

1 **Symptoms of depersonalisation/derealisation disorder as measured**
2 **by brain electrical activity: A systematic review**

3 Abbas Salami^{a*}, Javier Andreu-Perez^b, Helge Gillmeister^c

4 a. School of Computer Science and Electronic Engineering, University of Essex, Wivenhoe Park, Colchester, CO4
5 3SQ, UK, a.salami@essex.ac.uk

6 b. School of Computer Science and Electronic Engineering, University of Essex, Wivenhoe Park, Colchester, CO4
7 3SQ, UK, javier.andreu@essex.ac.uk

8 c. Department of Psychology and Centre for Brain Science, University of Essex, Wivenhoe Park, Colchester, CO4
9 3SQ, UK, helge@essex.ac.uk

10 **Abstract**

11 Depersonalisation/derealisation disorder (DPD) refers to frequent and persistent detachment
12 from bodily self and disengagement from the outside world. As a dissociative disorder, DPD
13 affects 1-2% of the population, but takes 7- 12 years on average to be accurately diagnosed. In
14 this systematic review, we comprehensively describe research targeting the neural correlates of
15 core DPD symptoms, covering publications between 1992 and 2020 that have used
16 electrophysiological techniques. The aim was to investigate the diagnostic potential of these
17 relatively inexpensive and convenient neuroimaging tools. We review the EEG power spectrum,
18 components of the event-related potential (ERP), as well as vestibular and heartbeat evoked
19 potentials as likely electrophysiological biomarkers to study DPD symptoms. We argue that acute
20 anxiety- or trauma-related impairments in the integration of interoceptive and exteroceptive
21 signals play a key role in the formation of DPD symptoms, and that future research needs
22 analysis methods that can take this integration into account. We suggest tools for prospective
23 studies of electrophysiological DPD biomarkers, which are urgently needed to fully develop their
24 diagnostic potential.

* Corresponding author.
E-mail address: a.salami@essex.ac.uk

1 **Keywords:** *Depersonalisation; derealisation; EEG; ERPs; biomarkers*

2 **Introduction**

3 Depersonalisation/derealisation refers to a state of mind in which a person feels detached
4 and disconnected from their bodies and own senses as well as from their surroundings (Phillips
5 and Sierra, 2003). This condition can be accompanied by a sense of unreality about the outside
6 world and by out-of-body experiences, and is believed to be a defensive mechanism of the brain
7 in order to protect the organism in acute anxiety or traumatic situations (Hunter et al., 2003;
8 Shilony and Grossman, 1993; Sierra and Berrios, 1998; Stein and Simeon, 2009). For instance,
9 temporary occurrences of depersonalisation have been reported by almost 50% of college
10 students (Dixon, 1963). Fatigue (Tibubos et al., 2018), sleep deprivation (van Heugten–van der
11 Kloet et al., 2015), or travelling to unfamiliar places can also be the cause of transient
12 depersonalisation/derealisation (Kaplan et al., 1998). However, in cases where the symptoms are
13 chronic, it is considered a type of dissociative disorder (depersonalisation/derealisation disorder
14 (DPD); Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) (American
15 Psychiatric Association, 2013)).

16 Although the exact cause of DPD is not yet known, traumatic experiences and childhood
17 anxiety are thought to be common triggers (Lee et al., 2012; Simeon et al., 2001b). It can also be
18 provoked by intense stress, depression, panic attacks, and ingestion of psychoactive substances
19 (Mathew et al., 1999; Medford et al., 2003; Simeon, 2004). Patients experience persistent and
20 frequent feelings of disembodiment or detachment from their physical self as well as emotional
21 numbness that may extend beyond the present moment to include memories and imagination.
22 Since derealisation is an inseparable aspect of DPD in most cases, the symptoms may also
23 include detachment from surroundings, as if the world around the patient is unreal, or a weakened

1 ability to respond to emotional circumstances, although the capacity for emotional expression and
2 reality testing remains intact (Hollander et al., 1992; Sierra and David, 2011). DPD can be
3 accompanied by anxiety, depression or schizophrenia (Stein et al., 1997), as well as difficulties in
4 concentration and memory retrieval (Lambert et al., 2001a), which can profoundly affect the
5 quality of life for patients and interfere with their daily activities and social relationships.
6 Identifying DPD, as well as its risks and neuroprotective factors, at early stages should thus be a
7 critical endeavour for clinical practice and research.

8 DPD has a prevalence of about 1-2% of the population (Hunter et al., 2004; Lee et al.,
9 2012; Michal et al., 2007), which is comparable to that of schizophrenia and obsessive-
10 compulsive disorder, with an equal gender ratio and an average onset age in early adulthood
11 (Baker et al., 2003; Michal et al., 2016; Simeon, 2004; Simeon et al., 2003). Nevertheless, DPD
12 is one of the most prevalent but under-diagnosed psychiatric disorders (Hunter et al., 2017;
13 Michal et al., 2010). Generally, there are no medical laboratory tests for diagnosis of dissociative
14 disorders, and since patients find it difficult to describe the symptoms of depersonalisation and
15 derealisation, it currently takes an average of seven to 12 years to correctly diagnose DPD
16 (Hunter et al., 2017). Diagnosis is hampered by a lack of awareness of DPD among medical
17 practitioners (Medford et al., 2005) and its symptomatology overlap with medical conditions such
18 as epilepsy and migraine (Devinsky et al., 1989; Lambert et al., 2002) and psychiatric conditions
19 such as depression and post-traumatic stress disorder (Armour et al., 2014). Therefore,
20 delineating the neurophysiological correlates of DPD may be of great importance for an early
21 diagnosis of DPD as discriminate it from its transient form and from other conditions.

22 In this review, we provide an overview of the structural and functional neurophysiology in
23 DPD, with a particular focus on studies aiming to characterise the cardinal symptoms of the

1 disorder such as feelings of disembodiment and emotional numbing by measuring the electrical
2 activity of the brain. Electrophysiological neuroimaging techniques are of great interest because
3 of their ease of application and cost-effectiveness for clinical practice. Therefore, we intend to
4 identify and introduce electrophysiological biomarkers associated with DPD symptoms, which
5 may have the potential to help with early recognition of this under-diagnosed psychiatric
6 condition. Our paper demonstrates both the urgent need to replicate promising findings on a
7 larger scale and the potential for further electrophysiological pattern analysis to characterise
8 DPD.

9 **Functional Nervous System Studies of DPD**

10 Several methods have been used to measure the functional characteristics of DPD
11 symptoms within the autonomic nervous system (galvanic skin response, heart rate) and the
12 central nervous system (EEG, ERPs, HEPs, fMRI, PET). The Galvanic Skin Response (GSR)
13 tracks changes in the conductivity of human skin due to sweating, reflective of the arousal related
14 to the intensity of emotional states. This property has made GSR a useful approach to investigate
15 emotional dysregulations in DPD. Studies using the GSR have elucidated differential autonomic
16 nervous system responses to salient stimuli in DPD, and the impairment is mostly in responding
17 to unpleasant and threatening emotional stimuli rather than pleasant ones (Michal et al., 2013;
18 Monde et al., 2013; Sierra et al., 2006). For instance, research by Dewe et al. (Dewe et al., 2016)
19 observed suppressed GSRs during the reception of body-threat-like stimuli (blood donation) in
20 DPD patients. Giesbrecht et al. (Giesbrecht et al., 2010) recorded a different temporal pattern of
21 GSRs in DPD patients compared to healthy individuals while watching an anxiety-inducing
22 movie scene. The response of the patients was characterized by an early peak and a flattened
23 pattern afterwards (even after clip offset), while the control group exhibited a more gradual

1 incremental pattern during the clip followed by a decreasing pattern after clip offset. Peak latency
2 was inversely associated with the severity of DPD symptoms, and patients also showed higher
3 baseline skin responses compared to the control group. Jay et al. (Jay et al., 2014) measured DPD
4 patients' galvanic skin responses and used repetitive transcranial magnetic stimulation (rTMS) to
5 confirm the causal role of ventrolateral prefrontal cortex in these atypical patterns of
6 physiological arousal.

7 Several neuroimaging studies in the literature have targeted central neural patterns and
8 possible abnormal activities in DPD with functional magnetic resonance imaging (fMRI)
9 (Phillips and Sierra, 2003; Röder et al., 2007), positron emission tomography (PET) (Simeon et
10 al., 2000), and electroencephalography (EEG). These studies predominantly compare the neural
11 substrates of DPD patients with control subjects and have mainly focused on two core aspects of
12 DPD, emotional numbing and disembodiment (Simeon et al., 2008). For instance, various fMRI
13 studies (Lemche et al., 2008; Lemche et al., 2007; Mancini-Marie et al., 2006) have investigated
14 the neural responses of DPD patients to emotional versus neutral stimuli (Medford et al., 2006;
15 Phillips et al., 2001). Results illustrate that emotional numbing (the attenuation of emotional
16 experiences as a result of inhibitory processes) in DPD is associated with reduced activity in
17 brain areas responsible for emotional processing, particularly the insula and limbic regions
18 including hypothalamus and amygdala (Medford et al., 2016). Lemche et al. (Lemche et al.,
19 2007) showed an inverse relationship between activity in hypothalamus and amygdala and the
20 intensity of positive and negative emotional stimuli in a group of DPD patients compared with
21 controls. fMRI studies also showed increased activation of right ventrolateral prefrontal cortex in
22 DPD patients exhibiting emotional numbness in response to aversive stimuli (Medford et al.,
23 2006; Phillips et al., 2001). Similarly, increased activation of dorsal prefrontal cortex, which

1 plays a role in emotional suppression (Etkin et al., 2006), was found during the processing of
2 both positive and negative emotional facial expressions in DPD patients (Lemche et al., 2007).
3 Dorsal prefrontal activation was inversely related to skin conductance levels. This suggests that
4 prefrontal regions actively suppress the operation of emotional cortical and limbic regions. In line
5 with this proposal, fifteen minutes of 1Hz inhibitory rTMS to the right ventrolateral prefrontal
6 cortex was found to result in an increase of skin conductance capacity, which reflects the capacity
7 of autonomic responses to emotional stimuli (Jay et al., 2014).

8 Investigations of disembodiment, another critical (but highly distinctive) characteristic of
9 DPD, can be found less frequently in the DPD literature. Nevertheless, Paul et al. (Paul et al.,
10 2019) recently conducted a comprehensive fMRI study on the functional connectivities between
11 brain areas that might be associated with depersonalisation/derealisation symptoms (such as
12 extrastriate body area, hippocampus, medial prefrontal cortex, and posterior and anterior insular
13 cortex) in patients with major depressive disorder. Results revealed that decreased functional
14 connectivity between extrastriate body area (which plays a role in the perception of body parts)
15 and default mode network (which is associated with the processing of self-relevant,
16 autobiographical information) is related to depersonalisation/derealisation symptoms in major
17 depressive disorder. Altered functional connectivity of the default mode network and particular
18 areas in the primary visual network has also been discovered by Derome et al. (Derome et al.,
19 2018) in transient depersonalisation.

20 Among the neuroimaging techniques for the analysis of brain activity, EEG holds great
21 promise as a diagnostic tool because of its non-invasive nature, low costs and simple setup. It
22 provides information about the ongoing neural processes in the cerebral cortex with high
23 temporal resolution. This paper aims to provide a review of studies on DPD using

1 electrophysiological signals to detect and introduce electrophysiological biomarkers associated
2 with DPD symptoms. It also addresses some recent developments in the theories of self-
3 consciousness that can potentially help to explain the unique symptomatology of DPD.

4 **Review Methodology**

5 The papers reported in this article are exclusively based on electrophysiological
6 approaches, and comprises of all the papers that have tried to explain symptoms of DPD using
7 scalp electrophysiological signals (for review of studies on DPD using other behavioural or
8 neuroimaging techniques see (Hunter et al., 2004; Sierra and David, 2011)). We categorized our
9 search based on the four major and distinct symptoms of DPD derived from factor analysis on the
10 Cambridge Depersonalisation Scale (CDS) (Sierra et al., 2005; Sierra and Berrios, 2000), which
11 is the most well-known benchmark questionnaire for quantification of DPD (Talbert, 2010). In
12 addition, we describe studies related to ‘other symptoms’ of DPD, such as those related to
13 perception, attention and working memory (see **Error! Reference source not found.**). We also
14 explicitly distinguished between papers based on whether they investigated transient or chronic
15 DPD, with transient DPD defined as episodes of depersonalisation in healthy individuals and
16 those with a primary diagnosis of another illness. Since the essence of depersonalisation is a self-
17 protective mechanism, its momentary symptoms can emerge in many healthy individuals during
18 their lifespan as the brain’s response to an overwhelmingly stressful or traumatic situation in
19 order to reduce its repercussions by creating a sense of physical and emotional numbness. Studies
20 have reported the prevalence of transient depersonalisation in the range of 34 to 70% in the non-
21 clinical population (Aderibigbe et al., 2001; Hunter et al., 2017). Besides, although a recent
22 comprehensive study has confirmed DPD as a distinct disorder (Sierra et al., 2012), transient
23 depersonalisation and derealisation are also common symptoms in several major psychiatric

1 illnesses such as anxiety (Baker et al., 2003), panic attacks (Harper and Roth, 1962), burnout
2 syndrome (Maslach and Jackson, 1981), and post-traumatic stress disorder (Lanius et al., 2012).
3 For instance, episodic depersonalisation attacks along with panic attacks have been jointly
4 observed in several cases (Davison, 1964; Dietl et al., 2005) and this symptomatic pattern has
5 been considered a distinct disorder, the "phobic anxiety-depersonalisation syndrome" (Roth,
6 1960). The dissociative subtype of post-traumatic stress disorder has been distinguished from its
7 nondissociative subtype symptomatically and by distinct patterns of central nervous system
8 activities (Lanius et al., 2010). In the dissociative subtype, patients show episodic
9 depersonalisation symptoms, which correlate negatively with the activation of amygdala and
10 right anterior insula (Hopper et al., 2007).

11 **Search Keywords and Information Sources**

12 Several combinations of keywords were used in this systematic search. The search
13 keywords consisted of one word from Set 1 and one word from Set 2 as follows (notice that
14 unlike Scopus, distinct results will be derived for British and American spelling of the keywords
15 in Google Scholar):

16 Set 1: "Depersonalization", "Depersonalisation", "Derealization", "Derealisation"

17 Set 2: "Electrophysiological", "EEG", "MEG", "Biomarker", "Interoception", "Exteroception"

18 The search was conducted in two major electronic databases, Google Scholar and Scopus. The
19 search was not restricted to any year ranges and selected papers covered publications from 1992
20 to February 2020. References of all the relevant papers were also scanned to find further potential
21 studies in the field.

1 **Articles Overview**

2 Papers selected (based on their title) from Google Scholar and Scopus created an initial
3 database of 104 studies after removing duplicate papers. The papers were manually filtered and
4 the number reduced to 70 based on their abstracts. Papers concerned with (neuroimaging)
5 techniques other than electrophysiology were excluded from the review. A final assessment of
6 papers was conducted based on an evaluation of the full text. The final number of selected papers
7 was 10, and these are presented as an overview in **Error! Reference source not found.**, and
8 described in detail in the next section.

9 **Electrophysiological Studies of DPD**

10 Earlier studies sought to investigate the oscillatory signatures associated with the
11 experience of depersonalisation. Locatelli et al. (Locatelli et al., 1993) examined EEG patterns in
12 depersonalisation states. They aimed to observe the probable dysregulation in the temporolimbic
13 regions of the brain in healthy subjects and panic disorder patients with and without
14 depersonalisation/derealisation using an odour discrimination task. The power of the EEG signals
15 in eight separate frequency bands covering 1 to 30Hz was analysed at six temporal electrodes.
16 The results revealed bilateral abnormalities in EEG of the temporal lobe in patients with
17 depersonalisation as compared with panic disorder patients without depersonalisation or
18 derealisation. Patients with depersonalisation/derealisation showed increased power in the delta
19 band and a bilateral lack of responsiveness in the upper alpha band during odour stimulation.
20 Hollander et al. (Hollander et al., 1992) reported EEG power changes in depersonalisation in a
21 different frequency band. They investigated the neurophysiological basis of depersonalisation in
22 a 23-year-old man, who had reported depersonalisation and derealisation symptoms after

1 suffering from severe anxiety for a period. Although the long-term resting-state EEG was
2 reported as normal, brain electrical activity mapping revealed frontal alpha overactivation and
3 increased temporal theta activity in the left hemisphere. They also reported enhanced N200
4 components of visual and auditory ERPs (~200ms post-stimulus) in the left temporal areas. DPD
5 was frequently found to be associated with abnormal theta activity over temporal regions. In an
6 alcohol-induced depersonalisation state, Raimo et al. (Raimo et al., 1999) observed a
7 significantly higher relative power in theta band compared with asymptomatic episodes. The
8 presence of abnormal theta activities in depersonalisation state was also confirmed in (Hayashi et
9 al., 2010) and associated with a large effect size. Hayashi et al. (Hayashi et al., 2010) showed that
10 depersonalisation symptoms in panic disorder patients could induce abnormalities in the EEG
11 pattern of patients, characterised by repeated slow wave (in the range of theta) bursts.

12 **Disembodiment feelings (desomatisation)**

13 One of the cardinal symptoms of depersonalisation is disembodiment – feeling detached or
14 estranged from one’s own body parts or whole body, when looking at them directly or in a
15 mirror. DPD patients also often complain about a lack of agency - feeling as if their speech or
16 movements are robotic and not their own. In other words, the disorder is characterized by
17 frequent and persistent experiences of a loss of the physical sense of self (the feeling of oneself as
18 the bodily subject of one’s experiences). Adler et al. (Adler et al., 2016) tried to explain
19 disembodiment in DPD patients using a somatosensory resonance paradigm, which taps into the
20 human mirror neuron system (Iacoboni et al., 1999; Molenberghs et al., 2012). The mirror neuron
21 system, which resides in the premotor cortex and inferior parietal cortex as well as associated
22 regions of sensory, motor and emotional processing (Molenberghs et al., 2009), is active both
23 when we perform an action (action execution) and when we observe someone else engaging in a

1 similar action (action observation) (Morales et al., 2019) and is thought to encode the functional
2 goal of an action (Le Bel et al., 2009). The mirror neuron system plays a crucial role in the adult
3 representation of the bodily self (Hu et al., 2016; Molnar-Szakacs and Uddin, 2013; Turjman,
4 2016) and in its development from infancy on the basis of contingencies between sensory and
5 motor information (Filippetti et al., 2014; Gallese and Sinigaglia, 2010). Adler et al. (Adler et al.,
6 2016) investigated the mirroring mechanism using somatosensory event-related potentials (SEPs)
7 for self-related information (synchronous visual-tactile stimulation on one's own face) and for
8 other-related information (synchronous visual-tactile stimulation on someone else's face). For
9 people with very infrequent symptoms of depersonalisation (low CDS scores), mirroring effects
10 for self-related information were observed at early stages of somatosensory processing (P45
11 component, ~45ms post-stimulus), while for other-related information they occurred at later
12 stages (N80 component, ~80ms post-stimulus) (both findings associated with a large effect size).
13 For persons with high levels of depersonalisation (high CDS scores), however, the authors did
14 not observe self-related mirroring effect at P45, but found other-related mirroring at N80 (finding
15 associated with a large effect size). At later cognitive stages (P200 component, ~200ms post-
16 stimulus), mirroring effects for self- and other-related information differed for individuals with
17 low CDS scores but not for those with high CDS scores (findings associated with a large and
18 medium effect size, respectively). In accordance with (Ketay et al., 2014), Adler et al. suggested
19 the lack of early (implicit) self-related information processing as a potential biomarker to explain
20 disembodiment feelings in DPD. A lack of self-other differentiation at later cognitive stages
21 (P200) may also contribute to this aspect of the DPD phenomenology.

22 In order to explain disembodiment in DPD, it is important to understand how the sense of
23 bodily self-attribution forms in humans. The “rubber hand illusion” (Botvinick and Cohen, 1998;

1 Ehrsson et al., 2004; Tsakiris and Haggard, 2005) and its full-body virtual reality equivalent
2 (Lenggenhager et al., 2007; Nakul et al., 2020; Pomés and Slater, 2013) have been instrumental
3 in showing that the integration of multisensory information from our environment, specifically
4 our bodily stimuli, forms the sense of bodily self-consciousness (Blanke et al., 2015; Ehrsson et
5 al., 2005; Noel et al., 2018; Tsakiris and Haggard, 2005) (for review see (Tsakiris, 2010)). In the
6 illusion, a participant's real hand receives tactile stimulation synchronously with a rubber hand,
7 while they only see the rubber hand being touched. Synchronous (but not asynchronous)
8 visuotactile stimuli result in changes in body ownership (the feeling that the rubber hand is part
9 of one's own body) and self-location (the felt location of one's own hand shifts toward the rubber
10 hand).

11 The multimodal integration of exteroceptive signals such as the tactile and visual stimuli
12 employed in the rubber hand illusion and in Adler et al.'s study are thought to occur in several
13 temporal and parietal lobe areas (Calvert and Thesen, 2004), especially the insula (Bushara et al.,
14 2001; Bushara et al., 2003), and disruptions in this process have been proposed as a possible
15 explanation for feelings of disembodiment in DPD (Farmer et al., 2019; O'Sullivan et al., 2018).
16 Indeed, participants with frequent symptoms of depersonalisation (high CDS scores) appear to be
17 more susceptible to feelings of illusory ownership of a rubber hand than those with infrequent
18 symptoms (Kanayama et al. 2009). It is worth noting that this association between biases in
19 multisensory information processing and anomalous bodily experiences is not limited to the
20 clinical population. For instance, Braithwaite et al. (Braithwaite et al., 2017) exposed the rubber
21 hand to a realistic threat following periods of synchronous vs. asynchronous visual-tactile
22 stimulation, and found no differences in GSRs in a group of persons predisposed to out-of-body

1 experiences while a control group showed elevated threat-related GSRs after synchronous
2 compared to asynchronous visual-tactile stimulation.

3 In addition to the integration of exteroceptive signals, several studies have confirmed the
4 role of interoceptive signals in bodily self-consciousness (Craig, 2009; Tsakiris et al., 2011) (for a
5 review see (Park and Blanke, 2019a)). Interoception refers to the processing of signals originating
6 from visceral organs and represents the internal state of the body (Khalsa and Lapidus, 2016).
7 The main brain regions responsible for interoception are insula, cingulate cortex, amygdala, and
8 somatosensory cortex (Craig, 2009). Notice that the role of these brain regions have been
9 revealed before in depersonalisation (Lemche et al., 2013), and abnormal activities in those brain
10 areas have been observed in DPD patients (Medford, 2012; Medford et al., 2016; Sierk et al.,
11 2018; Sierra et al., 2014). Since activity of insula is attenuated in DPD (Medford et al., 2016;
12 Phillips et al., 2001), attempts to explain disembodiment in DPD based on deficient interoception
13 were made in 2014 (Michal et al., 2014; Sedeño et al., 2014). Interoceptive functioning was
14 evaluated based on two heartbeat detection tasks (Schandry and Whitehead tasks (Schandry,
15 1981; Whitehead et al., 1977)) in both studies. However, Michal et al.'s DPD patients performed
16 similar to healthy subjects in heartbeat detection tasks while Sedeño et al.'s DPD patients showed
17 impaired performance. This contradiction may be explained by the inability of interoceptive
18 accuracy tests to reliably measure body awareness (Ferentzi et al., 2018). In fact, Michal et al.
19 (Michal et al., 2014) argued that patients with DPD have specific difficulties with sustained
20 attention to interoceptive signals as they show decreasing accuracy in the heartbeat perception
21 task over time, while healthy observers typically increase their accuracy. This pattern may
22 suggest deficits in sustaining attention to bodily sensations, rather than with bodily sensations per

1 se, in patients with DPD. However, a more robust index is needed for the investigation of
2 interoception and bodily self-consciousness in DPD.

3 One of the main indices of interoceptive signal processing are Heartbeat-Evoked Potentials
4 (HEPs) (Gray et al., 2007; Park and Blanke, 2019b; Pollatos and Schandry, 2004), which
5 correspond to the processing of cardiac signals in the brain. HEPs are obtained by averaging
6 brain signals time-locked with heartbeats in frontocentral regions of the brain, with the insula as
7 their primary origin (Park et al., 2017). They normally can be observed from 200 to 500ms after
8 the occurrence of the R-peak in the human electrocardiogram (Park and Blanke, 2019b; Park et
9 al., 2014a). Changes in HEPs can represent interoception and the level of attention to internal
10 signals. They also reflect distinct attentional mechanisms for interoceptive and exteroceptive
11 signals, such that interoception (tapping in line with one's own heartbeat) yields larger HEP
12 amplitudes compared with exteroception (tapping in line with a recording of a simulated
13 heartbeat) (García-Cordero et al., 2017). This difference was shown to be greater for people who
14 lack interoceptive awareness, as measured through the heartbeat detection task (Schandry, 1981),
15 and who may thus need more attentional effort to perceive their visceral signals (Montoya et al.,
16 1993). In this regard, and to understand the role of interoceptive signals in bodily self-
17 consciousness, Park et al. (Park et al., 2016) investigated the association between HEPs and
18 bodily self-consciousness. They showed that HEPs correspond to the strength of an induced
19 illusory sense of self in a full-body version of the rubber hand illusion. In addition, the authors
20 confirmed the role of insula, cingulate cortex, and amygdala in interoceptive signal processing
21 and bodily self-consciousness, which had been reported before (Heydrich and Blanke, 2013;
22 Ronchi et al., 2015).

1 Schulz et al. (Schulz et al., 2015) studied the patterns of HEPs in people with DPD and
2 compared them with healthy subjects through a heartbeat perception task. The objective was
3 finding an association between feeling of disembodiment in DPD and the cortical representation
4 of HEPs as an interoceptive signal. Healthy participants showed differential HEP amplitudes after
5 500ms from the onset of HEP between rest and heartbeat perception task, but such a difference
6 was not found in DPD patients (finding associated with a relatively large effect size). A later
7 study based on the analysis of cardiac responses to startle stimuli demonstrated that the altered
8 pattern of visceral-afferent signals in DPD is not limited to the cortical level, as similar effects
9 were observed in the brainstem (Schulz et al., 2016). It is worth noting that according to their
10 earlier report (Michal et al., 2014), DPD patients' performance in the heartbeat perception task
11 decreased over time. Patients with DPD showed higher initial performance than healthy controls,
12 but showed a decrease over time, while healthy individuals showed an increase over time,
13 resulting in a lack of difference in performance between the two groups overall.

14 Since it is likely that both interoception and exteroception are involved in the formation of
15 self-consciousness, researchers have attempted to define the role of their integration in bodily
16 self-consciousness (Aspell et al., 2013; Suzuki et al., 2013). For example, Sel et al. (Sel et al.,
17 2017) investigated whether the integration of visual and cardiac information, as an interoceptive
18 and exteroceptive signal respectively, can modify self-face recognition and neural responses to
19 heartbeats. For this purpose, a modified version of the enfacement Illusion (Tsakiris, 2008) as a
20 multisensory integration method was used. The participants saw an unfamiliar face being
21 morphed with their own face and also integrated with a pulsing shade synchronous or
22 asynchronous with their heartbeats. The results showed changes in the HEP amplitude between
23 195 and 289ms after the R-peak at centroparietal sites of the right hemisphere, with reduced HEP

1 amplitudes during synchronous cardio-visual stimulation compared with asynchronous
2 stimulation. The authors explained the reduced HEP amplitude as a result of a conflict created by
3 the external representation of private information (heartbeats) by an external agent (someone
4 else's face). Based on their argument, the brain resolves this conflict by attenuating the
5 prominence of interoceptive sensations in the formation of self-awareness, which manifests as
6 reduced HEP amplitudes and therefore leads to increased perceived similarity between self and
7 other. Similar results were later obtained by Heydrich et al. (Heydrich et al., 2018) for a cardio-
8 visual stimulation on a full body. Instead of HEPs, they used SEPs as a possible index for
9 changes in self-consciousness. Self-identification with the virtual body modulated SEP
10 component P45, which had previously been shown to reflect reduced implicit self-related
11 information processing in DPD (Adler et al., 2016).

12 In addition to impairments in the integration of exteroceptive and interoceptive body-
13 related signals, feelings of disembodiment in DPD may be exacerbated by deficits in attentional
14 processes (Adler et al., 2014; Guralnik et al., 2007), and this should be taken into account in
15 future studies of DPD (Gerrans, 2019).

16 **Emotional numbing (de-affectualisation)**

17 A second core symptom of DPD is emotional numbness (Blevins et al., 2013; Sierra et al.,
18 2002b). Self-reports from patients have asserted the lack of emotional responsivity to external
19 stimuli in DPD (Simeon, 2004), and fMRI studies have shown reduced activity in emotion
20 processing regions such as amygdala, hippocampus, temporal gyrus and anterior insula (Medford
21 et al., 2006). Quaedflieg et al. (Quaedflieg et al., 2013) examined the hypothesis of whether the
22 emotion-induced blindness effect differs in individuals with high versus low levels of
23 depersonalisation determined on the basis of scores on the CDS. Emotion-induced blindness

1 refers to a phenomenon in which one emotionally striking stimulus draws the attention of an
2 individual to such an extent that it reduces the processing capability for further subsequent
3 signals (Most et al., 2005). Due to the lack of patients' emotional responsivity (Simeon, 2004), an
4 inverse relationship between the level of depersonalisation and emotion-induced blindness was
5 expected. The Emotional Scenes Task (Most et al., 2005) was used to present emotional
6 distractors 200ms before the target in order to reduce the ability for correct target detection. As
7 expected, individuals with high levels of depersonalisation (high CDS scores) showed slightly,
8 but not significantly, less emotion-induced blindness than those with low levels of
9 depersonalisation (low CDS scores). The authors also examined visual ERPs during the above
10 task for the two groups. They found a meaningful positive correlation between the magnitude of
11 emotion-induced blindness and the ERP difference wave of emotional versus neutral distractors
12 in a 200–300ms time window at central and frontal electrodes. Interestingly, the ERP difference
13 wave at frontal sites was significantly smaller for high CDS compared to low CDS individuals in
14 the 200–300ms time window (finding associated with a relatively large effect size). Therefore,
15 the authors explained that the impact of an emotional distractor on subsequent processing is less
16 in people with high level of depersonalisation and is found at relatively early stages (200-300ms)
17 of information processing. They also showed that the lack of impact from emotional distractors
18 on these ERP components was associated with the derealisation factor of the CDS rather than
19 with levels of anxiety. In fact, depression and anxiety were related to ERP difference waves in
20 the 600–700ms time window at frontal electrodes. Their findings confirm that DPD is a distinct
21 psychological phenomenon from anxiety or depression (Simeon et al., 2001a; Stanton et al.,
22 2001).

1 The attenuation of the emotional response in DPD is thought to be caused by decreased
2 activities in emotional cortical (insula) and limbic (hypothalamus, amygdala) regions as well as
3 increased activities of the prefrontal cortex (Lemche et al., 2008; Lemche et al., 2007; Medford et
4 al., 2016; Sierra and David, 2011; Sierra et al., 2002b). The activation of posterior dorsal
5 prefrontal cortex, specifically, is thought to represent true inhibition of the intensity of an
6 emotional stimulus (Konishi et al., 2005; Phan et al., 2005) through the functional coupling
7 between prefrontal and limbic regions (Dolcos et al., 2006). In sum, it is hypothesised that
8 emotional numbing in DPD is due to early overactivation of these prefrontal regions, which
9 triggers the reduction of activity in limbic areas. The activation of this early defensive mechanism
10 could be due to the higher sensitivity of the brain to perceive an external emotional stimulus as a
11 threat (Sierra and Berrios, 1998).

12 This prefrontal-to-limbic suppressive mechanism can be further investigated using
13 electrophysiological signals. To do so, we suggest that researchers might consider EEG and ERP
14 markers associated with selective cortical inhibition of affective (e.g. aversive) processing, such
15 as alpha wave activity (Uusberg et al., 2013), frontal alpha asymmetries (Palmiero and Piccardi,
16 2017), delta–beta coherence (Putman, 2011), theta/beta ratio (Putman et al., 2010), and relatively
17 early (200-300ms) posterior negativities in visual ERPs, which are thought to be a consequence
18 of emotional stimulus appraisal in the amygdala (Luu and Tucker, 2003; Schupp et al., 2003), in
19 addition to the frontal and central emotional difference waves in the same time range (200-
20 300ms) that (Quaedflieg et al., 2013) showed to be attenuated in DPD.

21 **Anomalous subjective recall (de-ideation)**

22 Although functionally intact, memories in DPD can be subject to fragmentation, where
23 patients have difficulty forming sequential and coherent narratives of events (Giesbrecht et al.,

1 2010). DPD patients might also complain of their memories being “colourless” (Sierra and
2 David, 2011, p.4). Although patients can recall autobiographical memories, they describe them as
3 if they did not personally experience them, and as if they were an outside observer of the
4 incident. Sierra and David (Sierra and David, 2011) argued that autobiographical memory recall
5 entails two aspects, including retrieval of the incident and retrieval of the particular feelings
6 during that incident. Although the former aspect is intact in DPD patients, the absence of the
7 latter (Medford et al., 2006) results in actual memories becoming colourless and like a dream.
8 Similarly, a study of visual imagery and perception by Lambert et al. (Lambert et al., 2001b),
9 compared patients with DPD and a group of healthy individuals. DPD patients performed as well
10 as the control group in visual perception tests (Warrington and James, 1991) but showed
11 weakened ability in the imagination of visual information. Since the recall of autobiographical
12 events and the projection of one’s self into an imaginary future are similarly constructive
13 processes (Schacter, 2012), with largely overlapping neural underpinnings in limbic
14 (hippocampus) and medial prefrontal, medial parietal and temporal cortical regions (Martin et al.,
15 2011; Spreng and Grady, 2010), it is conceivable that both may feel similarly self-detached in
16 DPD.

17 However, and in addition to the questioning of de-ideation as an independent concept in the
18 factor structure of the CDS (Blevins et al., 2013), subjective recall and imagination in DPD have
19 not been adequately studied. In fact, no article was found in the literature on the investigation of
20 de-ideation using electrophysiological signals. However, Papageorgiou et al. (Papageorgiou et al.,
21 2002) observed an altered pattern of P300 during a working memory task in DPD patients. This
22 encoding-related electrophysiological signature could therefore be a potential biomarker to
23 investigate de-ideation in DPD (Amin et al., 2015). Moreover, observation of N200 and frontally

1 distributed N400 (FN400) components of ERP in DPD patients during a memory recall task
2 might also help to discover the underlying nature of de-ideation. A study by Proverbio et al.
3 (Proverbio et al., 2019) showed no distinction in N200 and FN400 components between the
4 retrieval of an old memory and the retrieval of more recent but emotionally salient memory, and
5 both scenarios evoked smaller components in comparison with a recent neutral memory. Since
6 these ERP components index familiarity of a stimulus (Curran, 1999; Curran, 2000), the authors
7 argued that both time and emotional valence have effects on memory recall. Enhanced N200 and
8 FN400 components in DPD patients could therefore mark patients' subjective unfamiliarity with
9 their memory. Finally, an additional biomarker of altered self-related memory and imagination in
10 DPD may be occipital alpha wave activity. Resting-state occipital alpha is an index of visual
11 cortical excitability (Romei et al., 2008), which has recently been associated with individual
12 differences in the strength of visual imagery (Keogh et al., 2020).

13 **Alienation from surroundings (derealisation)**

14 DPD refers to a chronic condition, and entails, as some researchers proposed (Sierra et al.,
15 2005; Simeon et al., 2008), four distinct symptoms, one of which is derealisation. However, in
16 the case of transient depersonalisation, derealisation is a distinct phenomenon (Dewe et al.,
17 2018), characterised by detachment from surroundings rather than from bodily self, with possible
18 distinct neurobiological mechanisms (Sierra et al., 2002a). For instance, in a recent study by
19 Heydrich et al. (Heydrich et al., 2019), the authors investigated the brain mechanism of
20 depersonalisation- and derealisation-like symptoms in patients with epilepsy. Patients were
21 divided into three groups of those with only depersonalisation-like symptoms, those with only
22 derealisation-like symptoms, and a control group consisting of patients with temporal lobe
23 epilepsy who had experienced Déjà vu or experiential hallucinations. The results from

1 multimodal neuroimaging study revealed that the majority of patients in the first group suffered
2 from frontal lobe epilepsy while the second group mostly suffered from temporal lobe epilepsy.
3 The epileptogenic zone in the group of patients with depersonalisation-like symptoms extended
4 from the mediodorsal premotor cortex to the medial prefrontal cortex. Heydrich et al.'s results
5 thus showed not only that depersonalisation and derealisation are two distinct transient
6 phenomena, but also that they are associated with two different sources of impairments.

7 No study was found in the DPD literature explicitly targeting derealisation symptoms using
8 electrophysiological methods. We propose that ERP signatures of familiarity and of attentional
9 engagement could serve as potential biomarkers of derealisation. Since derealisation is
10 characterised by a sense of unfamiliarity with one's surroundings, including with spaces and
11 objects that are intimately known, N200 and FN400, which we previously highlighted as
12 familiarity indexes (Curran, 1999; Curran, 2000), may differ less in DPD patients than in controls
13 during exposure to familiar versus unfamiliar scenery. Investigating the allocation of attention
14 within such scenes may also help to delineate the underlying nature of derealisation, as unfamiliar
15 contexts are likely to present a greater source of distraction than familiar contexts (Merriman et
16 al., 2016; Mruczek and Sheinberg, 2007; Park et al., 2014b). P300 has been shown to be
17 associated with cortical engagement in attentional tasks (Polich and Kok, 1995) and may serve as
18 a biomarker for feelings of alienation from one's surroundings. Indeed, abnormal P300 patterns
19 have already been observed in DPD patients in other tasks (Papageorgiou et al., 2002; Wise et al.,
20 2009). We further propose EEG/ERP indices of spatial cognition within egocentric and allocation
21 reference frames as potential measures of derealisation symptoms. For example, egocentric (vs.
22 allocentric) encoding of object locations in space has been associated with larger N1 amplitudes
23 and longer N2 latencies at left and bilateral inferior parietal sites, respectively (Lithfous et al.,

1 2014), possibly resulting from differential spatial discrimination and frame-dependent
2 localisation processes at these stages (Hopf et al., 2002; Luck and Hillyard, 1994; Vogel and
3 Luck, 2000). Gramann and colleagues (Gramann et al., 2010) found that the use of an egocentric
4 (vs. allocentric) reference frame during spatial navigation was associated with greater alpha
5 suppression in or near right primary visual cortex (vs. in occipito-temporal, bilateral inferior
6 parietal, and retrosplenial cortical areas). As a result of incoherent spatial referencing between
7 body and environment, such EEG/ERP signatures may be expected to be altered in persons
8 experiencing derealisation symptoms.

9 Another way to investigate derealisation (and other DPD) symptoms may be through the
10 probing of the vestibular system. The vestibular system includes sensory organs located in the
11 inner ear, which send information about the head's position, spatial orientation, and motion to the
12 brain (Khan and Chang, 2013), where vestibular signals are processed in distributed regions from
13 the temporo-parietal cortex to the prefrontal cortex (Ventre-Dominey, 2014). The vestibular
14 system plays a crucial role, not only in the sense of balance, motor coordination and spatial
15 orientation, but also more broadly for egocentric self-awareness (Lenggenhager et al., 2008;
16 Lenggenhager et al., 2015) by providing a gravitational reference to other bodily signals (Ferrè et
17 al., 2014). When signalling pathways are disturbed in peripheral vestibular disease, the brain fails
18 to generate a coherent spatial representation of the body with respect to the external world
19 (Renaud, 2015). An incoherent spatial frame of reference may also result in feelings of
20 detachment from the world (derealisation). Several studies in the literature indeed report a higher
21 tendency for DPD symptoms among patients with peripheral vestibular disease than among
22 healthy individuals. Sang et al. (Sang et al., 2006) first showed this in a sample group of 171
23 subjects (121 healthy, 50 patients), and later (Jáuregui-Renaud et al., 2008) reported that levels of

1 depersonalisation were negatively correlated with patients' ability to estimate spatial orientation
2 in an environment. Further substantiating the potential involvement of vestibular signals in DPD
3 symptoms, Tschan et al. (Tschan et al., 2013) found that detachment from memory, derealisation
4 and disembodiment in the general population were the three most substantial DPD symptoms
5 associated with feelings of vertigo and dizziness, the most frequent symptoms seen in vestibular
6 patients (Sang et al., 2006).

7 Future studies of DPD, specifically those interested in derealisation, may thus consider
8 activating the vestibular system through passive full-body motion or through direct artificial
9 stimulation of the (otolith) vestibular system (Ertl and Boegle, 2019), and probing EEG / ERP
10 markers pertaining to cortical vestibular processing (vestibular evoked potentials, EEG power
11 and EEG microstates). For instance, several vestibular evoked potentials can be measured over
12 posterior, frontal and central sites within 500ms of passive motion, acoustic or galvanic
13 stimulation (Ertl et al., 2017; Kammermeier et al., 2017; Kammermeier et al., 2015). Evoked
14 potentials can reflect different motion parameters and have been source-localised to the cingulate
15 sulcus visual area and the opercular-insular region (Ertl et al., 2017). These studies have also
16 identified evoked beta- and mu-band responses in central electrodes. EEG studies have further
17 shown that motion-induced vestibular stimulation caused bilateral temporal-parietal suppression
18 of alpha oscillatory activity (Gale et al., 2016; Gutteling and Medendorp, 2016), which was found
19 to be attenuated in patients with vestibular loss (Gale et al., 2016). Cortical EEG/ERP signatures
20 like these may thus be useful for studying the vestibular system in DPD, and egocentric self-
21 awareness in general.

1 **Other symptoms of DPD**

2 Standard neuropsychological test have detected broad perceptual and attentional alterations
3 in the pathophysiology of depersonalisation/derealisation (Guralnik et al., 2007; Guralnik et al.,
4 2000). Already Hollander et al. (Hollander et al., 1992) suggested that depersonalisation is
5 marked by dysfunctions in the emotional modulation and integration of perceptual information,
6 and they reported increased absolute values of visual and auditory N200 components of event-
7 related potentials (ERPs) over the left temporal cortex in a DPD patient, in addition to abnormal
8 theta oscillatory activity.

9 An electrophysiological alteration in early attentional functioning in DPD was later verified
10 in (Schabinger et al., 2018). Schabinger et al. used a spatial cueing paradigm (Posner and Cohen,
11 1984) to investigate the selective attentional mechanisms (Hillyard and Anllo-Vento, 1998;
12 Posner et al., 1980) in DPD and psychosomatic control patients, who were matched for
13 depression and anxiety. Each trial in this paradigm consisted of a target (ellipse) or non-target
14 (circle) visual stimulus in either the left or right area of the screen preceded by a central spatial
15 cue (arrow) indicating correctly, incorrectly, or neutrally the location of the upcoming stimulus.
16 Visual ERPs in response to cued stimuli were investigated for the two groups. Schabinger et al.
17 found diminished suppression of stimuli at to-be-ignored locations at the early sensory P1
18 component in DPD patients compared to control patients (findings associated with a large effect
19 size) while attentional effects at sensory N1 (enhancement of stimuli at to-be-attended locations)
20 and later cognitive components (including P300) were similar across patient groups. It was
21 proposed that the lack of early-stage suppression of irrelevant sensory inputs might be
22 responsible for the distractibility reported by DPD patients. Schabinger et al suggested visual
23 ERP component P1 as a potential biomarker for deficient attentional functioning in chronic DPD.

1 Papageorgiou et al. examined the potential alteration in the P300 ERP component in
2 transient depersonalisation (Papageorgiou et al., 2002). In a working memory test, lower P300
3 amplitudes (but no changes in latency) at central posterior brain regions were observed in
4 individuals with transient depersonalisation experiences compared with a control group (finding
5 associated with a large effect size). Since high P300 amplitudes are typically evoked by
6 conditions which demand more attention (Holdstock, 1995; Polich, 1998), the findings of the
7 above study appear to confirm attention problems in depersonalisation states. However, a later
8 study (Wise et al., 2009) reported a related but inverse finding regarding amplitude and latency
9 changes in P300 in depersonalisation state. Analysis of ERP components during an auditory
10 oddball task in patients with panic disorder revealed that patients who had experienced
11 depersonalisation symptoms showed reduced P300 latency (but no changes in amplitude) to a
12 striking target sound compared with healthy individuals (finding associated with a medium effect
13 size). Reduced P300 latency indicates accelerated information processing and stimulus
14 classification (Picton, 1992; Sur and Sinha, 2009). No such reduction in P300 latency was
15 observed in the comparison between panic disorder patients without depersonalisation and the
16 control group. In addition to the unchanged attentional effects at P300 in a visual-spatial task
17 comparing DPD with psychosomatic control patients (Schabinger et al., 2018), longer (rather
18 than reduced) P300 latencies were reported in panic disorder patients compared to healthy
19 individuals (Turan et al., 2002). In sum, although P300 may be a valuable electrophysiological
20 biomarker for attentional deficits in depersonalisation/derealisation, more studies with carefully
21 designed tasks are needed to examine its precise expression in each task and for each group of
22 patients. Additional ERP biomarkers for abnormalities in perceptual-attentional systems in DPD
23 may be found in P1 (Schabinger et al., 2018) and N200 (Hollander et al., 1992) components, and
24 these also require substantial replication through new studies of transient and chronic DPD.

1 **Summary and Conclusions**

2 Depersonalisation/derealisation disorder (DPD) can profoundly affect the quality of life for
3 patients and interfere with their social relationships and daily activities. It usually takes several
4 years to be correctly diagnosed (Hunter et al., 2017), and the symptoms of the disorder can be
5 intolerable until then. The present paper provided a systematic review of the studies targeting
6 transient and chronic symptoms of depersonalisation using electrophysiological neuroimaging
7 techniques. The aim was to describe what is presently known about the neurophysiological
8 correlates of DPD symptoms and to make recommendations for further study to improve the
9 diagnostic potential of this neuroimaging tool.

10 Before we summarise the EEG/ERP indices of DPD, it is worth noting the sparse use of
11 electrophysiology to delineate the neurophysiological correlates of DPD symptoms. Only ten
12 studies satisfied our criteria for inclusion in this review, two of which were single-case studies.
13 Yet, EEG/ERP methodologies are powerful techniques for eliciting human perception, cognition
14 and action independently of participants' cultural background or education levels. Unlike fMRI,
15 EEG/ERPs are direct measures of neural activity. Inexpensive, easy to implement, and well
16 tolerated by patients, their diagnostic potential has been successfully studied in other disorders,
17 including schizophrenia (Luck et al., 2011), which has a similar prevalence as DPD. We would
18 therefore urge researchers interested in depersonalisation/derealisation to invest more resources
19 into these techniques to develop their diagnostic potential for DPD beyond that which is presently
20 known.

21 Several studies have shown abnormal EEG activities in theta band in DPD patients, and the
22 severity of symptoms was found to be associated with increased theta activity. Higher theta wave
23 synchronisation has been observed for emotional compared to neutral stimuli, and this

1 synchronisation occurs earlier (around 200ms) when emotional stimuli are processed implicitly
2 but later (around 300ms) during the explicit recognition of facial emotions (Knyazev et al., 2009).
3 Therefore, increased theta activity in DPD patients might be associated with their greater effort or
4 involvement in processing emotional information (specifically unpleasant emotional information
5 (Quaedflieg et al., 2013; Sierra et al., 2002b; Sierra et al., 2006)). Another study (Kirmizi-Alsan
6 et al., 2006) showed that the theta wave represents the suppression of nontarget stimuli in the
7 go/nogo task, which requires both selective inhibition and arousal. Therefore, theta activity might
8 also represent the greater effort in the selective suppression of processing, which has been
9 observed to be deficient in DPD patients (Schabinger et al., 2018). Theta further plays a role in
10 memory maintenance in that higher theta activity is associated with the need for greater working
11 memory capacity (Jensen and Tesche, 2002; Raghavachari et al., 2001). Thus, the theta band of
12 the EEG power spectrum is likely to serve as a potential electrophysiological biomarker to study
13 DPD symptoms related to emotion, attention/inhibition and working memory. Future studies of
14 DPD should therefore focus on this oscillatory signature and investigate (a) the temporal
15 dynamics of event-related synchronisation in response to emotional stimuli, and (b) oscillatory
16 power during transient episodes of depersonalisation and in patients with chronic DPD, for
17 example. Note that it is important for future studies to consider a relatively prolonged time
18 window in order to analyse low-frequency components of EEG such as theta (practically, the
19 time window needs to contain at least three cycles of the target frequency), which may affect
20 stimulus design.

21 Analysis of cortical event-related and heartbeat-evoked potentials (ERPs and HEPs) can
22 also reveal valuable information regarding the underlying nature of DPD symptoms, as well as of
23 the sensorimotor integrative processes contributing to bodily self-consciousness in general. HEPs

1 and some ERP components have been introduced as potential valuable indices to investigate DPD
2 symptoms related to disembodiment. Somatosensory P45 reflects processing in the primary
3 somatosensory cortex and is known to be involved in attributing body ownership (Adler et al.,
4 2016; Otsuru et al., 2014; Rigato et al., 2019). Cortical HEPs are thought to primarily derive from
5 insula activity, which is attenuated in DPD (Medford et al., 2016; Phillips et al., 2001). A lack of
6 P45 modulation during visual-tactile stimulation related to the self (Adler et al., 2016), and a lack
7 of HEP modulation during focused attention to one's own heartbeat (Schulz et al., 2015), may
8 both serve as an electrophysiological biomarkers for feelings of disembodiment (desomatisation)
9 in transient and chronic DPD. Both somatosensory cortex and insula are part of the networks
10 responsible for interoception (Craig, 2009), and the integration of interoceptive, exteroceptive,
11 and interoceptive with exteroceptive sensory signals have been recently proposed as critical for
12 generating the moment-to-moment feeling of self-consciousness. When integrative processes like
13 these are transiently or chronically dysfunctional, feelings of disembodiment may ensue, and may
14 be further exacerbated by abnormal attentional processes (Gerrans, 2019). Our review has
15 highlighted the potential of somatosensory P45 and of HEPs for measuring these processes in
16 health and disease. It is worth mentioning that there might be a link between somatosensory P45
17 and the cortical HEP in the investigation of DPD symptoms. A recent study (Adler and
18 Gillmeister, 2019) showed that the activation of somatosensory P45 component in response to
19 personal visual-tactile stimulation (touch on subject's own hand) is stronger in people with a
20 higher level of interoceptive awareness. If interoceptive awareness modules HEPs (Petzschner et
21 al., 2019), measuring both P45 and HEPs in the same study may be able to test the relationship
22 between interoceptive and exteroceptive awareness (Al et al., 2019). In addition, researchers may
23 consider the inclusion of electrophysiological markers for proprioceptive and vestibular signal
24 processing to investigate the bodily self in health and disease. Vestibular processes are

1 increasingly recognised as critically involved in feelings of body ownership and egocentric
2 perception and vestibular disturbances bear a strong link with several cardinal DPD symptoms
3 (Lenggenhager et al., 2015; Tschan et al., 2013).

4 Another potential set of ERP biomarkers for DPD symptoms occur around 200-300ms
5 (Quaedflieg et al., 2013), including N200 (Hollander et al., 1992), P200 (Adler et al., 2016) and
6 P300 (Papageorgiou et al., 2002; Wise et al., 2009). In this article, we have referred to enhanced
7 temporal N200 as an aspect of alterations in the perceptual-attentional system (Hollander et al.,
8 1992), to lack of self-other differentiation in somatosensory resonance at frontocentral P200 as an
9 aspect of disembodiment (Adler et al., 2016), to lack of frontocentral 200-300ms differences
10 (Quaedflieg et al., 2013) as an aspect of emotional numbing, and to reduced amplitude/latency at
11 centro-parietal P300 (Papageorgiou et al., 2002; Wise et al., 2009) as an aspect of working
12 memory/attentional dysfunction. We have also suggested the potential of additional markers in
13 this time range, such as the N200 and frontal N400 related to stimulus familiarity. Partly due to
14 inconsistencies in the precise expression of P300 abnormalities in DPD, further studies are
15 urgently needed to systematically confirm P300 as a potential electrophysiological biomarker for
16 diagnosing and investigating DPD symptomatology related to attentional and working memory
17 dysfunction, as well as to symptoms of de-ideation and derealisation. Caution should be applied
18 when regarding the association between P300 and DPD symptoms because P300 changes also
19 occur with a number of other pathologies and physiological states (e.g. (Duncan et al., 2009;
20 Gangadhar et al., 1993; Mathalon et al., 2000)) and are thus not necessarily selective for
21 depersonalisation.

22 Reduced brain activities have been observed in DPD patients in sensory information
23 processing units (Medford et al., 2016) as well as regions responsible for the processing of

1 visceral signals (Lemche et al., 2013). Besides, the impairment is found mainly in the early stages
2 of information processing (Adler et al., 2016; Quaedflieg et al., 2013; Schabinger et al., 2018).
3 This impairment in the implicit processing of multimodal interoceptive and exteroceptive signals
4 could be a result of long-time severe stress or anxiety (Shilony and Grossman, 1993), which may
5 damage the sensory processing units and reduce their processing capacity (Sierra and Berrios,
6 1998). For instance, one dominant theory to explain emotional numbing in DPD (Sierra and
7 Berrios, 1998) defines a threshold for the level of anxiety (or any unpleasant salient stimuli) after
8 which the emotional processing units (including the anterior insula and amygdala) discontinue
9 translating emotions into perceived feelings, and DPD is associated with abnormalities in this
10 threshold or in how quickly it is reached (Jay et al., 2014). The higher GSR baseline and the
11 earlier peak in GSR response of DPD patients to emotional stimuli in (Giesbrecht et al., 2010)
12 represent a faster saturation of emotional capacity (Sierra et al., 2002b). Further, reduced capacity
13 in sensory processing units may also be the cause of concentration problems in DPD, in a way
14 that there may be a commensurate loss in the capacity to filter relevant from irrelevant signals in
15 sensory information. A related framework within which symptoms of DPD may be explained is
16 based on the loss of the brain's ability to make and update predictions about the internal body
17 state and the outside world (Gerrans, 2019; Seth et al., 2012; Seth and Tsakiris, 2018). With
18 reduced activity in emotional information processing units (such as insula), the brain faces a
19 relative sparsity of information for maintaining precision in predictions about one's self and the
20 outside world. The increasing inconsistencies may cause further suppression of emotional
21 processing and, in turn, give rise to DPD symptoms such as the feeling of disembodiment or
22 derealisation. Conflict-monitoring related electrophysiological markers such as the mismatch
23 negativity (MMN) and the error-related negativity (ERN) are good candidates for investigating
24 this theory further. MMN is a pre-attentive fronto-central response around 100-200ms after

1 omitted or perceptually deviant sensory events in a stimulus sequence, and is generated by a
2 network of temporal-prefrontal cortical regions (Garrido et al., 2009). ERN is generated by a
3 region in the anterior cingulate cortex (ACC) (Dehaene et al., 1994) and emerges around 100ms
4 after the onset of an erroneous motor response, even when the observer is unaware of making an
5 error and even when the error cannot be corrected (Luu and Tucker, 2003). Recent studies have
6 begun to describe both MMN and ERN within a predictive-coding framework as indexes of the
7 brain's monitoring of bodily processes, where MMN may represent the failed prediction of
8 visceral and other sensory inputs and thus the failed suppression of the prediction error (Garrido
9 et al., 2009; Pfeiffer and De Lucia, 2017). ERN may represent the monitoring of errors
10 committed as a consequence of failed interoceptive and exteroceptive predictions, with
11 imbalances in monitoring shown to be related to anxiety pathology (Sueyoshi et al., 2014; Tan et
12 al., 2019; Yoris et al., 2017). Thus, MMN and ERN may be useful for indexing errors in
13 predicting the internal and external state of the body in persons with DPD.

14 There is not enough evidence to confirm a clear hemispheric lateralisation of DPD
15 symptoms' neurophysiological correlates. Nevertheless, it is likely that such hemispheric biases
16 will eventually emerge with more targeted research. Some studies have already shown
17 abnormalities in left-hemispheric activation of DPD patients (Hollander et al., 1992; Jiménez-
18 Genchi, 2004) and of individuals with more frequent dissociative experiences (Spitzer et al.,
19 2004). Furthermore, based on the dominant role of the right hemisphere in emotional (Gainotti,
20 2019) and self-related processing (Hu et al., 2016), right-hemispheric biases in the dysregulation
21 of emotional processing and disembodiment in DPD may be expected. In support of this
22 argument, it may also be interesting to note that the right hemisphere may be more involved in
23 the perception and processing of negative emotions, while the left hemisphere deals

1 predominantly with positive sensations (Silberman and Weingartner, 1986), and that impairment
2 in emotional responsivity in DPD is often exclusive to unpleasant and threatening stimuli rather
3 than pleasant ones (Michal et al., 2013; Monde et al., 2013; Sierra et al., 2006). In addition,
4 inhibitory rTMS applied to the right ventrolateral prefrontal cortex can increase arousal capacity
5 (Jay et al., 2014) and rTMS applied to the right temporoparietal junction can reduce symptoms
6 (as measured by CDS total score) in DPD patients (Mantovani et al., 2011). Increased activation
7 in the angular gyrus of the right parietal lobe has also been found to be correlated with the level
8 of depersonalisation (Simeon et al., 2000). However, the DPD literature currently faces a lack of
9 direct investigations of hemispheric differences related to DPD symptoms; more studies on this
10 are urgently needed.

11 A schematic of the notable biological signals and associated electrophysiological
12 biomarkers introduced in this review as potential diagnostic tools are depicted in **Error!**
13 **Reference source not found.** Future studies in this area should consider both indexes of
14 interoceptive (such as HEPs) and exteroceptive signals (such as visual or somatosensory ERPs),
15 vestibular signals, and especially their interaction (including monitoring ERP markers like MMN,
16 ERN). For a comprehensive picture of DPD, it is useful to jointly investigate both peripheral
17 (autonomic) and central (cerebral) bodily responses, and both early (perceptual) and later
18 (cognitive) stages of central information processing. Additionally, there is a lack of research in
19 the analysis of EEG power spectra and their relative ratios and coherence. As this review has
20 uncovered that these may yield promising biomarkers for all cardinal DPD symptoms, further
21 studies need to consider different EEG waveforms and their roles in the formation of these
22 symptoms. For such analyses, the use of time-frequency and phase-based signal processing
23 (Mowlae et al., 2016) can be very insightful, since studies have suggested phase-alignment as a

1 fundamental phenomenon underlying the generation of ERPs and HEPs rather than evoked
2 potentials (Burgess, 2012; Park et al., 2018).

3 Further, the association between the vestibular system and the DPD symptoms can help the
4 design of experimental paradigms in future studies (Lopez et al., 2018). In this regard, a study by
5 Sang et al. (Sang et al., 2006) proposes caloric vestibular stimulation as an effective way to
6 provoke depersonalisation/derealisation-like symptoms in the non-clinical population. The
7 induced symptoms were similar to those experienced by patients with vestibular disease.
8 However, it should be carefully considered that there is also a close link between the vestibular
9 system dysfunction and out-of-body experiences (Blanke et al., 2004; Lopez and Elziere, 2018;
10 Lopez et al., 2008). For example, Lopez et al. (Lopez and Elziere, 2018) reported a higher
11 tendency for out of body experiences in patients with dizziness, and the relationship was more
12 significant in patients with peripheral vestibular disorder. Since out-of-body experiences are not
13 that common in depersonalisation/derealisation (Sierra and David, 2011), using methods to
14 dysregulate the vestibular system (such as caloric vestibular stimulation) to induce
15 depersonalisation/derealisation symptoms should be done carefully to prevent misinterpretation.

16 A correct diagnosis of DPD is an urgent matter in the area of psychological disorders, and
17 there is a need for finding diagnostic markers highly specific to DPD in order to distinguish it
18 from other alternative diagnoses. Understanding the potential of electrophysiological tools for the
19 identification of DPD symptoms can help to diagnose DPD quickly and effectively, and we
20 therefore appeal to researchers interested in the phenomena of self-awareness in health and
21 disease to consider using these tools more frequently.

22 **Declaration of Conflicting Interests**

- 1 The author(s) declared no potential conflicts of interest with respect to the research,
- 2 authorship, and/or publication of this article.

References

- Aderibigbe, Y., Bloch, R., Walker, W., 2001. Prevalence of depersonalization and derealization experiences in a rural population. *Soc. Psychiatry Psychiatr. Epidemiol.* 36, 63-69.
- Adler, J., Beutel, M.E., Knebel, A., Berti, S., Unterrainer, J., Michal, M., 2014. Altered orientation of spatial attention in depersonalization disorder. *Psychiatry Res.* 216, 230-235.
- Adler, J., Gillmeister, H., 2019. Bodily self-relatedness in vicarious touch is reflected at early cortical processing stages. *Psychophysiology* 56, e13465.
- Adler, J., Schabinger, N., Michal, M., Beutel, M.E., Gillmeister, H., 2016. Is that me in the mirror? Depersonalisation modulates tactile mirroring mechanisms. *Neuropsychologia* 85, 148-158.
- Al, E., Iliopoulos, F., Forschack, N., Nierhaus, T., Grund, M., Motyka, P., Gaebler, M., Vikulin, V.N., Villringer, A., 2019. Heart-Brain Interactions Shape Somatosensory Perception and Evoked Potentials. *bioRxiv*, 750315.
- American Psychiatric Association, 2013. *Diagnostic and statistical manual of mental disorders.*
- Amin, H.U., Malik, A.S., Kamel, N., Chooi, W.-T., Hussain, M., 2015. P300 correlates with learning & memory abilities and fluid intelligence. *J. Neuroeng. Rehabil.* 12, 87.
- Armour, C., Contractor, A.A., Palmieri, P.A., Elhai, J.D., 2014. Assessing latent level associations between PTSD and dissociative factors: Is depersonalization and derealization related to PTSD factors more so than alternative dissociative factors? *Psychol. Inj. Law* 7, 131-142.
- Aspell, J.E., Heydrich, L., Marillier, G., Lavanchy, T., Herbelin, B., Blanke, O., 2013. Turning body and self inside out: visualized heartbeats alter bodily self-consciousness and tactile perception. *Psychol. Sci.* 24, 2445-2453.
- Baker, D., Hunter, E., Lawrence, E., Medford, N., Patel, M., Senior, C., Sierra, M., Lambert, M.V., Phillips, M.L., David, A.S., 2003. Depersonalisation disorder: clinical features of 204 cases. *The British Journal of Psychiatry* 182, 428-433.
- Blanke, O., Landis, T., Spinelli, L., Seeck, M., 2004. Out-of-body experience and autoscapy of neurological origin. *Brain* 127, 243-258.
- Blanke, O., Slater, M., Serino, A., 2015. Behavioral, neural, and computational principles of bodily self-consciousness. *Neuron* 88, 145-166.
- Blevins, C.A., Witte, T.K., Weathers, F.W., 2013. Factor structure of the Cambridge Depersonalization Scale in trauma-exposed college students. *Journal of Trauma & Dissociation* 14, 288-301.
- Botvinick, M., Cohen, J., 1998. Rubber hands 'feel' touch that eyes see. *Nature* 391, 756.
- Braithwaite, J.J., Watson, D.G., Dewe, H., 2017. Predisposition to out-of-body experience (OBE) is associated with aberrations in multisensory integration: Psychophysiological support from a "rubber hand illusion" study. *JExPH* 43, 1125.
- Burgess, A.P., 2012. Towards a unified understanding of event-related changes in the EEG: the firefly model of synchronization through cross-frequency phase modulation. *PLoS One* 7.
- Bushara, K.O., Grafman, J., Hallett, M., 2001. Neural correlates of auditory-visual stimulus onset asynchrony detection. *J. Neurosci.* 21, 300-304.
- Bushara, K.O., Hanakawa, T., Immisch, I., Toma, K., Kansaku, K., Hallett, M., 2003. Neural correlates of cross-modal binding. *Nat. Neurosci.* 6, 190.
- Calvert, G.A., Thesen, T., 2004. Multisensory integration: methodological approaches and emerging principles in the human brain. *Journal of Physiology-Paris* 98, 191-205.
- Craig, A.D., 2009. How do you feel--now? The anterior insula and human awareness. *Nature reviews neuroscience* 10.
- Curran, T., 1999. The electrophysiology of incidental and intentional retrieval: erp old / new effects in lexical decision and recognition memory. *Neuropsychologia* 37, 771-785.
- Curran, T., 2000. Brain potentials of recollection and familiarity. *M&C* 28, 923-938.
- Davison, K., 1964. Episodic depersonalization: observations on 7 patients. *The British Journal of Psychiatry* 110, 505-513.
- Dehaene, S., Posner, M.I., Tucker, D.M., 1994. Localization of a neural system for error detection and compensation. *Psychol. Sci.* 5, 303-305.
- Derome, M., Fonseca-Pedrero, E., Badoud, D., Morosan, L., Van De Ville, D., Lazeyras, F., Eliez, S., Chan, R., Rudrauf, D., Schwartz, S., 2018. Resting-state networks of adolescents experiencing depersonalization-like illusions: Cross-sectional and longitudinal findings. *Schizophrenia Bulletin* 44, S501-S511.
- Devinsky, O., Putnam, F., Grafman, J., Bromfield, E., Theodore, W.H., 1989. Dissociative states and epilepsy. *Neurology* 39, 835-835.

- Dewe, H., Watson, D.G., Braithwaite, J.J., 2016. Uncomfortably numb: new evidence for suppressed emotional reactivity in response to body-threats in those predisposed to sub-clinical dissociative experiences. *Cogn. Neuropsychiatry* 21, 377-401.
- Dewe, H., Watson, D.G., Kessler, K., Braithwaite, J.J., 2018. The depersonalized brain: New evidence supporting a distinction between depersonalization and derealization from discrete patterns of autonomic suppression observed in a non-clinical sample. *Conscious. Cogn.* 63, 29-46.
- Dietl, T., Bien, C., Urbach, H., Elger, C., Kurthen, M., 2005. Episodic depersonalization in focal epilepsy. *Epilepsy Behav.* 7, 311-315.
- Dixon, J., 1963. Depersonalization phenomena in a sample population of college students. *The British journal of psychiatry* 109, 371-375.
- Dolcos, F., Kragel, P., Wang, L., McCarthy, G., 2006. Role of the inferior frontal cortex in coping with distracting emotions. *Neuroreport* 17, 1591-1594.
- Duncan, C.C., Barry, R.J., Connolly, J.F., Fischer, C., Michie, P.T., Näätänen, R., Polich, J., Reinvang, I., Van Petten, C., 2009. Event-related potentials in clinical research: guidelines for eliciting, recording, and quantifying mismatch negativity, P300, and N400. *Clin. Neurophysiol.* 120, 1883-1908.
- Ehrsson, H.H., Holmes, N.P., Passingham, R.E., 2005. Touching a rubber hand: feeling of body ownership is associated with activity in multisensory brain areas. *J. Neurosci.* 25, 10564-10573.
- Ehrsson, H.H., Spence, C., Passingham, R.E., 2004. That's my hand! Activity in premotor cortex reflects feeling of ownership of a limb. *Science* 305, 875-877.
- Ertl, M., Boegle, R., 2019. Investigating the vestibular system using modern imaging techniques—A review on the available stimulation and imaging methods. *J. Neurosci. Methods* 326, 108363.
- Ertl, M., Moser, M., Boegle, R., Conrad, J., zu Eulenburg, P., Dieterich, M., 2017. The cortical spatiotemporal correlate of otolith stimulation: Vestibular evoked potentials by body translations. *Neuroimage* 155, 50-59.
- Etkin, A., Egner, T., Peraza, D.M., Kandel, E.R., Hirsch, J., 2006. Resolving emotional conflict: a role for the rostral anterior cingulate cortex in modulating activity in the amygdala. *Neuron* 51, 871-882.
- Farmer, H., Cataldo, A., Adel, N., Wignall, E., Gallese, V., Deroy, O., Hamilton, A., Ciaunica, A., 2019. The Detached Self: Investigating the Effect of Depersonalisation on Self-Bias in the Visual Remapping of Touch.
- Ferentzi, E., Drew, R., Tihanyi, B.T., Köteles, F., 2018. Interoceptive accuracy and body awareness—Temporal and longitudinal associations in a non-clinical sample. *Physiol. Behav.* 184, 100-107.
- Ferrè, E.R., Lopez, C., Haggard, P., 2014. Anchoring the self to the body: vestibular contribution to the sense of self. *Psychol. Sci.* 25, 2106-2108.
- Filippetti, M.L., Lloyd-Fox, S., Longo, M.R., Farroni, T., Johnson, M.H., 2014. Neural mechanisms of body awareness in infants. *Cereb. Cortex* 25, 3779-3787.
- Gainotti, G., 2019. The role of the right hemisphere in emotional and behavioral disorders of patients with frontotemporal lobar degeneration: an updated review. *Front. Aging Neurosci.* 11, 55.
- Gale, S., Prsa, M., Schurger, A., Gay, A., Paillard, A., Herbelin, B., Guyot, J.-P., Lopez, C., Blanke, O., 2016. Oscillatory neural responses evoked by natural vestibular stimuli in humans. *J. Neurophysiol.* 115, 1228-1242.
- Gallese, V., Sinigaglia, C., 2010. The bodily self as power for action. *Neuropsychologia* 48, 746-755.
- Gangadhar, B., Ancy, J., Janakiraniah, N., Umapathy, C., 1993. P300 amplitude in non-bipolar, melancholic depression. *J. Affect. Disord.* 28, 57-60.
- García-Cordero, I., Esteves, S., Mikulan, E.P., Hesse, E., Baglivo, F.H., Silva, W., García, M.d.C., Vaucheret, E., Ciraolo, C., García, H.S., 2017. Attention, in and out: scalp-level and intracranial EEG correlates of interoception and exteroception. *Front. Neurosci.* 11, 411.
- Garrido, M.I., Kilner, J.M., Stephan, K.E., Friston, K.J., 2009. The mismatch negativity: a review of underlying mechanisms. *Clin. Neurophysiol.* 120, 453-463.
- Gerrans, P., 2019. Depersonalization Disorder, Affective Processing and Predictive Coding. *Review of Philosophy and Psychology* 10, 401-418.
- Giesbrecht, T., Merckelbach, H., van Oorsouw, K., Simeon, D., 2010. Skin conductance and memory fragmentation after exposure to an emotional film clip in depersonalization disorder. *Psychiatry Res.* 177, 342-349.
- Gramann, K., Onton, J., Riccobon, D., Mueller, H.J., Bardins, S., Makeig, S., 2010. Human brain dynamics accompanying use of egocentric and allocentric reference frames during navigation. *J. Cogn. Neurosci.* 22, 2836-2849.

- Gray, M.A., Taggart, P., Sutton, P.M., Groves, D., Holdright, D.R., Bradbury, D., Brull, D., Critchley, H.D., 2007. A cortical potential reflecting cardiac function. *Proceedings of the National Academy of Sciences* 104, 6818-6823.
- Guralnik, O., Giesbrecht, T., Knutelska, M., Sirroff, B., Simeon, D., 2007. Cognitive functioning in depersonalization disorder. *The Journal of nervous and mental disease* 195, 983-988.
- Guralnik, O., Schmeidler, J., Simeon, D., 2000. Feeling unreal: Cognitive processes in depersonalization. *Am. J. Psychiatry* 157, 103-109.
- Gutteling, T.P., Medendorp, W., 2016. Role of alpha-band oscillations in spatial updating across whole body motion. *Front. Psychol.* 7, 671.
- Harper, M., Roth, M., 1962. Temporal lobe epilepsy and the phobic anxiety-depersonalization syndrome: I: A comparative study. *Compr. Psychiatry*.
- Hayashi, K., Makino, M., Hashizume, M., Nakano, K., Tsuboi, K., 2010. Electroencephalogram abnormalities in panic disorder patients: a study of symptom characteristics and pathology. *Biopsychosoc. Med.* 4, 9.
- Heydrich, L., Aspell, J.E., Marillier, G., Lavanchy, T., Herbelin, B., Blanke, O., 2018. Cardio-visual full body illusion alters bodily self-consciousness and tactile processing in somatosensory cortex. *Sci. Rep.* 8, 9230.
- Heydrich, L., Blanke, O., 2013. Distinct illusory own-body perceptions caused by damage to posterior insula and extrastriate cortex. *Brain* 136, 790-803.
- Heydrich, L., Marillier, G., Evans, N., Seeck, M., Blanke, O., 2019. Depersonalization-and derealization-like phenomena of epileptic origin. *Annals of clinical and translational neurology*.
- Hillyard, S.A., Anllo-Vento, L., 1998. Event-related brain potentials in the study of visual selective attention. *Proceedings of the National Academy of Sciences* 95, 781-787.
- Holdstock, J., 1995. The effect of attention on the P300 deflection elicited by novel sounds. *J. Psychophysiol.* 9, 18-31.
- Hollander, E., Carrasco, J.L., Mullen, L.S., Truong, S., DeCaria, C.M., Towey, J., 1992. Left hemispheric activation in depersonalization disorder: a case report. *Biol. Psychiatry* 31, 1157-1162.
- Hopf, J.-M., Vogel, E., Woodman, G., Heinze, H.-J., Luck, S.J., 2002. Localizing visual discrimination processes in time and space. *J. Neurophysiol.* 88, 2088-2095.
- Hopper, J.W., Frewen, P.A., Van der Kolk, B.A., Lanius, R.A., 2007. Neural correlates of reexperiencing, avoidance, and dissociation in PTSD: Symptom dimensions and emotion dysregulation in responses to script-driven trauma imagery. *J. Trauma. Stress* 20, 713-725.
- Hu, C., Di, X., Eickhoff, S.B., Zhang, M., Peng, K., Guo, H., Sui, J., 2016. Distinct and common aspects of physical and psychological self-representation in the brain: A meta-analysis of self-bias in facial and self-referential judgements. *Neurosci. Biobehav. Rev.* 61, 197-207.
- Hunter, E., Phillips, M.L., Chalder, T., Sierra, M., David, A., 2003. Depersonalisation disorder: a cognitive-behavioural conceptualisation. *Behav. Res. Ther.* 41, 1451-1467.
- Hunter, E.C., Charlton, J., David, A.S., 2017. Depersonalisation and derealisation: assessment and management. *BMJ* 356, j745.
- Hunter, E.C., Sierra, M., David, A.S., 2004. The epidemiology of depersonalisation and derealisation. *Soc. Psychiatry Psychiatr. Epidemiol.* 39, 9-18.
- Iacoboni, M., Woods, R.P., Brass, M., Bekkering, H., Mazziotta, J.C., Rizzolatti, G., 1999. Cortical mechanisms of human imitation. *Science* 286, 2526-2528.
- Jáuregui-Renaud, K., Sang, F.Y.P., Gresty, M.A., Green, D.A., Bronstein, A.M., 2008. Depersonalisation/derealisation symptoms and updating orientation in patients with vestibular disease. *J. Neurol. Neurosurg. Psychiatry* 79, 276-283.
- Jay, E.-L., Sierra, M., Van den Eynde, F., Rothwell, J.C., David, A.S., 2014. Testing a neurobiological model of depersonalization disorder using repetitive transcranial magnetic stimulation. *Brain stimulation* 7, 252-259.
- Jensen, O., Tesche, C.D., 2002. Frontal theta activity in humans increases with memory load in a working memory task. *Eur. J. Neurosci.* 15, 1395-1399.
- Jiménez-Genchi, A.M., 2004. Repetitive transcranial magnetic stimulation improves depersonalization: a case report. *CNS spectrums* 9, 375-376.
- Kammermeier, S., Singh, A., Bötzel, K., 2017. Intermediate latency-evoked potentials of multimodal cortical vestibular areas: galvanic stimulation. *Front. Neurol.* 8, 587.
- Kammermeier, S., Singh, A., Noachtar, S., Krotofil, I., Bötzel, K., 2015. Intermediate latency evoked potentials of cortical multimodal vestibular areas: acoustic stimulation. *Clin. Neurophysiol.* 126, 614-625.

- Kaplan, H., Sadock, B., Grebb, J., 1998. Substance related disorders. Kaplan HI, Sadock BJ. Kaplan and Sadock's synopsis of psychiatry: behavioral sciences, clinical psychiatry. 8th ed. Baltimore: Williams & Wilkins, 419-426.
- Keogh, R., Bergmann, J., Pearson, J., 2020. Cortical excitability controls the strength of mental imagery. *Elife* 9, e50232.
- Ketay, S., Hamilton, H.K., Haas, B.W., Simeon, D., 2014. Face processing in depersonalization: An fMRI study of the unfamiliar self. *Psychiatry Research: Neuroimaging* 222, 107-110.
- Khalsa, S.S., Lapidus, R.C., 2016. Can interoception improve the pragmatic search for biomarkers in psychiatry? *Frontiers in psychiatry* 7, 121.
- Khan, S., Chang, R., 2013. Anatomy of the vestibular system: a review. *NeuroRehabilitation* 32, 437-443.
- Kirmizi-Aslan, E., Bayraktaroglu, Z., Gurvit, H., Keskin, Y.H., Emre, M., Demiralp, T., 2006. Comparative analysis of event-related potentials during Go/NoGo and CPT: decomposition of electrophysiological markers of response inhibition and sustained attention. *Brain Res.* 1104, 114-128.
- Knyazev, G., Slobodskoj-Plusnin, J.Y., Bocharov, A., 2009. Event-related delta and theta synchronization during explicit and implicit emotion processing. *Neuroscience* 164, 1588-1600.
- Konishi, S., Chikazoe, J., Jimura, K., Asari, T., Miyashita, Y., 2005. Neural mechanism in anterior prefrontal cortex for inhibition of prolonged set interference. *Proceedings of the National Academy of Sciences* 102, 12584-12588.
- Lambert, M.V., Senior, C., Fewtrell, W.D., Phillips, M.L., David, A.S., 2001a. Primary and secondary depersonalisation disorder: a psychometric study. *J. Affect. Disord.* 63, 249-256.
- Lambert, M.V., Senior, C., Phillips, M.L., Sierra, M., Hunter, E., David, A.S., 2001b. Visual imagery and depersonalisation. *Psychopathology* 34, 259-264.
- Lambert, M.V., Sierra, M., Phillips, M.L., David, A.S., 2002. The spectrum of organic depersonalization: a review plus four new cases. *The Journal of neuropsychiatry and clinical neurosciences* 14, 141-154.
- Lanius, R.A., Brand, B., Vermetten, E., Frewen, P.A., Spiegel, D., 2012. The dissociative subtype of posttraumatic stress disorder: Rationale, clinical and neurobiological evidence, and implications. *Depress. Anxiety* 29, 701-708.
- Lanius, R.A., Vermetten, E., Loewenstein, R.J., Brand, B., Schmahl, C., Bremner, J.D., Spiegel, D., 2010. Emotion modulation in PTSD: Clinical and neurobiological evidence for a dissociative subtype. *Am. J. Psychiatry* 167, 640-647.
- Le Bel, R.M., Pineda, J.A., Sharma, A., 2009. Motor–auditory–visual integration: the role of the human mirror neuron system in communication and communication disorders. *J. Commun. Disord.* 42, 299-304.
- Lee, W.E., Kwok, C.H., Hunter, E.C., Richards, M., David, A.S., 2012. Prevalence and childhood antecedents of depersonalization syndrome in a UK birth cohort. *Soc. Psychiatry Psychiatr. Epidemiol.* 47, 253-261.
- Lemche, E., Anilkumar, A., Giampietro, V.P., Brammer, M.J., Surguladze, S.A., Lawrence, N.S., Gasston, D., Chitnis, X., Williams, S.C., Sierra, M., 2008. Cerebral and autonomic responses to emotional facial expressions in depersonalisation disorder. *The British Journal of Psychiatry* 193, 222-228.
- Lemche, E., Brammer, M.J., David, A.S., Surguladze, S.A., Phillips, M.L., Sierra, M., Williams, S.C., Giampietro, V.P., 2013. Interoceptive–reflective regions differentiate alexithymia traits in depersonalization disorder. *Psychiatry Research: Neuroimaging* 214, 66-72.
- Lemche, E., Surguladze, S.A., Giampietro, V.P., Anilkumar, A., Brammer, M.J., Sierra, M., Chitnis, X., Williams, S.C., Gasston, D., Joraschky, P., 2007. Limbic and prefrontal responses to facial emotion expressions in depersonalization. *Neuroreport* 18, 473-477.
- Lenggenhager, B., Lopez, C., Blanke, O., 2008. Influence of galvanic vestibular stimulation on egocentric and object-based mental transformations. *Exp. Brain Res.* 184, 211-221.
- Lenggenhager, B., Lopez, C., Metzinger, T., Windt, J.M., 2015. Vestibular contributions to the sense of body, self, and others.
- Lenggenhager, B., Tadi, T., Metzinger, T., Blanke, O., 2007. Video ergo sum: manipulating bodily self-consciousness. *Science* 317, 1096-1099.
- Lithfous, S., Dufour, A., Blanc, F., Després, O., 2014. Allocentric but not egocentric orientation is impaired during normal aging: An ERP study. *Neuropsychology* 28, 761.
- Locatelli, M., Bellodi, L., Perna, G., Scarone, S., 1993. EEG power modifications in panic disorder during a temporolimbic activation task: relationships with temporal lobe clinical symptomatology. *The Journal of neuropsychiatry and clinical neurosciences.*
- Lopez, C., Elziere, M., 2018. Out-of-body experience in vestibular disorders—A prospective study of 210 patients with dizziness. *Cortex* 104, 193-206.

- Lopez, C., Halje, P., Blanke, O., 2008. Body ownership and embodiment: vestibular and multisensory mechanisms. *Neurophysiologie Clinique/Clinical Neurophysiology* 38, 149-161.
- Lopez, C., Nakul, E., Preuss, N., Elzière, M., Mast, F.W., 2018. Distorted own-body representations in patients with dizziness and during caloric vestibular stimulation. *J. Neurol.* 265, 86-94.
- Luck, S.J., Hillyard, S.A., 1994. Electrophysiological correlates of feature analysis during visual search. *Psychophysiology* 31, 291-308.
- Luck, S.J., Mathalon, D.H., O'Donnell, B.F., Hämäläinen, M.S., Spencer, K.M., Javitt, D.C., Uhlhaas, P.J., 2011. A roadmap for the development and validation of event-related potential biomarkers in schizophrenia research. *Biol. Psychiatry* 70, 28-34.
- Luu, P., Tucker, D.M., 2003. Self-regulation and the executive functions: Electrophysiological clues, *The cognitive electrophysiology of mind and brain*. Elsevier, pp. 199-II.
- Mancini-Marie, A., Fahim, C., Potvin, S., Beaugregard, M., Stip, E., 2006. Quetiapine: focus on emotional numbing in depersonalization disorder: an fMRI case report. *Eur. Psychiatry* 21, 574-577.
- Mantovani, A., Simeon, D., Urban, N., Bulow, P., Allart, A., Lisanby, S., 2011. Temporo-parietal junction stimulation in the treatment of depersonalization disorder. *Psychiatry Res.* 186, 138-140.
- Martin, V.C., Schacter, D.L., Corballis, M.C., Addis, D.R., 2011. A role for the hippocampus in encoding simulations of future events. *Proceedings of the National Academy of Sciences* 108, 13858-13863.
- Maslach, C., Jackson, S.E., 1981. The measurement of experienced burnout. *Journal of organizational behavior* 2, 99-113.
- Mathalon, D.H., Ford, J.M., Pfefferbaum, A., 2000. Trait and state aspects of P300 amplitude reduction in schizophrenia: a retrospective longitudinal study. *Biol. Psychiatry* 47, 434-449.
- Mathew, R., Wilson, W., Chiu, N., Turkington, T., DeGrado, T.R., Coleman, R., 1999. Regional cerebral blood flow and depersonalization after tetrahydrocannabinol administration. *Acta Psychiatr. Scand.* 100, 67-75.
- Medford, N., 2012. Emotion and the unreal self: depersonalization disorder and de-affectualization. *Emot. Rev.* 4, 139-144.
- Medford, N., Baker, D., Hunter, E., Sierra, M., Lawrence, E., Phillips, M.L., David, A.S., 2003. Chronic depersonalization following illicit drug use: a controlled analysis of 40 cases. *Addiction* 98, 1731-1736.
- Medford, N., Brierley, B., Brammer, M., Bullmore, E.T., David, A.S., Phillips, M.L., 2006. Emotional memory in depersonalization disorder: a functional MRI study. *Psychiatry Research: Neuroimaging* 148, 93-102.
- Medford, N., Sierra, M., Baker, D., David, A.S., 2005. Understanding and treating depersonalisation disorder. *Advances in psychiatric Treatment* 11, 92-100.
- Medford, N., Sierra, M., Stringaris, A., Giampietro, V., Brammer, M.J., David, A.S., 2016. Emotional experience and awareness of self: functional MRI studies of depersonalization disorder. *Front. Psychol.* 7, 432.
- Merriman, N.A., Ondřej, J., Roudaia, E., O'Sullivan, C., Newell, F.N., 2016. Familiar environments enhance object and spatial memory in both younger and older adults. *Exp. Brain Res.* 234, 1555-1574.
- Michal, M., Adler, J., Wiltink, J., Reiner, I., Tschan, R., Wölfling, K., Weimert, S., Tuin, I., Subic-Wrana, C., Beutel, M.E., 2016. A case series of 223 patients with depersonalization-derealization syndrome. *BMC Psychiatry* 16, 203.
- Michal, M., Beutel, M.E., Grobe, T.G., 2010. How often is the Depersonalization-Derealization Disorder (ICD-10: F48. 1) diagnosed in the outpatient health-care service? *Zeitschrift für Psychosomatische Medizin und Psychotherapie* 56, 74-83.
- Michal, M., Beutel, M.E., Jordan, J., Zimmermann, M., Wolters, S., Heidenreich, T., 2007. Depersonalization, mindfulness, and childhood trauma. *The Journal of nervous and mental disease* 195, 693-696.
- Michal, M., Koechel, A., Canterino, M., Adler, J., Reiner, I., Vossel, G., Beutel, M.E., Gamer, M., 2013. Depersonalization disorder: disconnection of cognitive evaluation from autonomic responses to emotional stimuli. *PLoS One* 8, e74331.
- Michal, M., Reuchlein, B., Adler, J., Reiner, I., Beutel, M.E., Vögele, C., Schächinger, H., Schulz, A., 2014. Striking discrepancy of anomalous body experiences with normal interoceptive accuracy in depersonalization-derealization disorder. *PLoS One* 9, e89823.
- Molenberghs, P., Cunnington, R., Mattingley, J.B., 2009. Is the mirror neuron system involved in imitation? A short review and meta-analysis. *Neurosci. Biobehav. Rev.* 33, 975-980.
- Molenberghs, P., Cunnington, R., Mattingley, J.B., 2012. Brain regions with mirror properties: a meta-analysis of 125 human fMRI studies. *Neurosci. Biobehav. Rev.* 36, 341-349.
- Molnar-Szakacs, I., Uddin, L.Q., 2013. Self-processing and the default mode network: interactions with the mirror neuron system. *Front. Hum. Neurosci.* 7, 571.

- Monde, K.-M., Ketay, S., Giesbrecht, T., Braun, A., Simeon, D., 2013. Preliminary physiological evidence for impaired emotion regulation in depersonalization disorder. *Psychiatry Res.* 209, 235-238.
- Montoya, P., Schandry, R., Müller, A., 1993. Heartbeat evoked potentials (HEP): topography and influence of cardiac awareness and focus of attention. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section* 88, 163-172.
- Morales, S., Bowman, L.C., Velnoskey, K.R., Fox, N.A., Redcay, E., 2019. An fMRI study of action observation and action execution in childhood. *Dev. Cogn. Neurosci.* 37, 100655.
- Most, S.B., Chun, M.M., Widders, D.M., Zald, D.H., 2005. Attentional rubbernecking: Cognitive control and personality in emotion-induced blindness. *Psychonomic bulletin & review* 12, 654-661.
- Mowlae, P., Kulmer, J., Stahl, J., Mayer, F., 2016. *Fundamentals of Phase-Based Signal Processing. Single Channel Phase-Aware Signal Processing in Speech Communication: Theory and Practice*, 33.
- Mruczek, R.E., Sheinberg, D.L., 2007. Context familiarity enhances target processing by inferior temporal cortex neurons. *J. Neurosci.* 27, 8533-8545.
- Nakul, E., Orlando-Dessaints, N., Lenggenhager, B., Lopez, C., 2020. Measuring perceived self-location in virtual reality. *Sci. Rep.* 10, 1-12.
- Noel, J.-P., Blanke, O., Serino, A., 2018. From multisensory integration in peripersonal space to bodily self-consciousness: from statistical regularities to statistical inference. *Ann. NY Acad. Sci* 1426, 146-165.
- O'Sullivan, N., de Bezenac, C., Piovesan, A., Cutler, H., Corcoran, R., Fenyvesi, D., Bertamini, M., 2018. I Am There... but Not Quite: An Unfaithful Mirror That Reduces Feelings of Ownership and Agency. *Perception* 47, 197-215.
- Otsuru, N., Hashizume, A., Nakamura, D., Endo, Y., Inui, K., Kakigi, R., Yuge, L., 2014. Sensory incongruence leading to hand disownership modulates somatosensory cortical processing. *Cortex* 58, 1-8.
- Palmiero, M., Piccardi, L., 2017. Frontal EEG asymmetry of mood: A mini-review. *Front. Behav. Neurosci.* 11, 224.
- Papageorgiou, C., Ventouras, E., Uzunoglu, N., Rabavilas, A., Stefanis, C., 2002. Changes of P300 elicited during a working memory test in individuals with depersonalization-derealization experiences. *Neuropsychobiology* 46, 70-75.
- Park, H.-D., Bernasconi, F., Bello-Ruiz, J., Pfeiffer, C., Salomon, R., Blanke, O., 2016. Transient modulations of neural responses to heartbeats covary with bodily self-consciousness. *J. Neurosci.* 36, 8453-8460.
- Park, H.-D., Bernasconi, F., Salomon, R., Tallon-Baudry, C., Spinelli, L., Seeck, M., Schaller, K., Blanke, O., 2017. Neural sources and underlying mechanisms of neural responses to heartbeats, and their role in bodily self-consciousness: an intracranial EEG study. *Cereb. Cortex* 28, 2351-2364.
- Park, H.-D., Bernasconi, F., Salomon, R., Tallon-Baudry, C., Spinelli, L., Seeck, M., Schaller, K., Blanke, O., 2018. Neural sources and underlying mechanisms of neural responses to heartbeats, and their role in bodily self-consciousness: an intracranial EEG study. *Cereb. Cortex* 28, 2351-2364.
- Park, H.-D., Blanke, O., 2019a. Coupling Inner and Outer Body for Self-Consciousness. *Trends Cogn. Sci.*
- Park, H.-D., Blanke, O., 2019b. Heartbeat-evoked cortical responses: Underlying mechanisms, functional roles, and methodological considerations. *Neuroimage* 197, 502-511.
- Park, H.-D., Correia, S., Ducorps, A., Tallon-Baudry, C., 2014a. Spontaneous fluctuations in neural responses to heartbeats predict visual detection. *Nat. Neurosci.* 17, 612.
- Park, H., Leal, F., Abellanoza, C., Schaeffer, J.D., 2014b. The formation of source memory under distraction. *Behavioral and Brain Functions* 10, 40.
- Paul, E.R., Farmer, M., Kämpe, R., Cremers, H.R., Hamilton, J.P., 2019. Functional Connectivity Between Extrastriate Body Area and Default Mode Network Predicts Depersonalization Symptoms in Major Depression: Findings From an A Priori Specified Multinetwork Comparison. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*.
- Petzschner, F.H., Weber, L.A., Wellstein, K.V., Paolini, G., Do, C.T., Stephan, K.E., 2019. Focus of attention modulates the heartbeat evoked potential. *Neuroimage* 186, 595-606.
- Pfeiffer, C., De Lucia, M., 2017. Cardio-audio synchronization drives neural surprise response. *Sci. Rep.* 7, 1-10.
- Phan, K.L., Fitzgerald, D.A., Nathan, P.J., Moore, G.J., Uhe, T.W., Tancer, M.E., 2005. Neural substrates for voluntary suppression of negative affect: a functional magnetic resonance imaging study. *Biol. Psychiatry* 57, 210-219.
- Phillips, M.L., Medford, N., Senior, C., Bullmore, E.T., Suckling, J., Brammer, M.J., Andrew, C., Sierra, M., Williams, S.C., David, A.S., 2001. Depersonalization disorder: thinking without feeling. *Psychiatry Research: Neuroimaging* 108, 145-160.
- Phillips, M.L., Sierra, M., 2003. Depersonalization disorder: a functional neuroanatomical perspective. *Stress* 6, 157-165.

- Picton, T.W., 1992. The P300 wave of the human event-related potential. *J. Clin. Neurophysiol.* 9, 456-479.
- Polich, J., 1998. P300 clinical utility and control of variability. *J. Clin. Neurophysiol.* 15, 14-33.
- Polich, J., Kok, A., 1995. Cognitive and biological determinants of P300: an integrative review. *Biol. Psychol.* 41, 103-146.
- Pollatos, O., Schandry, R., 2004. Accuracy of heartbeat perception is reflected in the amplitude of the heartbeat-evoked brain potential. *Psychophysiology* 41, 476-482.
- Pomés, A., Slater, M., 2013. Drift and ownership toward a distant virtual body. *Front. Hum. Neurosci.* 7, 908.
- Posner, M.I., Cohen, Y., 1984. Components of visual orienting. *Attention and performance X: Control of language processes* 32, 531-556.
- Posner, M.I., Snyder, C.R., Davidson, B.J., 1980. Attention and the detection of signals. *J. Exp. Psychol. Gen.* 109, 160.
- Proverbio, A.M., Vanutelli, M.E., Viganò, S., 2019. Remembering faces: The effects of emotional valence and temporal recency. *Brain Cogn.* 135, 103584.
- Putman, P., 2011. Resting state EEG delta–beta coherence in relation to anxiety, behavioral inhibition, and selective attentional processing of threatening stimuli. *Int. J. Psychophysiol.* 80, 63-68.
- Putman, P., van Peer, J., Maimari, I., van der Werff, S., 2010. EEG theta/beta ratio in relation to fear-modulated response-inhibition, attentional control, and affective traits. *Biol. Psychol.* 83, 73-78.
- Quaedflieg, C.W., Giesbrecht, T., Meijer, E., Merckelbach, H., de Jong, P.J., Thorsteinsson, H., Smeets, T., Simeon, D., 2013. Early emotional processing deficits in depersonalization: An exploration with event-related potentials in an undergraduate sample. *Psychiatry Research: Neuroimaging* 212, 223-229.
- Raghavachari, S., Kahana, M.J., Rizzuto, D.S., Caplan, J.B., Kirschen, M.P., Bourgeois, B., Madsen, J.R., Lisman, J.E., 2001. Gating of human theta oscillations by a working memory task. *J. Neurosci.* 21, 3175-3183.
- Raimo, E.B., Roemer, R.A., Moster, M., Shan, Y., 1999. Alcohol-induced depersonalization. *Biol. Psychiatry* 45, 1523-1526.
- Renaud, K.J., 2015. Vestibular function and depersonalization/derealization symptoms. *Multisensory research* 28, 637-651.
- Rigato, S., Bremner, A.J., Gillmeister, H., Banissy, M.J., 2019. Interpersonal representations of touch in somatosensory cortex are modulated by perspective. *Biol. Psychol.*, 107719.
- Röder, C.H., Michal, M., Overbeck, G., van de Ven, V.G., Linden, D.E., 2007. Pain response in depersonalization: a functional imaging study using hypnosis in healthy subjects. *Psychother. Psychosom.* 76, 115-121.
- Romei, V., Rihs, T., Brodbeck, V., Thut, G., 2008. Resting electroencephalogram alpha-power over posterior sites indexes baseline visual cortex excitability. *Neuroreport* 19, 203-208.
- Ronchi, R., Bello-Ruiz, J., Lukowska, M., Herbelin, B., Cabrilo, I., Schaller, K., Blanke, O., 2015. Right insular damage decreases heartbeat awareness and alters cardio-visual effects on bodily self-consciousness. *Neuropsychologia* 70, 11-20.
- Roth, M., 1960. The phobic anxiety-depersonalization syndrome and some general aetiological problems in psychiatry. *J. Neuropsychiatr.* 1, 293.
- Sang, F.Y.P., Jauregui-Renaud, K., Green, D.A., Bronstein, A.M., Gresty, M.A., 2006. Depersonalisation/derealisation symptoms in vestibular disease. *J. Neurol. Neurosurg. Psychiatry* 77, 760-766.
- Schabinger, N., Gillmeister, H., Berti, S., Michal, M., Beutel, M.E., Adler, J., 2018. Detached and distracted: ERP correlates of altered attentional function in depersonalisation. *Biol. Psychol.* 134, 64-71.
- Schacter, D.L., 2012. Constructive memory: past and future. *Dialogues Clin. Neurosci.* 14, 7.
- Schandry, R., 1981. Heart beat perception and emotional experience. *Psychophysiology* 18, 483-488.
- Schulz, A., Köster, S., Beutel, M.E., Schächinger, H., Vögele, C., Rost, S., Rauh, M., Michal, M., 2015. Altered patterns of heartbeat-evoked potentials in depersonalization/derealization disorder: neurophysiological evidence for impaired cortical representation of bodily signals. *Psychosom. Med.* 77, 506-516.
- Schulz, A., Matthey, J.H., Vögele, C., Schaan, V., Schächinger, H., Adler, J., Beutel, M.E., Michal, M., 2016. Cardiac modulation of startle is altered in depersonalization-/derealization disorder: evidence for impaired brainstem representation of baro-afferent neural traffic. *Psychiatry Res.* 240, 4-10.
- Schupp, H.T., Junghöfer, M., Weike, A.I., Hamm, A.O., 2003. Attention and emotion: an ERP analysis of facilitated emotional stimulus processing. *Neuroreport* 14, 1107-1110.
- Sedeño, L., Couto, B., Melloni, M., Canales-Johnson, A., Yoris, A., Baez, S., Esteves, S., Velásquez, M., Barttfeld, P., Sigman, M., 2014. How do you feel when you can't feel your body? Interoception, functional connectivity and emotional processing in depersonalization-derealization disorder. *PLoS One* 9, e98769.

- Sel, A., Azevedo, R.T., Tsakiris, M., 2017. Heartfelt Self: Cardio-Visual Integration Affects Self-Face Recognition and Interoceptive Cortical Processing. *Cereb. Cortex* 27, 5144-5155.
- Seth, A.K., Suzuki, K., Critchley, H.D., 2012. An interoceptive predictive coding model of conscious presence. *Front. Psychol.* 2, 395.
- Seth, A.K., Tsakiris, M., 2018. Being a beast machine: the somatic basis of selfhood. *Trends Cogn. Sci.* 22, 969-981.
- Shilony, E., Grossman, F.K., 1993. Depersonalization as a defense mechanism in survivors of trauma. *J. Trauma. Stress* 6, 119-128.
- Sierk, A., Daniels, J.K., Manthey, A., Kok, J.G., Leemans, A., Gaebler, M., Lamke, J.-P., Kruschwitz, J., Walter, H., 2018. White matter network alterations in patients with depersonalization/derealization disorder. *Journal of psychiatry & neuroscience: JPN* 43, 347.
- Sierra, M., Baker, D., Medford, N., David, A.S., 2005. Unpacking the depersonalization syndrome: an exploratory factor analysis on the Cambridge Depersonalization Scale. *Psychol. Med.* 35, 1523-1532.
- Sierra, M., Berrios, G.E., 1998. Depersonalization: neurobiological perspectives. *Biol. Psychiatry* 44, 898-908.
- Sierra, M., Berrios, G.E., 2000. The Cambridge Depersonalisation Scale: A new instrument for the measurement of depersonalisation. *Psychiatry Res.* 93, 153-164.
- Sierra, M., David, A.S., 2011. Depersonalization: a selective impairment of self-awareness. *Conscious. Cogn.* 20, 99-108.
- Sierra, M., Lopera, F., Lambert, M., Phillips, M., David, A., 2002a. Separating depersonalisation and derealisation: the relevance of the "lesion method". *J. Neurol. Neurosurg. Psychiatry* 72, 530-532.
- Sierra, M., Medford, N., Wyatt, G., David, A.S., 2012. Depersonalization disorder and anxiety: a special relationship? *Psychiatry Res.* 197, 123-127.
- Sierra, M., Nestler, S., Jay, E.-L., Ecker, C., Feng, Y., David, A.S., 2014. A structural MRI study of cortical thickness in depersonalisation disorder. *Psychiatry Research: Neuroimaging* 224, 1-7.
- Sierra, M., Senior, C., Dalton, J., McDonough, M., Bond, A., Phillips, M.L., O'Dwyer, A.M., David, A.S., 2002b. Autonomic response in depersonalization disorder. *Arch. Gen. Psychiatry* 59, 833-838.
- Sierra, M., Senior, C., Phillips, M.L., David, A.S., 2006. Autonomic response in the perception of disgust and happiness in depersonalization disorder. *Psychiatry Res.* 145, 225-231.
- Silberman, E.K., Weingartner, H., 1986. Hemispheric lateralization of functions related to emotion. *Brain Cogn.* 5, 322-353.
- Simeon, D., 2004. Depersonalisation disorder. *CNS drugs* 18, 343-354.
- Simeon, D., Guralnik, O., Hazlett, E.A., Spiegel-Cohen, J., Hollander, E., Buchsbaum, M.S., 2000. Feeling unreal: a PET study of depersonalization disorder. *Am. J. Psychiatry* 157, 1782-1788.
- Simeon, D., Guralnik, O., Knutelska, M., Hollander, E., Schmeidler, J., 2001a. Hypothalamic-pituitary-adrenal axis dysregulation in depersonalization disorder. *Neuropsychopharmacology* 25, 793-795.
- Simeon, D., Guralnik, O., Schmeidler, J., Sirof, B., Knutelska, M., 2001b. The role of childhood interpersonal trauma in depersonalization disorder. *Am. J. Psychiatry* 158, 1027-1033.
- Simeon, D., Knutelska, M., Nelson, D., Guralnik, O., 2003. Feeling unreal: a depersonalization disorder update of 117 cases. *The Journal of clinical psychiatry.*
- Simeon, D., Kozin, D.S., Segal, K., Lerch, B., Dujour, R., Giesbrecht, T., 2008. De-constructing depersonalization: further evidence for symptom clusters. *Psychiatry Res.* 157, 303-306.
- Spitzer, C., Willert, C., Grabe, H.-J., Rizos, T., Möller, B., Freyberger, H.J., 2004. Dissociation, hemispheric asymmetry, and dysfunction of hemispheric interaction: A transcranial magnetic stimulation approach. *The Journal of neuropsychiatry and clinical neurosciences* 16, 163-169.
- Spreng, R.N., Grady, C.L., 2010. Patterns of brain activity supporting autobiographical memory, prospection, and theory of mind, and their relationship to the default mode network. *J. Cogn. Neurosci.* 22, 1112-1123.
- Stanton, B.R., David, A.S., Cleare, A.J., Sierra, M., Lambert, M.V., Phillips, M.L., Porter, R.J., Gallagher, P., Young, A.H., 2001. Basal activity of the hypothalamic-pituitary-adrenal axis in patients with depersonalization disorder. *Psychiatry Res.* 104, 85-89.
- Stein, D.J., Schmeidler, J., Hollander, E., 1997. Feeling unreal: 30 cases of DSM-III-R depersonalization disorder. *Am. J. Psychiatry* 154, 1107-1113.
- Stein, D.J., Simeon, D., 2009. Cognitive-affective neuroscience of depersonalization. *CNS spectrums* 14, 467-471.
- Sueyoshi, T., Sugimoto, F., Katayama, J.i., Fukushima, H., 2014. Neural correlates of error processing reflect individual differences in interoceptive sensitivity. *Int. J. Psychophysiol.* 94, 278-286.
- Sur, S., Sinha, V., 2009. Event-related potential: An overview. *Industrial psychiatry journal* 18, 70.

- Suzuki, K., Garfinkel, S.N., Critchley, H.D., Seth, A.K., 2013. Multisensory integration across exteroceptive and interoceptive domains modulates self-experience in the rubber-hand illusion. *Neuropsychologia* 51, 2909-2917.
- Talbert, C., 2010. Construct Validity of Three Measures of Depersonalization in College-Exposed College Students.
- Tan, Y., Vandeput, J., Qiu, J., Van den Bergh, O., von Leupoldt, A., 2019. The error-related negativity for error processing in interoception. *Neuroimage* 184, 386-395.
- Tibubos, A.N., Grammes, J., Beutel, M.E., Michal, M., Schmutzer, G., Brähler, E., 2018. Emotion regulation strategies moderate the relationship of fatigue with depersonalization and derealization symptoms. *J. Affect. Disord.* 227, 571-579.
- Tsakiris, M., 2008. Looking for myself: current multisensory input alters self-face recognition. *PLoS One* 3, e4040.
- Tsakiris, M., 2010. My body in the brain: a neurocognitive model of body-ownership. *Neuropsychologia* 48, 703-712.
- Tsakiris, M., Haggard, P., 2005. The rubber hand illusion revisited: visuotactile integration and self-attribution. *JExpPH* 31, 80.
- Tsakiris, M., Jiménez, A.T.-, Costantini, M., 2011. Just a heartbeat away from one's body: interoceptive sensitivity predicts malleability of body-representations. *Proceedings of the Royal Society B: Biological Sciences* 278, 2470-2476.
- Tschan, R., Wiltink, J., Adler, J., Beutel, M.E., Michal, M., 2013. Depersonalization experiences are strongly associated with dizziness and vertigo symptoms leading to increased health care consumption in the German general population. *The Journal of nervous and mental disease* 201, 629-635.
- Turan, T., Esel, E., Karaaslan, F., Basturk, M., Oguz, A., Yabanoglu, I., 2002. Auditory event-related potentials in panic and generalised anxiety disorders. *Prog. Neuropsychopharmacol. Biol. Psychiatry* 26, 123-126.
- Turjman, O., 2016. On the role of mirror neurons in the sense of self. *Journal of Consciousness Exploration & Research* 7.
- Uusberg, A., Uibo, H., Kreegipuu, K., Allik, J., 2013. EEG alpha and cortical inhibition in affective attention. *Int. J. Psychophysiol.* 89, 26-36.
- van Heugten-van der Kloet, D., Giesbrecht, T., Merckelbach, H., 2015. Sleep loss increases dissociation and affects memory for emotional stimuli. *J. Behav. Ther. Exp. Psychiatry* 47, 9-17.
- Ventre-Dominey, J., 2014. Vestibular function in the temporal and parietal cortex: distinct velocity and inertial processing pathways. *Front. Integr. Neurosci.* 8, 53.
- Vogel, E.K., Luck, S.J., 2000. The visual N1 component as an index of a discrimination process. *Psychophysiology* 37, 190-203.
- Warrington, E.K., James, M., 1991. The visual object and space perception battery.
- Whitehead, W.E., Drescher, V.M., Heiman, P., Blackwell, B., 1977. Relation of heart rate control to heartbeat perception. *Biofeedback and Self-regulation* 2, 371-392.
- Wise, V., McFarlane, A.C., Clark, C.R., Battersby, M., 2009. Event-related potential and autonomic signs of maladaptive information processing during an auditory oddball task in panic disorder. *Int. J. Psychophysiol.* 74, 34-44.
- Yoris, A., García, A.M., Traiber, L., Santamaría-García, H., Martorell, M., Alifano, F., Kichic, R., Moser, J.S., Cetkovich, M., Manes, F., 2017. The inner world of overactive monitoring: neural markers of interoception in obsessive-compulsive disorder. *Psychol. Med.* 47, 1957-1970.

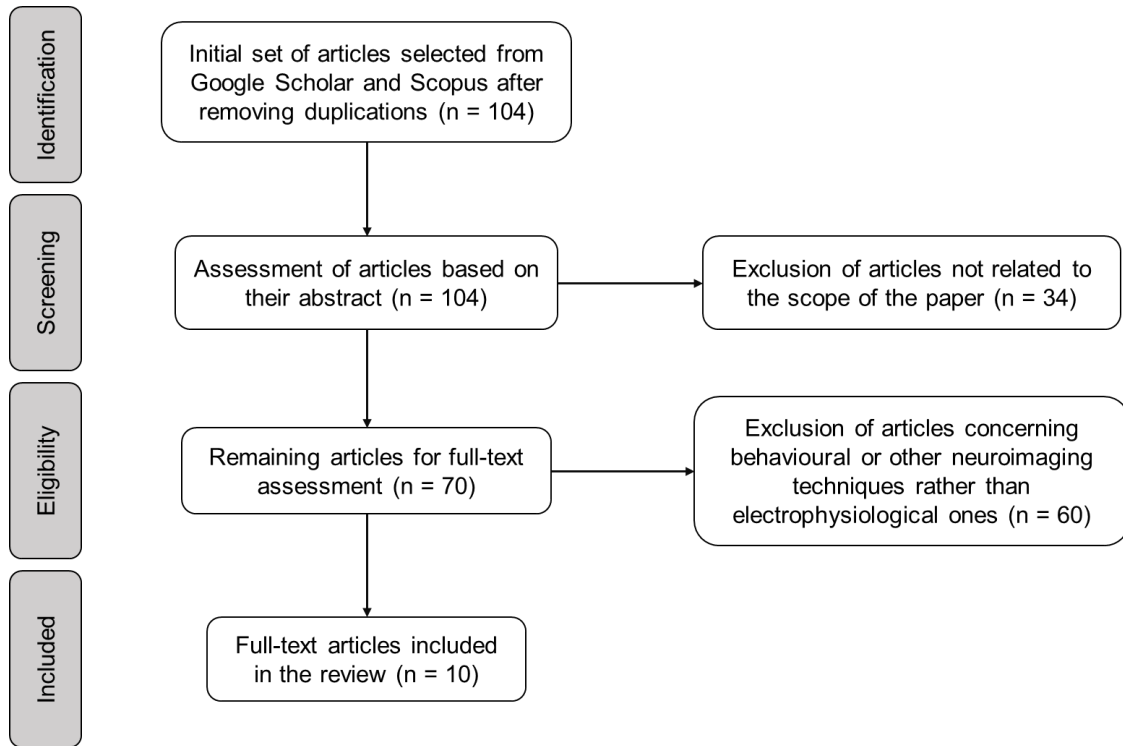


Figure 1 Flow diagram of the article selection process through the systematic review

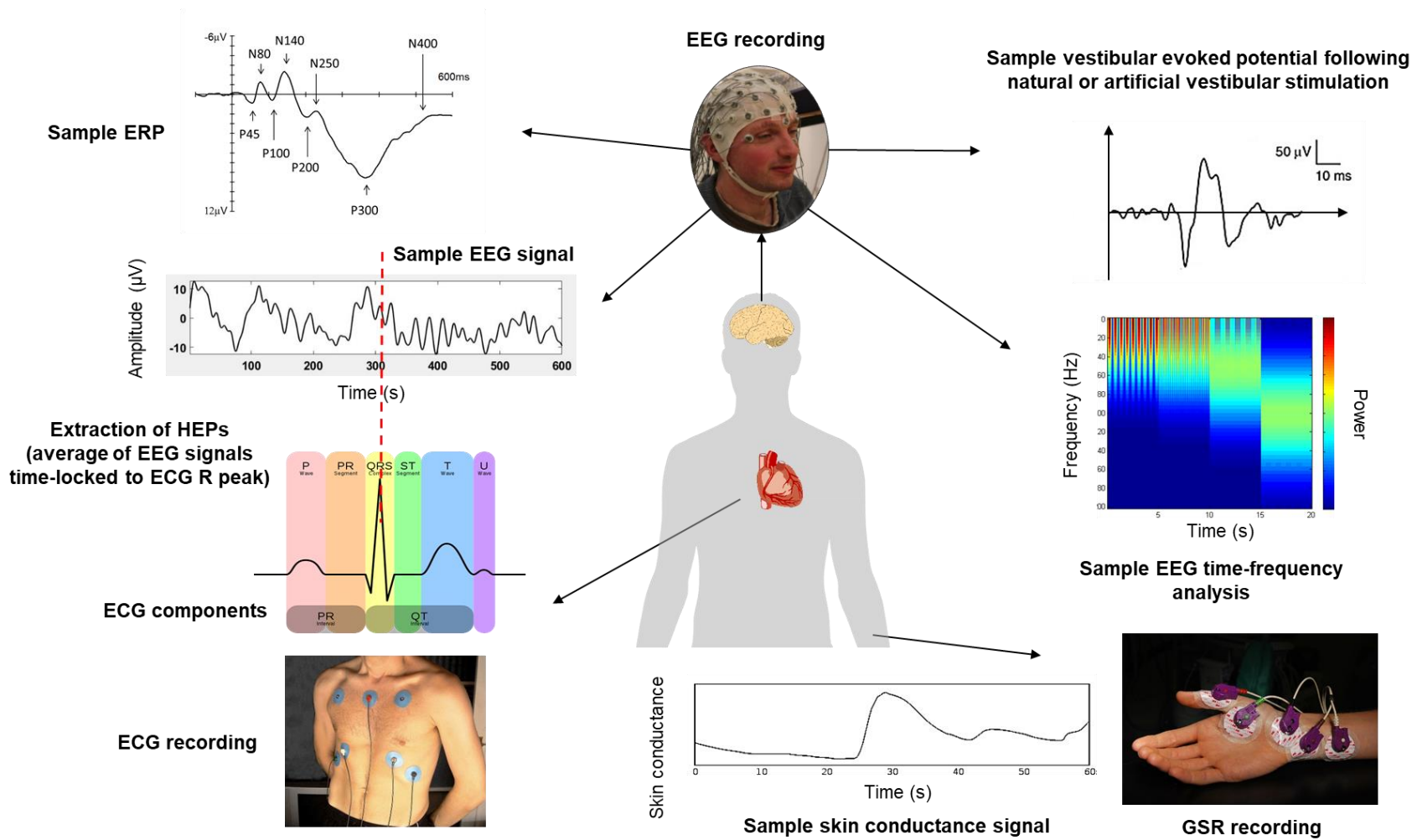


Figure 2 An overview of the biological signals and relevant electrophysiological biomarkers introduced in this review

Table 1 Four major symptoms of DPD (adapted from (Medford et al., 2005; Sierra and David, 2011)) and other associated processing differences

Disembodiment feelings (desomatisation)	Lack of body ownership or loss of agency
Emotional numbing (de-affectualisation)	Attenuation in emotional responsiveness
Anomalous subjective recall (de-ideation)	Disassociation between an incident and personal feeling in autobiographical memory retrieval
Alienation from surroundings (derealisation)	Detachment of the self from its surroundings
Other symptoms and processing differences	Impaired attentional functioning and processing speed or perceptual organisation

Table 2 Studies using electrophysiological neuroimaging techniques to characterise transient and chronic depersonalisation symptoms. Note that studies are ordered according to target symptom, and then chronologically. Reported effect sizes (interpretation): *d*: Cohen's *d* effect size (small (0.2), medium (0.5), and large (0.8)). η_p^2 : partial eta squared effect size (small (0.01), medium (0.06), and large (0.14)). OR: odds ratio effect size (small (1.5), medium (2.5), and large (4.3)).

Study (number of participants)	Task	Electrophysiological biomarker	Target symptom (transiency)	Findings
(Hollander et al., 1992) (n = 1)	None specified (a case report)	EEG power spectrum (alpha, theta); ERPs (visual and auditory; cognitive N200)	None specified (chronic)	Increased frontal alpha and temporal theta activity and enhanced N200 in visual and auditory ERPs over left brain regions in a DPD patient (case study).
(Locatelli et al., 1993) (n = 37)	Odour discrimination task	EEG power spectrum (delta, upper alpha)	None specified (transient)	Increased power in the delta band and a bilateral lack of responsiveness in the upper alpha band during odour discrimination in panic disorder patients with versus without depersonalisation (unable to obtain effect size from available data).
(Raimo et al., 1999) (n = 1)	None specified (a case report)	EEG power spectrum (theta)	None specified (transient)	Significantly higher relative power in theta band during induced depersonalisation episodes by absolute alcohol consumption compared with asymptomatic episodes (case study).
(Hayashi et al., 2010) (n = 70)	Intermittent Photic Stimulation (IPS)	EEG power spectrum (theta)	None specified (transient)	Abnormal theta activity (repeated slow waves) in 17 of 70 panic disorder patients, which was associated with three panic disorder symptoms (depersonalisation, nausea, and paresthesias) (OR = 13.92 for association with depersonalization/derealization).

(Schulz et al., 2015) (n = 47)	Heartbeat perception task	HEPs	Disembodiment (chronic)	Reduced differential HEP amplitudes after 500ms between rest and heartbeat tracking in DPD patients (n= 23) compared with healthy controls (n = 24) ($\eta_p^2 = 0.10$ for the two-way interaction between group and experimental task).
(Adler et al., 2016) (n = 27)	Somatosensory resonance paradigm	ERPs (somatosensory; perceptual P45, cognitive P200)	Disembodiment (transient)	Reduced somatosensory resonance for self-related information at P45 (no changes for other-related information at N80) in central-parietal electrodes in individuals with high (n = 14) versus low (n = 13) CDS scores (P45: $\eta_p^2 = 0.46$ for self-face touch in low CDS group only; N80: $\eta_p^2 = 0.29$ for other-face touch in all participants). Reduced self-other differences in resonance at cognitive P200 in fronto-central electrodes in individuals with high versus low CDS scores ($\eta_p^2 = 0.06$ versus $\eta_p^2 = 0.41$ for interaction between observed touch and observed face in each group).
(Quaedflieg et al., 2013) (n = 30)	Emotion-induced blindness (EIB)	ERPs (visual; cognitive 200-300ms)	Emotional numbing (transient)	Smaller difference in ERP amplitudes in a 200–300ms time window between emotional and neutral distractors in frontal electrodes in individuals with high (n = 15) versus low (n = 15) CDS scores ($d = 0.71$ for differential activation at Fz in 200–300ms time window between the two groups).
(Papageorgiou et al., 2002) (n = 30)	Working memory test	ERPs (auditory; cognitive P300)	Other (working memory) (transient)	Lower P300 amplitudes (no changes in latency) in response to single sound presenting the start of working memory tests at central posterior brain regions in healthy individuals with transient depersonalisation (n = 15) compared with a control group (n = 15) ($d = 1.62$ for group difference in P300 amplitudes).

(Wise et al., 2009) (n = 75)	Auditory oddball task	ERPs (auditory; cognitive P300)	Other (attentional dysfunction) (transient)	Reduced P300 latency (no changes in amplitude) in response to striking (target) tone in panic disorder patients with transient depersonalisation (n = 25) compared with matched healthy controls (n = 50) ($d = 0.62$ for group difference in P300 latency).
(Schabinger et al., 2018) (n = 28)	Spatial cueing paradigm	ERPs (visual; perceptual P1)	Other (attentional dysfunction) (chronic)	Reduced attentional suppression of irrelevant sensory inputs at P1 in occipito-parietal electrodes in DPD patients (n = 14) compared with anxiety- and depression-matched psychosomatic patients without DPD (n = 14) ($\eta_p^2 = 0.66$ vs. $\eta_p^2 = 0.19$ for effect of cue validity (valid vs .neutral vs. invalid) in DPD vs. control group).