* 2018). These results suggest cognitive disruption from over-exposure to stress mediators occurs over a lifetime. This suggests the stress/age interaction may also affect other cognitive domains, such as attention. Furthermore, do classical theories of stress or new ones such as GUTS better explain these findings? Before attempting to answer these questions, it is important to understand in more detail what the stress response is, and what its effect is on cognition.

1.1.2 The Biology of Stress

The stress response is the classic fight or flight response upon the perception of threat. While there are some universal threats, what constitutes a threat is subjective and seems to depend on a mixture of genetics and past experience (McEwen and Stellar, 1993). This subjective state of perceiving threat is called stress. Information related to the stressor is sent from sensory systems to the brain, which in turn activates neural and neuroendocrine systems to minimise the potential cost of the stressor (Ulrich-Lai & Herman, 2009). This leads to the activation of a tide of stress mediators that cause cascading effects within the body. This is the stress response, otherwise known as an allostatic state or allostasis. Allostasis is the term for when the body tries to correct homeostatic deviation. The need to deal with systemic physiological threats, such as pain or infection, is immediate and so allostasis produces an immediate behavioural effect. Furthermore, psychogenic stressors, that is to say non-physiological stressors, also facilitate allostasis. The former involves the autonomic nervous system (ANS) while the latter requires processing in the forebrain to initiate. Allostasis also facilitates memory consolidation as a way to learn and adapt for future encounters with the same stressor (Krugers, *et al.*, 2012). In this way, stress and allostasis are adaptive and a two-step process. There are different types of stressors (physical, psychological, short and long-term) and so there are also many types of stress mediators that cause differential effects. For example, different areas of the hippocampus and amygdala show increased activation depending on whether the stressor is systemic or psychogenic (Jankford & Herman, 2008; Joëls & Baram, 2009; Ulrich-Lai & Herman, 2009). However, there is a large overlap between the effects of these mediators and even though the systems themselves are segregated, they act within the central nervous system (CNS) to affect the entire system (Joëls & Baram, 2009). Nevertheless, as mentioned above, allostasis is a two-step process that involves two distinct pathways and two principal components. (1) Stress in response to systemic stressors is facilitated by the activation of the sympathetic–adrenal–medullary (SAM) axis and subsequent release of adrenaline and noradrenaline (Chrousos & Gold, 1992) which occurs within in seconds after the onset of a

stressor (Joëls, *et al.*, 2006). (2) The slower acting and longer lasting response (Joëls & Baram, 2009) is triggered by the activation of the hypothalamo-pituitary-adrenocortical (HPA) axis in response to both systemic and psychogenic stressors. This results in the release of corticotropin-releasing hormone (CRH) and elevated circulating glucocorticoids (GC) (Chrousos & Gold, 1992).

SAM and HPA axes

The basic pathways of allostasis are the SAM axis and HPA axis and their intercommunication pathways. The activation of one will lead to the activation of the other and the type of stressor is the determinant of which activates first. Generally, if the stressor is systemic, the SAM axis is the first to activate, while the HPA is activated first following psychogenic stressors.

1.1.2.1 Sam and Nor/Adrenaline

The SAM axis is reflexive in nature and makes use of the peripheral nervous system (PNS), which consists of nerves outside the brain and spinal cord, referred to as the CNS. The PNS is divided into the somatic (voluntary control such as movement) and the autonomic (ANS; involuntary control that regulate physiological functions) nervous systems (Laight, 2013). The ANS is a self-regulatory system that tracks and maintains homeostatic functions that organisms do not have voluntary control over, such body temperature and heart rate (Laight, 2013). The ANS can also be divided into the parasympathetic and sympathetic nervous systems. Both are important to maintaining homeostasis within an organism. The parasympathetic system is largely responsible for homeostatic functions and regulation such as ingestion, digestion and resting. The sympathetic system is responsible for the 'fight or flight' reaction. To put it crudely, innervation from the parasympathetic system and sympathetic system have the opposite effect on the target organ and can often act as inhibitory factors for each other. However, the interactions between the two arms are not that simple (Goldberg *et al.,* 1975; Olshansky, *et al.*, 2008). As the ANS is tonically active and

organs within the PNS purview are innervated by both arms of the ANS, the body is constantly subject to sympathetic or parasympathetic stimulation. As noted by Cannon (1929), simply acting within the environment brings about changes within the *milieu interne* (Bernard, 1878) and as the *milieu interne* must remain homeostatic, the ANS and its two arms are constantly in flux to maintain homeostasis, which often occurs unconsciously. However, threat can bring the body into dominant sympathetic stimulation.

The rapid response of the ANS and the secretion of adrenaline can be facilitated in one of two ways. The first is when homeostatic disturbances (or systemic stressors) are signalled to the brainstem. The ANS responds reflexively to stimulate the adrenal medulla and sympathetic neurons within the spinal cord (Herman *et al*., 2003: Joëls & Baram, 2009; Ulrich-Lai & Herman, 2009) and begins the activation for the SAM axis (Wetherell, *et al.,* 2006). Nor/adrenaline signals are then sent from the medulla upstream to higher-order autonomic systems within the brain such as the hypothalamus, in particular, to the paraventricular nucleus (PVN) within the hypothalamus (Kandel *et al.,* 2000; Ulrich-Lai & Herman, 2009). It is from this signal that the HPA axis becomes active and begins the process of releasing glucocorticoids (GCs; further described in the following paragraph). The second comes from the innervation of the pituitary gland following activation of the HPA axis by the amygdala upon the perception of threat. In both cases, the target organ for innervation is the adrenal medulla in order to stimulate the release of adrenaline into the system. Clearly, the SAM axis and HPA axis act in concert during the stress response via feedforward and feedback mechanisms. The release of nor/adrenaline occurs within seconds of a stressor (Joëls & Baram, 2009; Romero & Butler, 2007) and scarcely lasts longer than exposure to the stressor and returns to baseline levels within an hour (Quirarte, *et al.,* 1997).

Whether through feedforward via the brainstem, or feedback mechanisms via the hypothalamus, activation of the sympathetic system leads to the release of adrenaline throughout the body and noradrenaline within the brain, which act in concert to prepare the body and mind in a number of ways for activity. To this end, adrenaline increases blood flow

to the skeletal muscles, heart rate and blood pressure (Allen, *et al.*, 1946; HåRkanson, *et al.*, 1986). Additionally, adrenaline aids the release of glucose and increases systematic oxygen uptake (HåRkanson, *et al.*, 1986). As parasympathetic activity is suppressed during sympathetic activity, digestion and the release of the growth hormone (somatotropin) are suppressed. The net result of this is increased physical performance and inhibition of non-vital activities (Romero & Butler, 2007). On the other hand, noradrenaline works within the CNS via the locus coeruleus (LC; Berridge & Waterhouse, 2003). The LC is located within the brainstem, and functions to heighten sensory responses in the visual (Maclean & Waterhouse, 1994; Gelbard-Sagiv, *et al.*, 2018), somatosensory (Lecas, 2004), auditory (Foote, *et al*, 1975) and olfactory (Bouret & Sara, 2002) modalities, as well as increasing attentional performance (Booth & Sharma, 2009). Elevated noradrenaline increases the processing of salient sensory information by increasing and directing an organism's attention towards that information. This is known as the orienting reflex (Aston-Jones, *et al.,* 1999; Sara & Bouret, 2012). In many ways, this mirrors attentional mechanisms themselves. For example, noradrenaline improves the signal-to-noise ratio of salient information (Foote *et al.,* 1975; Waterhouse, *et al.*, 1990), lowers the response thresholds of sensory information (Foote *et al.,* 1975; Waterhouse, *et al.*, 1990) and shortens response latencies (Lecas, 2004). The result is heightened awareness of salient or threatening sensory information and a shift from focused attention to a general scanning attention (Rajkowski, *et al.*, 1994). Additionally, signals through β-adrenergic receptors facilitate the induction of hippocampal long-term potentiation increasing the likelihood of memory of the stressor (Thomas, *et al.*, 1996). If the stressor was dealt with successfully, this long-term potentiation leads to competency, reducing the stress response to the stressor (Shields, *et al*., 2016). If not, this could lead to learned helplessness, a maladaptive response, best described as an escape/avoidance deficit towards the stressor (Maier & Seligman, 1976).

In summary, noradrenaline and adrenaline work in tandem to increase physical responses to threat by modulating physiological factors as well as cognitive factors. Cortisol is the slower acting stress hormone and works in parallel with nor/adrenaline.

1.1.2.2 HPA Axis and Cortisol

When threat is detected, there is also a delayed and prolonged neuroendocrine response (Norman & Hearing, 2002; Sorrells, *et al.*, 2009). The amygdala signals the hypothalamus to release CRH. This in turn activates the HPA axis (Jankord & Herman, 2008), finally triggering the release of adrenocorticotropic hormone (ACTH) from the anterior pituitary gland. ACTH is released into the bloodstream where it signals for the release of cortisol from the adrenal cortices, situated on the kidneys (Ehlert, *et al.*, 2001). From here, cortisol levels rise within the bloodstream and remain elevated for several hours (Blackburn-Munro & Blackburn-Munro, 2003; Dedovic, *et al.,* 2009). Cortisol is also lipophilic so it can pass the blood-brain barrier and bind with receptors within the brain (Lupien, *et al.,* 2007). However, the multistage nature of this response necessarily creates a delay compared to the release of nor/adrenaline. Generally, elevated cortisol levels alter an organism in five ways: increased glucose in the blood (Dallman, *et al*., 1993), inhibiting sexual reproduction (Romero & Wingfield, 2001), immune system modulation (Heim, *et al.*, 2000) and inhibiting growth (Sapolsky, 1992). The net outcome is re/allocation of energy. Energy that would be used for non-vital functions are reallocated to muscle and increased glucose in blood further heightens the available fuel. The fifth and final way cortisol alters an organism is through behaviour by modulating top-down control (Ulrich-Lai & Herman, 2009).

GCs (cortisol in humans) bind to receptors found in the hippocampus, amygdala and PFC brain areas. Within these brain structures, cortisol has a high binding affinity with two receptors: mineralocorticoid (MRs) and glucocorticoid (GRs; Joëls, 2006). MRs have a much higher affinity for cortisol than GRs, whereby cortisol more readily binds to MRs than GRs. The circadian rhythm produces a natural peak of cortisol in the morning upon awakening that slowly tapers off during the rest of the day. During cortisol peaks (in the morning) or during a stress response cortisol is able to bind to both receptors (Joëls & Baram, 2009). As the levels of cortisol increase and MRs become saturated, GRs now too becomes saturated. During troughs in cortisol concentration, there is less than 10% occupation of GRs while there is a 90% occupation of MRs (Lupien, *et al.,* 2007). This is important because only GRs

are expressed in the PFC while MRs and GRs are both expressed in the hippocampus and amygdala (Joëls & Baram, 2009). Furthermore, MRs are associated with positive/enhancing effects while GRs are associated with negative/inhibiting effects such that emotional memory (handled by the hippocampus and amygdala) performance can be expressed as an inverted-U. While, on the other hand, executive function performance (mostly processed by the PFC) suffers with higher cortisol concentrations (Ouanes & Popp, 2020). Therefore, performance suffers on tasks associated with brain areas predominantly expressing GRs, while performance on tasks associated with brain areas expressing both MRs and GRs increase during a stress response. In short, this expression of MRs and GRs within the brain during an acute stress response is adaptive in nature as it results in learning and acquiring new behavioural strategies (Lupien, *et al*., 2007). It also promotes competence as the stress response to repeated exposure to the same stressors decreases (Shields, *et al*., 2016). However, it is not as simple to claim that cognitive performance increases or decreases during a stress response, indeed, even different forms of memory are differently affected by a stress response. For example, declarative and verbal memory performance is reduced, however, emotional or 'flash-bulb' memory performance is increased (Vedhara, *et al.,* 2000). Changes in performance with regards to attention and cortisol are also mixed. For example, Vedhara et al. (2000) reported decreases in divided attention but no change in selective attention; whereas, Putman et al. (2010) reported a decrease in selective attention. The exact effect cortisol has on different aspects of cognition is not fully understood. Of course, cortisol and noradrenaline (as well as other neurotransmitters) also interact within the brain to produce different effects (Krugers, *et al*, 2012) further complicating the matter.

The stress response is clearly adaptive when acute in nature, promoting focused attention, alertness and vigilance. Furthermore, it promotes memory formation about the stressful event so that an organism learns from the event, resulting in adaptation to the same or similar events in the future. In order to achieve this response, cortisol and noradrenaline alter brain cell properties, forcing brain structures involved in stress into 'hyper-drive' (Joëls, *et al.,* 2006). Following a stressful event, it is important to return brain function back to

normal from this heightened state to avoid cell degradation. Prolonged exposure to increased cortisol leads to dendritic atrophy in the hippocampus (Uno, *et al.*, 1994) leading to memory deficits (Manikandan, *et al.,* 2006). Dendritic atrophy also occurs in pyramidal cells within the PFC (Brown, *et al.,* 2005) accompanied by an overall decrease in cell volume (Cerqueira, *et al.,* 2005). This leads to an increase in memory deficits and a decrease for performance on executive functions. Cortisol also reduces neurogenesis in general, consequently decreasing cell volume further (Mirescu & Gould, 2006). Finally, cortisol increases dendritic length for pyramidal cells in the amygdala leading to increased fear learning (Mitra, *et al.,* 2005) and thus sensitising persons to feared stimuli as well as salient stimuli (Seeley, *et al.,* 2007).

1.1.2.3 Summary

Biologically, stress produces a host of physical and cognitive changes within an organism. It is brought about by a cascade of hormones and neurotransmitters activated by the HPA and SAM axes in response to real and imagined threat. The stress response is adaptive in nature as it readies the body to deal with the threat, promotes learning to overcome the same threat in the future and consolidates memories of the threat. However, this acute stress response is not sustainable long-term as both cortisol and nor/adrenaline can produce maladaptive states and even physiological harm. Understanding these different aspects of stress could also account for the discrepant data for the effect of stress on cognition reported above. Indeed, when, and how stress becomes maladaptive, or how these changes affect cognition (for example, attention) are questions that need exploration. In the following sections, we summarise theories related to the stress response, in particular, those that deal with the effects of increased exposure to stress hormones and their maladaptive effects.

1.1.3 The Long Road of Stress: Introducing the Theories

It must be noted that pre-1930s, the term stress was not used in terms of psychological distress as it is today and was mainly used to describe mechanical pressure exerted on an object. It is a difficult endeavour to trace the origins of stress as it relates to physiology. The change seen in the 1930s is due in part to stress being used to refer to the noxious agents that caused the stress response, as in the "pressure" noxious agents exerted on the body. While Selye (1956) is often credited for the discovery of general stress (Goldstein & Kopin, 2007), its definitional shift during the 1930's was due to the work on homeostasis by Cannon whose work focussed on what Selye would later term 'the syndrome of just being sick' (Selye, 1965, page 97). With that said, the work of the latter drove the contemporary concept of stress (Viner, 1999; Goldstein & Kopin, 2007). While stress theories have certainly moved on from the 1930s, these early academic works laid the groundwork for future theories such as allostasis (Sterling & Eyer, 1988), allostatic load (McEwen & Stellar, 1993) and more recently, GUTS (Brosschot, *et al.*, 2016).

1.1.3.1 Homeostasis

Cannon (1929) referenced 18th century biologists who asserted the body is self-regulatory and strives for internal stability without which the living being would not exist in the face of external forces (Bernard, 1878; Fredericq, 1885; Pflüger, 1887; Richet, 1900). From this early biological concept, it is easy to see the beginnings of the idea that an organism needs to adapt in the face of external threat. While investigating heat regulation Bernard (1865) discovered blood regulation by sympathetic nerves, an unexpected and seemingly unrelated response. From this, he laid the foundations for homeostasis. He noted that all internal structures are bathed in bodily fluid which he termed the '*milieu interne'* (Bernard, 1878) and that this *milieu interne*, which Cannon (1929) later called the fluid matrix, must remain stable. In other words, physiological variables such as body temperature are regulated so that they are maintained within a narrow operating range between two set points. It is within this stable homeostatic internal environment that an organism can operate

optimally. Simply acting within the environment or experiencing changes in the environment elicit reactions within the body such that stability within the fluid matrix is disturbed. These disturbances are constrained within an acceptable range for an organism to remain healthy. This concept is known as homeostasis (Cannon, 1929), the body's corrective reaction to a perturbation of a regulated physiological variable. Homeostatic systems are comprised of sensors and effectors. Sensors detect deviations from the acceptable range of physiological variables and effectors act to reduce those deviations. Cannon asserted that threats to homeostasis activated the adrenal medulla and sympathetic nervous system, releasing adrenaline and noradrenaline, the effectors of homeostasis (Cannon & Lissak, 1939; von Euler, 1946). Regardless of the threat to homeostasis, Cannon (1929) found the sympathoadrenal response was consistent. Since the landmark work of Cannon, it has been discovered that adrenaline, noradrenaline and sympathetic activity are not only associated with emergencies but with everyday movements including simply changing posture (Lake, *et al.,* 1976). Merely acting in the world requires a sympathetic response. Threats to homeostasis do not always produce a stress response or the 'fight or flight response' as Cannon described it. It appears the body can, and will, naturally correct homeostatic deviations without the need to resort to fight or flight, using the sympathetic system. While the concept of stress and its long-term effects was not yet fully realised, the concepts of internal self-regulation to maintain the stability of the fluid matrix and the sympathoadrenal system set the stage for future investigation as there did seem to be an associated cost with this adaptive function.

1.1.3.2 General Adaptation Syndrome

During the mid-1930s and throughout his long career Selye noted that during animal experiments involving rats, the physiological response (regardless of the stressor) was stereotypical in nature, in that the response always produced gastrointestinal ulcers, adrenocortical enlargement and involution of the thymus and lymph nodes (Selye, 1936, 1950, 1951, 1976). Selye and his colleagues surmised this robust response that reacted to

all manner of specific effects represented the body's reaction to stress. With this realisation and drawing from the work of Cannon and Bernard, among others, Selye attempted to unify these findings and concepts together which, at the time, were thought to be interconnected (Selye, 1950). Selye reasoned that, that which causes stress is necessarily something that threatens life, and that it would require an adaptive response to overcome. This adaptive response is the stereotypical physiological response mentioned above and which Selye called the General Adaptation Syndrome (GAS). GAS is the integrated syndrome of non-specific adaptive reactions to stressors. GAS manifests as an interaction of non-specific damage and active defence (Selye, 1950), which was a common theme that continued with the theories of allostatic load (McEwen & Stellar, 1993) but is ultimately not always true (Pacak, *et al.,* 1998).

GAS is composed of three distinct stages: Alarm Reaction, Stage of Resistance and the Stage of Exhaustion. What is stereotypically thought of as the stress response (i.e. fight or flight) manifests within the Alarm Reaction stage. This includes the physiological reactions mentioned above and includes activation of the adrenal medulla, which releases adrenaline and the adrenal cortex, which produces GCs. The end goal of this reaction is to provide energy and increase blood circulation to provide an individual the necessary means to fight or avoid the stressor as quickly as possible. The activation of certain physiological structures and release of chemicals is an effort to restore homeostasis. The Stage of Resistance comes after the initial endocrine cascade of the Alarm Reaction. It is either a stage that leads to adaptation or leads to the Stage of Exhaustion. If the stressor has been removed from the situation the body will have adapted to the threat and return to normal functioning. If, however, this does not happen, the body remains in an alarm state and does not revert to normal functioning, then it is from this outcome of the Stage of Resistance that the Stage of Exhaustion is reached (Selye, 1950). Prolonged exposure to the stress response leads to what Selye (1976) called the diseases of adaptation. These occur in response to prolonged exposure to CRF and ACTH and include migraines, insomnia, hypertension and cardiovascular disease (Selye, 1976).

This is the paradox of the stress response mentioned earlier. A stress response is a corrective response to dangerous physiological imbalances that could cause damage but it, itself can cause physiological damage. However, it was never addressed within the framework of GAS. Which is somewhat surprising as converging evidence has since corroborated some, but not all, of the physiological manifestations of the Alarm Stage and the detrimental effects of chronic stress as highlighted by McEwen (1998). Evidence that outright contradicts GAS regards whether the stress response is homogeneous or heterogeneous in nature. GAS clearly states that the stress response is homogenous or stereotypical in response to a multitude of distinct stressors. That is to say, no matter the stressor, the stress response will be the same. Pacak *et al.* (1998) tested this rather straightforward prediction by measuring some biological markers for stress (ACTH, noradrenaline, and adrenaline) in rats after exposing them to various stressors such as cold, immobilisation or haemorrhage. GAS would predict no difference in the magnitude of response between the responses to these stressors. In contrast with that prediction, ACTH, noradrenaline, and adrenaline levels were inconsistent between stressors but consistent within stressors. The authors suggested the results indicate that stressors have their own central neurochemical and peripheral neuroendocrine signature (Pacak, *et al.,* 1998). Further theoretical problems exist within the GAS framework. The concept of homeostasis, one of the central tenants of GAS, began to run into definitional problems, as more aspects of stress were uncovered (Sterling & Eyer, 1988; McEwen & Stellar, 1993). Homeostatic function by its definition requires that the *milieu interne* is regulated and remains stable within a strict operating range lest the organism suffers and, in extreme cases, dies. However, this is not exactly how the body functions. The physiological factors that account for the *milieu interne* continually fluctuate and can settle on different operational steady states depending on environmental challenge (McEwen, 2005). Another problem with the concept of homeostasis within the GAS framework is that it does not accurately account for stress-related pathologies, as the exhaustion stage of GAS does not specifically pinpoint how and why prolonged stress causes such pathologies (McEwen & Stellar, 1993; McEwen,

2005). With that said, GAS is often still used as a framework within which to study stress (Csaba & Pállinger, 2009; Fink, 2017). At the very least, it certainly brought the idea of stress to the public and academia. For example, following on GAS, newer concepts have been introduced to explain how and why chronic stress can lead to dysfunction. Thus, allostasis and allostatic load were conceptualised to compensate for the limits of homeostasis and GAS in general (Sterling & Eyer, 1988; McEwen & Stellar, 1993).

1.1.3.3 Allostasis

The stability and uniformity of the *milieu interne* certainly needs to be maintained to prevent harmful effects on the body. Allostasis, first defined in 1988, refers to the operating range and the ability to adapt physiological function to a new operational steady state when confronted with challenge (Sterling & Eyer, 1988; McEwen & Stellar, 1993). While physiological factors operate optimally within a specific range, some of these factors often operate outside of this range for varying periods of time depending on whether the stress is acute or chronic. Both homeostasis and allostasis refer to the need for stability and uniformity within the body for healthy physiological function and refer to the body's attempt to restore physiological functions back to stability when faced with challenge. However, allostasis specifically refers to the superordinate system through which the body maintains stability through change (McEwen, 2005). Therefore, homeostasis is the maintenance of an internal stable environment and refers to a limited number of physiological variables essential for life such as glucose levels, oxygen tension and body temperature (McEwen, 2005). Allostasis is the process, through change, by which stability is re/achieved. This difference takes into account the variability that is observed when the body responds to homeostatic fluctuation in its attempt to correct these fluctuations. For example, body temperature is a homeostatic variable, as it needs to be maintained within two set points that form a strict operating range. If body temperature exceeds the limits of the operating range, it is now in an allostatic state. If body temperature continues to operate outside its normal range this can lead to detrimental physiological effects and eventual death. When this

fluctuation is detected, allostatic mediators are employed to elicit change (physiological and behavioural) to bring body temperature back within its acceptable homeostatic range (McEwen 2005; Ramsay & Woods, 2014). During allostatic states, non-homeostatic physiological variables such as heart rate, blood pressure and neural activity will change to a new operating steady state that may be outside their normal operating range in order to restore homeostasis (McEwen & Stellar, 1993). If body temperature increases due to environmental pressure, in order to restore body temperature back to its normal homeostatic operating range, an individual's heart rate may increase to deal with the environmental pressure. In simpler terms, when the body detects deviation or potential deviation from homeostatic function it enters an allostatic state whereby stability is re-established by changing the operating range of allostatic functions. As Richet (1900) noted, the body is able to maintain the uniformity of the fluid matrix only because it is capable of adjusting itself in order to deal with the incoming stimulation that would negatively impact the fluid matrix. To quote Richet (1900; page 72), 'in a sense it is stable because it is modifiable'. However, even with this definitional shift, homeostasis and allostasis do not consider the long-term effects of an allostatic state, or in terms of GAS, the long-term effects of the alarm reaction stage that led to the exhaustion stage. But there is plenty of evidence demonstrating the harmful effects of chronic stress. Selye (1936) recognised the fact that the physiological systems responsible for the restorative effects during allostasis, are the same systems that can damage the body. It is only within the last 30 years that the reason for this paradoxical effect has been explored. McEwen (2004) suggests this dual effect is explained by 'allostatic load', whereby continued exposure to allostasis gradually wears down biological structures such that dysfunction occurs.

1.1.3.4 Allostatic Load

In short, allostatic load is the general wear and tear the body experiences from prolonged allostasis. Acute stress is adaptive in that it promotes survival by providing the necessary physical energy and strength to overcome the perceived threat. Acute stress

promotes memory encoding of the situation so that successful solutions are remembered and can be integrated into a successful behavioural strategy in the future in similar situations (Seery, *et al.,* 2010; Shields, *et al*., 2016). Repeatedly facing a similar threatening situation successfully builds competency and reduces the perception that that situation is threatening in some people but not all (Shields, *et al*., 2016). As that happens, the allostatic response is no longer triggered in that situation. In this way, acute stress is adaptive for the present and the future and it suggests the allostatic response is triggered on the subjective appraisal of threat (Ehlert, *et al.,* 2001). Clearly then, nor/adrenaline and cortisol, and the allostatic response, provide enormous immediate benefits for survival but are not beneficial when prolonged. Acute stress is brief and triggered upon the perception of threat and subsides once the threat has been successfully dealt with (Joëls & Baram, 2009). Chronic stress is a continued allostatic response lasting for at least a month after the initial perception of threat (Baum, *et al.,* 1993). Unfortunately, consistent, and continued activation of the allostatic response can lead to nor/adrenaline and cortisol dysfunction which may result in physiological and psychological trauma. There is plenty of evidence suggesting severe consequences resulting from chronic stress caused by cortisol dysfunction. As a reminder, chronic stress is associated with suppressed immune systems and increased susceptibility to disease (Khansari, *et al.,* 1990). It is also positively associated with cardiovascular disease (Rozanski, *et al.*, 1999), has deleterious effects on hippocampal cells resulting in memory impairment (McEwen, 1999; Sapolsky, *et al.*, 1990; Woolley, *et al.*, 1990; Gould, *et al.*, 1998), and disrupts healthy appetite (Diz-Chaves, 2011; for review see Yaribeygi *et al.,* 2017). Despite the evidence suggesting the destructive consequences of chronic stress on physiological integrity, research to date reveals the disruption of cognitive processes produces mixed/discrepant results.

It is important to reconcile these discrepancies because physiological data demonstrates the destructive consequences of allostatic load on brain structures, and this should come with at least some cognitive cost. One reason for these discrepancies may be

due to the time it takes for physiological damage to negatively affect cognitive processes. As such, the cognitive cost for stress may only manifest during advanced aging.

Age is often accompanied by cognitive decline because of general degradation from the ageing process. However, there are discrepant results reported here too. One longitudinal study tested for mediators of cognitive decline during ageing and found that above all, exposure to stress was the strongest predictor of cognitive decline during ageing (Peavy, 2009). Subsequently, a series of studies then tested the interaction of age and stress on cognitive decline. In these studies, performance on memory and response inhibition was significantly worse for older participants in a high stress group (i.e. the group that had experienced more stress throughout their lives), while younger participants regardless of stress exposure performed equally well, along with older low stress participants. Furthermore, this was accompanied by abhorrent neuro-oscillations in the older high stress group, which was attributed to the destructive consequences of chronic stress on the brain (Marshall, *et al.,* 2016a; Marshall, *et al.,* 2016b; Marshall, *et al.,* 2018). For example, compared to the younger low and high stress groups as well as the older low stress group, participants in the older high stress group had an increase in theta event-related synchronisation in a spatial discrimination task. This increase in theta was attributed to a damaged hippocampus, which in turn explained the poorer behavioural performance by the same group (Marshall, *et al.,* 2016b). This result is interesting because it presents two key observations. The first is that cognitive decline during ageing is a function of exposure to stress. The second is that younger participants with high stress exposure do not show cognitive disruption from the high stress. These results suggest that cognitive degradation due to stress exposure takes time. These studies help explain the discrepant results found in the stress and ageing literature and connects these two areas. This could even help address discrepant results describing the relationship between cortisol and attention. For now, another question that still needs an answer is how stress is maintained for it to become chronic. No previous theories adequately addresses this, but the more recent General Unsafety Theory of Stress (GUTS) attempts to answer this question.

1.1.3.5 General Unsafety Theory of Stress (GUTS)

Brosschot et al. (2016) argue that previous theories of stress cannot explain stress maintenance because of their focus on threat perception. The authors argue that in previous theories, the maintenance of stress is reliant on the constant perception of threat when there is none. In previous theories, this perception is generated by threat cues, and our internal monologue and maintained through rumination. However, Brosschot et al. (2016) argue that even in the most severe cases of chronic stress, it is hard to imagine one ruminating to such an extent as to generate an allostatic response constantly. Furthermore, the authors argue the world is generally, overtly safe with a lack of threatening cues especially in circumstances where there are none, such as the workplace or at home. Yet, workplace stress is reported commonly and globally (Europe 51%, Safety at Work, 2013; United States 83%, The American Institute of Stress, 2021; Japan 53%, www.Stastista.com; Australia 64%, Casey & Liang, 2014). With that said, ambiguous stimuli are initially interpreted negatively. Perhaps then, ambiguous stimuli/situations account for the maintenance of chronic stress as work outcomes and home life are not always set in stone and are therefore ambiguous. Brosschot et al. (2016) argue that through routine and habit, ambiguity is almost absent from modern, everyday life. Furthermore, rumination and our internal monologue cannot explain the continuous physiological activity associated with chronic stress, because as stated previously worry and rumination are themselves not continuous according to Brosschot et al. (2016). Indeed, chronic stress is associated with low heart rate variability (HRV) but HRV is not associated with rumination (see below for why HRV is important in this context; Hoehn-Saric *et al.,* 2004; Licht, *et al.,* 2009; Thayer, *et al.*, 1996). GUTS proposes that it is the lack of safety cues that causes an allostatic response and that chronic stress is maintained from this continuous lack of safety cues and not from the perception of threat cues. Furthermore, GUTS proposes that allostasis is persistent and not triggered, it is through learning safety cues and then perceiving them that allostasis is inhibited.

Here we can see the divergence of GUTS from the theories that came before it. Stress is a response to the lack of safety, not the perception of threat and it is disinhibited (or

'let go') instead of 'turned on'. To increase energy efficiency and response times it is better to have to disinhibit a default allostatic response instead of having to trigger it (Waldvogel, *et al.,* 2000). If one were suffering from chronic stress from a lack of safety cues and not necessarily threat or rumination, this would explain the association between chronic stress and a cardio-physiological phenomenon that usually accompanies it - low heart-rate variability (HRV). HRV (as its name suggests) is a measure of the variability of one's heart rate; with increased HRV often seen as a measure of increased parasympathetic activity and therefore sympathetic withdrawal (Thayer, *et al.*, 2012). In practical terms, HRV is employed as an indication of an allostatic state. In relation to parasympathetic activity (in this context, operating largely through the vagus nerve), during an allostatic response, low HRV is regarded as vagal withdrawal and therefore an increase in sympathetic activity. Furthermore, a high HRV, which reflects parasympathetic activity and sympathetic inhibition, is also linked with prefrontal inhibition of the subcortical areas that are responsible for generating allostasis. HRV is therefore an important indicator of GUTS as Brosschot et al. (2016) claim a low HRV is linked to GU, which in turn maintains chronic stress. To overcome GU and inhibit allostasis, one needs to learn and recognise safety cues. Brosschot et al. (2016) assert that soon after birth, humans are adept at learning safety cues. For example, satiation of hunger and thirst is associated with increased HRV (Porges, 2007), which is associated with decreased chronic stress. As we get older, and the complexities of life increase so should the contingencies of safety cues and their generalisability. Unfortunately, the same is true for fear learning (Glenn, *et al.,* 2012).

Brosschot and colleagues (2016) use the results from conditioning studies to support these claims. In these studies, chronic stress elicits a fear response from both unconditioned and conditioned stimuli, whereas the same response is only elicited from conditioned stimulus in healthy controls. Furthermore, chronic-stress participants were slower to unlearn the conditioned stimulus (Duits, *et al.,* 2015). Taking these findings together, Brosschot et al., (2016) argue that participants with chronic stress do not recognise the safety cues in the unconditioned stimulus or in the stimulus that is unpaired and therefore safe. Low HRV is

associated with both of these effects in conditioning paradigms (Pappens, *et al.,* 2014; Wendt, *et al.,* 2015). Additionally, fear learning progresses from general fear to specific fear instead of from no fear towards fear. Brosschot et al. (2016) propose individuals start with a default allostatic response and learn to predict and how to control threats. It is by learning about the predictability and controllability of threats in life that GU is lowered and this in turn inhibits the default allostatic response. Here Brosschot et al. (2016) conflate predictability and controllability but point out that both have the same (or similar) effect of perceived safety (Christianson, *et al,* 2008). Regardless, there is evidence that the experience of control when facing threat 'inoculates' against future uncontrollable threats and safety is generalised to similar threats (Maier, 2015). Unfortunately, insufficient safety learning can instead generalise the lack of safety in inappropriate situations and so increase GU. This can be caused by genetics, early prenatal stress and psychological vulnerability. Safety learning can also be compromised later in life through distinct domains. Brosschot et al. (2016) put forward one's social network, one's body and one's context as three key domains. When these domains are compromised, increased GU occurs because the perception of safety is undermined. Support for the importance of these domains in the context of stress comes from the following observations: social support is associated with high HRV (Porges, 2007) while social anxiety is often linked with low HRV compared to healthy participants, (Gaebler, *et al.,* 2013; Licht, *et al*., 2009; Pittig, *et al*., 2013). For the body domain, low aerobic fitness, old age and obesity are all associated with low HRV (Thayer*, et al*., 2010; Zulfiqar, *et al.,* 2010). The context domain refers to the generalisation of safety through learning or context conditioning (Melzig, *et al.,* 2009; Grillon, *et al.,* 2006) into non-threatening environments or situations. When compromised, generalising safety to separate but similar contexts does not occur, leading to GU.

Despite the theoretical arguments for GUTS, it has not been tested empirically (as far as the authors are aware) and some weaknesses are apparent. For example, Brosschot et al. (2016) specifically name age as a factor that belongs in the body domain. A weaker body should lead to increased GU and chronic stress. However, data suggests that increased age

is associated with happiness, not the negative effect associated with chronic stress (Witt, *et al.,* 1980; Buijs, *et al*., 2021). Without testing, it is hard to reconcile this discrepancy. Another issue is measuring GU; how should one capture GU present in participants? It seems likely that GU would be associated with perceived stress. The less safety cues the more stress one should perceive manifesting in their lives. However, data suggests there is no association between perceived stress and accumulated stress or ageing (Marshall, *et al.,* 2016a; Marshall, *et al.,* 2016b; Marshall, *et al.,* 2018). In these studies, age per se was not the cause of cognitive decline during ageing but the interaction of ageing and accumulated life stress, providing discrepant results from what the body domain of GUTS predicts. This also suggest that GUTS may explain one's perception of stress but not necessarily the effects of stress. This is an avenue in need of investigation. Another shortcoming of GUTS is the lack of description for a non-compromised domain. For example, self-esteem has often been negatively associated with stress (Kreger, 1995; Martyn-Nemeth, *et al*., 2009) and could therefore represent a healthy domain although it is not apparent in which domain it would belong.

1.1.4 Summary

Stress first became prevalent when early researchers noted the body's *milieu interne* needs to maintain a consistency in order to remain healthy. This process is called homeostasis. However, there is an associated physiological cost to continually maintaining homeostasis. A stressor is something by definition that causes harm and may negatively affect the *milieu interne* which in turn affects homeostasis. The body needs to adapt to overcome these stressors. The physiological damage caused by stress comes from a lack of successfully adapting to the stressor. However, not all physiological factors operate within a rigid set of parameters. Indeed, some physiological factors need to act outside their optimal parameters in order to return stability to factors that do need to act within a rigid set of parameters. Homeostasis is the maintenance of the latter factors while the change associated with this maintenance by the former factors is known as allostasis. The

physiological cost is explained by allostatic load, prolonged allostasis causes wear and tear on the physiological factors acting for sustained periods outside of their optimal parameters. This usually occurs in those suffering from chronic stress or from increased accumulated stress. GUTS attempts to address how chronic stress is maintained to the point of allostatic load, as this is not addressed in previous theories. However, how chronic stress is maintained is still an open question as GUTS has not been empirically tested.

1.1.5 Open Questions

The effects of allostatic load on cognition have produced discrepant results (Booth & Sharma, 2009; Braunstein-bercovitz, 2003; Kan, *et al*., 2019). Recent evidence suggests that cognitive impairment from allostatic load requires time and manifests during ageing (Marshall, *et al.,* 2016a; Marshall, *et al.,* 2016b; Marshall, *et al.,* 2018; Peavy, 2009). This suggests prolonged exposure to stress hormones, either through chronic or accumulated stress, could account for these discrepancies. However, this evidence relates to memory and inhibition and there are still discrepant results for the effects of allostatic load on attention (Liu, et al., 2020; Liston, et al., 2006; Öhman, et al., 2007). Perhaps the stress/age interaction could also account for these discrepant results? Additionally, GUTS attempts to explain the maintenance of chronic stress but remains hitherto untested. The domains suggested by GUTS provide a way to test the theory by investigating their association with levels of stress. Consequently, this thesis sets out to investigate the following questions: the first question to be addressed is: is there an age/stress interaction on attentional performance? The second question to address concerns the validity of GUTS: do individual differences in the GUTS domains predict chronic stress? First though, it is important to summarise what is known about stress and attention as well as attention and ageing.

1.2 Attention

1.2.1 Attention, Physiology and Stress

As William James famously noted “everyone knows what attention is” which is to say that attention is understood instinctively. James continues, “It is the taking possession by the mind, in clear and vivid form, of one out of what seems several simultaneously possible objects or trains of thought. Focalization, concentration of consciousness are of its essence. It implies a withdrawal from some things in order to deal effectively with others” (James, 1890; page 403). Our sensory systems are bombarded by incoming stimuli, generating huge amounts of sensory information that need to be processed so that meaningful behavioural interactions can occur. This is especially true of our visual and auditory systems. It is hard to dampen or prevent incoming auditory stimuli and most of human experience is driven by the visual domain, indeed a large proportion of the brain is involved in visual processes. The brain is constrained by a limited number of resources (known as cognitive resources) with which to process all this incoming information. There is far more unprocessed information coming in than cognitive resources within the brain to process it all. Itti and Koch (2001) suggested that as much as 10^7 - 10^8 bits per second of information pass through the optic nerve and there is simply not enough processing power for all that information in the human brain. Instead of processing the whole scene in parallel, the strategy is rapid, localised serial processing. Much of what comes in must be discarded and a tiny percent is kept for further processing. The mechanism by which this selection is made is referred to as ‘attention’ and it can be conceptualised as a mechanism that controls limited resources (Lindsay, 2020). Early visual processing captures and encodes all incoming visual information, but consciously sifting through all the information for what is behaviourally relevant costs time and energy. Giving priority to visual information that is more pertinent to current behavioural goals or to salient stimuli ensures the limited cognitive resources are put to processing the most important stimuli within a visual scene. Therefore, visual attention is the mechanism by which a subset of visual information is prioritised at the expense of the rest of the scene (Moore & Zirnsak, 2017). High visual fidelity is largely the work of a comparatively small part

of the retina, the fovea. Attentional benefits include a heightened perceptual performance toward the selected target or location and faster reaction times towards behavioural targets or salient stimuli (Jonikaitis, 2019). How these benefits are achieved include increasing the signal-to-noise ratio of the neural representation of the attended stimuli and by the generation of priority maps that distinguish target from distractor stimuli (Fecteau & Munoz, 2006), which aid in target selection (Serences & Yantis, 2006). Increases in signal-to-noise ratio are achieved by modulating the neuronal responses within brain areas encoding the attended stimulus (Ciombor, *et al.,* 1999; Waterhouse, *et al.,* 1990). The priority map is generated from a summation of top-down and bottom-up attentional influences (Stemmann & Freiwald, 2019). This dichotomy is represented by visual attention being carried out over large, interconnected brain regions. These are either divided into two regions: the control regions and the sensory processing regions (Corbetta & Shulman, 2002; Scolari, 2015) or are separated into networks based on brain structure (Posner & Petersen, 1990; Petersen & Posner, 2012). These are not the only distinctions that can be made when classifying and investigating attention.

However, attention is not easily defined and the there is still much debate on distinct forms of attention. For example, there is also debate whether event history is a part of top-down influence or a distinct process, which has consequences for what constitutes a top-down mediated behaviour (Gaspelin & Luck, 2018; Theeuwes, 2018). Definitional difficulties are due to a number of reasons. Some studies combine certain aspects of attention but do not clearly define this combination. Most importantly, however, the term ‘attention’ is used as a catchall phrase for distinct neural processes and mechanisms that encompass a wide array of processes (Hommel, *et al.,* 2019; Lindsey, 2020). Furthermore, some aspects of attention have been given far more scrutiny than others, such as the distinction between top-down and bottom-up attention. Top-down attention has been subject to more inquiry than bottom-up attention despite being opposite sides of the same coin (Moore & Zirnsak, 2017). For these reasons, this chapter will focus on highlighting important aspects of attention.

These include top-down and bottom-up attention and the neural brain structures, neural oscillations and neuromodulators involved in visual attention.

1.2.2 Introducing the Biology of Attention

1.2.2.1 Attention, Brain Structures and Pathways

Vision starts with light reaching the retina, which sends information to the lateral geniculate nucleus (LGN), and the superior colliculus (SC; Werblin, *et al.*, 2001). The LGN receives the most information, at approximately 90%, while the SC receives the rest. From the LGN information is sent to the visual cortex where information is feedforward through a hierarchy of increasing visual processing complexity starting with area V1. This stream, known as the ventral stream, consists of V1, V2, V3, V4 and the inferotemporal gyrus (IT; Baluch & Itti, 2011). Additionally, V1 also projects information to the medial temporal (MT) area and parietal cortices for motion processing. This stream is known as the dorsal stream. From V4 in the ventral stream and the MT in the dorsal stream salient information is sent to the frontal eye fields (FEF) via the posterior medial wall of the intraparietal sulcus (IPS; Koyama, *et al.,* 2004; Grefkes & Fink, 2005). Information from the SC via the pulvinar is also sent to the FEF (Shipp, 2003). Finally, information from the FEF and IT are projected to the PFC, which is involved in executive functions (Desimone & Duncan, 1995). These functions include short-term memory and attentional processes (Baluch & Itti, 2011). This network, encompassing multiple pathways to the PFC, transmits bottom-up information. Top-down information is fedback from the PFC, FEF, IT and IPS to the MT, V4 and the SC via the pulvinar (Cutrell & Marrocco, 2002; Baluch & Itti, 2011; Ungerleider, *et al.,* 2008; Tomita *et al.,* 1999; Moore & Armstrong, 2003). Attentional modulation has little effect on earlier visual areas but gradually increases in magnitude through higher areas in the visual hierarchy. The FEF also has a direct connection to area V4 (Moore & Armstrong, 2003; Winkowski & Knudsen, 2008). The take-away message from this elaboration is that attention is the sum of the collected communication between multiple distinct brain areas. The distinction between top-down and bottom-up, while useful, certainly does not convey the true scope of attention

(Cooper, 2003). As such, this is not an exhaustive description of the complex and interconnected nature of the attentional system within the brain, but it is important to know so that brain areas affected by stress can be mapped on to the attentional areas. These areas include the PFC and hippocampus and are discussed later.

1.2.2.2 Attention and Neural Oscillations

Attention modulates the firing rate in neurons representing the selected-for target, which increases the signal to noise ratio of the neural representation for that target. Evidence suggests the priority map is generated within the IPS (Ipata, *et al.,* 2009) by the intra-communication of the attentional network that spans at least the occipital, parietal, and prefrontal cortices. Attentionally enhanced firing rates of neurons have also been reported in all these areas, as well as subcortical areas such as the SC (Paneri & Gregoriou, 2017). Attention also modulates the method in which different brain areas within the attentional network project and receive information. Coherent long-range communication between different areas is necessary as no brain area processes information independently and, as such, the brain is abundantly interconnected. Neural oscillations are a feature of neural activity, believed to be mechanisms for neural communication. Neural oscillations refer to the rhythmic variation of neural activity and are represented by voltage fluctuations (Schnitzler & Gross, 2005). Generally, neural oscillations are divided into frequency bands such as theta (4 – 7 Hz), alpha (8 – 12 Hz), beta (13 – 30 Hz) and gamma (30 - 80 Hz). Different frequency bands play a role in different cognitive processes, including attention. Using electroencephalogram (EEG) we can detect and measure these frequency bands. The advantage of using EEG to measure neural oscillations is its high temporal resolution. This is especially useful when measuring a rapid cognitive function such as attention.

An example of how this has been investigated can be seen in the following visual search task that manipulated bottom-up and top-down attention (Riddle, *et al.*, 2019). After being shown a sample stimulus participants would have to perform a saccade to one of four probe stimuli that matched the sample stimulus. Distractors were either uniform and created

a pop-out effect for the target stimulus (feature task), requiring bottom-up attention, or each distractor shared at least one feature with the target stimulus (conjunction task) requiring more top-down attention. Importantly, participants had transcranial magnetic stimulation (TMS) in either the gamma or the beta frequency band before the task. TMS was applied either to the IPS, which the authors claim is the human analogue of the FEF, or superior precentral sulcus (sPCS). (As an aside, it is probably more accurate to describe the human FEF as a brain region within the sPCS (Amiez, *et al.*, 2006). Gamma TMS to the sPCS during both tasks slowed the saccadic responses to the target, reducing reaction times, while beta TMS to the sPCS and the IPS decreased search accuracy only on the conjunction task. The authors argued therefore that the gamma frequency band carries bottom-up salient stimuli from visual areas to the sPCS for further processing. While the beta frequency oscillations between the IPS and sPCS represent top-down attention, citing the top-down modulatory effects of beta oscillations on gamma oscillations (Riddle, *et al.,* 2019).

Furthermore, trait attentional control has been associated with the theta/beta ratio within the PFC, with greater beta than theta power representing greater top-down control (Putman, *et al.,* 2014; Schutter & van Honk, 2005a). This further implicates the role of beta oscillations during top-down attentional mechanisms. Another frequency band associated with top-down visual control is the alpha band, with non-occipital alpha theorised to be generated in either the IPS or FEF (Klimesch, *et al.*, 2007). Alpha power has been associated with inhibitory control processes during visual search tasks in task-irrelevant regions of the visual field and has been expanded into the alpha-inhibition hypothesis (Cooper et al., 2003; Klimesch, *et al.*, 2007; Händel, *et al.*, 2011). In one study, participants were instructed to covertly attend one of two random dot kinematograms (RDK; two or more groups of dots that move coherently or incoherently; when coherent, the dots give the illusion of an overall shape moving in the coherent direction of the dots) presented in both hemifields. After 1.5 seconds, a second cue indicated which of the two RDKs the participants should report the motion of. Alpha power was higher in the contralateral hemisphere to the unattended visual hemifields. Furthermore, when incongruently cued increased alpha power

was correlated with worse behavioural performance in detecting the motion of a kinematograms in the unattended hemisphere. The authors concluded that this was evidence for the inhibitory effect of the alpha frequency on task-irrelevant stimuli in task-irrelevant visual regions (Händel, *et al*., 2011). However, a competing account argues that the alpha frequency band does not suppress distractors but enhances the target's neural representation (Foster & Awh, 2019). A third option could be that these two accounts could be complementary, but the debate is still ongoing (Cehlazzi, *et al.,* 2019). With that said, there is little doubt the alpha frequency band plays a role during attention. Overall, there is strong evidence that theta, beta, alpha and gamma all play a specific role during visual attention, whether timing, carrying or inhibiting information.

1.2.2.3 Attention and Neuromodulators

Neuromodulators are specific types of neurotransmitters that modulate or influence synaptic transmission between neurons. They are not investigated as often regarding attention compared to the timing (EEG) or location (BOLD) of attentional processes. Nevertheless, there is evidence to suggest the neuromodulators, particularly acetylcholine (Ach), dopamine (DA) and noradrenaline (NA), are involved in the attention process. In their review, Moore & Zirnsak (2017) point out these neuromodulators have distinct origins within the midbrain, with far reaching projections reaching subcortical and cortical structures associated with attentional processes (Cooper, *et al.*, 2003; also see Noudoost & Moore, 2011). The nuclei responsible for synthesising and releasing these neuromodulators also receive projections from the PFC (Arnsten & Goldman-Rakic, 1984; Carr & Sesack, 2000; Ghashghaei & Barbas, 2001). There is far more research for the role of ACh and DA during attentional processes than noradrenaline but due to the role it plays during allostasis it is a neurotransmitter of interest here. In brief, ACh's points of origin are the nucleus basalis of Meynert, the substantia innominata and the diagonal band of the basal forebrain (Furey, *et al.,* 2008). It is associated with bottom-up processes such as visual selective attention (Furey, *et al*., 2008), increases sensory signal strength in posterior regions (Goard & Dan,

2009) and establishing stimulus biases (Furey, *et al.,* 2008) and orientation (Voytko, et al., 1994).

DA, meanwhile, is synthesised in mid-brain areas, such as the substantia nigra pars compacta, and projects widely in the cortex. Contrary to Ach, evidence implicates DA in top-down attention, as increased DA in frontal areas is associated with increased representations of a target in the receptive fields of downstream visual areas such as area V4 (Noudoost & Moore, 2011). Furthermore, abnormal DA levels within the PFC (Ernst, *et al.,* 1998) accompany attentional problems (Mason, et al., 2003) in Attention-Deficit Hyperactivity Disorder (ADHD). In their review, Wender et al. (2001) conclude that drugs that reduce ADHD symptoms are indirect DA agonists, therefore increasing DA levels to resolve attentional deficits.

The role of noradrenaline on attentional processes is less understood and it is difficult to ascertain whether its role is purely involved in motor responses or if it does indeed supplement attention processes. Noradrenaline is synthesised centrally by neurons within the LC and is released widely throughout subcortical and cortical structures (Moore & Zirnsak, 2017). Evidence seems to suggest that noradrenaline is involved in general arousal. For example, noradrenergic receptors in the LC activate selectively to salient stimuli (Foote, *et al*., 1980, Grant*, et al.,* 1988) but also to learned targets (Aston-Jones & Cohen 2005). Noradrenaline is heavily involved in the allostatic response, which modulates attentional processes making its role on attention processes contingent on the current state of an organism.

1.2.3 Connections to Stress

The obvious place to start is the behavioural overlap of attention and stress on task performance before comparing attentional and stress mechanisms within the brain. When summarising the effect of stress on attention it is important to separate the effects of acute and chronic stress.

Summarising the effect acute stress has on attention is not straightforward because of the widely discrepant results reported within the literature. For example, one study reported acute stress impaired selective attention by increasing interference from task irrelevant information on a negative priming task (Braunstein-Bercovitz, 2003). While another study reported increased selective attention by decreasing interference from task irrelevant information on a Stroop task (Booth & Sharma, 2009). Of course, two different tasks were used but both claim the opposite effect. Using an attentional blink task, Kan et al. (2019) also reported an increase in performance due to acute stress that promoted selective attention. Perhaps then, acute stress promotes certain aspects of attention. There does seem to be a pattern for the negative/positive effects of acute stress based on the task used and what nature of attention that task is investigating. On the positive end, acute stress seems to promote quicker reaction times and increased vigilance during flanker, attentional blink and probe tasks (Kan, *et al.,* 2019; Qi & Gao, 2020) which are tasks that require fast reactions and vigilance for task relevant stimuli. On the negative end, acute stress impairs sustained attention whereby continual monitoring for change is required (Eck, *et al*., 2020), which is a slower more drawn-out task than those mentioned previously. Acute stress also impairs top-down attention in the presence of irrelevant but salient distractors (Sänger, *et al.,* 2014). While the merits of separating attention into top-down and bottom-up are not always appropriate, to summarise grossly, evidence to-date suggests that acute stress appears to promote bottom-up attention and impair top-down attention.

The effect of chronic stress on attention is less explored but the overall effect is negative with slower reaction times, decreased accuracy (Liu, *et al.,* 2020), impaired divided attention (Öhman, *et al.,* 2007) and impaired attentional set-shifting (Liston, *et al.,* 2006). The lack of research in this area is surprising given that Morrison (2014) has suggested life stress interacts with the attentional negativity bias by increasing the negativity bias. This suggests a link to the “Vicious Cycle of Stress” (Justice, 2018; page 127) which is discussed later in this chapter. The gist is that stress and neuropathology (that leads to cognitive decline) generate a negative feedback loop with each other that accelerates cognitive

decline. Furthermore, one study reported *reversible* PFC disruption caused by social stress. This disruption lead to impaired attentional control (Liston, *et al.,* 2009). However, the interaction of stress and age on other cognitive functions (Marshall, *et al.,* 2016a; Marshall, *et al.,* 2016b; Marshall, *et al.,* 2018) would suggest damage from lifetime stress is not reversible. Furthermore, the underlying mechanisms causing attentional decline from chronic stress are less explored. The stress/age interaction could be one mechanism (explored in this thesis), while perceived stress could be another (Forrester, 2017). Regardless, there does seem to be a connection between attention and chronic stress that warrants further investigation. There are some obvious overlaps in brain areas, neurotransmitters, and oscillation related to both the allostatic response and the attentional network. Noradrenaline is essential for arousal during everyday attention to both task-relevant and salient stimuli (Foote, *et al*., 1980, Grant*, et al.,* 1988; Aston-Jones & Cohen 2005). During an allostatic response, noradrenaline increases leading to increased awareness of salient and threatening stimuli (Rajkowski, *et al.*, 1994). Prolonged exposure to noradrenaline due to chronic or accumulative stress sensitises subjects to further stress (Adell, *et al*., 1988) and incidentally may be a key factor for the development of anxiety and depression (Leonard, 1997; Seki, *et al.,* 2018). The role of the PFC in attention and its deterioration from long-term exposure to cortisol further links attention and stress together. The PFC is responsible for executive function, including attentional control (Desimone & Duncan, 1995) and is susceptible to cortisol-related damage. GRs expression in the PFC during an allostatic response decreases executive function via cortisol binding (Ouanes, *et al.,* 2020; Ouanes & Popp, 2019). Prolonged exposure to cortisol from chronic or accumulated stress leads to dendritic atrophy in pyramidal cells within the PFC (Brown, *et al.,* 2005) and an overall decrease in cell volume (Cerqueira, *et al.,* 2005). This degrades performance on executive functions such as inhibition and memory (Marshall, *et al.,* 2016a; Marshall, *et al.,* 2016b; Marshall, *et al.,* 2018; Peavy, 2009). However, this issue has not been explored for attention. Due to the effect chronic stress has on the PFC one would expect attentional detriments as well. Further evidence for this hypothesis is reflected in changes to neural oscillations

whereby chronic stress disrupts normal oscillatory activity within the PFC during executive functions. The theta/beta ratio within the PFC is important for executive function; however, chronic stress increases theta oscillations disrupting executive function as well as PFC communication with other brain areas such as the hippocampus (Marshall, *et al*, 2016b; Marshall, *et al*, 2018). Furthermore, long-term stress also brings reductions in gamma oscillations disrupting communication from sensory areas to the PFC (Marshall, *et al*., 2015; for a review of oscillations and stress see Negrón-Oyarzo, *et al.,* 2016). This leads to slower reaction times on tasks that require executive function and increased errors on tasks requiring bottom-up precision. Therefore, these oscillatory disruptions should also bring about attentional deficits. Clearly then, evidence suggests that chronic stress should negatively impact attentional performance. Furthermore, work by Marshall et al. (2015, 2016a, 2016b, 2018) highlight the interaction of age and chronic stress on cognitive decline and not necessarily the effect of chronic stress or ageing in themselves. Their results suggest the negative effects of chronic stress on cognition only start to manifest after a long period of time (e.g. a life-time). This suggests that chronic stress could negatively affect attention but only after sufficient exposure to the stress hormones. Evidence from EEG, stress hormones and behavioural performance for other cognitive domains other than attention suggest the possibility of the same link between attention and chronic stress.

1.2.4 Summary

Perception is vitally important for making meaningful choices in the world either through proactive or reactive behaviours. Like all brain functions, it is limited by the amount of cognitive resources available within the brain and so not all stimuli can be, or even should be, processed. Attention is the mechanism by which resources are allocated to priority stimuli. It is an all-encompassing term that sparks debate and demands investigation. Common among the very many studies of attention are the concepts of bottom-up and top-down mechanisms of attention, but, although this distinction is useful, it is arguably a gross simplification. Oscillations within the gamma frequency band are associated with

feedforward processes and thus implicated in bottom-up mechanisms by increasing the signal strength of the selected-for target in higher order areas. Feedback attentional mechanisms produce a bias towards stimuli related to task demands, prior memory and planning. Originating from the FEF, top-down signals are fedback to area V4 modulated by DA, while the FEF is also involved in generating saccades towards the selected-for targets. The feedback signal is associated with the beta frequency band and modulates neural activity within the visual stream such that there is increased neural activity relating to the selected-for stimulus. The combined outputs of bottom-up and top-down mechanisms result in the priority map, whereby visual stimuli are given preference as saccadic targets. Overall, attention is an important mechanism to guide visual selection towards stimuli that affect behavioural goals at the expense of the rest of the visual scene. The effect of stress on attention seems to depend on the task requirements and whether stress is acute or chronic. Acute stress seems to increase vigilance and reaction times but hinders tasks requiring sustained monitoring attention. Chronic stress slows reaction times and decreases target accuracy. This seems to come about from the long-term damage to the PFC and hippocampus caused by over exposure to cortisol. Amongst other effects, this damage atrophies PFC dendrites and disrupts normal oscillatory function leading to decreased attentional function.

1.2.5 Open Questions

Converging evidence suggests that a mechanism for the negative effect of prolonged exposure to stress comes about from neuron degradation from over exposure to cortisol resulting in dendritic atrophy and volume loss. This results in communication disruption between the PFC and other brain areas as noted by aberrant neural oscillation in the theta and gamma frequency range and is accompanied by memory and inhibitory deficits. However, the amount of work on the topic is sparse. This link between chronic stress and other cognitive functions, such as attention is yet to be investigated. Finally, evidence suggests cognitive decline from chronic stress only manifests after long-term exposure.

Following on from previous work, the effects of this interaction on attention should be investigated.

1.3 Ageing

1.3.1 The Ageing Mind

Anecdotally the ageing process is often associated with cognitive decline, be it working memory, spatial learning or attention. Empirically there is evidence to support this with the normal ageing process being associated with physiological and cognitive decline (Colsher, & Wallace, 1991; Evans, *et al.,* 1993; Kausler, 1994; Wilson, *et al*., 1999). This effect of ageing on cognitive decline appears to be cross-cultural (Yu, *et al*., 1989; Jin, *et al*., 1989). In addition, it is reported for memory, language and perceptual performances (Wilson, *et al*., 1999; Wilson, *et al.,* 2002). The total number of people over 60 years of age is increasing, expecting to reach 2 billion by 2050, exceeding the total number of children (UN, 2013). Couple this with retirement age being around 60 – 65, and evidence of cognitive decline during ageing; a huge uptick in older persons would have major economic consequences. It is therefore important to investigate the causes of cognitive decline in aging. However, ageing itself may not necessarily be the determinant for the rate of cognitive decline (Marshall, *et al.,* 2016; Peavy, *et al*., 2009; Wilson, *et al.,* 2002). For this reason, it is important to explore what contributes to the rate of decline in cognition for older persons.

As Wilson and colleagues (2002) noted, despite the evidence of cognitive decline during ageing, the decline rate between individuals has high variability. They suggested ageing itself does not drive cognitive decline and proposed the decline was due to other individual differences. There is evidence for this with one study reporting the association between high neuroticism and cognitive decline (Luchetti, *et al*., 2016). Another factor that has been investigated regarding cognitive decline during ageing is education. Earlier work noted the level of educational attainment seemed to buffer cognitive decline (Colsher & Wallace, 1991; Evans, *et al*., 1993) regardless of age, place of birth, occupation and income (Evans, *et al.,* 1993). However, other results reported no such effect (Carmelli, *et al.,* 1997;

Hultsch, *et al.,* 1998). Lenehan et al. (2015) noted this discrepant trend throughout the 2000s and after review, reported education had no such buffering effect on cognitive decline during ageing. However, they did note that education was associated with cognitive performance in general (Lenehan, *et al*., 2015). At the very least, the evidence for education as a factor involved in cognitive decline is inconclusive. Another prominent factor in cognitive decline during ageing is neuropathology, in particular Alzheimer's disease (AD). One longitudinal study found that cognitive decline for memory, language and perception was only present in two subgroups: the AD group and the group that later developed AD over the course of the study. The third and final subgroup, free of AD, did not suffer from cognitive decline (Wilson, *et al*., 1999). More recently, the link between neuropathology and cognitive decline was further explored (Boyle, *et al.,* 2017). The decline was linked with the deleterious effects of AD on the different brain areas, including the hippocampus (DeTure & Dickson, 2019), important for memory, and the PFC (Wenk, 2003), important for executive function. Taken together this evidence suggests ageing *per se* may not be the central cause of cognitive decline. Of note here is the link between the brain areas mentioned and the brain areas associated with stress and attention. Studies have linked accumulated life stress to cognitive decline. This is particularly interesting as chronic and accumulative stress are involved in the genesis and progression of disease (for review, see: Bjorntorp, 1997; Martocchia et al., 2016; Selye, 1950; Shin, *et al*., 2016) and this includes AD (Justice, 2018).

1.3.2 Stress, ageing and Alzheimer's disease

From evidence suggesting a strong association between chronic stress and memory loss (Lupien, *et al*., 1997; Wilding, *et al*., 2007), Peavy et al. (2009) investigated the long-term effects of stress on memory. Using a longitudinal design, they found chronic stress was associated with faster cognitive decline in participants who already had mild cognitive impairment but the same was not true for cognitively normal participants. Following from this, further work investigated the interaction effect of age and accumulated stress on memory and response inhibition (Marshall, *et al.,* 2016a; Marshall, *et al.,* 2016b; Marshall, *et al.,*

2018) as described previously. To reiterate, in this series of studies participants were in one of four groups: older high/low stress or younger high/low stress. Behavioural performance between the young groups and the older low stress groups were not significantly different, however the older high stress group consistently performed worse on all tasks. This is significant for two reasons, as it suggests age (performance for the older low stress group) and stress (performance from the younger high stress group) in isolation do not contribute to cognitive decline. The long-term effects of stress provoke cognitive decline during advanced ageing.

One mechanism for this decline is the deleterious effects prolonged exposure to stress neurotransmitters and hormones have on the brain, particular in the hippocampus (McEwen, 1999; Sapolsky, *et al.*, 1990; Woolley, *et al.*, 1990; Gould, *et al.*, 1998) and PFC (Brown, *et al.,* 2005; Cerqueira, *et al.,* 2005). However, yet another putative mechanism that could lead to cognitive decline is the "Vicious cycle of Stress" and its link to neuropathology (Justice, 2018; page 127). Previously, the rate of cognitive decline was associated with AD or the subsequent development of AD, with faster rates of decline associated with greater progression of AD (Wilson, *et al*., 1999). This has led to notion of the "Vicious Cycle of Stress" whereby stress leads to, and accelerates the progression of neurological disease, which in turn leads to the disruption of stress mechanisms that would produce neuropsychiatric symptoms. Moreover, the cycle repeats and accelerates itself (Justice, 2018).

Given the effects of stress hormones on the brain and the evidence from age/stress interaction on memory and inhibition (Marshall, *et al.,* 2016a; Marshall, *et al.,* 2016b; Marshall, *et al.,* 2018) we previously posited that this interaction could also explain attentional deficits related to advanced ageing. This includes slower RTs, decreased cognitive accuracy (Li, *et al*., 2013), attentional control (Sweeney, *et al.,* 2001), attentional speed (Georgiou-Karistianis, *et al*., 2007), attentional efficiency (Commodari & Guarnera, 2008), and decreased ability to sustain attention (Georgiou-Karistianis et al., 2007). Furthermore, one study noted that cognitive decline in one domain would be associated with

decline in another domain (Wilson, *et al*., 2002). Given this, the link to stress and the association between stress and neuropathology (which itself is linked to cognitive decline) begs the question; will the pattern of results for the effect of stress and age on attention mirror the results for stress and age on memory?

1.3.3 Physiological Overlap

There are physiological data, which support the hypothesis that the stress/age interaction would negatively affect attention. In general, older persons show shrinkage in grey and white matter unequally spread throughout the brain with the frontal lobe displaying the highest shrinkage, and the occipital lobe having the least (Kemper, 1994; Raz, 2000). This affects executive functions such as attention and inhibition as previously discussed. However, the brain also shows less specificity during cognitive tasks with age. As the cognitive load of a task increases, processing becomes more generalised with greater PFC recruitment during tasks for older persons compared to younger persons (Li, *et al.,* 2013; Smith, *et al.,* 2001), possibly as a way to compensate for atrophy in other brain areas (Park, *et al.,* 2022). This may also account for slower reaction times but help maintain accuracy. Reaction times and stimulus accuracy may also be hampered by alterations within gamma frequency oscillations, whereby older persons show a reduction in synchronous gamma activity (Insel, *et al*., 2012) associated with decreased performance on attention tasks (Elshafei, *et al.,* 2020).

Cortisol is also affected by ageing. The cortisol awakening response (CAR), whereby cortisol concentrations peak in the morning and slowly decrease over the course of a day, becomes flattened in older persons. This is due to an increase in cortisol at the tail end of the day (Rehman & Masson, 2001), increasing cortisol exposure to the PFC of the older person which may increase saturation of GRs within the PFC, inhibiting frontal activity (Ouanes & Popp, 2020). The CAR is also affected by chronic stress. Chronic stress is associated with an increased CAR from work burn out (Steptoe, *et al.,* 2000) and a compromised social life (Wüst, *et al.,* 2000). Experiencing chronic stress or accumulating

more stress over a lifetime may exacerbate cortisol exposure during ageing, especially altering the CAR, increasing the risk of mild cognitive impairment and AD. This would ultimately lead to decreased cognitive ability before the actual onset of AD as seen in the Wilson et al. (1999) study.

Finally, noradrenaline decreases during ageing. Those with the lowest noradrenaline concentrations often develop AD (DeKosky & Palmer, 1994). Indeed, decreased structural volume of the LC, the brain area that synthesises NA (Moore & Zirnsak, 2017), predicts development of AD (Dutt, *et al*., 2020). One hypothesis is that LC degradation caused by ageing or stress increases tonic activity within the LC, which can lead to cognitive impairment and AD (Mathers, 2021). However, there is contrasting evidence as to whether noradrenaline protects or accelerates cognitive decline, especially in the development of AD (for review see Mathers, 2021). Noradrenaline binds to one of two receptors, the low affinity β receptors or the high affinity α2 receptors (Marzo, *et al.,* 2009; Salgado, *et al.,* 2012), with the latter responsible for the allostatic response (Musheshe, *et al.,* 2018). β-adrenergic activation stops the build-up of Aβ peptides (Li, *et al.,* 2013), produced as a by-product of brain activity, which are flags for AD before the development of AD, in post-mortem study (Herrup, 2015). However, once AD develops, β-adrenergic activation accelerates the progression of AD (Koivunen, *et al.,* 2011). This is important as stress increases noradrenaline concentrations, which may accelerate cognitive decline during ageing if already cognitively impaired but may actually help those not cognitively impaired.

Therefore, there is some physiological evidence that the stress/age interaction should decrease attentional performance. Both stress and ageing increase cortisol levels, and both are associated with atrophy within the brain. Noradrenaline is a large component in cognitive decline during ageing, either positively or negatively and evidence suggests an effect of stress on the LC. Finally, AD is intimately linked with cognitive decline which itself is accelerated by cortisol and noradrenaline.

1.3.4 Summary

Attentional ability declines during ageing. Prior evidence suggests the stress/age interaction may cause attentional deficits during ageing. Circumstantial evidence comes from studies that have investigated this interaction with other cognitive functions. Other evidence indicates stress seems to interact and overlap with the ageing process producing or accelerating cognitive decline. This is because significantly worse cognitive performance is associated with mild cognitive impairment, or those that go on to development AD. As cortisol and noradrenaline, both primary hormones/neurotransmitters involved in the allostatic response, are associated with mild cognitive impairment and AD, it is reasonable to suggest that lifetime exposure or heavily accumulated stress over a lifetime could contribute to attentional deficits, which only manifest during increased ageing. However, the stress/age interaction effect on attention, regardless of the proposed mechanisms have, to date, not been investigated.

1.4 General Summary

Stress is an adaptive mechanism, which prepares an organism to deal with incoming threat. However, chronic stress or increased accumulated stress leads to an over exposure to cortisol leading to maladaptive behaviours and brain degradation in the PFC and hippocampus, which are areas responsible for executive functions such as memory, inhibition, and attention. While not immediate, these deleterious effects seem to produce cognitive deficits during advanced ageing where the negative effects of the stress hormones have had time to significantly harm the brain. In ageing research, cognitive decline is associated with mild cognitive impairment and AD. It is interesting to note that both mild cognitive impairment and AD are associated with the prevalent stress hormones: cortisol and NA. This may help to explain the age/stress interaction on cognitive performance, as well as explain the common conception that ageing is accompanied with cognitive deficits.

In this regard, previous research found that only older persons with high exposure to stress performed significantly worse on memory and inhibitory tasks than other older

persons and young persons. However, scientific investigation has not extended this effect to attentional performance. Attention is the cognitive mechanism that filters out unnecessary stimuli from the environment and allocates cognitive resources to relevant stimuli. Attentional mechanisms overlap with brain areas already known to be affected by stress and ageing, with particular focus on the PFC. Attention is also affected by cortisol and noradrenaline, hormones involved in the allostatic response and the maladaptive ageing process described above. Therefore, attentional performance during advanced ageing could also be affected by the stress/age interaction.

Finally, current theories do not adequately address how stress is maintained so that it becomes chronic. One relatively new theory (GUTS) suggests allostasis is avoided by learning and generalising safety cues. If this process is compromised, safety cues are missed, or fear learning happens instead, which leads to the maintenance of chronic stress. Furthermore, compromised life domains (physical, social and contextual) can contribute to increased 'generalised unsafety', which also leads to the maintenance of chronic stress. This theory and the life domains it proposes to be associated with feelings of unsafety have not been empirically tested.

Consequently, this thesis aims to investigate two questions: 1) Will the stress/age interaction previously observed for memory and inhibition also be seen for attention? 2) Are compromised life domains suggested by GUTS associated with chronic stress?

Chapter 2 – Paying Attention: The Cost of Stress During Aging

2.1 Abstract

Conventional wisdom and experimental data express the negative effects of stress and ageing on cognitive decline. Recent studies investigated the interaction between ageing and stress on memory and found that only older, high stress participants performed significantly worse than both the younger, high and low stress groups and, most importantly, the older low stress group. It is not clear whether the stress/age interaction extends to other cognitive functions such as attention, especially as evidence shows overlap in brain area associated with both memory and attention. Therefore, this study investigated the interaction of age and stress on attention. 146 participants, with an age range of 61 (*M* = 38, *SD* = 22), completed a measure of the amount of stressful experiences encountered over the course of their lifetimes (either the Social Readjustment Rating Scale or the Life Events Scale for Students). Additionally, participants completed an attentional blink task where they had to identify two target words in a rapid serial visual presentation where recall accuracy was measured. The two targets could either be neutral (e.g. book) or aversive (e.g. kill) resulting in four conditions (neutral/neutral, neutral/aversive, aversive/neutral or aversive/aversive), and either appeared 300ms or 800ms apart. Age and life stress were regressed on the magnitude of the accuracy between target 1 and 2 words. Overall, older participants were less accurate than younger participants were but importantly, there was an interaction effect of age and stress. Older participants who had experienced more accumulated life stress performed worse than their less stressed counterparts and younger low and high stress participants. When considering the word combinations separately, the stress/age interaction effect remained for all conditions except when the first target was aversive and the second target was neutral. Our study provides evidence that attentional decline during aging may be driven by the negative long-term effects of stress, in addition to the aging process itself. Furthermore, aversive stimuli still show a strong attentional effect, regardless of age or stress as aversive stimuli readily captures, and holds attention in a bottom-up fashion more

powerfully than neutral stimuli. Future research should explore this difference between stimulus effects by using an attentional task more related to top-down attention.

2.2 Introduction

Stress and ageing are not specifically related (although living longer can expose one to more stressful situations) but conventional wisdom suggests that both come with a suite of negative physiological, cognitive and behavioural effects. The disastrous physiological effects of chronic stress are well documented and include increased cardiovascular disease (Rozanski, *et al.*, 1999), suppressed immune systems and increased susceptibility to disease (Khansari, *et al.,* 1990), and healthy-appetite disruption (Diz-Chaves, 2011; for review see Yaribeygi *et al.,* 2017). Furthermore, chronic stress is strongly associated with inflammatory related disorders such as mild cognitive impairment and Alzheimer's disease (Sorrells, *et al.*, 2009; Candore, *et al.,* 2010; Jaroudi, *et al.,* 2017). The physiological effects can also lead to psychological deficits such as the deleterious effects on hippocampal cells resulting in memory impairment (McEwen, 1999; Sapolsky, *et al.*, 1990; Woolley, *et al.*, 1990; Gould, *et al.*, 1998). It also interrupts prefrontal cortical (PFC) communication with other brain areas resulting in impaired top-down control in cognitive processes such as planning and attention (Desimone & Duncan, 1995; Miller & Cohen, 2001). The process of ageing is also associated with an overall decrease in episodic, working and semantic memory, as well as decreased perceptual speed and visuospatial ability (Wilson, *et al.,* 2002; Colsher & Wallace, 1991). Furthermore, accompanying the ageing brain are shrinking cell bodies, a loss of dendritic spines and changes in the receptors of neurotransmitters (Rehman & Masson, 2001). While this is cause for concern as the population is steadily ageing (UN, 2019) and the prevalence of stress within the population is increasing, especially in young adults, it is not the complete picture. A longitudinal study found that when unaffected by Alzheimer's disease, advancing age was not associated with cognitive decline (Wilson, *et al.*, 1999). Some years later, another longitudinal study investigated several factors that may contribute to the cognitive decline associated with ageing. This study

highlighted chronic stress and accumulated life stress as significant contributing factors towards cognitive decline and not simply the process of ageing *per se* (Peavy, *et al.,* 2009). In order to investigate this issue in more depth, a series of studies examined the effect of cumulative life stress on memory performance and inhibition (Marshall, *et al.*, 2015; Marshall, *et al.*, 2016a; Marshall, *et al.,* 2016b; Marshall & Cooper, 2017; Marshall, *et al.*, 2018). This series of studies found that accumulated life stress was associated with cognitive decline in older, high stress individuals compared to younger, low and high stress individuals as well as other older low-stress individuals. This series of results would suggest that cognitive decline during ageing is, at least in part, driven by the exposure to stress hormones, such as cortisol, over the course of a lifetime. In line with chronic stress, accumulative stress exposes one to more stress hormones (such as cortisol) increasing the risk of allostatic load. Continuing this line of inquiry it is important to investigate if this stress/age interaction extends into other cognitive domains given that areas of the brain which are responsible for memory and attentional processes are both susceptible to the permanent damaging effects of chronic/accumulative stress and cortisol (Arnsten, 2009; McEwen & Sapolsky, 1995).

Allostatic load is a process whereby continued exposure to the allostatic response gradually wears down biological structures such that dysfunction occurs. Therefore, the longer one is exposed to stress and cortisol the higher the chance of cortisol dysfunction and damage to brain structures susceptible to cortisol. Evidence strongly suggests that it is through this process the cognition declines during the ageing process (Marshall, *et al.*, 2015; Marshall, *et al.*, 2016a; Marshall, *et al.,* 2016b; Marshall & Cooper, 2017; Marshall, *et al.*, 2018; Peavy, *et al.,* 2009). It could also be argued that being alive for longer has the potential to expose an individual to more life stressors, leading to an accumulation of micro lesions in the brain caused by cortisol (Peavy, *et al.,* 2009). This is the difference between chronic and accumulated stress. Chronic stress is pathological in nature while accumulated stress is merely the result of living. Nevertheless, chronic stress and accumulated stress

lead to increased exposure to cortisol. With increased exposure to cortisol, brain areas associated with memory, such as the hippocampus, atrophy over time causing abhorrent brain activity compared to healthy brains (Shi, *et al.*, 2015); while the frontal cortex may suffer damage in the form of micro lesions caused by hypertonic blood flow, itself induced by stress (Rabbitt, 2005). However, previous studies investigated the effect of stress and ageing on memory but did not investigate the same effects on attention. It is therefore imperative to continue this line of inquiry by investigating the effects of age and stress on attention.

As there are not enough cognitive resources to process all incoming stimuli, attention is the mechanism by which awareness is directed towards some phenomena at the exclusion of others (Moore & Zirnsak, 2017). As a result, some stimuli receive priority over other stimuli. Over the course of evolutionary selection, this has tended to favour negative over positive stimuli for simple survival purposes (Taylor 1991; Jonikaitis, 2019). For example, there is a considerable amount of experimental evidence that indicate aversive and emotional stimuli hold privileged access to cognitive resources; this is especially true for attentional resources in response to negative stimuli (Arnell, *et al.*, 2007; Ellenbogen, *et al.*, 2002; Kan, *et al.,* 2019; Kan, *et al.,* 2021; Schwabe & Wolf, 2010). Similar to memory, attention also declines during ageing (Greenwood, *et al.*, 1997; Sweeney, *et al.*, 2001). As memory decline in old age is linked with lifetime stress, it is important to explore whether the same pattern would be true for attention. To date, this has not been investigated and that is the goal of the current research.

The 'Attentional Blink' (AB) is a phenomenon whereby the recall accuracy of the second (T2) of two target stimuli is significantly lower if presented within 500ms of the first target (T1) when embedded in a rapid serial visual presentation (RSVP; Raymond, *et al.*, 1992). A behavioural task utilising the attentional blink, known as the AB task, involves trials in which two target stimuli, usually a word or picture, are embedded in a stream of distractor stimuli - other non-related words or pictures. Targets have features, which are distinct from

distractor stimuli such as colour or content. Each stimulus within the stream is presented rapidly (around 100ms) whereby a stream containing 18 total stimuli lasts less than 1.8 seconds - the length of each trial. At the end of each trial, participants must indicate what the two target stimuli were in the RSVP. Early experimentation with the AB task used letters and numbers. Stimuli that are more sophisticated were introduced over time, such as words and pictures, with concurring results (Raymond, *et al.*, 1992; Kawahara & Sato, 2013; Schwabe & Wolf, 2010; Kan *et al*., 2019; Kan *et al.,* 2021). The proposed reason for the inaccuracy of the second target is thought to be related to working-memory consolidation. Attention to the T1 effectively ties up available cognitive resources for the first target, leaving little attentional resources for the second target (Jolicœur, 1999; Jolicœur, *et al.*, 2001; Schwabe & Wolf, 202; Kan *et al.,* 2021). The prefrontal cortex (PFC) is responsible for memory and attentional processes and susceptible to the permanent damaging effects of chronic stress and cortisol (Arnsten, 2009; McEwen & Sapolsky, 1995). In fact, evidence suggests working memory is, in part, responsible for top-down attention, which is often thought of as goal-directed or motivated attention (Baluch & Itti, 2011; Theeuwes & Van der Berg, 2013). Regardless, this damage to brain areas responsible for attention, caused by the long-term exposure to cortisol would suggest a similar pattern of behavioural outcome for attention as memory. Namely, poorer performance for older individuals who have, either through chronic or high-accumulated lifetime stress, been exposed to cortisol more than their older non-stressed counterparts have and younger individuals.

Related to the current study, stress, age and emotion have been shown to interact with the AB. For example, stress-induced participants (participants experiencing acute stress) showed an increase in accuracy for T2 (Schwabe & Wolf, 2010; Kan *et al*., 2019; Kan *et al.,* 2021), indicating that acute stress attenuates the AB window, reflecting the narrowing of attentional focus and a decrease in the AB window. With that said, there is no data on the effect of chronic stress specifically on the AB but there is evidence that chronic negative mood states decrease attentional ability. MacLean, et al. (2010) found that participants with self-reported negative affect had a larger AB window than participants with a self-reported

positive affect. Furthermore, older participants perform significantly worse than younger participants on the AB task as reflected by lower accuracy scores for T2 detection (Lahar, *et al.*, 2001; van Leeuwen, *et al.*, 2009). Manipulating the target words so that they are either aversive or neutral has also been investigated. For example, an aversive T2 shortens the AB window if T1 is neutral; increasing accuracy rates to the second target under 500ms (Schwabe & Wolf, 2010), effectively decreasing the magnitude of the AB. This effect was observed to be greater in the stress group compared to the neutral group. Additionally, regardless of the emotional content of T2, an aversive T1 will always increase the magnitude of the AB, thereby increasing the AB effect, (Schwabe & Wolf, 2010; *see also* McHugo, *et al.*, 2013). Evidence suggests there may be an interaction between stress and age on the AB; however, this interaction has not been investigated. Therefore, demonstrating that these changes in attentional ability with age are also, at least in part, moderated by lifetime exposure to stress would add considerable strength to our understanding of cognitive decline.

In the present study, we investigated the interaction between stress and ageing on performance on the AB task. Participants completed an AB task, with a combination of aversive and neutral target words, and provided life stress scores for comparison. We expected to find similar results to previous studies: overall, older participants would have decreased second target accuracy resulting from a larger attentional blink, and older participants who have experienced more stress over a lifetime would have further decreased second target accuracy also resulting from a larger magnitude of the attentional blink. Furthermore, if T1 was aversive there would be a decreased accuracy for T2, while if T1 was neutral there would be an increased accuracy for an aversive T2. The main hypothesis is the replication of the same pattern of results as Marshal *et al*. (2016a; 2016b) in that we expected an interaction of stress and age on performance, and that specifically older participants who have experienced more lifetime stress would have the largest attentional blink magnitude. Conversely, older participants with lower lifetime stress would have

performance comparable to younger participants regardless of their lifetime stress. This effect was expected across all word combinations.

2.3 Methods

2.3.1 Participants and Design

Participants (*n* = 146) were recruited from the University of Essex (where students complete studies for course credit) and online via social media (nextdoor.com and facebook.com). This was to ensure a good mix of ages. Recruitment continued until there were at least 40 participants under 30 years old (*n* = 88), Mean age = 20.90, *SD* = 2.84; and at least 40 over 60 years old (*n* = 58); Mean age = 65.04. *SD* = 5.29. Marshall and colleagues consistently aimed for 30 participants in each group. Given this study did not include electroencephalogram (EEG) and therefore we were free of the typical EEG time constraints, we aimed to recruit more participants. We left the online posts advertising the study online for two months foreseeing trouble recruiting older participants[1] and allowed all those that were eligible to take part. Overall, participants comprised 72% women, 76% white, 12% Asian and 7% black. 70% of the participants had an A-level qualification or higher. We used a within participant design and the study was completed online. All participants completed the study online with all blocks of the AB task completed though Inquisit and all the questionnaires completed through Qualtrics. Younger participants completed the Life Event Scale for Students (LESS: Clements & Turpin, 1996) while older participants completed the Social Readjustment Social Scale (SRSS: Holmes & Rahe, 1967). Both scores were standardised and combined (please see below for justification).

[1] We planned to recruit from the University of the 3rd Age. It is a UK wide movement that aims to bring people no longer in full-time work together to promote non-formal learning. Marshall and colleagues recruited their older participants from u3a, however due to COVID they did not want to be involved.

2.3.2 Materials

2.3.2.1 Questionnaires

Questionnaires were used to ascertain the accumulated life stress of participants, trait anxiety as well as perceived stress, with the latter two acting as control variables.

The LESS and the SRSS measured accumulated life stress. Both questionnaires are analogous to one another but are used for different age groups and were used in the Marshall (2015, 2016a, 2016b, 2017 & 2018) studies. Within each questionnaire is a set of statements reflecting life events that participants may have encountered (e.g. 'The death of a spouse' or 'been on holiday') and are assigned a value, with higher values indicating the statement represents a higher stress event and vice versa for lower values. Participants indicate if they have experienced the life event expressed in the statement and the scores from all the statements are added together, a higher score would indicate higher accumulated life stress. There are 43 items on the SRSS (with total scores ranging from 0 to 1466) and 36 items on the LESS (with total scores ranging from 0 to 1849). The LESS is used for participants aged under 30, while the SRSS is used for participants aged over 60. While very similar, the two questionnaires differ slightly to better reflect the age of the participant. To be compared and averaged together across age groups, the scores will be standardised. As noted by Marshall *et al.* (2015), it is not best practice to equate scores from distinct questionnaires, but it is unavoidable in this case because older participants will have inevitably experienced more stress than younger participants simply because they have lived longer. Furthermore, the questionnaires are analogous in structure and layout and the differences are subtle. The Marshall papers also found robust results over the course of several studies that suggest the use of the two questionnaires was not a detriment to scientific enquiry.

Stress and anxiety are often present simultaneously and the effect of one on behaviour may confound the effect of the other. For example, acute stress and anxiety increase bottom-up attentional focus towards negative stimuli and decrease top-down

control (Arnell, *et al.,* 2007; Most, *et al.*, 2007; for an overview see McHugo, *et al.*, 2013). For this reason, it was necessary to control for anxiety. Anxiety was measured using the Trait Anxiety Inventory (TAI; Spielberger, *et al.*, 1971) to measure trait anxiety (general levels of anxiety). The TAI comprises a 20-item questionnaire. Participants rate their (dis)agreement to a presented statement (e.g. 'I am always nervous' or 'I currently feel nervous') on a 4-point Likert scale ranging from 1 ('Not at all') to 4 ('Very much'). Higher scores indicate higher levels of trait anxiety (total score range: 20 – 80).

For the LESS and SRSS, each statement is preassigned a value that is separate from any subjective attitude toward stress or perception of stress on the part of the participant. 'Breaking the law' would be, presumably, stressful to most but for others, this may not be the case, yet the assigned value is the same regardless of participant. To this end, the Perceived Stress Scale (PSS; Cohen, *et al.*, 1983) was used to measure the participant's perception of stress. The score captured by the PSS was used as a control because the PSS was originally designed to account for the subjective perception of stress. It is a subjective measure of how much one appraises events in their life as stressful. Therefore, if there is an effect of stress and age regardless of perceived stress then the effect is more objective than subjective in nature because the effect is due to the structural changes to the brain caused by cumulative stress (Peavy, 2009; Marshal *et al.,* 2016; Sapolsky, *et al.,* 1990). The statements in the PSS are non-specific and make no inquiry to the nature of the events themselves. It asks participants to rate their dis/agreement to statements (e.g. 'In the last month, how often have you felt nervous and "stressed"?') on a 4-point Likert scale ranging from 1 ('Never') to 4 ('Very often'). There are three versions of the PSS: 4-, 10- and 14- item versions. The 10 item PSS has the highest validity and reliability and was the version we used (Lee, 2012). Higher scores indicate more stressful appraisals than a lower score (total score range: 10 – 40).

2.3.2.2 Attentional Blink Task

The ABT was created and run through Inquisit (Inquisit 5 [Computer software]. (2016). Retrieved from https://www.millisecond.com). Items were presented in each RSVP stream whereby T1 could appear as item 5 or item 8 and T2 was either 3 or 8 items later (lag 3 and lag 8 respectively). Items were presented for 100ms; therefore, a stream lasted 1.8 seconds (figure 2.1). Words were in Arial font and were set to be 10% of the screen height to account for the varying screen sizes participants would use.

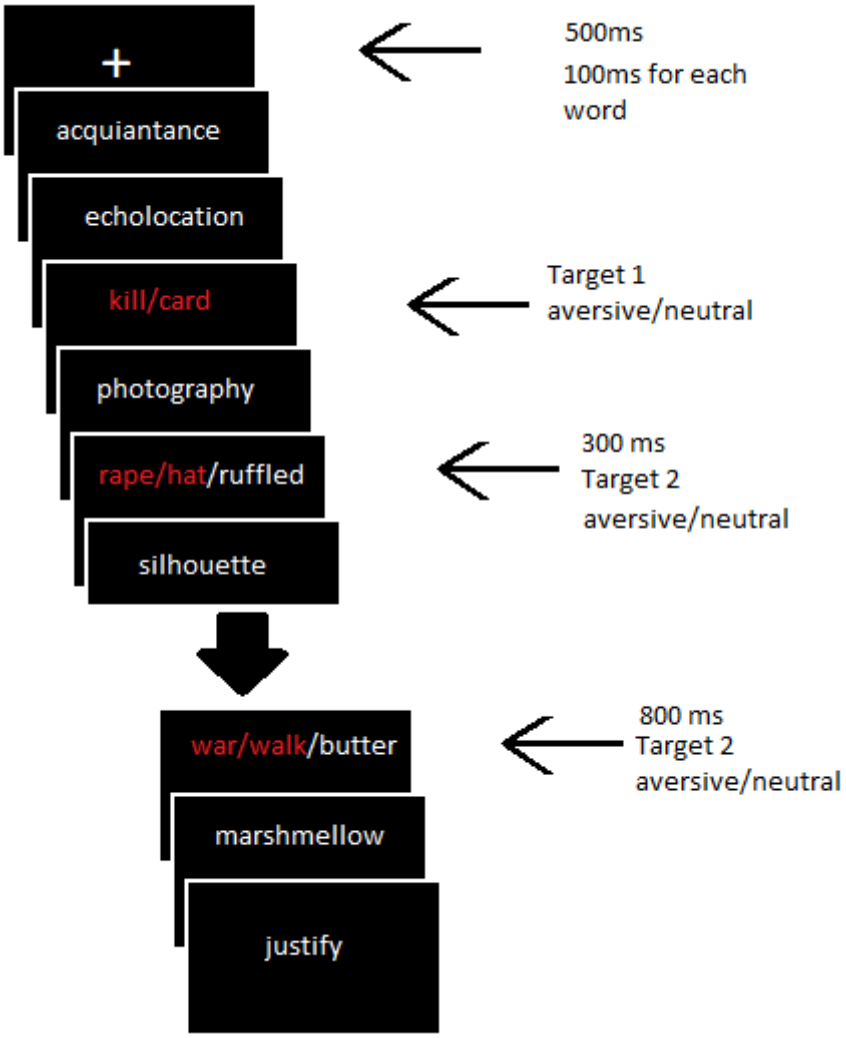

Figure 2.1 RSVP example

Similar to Schwabe (2010) target words were red and neutral distractor words were white centred on a black screen. Participants were asked to recall the red words (i.e. the

target words) after the stream ended with two multiple-choice questions, one for each of the targets, consisting of the target word and three incorrect words that could have been the target. Target words were length matched and substantially shorter (3 – 4 letters) in length than distractor words (6 – 12 letters) so that targets were forward and backward masked. Words were taken from several studies so that they were already validated (Arnell *et al.,* 2007; Schwabe & Wolf, 2010) leading to a total of 18 aversive (e.g. 'rape', 'cut') and neutral (e.g. 'fish', 'gel') target words and 18 distractor words. T1 and T2 could be either aversive or neutral and each word in either list was used at least once.

Before the task started proper, participants were presented with 16 practice trials, one for each combination of target words and for each combination of their location and lag. There were four conditions depending on the T1/T2 combinations. In one condition both target words could be neutral (N-N), another where each target was aversive (A-A), a condition where T1 was neutral and T2 was aversive (N-A) and the final condition where T1 was aversive and T2 was neutral (A-N). Each condition could be presented with an early or late T1 and lag 3 or lag 8 T2. Each condition and combination was repeated 18 times totalling 288 trials. This was divided into blocks of 72 in between which participants were offered a break.

2.3.3 Procedure

After participants read the study information and provided written consent in the form of a check box, they answered sociodemographic questionnaires followed by completing the questionnaires, presented in random order. Finally, they completed the AB task described above.

2.3.4 Data Preparation

Data for T2 accuracy was only used in the analyses if the respective T1 was accurate. The dependent variable was the magnitude of the AB, which was calculated by subtracting accuracy of T2 at the early latency (300ms: lag 3) and accuracy of T2 at the later

latency (800ms: lag 8) as a means of accounting for general ability to detect targets on the task (Arnell, *et al.,* 2006; Georgiou-Karistianis et al., 2007). This was done for each T1/T2 combination and represents overall performance on the AB task with higher values representing a larger blink magnitude and therefore worse performance.

The attentional performance of the AB task (magnitude of the AB) was analysed by hierarchical regression. Attentional performance, in the form of the blink magnitude, was regressed on experienced stress and age where age was coded 0 (participants < 30 years of age) and 1 (participants > 60 years of age). In the second step, the stress by age interaction term was included. The interaction term was created by multiplying participants' age by their standardised stress scores. Data above 2.5 SD from the mean were excluded from analysis. Finally, we controlled for trait anxiety, gender and perceived stress.

Before running hierarchical regression for each T1/T2 word combination, we utilised an ANOVA for two reasons. The first was to test if there was a difference in performance between combinations of T1/T2, as we speculated different attentional performance based on the T1/T2 combinations. Secondly, before running separate hierarchical regressions for each T1/T2 word combination it was useful to first analyse if performance differed between the combinations as a function of age and stress by using a mixed factors ANOVA. Using a median split participants were divided into two age groups (young and old) and two stress groups (low and high). While there is merit to using a median split in general, in this case, concerning stress, it may not be appropriate. Stress scores were standardised and so a median split naturally places scores that are very close together in separate groups (see table 2.1 and figure 2.3 for descriptive statistics). However, we felt it necessary to first investigate whether there were statistical grounds for running separate hierarchical regressions for the different T1/T2 word combinations. To be clear this would be an interaction of stress and age on performance as well as an interaction of stress, age and word combination on performance. The factorial ANOVA was a 4 (T1/T2 combination: NN vs NA vs AN vs AA) x 2 (age: young vs old) x 2 (stress: low vs high) design. Age and stress

were between subjects' factors while the T1/T2 word combinations were within subjects' factor.

2.4 Results

2.4.1 Manipulation Check

To test whether the AB was successfully manipulated a paired sample t-test was run between accuracy rates of T2 at a latency of 800ms (lag 8; *M* = 81.63, *SD* = 32.48) and a latency of 300ms (lag 3; *M* = 67.58 *SD* = 30.09) and found to be significant t(146) = 12.74, *p* < .001, *d* = 1.06. This process was repeated for each of the different T1/T2 word combination types and summarised in table 2.1.

Table 2.1: *Descriptive statistics for the accuracy rate of T2 at lag 3 and lag 8*

Combination	Lag 3 Accuracy	Lag 8 Accuracy
N-N	21.42 (10.22)	26.30 (11.55)
A-N	22.89 (9.96)	27.58 (10.44)
N-A	22.33 (10.54)	26.97 (10.66)
A-A	21.86 (10.63)	26.08 (11.34)

Overall, the AB was successfully manipulated regardless of the word combination for T1/T2 as accuracy was always significantly better for T2 when it was displayed with a latency of 8 compared to a latency of 3. For *N-N,* t(145) = 8.24, *p* < .001, *d* =.68, while *N-A* was t(145) = 9.40, *p* < .001, *d* = .78. When the combination was *A-N,* t(145) = 9.68, *p* < .001, *d* = .80 and finally when the combination was *A-A,* t(145) = 8.03, *p* <.001 , *d* = .66. As participants were always more accurate when T2 had a latency of 8 than 3, the AB was successfully manipulated.

2.4.2 Overall Magnitude

Before standardising the stress scores older participants had an average stress score of 705.66 (*SD* = 116.25) indicating scores in the middle of the total range for the SRRS. Younger participants had and average stress score of 645.57 (*SD* = 285.24) indicating younger participants had not experienced that much life time stress (total stress score could be 1849). The average perceived stress score was 23.64 (*SD* = 5.84) and trait anxiety score was 45.34 (*SD* = 11.75). For the overall blink magnitude, the first model was significant, accounting for 12% of the variance of the AB magnitude $f(2,142) = 9.8$, $p < 0.001$. Both stress ($\beta = 0.277$, $p < 0.001$) and age ($\beta = 0.221$, $p = 0.006$) were associated with an increased blink magnitude, indicating that the older participants and participants who experienced more stress performed worse on the ABT. An additional 12% (24% in total) of the variance was accounted for after adding the interaction term of age and stress $f(3,141) = 14.52$, $p < 0.001$. The interaction term ($\beta = 1.01$, $p = 0.001$) moderated the association of stress ($\beta = -0.682$, $p = 0.002$) but not age ($\beta = 0.235$, $p = 0.002$). This pattern of results indicates that when taking the interaction of stress and age into account older participants who have experienced more life stress performed the worst and that stress independently increases AB performance while age is associated with poorer performance (figure 2.2). A simple slope analysis was used to investigate the interaction and found that the magnitude of the attentional blink was significantly larger for older participants who also experienced more life stress $t(144) = 5.93$, $p < 0.001$. Importantly, the interaction term was still significant when controlling for gender, perceived stress and trait anxiety. Indeed, stress, age and the interaction term remained significant when controlling for gender, perceived stress and trait anxiety.

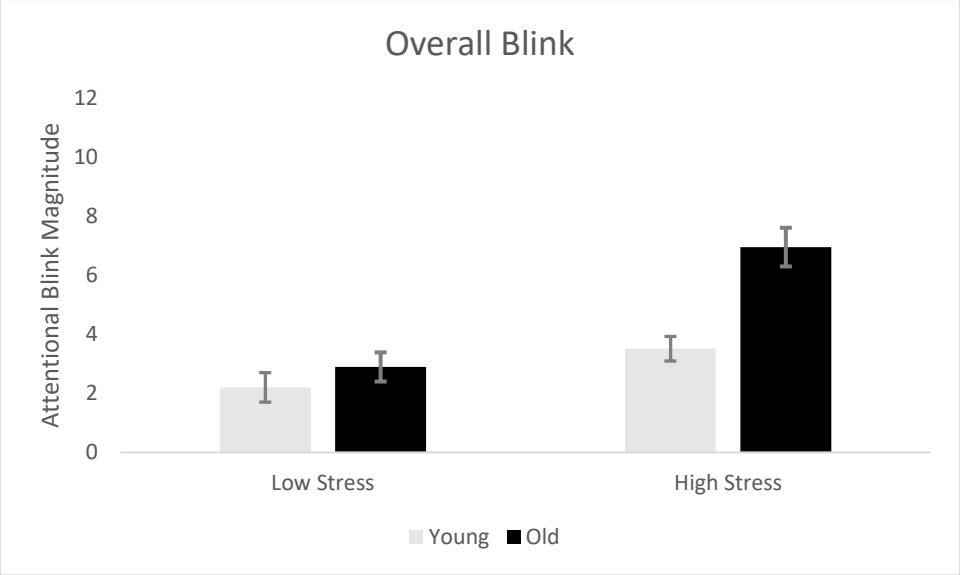

Figure 2.2 Results for overall blink magnitude

2.4.3 Decomposing T1/T2 word combinations (ANOVA)

There was no difference in performance between the different combinations of T1/T2 (p = 0.296) suggesting performance was not significantly different between the different word combination types. Participants who experienced more life stress (M = 5.37, SD = 0.39) performed worse on the ABT compared to participants with less life stress (M = 2.55, SD = 0.35) as there was a significant main effect of stress $f(1,141) = 28.96$, $p < 0.001$, $\eta^2 = 0.17$, indicating a large effect size. Additionally, older participants (M = 5.06, SD = 0.41) in general performed worse than younger participants (M = 2.86, SD = 0.32) as there was also a significant main effect of age $f(1,141) = 17.67$, $p < 0.001$, $\eta^2 = 0.11$, indicating a large effect size. These two main effects were qualified by a two-way interaction of stress and age $f(1,141) = 8.33$, $p = .005$, $\eta^2 = 0.05$, indicating a medium effect size, as well as a two-way interaction of word combination and stress $f(3, 423) = 2.81$, $p = .039$, $\eta^2 = 0.02$, indicating a small effect size. Both two-way interactions were further qualified by a significant three-way interaction of word combination, stress and age $f(3,423) = 4.53$, $p = .004$, $\eta^2 = 0.03$, indicating a small to medium effect size. The significant 3-way interaction suggests that behavioural performance differed as a function of stress, age and T1/T2 word combination.

For this reason, it was statistically appropriate to continue with separate hierarchical regressions for each T1/T2 word combination.

2.4.3.1 N-N

For the blink magnitude when both the T1 and T2 were neutral words, the first model was significant, accounting for 10% of the variance of the AB magnitude $f(2,142) = 7.49$, $p < 0.001$. Only stress ($\beta = 0.284$, $p < 0.001$) and not age ($p = 0.099$) was associated with an increased blink magnitude. An additional 13% (24% in total) of the variance was accounted for after adding the interaction term of age and stress $f(3,141) = 13.88$, $p < 0.001$. The interaction term ($\beta = 1.093$, $p < 0.001$) moderated the association of stress ($\beta = -.746$, $p = 0.001$) such that stress increased performance and was only detrimental to attentional performance when interacting with age, in that older participants who experienced more stress performed the worst when both targets were neutral. A simple slope analysis was used to investigate the interaction and found that the magnitude of the attentional blink was significantly larger for older participants who also experienced more life stress $t(144) = 6.23$, $p < 0.001$. Stress and the interaction term were still significant when controlling for gender, perceived stress and trait anxiety.

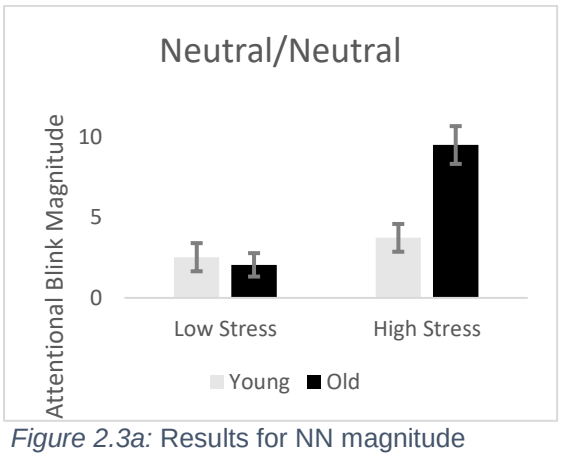

Figure 2.3a: Results for NN magnitude

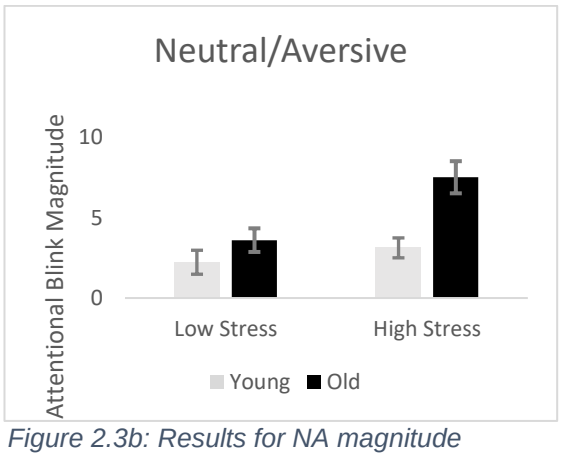

Figure 2.3b: Results for NA magnitude

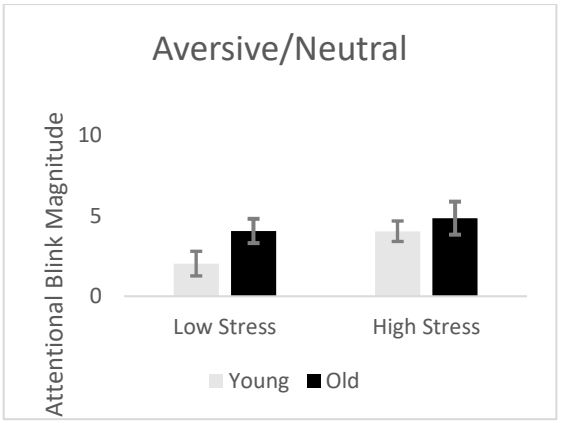

Figure 2.3c: Results for AN magnitude

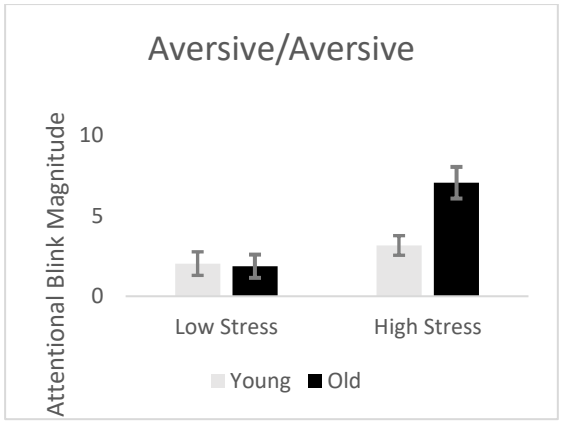

Figure 2.3d: Results for AA magnitude

Table 2.2: *Descriptive statistics for each combination of T1/T2 performance scores (subtracting performance at lag 3 from lag 8, higher numbers shows decreased performance) as a function of stress/age*

Neutral/Neutral	Low Stress	High Stress
Young	2.53 (0.88)	3.73 (0.73)
Old	2.05 (0.86)	9.5 (1.17)
Neutral/Aversive	Low Stress	High Stress
Young	2.22 (0.74)	3.12 (0.62)
Old	3.60 (0.74)	7.50 (0.99)
Aversive/Neutral	Low Stress	High Stress
Young	2.03 (0.76)	4.04 (0.64)
Old	4.05 (0.75)	4.85 (1.03)
Aversive/Aversive	Low Stress	High Stress
Young	2.03 (0.73)	3.15 (0.61)
Old	1.87 (0.72)	7.05 (0.98)

2.4.3.2 N-A

For the blink magnitude when T1 was neutral and T2 was aversive, the first model was significant, accounting for 9% of the variance of the AB magnitude $f(2,142) = 6.88$, $p = 0.001$. Both stress ($\beta = 0.188$, $p = 0.021$) and age ($\beta = 0.237$, $p = 0.004$) were associated with an increased blink magnitude indicating that the older participants and participants who experienced more stress performed worse on the ABT. An additional 6% (15% in total) of the

variance was accounted for after adding the interaction term of age and stress $f(3,141) = 8.39$, $p < 0.001$. The interaction term ($\beta = 0.754$, $p = 0.002$) moderated the association of stress ($\beta = -0.523$, $p = 0.026$) but not age ($\beta = 0.248$, $p = 0.002$). This pattern of results indicate that when taking the interaction of stress and age into account, older participants who have experienced more life stress performed the worst and stress independently increases AB performance while age is associated with poorer performance when T1 was neutral and T2 was aversive. A simple slope analysis was used to investigate the interaction and found that the magnitude of the attentional blink was significantly larger for older participants who also experienced more life stress $t(144) = 4.04$, $p < 0.001$. Importantly, the interaction term was still significant when controlling for gender, perceived stress and trait anxiety. Indeed, stress, age and the interaction term remained significant when controlling for gender, perceived stress and trait anxiety.

2.4.3.3 A-N

For the blink magnitude when T1 was aversive and T2 was neutral, the first model was not significant, only accounting for 2% of the variance of the AB magnitude $f(2,142) = 1.30$ $p = 0.275$. An additional 2% of the variance was accounted for after adding the interaction term of age and stress but this was not significant ($p = 0.414$). Therefore, when the T1 was aversive and T2 was neutral neither age, stress or their interaction was significantly associated with performance on the ABT

2.4.3.4 A-A

For the blink magnitude when T1 and T2 were both aversive, the first model was significant, accounting for 5% of the variance of the AB magnitude $f(2,142) = 3.51$ $p = 0.032$. Only stress ($\beta = 0.191$, $p = 0.021$) and not age ($p = 0.178$) was associated with an increased blink magnitude indicating more experienced life stress was associated with a poorer performance on the ABT. An additional 5% (10% in total) of the variance was accounted for after adding the interaction term of age and stress $f(3,141) = 5.09$, $p = 0.002$. The

interaction term (β = 0.675, p = 0.006) moderated the association of stress (p = 0.066) such that it was no longer associated with performance on the ABT. This pattern of results indicate that when taking the interaction of stress and age into account, older participants who have experienced more life stress performed the worst while stress and age alone are not associated with ABT performance when both targets were aversive. A simple slope analysis was used to investigate the interaction and found that the magnitude of the attentional blink was significantly larger for older participants who also experienced more life stress $t(144) = 3.67$, $p < 0.001$. Importantly, the interaction term was still significant when controlling for gender, perceived stress and trait anxiety.

2.5 Discussion

The present study explored the impact of lifetime stress on attention during ageing, which expands on previous research that looked at the impact of lifetime stress on memory. Participants' lifetime stress was captured and, along with their age, was used as predictor variables for attentional performance on an AB task. Overall, both stress and age were significant independent predictors of attentional performance in that increased age and lifetime stress was associated with decreased performance.

The effect of age on the blink magnitude is a robust and highly replicable finding. Previous work consistently shows that increased age is associated with cognitive deficits, attention chief among those (Lahar, *et al.,* 2001; van Leeuwen, *et al.,* 2009; Sklenar & Mienaltowski, 2019). Performance for older participants (compared to younger participants) when using the AB is characterised with either lower T2 accuracy or an increased AB magnitude (which itself represents a lower T2 accuracy). Here we reported a main effect of age whereby performance on the AB task was worse for older participants compared to younger participants, indicated by an increased AB magnitude. Our current findings therefore fit the current literature on aging and attentional performance; aging seems to bring with it cognitive deficits.

In addition, acute stress has been demonstrated multiple times to attenuate the AB magnitude (Schwabe & Wolf, 2010; Kan, *et al.,* 2021) and this represents the adaptive side of stress. Acute stress narrows focus, reducing the AB magnitude, which allows for an increase in T2 accuracy. This effect also applies to aversive and emotional targets within an AB (Mathewson, *et al.,* 2008; Kan, *et al.,* 2021). To our knowledge there has been no work investigating the effect of accumulative stress on the AB. As overexposure to stress is maladaptive and, negative affect increases the AB magnitude (MacLean, *et al.,* 2010) it is likely that lifetime exposure to stress would also produce deficits in attention (the opposite effect of acute stress), such as increasing the blink magnitude. Here we extend the literature on the effect of stress on cognition by reporting the maladaptive effects of lifetime exposure to stress. In this study, an increased AB magnitude was associated with an increased lifetime exposure to stress, corroborating previous work that demonstrated the maladaptive effect of accumulative stress on cognition (Desimone & Duncan, 1995; Miller & Cohen, 2001; Marshal, *et al.,* 2015). This also fits the results reported for negative affect on attention (MacLean, *et al.,* 2010) as long-term stress assumes a negative effect. This work adds to the growing evidence for the negative effect of cumulative stress on cognition.

Additionally, we hypothesised that the main effect of both age and stress would be qualified by a cumulative stress/age interaction. Here older participants, with increased lifetime exposure to stress performed significantly worse on the ABT compared to younger participants and importantly older low stress participants. This extends the literature by examining the stress/age interaction on attention and fits the pattern of previous results that investigated this interaction on memory and inhibition. As many studies investigating stress on the AB task use acute stress, we based our predictions specifically on previous results that investigated the stress/age interaction (Marshall, *et al.,* 2015; Marshall, *et al.,* 2016a; Marshall, *et al.,* 2016b; Marshall & Cooper, 2017; Marshall, *et al.,* 2018). In these studies, the stress/age interaction effect on cognition was robust; decreased cognitive performance was associated with increased age only if co-occurring with increased accumulative life stress. Older participants with lower lifetime exposure to stress performed equally as well as

the younger participants, indicating age itself was not the driving factor in cognitive performance. Just as important was the finding that young participants with higher accumulative life stress performed just as well as other young low stress participants and older low stress participants. This indicates that stress itself is not the driving factor behind the poorer cognitive performance. It is the exposure to stress over a lifetime, typically associated with advancing age, which seems to be a driving factor for cognitive decline during aging.

Furthermore, we investigated different word type combinations of T1/T2 and hypothesised an aversive T1 would increase the AB window whereas a neutral T1 and an aversive T2 would decrease the AB window. However, we found no difference in performance across the different T1/T2 combinations, which does not support previous findings or our hypothesis as aversive stimuli in different combinations have shown to attenuate or increase the AB window. Previous work demonstrated that an aversive T2 decreased the AB window if T1 was neutral and that an aversive T1 extends the AB window regardless of the type of T2 (Schwabe, & Wolf, 2010; Kan *et al.,* 2021; Sklenar & Mienaltowski, 2019) but here the performance across T1/T2 word combinations was not significantly different. However, we did find a three-way interaction of word combination, stress and age. Besides the A-N combination, the interaction of stress/age had an effect on the AB window with same pattern (i.e. older high stress participants had the largest blink magnitude) reported previously. There was no effect of stress, age or an interaction in A-N word combination, all participants performed equally in this condition. This is what drove the three-way interaction. This does not fit previous results examining T1/T2 combinations specifically. However, previous work focused on acute stress, whereas here, we measured accumulative stress, and this may explain the differences. It does fit the previous work on the effect of stress/age on cognition, except for the A-N word combination. In general, we found the same pattern of results of a stress/age interaction across the different word combinations, in that experiencing more lifetime stress during advanced ageing resulted in a declining performance on the ABT.

Based on these findings and the work of Marshall *et al.* (2016) and Peavy *et al.* (2009) there clearly seems to be an interaction effect of stress and ageing on cognition. Previous studies found this effect on several memory tasks including the Sternberg and N-back tasks (Marshall, *et al.,* 2015), a spatial memory task (Marshall, *et al.,* 2018), episodic memory (Peavy, *et al.,* 2009) as well as a Flanker task (Marshall, *et al.,* 2016). This pattern of effects is extended in the present study using an attentional task. Physiologically this makes sense as cortisol has been shown to detrimentally affect similar brain areas involved in both memory and attention (Arnsten, 2009; McEwen & Sapolsky, 1995). Regardless of the debate concerning the independence of memory and attention as separate functions, the results reported here still fit with the stress literature and it is not surprising that overall we observed the same pattern as found with regard to previous memory research. Indeed, if attention and memory are in fact not distinct functions then it makes sense that as one declines so would the other. If they are distinct functions, the brain areas that subserve both functions are both affected by the long-term effects of cortisol, so that as one declines, it is likely so would the other. What is important in this pattern is the comparable behavioural results of old participants who experienced less life stress (compared to other older participants) and the younger participants. The pattern suggests that it is not age *per se* that determines the extent of cognitive decline but a lifetime exposure to stress and, conversely, it is not just stress that determines cognitive decline as younger higher stressed participants performed as well as their younger counterparts. Indeed acute stress carries important fitness functions, one of which is to modulate attentional and memory processes and can include increased performance on the AB task (Schwabe & Wolf, 2010; Kan *et al.,* 2019; Kan, *et al.,* 2021). The decline in function and performance comes from the over-exposure to stress hormones such as cortisol and noradrenaline over many years. Taking this a step further, it is not the over exposure to modulated cognitive function (i.e. habituation) itself which contributes to cognitive decline but the physiologically damaging effects of long-term exposure to stress hormones.

Parsing out the effect of the stress/age interaction on aversive stimuli is a little more complicated; especially given the present results on the surface do not coincide with previous results. Previous research observed a clear difference in performance depending on the aversive/neutral nature of T1 and T2. For example, Schwabe and Wolf (2010) found that an aversive T1 increased the blink magnitude and an aversive T2 attenuated the blink magnitude if T1 was neutral, with similar results in prior and subsequent studies (Arnell *et al.,* 2007; Kan *et al.,* 2019; McHugo, *et al.,* 2013). Previous work demonstrated aversive stimuli hold some kind of attentional privilege whereby they are detected easier (Dijksterhuis & Aarts, 2003) and for longer (Mathewson, *et al.,* 2008). This is due to either lowered activation thresholds or increased attentional resources for aversive stimuli (Anderson, 2005). Regardless of explanation, an aversive T2 should wrestle attention back from a neutral T1, whereas, this would be harder if T1 was also aversive. This was not replicated here as no main effect of T1/T2 word combination was found, performance on both the *A-A* and *N-A* combinations were similar. In these instances, it may be that an aversive T2 was enough to gain some attention despite the nature of T1. One explanation could be the lower activation threshold for aversive stimuli (Anderson, 2005). Schwabe and Wolf (2010) rejected this explanation based on their observed results stating that aversive stimuli demand more cognitive resources therefore negating the effect of an aversive T2. Dijksterhuis and Aarts (2003) found that participants were more successful at categorising subliminal aversive words than positive or neutral words and that this was driven by the effect of the word. In other words, even if additional cognitive resources are consumed by an aversive T1, the lower activation threshold for an aversive T2 is enough to regain attention. The null result of the *A-N* combination is the only T1/T2 word combination that does not support the hypothesis that performance on the AB task would be worse for all older high stressed participants compared to other participants. That said the *A-N* result coincides with previous results (Dijksterhuis & Aarts 2003; Schwabe & Wolf, 2010; Kan *et al.,* 2019). A neutral T2 does not have enough attentional sway to pull attention away from an aversive T1 because of the attentional privileges aversive stimuli possess (Anderson, 2005). This may

also explain why the stress/age interaction term did not predict performance on this T1/T2 word combination but did predict the other word combinations.

When parsing out the results of the different T1/T2 combination in relation to stress and age, we observed both similar and dissimilar results to the results described in the preceding paragraph. For example, the interaction term of stress and age significantly predicted AB task performance for each T1/T2 combination except for the *A-N* T1/T2 combination. The *N-N* combination is the classic AB task result (Raymond, *et al.,* 1992) and as such, the results are not surprising given the work by Marshal et al. (2016). If the lower-threshold explanation for the aversive T2 combinations (*A-A* and *N-A*) are correct then the stress/age interaction effect would also make sense as the AB task performance would simply remain constant between the two combinations as well as the *N-N* combination and the same interaction effect would be observed. Where *A-N* is concerned, the strong attentional influence of an aversive T1 over a neutral T2 also falls in line with previous results, but age, at the very least, should still predict performance on this combination especially given the robust nature of age on AB task performance. One explanation is that the attentional bias of aversive stimuli remains intact throughout one's lifetime due to its adaptive advantages. Recently, Sklenar and Mienaltowski (2019) reported that when their T1 was aversive and their T2 was neutral there was no effect of age and suggested the lifetime effect of negative stimuli on attention remains strong even during advanced ageing. Why there was no effect of stress for the *A-N* combination may be because cortisol damages the hippocampus and the PFC, both areas responsible for attentional control and top-down attention. However, for a rapid response to threat, visual stimuli are simultaneously passed through the amygdala as well as the visual cortex, allowing for a rapid response to the aversive stimuli. This has evolutionary benefits as rapid response to threat and danger allows an organism to live another day (LeDoux, 1996; Kandel *et al.,* 2000; Ulrich-Lai & Herman, 2009; Brosschot, *et al.,* 2016). Threatening and aversive stimuli are flagged in the amygdala and as a result, rapid attention towards that particular stimulus is generated (Ulrich-Lai & Herman, 2009). As aversive stimuli are quickly processed in the amygdala and

amygdala activation in response to aversive stimuli remains constant through life (Mather, *et al.,* 2004), and does not atrophy over time in response to long-term exposure to cortisol (McEwen, 2004), the strong negative bias in attention remains intact. Therefore, a lifetime exposed to stress is not enough to affect performance on tasks reliant on bottom-up attention. However, the damage to the PFC and hippocampus debilitate top-down selective attention which may impair individuals ability to override attention to the aversive T1 word and detect a neutral T2. Future work could include tasks associated independently with bottom-up and top-down performance to tease this apart. Nevertheless, the *A-N* combination is robust enough that neither age nor stress is enough to impact performance.

One potential issue in this study is the use of two separate measures for young and older participants. However, this is necessary as people who have lived a longer life will have been exposed to more stressors than younger people will and therefore, using one measure for both might have issues with item weighting. What is stressful for a younger person may not be the same for an older person and using one measure would overlook this as items would be weighted the same. It should be noted that both scales measure lifetime events (adapted to the age group) and are analogous to one another. Furthermore, this approach has been used successfully in previous work (Marshall *et al*, 2015; Marshall *et al*, 2016a; Marshall *et al*, 2016b; Marshall, & Cooper, 2017; Marshall *et al.*, 2018), where the measures were paired with physiological data taken from EEG recordings. Throughout those studies, there was a clear association between the questionnaire responses and the EEG data. For this reason, their inclusion here is valid. The three-way interaction between T1/T2, stress and age could be spurious in nature. Performance on all 4 T1/T2 word combinations was very similar, highlighted by the non-significant main effect in the ANOVA. What seemed to drive the three-way interaction was the lack of a stress/age interaction on the *A-N* word combination compared to the other word combinations which all showed the same interaction with stress/age. To add to the spurious nature of this three-way interaction stress and age did not significantly predict performance on the *A-N* word combination.

With that said, adding physiological data that directly measures experienced stress is a clear step forward for future research as it could directly measure exposure to stress without the reliance on separate self-report questionnaires. For example, research investigating chronic stress has used hair cortisol as physiological marker for chronic stress (Russel, *et al.,* 2012; Greff, *et al.,* 2019; Staufenbiel, *et al.,* 2013). It is common to measure cortisol for acute stress (Kawahara, & Sato, 2013; Schwabe, & Wolf, 2010; Kan, *et al*., 2019) but as hair grows it absorbs cortisol and captures exposure to cortisol from the prior three months (Greff, *et al.,* 2019). This provides a snapshot of cortisol exposure over an extended period of time that represents chronic stress more than acute stress. (Heart rate variability (HRV) has also been associated with experienced stress, whereby chronic stress is associated with decreased HRV (Thayer, *et al.,* 2012). Directly measuring the physiological markers of chronic stress in the continued research of the stress/age interaction effect cognition could strengthen the results reported here and previously.

Overall, this study showed support for the idea that the ageing process itself is not enough to cause cognitive decline in the attentional blink task. This study adds to the literature by providing evidence that cognitive decline during ageing is linked with lifetime exposure to stress. This study builds on similar studies that previously investigated the effects of stress and ageing on memory performance and expands to the effects of stress and ageing on attentional performance. The overall interpretation of the results and the interpretation of *A-N* word combination are consistent with previous results. When parsing out the different T1/T2 word combinations, the previous patterns of results remain except when T1 is aversive and T2 is neutral. This may point to the attentional privilege aversive stimuli have over neutral stimuli, especially when the stimuli is attracted by bottom-up attention. Ultimately, the stress/age interaction associated with cognitive decline during ageing may be restricted to certain forms of cognition such as top-down attention and memory and should be addressed in future research.

Chapter 3 – The Cost of Stress? An EEG Study

3.1 Abstract

In Chapter 2, we reported a stress/age interaction on attention during an attentional blink (AB) task. Specifically, older higher stress participants performed significantly worse than older low stress participants, who in turn performed as well as younger participants. Furthermore, research has reported the same pattern of the stress/age interaction in electroencephalographic resting state delta and alpha frequency bands with delta/alpha power associated with older high stress participants.

We aim to expand on both these findings by investigating whether resting state delta/alpha power would also be associated with stress, age and performance on the AB task and hypothesised we would find the same pattern of results in the AB task, which in turn would be associated with increased delta/alpha power. 76 participants with an age range of 64 and at least 30 under 30 and 30 over 60 years of age participated in the study. Participants completed a stress questionnaire measuring accumulated life stress and completed an attentional blink task in which they were instructed to identify two target words in a rapid serial visual presentation where recall accuracy was measured. During analysis, task performance was measured as raw accuracy or by taking base rate task performance into account. The results failed to replicate the stress/age interaction for either measurement, but increased age was associated with poorer task performance when not considering base rate performance. Stress was positively associated with task performance when base rate was taken into account and the second target was neutral. We found no association between delta/alpha power and task performance. Besides the effect of age, the findings in general went against prediction. The positive association between stress and task performance may reflect a measurement issue with stress in this investigation.

3.2 Introduction

Stress is an adaptive process in that it prepares the body for action by altering the operational states of different systems within the body. For example, by suppressing immune function (Khansari, *et al.,* 1990), energy usually required by this system is reallocated to another system, such as the cardiovascular system, whereby heart rate is increased (Allen, *et al.*, 1946; HåRkanson, *et al.*, 1986). This altered state, known as allostasis (McEwen and Stellar, 1993) increases physiological and cognitive performance to deal with immediate threat in order to prevent death in an organism. However, from the basic example just given, it is easy to see that an allostatic state is not sustainable long-term. Prolonged allostasis from chronic stress can lead to allostatic load, which is the accumulation of general wear and tear on the body from allostasis. Allostatic load has detrimental physiological (Diz-Chaves, 2011; Rozanski, et al., 1999) and cognitive (Desimone & Duncan, 1995; Sapolsky, *et al.*, 1990) consequences and is associated with inflammatory-related disorders such as Alzheimer's disease (AD; Sorrells, *et al.*, 2009). Allostatic load can also occur from accumulated exposure to an allostatic state regardless of whether the state is acute or chronic. As with stress in general, the ageing process is also associated with physiological and cognitive decline. This decline is often attributed to the ageing process itself, but research indicates that prolonged stress exposure, through accumulation or chronic exposure, may be one of the triggers for the cognitive decline especially given the link between chronic stress and AD (Goosens & Sapolsky, 2011; Justice, 2018; Prenderville, *et* al., 2015; Sotiropoulos, *et al.,* 2011). Strengthening this link between stress and AD is evidence that increased cortisol exposure exacerbates AD symptoms (Justice, 2018; Sotiropoulos, *et al.,* 2011). While chronic and accumulated stress differ, both increase one's exposure to cortisol and therefore both increase the risk of cognitive decline.

Indeed, cumulative stress has been associated with changes in cognitive performance with age. A series of studies investigated the interaction of stress and ageing on spatial memory (Marshall, *et al.,* 2016b; Marshall, *et al.*, 2018), inhibitory performance on a flanker task (Marshall, *et al.*, 2016a) and working memory (Marshall, *et al.*, 2015) and

consistently found an interaction of age and stress on performance. The younger and low stress participants always outperformed older high stress participants. Older low stress participants performed as well as the younger participants. The authors attributed this effect to the deleterious effect prolonged cortisol exposure has on the prefrontal cortex and hippocampus; it takes decades for the negative behavioural effects to manifest, appearing only during advanced ageing. Given this evidence results from tasks that tap into different cognitive processes, it suggests an age/stress interaction effect may also be found for other cognitive processes, such as attention.

In Chapter 2, this interaction effect was investigated in relation to attention. Specifically, we used the attentional blink task whereby participants often miss the second of two target (T2) stimuli if the second target appears within 300ms of the first target (T1) in a rapid serial visual presentation (RSVP; Raymond, *et al.*, 1992). This attentional blink (AB) effect is moderated by age in that age is negatively correlated with performance in AB experimental trials (T2 within 300ms of T1), baseline trials (T2 after 300ms, typically at 800ms after T1) and increases the length of the blink window (Georgiou-Karistianis, *et al.,* 2007). Acute stress on the AB generally increases T2 accuracy (Schwabe & Wolf, 2010; Kan, *et al.,* 2019; Kan, *et al.,* 2021) but to the best of our knowledge the effects of accumulated stress on the AB has only been investigated once, in Chapter 2, where stress was also negatively correlated with performance on the AB task. There we reported the stress/age interaction, replicating previous stress/age interactions found on other cognitive tasks (Marshall, *et al.,* 2015; Marshall, *et al.,* 2016a; Marshall, *et al.,* 2016b; Marshall, *et al.,* 2018).

Given the results of Chapter 2 and the explanation for the results one would expect to see differences in brain activity to accompany the behavioural results. Indeed Marshall et al. (2015; 2016a; 2016b; 2018) paired electroencephalogram (EEG) data with behavioural data and consistently reported differences in brain activity for older high stress participants compared to all other participants. Intriguingly, Marshall et al. (2017) also reported higher

levels of resting state delta/alpha power (i.e., while not engaged in a task) in mid frontal, and right and left parietal areas for older high stress participants compared to other participants. Taken together, the presented evidence suggests the resting state EEG power in the delta and alpha frequency bands may be associated with decreased performance on cognitive tasks, including the AB task. The aim of this study is to first replicate the stress/age effect reported in Chapter 2 and second investigate the association between resting delta/alpha power and attentional performance.

We reported (Chapter 2) a similar age/stress interaction effect on AB task performance across multiple conditions made from different T1 and T2 word combinations made from neutral and aversive words. Here we will constructively replicate that work by combining it with EEG resting state power in the delta and alpha frequency bands in new participants. In line with Chapter 2 and the previous work of Marshall et al., we hypothesise a stress/age interaction on AB task performance where older high stress participants will have the worst performance compared to older low stress participants and younger low/high stress participants. Furthermore, we hypothesise increased resting delta/alpha power in mid frontal, and right and left parietal areas will be associated with decreased performance on the AB task.

3.3 Methods

3.3.1 Participants and Design

Participants (*n* = 76) were recruited from the University of Essex (where *n* = 37 students participated for course credit) and online via social media (nextdoor.com and facebook.com) with an overall mean age of 46.95 (24.01) and invited to the laboratory to take part in the study. This was to ensure a good mix of ages. Recruitment continued until there were at least 30 participants under 30 years old (*n* = 35), Mean age = 23.14, *SD* = 2.94; and at least 30 over 60 years old (*n* = 33); Mean age = 72.18. *SD* = 6.22. This was to match the previously mentioned Marshal studies (Marshall, *et al.,* 2015, 2016a, 2016b and

2018) that collected data from 60 participants with 30 under 30 and 30 over 60. In these studies a median split in stress was then used to further divide participants into low and high stress groups. Overall, participants comprised 66% women, 67% white, 29% Asian and 3% black. 63% of the participants had a bachelor's qualification or higher. We used a within participant design (except for the life stress questionnaires) and the study was completed in person. Younger participants (< 30) completed the Life Event Scale (LESS: Clements and Turpin, 1996) while older participants (> 30) completed the Social Readjustment Social Scale (SRSS: Holmes & Rahe, 1967). Both scores were standardised and combined (see Chapter 2 for justification).

3.3.2 Materials

3.3.2.1 Questionnaires

The LESS and the SRSS measure accumulated life stress. Both questionnaires are analogous to one another but are used for different age groups and were used previously (Marshall, *et al.,* 2016). Each contains a set of statements reflecting life events (e.g. 'The death of a spouse' or 'been on holiday') with a preassigned value, with higher values representing a higher stress event and vice versa for lower values. Participants indicate if they have experienced any of the life events over their lifetime. Preassigned scores from experienced life events are added together to create a total, regardless of the frequency for each event as including the frequency does not increase the predictive power of either questionnaire (Wilker, *et al.,* 2015). As such, each event was only included once when calculating stress scores. The SRSS comprises 43 items (with total scores ranging from 0 to 1466), while the LESS comprises 36 (with total scores ranging from 0 to 1849). Scores from both were standardised. The LESS is used for participants aged under 30, while the SRSS is used for participants aged over 30 with statements in each better reflecting the age of the participant. As noted by Marshall *et al.* (2015), it is not best practice to equate scores from distinct questionnaires, but it is unavoidable in this case because older participants will have inevitably experienced more stress than younger participants. Due to their analogous nature,

they have been used in conjunction previously with robust results (Marshall, *et al.*, 2015; Marshall, *et al.*, 2016a; Marshall, *et al.,* 2016b; Marshall & Cooper, 2017; Marshall, *et al.*, 2018).

Perceived Stress Scale (PSS; Cohen, *et al.*, 1983) was used to measure the participant's perception of stress. The score captured by the PSS was used as a control variable (see Chapter 2). It asks participants to rate their dis/agreement to statements (e.g. 'In the last month, how often have you felt nervous and "stressed"?') on a 4-point Likert scale ranging from 1 ('Never') to 4 ('Very often'). There are three versions of the PSS: 4-, 10- and 14- item versions. The 10 item PSS has the highest validity and reliability and was the version we used (Lee, 2012). Higher scores indicate more stressful appraisals than a lower score with a range of 10 - 40. The PSS within this study had a strong internal validity (Cronbach's alpha = .816).

The Stress Mindset Measure (SMM; Crum, *et al.*, 2013) is an 8-item measure used to assess one's mindset towards stress as a control variable (see Chapter 2). Participants rate their agreement on a 4-point Likert scale from 1 ('strongly disagree') to 4 ('strongly agree') for statements such as 'The effects of stress are negative and should be avoided' and 'experiencing stress facilitates my learning and growth'. Negative items are reversed scored (items 1, 3, 5 and 7) before all items are summed so that a higher score is associated with a more positive mindset towards stress with scores ranging from 8 - 32. The SMM had an acceptable internal validity (Cronbach's Alpha = .799) and was used as another control variable.

3.3.2.2 Attentional Blink Task

The ABT was created and run through Inquisit (Inquisit 6 [Computer software]. (2016). Retrieved from https://www.millisecond.com). 18 Items were presented in each RSVP stream whereby T1 appeared as item 5 and T2 was either 3 or 8 items later (lag 3 and lag 8 respectively). Items were presented for 100ms; therefore, a stream lasted 1.8

seconds (figure 3.1). Items (words) were in Arial font and were set to be 10% of the screen height.

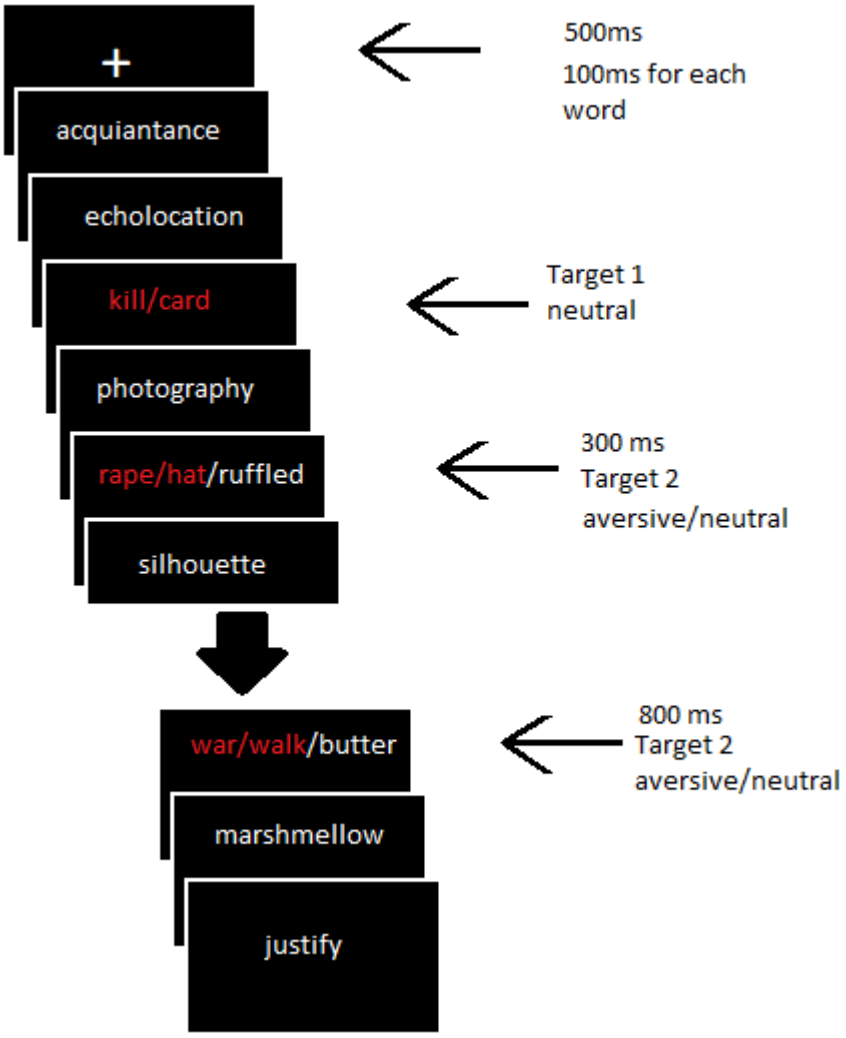

Figure 3.1 RSVP schematic

Similar to Schwabe (2010; and Lahar, *et al.,* 2001) target words were red and neutral distractor words were white centred on a black screen. Participants were asked to recall the red words (i.e. the target words) after the stream ended with two multiple-choice questions (with 4 options), one for each of the targets, consisting of the target word and three incorrect words (randomly selected from the same pool of words as the target word) that could have been the target. All words were length matched (3- 5 letters) and were either taken from Bradley & Lang (1999) where neutral targets and distractor words were matched for valence

(~5) and arousal (~3.6). Aversive words were also matched for valance (~2.5) and arousal (~7). In total, there were 48 neutral target words (e.g. arm, cork, plant and seat) 16 aversive words (e.g. abuse, burn, kill and rape) and 60 neutral distractor words (e.g. book, cane, dish and slow). Trials could either have a T2 at lag 3 or at lag 8 and either a neutral or aversive T2. T1 was always neutral which produces two conditions, a neutral T1 and T2 (N-N condition) and a neutral T1 and aversive T2 (N-A condition). Each word in the neutral and aversive word list were presented four times at T2, once at lag 3 and once at lag 8 generating 128 trials. Before starting the task proper, participants completed 4 practice trials with each combination of lag and T2 type. When pairing the task with EEG, we necessarily endeavoured to reduce the task time compared to chapter 2 in order to prevent boredom, fidgeting (with subsequent EEG artifact) and overall test time. Boredom has been known to increase random error and increase outliers (D'Angiulli & LeBeau, 2002; Ratcliff, 1993). The total task time in Chapter 2 was 40 – 60 minutes and if paired with EEG setup and take down could easily have taken over 3 hours. This necessitated protocol changes between this chapter and chapter 2. In chapter 2, T1 could appear at position 5 or 8 in the RVSP stream, T1 could also be either neutral or aversive (leading to two more T1/T2 combinations) and totalled 288 trials. Here we removed T1 position variation and the aversive T1, reducing the number of trials to 72. To increase the total trials we increased the amount of neutral words in the neutral word pool to account for only neutral T1s. In chapter 2, there were effectively 16 conditions Here we effectively have four conditions, T2 word type (neutral or aversive) and T2 lag (300ms or 800ms) with a total of 130 trials.

3.3.3 Procedure

Participants read the study information and provided written consent. They then answered sociodemographic questionnaires followed by completing the stress questionnaires, presented in random order. Before participants completed the ABT task they were asked to remain still and keep their eyes closed for 2 minutes in a dark and sound dampened room while EEG recorded brain activity.

3.3.4 EEG recording and Data Preparation

EEG was recorded from 64/AgCl electrodes (BrainCap, Brain Products placed within a soft-cap according to the 10–20 method of electrode positioning. The ground electrode was positioned on the left mastoid. Two electrodes were placed at the outer canthi of both eyes to monitor horizontal eye movement (HEOG), and another set of two electrodes are positioned above and below the left eye (VEOG). Recordings were referenced to the mastoid behind the left ear. Impedances were lowered to below 20 kΩ in all electrodes before acquisition conductive gel, and signals are amplified and sampled at 1000 Hz by a 64-ch SynAmps RT (Compumedics Neuroscan). EEG signals were recorded and subsequently cleaned using a Curry 8 (Compumedics, Neuroscan). Data was collected at a sampling rate of 1000 Hz with a band-pass filter of .05 - 200 Hz. The stimuli are presented with a Windows 10 computer displaying to a monitor (Dell S2419HGF) and responses are collected from a desktop QWERTY keyboard. This lab is located in UK, where line noise frequency is 50 Hz. Acquired data was visually inspected and noisy data blocks, general artefacts and bad electrodes were rejected. Electrodes with high variability or no variability were rejected. Blink and movement artefacts were marked and removed from further analysis. All data was re-referenced to a common average reference and segmented into 4-second epochs (Putman, *et al.,* 2012; Putman, 2011) resulting in a maximum total of 30 epochs. Due to bad blocks the amount of epochs between participants varied resulting in an average of 19.62 (*SD* = 5.36, Min = 10, Max = 30) epochs per participant. 10 epochs was deemed acceptable as Marshall et al. (2017) used 40 seconds of resting state data, here 10 epochs is 40 seconds. Data was then divided into the delta (0.5–4 Hz), theta (4 - 6 Hz), alpha (8 - 12 Hz), beta (12 - 20 Hz) and gamma (30 – 70 Hz) frequency range by means of a digital Fast Fourier Transform-based spectrum analysis (frequency domain). Absolute power for each electrode was then obtained by averaging each frequency band and each epoch together to create an absolute power for each electrode and each frequency band for each participant. Delta and alpha power from each electrode were normalised using Z-scores and electrodes with power scores above 2.5 SD were excluded from analysis.

3.3.5 ABT Data Preparation and Analyses

As the AB effect is contingent on participants correctly identifying T1, T2 accuracy was only included in the analysis if the corresponding T1 was correct. We calculated the percentage correct at both lag 3 and 8 for T2. Previously, (Chapter 2) we used a baseline correction by subtracting accuracy at lag 3 (AB effect) from lag 8 (baseline AB performance) to create an overall blink magnitude score whereby a higher magnitude score indicated more of an effect of the AB. This was taking account of general detection performance. However, there are issues with this[2]. Therefore, we elected to use both the magnitude and percentage correct at lag 3 (Dent & Cole, 2019; Schwabe & Wolf, 2010) to compare methods. We refer to the former as magnitude performance and the latter as general performance.

The attentional performance of the ABT was analysed by hierarchical regression. Attentional performance (both magnitude performance and general performance) was regressed on experienced stress and age. In the second step, the stress by age interaction term was included. The interaction term was created by multiplying participants' age by their standardised stress scores. In the third step, we included any region of interest (ROI) generated from the EEG data. Finally, we controlled for stress mindset, gender and perceived stress.

3.4 Results

3.4.1 Descriptive Statistics

Before standardising the stress scores older participants had an average stress score of 710.87 (*SD* = 147.76) indicating scores in the middle of the total range for the SRRS. Younger participants had and average stress score of 647.14 (*SD* = 234.55) indicating younger participants had not experienced that much life time stress (total stress

[2] For example, if the maximum score at both lags was 50. Participant A could show a relatively low magnitude by scoring 8 at lag 8 and 3 at lag 3 which would indicate a magnitude of 5. Participant B could score 50 at lag 8 and 25 at lag 3 producing a magnitude score of 25. Clearly, overall Participant B performed better but according to the magnitude score Participant A was less affected by the AB magnitude.

score could be 1849). The average perceived stress score was 23.01 (*SD* = 4.77) and the average stress mindset score was 18.41.34 (*SD* = 3.81).

3.4.2 EEG: ROI

3.4.2.1 Magnitude Performance

Following from Marshall *et al*. (2017) the mid frontal, and right and left parietal electrodes in the delta frequency (FP1, FPz, FP2, AF3, AF4, F3, F1, Fz, F2, F4, T7, TP7, P7, P5, PO7, PO8, T8, TP8, P8 and Pz) were correlated with overall attentional blink magnitude, magnitude at N-N and magnitude at N-A. However, there were no significant correlations. This was repeated for the alpha frequency (FP1, FPz, FP2, AF3, AF4, F7, F5, F3, F1, Fz, F2, F4, F6, FT7, FC5, FC3, FCz, FC2, FC4, FC6, FT8, C2, CP3, TP8, P1, P4, P6, PO4, PO8 and O1). Again, there was no significant correlation between performance and alpha power in any electrodes. Therefore, the ROI variable was excluded from the magnitude analysis.

3.4.2.2 General Performance

As above, the electrodes in the delta frequency (FP1, FPz, FP2, AF3, AF4, F3, F1, Fz, F2, F4, T7, TP7, P7, P5, PO7, PO8, T8, TP8, P8 and Pz) were correlated with general performance, performance at N-N and performance at N-A. However, there were no significant correlations.

This was repeated for the alpha frequency (FP1, FPz, FP2, AF3, AF4, F7, F5, F3, F1, Fz, F2, F4, F6, FT7, FC5, FC3, FCz, FC2, FC4, FC6, FT8, C2, CP3, TP8, P1, P4, P6, PO4, PO8 and O1). However, there was no significance between performance and alpha power in any electrodes.

3.4.3 Manipulation check for the attentional blink

To test whether the AB was successfully manipulated, a paired sample t-test was run between accuracy rates of T2 at a latency of 800ms (lag 8; *M* = 82.21, *SD* = 14.25) and a latency of 300ms (lag 3; *M* = 47.19 *SD* = 16.76) regardless of stimulus type and a significant difference was found $t(63) = 21.42$, $p < .001$, $d = 2.68$. This indicates performance at lag 8 was much better than at lag 3 (indicative of an attentional blink affect). This process was repeated for the neutral-neutral (N-N) and neutral-aversive (N-A) conditions (descriptive statistics are summarised in table 3.2).

Table 3.2: *Descriptive statistics for the accuracy rate of T2 at lag 3 and lag 8*

Combination	Lag 3 Accuracy	Lag 8 Accuracy
N-N	46.99 (18.63)	82.71 (16.15)
N-A	47.42 (17.27)	82.21 (14.36)

Overall, the AB was successfully manipulated as accuracy at lag 8 was always significantly better than lag 3. For *N-N,* $t(63) = 16.78$, $p < .001$, $d = 2.01$, while *N-A* was $t(63) = 19.74$, $p < .001$, $d = 2.47$. Furthermore, there was no difference in performance between neutral (*M* = 65.17, *SD* = 15.22) and aversive (*M* = 64.81, *SD* = 14.21) T2 targets, $t(63) = .318$, $p = .752$, $d = .04$. Overall, participants performed equally regardless of the valence of T2.

3.4.4 Hierarchical regression of attentional performance

In each regression performance (magnitude or general) was regressed on by age and stress (step 1) the stress/age interaction term (step 2) and perceived stress, stress mindset and gender (step 3, the control variables).

3.4.4.1 Magnitude Performance

3.4.4.1.1 Overall Blink Effect

Only participants who had an overall accuracy above 50%[3] (McLean, *et al.,* 2009) at lag 8 were considered in the analysis. For the overall blink magnitude, the first model was not significant, accounting for 8% of the variance of the AB effect $f(2,61) = 2.95$, $p = .060$. Neither age ($\beta = .215$, $p = .086$), nor stress ($\beta = -.182$, $p = .144$), was associated with an increased blink magnitude. The additional steps did not add significantly to the model (model 2 change statistic $p = .361$, model 3 change statistic $p = .468$), including the stress/age interaction term ($\beta = .241$, $p = .361$).

3.4.4.1.2 N-N

Only participants who had an overall accuracy above 50% at lag 8 in the N-N condition were considered in the analysis. For the N-N magnitude, the first model was significant, accounting for 9% of the variance of the AB effect $f(2,59) = 4.04$, $p = .023$. Stress ($\beta = -.266$, $p = .034$), but not age ($\beta = .193$, $p = .121$), was associated with an increased blink magnitude. Those with higher experienced stress had a smaller AB magnitude than those with lower experienced stress indicating higher stress was associated with increased performance. The additional steps did not add significantly to the model (step 2 change statistic $p = .193$, step 3 change statistic $p = .524$), including the stress/age interaction term ($\beta = .336$, $p = .361$) and the control variables. However, stress remained significant in both step 2 ($\beta = -.558$, $p = .031$) and step 3 ($\beta = -.629$, $p = .019$).

3.4.4.1.3 N-A

Only participants who had an overall accuracy above 50% at lag 8 in the N-A condition were considered in the analysis. For the N-A magnitude, the first model was not

[3] It should be noted that 7 of the 8 exclusions were older adults, which in itself suggests a direct effect of age on the task. This was similar for both the N-N (9 of the 10 were older) and N-A (8 of the 10 were older) conditions. This is the same for general performance.

significant, accounting for 8% of the variance of the AB effect $f(2,59) = 2.59$, $p = .083$. Despite this, age ($\beta = .263$, $p = .039$), but not stress ($\beta = -.09$, $p = .473$), was associated with an increased blink magnitude. Older participants had a larger AB magnitude than younger participants indicating increased age was associated with decreased performance. The additional steps did not add significantly to the model (step 2 change statistic $p = .678$, step 3 change statistic $p = .266$), including the stress/age interaction term ($\beta = -.110$, $p = .678$).

3.4.2.2 General Performance

3.4.4.2.1 Overall Blink Effect

Only participants who had an overall accuracy above 50% at lag 8 were considered in the analysis. For the overall blink effect, the first model was significant, accounting for 38% of the variance of the AB effect $f(2,59) = 19.95$, $p < .001$. Age ($\beta = -.631$, $p < .001$), but not stress ($\beta = .059$, $p = .589$) was associated with performance. This indicates that increased age was associated with decreased performance on the AB task. The additional steps did not add significantly to the model (model 2 change statistic $p = .670$, model 3 change statistic $p = .162$), including the stress/age interaction term ($\beta = .091$, $p = .670$).

3.4.4.2.2 N-N

Only participants who had an overall accuracy above 50% at lag 8 in the N-N condition were considered in the analysis. For the N-N magnitude, the first model was significant, accounting for 37% of the variance of the AB effect $f(2,57) = 18.56$, $p < .001$. Age ($\beta = -.604$, $p < .001$), was significantly associated with an increased AB effect but not stress ($\beta = .08$, $p = .427$), indicating increased age was associated with decreased performance on the AB task. The inclusion of the interaction term and the control terms did not significantly add to the model (all change statistics $p > .05$). Although age remained significantly associated with AB performance throughout each step.

3.4.4.2.3 N-A

Only participants who had an overall accuracy above 50% at lag 8 in the N-A condition were considered in the analysis. For the N-A magnitude, the first model was significant, accounting for 30% of the variance of the AB effect $f(2,57) = 13.83$, $p < .001$. Age ($\beta = -.572$, $p < .001$), but not stress ($\beta = .002$, $p = .985$), was associated with an increased AB. This indicates that increased age was associated with decreased performance. The inclusion of the interaction term and the control terms did not significantly add to the model (all change statistics $p > .05$). Although age remained significantly associated with AB performance throughout each step.

3.5 Discussion

In this study, we attempted to constructively replicate the previous stress/age interaction effect on the AB task reported in Chapter 2 and investigated the association between resting state delta/alpha power and performance on the AB task. Additionally, we compared two separate ways of measuring performance on the AB task. We failed to replicate the stress/age interaction effect for both ways of measuring performance on the AB task. With that said, increased age was consistently associated with poorer general performance but not for magnitude performance. We also report an association between stress and magnitude performance for the Neutral-Neutral condition in the opposite direction than predicted. We do not, however, report any evidence of an association between resting state delta/alpha power and AB task performance .The data reported here also highlights that the way in which performance is measured influences the outcome of the results and will be explored more fully below.

3.5.1 Age

The effect of age on general performance is not surprising. The literature commonly reports a robust, negative association between age and AB task performance (Georgiou-Karistianis et al., 2007; Maciokas & Crognale, 2003; van Leeuwen, *et al.*, 2009) and we

reported this same finding in Chapter 2. This is generally attributed to reduced sustained attention and ineffectual inhibitory mechanisms compared to younger people (Chao & Knight, 1997; Pagnoni & Cekic, 2007). The lack of the stress/age interaction here suggests that detriments in cognitive performance during ageing are attributed to the ageing process itself and not the deleterious effects of long-term cortisol exposure, at least for the AB task, as hypothesised here and reported elsewhere (Chapter 2). However, here the age effect on the AB task depends on how performance was measured. For magnitude performance there was no effect of age while there was an age effect on general performance. A possible reason why there was an association of age and magnitude performance in chapter 2 and not here is discussed in the stress/age interaction section. General performance can be thought of as raw performance when under AB effect conditions (I.e., T2 correct when T1 is correct) and is the common way to calculate performance (Dent & Cole, 2019; Georgiou - Karistianis et al., 2007; Maciokas & Crognale, 2003; Lahar, *et al.,* 2001; Schwabe & Wolf, 2010; Georgiou; van Leeuwen, *et al.*, 2009; Wynn, *et al.,* 2006). However, this does not consider how good participants are at just detecting targets in an RSVP. The AB task is used as a measure for attentional ability in general, as was the case here and Chapter 2. Not accounting for the base detection rate of participants is also useful for investigating performance at different lag intervals, but it is not really measuring how much the AB effect affects different people or what affects the AB effect itself. For this, overall detection performance can be considered by measuring and taking into account false hits (Arnell, *et al.,* 2007; Dale & Arnell, 2013) or by subtracting performance on a hard trial (lag 3) from an easy trial (lag 8; Arnell, *et al.,* 2006; Chapter 2). When investigating the actual AB effect (besides lag differences) this is probably the better performance metric but as a broad-spectrum measure for attention, general performance is better. You can see these differences in measurements here with age. General performance was affected by age (raw performance) but when taking in overall target detection (magnitude performance) the effect of age disappeared. This does not mean older people performed better, just that they were generally worse at the task which is what we were investigating here. Taken together this

suggests older participants were attentionally worse but they were no more affected by the AB effect than younger participants were. This difference in measurement can also be seen when considering stress and suggests stress affects the AB effect itself but not general detection performance. This suggests general performance is better for age and magnitude performance is better for stress. This may be another reason we failed to find the stress/age interaction.

3.5.2 Stress

There was no effect of stress for general performance but there was for the N-N condition for magnitude performance. This suggests that attentional performance is not affected by stress but the AB effect itself is affected by accumulated stress. However, the effect was in the opposite direction than predicted, as increased accumulated stress was associated with better performance. What could make this particular set of results more confounding is the lack of a stress effect on the N-A condition given previous evidence that acute stress increases performance and an aversive T2 after a neutral T1 is easier to detect (Schwabe & Wolf, 2010; Kan, *et al.,* 2019). However, upon consideration this may not be that surprising. If aversive enough, outside factors may not have as much of an influence on attention because regardless of context an aversive enough stimulus will capture attention. When stimuli are sub-threshold for attentional capture, outside factors such as stress, come into play and may account for the effect of stress in the N-N condition but not the N-A condition. Even if true, this explanation does not explain the direction of results. Typically, long-term exposure to stress produces an overall negative effect on attention (Liston, *et al.,* 2006; Liu, *et al.,* 2020; Öhman, *et al.,* 2007). However, here we measured accumulated stress, which while often associated with chronic stress is not the same as chronic stress. There is mixed, if limited, evidence that chronic and accumulative stress produce different effects with some reporting a difference (Grover, *et al.,* 2009; Harris, *et al.,* 2017) while others do not (Ostiguy, *et al*., 2009). Furthermore, Schwabe and Wolf (2010) and Kan, *et al.,* (2019) reported a positive association between acute stress and AB performance. While

unlikely, it is possible that what we captured here with this sample is more closely related to acute stress than chronic stress. As both Schwabe and Wolf (2010) and Kan et al. (2019) also used physiological markers of stress (EEG, blood pressure and cortisol), to address the results here, future research should include physiological measures of chronic stress. Pieper and Brosschot (2005) reviewed different physiological measures of chronic stress and suggested using blood pressure and heart rate. Pairing up such measures would allow for a more accurate measure of chronic stress that could then be used to separate out different types of stress effects and provide more definitive evidence for one or the other. Either way, this highlights the difficulty of measuring long-term stress in either its chronic or accumulated form. The LESS/SRRS (the stress measures used here) assume threatening situations produce an allostatic response. By weighting these events and noting if they occur we arrive at a general accumulated stress score. This does not consider how well people can deal with stress or if they have social support which may reduce the allostatic response. The General Unsafety Theory of Stress (GUTS; Brosschot, *et al.,* 2016) suggests what produces stress is not threat but the lack of safety from compromised coping and support systems which would include social support. This offers another avenue for future exploration and an explanation for the minimal stress effects reported here, which includes the lack of stress/age interaction effect. Furthermore, within the GUTS framework increased age contributes to compromised systems. Given the association of age reported here and chapter 2 provides another reason to investigate stress and age within the GUTS framework.

3.5.3 The Stress-Age interaction

That the stress/age interaction was not replicated (for either magnitude performance or general performance) is a surprise given how robust the interaction seems to be, as reported across several studies and several cognitive tasks (Marshall, *et al.*, 2015; Marshall, *et al.*, 2016a; Marshall, *et al.,* 2016b; Marshall & Cooper, 2017; Marshall, *et al.*, 2018; Peavy, *et al.,* 2009; Chapter 2). It is possible that the lack of a finding comes down to the differences between the methods in this study and Chapter 2. There were almost 3 times the number of

participants and double the amount of trials overall in Chapter 2, leading to greater statistical power. However, there were more T1/T2 combinations in Chapter 2 with 72 trials in each and in all but one condition (T1 aversive and T2 aversive) the stress/age interaction was found. Here we had 128 trials in total and did not report this effect which indicates, at the very least, we had enough trials but not enough participants. Furthermore, in Chapter 2, T1 placement varied to prevent participants anticipating the appearance of T1, which has a knock-on effect of T2 placement leading to greater overall variation in target placement compared to this study. It is possible without the variations participants who might have performed worse, were able to compensate by anticipating when targets would appear. Individually, each presented reason for the lack of a stress/age interaction effect, and indeed why age was associated with magnitude performance in chapter 2 and not here, may not have had a large impact on the results overall but taken together could compound to largely impact the study and the results.

3.5.4 EEG activity in the Delta bandwidth

Finally, we did not present data any data showing an association between alpha/delta power and task performance on the AB task for either magnitude or general performance. We originally predicted a negative association between task performance and delta/alpha power. This particular prediction was based on the stress/age interaction of resting delta power reported by Marshall et al. (2017) whereby older high stress individuals had higher delta/alpha power across several brain regions (left and right parietal and frontal regions) compared to other participants. The authors point out that increased delta power is associated with Alzheimer's disease (Coben, *et al.,* 1985) and considering this, suggested their pattern of results may be an indication of early stages of development of inflammatory diseases such as Alzheimer's. As we did not report a stress/age interaction effect perhaps it is not surprising that a similar pattern in relation to task performance was not found. Delta power is not usually associated with cognitive tasks and is generally related to sleep (Amzica & Steriade, 1998; also see Harmony, 2013). With that said increased delta power during

cognitive tasks has occasionally been positively associated with cognitive performance (Douw, *et al.,* 2011; Harmony, *et al.,* 1996), including attentional tasks (Harmony, 2013). Furthermore, resting state delta/beta correlation has been suggested to represent emotional regulation (Schutter & van Honk, 2015b), with Putman (2011) reporting attentional avoidance in a dot probe task (an attentional task) to threatening stimuli in those lose with low delta/beta coherence. While we did not measure delta/beta coherence this suggests a role in resting state delta power and negative stimuli processing which could be addressed in future research. Resting state alpha power is also linked with cognitive health and ageing (Babiloni et al., 2015; Koenig et al., 2005) but, again, we did not report a stress/age interaction associated with alpha power. Furthermore, resting state alpha has not been associated with performance on attentional tasks (Anderson & Perone, 2018; Douw, *et al.,* 2011). Our results here regarding resting state frequency bands fit within the general literature but are not in line with Marshall et al. (2017) most likely due to the lack of a stress/age interaction here.

3.5.5 Conclusion

The aim of this study was to replicate the stress/age interaction on AB task performance and investigate the association between resting delta/alpha power and performance on the task. We failed to replicate the stress/age interaction, which may be due to a lack of variation for T1 and/or fewer trials and participants. This may imply that pairing EEG with this specific investigation was not well suited due to the time constraints. During analysis, the potential differences in performance measurement was highlighted leading to a comparison between two separate measurements. For general performance there was a strong consistent effect of age but when taking the magnitude performance this effect disappeared implying that in general, the task was more difficult for older people. In terms of stress there was only an effect of positive association in the N-N condition, in the opposite direction of what was predicted, which may be in part due to the method by which stress was measured here. Finally, we report no evidence for an association resting state delta/alpha power likely due to the lack of a stress/age interaction reported here.

Chapter 4 – Staying GUTsy During Aging

4.1 Abstract

Classic stress theory cannot explain how rumination and worry can lead to the maintenance of chronic stress, given that for most people, the world is overtly safe at least according to Brosschot et al. (2016). Recently, the Generalised Unsafety Theory of Stress (GUTS) claimed that threat perception was not the cause of an allostatic response. Instead, it was the lack of perception for safety (generalised unsafety; GU). According to GUTS, safety cues are learnt but there are certain life domains which, when compromised, can lead to GU causing chronic stress. These domains include one's social network and physical health (referred to here as the body domain). This study investigated the predictive strength of participants' social network and body domains for perceived stress, in contrast to exposure to stressful events, which would represent classic stress theory. 452 participants completed a variety of questionnaires that measured their social network domain (social support, loneliness and self-esteem), their body domain (physical fitness and activity as well as age) and their exposure to stressful events during the course of their lives (the life events and social readjustment scales). These were regressed on their measure of perceived stress. Overall, the social network domain strongly predicted perceived stressed, whereas the body domain did not. Furthermore, exposure to stressful events significantly predicted perceived stress but with much less strength than the social network domain. These results provide some preliminary support for the Generalised Unsafety Theory of Stress but also show that the domains within the framework require more investigation.

4.2 Introduction

In recent years, stress has become recognised as a worldwide problem. When polled, 51% of European employees reported stress as a common problem in their workplaces (Safety at Work, 2013). This is similar across the world, as seen in the United States (83%; The American Institute of Stress, 2021; see also Moreno, *et al*., 2020), Japan

(53%, www.Stastista.com) and Australia (64%; Casey & Liang, 2014, see also Ribeiro Santiago, *et al.,* 2020). This coincides with high absenteeism because of stress (McDaid, *et al.,* 2005) and accounting for 60 – 80% of lost productivity when direct health and social care costs are controlled for (Knapp, *et al.,* 2004). The cynical may attribute this to 'made up' excuses by some to get off work when not actually sick, but stress is the stated reason for up to 66% of doctor's visits (Pikhart & Pikhartova, 2015) and so simple malingering or factitious disorder is unlikely. According to the Mental Health Organisation (2018) 3 quarters of the adult population suffer from chronic stress in the United Kingdom. It is therefore not difficult to understand the negative perception of stress. Stress is often described in terms of the fight or flight response which itself conveys the negative connotation that one is required to fight or flee from some perceived threat. However, the allostatic response is not entirely negative. The fight or flight response (the allostatic response) is an adaptive bodily state, known as allostasis (McEwen, 2004), that is triggered to deal with any detected threats to homeostasis (Cannon & Lissak, 1939; von Euler, 1946). The key idea here is *perceived threat*, which is defined as the cognitive appraisal that one may not have the necessary resources to deal with the current demands placed on them (Denson, *et al.,* 2009). Allostasis puts the body in a state of action preparedness so that a physical advantage is gained when facing a threat. With that said, stress and allostasis are only adaptive insofar that they are transient. Unfortunately, the internal mechanisms responsible for appraising threat have not changed since humanity was avoiding predators and fighting or fleeing were quick, efficient solutions to an immediate threat. Modernity presents threats where fighting or fleeing are no longer viable or appropriate. Taxes, money, traffic, work life and deadlines are examples of stimuli that are perceived through the same lens as snakes, other predatory animals or even invading tribes. While abstract, the body can, and does react to the problems of modernity as if they were such threats. That is to say, by triggering allostasis over a prolonged period of time due to the prolonged and often drawn out nature of modern problems. Even worse, is the perception of threat in neutral or even safe settings such as social interaction, which is a symptom of long term exposure to stress, which is referred to as prolonged allostasis. In this

context, allostasis is the bodily state when reacting to a stressor (Sterling & Eyer, 1988; McEwen, 1998, 2005). This state includes increased muscle tension, heart rate (Taelman, *et al.,* 2009) and glucose production (Sapolsky, *et al.,* 2000). Prolonged allostasis or chronic stress leads to wear and tear on the body from over exposure to the stress hormone cortisol (McEwen, 1998, 2005). This is known as allostatic load and increases the chances of cardiovascular disease (Rozanski, *et al*, 1999), susceptibility to disease (Khansari, *et al.,*1990), and causes appetite disruption amongst many other negative effects (Diz-Chaves, 2011; for review see Yaribeygi, *et al.,* 2017). For example, the risk of cardiovascular disorders such as heart attack doubles for the top 25% most stressed (Rosengren, *et al.,* 2004), which conveys the same risk factor as smoking or obesity (Cartwright & Cooper, 2011; Cox *et al.,* 2000). As such, it is important to understand what triggers and maintains an allostatic state, which leads to chronic stress. The physiological mechanisms of allostasis are well understood but the psychological triggers are not. In fact, current theory cannot adequately explain how chronic stress is triggered or even maintained. According to Brosschot et al. (2006) a core, causal factor of chronic stress is habitual worrying, or rumination. In order to understand the psychological mechanisms for chronic stress it is important to understand the maintenance of rumination.

Classic models of stress place their emphasis on the perception of threat as a trigger for allostasis. Threats are often innate and are subject to attentional biases. Attention is the cognitive mechanism that ranks incoming phenomena by importance and allocates limited cognitive resources accordingly (Moore & Zirnsak, 2017) thereby excluding some stimuli in favour of subjectively more important stimuli. Threatening stimuli usually gain the highest priority (Kan, *et al.,* 2019; Kan, *et al.,* 2021; Schwabe & Wolf, 2010; Arnell, *et al.*, 2007; Ellenbogen, *et al.*, 2002). This negative attentional bias is well known and often explained in evolutionary terms. A false alarm (i.e. the perception of threat when there is none) outweighs the potential cost of a false negative (i.e. the lack of perception of threat when there is danger) in that some wasted energy expenditure is better than death (Taylor, 1991;

Jonikaitis, 2019). This negative bias is also applied to ambiguous stimuli whereby an unclear phenomenon is treated as a threat first before investigation can overwrite this and label the phenomena as non-threatening. For example, reaction times are longer when ambiguous faces are categorised as safe compared to ambiguous faces being categorised as threatening (Kim, *et al*., 2003), a bias exacerbated by chronic stress (Maoz *et al.,* 2016). Erring on the side of danger provided enough reproductive benefit that evolutionary pressure gave rise to this negative attentional bias. This explains the transient, acute form of stress, in which it is adaptive. However, both this cognitive bias and the evolutionary framework from which it arose cannot explain chronic stress maintenance or indeed rumination.

Brosschot et al. (2016) argue that attentional biases towards threat cannot explain chronic stress in a world that they regard as overtly safe. Through habit and routine, especially in modern life, there is not much ambiguity or threat left to grab and maintain attention on such a chronic level. One may counter with the idea that worry and rumination are maintained in order to prevent panic-attacks (Borkovec, 1994), acting as a buffer against strongly conflicting emotions (Newman & Llera, 2011). This may be true in many cases but cannot explain chronic stress in animals. Animals too, can suffer from chronic stress (Mastorci *et al.,* 2009) but these defence mechanisms require higher order abstraction typical for humans but not for animals (Brosschot, *et al*., 2016). One may then point to perseverative cognition (PC) as the trigger for chronic stress, where PC is defined as "*the repeated or chronic activation of the cognitive representation of one or more psychological stressors*" (Brosschot, *et al.,* 2006), an umbrella term for worry, rumination and everything in between. What sets it apart from rumination is that PC has both a conscious and unconscious component and therefore can explain an allostatic response in a safe world in terms of an unconscious but pervasive reaction (Brosschot, 2010). However, PC cannot account for the chronic nature of worry in the putative overtly safe world described by Brosschot et al. (2016). Furthermore, PC does not account for continuous low heart rate variability (HRV), a robust symptom of chronic stress (Hoehn-Saric *et al.,* 2004; Licht, *et al.,* 2009; Thayer, *et al.*, 1996). Brosschot et al. (2016) suggest that worry and rumination, even

in the most stressed, is not continuous and does not therefore effect HRV continuously. An evolutionary account also does not explain chronic stress when there are no objective threats. It is true that threat is subjective in nature and depends on current health, environment and learnt behaviours (Trimmer, *et al*., 2013) but even this does not explain the prolonged physiological response caused by chronic stress while sitting at home, when there are no threats to perceive. Brosschot et al. (2016) proposes the core of chronic stress is the inability to recognise safety cues that result in a disinhibited default allostatic response. It is therefore the uncertainty of safety rather than threat (the perception of generalised unsafety; GU) that is the basis for the maintenance of chronic stress. This has been termed the Generalised Unsafety Theory of Stress (GUTS).

4.2.1 GUTS

GUTS proposes that the default state of an organism is a state of allostasis and that this state is inhibited only when safety is perceived. It is therefore not the perception of threat that triggers allostasis but the lack of perception for safety which disinhibits it (Brosschot, *et al*., 2016). This means that GUTS differs from classic stress theory in two ways. The first is the distinction between the presence of threat and the lack of safety. GUTS supposes it is not the presence of threat that leads to an allostatic response but the lack of perception for safety. The second is that the allostatic response is not *triggered* in GUTS, it is always on. It is the default response in a world where evolution was driven by erring on the side of caution. If an allostatic response is meant to be as rapid as possible it is quicker and more energy efficient for it to be disinhibited instead of being triggered (Waldvogel, *et al.,* 2000). In this way, GUTS explains low HRV in chronic stress where PC could not. This is important as HRV is used as a measure for parasympathetic activity and is an important component for GUTS. The parasympathetic nervous system (PSNS) (in this context, operating largely through the vagus nerve) is responsible for body function when at rest, which is known as homeostatic function. The PSNS works in tandem with the sympathetic nervous system (SNS), which is the system that triggers the allostatic response. These two arms of the

autonomic nervous system tend to have an inhibitory relationship with each other and generate opposite activity in the bodies organs. Low HRV is regarded as vagal withdrawal, reflecting PSNS inhibition and SNS disinhibition. Furthermore, a high HRV, which reflects PSNS activity and SNS inhibition, is also linked with prefrontal inhibition of the subcortical areas, which themselves are responsible for generating allostasis. HRV is therefore an important component of GUTS as Brosschot et al. (2016) claim a low HRV is linked to GU.

In order to support this, it is important to understand the roles of GU and HRV in GUTS. In conditioning studies, fear responses were elicited from participants with chronic stress by the conditioned and unconditioned stimulus whereas fear was only elicited by healthy controls in the conditioned response. Furthermore, chronic stress participants were slower to unlearn the conditioned stimulus (Duits, *et al.,* 2015). Brosschot et al. (2016) suggest this is because those suffering from chronic stress do not recognise the safety for unconditioned stimuli and struggle to learn that the unpaired conditioned stimuli is now safe. Low HRV is associated with both of these effects in conditioning paradigms (Pappens, *et al.,* 2014; Wendt, *et al.,* 2015). What makes chronic stress insidious is that it increases contextual fear conditioning (Melzig, *et al.,* 2009) so that allostasis is generalised to wider, often inappropriate contexts. To overcome GU and inhibit allostasis, one needs to learn and recognise safety cues. Brosschot et al. (2016) assert that humans are pre-packaged with a default allostatic response but that soon after birth we are adept at learning safety cues. For example, satiation of hunger and thirst is associated with increased HRV (Porges, 2007) which is associated with decreased chronic stress. As we get older the complexities of life increase as should the contingencies of safety cues and their generalisability. Unfortunately, the same is true for fear learning (Glenn, *et al.,* 2012).

Further support for the idea of a default allostatic response is that fear learning is from general fear to specific fear instead of no fear towards fear. Brosschot et al. (2016) proposes individuals start with a default allostatic response and learn to predict and how to control threats. It is by learning about the predictability and controllability of threats in life that GU is lowered and this in turn inhibits the default allostatic response. Here Brosschot et al.

(2016) conflate predictability and controllability but point out that both have the same (or similar) effect of perceived safety (Christianson, *et al,* 2008). Regardless, there is evidence that the experience of control when facing threat 'inoculates' against future uncontrollable threats and safety is generalised to similar threats (Maier, 2015). Unfortunately, insufficient safety learning can instead generalise threat to where there is none and so increase GU. This can be caused by genetics, early prenatal stress and psychological vulnerability. Safety learning can also be compromised later in life in distinct life domains. Brosschot et al. (2016) argue that these domains are our social network, our body and the context domains. When compromised these domains increase GU by failing to add to the perception of safety in general.

Humans are social animals and a lot of our perception and cognition is geared towards social processing. A functioning social network can provide distractions to the everyday stresses of life, provide social support (Cacioppo, *et al.,* 2015) and is linked to increased HRV (Porges, 2007). When compromised, an individual loses a large source of safety and predictability in their life, which is replaced with social anxiety and/or loneliness. Social anxiety is the fear of social interaction or perceiving social interactions as threatening when most are not only non-threatening but instead a positive experience. Brosschot et al. (2016) argue this leads to the distrust of a primary source of safety (a social network) which leads to an increased GU and a disinhibited allostatic response. Social anxiety is often linked with low HRV compared to healthy participants, (Gaebler, *et al.,* 2013; Licht, *et al*., 2009; Pittig, *et al*., 2013) however, non-significant results have also been reported (Klumbies, *et al*., 2014). Loneliness is increasing in prevalence and is strongly associated with morbidity, mortality, and chronic stress (Cacioppo, *et al.,* 2015). It is interesting that loneliness fits well within the framework of GUTS because it produces chronic stress without a specific threat or stressor. Both social anxiety and loneliness represent a compromised social network. In addition, it may be the case that social support and self-esteem represent a healthy social network. For example, self-esteem has often been negatively associated with stress (Kreger,

1995; Martyn-Nemeth, *et al*., 2009), with low self-esteem increasing levels of cortisol (Galanakis, *et al.,* 2016), while high self-esteem may act as a buffer against stress (Rector & Roger, 1997). Self-esteem may arise from multiple life domains such as physical fitness, social standing or status. However, previous data suggests it is not correlated with physical activity (Hubbs, *et al.*, 2012) but it is associated with social capital (Wahl, *et al.,* 2010; for review see Han, 2015). As such, it may connect to the social network domain but overall these concepts have not been directly tested and remain vague.

As mentioned previously, safety depends on more than the surrounding environment and incoming signals. It also depends on the physical state of the individual (Nesse, 2005). Early in humanity's evolutionary history, the world was less safe and an unfit body could drastically lower the ability to fight or flee. The world was inherently more dangerous if one could not act efficiently within it because of physical degradation or injury. Evidence for this comes from physical conditions that are associated with low HRV. For example, low aerobic fitness, old age and obesity are all associated with low HRV and as mentioned earlier, low HRV is a symptom of chronic stress. It therefore makes sense that these physical states could lead to a compromised body, which generates GU. Evidence comes from studies that report physical unfitness is associated with the overestimation of physical challenge (Proffitt, 2006). For example, participants with low physical fitness who need to climb a hill will overestimate the height of the hill compared to fitter participants. The evidence cited provides theoretical support for a compromised body domain within the framework of GUTS. With that said, previous work has shown an interaction of cumulative stress and aging on cognitive decline during aging (Marshall, *et al.,* 2016a; Marshall, *et al.,* 2016b; Marshall, *et al.,* 2018). In these studies, participants recorded exposure to stressful events from the participant's life and performed various memory, inhibitory and spatial tasks. The authors consistently reported a stress/age interaction whereby only older participants, who had experienced more stressful life events, performed significantly worse than other participants on the cognitive tasks. This included other older participants with fewer stressful life events, and both younger low and high cumulative stress participants (Marshall, *et al.,* 2016a;

Marshall, *et al.,* 2016b; Marshall, *et al.,* 2018). This suggests that age itself may not itself be a contributing factor to stress perception but its interaction with exposure to stressful events. GUTS does not take these nuances that may exist into account. Indeed, to date, no direct research has tested whether a compromised body leads to increased perceptions of stress and there is no direct evidence for the connection between compromised physicality and GU.

To complicate the conceptualisation of GUTS domains further are phenomena not directly related to the domains but have an effect on perceived stress. For example, a positive stress mindset towards stress acts as a positive buffer against the negative effects of stress (Crum, *et al.,* 2013; Crum, *et al.,* 2017). Someone, with a positive stress mindset views stress as a healthy part of life and a motivator, whereas a negative mindset includes the belief that stress is negative, harmful and should be avoided at all costs. The stress mindset is an attitude towards stress and is distinct from threat perception and GU. However, it is an important phenomenon that moderates an allostatic response and should be included in any theory of stress. The findings reported in the last two paragraphs highlight that the first step in testing GUTS is to determine which phenomena contribute to each putative domain and whether there are other domains yet to be included.

Despite the theoretical arguments for GUTS and the domains it proposes as being compromised leading to GU, both mentioned domains have not been directly tested. It is also important not to test GUTS in a vacuum; one needs to take into account stressful events that can constitute threats, which would reflect a classical approach to chronic stress. For example, a lifetime of traumatic events is associated with increased cortisol levels (Schreier, *et al.*, 2016), which is a biomarker of chronic stress. Additionally, increased exposure to stressful life events elevates the risk of cardio-vascular disease (Berntson, *et al.*, 2017) caused by hypothalamo-pituitary-adrenocortical (HPA) axis dysregulation, another biological marker often associated with chronic stress (Mizoguchi, *et al.*, 2008). Both of these cases provide evidence for the classic framework for stress and not for GUTS. Furthermore,

there is evidence that long term exposure to stress is a contributing factor for cognitive decline during aging and not the aging process itself (Marshall, *et al.,* 2016a; Marshall, *et al.,* 2016b; Marshall, *et al.,* 2018) further adding empirical support for classic stress theories. While GUTS has a strong theoretical rationale, classic stress theory has empirical support. Regardless of the cause for chronic stress (i.e. threat or GU), chronic stress is associated with the increased perception of stress. Therefore, this study will test the domains suggested by GUTS using measures of one's social network (social support, loneliness etc.) and physical fitness alongside measures of cumulative stressful life events (as a stand in for increased exposure to stress) to find the best the predictors for perceived stress.

As GUTS has not been formally tested and there is already empirical data for the classical stress framework, a clear hypothesis is difficult to formulate. Further complicating the matter is the fact that each domain comprises distinct phenomena grouped together. Specifically, Brosschot et al. (2016) suggest that the compromised social network domain comprises social fear and loneliness. Therefore, both should predict increased perceptions of stress. However, if that is true then a healthy social network domain would predict less perceived stress but this was not discussed within their original paper making the domains somewhat vague. To shed some light on this issue, we will include measures of self-esteem and perceived social support. Additionally, Brosschot and colleagues also suggest that age, obesity and physical fitness should compromise the body domain, and therefore older age, physical unfitness and obesity should predict increased perceived stress. We will therefore include measures of these characteristics in our study. If GUTS is correct, then measures for the social network and body domains will predict increased perceived stress separately from stressful life events. It is likely a mixture of measures may predict perceived stress within the social and body domains as well as stressful life events. In this case, GUTS and classic stress theories will need some form of integration. In order to do that the aim of this study is to 1) test the theoretical predictions of GUTS by testing the predictive power of the domains for perceived stress. 2) Distinguish which phenomena do and do not contribute to

each domain and finally, 3) compare the predictive power of classic stress exposure and GUTS domains.

4.3 Methods

4.3.1 Participants and Design

Participants (N = 585) were recruited online through Prolific (www.prolific.co) where they were either paid or, if they were students from the University of Essex, were awarded course credit for participation. They then completed the study online through Qualtrics. The sample size was based on similar studies that investigated perceived stress and social support (Chao, 2012), exercise (Olefir, *et al.,* 2019) and loneliness (Campagne, 2019). Participants who did not complete all the questionnaires/scales or who failed attention checks were excluded resulting in 452 participants. 68% were women (31% men and 1% other). The age ranged from 18 to 72 years (M = 24.69, SD = 8.39). Younger participants (under 30 years of age: n = 377: M_{age} = 26.47, SD_{age} = 9.64: 69% women, 30% men and 1% other) completed the Life Event Scale (LESS: Clements and Turpin, 1996) while older participants (over 30 years of age: n = 75: M_{age} = 40.22, SD_{age} = 9.54: 60% women, 40% men) completed the Social Readjustment Social Scale (SRSS: Holmes & Rahe, 1967). Both scores were standardised and combined (see chapter 2 for justification). The design was cross sectional with perceived stress acting as the predicted variable and the social, physical and accumulated stress measures acting as the predictor measures.

4.3.2 Materials

4.3.2.1 Body Domain

Along with age and gender, participants were asked to fill out the International Physical Activity Questionnaire (IPAQ; Hagströmer, *et al.,* 2007) in order to measure physical activity. In the IPAQ, participants are first asked to give their height (m) and weight (kg) so that their body mass index (BMI) could be calculated (weight/height^2) with higher scores indicating increased weight while lower scores indicate decreased weight. A link to a

unit converter was provided so that imperial measurements could be converted into the required metric units. Participants were then asked to record how many days in the past week they had performed vigorous activity (that lasted at least 10 minutes), such as heavy lifting, digging or aerobics; as well as their moderate activity, such as carrying light loads and regular, paced bicycling. They were also asked the same question but for light activity (walking). Participants were asked to provide the minutes per day spent on vigorous activity, moderate activity and walking when they perform such activities and how many days a week they perform these activities. From this, a ratio of participants' working metabolic rate relative to resting metabolic rate was calculated and defined as 1 kcal/kg/hour and measured in METs (Hagströmer, *et al.,* 2007). The IPAQ assigns a weighting score for each of the above categories so that vigorous activity (8) is worth more METs than moderate activity (4) which in turn is worth more than walking (3.3). MET scores for each category were calculated as follows:

((Minutes on activity * days in a week spent on activity) / 7) * weight score.

This represents average MET scores per day for each activity with a higher MET score indicating more activity. For a total MET score, each category score was summed.

4.3.2.2 Social Domain

Several scales were used to capture different potential aspects of the social domain. The Liebowitz Social Anxiety Scale (Liebowitz, 1987) is a 24-item scale that measures social fear and social avoidance. Participants indicate their fear of several social statements (e.g. "Using a telephone in public" and "Going to a party") on a 4-point Likert scale from 1 ('none') to 4 ('severe'). They are also asked to rate their avoidance of the same statements on a 4-point Likert scale from 1 ('never') to 4 ('usually'). Scores for each statement are summed together and produce a total social anxiety score. Higher scores indicate higher social anxiety (total score range: 48 – 192).

The Multidimensional Scale of Perceived Social Support (MSPSS; Zimet, *et al.,* 1988) is a 12-item scale. It was used to measure participants' perceived social support by

asking them to rate their agreement to statements such as ‘there is a special person who is around when I am in need’ on a 7-point Likert scale from 1 (‘Very strongly disagree’) to 7 (‘Very Strongly Agree’). Scores are summed together with higher scores indicating higher perceived social support (total score range: 12 – 84).

Loneliness was measured using the 20-item UCLA Loneliness Scale (ULS; Russell, 1996). Participants read statements such as ‘I lack companionship’ and are asked to indicate how often they feel that way on a 4-point Likert scale from 1 (‘I often feel this way’) to 4 (‘I never feel this way’). Scores are summed to produce a total loneliness score with higher scores indicating increased feelings of loneliness (total score range: 20 – 80).

The Rosenberg Self-Esteem Scale (Rosenberg, 1965) was used to capture the self-esteem of participants. It is a 10-item scale where participants are asked to rate how much they agree with statements such as ‘I wish I had more respect for myself’ and ‘I take a positive attitude toward myself’. It is rated on a 4-point Likert scale from 1 (‘Strongly agree’) to 4 (‘Strongly disagree’). Items 1, 3, 4, 7 and 10 are reverse scored and then all the scores are summed so that a higher score represents higher self-esteem (total score range: 10 – 40).

4.3.2.3 Stressful Events

The LESS and the SRSS measure exposure to stress or life-threatening events. Both questionnaires are analogous to one another but were used for different age groups and have been used in such a way previously used by Marshall et al. (2016). While very similar, the two questionnaires differ slightly to better reflect the age of the participant. So that they could be compared and averaged together across age groups, the scores were first standardised and then combined. As noted by Marshall et al. (2016), it is not best practice to equate scores from distinct questionnaires, but it is unavoidable in this case because older participants will have inevitably experienced more stress than younger participants simply because they have lived longer. Furthermore, the questionnaires are analogous in structure and layout and the differences are subtle.

Within each questionnaire is a set of statements reflecting life events that participants may have encountered (e.g. 'the death of a spouse' or 'been on holiday') and are assigned a value, with higher values indicating the statement represents higher stress associated with the event and vice versa for lower values. Participants indicate if they have experienced the life event expressed in the statement and the scores from all the statements are added together, a higher score would indicate higher exposure to life stress. There are 43 items on the SRSS and 36 items on the LESS. The LESS is used for participants aged under 30, while the SRSS is used for participants aged 30 and over.

4.3.2.4 Control and Dependent Variable

The Perceived Stress Scale (PSS; Cohen, *et al.*, 1983) was used to measure the participant's perception of stress, which was the dependent variable. The statements in the PSS are non-specific and make no inquiry to the nature of the events themselves. This is useful for testing GUTS, as its central claim is that chronic stress is perceived stress (through either perceived threat or GU) in the absence of specific stressors. It asks participants to rate their dis/agreement to statements (e.g. 'In the last month, how often have you felt nervous and "stressed"?') on a 4-point Likert scale ranging from 1 ('Never') to 4 ('Very often'). There are three versions of the PSS: 4-, 10- and 14- item versions. The 10-item PSS has the highest validity and reliability, and was the version used in this study (Lee, 2012). Scores for each item were summed with higher scores indicating more stressful appraisals than a lower score (total score range: 10 – 40).

The Stress Mindset Measure (SMM; Crum, *et al.*, 2013) is an 8-item measure used to assess one's mindset towards stress. Participants rate their agreement on a 4-point Likert scale from 1 ('strongly disagree') to 4 ('strongly agree') for statements such as 'The effects of stress are negative and should be avoided' and 'experiencing stress facilitates my learning and growth'. Negative items are reversed scored before all items are summed so that a higher score is associated with a more positive mindset towards stress (total score range: 8 – 32).

4.3.3 Procedure

After participants read the study information and provided written consent in the form of a check box, they answered sociodemographic questionnaires (age and gender) followed by completing all of the previously mentioned questionnaires, presented in random order.

4.3.4 Data Analysis

We first used two separated hierarchical regressions (i.e. the physical and social domain taken from GUTS) to first exclude domain specific non-significant variables before conducting the overall regression. This was to fulfil the second aim of this study, to decompose what concepts comprise each of GUTS domains.

In the first regression, stress perception was regressed on height, weight, BMI, age, gender and the total MET scores as well as the subset of MET scores for vigorous and moderate activity, and walking. This regression represented the body domain. In the second regression (representing the social domain), stress perception was regressed on social support, loneliness, social fear and social avoidance and finally self-esteem.

In the overall regression, participants' exposure to adverse life events as well as its interaction with age and the variables that significantly predicted stress perception from each domain were included. In this final regression stress perception was regressed on stress exposure/interaction with age (step 1), measures from the body domain (step 2), measures from the social domain (step 3), and a stress mindset (step 4).

4.4 Results

See table 4.1 for a zero order correlation table between perceived stress scores, all the body and social domain variable scores, as well as the stress mindset score.

Table 4.1: Zero order correlations between all variables included in the social and physical domains (significance values in brackets).

	Perceived Stress	Age	Gender	Vigorous Exercise	Moderate Exercise	Walking	BMI	Social Support	Lonely	Social Anxiety	Self-Esteem
Age	-.332 (<.001)										
Gender	.223 (<.001)	-.099 (.036)									
Vigorous Exercise	-.035 (.462)	-.032 (.502)	-.063 (.179)								
Moderate Exercise	.023 (.633)	-.043 (.358)	.051 (.275)	.453 (<.001)							
Walking	.049 (.304)	-.093 (.049)	.082 (.083)	.158 (.001)	.329 (<.001)						
BMI	.072 (.129)	0.177 (<.001)	<.001 (0.993)	.094 (.045)	.011 (.814)	-.002 (.963)					
Social Support	-.148 (.002)	.090 (.055)	.135 (.004)	-.035 (.461)	-.030 (.525)	-.006 (.905)	-.011 (.809)				
Lonely	.531 (<.001)	-.299 (<.001)	.064 (.174)	.021 (.663)	.044 (.346)	.007 (.787)	.094 (.046)	-.537 (<.001)			
Social Anxiety	.526 (<.001)	-.238 (<.001)	.246 (<.001)	-.051 (.279)	.026 (.577)	.068 (.150)	.079 (.095)	-.128 (.006)	.443 (<.001)		
Self-Esteem	-.548 (<.001)	.282 (<.001)	-.085 (.072)	-.011 (.807)	-.036 (.446)	-.053 (.262)	-.054 (.254)	.256 (<.001)	-.523 (<.001)	-.430 (<.001)	
Stress Mindset	-.296 (<.001)	.034 (.466)	-.115 (.014)	.074 (.118)	.018 (.697)	.076 (.106)	-.001 (.978)	-.054 (.250)	-.065 (.165)	-.170 (<.001)	.102 (.031)

4.4.1 Body domain

On average, participants were 1.68 (*SD* = 0.15) metres tall and weighed 69.43 (*SD* = 17.59) kg leading to an average BMI of 24.53 (*SD* = 6.09). In terms of physical exercise participants' MET scores per day were as follows: walking was 282.08 (*SD* = 472.95), moderate exercise was 131.31 (*SD* = 273.85), while vigorous exercise was 203.96 (*SD* = 333.87). This led to an overall average MET score of 617.35 (*SD* = 792.21). Height, weight, BMI and MET scores may have a quadratic relationship with perceived stress (De Wit, *et al.,* 2009; Bohon & Welch, 2021). For example, a low BMI score equates to an unhealthy low weight, while a high BMI score equates to an unhealthy high weight. For this reason, residuals for each listed variable were plotted against predicted scores and inspected; they suggested there may be some slight heteroscedacity. That is to say the weighting of scores for these variables when predicting perceived stress may not be the same. If so, it is inappropriate to use them in a linear regression and would be better in a quadratic regression. However, follow-up Breush Pagan tests failed to support this (all $p > 0.05$). As

such, the above-mentioned variables were used in linear regression. A test of collinearity indicated that multicollinearity was a concern for height (tolerance = .132, VIF = 7.59), weight (tolerance = .06, VIF = 16.59) and BMI (tolerance = 0.7, VIF = 14.59). As BMI is calculated from both height and weight we removed height and weight from the model but kept BMI.

Overall, the physical model was significant, accounting for 17% of the variance $f(6,444) = 14.8$, $p < 0.001$. Age ($\beta = -0.338$, $p < 0.001$), gender ($\beta = 0.186$ $p < 0.001$) and BMI ($\beta = 0.138$, $p = 0.002$) were significantly associated with perceived stress wherein increased age was associated with less perceived stress and women/increased BMI were associated with increased perceived stress. As such, age, gender and BMI were included in the overall model. That is to say, none of the physical activity measures from the IPAQ, ($p > .05$) and thus were excluded from the overall regression.

4.4.2 Social Domain

On average, participants' perceived social support score was 61.81 (*SD* = 13.39). Their loneliness score was 46.17 (*SD* = 13.41) and participants averaged a self-esteem score of 26.98 (*SD* = 4.83). In terms of social anxiety, participants had a total social anxiety score of 60.49 (*SD* = 28.71).

Overall, the social domain model was significant, accounting for 45% of the variance, $f(4,447) = 94.91$, $p < 0.001$. Loneliness ($\beta = 0.335$, $p < 0.001$), social anxiety ($\beta = 0.269$, $p < 0.001$) and social support ($\beta = 0.142$, $p < 0.001$) were all positively associated with perceived stress indicating that increased loneliness, social anxiety and perceived social support were associated with increased perceived stress. Self-esteem was negatively associated with perceived stress ($\beta = -0.293$, $p < 0.001$) indicating that as one's self-esteem increases so their perceived stress decreases. All social domain variables were added to the overall model.

4.4.3 Overall Model

In the final model, perceived stress was regressed on experienced stress (step 1), age, gender and BMI (step 2: the body domain), perceived social support, loneliness, social anxiety and self-esteem (step 3: the social domain). Finally the stress mindset was added (step 4: the control variable; see table 4.2 for standardised beta coefficients); with the average stress mindset for participants being 17.29 (3.84).

Table 4.2 shows the beta coefficients for each variable for each step within the overall regression. The first step was significant accounting for 1% of the variance, $f(1,450) = 6.16$, $p = 0.013$. Experiencing more life stress was significantly associated with increased perceived stress.

The second step (body domain) was also significant, accounting for an additional 17% of the variance for a total of 18% of the variance, $f(4,447) = 24.46$, $p < 0.001$. Likewise, the change statistic was also significant $f(3,447) = 30.16$, $p < 0.001$. Experienced stress remained significantly and positively associated with perceived stress. Age was negatively associated with perceived stress such that older participants perceive less stress. Conversely, gender was positively associated with perceived stress indicating that women perceive more stress than men do. BMI was also positively associated with perceived stress indicating that participants with a higher BMI perceived more stress.

Table 4.2: The beta coefficients of experienced stress, the body domain, the social network domain and a stress mindset on perceived stress (significance values in brackets).

Independent Variable	Step 1	Step 2	Step 3	Step 4
Experienced Stress	0.116 (.013)	0.129 (.003)	0.113 (.001)	0.106 (.002)
Age		-0.348 (<.001)	-0.126 (<.001)	-0.130 (<.001)
Gender		0.183 (<.001)	0.092 (.010)	0.080 (.021)
BMI		0.116 (.008)	0.020 (.579)	0.024 (.484)
Social Support			0.100 (.016)	0.084 (.038)
Loneliness			0.295 (<.001)	0.290 (<.001)

Social Anxiety	0.237 (<.001)	0.211 (<.001)
Self-Esteem	-0.270 (<.001)	-0.261 (<.001)
Stress Mindset		-0.191 (<.001)

Gender coded as 1 = man, 2 = woman.

When the social domain variables were added in the third step, the model was significant accounting for an additional 31% variation to the model for a total of 48%, $f(8,443) = 53.56$, $p < 0.001$. The change statistic was also significant $f(4,443) = 68.01$, $p < 0.001$. All were significantly associated with perceived stress. Predictably, social anxiety and loneliness were positively associated with perceived stress indicating that the more these feelings are felt the more stress one perceives. Interestingly, perceived social support was positively associated with perceived stress, which indicates that the more social support one perceives the more stress one perceives. Self-esteem was negatively associated with perceived stress, whereby the more self-esteem one has the less stress one perceives. Experienced stress, age and gender were still associated with perceived stress but the association had diminished in strength. In this step BMI was no longer significantly associated with perceived stress indicating that the social domain variable mediated BMI out of the model.

In the final step the model was significant when the stress mindset measure was added, increasing the accounted for variance by 3% (52% total for the model), $f(9,442) = 54.66$, $p < 0.001$. The change statistic was also significant $f(1,442) = 32.77$, $p < 0.001$. A positive mindset was negatively associated with perceived stress whereby a positive mindset towards stress was associated with less perceived stress.

To summarise, we tested the predictive power of the experienced stress of participants, their body domain and social domain scores with their perception of how stressed they currently feel. Experienced stress remained significant in all 4 steps of the model and remained relatively constant once the body & social domain variables were added. The body domain was also initially significant with age, gender and BMI; but only age and gender remained significant but their predictive power was reduced by more than 50%

when the social domain was added to the model. This indicates that the physical and social domains are not completely distinct domains from each other as variables in one domain mediated variables in the other domain. The social domain variables were also significantly associated with perceived stress, this was still true when a stress mindset variable was added to the model and taken into account.

4.5 Discussion

In the present study, the predictive strength of GUTS domains (social network and the body domain) and participants' exposure to adverse life events for perceived stress were contrasted. In relation to GUTS, results provide support for many elements that make up the social network domain whereas only age and gender were significant for the body domain. Support was also found for the classic framework for stress. One's social network was by far the strongest predictor of perceived stress followed by age (in the opposite direction than hypothesised), with exposure to stress adding a significant albeit small contribution to the overall model. As suggested earlier, the results report here suggest a mix of GUTS and classic stress frameworks in predicting perceived stress.

The first aim of this study was to test the predictive power of the social network domain and the body domain from GUTS on perceived stress. GUTS provides a well-argued explanation for prolonged allostasis when there is no present threat to perceive but was hitherto not formally tested. The results reported here provide evidence that compromised elements within each domain can indeed lead to increased perceived stress. Furthermore, other elements were significant in the opposite direction than what was predicted by Brosschot et al. (2016). Further discussion on the first aim will be in conjunction with an assessment of the second aim of this study, which was to ascertain which components could be included in each domain and the nature of their relationship with perceived stress.

4.5.1 Social Network Domain

According to GUTS, a compromised social network should increase perceived stress. Brosschot et al. (2016) suggested social anxiety and loneliness comprise a compromised social network. Here we report strong evidence for this. Measures of both loneliness and social anxiety strongly predicted perceived stress. Social support predicted perceived stress in the opposite direction than predicted, increased perception of social support was associated with increased perceived stress instead of decreasing perceived stress as GUTS predicts. Various studies have reported contradictory results in that increased perceived social support is negatively associated with perceived stress and vice-versa (Cohen & Wills, 1985; Hamdan-Mansour & Dawani, 2008; Matvienko-Sikar, *et al*., 2021). This contradictory evidence may be due in part to gender differences as two thirds of the participants in the current study were women and their responses may have driven the results in this direction. Recently, Yalcin-Siedentopf et al. (2021) investigated sex differences in perceived stress and perceived social support. They reported that the association between social support and perceived stress was fully mediated by resilience for men but only partially mediated for women and that women reported higher levels of perceived stress than men and also higher levels of perceived social support (Yalcin-Siedentopf, *et al*., 2021). This is not an uncommon finding as previous work reports the same pattern (Park *et al.,* 2015; Padkapayeva, *et al.,* 2018) and Yalcin-Siedentopf et al. (2021) suggest that as women are more empathetic and emotional (Park, *et al.,* 2015), they seek out social support more than men (Adamczyk, 2016). In this way social support does not lead to increased perceived stress. Rather, it is the perception of stress that leads to women seeking out social support. This may help to explain the results reported here. This study also included self-esteem as a measure of a healthy social network domain and was significantly and negatively associated with perceived stress. As such, it may act as a buffer against stress, inhibiting allostasis whereas low self-esteem causes HPA activation and the release of cortisol (Galanakis, *et al.,* 2016). When viewed through the lens of GUTS, self-esteem may represent an individual's state where they have successfully generalised safety cues across disparate situations. We

included variables to measure both a compromised and a healthy social network. There is evidence for the social network domain but what base elements constitute the total domain remain difficult to define.

4.5.2 Body Domain

To test the body domain, we included measures of physical activity and physical health (BMI) but only BMI predicted perceived stress. However, BMI was completely mediated out of the model by the social domain variables. This somewhat goes against the predictions of GUTS, as obesity and unfitness were specifically predicted to increase GU (Brosschot, *et al*., 2016). Furthermore, increased age was predicted by GUTS to increase perceived stress but here it was associated with less perceived stress, not more. The argument for a compromised body comes from Brosschot et al. (2016) with the idea that an allostatic response was ubiquitous for our ancestors, as life in the open was far more dangerous than it is today. Without a fit body, we do not have accurate information regarding physical exertion (Proffitt, 2006) or sufficient somatic information in order to predict safety (Smith, *et al.*, 2015) leading to increased perceived stress. Brosschot et al. (2016) argue that modernity has not existed long enough for evolution to overcome this. However, the allostatic system is a general-purpose system and the context in which the body is perceived has changed even if the system itself has not. For example, usually, we no longer have to fight off invaders or predators, food is never far away, and doctors and hospitals abound. Perhaps for physical (un)fitness and obesity there are enough safety signals to inhibit the default allostatic response. On the other hand, an explanation for age is not readily available. In 1980, it was noted that at the time a new trend was emerging where a positive association between age and happiness was routinely being reported (Witt, *et al.,* 1980). This emergent trend could not readily be explained at the time and it remains a mystery to this day (Frijters & Beatton, 2012; Buijs, *et al*., 2021). Furthermore, this effect is found worldwide across well over 100 countries (Blanchflower, 2021) and there is very weak evidence that the effect is due to different life needs between different groups of people (Buijs, *et al*., 2021). What is

known is that the age/happiness relationship is U-shaped (Frijters & Beatton, 2012) although it is slightly more complex. For example, there is no agreement at what age happiness begins to rise, or at what age happiness seems to cap out at; there are also slight gender differences (Laaksonen, 2018). With this in mind, and when viewing the results presented here through the lens of GUTS, it may be that this happiness associated with age acts as a buffer against stressors and is enough to inhibit the default allostatic response. If this is the case then age should not belong in the body domain but in the context domain, another domain described by GUTS but not explicitly tested here (Brosschot, *et al.,* 2016). Briefly, the context domain is the generalisation of safety, through learning or context conditioning (Melzig, *et al.,* 2009; Grillon, *et al.,* 2006) into non-threatening environments or situations. It is also possible that age could belong in a new domain. Gender was also associated with perceived stress in the final model. Gender was included in the body domain because of the physical strength differences between men and women. Men are more physically active in their free time for example (Azevedo, *et al.,* 2007; Trost, *et al*., 2002). However, these differences begin to disappear with age (Trost, *et al*., 2002). Furthermore, given the lack of evidence for physical activity as a predictor of perceived stress in this study, gender may predict perceived stress because of affective differences in gender and not physical differences as previously discussed. Women experience more perceived stress and chronic stress than men do (Graves, *et al.,* 2021; Matud, 2004) despite experiencing the same number of stressors as men. Related to GUTS, women perceive less control than men do with increased control being negatively associated with perceived stress (Matud, 2004). Furthermore, a strong negative association between self-esteem and perceived stress was reported in the present study. Given that women often report lower self-esteem than men (Conley, *et al.*, 2020; Kling, *et al.*, 1999), this suggests an affective link between GU and gender and not a physical one. . The results reported for the body domain highlight the vagueness of the original definition of each GUTS domain. Especially when one has to consider what concepts fit within each domain. Based on the evidence presented here, we

suggest the body domain has no support and should possibly be removed from GUTS if further studies cannot find such support.

4.5.3 Stress Exposure

The third and final aim of this research was to compare stress exposure to the domains of GUTS. The data reported here is in line with the claims of Brosschot et al. (2016) that GUTS provides more predictive power for perceived stress than classic threat models. Exposure to life stressors only accounted for 3% of the variance in perceived stress whereas the social network and age accounted for 50%. Even though life stressors are associated with increased HPA axis activity and increased cortisol (Mizoguchi, *et al.*, 2008) how these fit within the framework of GUTS is unknown. Life stressors may provide a means for maladaptive conditioning to occur between the stressful events and other similar but non-threatening situations. Once this has happened safety cues are replaced with negative associations to the environment and situation of the stressful event, leading to increased perceived stress. This also seems to contradict previous work, specifically, work that reported a stress/age interaction effect on cognitive ability (Marshall, *et al.,* 2016a; Marshall, *et al.,* 2016b; Marshall, *et al.,* 2018), but upon reflection it does not. In the stress/age interaction studies, memory or response inhibition was regressed on by stress and age - not perceived stress, as it was a control. Indeed, in the Marshall et al work, cumulative lifetime stress and age did not correlate with perceived stress. Thus, exposure to stressful events over the course of one's lifetime may detrimentally affect cognitive ability as we age without changing one's current perception of stress. On the other hand, one's social network and age does moderate this perception. This may also suggest another useful avenue of research to pursue. By utilising a behavioural task in conjunction with GUTS variables, as identified here, as well as experienced stress, one could test whether the above is true. A further bonus to this continued avenue of research would be the integration of GUTS and experienced stress into a single stress theory. We included participants stress mindset as a control variable as it did not fit neatly within the social network and body domains but like

stressful life events may fit within the context domain. However, as with the social network domain and self-esteem, GUTS does not describe what would constitute a healthy domain. The stress mindset is the perception that stress can be natural and healthy and something to learn from (Crum, *et al.*, 2017). For this reason, within GUTS, it can be conceptualised as the perception of control in what would normally be considered stressful, especially as perceived stress is negatively associated with perceived control (Matud, 2004) and the role perceived control plays within GUTS framework. Data here suggest those with a healthy stress mindset perceive less stress than those without one. It may then represent a healthy context domain in that fear learning is not readily generalised.

4.5.4 Limitations and Future Directions

GUTS is an intriguing framework to explain how chronic stress is maintained. The lack of safety (not threat) disinhibits (instead of triggering) the allostatic response. When compromised, different domains cause GU, leading to an allostatic state. However, here we would add that when functioning properly, healthy domains decrease GU and inhibit the allostatic state. Within GUTS, an emphasis is placed on learning safety cues that are generated by each domain. As stated previously, the concept of a domain *per se* and the proposed GUTS domains can be vague or incomplete as there is no mention of what constitutes a healthy domain. As we have argued, it is difficult deciding on a domain and what to include in it. For example, we included self-esteem as a measure of a healthy social network due to its association with social capital and negative association with stress (Kreger, 1995; Martyn-Nemeth, *et al*., 2009; Wahl, *et al.*, & 2010). However, self-esteem can stem from any number of life domains such as work and school success (Baumeister, *et al.*, 2003). Furthermore, a stress mindset could represent a healthy context domain as suggested previously. The data here also provide little support for the body domain in generating GU when compromised. Only gender and age were significantly associated with perceived stress, despite the inclusion of direct measures of physical activity and health. Not

only that, age should generate more GU not less according to GUTS (Brosschot, *et al*., 2016) but here we report the opposite. However, along with gender, age does not fit well within the proposed domains (i.e., context, social network and body). It may be useful to replace the body domain with another domain. As both gender and age have an emotional component that seems to be the driving factor behind predicting perceived stress, as discussed previously. Another area with which to continue work with GUTS is to explore the directionality of concepts within each domain in relation to perceived stress and thus GU. Social support seems to be sought out after achieving an allostatic state, not before (Adamczyk, 2016) and therefore, social support cannot act as a buffer against it. This also means that social support should be removed from GUTS because it does not produce or inhibit perceived stress and is instead a coping mechanism once the body is in an allostatic state (Yalcin-Siedentopf, *et al.,* 2021). Currently, we suggest a context domain, social network domain and an affective domain. The context domain would include a stress mindset that reduces GU and experienced stress that increases GU. The social network domain would include loneliness and social fear which increase GU while self-esteem decreases GU. Finally, a new domain would include gender and age. Increased age would decrease GU while women are associated with increased GU, and men are associated with decreased GU. As mentioned above, HRV is an important component of GUTS; Brosschot et al. (2016) claim a low HRV is linked to GU. Ambiguous or uncertain contexts are considered unsafe (Luyten, *et al.,* 2011) and Brosschot et al. (2016) argue, therefore, that tolerance towards uncertainty is an inbuilt and default state of being. GUTS proposes that stress is triggered by lack of safety, or uncertainty of safety and this causes low HRV and worry, which are symptoms of chronic stress. From this, Brosschot et al. (2016) argue that uncertainty is enough to generate GU. Future work could also include the Tolerance of Uncertainty Scale (Carleton, *et al.,* 2006), which would allow one to further test the validity of GUTS by testing the association tolerance towards to uncertainty to perceived stress. Furthermore, it would be useful to provide data in the form of behavioural and physiological measures that could provide converging evidence for GUTS, especially concerning the

stress/age interaction. As mentioned previously, an effect of chronic stress on ambiguous face perception has been reported (Maoz, *et al.,* 2016) which could be a useful next avenue of investigation. HRV could also be measured in relation to GUTS given the strong evidence of its association with chronic stress (Hoehn-Saric, *et al.,* 2004; Licht, *et al.,* 2009; Thayer, *et al.,* 1996) and its important role within GUTS.

4.5.5 Conclusion

In this study, we set out to test the validity of GUTS, a new theory that explains the maintenance of chronic stress. It proposed specific life domains that, when compromised, lead to chronic stress. Despite the vagueness of the domains, we provided the first empirical support for parts of GUTS; specifically, we found evidence for the social network domain but little evidence for the body domain. That is to say that generally, a compromised social network leads to increased perceived stress while a healthy social network decreases perceived stress. Gender and age did predict perceived stress but either does not seem to belong in GUTS body domain, as previously suggested (Brosschot, *et al.,* 2016). While not specifically tested, we also suggest that stress mindset be included in the context domain and we proposed a novel domain, incorporating age and gender. GUTS research is still in its infancy but parts of it appear useful in predicting perceived stress. However, classical stress theories also predicted perceived stress and so work to understand and integrate the two frameworks should now follow. Indeed, GUTS also provides many predictions with which further work can test, such as investigating the role of perceived control. Overall, the results reported here suggest the domains within GUTS are incomplete, however, they still provide some evidence for the use of this novel theory when attempting to understand the causes and consequences of stress.

Chapter 5 – GUTS in the Face of Stress

5.1 Abstract

Recently, a new theory of stress has been proposed. The Generalised Unsafety Theory of Stress (GUTS) aims to explain how the allostatic response is maintained during chronic stress, for which classic theories of stress do not adequately account. In GUTS, the perception of generalised unsafety (GU) is the contributing factor to maintaining chronic stress. According to GUTS, compromised life domains such as one's social network or one's physical fitness can lead to GU later in life. However, to date, GUTS does not have behavioural evidence to support this.

In chapter 4 we found self-report evidence for some domains of GUTS and suggested pairing GUTS self-report measures with behavioural performance. Here, we tested the predictive strength of GUTS domain specific variables on an emotion recognition task in faces. 193 participants completed surveys to capture measures of two domains proposed to be central to GUTS: their social network (social support, loneliness and self-esteem) and their body (physical fitness, activity and age). They then judged happy, angry and surprised faces as negative or positive as previous work has revealed that increased stress increases negative judgements of ambiguous faces. The domain measures were regressed on facial judgments and reaction times to the faces. This study had three aspects: 1) We previously found support for the social, but not the body domain for GUTS. Therefore, we hypothesised increased social scores would be associated with decreased perceived stress; but there would be no association between physical scores and perceived stress. 2) Previous work reports faster reaction times (RTs) to happy faces followed by angry and ambiguous faces. We hypothesised this same pattern of results. 3) As stress promotes a negative attentional bias, and previously (chapter 4) we suggested the body domain may influence behaviour but not perception, we hypothesised lower physical and social scores would be associated with faster RTs towards angry faces and slower RTs to happy faces. When the face was ambiguous, we hypothesised lower social and physical scores would be

associated with a higher proportion of negative judgements than positive judgements, and slower RTs on negative judgements compared to positive judgements. We report evidence to support part 1 and 2 but not 3. The pattern of behavioural results for 1 and 2, while correctly predicted, were not driven by compromised GUTS domains. The results and implications are discussed.

5.2 Introduction

Conventionally, stress is often associated with a host of negative effects that include physical (McEwen, 1999; Sapolsky, *et al.*, 1990; Woolley, *et al.*, 1990; Gould, *et al.*, 1998), cognitive (Desimone & Duncan, 1995; Jaroudi, *et al.,* 2017) and behavioural (Wilson, *et al.,* 2002; Colsher & Wallace, 1991) domains. It is often named as a common workplace problem (around 50% of all work place problems are reportedly stress-related) reported globally and cross culturally (Casey & Liang, 2014; Moreno, *et al*., 2020 Ribeiro Santiago, *et al.,* 2020). Stress in the workplace results in lost productivity (60 to 80%) due to high-stress related absenteeism (McDaid, *et al.,* 2005; Knapp, *et al.,* 2004) and accounts for up to two thirds of all doctors' visits (Pikhart & Pikhartova, 2015; Wilkinson & Marmot, 2003). With this in mind, it is easy to understand why stress is maligned.

An aspect of stress that is often missed is that it is adaptive when it is transient and only becomes maladaptive when sustained. It serves a vital survival function meant to prolong an organism's existence long enough to pass on its genetic code. In practical terms, stress provides behavioural advantages in perceived dangerous situations where threat perception is generated either from the environment or from one's own thoughts. Classically, when threat is detected, the body is put into a state of action preparedness to deal with the threat in the here and now. Physically, adrenaline is released which increases blood flow to the skeletal muscles and heart rate and blood pressure are increased (Allen, *et al*, 1946; HåRkanson, *et al.*, 1986). Additionally, adrenaline aids the release of glucose and increases systematic oxygen uptake (HåRkanson *et al.*, 1986) which increases physical performance. Neurologically, stress increases the signal to noise ratio for salient and threatening stimuli

(Foote *et al.,* 1975; Waterhouse, *et al.*, 1990), lowers the response thresholds of sensory information (Foote *et al.,* 1975; Waterhouse, *et al.*, 1990) and shortens response latencies to incoming stimuli (Lecas, 2004). Furthermore, attention shifts from focused attention to general scanning (Rajkowski, *et al.*, 1994). The net result is that attention becomes attuned for salient and threatening stimuli. In short, the body is physically prepared to deal with the threat (i.e. fight or flight) and, attention scans for threat. This state of preparedness is physically enabled by a state referred to as allostasis (McEwen, 2004) and is turned off once the threat is dealt with, returning the body to normal functioning. However, prolonged allostasis can lead to the wear and tear on the body and is known as allostatic load (McEwen, 2004). For example, those suffering from chronic stress and therefore experiencing allostatic load have less attentional control, require more cognitive resources with target conflict and have difficulty remaining alert (Liu, *et al.,* 2020). Allostasis provides such a substantial evolutionary advantage that attentional mechanisms are subject to a negativity bias whereby threatening stimuli have the highest priority compared to non-threatening stimuli (Kan, *et al.,* 2019; Kan, *et al.,* 2021; Taylor, 1991). This can result in false alarms and erroneous allostasis to non-threats, however, it is better to err on the side of caution and waste energy than die from false negatives (Taylor, 1991; Jonikaitis, 2019). Practically this means that ambiguous stimuli are often perceived as threatening, an effect that is increased as a function of chronic stress (Maoz *et al.,* 2016). Classically, the perception of threat (real or imagined) is thought to generate allostasis. What is less clear is how allostasis is maintained during chronic stress.

In order to be maintained at the chronic level, the perception of threat would also need to be chronic, but it has been suggested by Brosschot et al. (2016) that it is hard to imagine that even the most severely chronically stressed individuals perceive stress in this way. Instead, Brosschot et al. (2016) argue that threat does not generate allostasis; they propose that a lack of safety perception does. In other words, it is this perception of a lack of safety, which they term “generalised unsafety” (GU) that generates allostasis. Brosschot et al. (2016) suggest that ones’ social network, one’s physical body, and the context (the ability

to generalise safety cues from context to a similar context) domains as potential life domains that could become compromised. By itself, a compromised life domain is not necessarily threatening but it contributes to perceiving less safety. For example, a compromised body and social network provide one with less means to deal with incoming threats making the world inherently less safe, which is then generalised to similar situations that encompass those domains leading to a lack of safety perception and (Brosschot and colleagues argue) the maintenance of chronic stress. For example, a social gathering, which is not by itself threatening, may be perceived as unsafe if the social network domain is compromised leading to GU and maintenance of chronic stress. This theory was named the Generalised Unsafety Theory of Stress (GUTS; Brosschot, *et al*., 2016, 2017, 2018).

GUTS and its social and body domains were described and explained as well as tested in Chapter 4. There we provided significant evidence for the social network domain but there was no evidence for the body domain. The social network domain variables significantly predicted self-reported perceived stress, which was in line with what GUTS predicted. Age and gender were originally included in the body domain but, we argued they do not belong in the body domain. We reported age negatively predicted perceived stress (the opposite of what was predicted) and that being a woman was associated with increased perceived stress, and we argued this was related to the social domain and not the body domain. We suggested the lack of evidence for the body domain might be due to a lack of a behavioural task in the paradigm. A series of previous studies provided evidence that the interaction of age and accumulated life stress was associated with a decrease in cognitive performance (Marshall, *et al.,* 2016a; Marshall, *et al.,* 2016b; Marshall, *et al.,* 2018) but not perceived stress. Therefore, the body domain may predict behavioural outcomes, such as the age/stress interaction but not necessarily self-report measures of perceived stress such as the social network variables do. Indeed, we included this interaction previously and it accounted for 50% less variance than the social network variables when regressed on perceived stress (see Chapter 4). That is to say, the lack of evidence for the body domain

may be due to the lack of a behavioural component in the previous methodological design. Thus, one's social network domain could moderate this stress perception while the stress/age interaction and the body domain detrimentally affect cognitive ability without changing one's current perception of stress.

To expand on these previous results, we will use the same methodological design (see Chapter 4) but include a behavioural task. Here we introduce a forced choice task using ambiguous (surprised faces) faces, where participants have a time limit to decide if a face is negative or positive. There is evidence that surprised faces without surrounding context are perceived positively by some and negatively by others (Kim, e*t al.,* 2003), meaning they are ambiguous in nature (Neta, *et al.,* 2009; Neta, *et al.,* 2021). This makes using surprised faces useful as they provide ambiguity without needing to manipulate the faces themselves. The basis for using these faces is that ambiguous, yet neutral, stimuli are often categorised as threatening by those who suffer with high stress compared to those who are not experiencing stress. In one study, participants were asked to judge faces as either happy or angry where face stimuli were created by morphing a happy and an angry face together. Faces were blended along a spectrum so that at one end the face was 100% happy, while at the other end the face was 100% angry, with the most ambiguous face being in the middle consisting of a 50/50 blend of happy and angry. Participants suffering from symptoms of chronic stress were more likely to judge the ambiguous faces as angry compared to their healthy counterparts (Maoz, *et al.,* 2016). Related to GUTS, Brosschot, *et al.* (2016) suggest a reason for this is that chronic stress may lead to perceiving the lack of safety in ambiguous faces as opposed to perceived threat detection. To substantiate this claim Brosschot et al. (2016) point out that in fear conditioning paradigms, chronic stress produces a fear response to a conditioned stimulus coupled with a threatening stimulus but also to the uncoupled unconditioned stimulus (for a review see Duits et al., 2015). They suggest that these participants fail to recognise the safety in the unconditioned stimulus but not threat, as there is no threat to perceive. A compromised social network domain or body domain should predict whether a participant labels a surprised face as negative or positive. Furthermore,

there is evidence that stress also has an effect on reaction time (RT) when judging ambiguous faces. Maoz et al. (2016) reported that increased stress produced an RT bias in which participants were slower to judge surprised faces angry compared to when they were judged happy. This effect was absent from non-stressed individuals. When faces are unambiguous, increased stress is associated with faster RTs towards angry faces (Rued, *et al.,* 2019) and slower RTs for happy faces (Tipura, *et al*., 2022). When responding to angry or happy faces, in a stress-free context, there is a slight effect of valence where happy faces are responded to faster than angry faces but not significantly (Brüne, *et al.,* 2013) but ambiguous faces consistently have the slowest response times (Neta, *et al.,* 2009). If correct, GUTS would predict that compromised social network and body domains would produce a similar pattern of results. Compromised domains would predict faster RTs for angry faces and slower RTs for happy faces. When categorising a surprised face, compromised domains would predict slower RTs when judging a surprised face as angry compared to judging a surprised face as happy.

There are three aspects to the current study. The first tests the predictive power of the GUTS life domains on perceived stress, a replication of previous work (see Chapter 4). In the second, we compare reaction times for each of the different kinds of faces (happy, angry and surprised) as well as the RTs to surprised faces judged as negative and those judged as positive. This is to ensure that the face manipulation worked as intended. Finally, we test the predictive power of the domains on the forced choice task using ambiguous faces (surprised faces), which will include RTs for each face (same as part 2) and the proportion of surprised faces judged as negative/positive. Following previous results, for part 1, we hypothesise that lower scores on the social measures will be associated with increased perceived stress but not the physical activity measures except for age (decreased perceived stress) and gender (women will have increased perceived stress). For general response times to faces (part 2), we hypothesise that happy faces will be responded to the quickest followed by angry faces and finally surprised faces. There will be no difference in response times to surprised faces judged as negative compared to surprised faces judged

as positive (Maoz, *et al.,* 2016). In part 3, we test GUTS predictions and hypothesise that lower scores on both the social network and body domain measures will be associated with faster RTs with judging angry faces and slower RTs when judging happy faces. We hypothesise that when the face is ambiguous (a surprised face), lower scores on both the social network and body domain measures will be associated with slower RTs when judging surprised faces as angry compared to when surprised faces are judged as happy. Finally, we hypothesise that lower scores on both domains will be negatively associated with the proportion of surprised faces judged as negative.

5.3 Methods

5.3.1 Participants and Design

Participants (*n* = 267) were recruited online through Prolific (www.prolific.co) where they were either paid or, if they were students from the University of Essex, were awarded course credit for participation. The study was completed online. Participants who did not complete all the questionnaires/scales or who failed attention checks were excluded resulting in 193 participants in the final sample. 49% were women (50% men and 1% other). The age ranged from 18 to 71 years (*M* = 34.87, *SD* = 14.27). 43% had an A-Level qualification or equivalent as their highest form of education, while 8% had a GCSE or lower and 49% had a Bachelor's Degree or higher. Most participants were White (68%) while some were Black (10%) and Asian (10%); a small portion were Mixed (7%), another ethnic group (4%) or preferred not to say (1%).

The design was fully within-subjects. All participants completed all the questionnaires and rated all the faces. RTs for angry, happy and surprised faces were the dependent variable as well as the proportion of surprised faces rated as negative.

5.3.2 Materials

5.3.2.1 Body Domain

Besides age and gender, participants filled out the International Physical Activity Questionnaire (IPAQ; Hagströmer, *et al.,* 2007) in order to measure physical activity and fitness. In the IPAQ, participants give their height (m) and weight (kg) which can be used to calculate their body mass index (BMI; weight/height^2) which represents weight by controlling for height. Like weight, BMI has an inverted-u shape when thinking about health, as lower scores represent too little weight, and higher scores represent too much weight in relation to height. A link to a unit converter was provided so that imperial measurements could be converted into the required metric units. The IPAQ has participants record how many days in the past week they performed vigorous activity (that lasted at least 10 minutes), such as heavy lifting, digging or aerobics; as well as their moderate activity (that lasted at least 10 minutes), such as carrying light loads and regular, paced bicycling. They were also asked the same question about walking. Participants were asked to provide the minutes per day spent on each of the above activities and how many days a week they perform these activities. From the information provided, a ratio of participants' working metabolic rate relative to resting metabolic rate was calculated and defined as 1 kcal/kg/hour and measured in metabolic equivalent of task (METs; Hagströmer, *et al.,* 2007). The IPAQ assigns a weighting score for each of the above activities so that vigorous activity (8) is worth more METs than moderate activity (4) which in turn is worth more than walking (3.3). MET scores for each activity were calculated as follows:

((Minutes on activity * days in a week spent on activity) / 7) * weighted score.

This represents average MET scores per day for each activity with a higher MET score indicating increased metabolic rate. A total MET score is calculated by summing each activities MET score together. This was done because the MET scores were positively skewed.

5.3.2.2 Social Domain

The Liebowitz Social Anxiety Scale (Liebowitz, 1987) is a 24-item scale that measures social fear and social avoidance. The LSAS has high reliability and validity (Heimberg, *et al.,* 1999) as well as test-retest reliability (Baker, *et al.,* 2002). Participants respond to each item twice, once indicating their fear of the item on a 4-point Likert scale from 1 ('none') to 4 ('severe') and again to indicate their avoidance of the item on a 4-point Likert scale from 1 ('never') to 4 ('usually'). Items range from "Using a telephone in public" to "Going to a party". Fear scores for each item are summed for a social fear score. The same is done for avoidance to produce a social avoidance score. A total social anxiety score is produced by adding the previous two totals. Higher scores indicate higher social fear and avoidance.

The Multidimensional Scale of Perceived Social Support (MSPSS; Zimet, *et al.,* 1988) is a 12-item scale. It has been validated cross-culturally and repeatedly shown to be reliable (Başol, 2008; Osman, *et al.,* 2014; Trejos-Herrera, *et al.,* 2018; Wongpakaran, *et al.,* 2011). It consists of three subscales, namely the significant other subscale ('there is a special person who is around when I am in need'), the family subscale ('I get the emotional help & support I need from my family') and the friends subscale ('I have friends with whom I can share my joys and sorrows'). Each captures perceived social support from each group on a 7-point Likert scale from 1 ('Very strongly disagree') to 7 ('Very Strongly Agree'). Scores are summed together with higher scores indicating higher perceived social support. A total perceived social support score is calculated by adding the scores of all the subscales.

Loneliness was measured using the 20-item UCLA Loneliness Scale (ULS; Russell, 1996) and verified as reliable and valid (Lasgaard, 2007). Participants rate how often they feel the statements for each item ('I lack companionship') on a 4-point Likert scale from 0 ('I often feel this way') to 3 ('I never feel this way'). Scores are summed to produce a total loneliness score with higher scores indicating increased feelings of loneliness.

5.3.2.3 Additional Variables

The Perceived Stress Scale (PSS; Cohen, *et al.,* 1983) was used to measure the participant's perception of stress as a stand in for GU. It asks participants to rate their dis/agreement to statements (e.g. 'In the last month, how often have you felt nervous and "stressed"?') on a 4-point Likert scale ranging from 1 ('Never') to 4 ('Very often'). There are three versions of the PSS: 4-, 10- and 14- item versions. The 10-item PSS has the highest validity and reliability of the three (Lee, 2012). It was therefore the version used in this study. Scores for each item were summed with higher scores indicating more perceived stress than a lower score.

The Rosenberg Self-Esteem Scale (Rosenberg, 1965) was used to capture the self-esteem of participants; reliability and validity for the scale have been confirmed since the scales inception (Cong & Cheong, 2022; Martín-Albo, *et al.,* 2007). It is a 10-item scale where participants are asked to rate how much they agree with statements such as 'I wish I had more respect for myself' and 'I take a positive attitude toward myself'. It is rated on a 4-point Likert scale from 1 ('Strongly agree') to 4 ('Strongly disagree'). Items 1, 3, 4, 7 and 10 are reverse scored and then all the scores are summed so that a higher score represents higher self-esteem.

5.3.3.4 Faces

Faces were taken from The Karolinska Directed Emotional Faces (KDEF, https://kdef.se/; Lundqvist, *et al.*, 1998). It is a database of emotional facial expressions. The age of all the models were between 20 and 30 years of age and were instructed to evoke the necessary expression. All models were screened for beards, moustaches, earrings, eyeglasses, and visible make-up prior to taking the photographs. The faces have been validated on emotion, intensity and arousal by test-retest reliability with mean correlations across all pictures of .75 and .78 respectively (Goeleven, *et al.,* 2008). 10 angry (fig 5.1a), 10 happy (fig 5.1b) and 20 (fig 5.1c) surprised faces were chosen with equal split of men and women. This led to a total of 40 faces all presented once. Each face was 249px x 340px and

presented in the middle of the screen. Participants were presented with a single picture of a face and rated it either as positive or negative. Faces were presented for a maximum of 5 seconds or until the participant rated the valence of the face. RT for each trial was calculated by subtracting start time by click time. Trials where happy faces were rated as negative were excluded from analysis and the same was true for trials for angry faces rated as positive. In cases where all happy faces were rated negative and/or all angry faces were rated as positive the participant was excluded from the analysis for failing to follow instructions making their ratings of surprised faces unreliable. The proportion of surprised faces rated as negative (and therefore positive as well) was also calculated.

Figure 5.1. From left to right an example of an angry, happy and surprised face used.

5.3.3 Procedure

After participants read the study information and provided written consent in the form of a check box, they answered socio-demographic questionnaires (age, gender, ethnicity and highest academic achievement) followed by completing all questionnaires, presented in a random order. Participants then completed a practice block consisting of 6 trials (which did not include faces from the main experiment) for the facial emotion recognition task (Maoz, *et al.,* 2016). After which they rated all forty faces. Faces were presented in random order.

5.3.4 Data Analysis

All reaction time scores, and all MET scores were positively skewed and so were log transformed (base of 2) to normalise their distributions after adding 1 to each score. Adding 1 to each score was to avoid log transforming a score of 0. The proportion of surprised faces labelled as negative for each participant was also calculated and called the negative proportion (NP).

The difference in RTs for happy, angry and surprised faces (as well as surprised faces rated negative vs positive) were analysed using a one-way ANOVA.

In order to test the GUTS domains on perceived stress, we first ran two separate hierarchical regressions (i.e. the physical and social domain taken from GUTS) to first exclude domain specific non-significant variables before conducting the overall GUTS regression. In the first regression, representing the body domain, stress perception was regressed on BMI, age, gender and the total MET scores as well as the subset of MET scores for vigorous and moderate activity, and walking. In the second regression, representing the social domain, stress perception was regressed on social support, loneliness and social anxiety. In the overall GUTS analysis, significant predictors of perceived stress from the social and body domain were used. Additionally, self-esteem was also added as a possible measure of a functioning social network domain. Significant variables would then also be used in further regression analyses for RTs and the NP. A correlation was also run between the body domain variables and the RTs and the NP in order to determine which variables, if any, should be included in the regressions for RTs and NP. As discussed, the reasoning is the previous lack of association between the body domain and perceived stress but the possible association between the body domain and behavioural performance. This led to a further 6 regressions; one for each RT (happy/angry/surprised and surprised faces labelled negative/positive) and one for the NP.

5.4 Results

5.4.1 GUTS

See table 5.1 for a zero order correlation table between perceived stress scores and all the body and social domain variable scores.

Table 5.1: Zero order correlations between all variables included in the social and physical domains (significance values in brackets).

	Perceived Stress	Age	Gender	Vigorous Exercise	Moderate Exercise	Walking	BMI	Social Support	Lonely	Social Anxiety
Age	-.365 (<.001)									
Gender	.307 (<.001)	-.214 (.003)								
Vigorous Exercise	-.047 (.517)	-.066 (.363)	-.138 (.055)							
Moderate Exercise	.013 (.858)	-.011 (.884)	.024 (.738)	.271 (<.001)						
Walking	.025 (.727)	-.109 (.130)	.141 (.051)	.136 (.059)	.409 (<.001)					
BMI	-.089 (.217)	0.311 (<.001)	-.044 (0.541)	-.105 (.145)	.042 (.588)	-.026 (.715)				
Social Support	-.249 (<.001)	.227 (.002)	.-.092 (.204)	.091 (.206)	-.115 (.113)	-.038 (.601)	.009 (.905)			
Lonely	.538 (<.001)	-.270 (<.001)	.122 (.091)	-.072 (.318)	.136 (.059)	.059 (.413)	.005 (.0950)	-.555 (<.001)		
Social Anxiety	.515 (<.001)	-.182 (.011)	.273 (<.001)	-.120 (.096)	.011 (.881)	.011 (.881)	.025 (.729)	-.255 (<.001)	.482 (<.001)	
Self-Esteem	-.641 (<.001)	.348 (<.001)	-.131 (.069)	.044 (.540)	-.018 (.806)	-.018 (.806)	-.012 (.867)	.357 (<.001)	-.658 (<.001)	-.570 (<.001)

5.4.1.1 Body Domain

On average, participants were 1.71 (*SD* = 0.78) metres tall and weighed 75.21 (*SD* = 18.82) kg leading to an average BMI of 25.68 (*SD* = 5.97). In terms of physical exercise participants' MET scores per day were as follows: walking was 207.9 (*SD* = 4229.64), moderate exercise was 133.45 (*SD* = 249.12), while vigorous exercise was 191.29 (*SD* = 280.95). This led to an overall average MET score of 532.73 (*SD* = 544.12). BMI and MET scores may have a quadratic relationship with perceived stress (De Wit, *et al.,* 2009; Bohon & Welch, 2021). For example, a low BMI score equates to an unhealthy low weight, while a high BMI score equates to an unhealthy high weight. For this reason, residuals for each listed variable were plotted against predicted scores and inspected; they suggested there

may be some slight heteroscedasticity. That is to say, the weighting of scores for these variables and the ends of the distribution when predicting perceived stress may not be the same. If so, it is inappropriate to use them in a linear regression and would be better in a quadratic regression. However, follow-up Breush Pagan tests failed to support this (all $p > 0.05$). As such, the above-mentioned variables were used in linear regression.

Overall, the physical model was significant, accounting for 20% of the variance $f(7,185) = 6.62$, $p < 0.001$. In this model, age ($\beta = -0.334$, $p < 0.001$) and gender ($\beta = 0.22$ $p = 0.001$) were both significantly associated with perceived stress wherein increased age was associated with less perceived stress and women were associated with increased perceived stress. As such, age and gender were included in the overall model. None of the physical activity measures from the IPAQ, weight, height or BMI were significant (*ps* > .241) and thus were excluded from the overall regression for perceived stress.

5.4.1.2 Social Domain

On average, participants' perceived social support score (minimum score = 12[4], maximum score = 84) was 59.55 (*SD* = 14.19). Their loneliness score was 43.55 (*SD* = 13.24; with a minimum score of 20 and a maximum score of 80). In terms of social anxiety, participants had a score of 55.86 (*SD* = 30.15; minimum score = 0, maximum score = 144).

Overall, the social domain model was significant, accounting for 37% of the variance, $f(3,188) = 37.88$, $p < 0.001$. In this model, loneliness ($\beta = 0.415$, $p < 0.001$) and social anxiety ($\beta = 0.333$, $p < 0.001$) were positively associated with perceived stress indicating that increased loneliness and social anxiety were associated with increased perceived stress. Therefore, the loneliness and social anxiety were included in the overall regression for perceived stress. Social support ($p = .315$) was not significant and was therefore omitted.

[4] All minimum and maximum scores are the absolute scores of each scale.

5.4.1.3 Overall Model

In the final model, perceived stress was regressed on age and gender (step 1: the body domain), loneliness and social anxiety (step 2: the social domain). Finally, self-esteem (minimum of 10 and a maximum of 40) was added (step 3: the control variable; see table 5.2 for standardised beta coefficients); with the average self-esteem score for participants being 28.36 (*SD* = 6.25).

The first step (body domain) was significant, accounting for 19% of the variance, $f(2,189) = 21.61$, $p < 0.001$. Age was negatively associated with perceived stress such that older participants perceive less stress. Conversely, gender was positively associated with perceived stress indicating that women (coded as 2) perceive more stress than men (coded as 1) do.

When the social domain variables were added in the second step, the model was significant accounting for an additional 25% variation to the model for a total of 44%, $f(4,187) = 36.37$, $p < 0.001$. The change statistic was also significant $f(2,187) = 41.81$, $p < 0.001$. Both were significantly associated with perceived stress.

Table 5.2: Linear regression models of the body domain, the social network domain and self-esteem on perceived stress (significance in brackets).

Independent Variable	Step 1	Step 2	Step 3
Age	-0.312 (<.001)	-0.173 (.001)	-0.110 (.028)
Gender	0.239 (<.001)	0.145 (.011)	0.209 (.002)
Loneliness		0.330 (<.001)	0.167 (.024)
Social Anxiety		0.281 (<.001)	0.161 (.024)
Self-Esteem			-0.364 (<.001)

Gender coded as 1 = man, 2 = woman.

Predictably, social anxiety and loneliness were positively associated with perceived stress indicating that the more these feelings are felt the more stress one perceives. Age

and gender were still associated with perceived stress but the association from both had diminished in predictive strength.

In the final step the model was significant when the self-esteem measure was added, increasing the accounted for variance by 7% (51% total for the model), $f(5,186) = 38.01$, $p < 0.001$. The change statistic was also significant $f(1,186) = 25.74$, $p < 0.001$. Self-esteem was negatively associated with perceived stress whereby higher self-esteem was associated with less perceived stress. The previous variables remained significant.

5.4.1.4 Summary

We tested the predictive strength of participants' body domain and social domain scores, and self-esteem with their stress perception. The body domain was initially significant with both age and gender and remained significant after each step. T. The social domain variables were also significantly associated with perceived stress. This was still true when self-esteem was added to the model. Self-esteem itself was highly associated negatively with perceived stress. Taken together these results provide some evidence for the body/social domains of GUTS because of their association to perceived stress. For the most part (besides social support) these results are congruent with the results reported in chapter 4 and supports hypothesis 1. Therefore, all these variables were added to the RT and NP regressions.

5.4.2 RT

RTs were measured in milliseconds. Of the three main emotions, happy faces (M = 1674.03, SD = 436.31) were responded to the quickest followed by angry faces (M = 1731.19, SD = 471.74), with surprised faces (M = 1924.98, SD = 468.87) having the slowest response time. SNeg faces (M = 1918.88, SD = 489.24) had a quicker RT than SPos faces (M = 2015.01, SD = 568.85) when splitting surprised faces into those judged as negative or positive, both of these faces were still slower than happy and angry faces. This indicates that when the emotion of the face was easy to infer, RTs were quicker, as happy and angry faces

were identified faster than surprised faces. A one-way ANOVA showed that overall, these RTs were significantly different $f(4,748) = 23.813$, $p < .001$, $\eta p^2 = .11$. Follow-up pairwise comparisons using a Bonferroni correction indicated that all five RTs were significantly different from each other except for surprised faces and surprised faces judged as negative ($p = 1$). Happy faces were responded to significantly faster than angry faces ($p = .001$), surprised faces rated negative ($p < .001$), surprised faces ($p < .001$) and surprised faces rated positive ($p < .001$). Angry faces were responded to significantly faster than surprised faces rated negative ($p = .003$), surprised faces ($p = .001$) and surprised faces rated positive ($p < .001$). Surprised faces rated negative ($p = .041$) and surprised faces ($p = .014$) were responded to significantly faster than surprised faces rated positive.

5.4.3 RT and GUTS

Multiple correlations were run between the body domain variables and the RTs to faces as the body domain may be associated with behavioural performance but not the perception of stress. There were only 4 significant correlations between the body domain variables and the RTs and NP. Age was positively correlated with RT's for surprised faces, $r(192) = .152$, $p = .035$ and SNeg faces, $r(192) = .164$, $p = .024$. Both of these indicate that older age was associated with slower reaction times with surprised faces and surprised faces labelled negative. There was also a significant correlation between walking and SPos faces, $r(190) = -.191$, $p = 0.008$. Participants who spent more time walking were faster at responding to surprised faces when they labelled them positive. Finally, gender was significantly correlated with NP, $r(192) = .177$, $p = .014$. Thus, women (coded as 2) were more likely to label surprised faces as negative compared to men (coded as 1).

5.4.3.1 Happy/Angry Faces

The happy/angry face regression included gender in the first step, followed by, loneliness and social anxiety in the second step and finally self-esteem was added in the third step. There was no significance at any step of the model (all p's > 0.283).

5.4.3.2 Surprised Faces

The surprised face regression included gender and age in the first step, followed by loneliness and social fear in the second step, and finally self-esteem was added in the third step. Overall, the model was not significant $f(2,189) = 2.3$, $p = 103$. However, age was a significant predictor of reaction times for surprised faces in all 3 steps ($\beta = 0.158$, $p = 0.033$, $\beta = 0.191$, $p = 0.012$ and $\beta = 0.209$, $p = 0.008$ respectively). This indicated that slower reaction times for surprised faces were associated with higher age. The same regression was run for SNeg faces with the same results as surprised faces with a non-significant overall model, $f(2,186) = 2.61$, $p = .076$, but age being a significant predictor of reaction times for SNeg faces ($\beta = 0.169$, $p = 0.023$, $\beta = 0.206$, $p = 0.008$ and $\beta = 0.225$, $p = 0.005$ respectively). Again, this indicates an association between longer reaction times for surprised faces rated as negative and increased age.

The SPos regression replaced age with walking time in the first step because of the above correlations. The model was non-significant $f(2,186) = 2.071$, $p = 0.129$. Similar to age in the above analyses the amount of time spent walking was a significant predictor of reaction times for surprised faces rated as positive in all 3 steps ($\beta = -0.149$, $p = 0.043$, $\beta = -0.157$, $p = 0.034$ and $\beta = -0.156$, $p = 0.035$ respectively). This indicated that faster reaction times for surprised faces rated as positive were associated with increased walking.

5.4.3.3 Faces Rated Negative

The steps in the regression for the NP were the same as the happy/angry faces. The first step was significant accounting for 3% of the variation, $f(1,190) = 6.79$, $p = 0.01$, with gender significantly predicting NP ($\beta = 0.186$, $p = 0.01$). This indicates that women had a higher proportion of surprised faces labelled as negative compared to men. The second and third steps were non-significant (all p's > 0.05). Gender remained a significant predictor in all three steps ($\beta = 0.169$, $p = 0.024$, $\beta = -0.167$, $p = 0.026$ respectively).

5.4.3.4 Summary

We tested the predictive power of the GUTS domain variables on RTs for valence judgements for happy, angry and surprised faces, as well as the GUTS domain variables on the surprised face ratings (positive vs negative). Only the NP conditions were significant in the regression whereby gender predicted NP. While age significantly predicted RTs for surprised and SNeg faces and walking predicted RTs for SPos faces the overall models were non-significant. Both models for happy and angry faces were not significant.

5.5 Discussion

This study consisted of three parts. In the first part, we tested the predictive strength of the social network and body domains for perceived stress. This was to test the validity of GUTS and was a replication of Chapter 4. In the second part, we compared RTs when judging angry, happy and surprised faces as either positive or negative to ensure we correctly manipulated the valence of the faces. Finally, we tested the predictive strength of the GUTS domains on the RTs for each face type, surprised faces judged negatively and positively, and the proportion of surprised faces judged as negative. Here we report data to support the hypotheses for part 1 and 2 of the study but not part 3.

For the first part of the study, we hypothesised that only the social network domain would predict perceived stress and only age and gender would predict perceived stress from the body domain. The hypothesis was mostly, but not completely confirmed. Brosschot et al. (2016) originally suggested social anxiety and loneliness would represent a compromised social network and we report that here. According to GUTS, the world is inherently less safe without the safety net provided by social support (including family, friends and significant others) therefore loneliness, the absence of peers, would mean an inherently less safe world for the lonely. As social safety cues are learnt, GU from social anxiety can arise from either failing to initially learn these safety cues or generalising a previous threat during a social event to other social events. In opposition to loneliness, the more social support one

perceives, the more of a general safety net they perceive, making the world safer and generating less GU (or perceiving less stress). Here we do not provide evidence for this, contrary to chapter 4. In the overall model in chapter the beta coefficient was .084, while here the coefficient was .07 which is not a wildly different outcome. Chapter 4 did have a much larger sample size (452 vs 193) and perhaps this increased statistical power lead to a significant finding previously. With that said, in chapter 4 increased social support was associated with increased perceived stress, which is the opposite of what GUTS predicts. There we argued one may turn to peers once stress has already been perceived leading to a positive association between support from friends and perceived stress. Either

For the body domain, only age and gender were significantly associated with perceived stress. Participants BMI, height, weight, and amount and type of exercise did not predict perceived stress. However, as age brings with it a compromised body, GUTS predicts increased age should be associated with increased perceived stress, but the opposite was found. Brosschot et al. (2016) argue that our ancestors would have been in more fight or flight situations while hunting or defending a tribe from another tribe or animal attack and that modernity has not existed long enough for evolution to overcome this. While this may be true, it may be that safety cues due to physical un/fitness are not compromised in today's world. We no longer have to fight off invaders or predators, food is never far away, and doctors and hospitals abound. Furthermore, age has been associated with happiness (Blanchflower, 2021) and may actually act as a buffer against threat when viewed through the lens of GUTS.

Gender was included in the body domain because of the physical strength differences and time spent on physical activities between men and women (Azevedo, *et al.,* 2007; Trost, *et al*., 2002). Given the lack of evidence for physical activity as a predictor of perceived stress in this study, gender may predict perceived stress because of affective or social differences in gender and not physical differences as previously discussed (chapter 4). Furthermore, women, in general, perceive more stress and experience more chronic stress than men do (Graves, *et al.,* 2021; Matud, 2004) despite both genders experiencing

the same number of stressors. Related to GUTS, women perceive less control than men do with increased control being negatively associated with perceived stress (Matud, 2004). As such, less perceived control may lead to more perceived stress and in turn more GU. According to GUTS, one of the causes for GU is the intolerance towards uncertainty and so this may be a driving factor as to why gender is associated with perceived stress (Brosschot, *et al*., 2016).

The data reported here supports the association between stress perception and a compromised social network domain but not between a compromised body domain and stress perception. The relationship between age and gender, and GU may not be due to physical fitness but another factor such as happiness, sense of control, social support or an interaction between any of these variables.

The second part of the study was a replication of previously reported RTs and validation of the experimental manipulation when reacting to faces with different emotions. We provide evidence for all but one of the proposed hypotheses regarding RTs to different faces. Neta et al. (2009) reported faster RTs to happy faces compared to angry faces but not significantly so, here the difference was in the same direction and statistically significant. Additionally, we report the slowest RTs to surprised (ambiguous) faces that has also been previously reported (Neta, *et al.,* 2009). Surprised faces are ambiguous and slower to be judged compared to happy and angry faces, due to the lack of valence associated with ambiguous faces (Neta, *et al.,* 2009). Finally, Brüne et al. (2013) and Maoz et al. (2016) reported no difference in RTs when judging surprised faces as angry compared to when they were judged happy in the control groups; however, here we found surprised faces judged as angry were responded to faster than faces judged as happy. While the significances are not the same the overall pattern of results are in the same direction here and elsewhere (Brüne, *et al.,* 2013; Maoz, *et al.,* 2016). This provides validation for the experimental manipulation presented here.

The third part and main impetus of this study was the investigation of the predictive strength of GUTS domains on the RTs of ambiguous faces as well as the proportion of faces judged as negative. Overall, there was no evidence that any of the GUTS domains were associated with these RTs, or at the very least very little evidence. Age was associated with RTs to surprised faces, which may represent a general cognitive slowing present during ageing. Time spent walking was associated with positive judgments of surprised faces whereby RTs were quicker the more one walked. Finally, gender was associated with negative judgements of faces, where women judged surprised faces as negative more often than men did. However, in all three cases the overall model was not significant. Brüne et al. (2013) induced stress in participants (therefore acute stress) whereas here we were more interested in the maintenance of chronic stress which may led to the discrepant results. We measured and tested the variables that could lead to the maintenance of chronic stress through GU. Brüne et al. (2013) reported slower reaction times for the stress group compared to the control group which is what one would expect from chronic stress. For example, Maoz et al. (2016) reported slower reaction times to ambiguous faces in the socially anxious group compared to the control group. Therefore, either way (acute or chronic stress) one would expect that variables leading to the maintenance of chronic stress (as described by GUTS) would be associated with reaction times for ambiguous faces as previously reported. However, here we did not find this association. Therefore, the results reported here do not support GUTS at a behavioural level.

5.5.1 Limitations and Future Directions

The reason for the lack of evidence for an effect of the GUTS domains on perception of angry and happy faces may be due in part to the clear valence of the faces. When the valence of a face is clear, there is less of an impact of individual differences (Neta, *et al.,* 2009). This may help to explain the lack of associations between the GUTS domains and RTs for these particular faces. An explanation for the lack of an association between the GUTS domains and the RTs to surprised faces and the proportion of surprised faces judged

as negative is far less clear; especially given the clear association between the social domain network and perceived stress. There are reports of a stress effect on RTs towards ambiguous faces and their judgement (Brüne, *et al.,* 2013; Maoz. *Et al.,* 2016; Neta, *et al.,* 2021). Through the lens of GUTS, compromised domains would be associated with these effects. For example, increased loneliness and social anxiety represent a compromised social network domain, when a domain is compromised there is increased GU, leading to the disinhibition of allostasis. The net result is stress and therefore the factors included in each domain should be associated with performance on a task known to be associated with a stress effect. Again, perhaps the social network domain contributes to perceived stress but not behavioural outcomes, while the body domain should be removed from GUTS in general. With that said, GU from compromised social domains predicts increased perception of stress with empirical evidence from this chapter and Chapter 4, providing at least some evidence for GUTS (see also Chapter 4). However, perceived stress itself did not predict performance on the face judgement task either. There may be two reasons for this. Perhaps perceived stress is not a good stand in for perceived GU. Although, this begs the question that was brought up in chapter 4, how does one measure perceived GU? A question that has no easy answer and is beyond the scope of this chapter. It may also be that there is no issue with GUTS or the measures here but perhaps the task and measures in combination were ill-fitted for testing GUTS. Indeed, previous work investigating the effects of long-term stress exposure on cognition found no association between perceived stress and behavioural performance but did find an association with more direct measures of the effects of long-term exposures to stress (Marshall, *et al.,* 2016a; Marshall, *et al.,* 2016b; Marshall, *et al.,* 2018). In their series of studies, the authors used the social readjust rating scale (Holmes & Rahe, 1967) and the life events scale for students (Clements and Turpin, 1996) which specifically reflect the amount of stress participants could have faced in their life already. Therefore, higher scores indicate higher involvement in stressful situations and not the mere perception of stress. To add to this, one study addressed discrepant results of ambiguous

face judgements RTs by measuring facial muscle movement (Neta, *et al.,* 2009). The measures here, namely RTs, may not be sensitive enough to capture a stress effect.

Another method to test the validity of the GUTS domains would be to measure accumulated life stress (Marshall, *et al.,* 2016a; Marshall, *et al.,* 2016b; Marshall, *et al.,* 2018) and physiological measures of stress such as cortisol (Brüne, *et al.,* 2013; Neta, *et al.,* 2009) so that GUTS can be tested alongside classical measures of chronic stress. For example, previous work has shown an interaction of chronic stress and ageing on cognitive decline during ageing (Marshall, *et al.,* 2016a; Marshall, *et al.,* 2016b; Marshall, *et al.,* 2018) while using the same measures suggested here. By replicating the paradigm used by Marshal et al. (2016a, 2016b, 2018) one could compare the effect of the GUTS domains against more classical stress measures on behavioural performance. Furthermore, while the faces used here have been used before in similar studies (Brüne, *et al.,* 2013; Neta & Whalen, 2009; Neta, *et al.,* 2021) their utilisation was different. We simply used the faces as they are, while previously the faces were modified, for example, to create high or low spatial frequencies (Neta, *et al.,* 2021). In studies where faces were not modified a different set of faces were used (Maoz, *et* al 2016). This difference may also explain the lack of GUTS association with the proportion of faces judged as negative. In previous work, ambiguous faces were created by morphing a happy and angry face along a spectrum whereby the ambiguous face was a blend of happy and angry characteristics, not surprised faces (Maoz, *et al.,* 2016). While there is no evidence for GUTS in terms of behaviour, there is still evidence for GUTS and in particular, the relationship between stress and one's social network domain. As suggested, there are still avenues of research with which to continue the investigation of GUTS.

5.5.2 Conclusion

The main aim of this study was to investigate the validity of GUTS and its domains. We tested whether the GUTS domains, namely those of the social network and physical fitness, were associated with known effects of stress on judging ambiguous faces. We first

replicated previous data that showed evidence for the social network domain. We then reproduced previous behavioural results typical of RTs and facial judgements towards ambiguous faces from previous work. That is to say, the manipulation and measures used were in line with previous work. However, there was a negligible effect of the GUTS domains on the RTs for the face judgements and the judgements themselves. This may be due to methodological differences between this and previous work and/or it may highlight the difficulties in objectively capturing stress levels. Acknowledging present and previous results there is evidence to support the social network domain. More research into GUTS should include more physiological measures of stress as well as classic self-report measures of cumulative stress.

Chapter 6 – General Discussion

6.1 Overview and Aims

There were two main aims of this thesis: 1) investigate possible associations between stress, age and attentional ability and 2) investigate whether compromised life domains, as suggested by the Generalized Unsafety Theory of Stress (GUTS; Brosschot, *et al*., 2016), are associated with stress. In Chapters 2 and 3, we report mixed evidence for the first aim and in Chapters 4 and 5, we report support for some of the GUTS domains. Additionally, we also assessed different ways of measuring performance on the attentional blink (AB) task in Chapter 3, and the relationship between the stress/age interaction and GUTS in Chapter 4. This chapter will summarise each previous chapter, then link and discuss the overall results of the stress/age interaction and GUTS, including limitations and future directions.

6.1.1 Chapter 2

Published work (Marshall *et al*, 2015; Marshall *et al*, 2016a; Marshall *et al*, 2016b; Marshall, & Cooper, 2017; Marshall *et al.*, 2018), consistently found a robust stress/age interaction effect on various cognitive abilities (such as working and spatial memory and task-related inhibition), where older high stress participants displayed the lowest cognitive ability on cognitive tasks. These sets of results suggest ageing itself may not be solely responsible for cognitive decline during ageing but a combination of stress and age. In Chapter 2, we sought to continue[5] this line of inquiry by investigating the stress/age interaction on attention. We used questionnaires to measure stress and the attentional blink (AB) task as a measure of attentional performance. The AB task involves identifying two targets in a rapid serial visual presentation (RSVP). The difficulty in identifying the second target (T2) is a function of time between it and the first target (T1). It is far harder to identify

[5] Originally, we were going to include EEG measures as these were previously paired with cognitive performance in the Marshall papers. Due to COVID-19 this was not possible.

T2 if it appears within 300ms of T1, whereby identifying T1 creates an attentional blink window so that T2 is missed. When T2 is out of this blink window (here we used 800ms) identifying it is a measure of baseline ability. The AB window depends on individual differences in attentional ability and other factors that may affect this, such as age and stress. Generally, attentional ability decreases with age and increased chronic stress. However, the effect of stress on attention is generally mixed and depends on the type of stress as well as the valence of the stimuli. For this reason, we were rather thorough with the AB task in Chapter 2. In total there were 16 conditions across 288 trials. We varied T1 placement, the valence of T1 and T2 and varied the time lag between T1 and T2. We measured overall performance as well as performance across the four different T1/T2 valence combinations by subtracting performance at hard T2 (short time lag) from easy T2 trials (long time lag).

Overall, we found both age and stress were associated with attentional performance on the AB task. This was true for all T1/T2 valence combinations except where T1 was aversive and T2 was neutral, where there was not an association between age or stress and performance. Crucially, we reported the same stress/age interaction on attentional performance as reported by Marshall et al. (2015; 2016a; 2016b; 2018) in all but the Aversive-Neutral condition. Given the damaging effects long-term cortisol exposure has on the PFC this is not surprising. That the Aversive-Neutral condition was unaffected by stress or age is also not surprising given that aversive stimuli hold privileged access to attentional mechanisms, controlled by brain areas not usually negatively affected by the damaging effects of long-term cortisol exposure (Mather, *et al.,* 2004). In this case, an aversive stimulus paired with, and coming before, a neutral stimulus will necessarily engage attention and increase the AB window. Furthermore, the data reported here demonstrate the differences acute and long-term stress have on cognition, as work on acute stress shows an effect of stress on AB performance when T2 is aversive compared to neutral. Here, we did not report a difference in performance between the different T1/T2 valence conditions.

Overall, this chapter coincided with what the current literature would predict and contributed to it, extending the stress/age interaction effect into the realm of attentional processing.

6.1.2 Chapter 3

Continuing from Chapter 2, we extended the work by including resting state delta/alpha EEG power as a potential predictor of performance on the AB task. As noted above, the Marshall et al papers (2015; 2016a; 2016b; 2018) paired EEG data with behavioural data but additionally, they showed the resting state delta/alpha power was also associated with the stress/age interaction: Older high stress participants had increased resting state delta/alpha power in left/right parietal and frontal electrodes compared to other participants. In this chapter, we attempted to replicate the findings of Chapter 2 and, using the same electrodes (scalp regions of interest) as Marshall and colleagues, investigated whether resting state delta/alpha power was associated with the expected pattern of performance reported in Chapter 2.

Previously the AB task lasted between 40 and 60 minutes, which could easily extend well beyond 2 hours if paired with the set-up and take-down of EEG. Hence, to reduce the possible effects of boredom (given the nature of the task was attention), we reduced the complexity in the AB task design. To decrease the overall task time, conditions were lowered from 16 to 4. We removed aversive T1's and T1 starting variation. Here, an unexpected consideration arose when calculating performance on the AB task: whether baseline performance should be considered (in line with Chapter 2 and termed magnitude performance) or not (termed general performance). We reported performance for both, which produced different results, justifying the consideration. Overall, we did not find the previous stress/age interaction, failing to replicate Chapter 2. We also did not find any association between performance and resting state alpha/delta power. For general performance, there was an overall negative association of age (older participants performed

worse). The association of age was independent of the valence of T2. For magnitude performance, there was no overall association with any of the variables except when T2 was aversive, when there was a positive association between performance and stress. The differences between general and magnitude performance for age can be explained as follows: our general performance measure only includes hard trials and therefore does not take into account how good a participant is at just detecting targets in an RSVP. By incorporating performance on easy trials, when calculating magnitude performance, you take this into account by subtracting performance on hard trials from performance on easy trials. Doing this removes the association between increased age and worse performance on the AB task. There was less variation for older participants compared to younger participants when considering performance on hard trials. Their scores clustered around 20 - 40% accuracy whereas younger participants scores varied from 20 to 90% accuracy. When considering performance on easy trials the opposite was true, there was less variation for younger participants compared to older participants. The scores of younger participants typically clustered around 80 -100% whereas older participants scores varied from 20% - 80% accuracy. This pattern suggests that older participants were just worse at detecting targets in a RSVP compared to younger participants. This means the magnitude performance scores for younger participants are pulled down by variation on the hard trials. For older participants, the variation on the easy trials pulls up the magnitude performance. What are left are performance scores that are similar between the older and younger participants. In turn, this would account for the lack of stress/age interaction for magnitude performance. This is different from Chapter 2 and the reasons why may also explain the lack of the stress/age interaction effect. As explained above, there were fewer trials and participants, making it harder to detect any associations. The lack of T1 starting variation also meant T2 placement was easier to predict compared to Chapter 2 and may have allowed those who would have performed worse a compensatory mechanism to improve performance. This would eliminate the variance that otherwise might have been present (McLean & Arnell, 2012). For stress, the lack of association with general performance may

be due to the large variation in performance accounted for by age (35 – 42%). To support this, when age was controlled for in the magnitude performance there was an association of stress and performance when the T2 was neutral, albeit in the opposite direction than predicted. Previous work has reported a positive association between acute stress and performance on the AB task (Kan, *et al.,* 2019; Schwabe & Wolf, 2010), therefore, while unlikely, we may have measured acute stress here and not accumulated stress. Measuring any form of long-term stress is difficult, especially when comparing age groups, which requires using distinct questionnaires dependent on age.

Finally, we failed to report an association between resting state right delta/alpha power and AB task performance. This prediction was based on Marshall et al (2017), who found increased delta power associated with the stress/age interaction pattern. As we did not find a stress/age interaction, the lack of an association here may not be surprising.

6.1.3 Chapter 4

Here, we enlarged the scope of our investigations beyond the stress/age interaction and tested the validity of GUTS: A new framework of stress that attempts to explain the maintenance of chronic stress. Brosschot et al. (2016) proposed the framework in the light of a lack of an explanation for the maintenance of chronic stress within our current understanding of stress, given that chronic stress is maintained through situations with no obvious threat cue. GUTS proposes that a lack of perception for general safety, or more accurately, the perception of general unsafety (GU) is what disinhibits the stress response, not the perception of threat. When safety is perceived, the stress response is inhibited. When uncertain of safety, we err on the side of caution and disinhibit the stress response.

Later in life one's social network domain and body domain can become compromised leading to GU in situations that are not overtly threatening but still maintain allostasis.

Brosschot et al. (2016) provided a lot of theoretical evidence in support for GUTS but as a whole, GUTS remained untested (as far as we were aware at the time). We therefore decided to test the social network and body domains on GU by measuring a multitude of variables that would fit into each domain, including variables that would suggest a healthy social network and body domain. Measuring GU proved tricky, but we argued perceived stress could be used as a stand-in for GU. As chronic stress is associated with perceived stress and, classically, stress is triggered, and therefore maintained by threat, we also measured accumulated exposure to stress. For the body domain we found no association between frequency and intensity of exercise and perceived stress. Age was associated with less perceived stress (opposite of what was predicted) and therefore does not represent a compromised body domain when viewed through the lens of GUTS. Increased BMI was associated with increased perceived stress but was mediated out in the final model by social network domain variables. In the final model, gender (as a body domain variable) was also significantly associated with perceived stress. We argued that gender should not be considered part of the body domain but rather part of the social network domain. Furthermore, in the social domain, loneliness and social anxiety (explicitly named as variables within GUTS) were strongly positively associated with perceived stress as predicted. Social support was also positively associated with perceived stress, the opposite of what was predicted. This can be explained by noting that support is often sought out once one is already stressed.

We also argued that self-esteem and a positive stress mindset would constitute a healthy social network domain and we reported evidence to support this. Despite this, it was noted that deciding what should be included in each domain is tricky because of contradicting evidence for inclusion (see age), strong links with variables in other domains (see gender) or describing what would constitute a healthy domain (self-esteem or a positive stress mindset). Furthermore, increased accumulated exposure to stress was not mediated out by the GUTS domains as it was still associated with perceived stress; however, it was

moderated by the GUTS domains. Overall, this provides evidence for the importance of the social network domain but not the body domain in the perception of stress. It therefore seems that the GUTS model is incomplete and needs integration with classical stress theories. Finally, we suggested that the social network domain might predict our perception of stress (or the perception of GU) whereas the body domain may predict behavioural outcomes associated with stress. In this chapter, we provided the first piece of empirical evidence for the social network domain and GUTS. However, it should be noted that the link between loneliness and stress (Hawkley & Cacioppo, 2003) as well as the link between stress and social anxiety (Pittig, *et al.,* 2013) has been posited before. We may have therefore also found evidence to support these links. Future work will need to examine whether these relationships are best described in terms of a generalised anxiety model or if they are independent of GUTS.

6.1.4 Chapter 5

Continuing from Chapter 4, we tested our own suggestion that the body domain within GUTS may predict behavioural outcomes associated with stress but not the perception of stress (which we were using as a proxy for GU), and the opposite would be true for the social network domain. To test this, we used the same questionnaires as Chapter 4 and included a valence discrimination task, using surprised faces. From an evolutionary standpoint, and as Brosschot et al. (2016) acknowledge, when uncertain of safety, it is better to err on the side of caution. In practical terms, this means that ambiguous stimuli are initially interpreted as negative, rather than positive (Kim, *et al*., 2003). Evidence suggests surprised faces are ambiguous and interpreting their valence is affected by stress (Maoz *et al.,* 2016), where increased chronic stress is associated with increased negative interpretations of surprised faces. Furthermore, surprised faces judged as negative are responded to quicker than surprised faces judged as positive (Kim, e*t al.,* 2003; Neta, *et al.,* 2009; Neta, *et al.,* 2021).

In this context, we had three aims: constructively replicate Chapter 4 (i.e. testing the validity of the social network and body GUTS domains); perform a manipulation check on the faces; and investigate whether any of the GUTS domains were associated with the stress effects noted above. We successfully replicated Chapter 4 and successfully manipulated face valence. However, we found no evidence for the association between GUTS domains and the known stress effects on judging surprised faces or the RTs associated with these judgements. We suggested and reiterated that the social network domain contributes to the perception of stress but not to the behavioural influence of stress. Given the lack of evidence for the body domain across both this and Chapter 4, we also suggested the body domain be removed from GUTS. With that in mind, perceived stress (our stand-in for the perception of GU and the crucial feature of GUTS) was also not associated with behaviour in this chapter. We suggested that 1) perceived stress may not be a good stand-in for perceived GU and 2) the task and measures were ill-fitted for testing GUTS. If suggestion 1 is true, it is not obvious how one would measure perception of GU (further discussion below). For suggestion 2, we point out that previous measures used more than just RTs and valence judgements to address differences in judgements of ambiguous faces. This suggests our RTs and judgements may not be sensitive enough to capture these effects. We did not include measures of long-term stress exposure in this study as we had done in previous studies and suggested this be done in the future. If this measure is also not associated with the known effects of long-term stress on facial judgments, it would provide evidence for the second suggestion. If long-term stress exposure is associated with behaviour, then that would suggest GUTS does not predict the behavioural outcomes one would expect. Overall, we provided further evidence for the role of the social network domain and GU within the GUTS framework but not for the role of GUTS on valence-discrimination behaviour.

6.2 What We Have Learned about Age and Stress

Overall, we provide mixed evidence for the stress/age interaction effect on attention by using the attentional blink task. There may be several reasons for the incongruent pattern of results reported in Chapter 2 compared to Chapter 3 and the literature (discussed in Chapter 6.2.2 below). We will discuss why this may be by considering the AB task itself in conjunction with age and how we measure stress. Finally, we will discuss the possible reasons why we did not find a stress/age interaction in Chapter 3.

6.2.1 AB Task and Age

Performance on the AB task can be quantified in a number of ways. One way is to measure performance just on hard trials. The other is to take into account how good a participant generally is at spotting targets in a rapid sequence by making use of performance on the easy trials. Depending on how performance is quantified, one can expect different results as we reported here. Performance only considering hard trials (Chapter 3) revealed a strong effect of age and no effect of stress or a stress/age interaction, suggesting the task is just harder for older participants and that stress does not play a role in performance. This does not support the stress/age interaction reported in Chapter 2 and by Marshall and colleagues (2015; 2016a; 2016b; 2018). Upon reflection, this is not so surprising. The previous cognitive tasks used by Marshall and colleagues had longer trial times or were modified to accommodate older participants. For example, when measuring the stress/age interaction within spatial discrimination, participants had between 2 and 4 seconds to encode stimulus arrays in space. After a maintenance period (about 3 seconds) participants were presented with the stimulus again and asked if it occupied the same space as previously presented during encoding. Another example is the *N*-back task used by Marshall *et al.,* (2015) where each stimulus was presented for 500ms with only 4 stimuli to keep track off (the numbers 1-4). While experiments have employed 4 stimuli in an *N*-back task (Bartova, *et al.,* 2015; Borkowska, *et al.,* 2009), they can also consist of 18 stimuli (Nystrom, *et al.,*

2000; Braver, *et al.,* 1997). The point being that the AB task used here is more cognitively taxing than the cognitive tasks used by Marshall and colleagues (2015; 2016a; 2016b; 2018). That is not to say that generally the AB task is more cognitively demanding than a typical *N*-back task. Rather the *N*-back task as utilised by Marshall and colleagues (2015: for the reasons described above) is less cognitively demanding than the AB task as utilised here. The AB task here is rapid with the target stimulus visible for 100ms, a whole trial lasting 1.6 seconds, and with participants having a choice of 4 possible targets. These overall differences in speed and number of choices may increase the number of error rates for the ageing participants as the AB procedure may be more difficult especially when considering the factor of speed. Indeed, when measuring the stress/age interaction on inhibition using a flanker task, the task needed to be modified to reduce elderly error rates (Marshall, *et al.,* 2016a) and when excluding participants here due to low correct responses (in Chapter 3) most exclusions were elderly. This indicates that when speed is involved, cognitive tasks seem to be more difficult for elderly participants (Lu, *et al.,* 2013; Stomrud, *et al.,* 2011) regardless of stress. Furthermore, when considering general ability of the AB task (i.e. taking performance on easy trials into account), the age effect disappeared indicating that overall, older participants were worse at the task compared to younger participants.

Overall, older participants just perform worse than younger participants on the AB task and this fits the current literature for the AB task (Lahar, *et al.*, 2001; van Leeuwen, *et al.*, 2009) and cognitive performance in general (Colsher, & Wallace, 1991; Evans, *et al.,* 1993; Kausler, 1994; Wilson, *et al*., 1999). Supporting this claim, age accounted for about a third of the variation in performance (when not considering general ability) in chapter 3. It has been suggested that older persons switch from specific to generalised processing as cognitive load increases (Li, *et al.,* 2013; Smith, *et al.,* 2001) in order to maintain accuracy at the cost of processing speed. As the AB task is rapid, this may explain the poorer performance by the older participants. Speed itself may not be the only reason for the poorer performance for older compared to younger participants. It may also be due to older

participant's inability to inhibit distractor stimuli (Maciokas, & Crognale, 2003). Performance on the AB task has been associated with individual ability to attenuate distractors (Visser & Ohan, 2012) and age differences for inhibition have been reported within the literature where older participants had worse inhibitory function compared to younger participants (Earles, *et al.,* 1997).

6.2.2 Stress

When considering the long-term negative effects of cortisol exposure, one would expect cognitive performance to decrease, as reported in Chapter 2 and by Marshall and colleagues (2015; 2016a; 2016b; 2018) but, the opposite was reported in Chapter 3. This makes placing the results within the broader literature somewhat difficult. In chapter 3, we suggested that what we measured may have been closer to acute stress than to chronic stress (this does raise the issue of how long-term stress was measured here and is discussed below). The stress response, allostasis, is a mechanism that transiently puts the body in a state of action preparedness (Denson, *et al.,* 2009). Nor/adrenaline and cortisol acts within the body and brain to increase physical performance and attentional performance to salient stimuli (Foote *et al.,* 1975; Waterhouse, *et al.*, 1990). Therefore, acute stress improves attentional performance on the AB task by narrowing the blink window, or at least allows the salient targets to break through the blink window (Schwabe & Wolf, 2010; Kan *et al*., 2019; Kan *et al.,* 2021). However, prolonged cortisol exposure within the PFC and hippocampus results in dendritic atrophy in the PFC (Brown, *et al.,* 2005; Uno, *et al*., 1994).

It would therefore make sense that this over exposure to cortisol could lead to decreases in cognitive performance over time, especially for cognition associated with PFC and hippocampal activity. This includes memory, executive function and attention. However, the results reported throughout the literature are not clear and the results here reflect that. This is true for both acute and chronic stress. Vedhara et al. (2000) report no association

between acute stress and selective attention; however, Kan et al. (2019) report a positive association between selective attention and acute stress. Generally, chronic tress is associated with poorer cognitive performance but it is selective, as it does not affect all forms of cognition and this does depend on task load (Öhman, *et al.,* 2007). By varying T1 positioning within the AB task in one study but not the other, we may have inadvertently lowered task load. Removing the variation would make it easier to predict when T1 will appear, overall lowering the task load reducing the amount of cognitive resources required for processing T1. This would leave additional resources that would be normally tied up in T1 processing, free for T2 processing (Zivony & Lamy, 2021). Chronic stress drains cognitive resources decreasing attentional accuracy and slowing attentional reaction times (Liu, *et al.,* 2020). Reducing the task load of the AB task in chapter 3 may have therefore eliminated the negative effect of long-term stress exposure. If so, this would explain the results reported here. With the increased task load in chapter 2, we found the detrimental effects of chronic stress on attention. With the lower task load in chapter 3, stress was positively associated with performance and not negatively associated with performance as reported in chapter 2. Overexposure to cortisol can increase the dendritic spine density within the amygdala, which produces sensitisation to feared and salient stimuli (Mitra, *et al.,* 2005). Without the extra cognitive load and increased sensitivity to salient stimuli (i.e. red words against a black background in AB task) chronic stress may actually improve performance on the AB task. In other words when task load is low (non-varied T1) and the strong effect of age is taken into account (by considering both easy and hard trials) one may find accumulated stress is associated with increased performance.

Here and elsewhere (Marshall, *et al.,* 2015, 2016a, 2016b, 2018), accumulated and not chronic stress was measured in participants using two separate questionnaires, one for the younger participants (Life Event Scale for Students: Clements and Turpin, 1996) and one for the older participants (Social Readjustment Social Scale: Holmes & Rahe, 1967). This was deemed necessary as life stressors and life experiences change depending on

age. As this was a constructive continuation of the Marshall studies, the same questionnaires were used. However, two limitations to the studies performed here were raised. The first is that two separate questionnaires, though analogous, were combined under the assumption they are measuring the same thing. The second is that we measured accumulated stress and not chronic stress, and arguably chronic stress is the more dangerous of the two forms of stress. However, there are two separate questionnaires for measuring chronic stress in adults (Hammen, *et al.,* 1987) and adolescents (de Bruin, *et al.,* 2018) as well. While this presents similar issues as using the accumulated stress questionnaires (i.e. two separate questionnaires for different age groups) future work investigating the effect of long-term stress exposure on cognition should investigate the use of these chronic stress questionnaires.

The first limitation may be unavoidable when investigating any form of long-term stress exposure in young and old participants using questionnaires. Stressful experiences will just differ between those under 30 and those over 60 – for instance, because older participants have simply had longer to potentially experience for stressful life events. Also, what may be considered stressful for one group may not be the same for the other group due to cultural/generational differences and priorities. For example, there are differences in coping strategies, due to developmental and contextual factors (Folkman, *et al.,* 1987); and differences in defence mechanisms where younger people use more maladaptive mechanisms such as ‘acting out’ compared to older people (Segal, *et al.,* 2006). Another factor to consider is resilience. Being exposed to risk (Masten, 2001) or a controllable stressor (Maier, 2015) in adolescence builds resilience to stressors later in life and this may differ between generations. This reiterates the idea that similar stress is experienced differently between people but to add that the negative effects may be less prominent in those with earlier exposure to stress. In future research, one way to overcome these issues and take account of resilience may be to use the cumulative lifetime adversity measure (Seery, *et al.,* 2010). It can be administered to both young and older participants and has been validated in a very large data set using young and old participants (Carstensen, *et al.,*

2020). This is still a measure of cumulative stress however, and the differences between this form of stress and chronic stress for understanding a stress/age effect are important

Measuring chronic stress is actually rather difficult. For all the above-mentioned reasons, there are many factors to consider and take account for. Considering that everyone will experience acute stress at some point in their life, it is therefore natural that everyone will have experienced accumulated stress but not everyone experiences cognitive decline due to stress. By themselves these brief moments in which one is exposed to cortisol is not enough to produce the detrimental effects found in the brain as one ages. It may not be the frequency of these events but the duration of each event or at least a prolonged allostatic state (i.e. chronic stress) from each event that causes the damage, as it exposes an individual to cortisol for the length of time needed for damage to occur (i.e. allostatic load). This would be hard to capture in retrospect using questionnaires and there are caveats even when using physiological measures of chronic stress. Hair absorbs cortisol as it grows and can provide a 3-month snapshot of how much cortisol has accumulated in an individual (Greff, *et al.,* 2019; Staufenbiel, *et al.,* 2013). This snapshot is adequate to suggest current chronic stress. The argument is that a lifetime of stress is needed for cortisol to cause enough damage to produce behavioural effects and clearly hair cortisol does not capture lifetime chronic stress. Another physiological measure is heart rate variability (HRV) which is also associated with a chronic stress. HRV is associated with vagal nerve activity with low HRV often representing sympathetic activation indicating allostasis (Wendt, *et al.,* 2015). Again, HRV is enough for the here and now but does not actually confirm a lifetime of chronic stress. It seems that to truly measure and capture allostatic load one needs to employ a longitudinal study design, similar to that implemented before (Graves & Nowakowski, 2017) but with the extra measures described above.

6.2.3 Stress/Age Interaction

The stress/age interaction was a robust finding from the work of Marshall et al (2015; 2016a; 2016b; 2018) and we investigated whether it would be the same for attention using the AB task. We reported mixed results to support the stress/age interaction effect for the AB task where we found evidence for the stress/age interaction in chapter 2 but not in chapter 3. Of course, the lack of an effect of stress (when only considering hard trials) and the lack of an effect of age (when considering both easy and hard trials) in chapter 3 means there will not be an interaction effect involving those factors. Here we consider what leads to these differences in effect and what contributes to the stress/age interaction. When considering the above discussion on age and stress together it seems that the stress/age interaction on attention (or at the very least performance on the AB task) is at least to some degree dependent on task load. The tasks used by Marshall et al (2015; 2016a; 2016b; 2018) lowered task load in order to compensate for age and thereby found an effect of stress. This suggests the effect of age is so strong that it may sometimes eclipse any effect of stress. Both the hippocampus and the frontal cortex decline with age and increased cortisol exposure (Hedden & Gabrieli, 2010; Rottschy, *et al.,* 2012) linking their associated cognitive process to age and stress exposure. When the task load in chapter 3 was unintentionally decreased (lack of T1 variation), this strong effect of age drowned out any subtler effect of stress (performance without considering easy trials). Additionally, when task load was low and the effect of age was accounted for (performance considering easy trials) in chapter 3 stress was associated with increased performance on the AB task. Attentional processes involving salient stimuli recruit the amygdala (Mitra, *et al.,* 2005), which is thought to be unaffected by the ageing process (Jernigan, *et al.,* 2001) and cortisol increases spine density in the amygdala (Mitra, *et al.,* 2005) thereby allowing increased performance on a task with low task load with salient stimuli because of the increased availability of cognitive resources. In chapter 2, when task load was high (varied T1) and the effect of age was accounted for, reducing the strong effect of age, the increased spine density of the amygdala

was not enough to overcome the task impairment from possible damage to the frontal areas and hippocampus leading to an association of increased accumulated stress and decreased performance. This may be due to the lack of additional cognitive resources tied up from the high task load. Therefore, on the AB task, it is arguable that in order to see an interaction effect of stress and age, whereby increased accumulated stress is associated with decreased performance you need high task load (i.e. varied T1) and to take the strong effect of age into account (by considering both easy and hard trials).

6.3 GUTS

GUTS is an interesting theory to explain how chronic stress is maintained as current theory does not adequately account for this. While we could not test the theory in its entirety, we did provide evidence for the association between the proposed social network domain and perceived stress but not the body domain. The reasons for this were discussed and reiterated in Chapters 4 and 5. What is more important to discuss here is the conceptualisation of GUTS versus the methodological implementation of GUTS. For example, the concept of generalised unsafety (GU) is a well-argued concept and an important component of GUTS, as its perception leads to the maintenance of stress but, methodologically, it is unclear how one measures GU. Conceptually, the social network and body domains make sense but methodologically, any number of measures could be used to represent each domain. Furthermore, as we reported, some concepts such as self-esteem could represent a healthy domain but it is unclear to which domain it would belong. Another issue is the lack of evidence reported here for GUTS when considering behaviour.

Since its initial proposal GUTS has seen some traction, especially in review articles (Abend, 2023; Freeston & Komes, 2023; O'Conner, *et* al., 2021; Pickering, *et al.,* 2020; Smith, *et al.,* 2019; Thayer, *et al.,* 2020). Usually, in relation to uncertainty. This is somewhat surprising, given that the unique aspects of GUTS, as mentioned a few times throughout this

thesis, is the switch from threat to safety and the switch from turned on to always on. In fact it is unclear how GUTS and threat based theories differ in their predictions from uncertainty. GUTS claims that the mere uncertainty of safety is intolerable and leads to stress (Brosschot, *et al*., 2016). Threat based theories posit the negativity bias where ambiguous (uncertain) stimuli are treated as negative by our attentional systems (Taylor 1991; Jonikaitis, 2019). Either way, both claims lead to a stress response and disentangling the difference is not simple. Where GUTS does differ is not the outcome of stress but the cause of the outcome, namely GU. Indeed the domains generating GU (when compromised) which in turn generates stress is the core difference of threat based theories and GUTS. Compromised domains (discussed below) generate GU even in overtly safe environments, devoid of threat according to GUTS (Brosschot, *et al.,* 2016). A classic threat based theory would not predict a stress response from a physically unfit individual sitting in their safe room but GUTS would. The same is true when considering a lonely individual safely sitting in their room. For this reason, we found it important to test these domains directly however, besides here, these domains have not been tested. Interestingly, when GUTS and GU have been test directly there has been mixed (Morse, 2021; which is similar to the results reported in this thesis) or no (Huskey, *et al.,* 2022) evidence. This may be due in part to the problem of operationalising GU though (discussed below).

6.3.1 Generalised Unsafety

An issue when testing GUTS is operationalising GU so that it can be measured. In GUTS the perception of GU results in the perception of stress in the absence of specific stressors. The questions in the perceived stress scale are non-specific and measure the perception of stress; therefore, we used perceived stress as a stand-in for GU. Other studies have used a measure of fear inhibition (Huskey, *et al.,* 2022) while Morse (2021) used heart rate variability (HRV) but neither found full support for GUTS. Therefore, the question remains, what is a suitable stand in for the perception of GU? This remains a limitation within

this thesis. There are, however, some ways to provide converging evidence for perceived stress/fear inhibition/HRV as a stand-in for the perception of GU. As mentioned previously, resilience to stress is built in adolescence. This is a key part of GUTS as Brosschot et al. (2016) argue that when learning to deal with stressors in adolescence one is learning to recognise safety cues and then generalise those safety cues to similar stressful situations; it is this mechanism by which resilience is built. However, this 'contingency learning' (Brosschot, *et al.,* 2016; page 19) can go awry for a number of reasons, such as neuroticism and intolerance of uncertainty (proposed by Carleton, 2012), which would lead to perceptions of GU (Brosschot, *et al.,* 2016). Therefore, one could measure participant's neuroticism and intolerance of uncertainty along with perceived stress in order to check for any association. This could provide converging justification for using any of the above mentioned measures as a proxy for perceived GU. By locking in a measure for the perception of GU, one could more confidently test the validity of each of the domains that GUTS predicts could lead to GU perception when compromised.

6.3.2 Domains

While genetics, early childhood experiences and/or other individual differences can lead to deficient safety learning, deficient safety learning can also occur later in life, in three major life domains if compromised. Here we tested both the social network and body domains by measuring their association to a proxy of GU (i.e. perceived stress). When deciding what to include for each domain it becomes apparent that a large number of factors could contribute to a compromised domain and deciding what factor belongs in each domain can be difficult. For example, Brosschot et al. (2016) specifically cite loneliness and social anxiety as contributors to a compromised social network domain (which we found significant support for) but not perceived social support, or lack thereof. Yet, within their paper, they state, "belonging to a cohesive and supporting social network or simply perceiving sufficient friendly people around appears vital" (Brosschot, *et al.,* 2016; page 25). This would suggest

that lacking social support would contribute to a compromised social network domain and so we tested this factor. However, we reported the opposite finding for social support that GUTS would predict: increased perceived social support was associated with increased perceived stress. It is arguable that one seeks out support when stressed but as with any correlation, the direction of the relationship is unclear. Another example is the contribution of age to a compromised body domain. We found the opposite of what GUTS predicted (i.e. we found a negative association between age and perceived stress instead of a positive association; older participants perceived less stress than younger participants did). Furthermore, the wider literature reports that increased age is associated with positive, not negative effects (Frijters & Beatton, 2012; Buijs, *et al*., 2021). Which domain, therefore, would age belong too? If increased age is associated with decreased stress perception, as is self-esteem and a positive stress mindset (two more factors that could fit within GUTS but it is unclear in which domain), then clearly some factors could also represent a *healthy* life domain but this is not discussed within the framework of GUTS. This is clearly an aspect of GUTS that needs to be expanded upon in future work given the evidence for it reported here. Despite these issues, we provided very strong evidence overall for the importance of one's social network domain on stress, when using self-report measures.

6.4 Conclusions

Overall, this thesis investigated 2 main aims by testing 1074 individuals: 1) Whether there would be a stress/age interaction effect on attention, in which older high stress participants would perform worse than younger low and high stress participants as well as low stress older participants. 2) Whether GUTS provides a useful model for understanding long-term stress. We found mixed evidence for both.

We investigated possible stress/age interactions on attention across two studies and found support for it in one but not the other. Overall, the results suggest that older people are simply worse at the attentional tasks measured, especially when speed is involved. When

taking general ability on the AB task into account, the effect of age disappeared (further indicating an effect of age on performance) and an effect of stress emerged. Interestingly, this effect of stress was in the opposite direction across two studies. We suggest that due to the different effects of cortisol on different brain areas recruited during attentional processes on the AB task, that high task load reveals a stress/age interaction but low task load does not. We also highlighted the difficulties in measuring long-term exposure to stress. Nevertheless, we still provide evidence that stress is associated with cognitive performance but that it may not always interact with age on cognitive performance. However, we did not find evidence of an association between resting state delta/alpha power and attentional performance.

Across two studies, we also investigated the validity of GUTS. We found strong self-report evidence that a compromised social network contributes to the perception of stress, a proxy for generalised unsafety, which, as GUTS predicts, would lead to the maintenance of chronic stress. However, we did not find evidence for a compromised body domain and in fact argue against the inclusion of the domain within the GUTS framework, we found no behavioural support for GUTS. It could be that GUTS is associated with the perception of stress but not necessarily with the behaviour often associated with stress. We also suggest avenues for future research in which we can check this suggestion by comparing GUTS variables to stress variables. It could also be that perceived stress is not the best proxy for GU perception. This does raise the question of how one would actually capture GU. We suggest measuring factors that are claimed to be associated with GU to potentially provide converging support for perceived stress as a measure of GU. GUTS is an intriguing theory but it is clear much more work is needed to validate it.

6.5 Final Remarks

Over the course of completing this PhD it has become apparent how complicated stress and attention are as individual concepts, let alone trying to incorporate them into a

single study. The literature on both has produced many discrepant results and that is reflected in this thesis, especially in chapters 2 and 3. Both have several components that contribute to a greater whole. The stress/age interaction effect that has been reported before this thesis can be viewed as optimistic, with the cognitive deficits usually associated with ageing not always being inevitable. However, the one robust finding in this thesis is that age is usually associated with poorer attentional performance. This is not as bleak as it first appears though. The cognitive tasks used were purposefully difficult (e.g. AB task) in order to elicit variation in performance between people. It is not clear that everyday life includes such strenuous cognitive activity.

When this thesis diverged and investigated GUTS, age was again associated with stress – but contrary to what was predicted, older participants perceived less stress in their life than younger participants. Furthermore, evidence suggests age is associated with happiness, despite the extra stress that comes from simply living longer. Likewise, stress is not always negative as it can improve performance and act as a motivator for change. From this, it seems the take home message is: accept stress and ageing for what they are because they are neither wholly negative nor positive.

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