Neuroscience and Biobehavioral Reviews 138 (2022) 104704

Contents lists available at ScienceDirect

Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev

A predictive coding account of value-based learning in PTSD: Implications for precision treatments

Andrea Putica[a,*], Kim L. Felmingham[b], Marta I. Garrido[b], Meaghan L. O'Donnell[a], Nicholas T. Van Dam[b]

[a] Phoenix Australia Centre for Post-traumatic Mental Health, Department of Psychiatry, University of Melbourne, Parkville, VIC, Australia
[b] Melbourne School of Psychological Sciences, University of Melbourne, Parkville, VIC, Australia

ARTICLE INFO

Keywords:
Active inference
Perceptual inference
Bayesian brain
Posttraumatic stress disorder
Predictive coding
Interoception

ABSTRACT

While there are a number of recommended first-line interventions for posttraumatic stress disorder (PTSD), treatment efficacy has been less than ideal. Generally, PTSD treatment models explain symptom manifestation via associative learning, treating the individual as a passive organism - acted upon - rather than self as agent. At their core, predictive coding (PC) models introduce the fundamental role of self-conceptualisation and hierarchical processing of one's sensory context in safety learning. This theoretical article outlines how predictive coding models of emotion offer a parsimonious framework to explain PTSD treatment response within a value-based decision-making framework. Our model integrates the predictive coding elements of the perceived: self, world and self-in the world and how they impact upon one or more discrete stages of value-based decision-making: (1) mental representation; (2) emotional valuation; (3) action selection and (4) outcome valuation. We discuss treatment and research implications stemming from our hypotheses.

Current understanding and treatment of post-traumatic stress disorder (PTSD) is heavily influenced by fear extinction learning (see Zuj and Norrholm, 2019). Such models posit that individuals with PTSD fail to adapt to intense, novel stimuli and learn in maladaptive ways. Current first-line treatments of PTSD are trauma-focused in that they present the trauma stimuli in objectively safe contexts resulting in the inhibition of conditioned associations. In contrast to fear extinction models (which build on conceptualisations of stimulus-response systems), predictive coding models situate learning around an 'active self' that: (1) predicts the sensory input that it will receive if one or another course of action is taken, (2) selects action to achieve the most desired outcome, (3) experiences the outcome of action selection, (4) adjusts itself (subjective expectation or interoceptive state) and (5) updates pre-existing models as a result of surprising outcomes. The active self also acts upon the environment and changes it to suit expectations and desires. To give context to the way in which predictive coding models impact behaviour, value-based models of decision-making (VBDM) provide a useful applied framework. The integration of these two frameworks situates the way in which an embodied self, based on active inference of interoceptive and exteroceptive signals, anticipates experiences, compares experiences to predictions, and evaluates the way in which mismatches of predictions and experiences themselves are used to inform future predictions. Such models may not only be able to account for historical successes of fear extinction learning but may also help to explain why some individuals do not respond to trauma-focused treatments. The key to the ability of such models to integrate pre-existing research and conceptualisations to explain exhibition of, and recurrent failure to, learn with respect to: 1. Mental representation biases perpetuated by rigidly held beliefs (i.e. strong threat priors - "I will never be safe"), inaccurate bias towards and predictions of negative outcomes (i.e. prediction errors – "I am in danger", "I will be hurt or killed"), and a de-emphasis or poor updating from safety prediction errors (i.e. low-precision weighting – "That I escaped safely this time was a fluke"); 2. Emotion valuation difficulties due to a discordance of memory, experience and engagement impact an individual's sense of emotional presence and agency (e.g. an over-reliance on negative salience despite no fear cues, i.e. emotion discordance or threat detection); 3. Action-selection inflexibility impacting the use of novel and varying strategies to resolve discrepancies between expected (danger) and desired states (safety) (e.g. flexibly choosing available actions to resolve the discrepancy between perceived and desired states, i.e. limited emotion regulation repertoire); 4. Outcome evaluation inaccuracies due

* Correspondence to: Phoenix Australian Centre for Post-traumatic Mental Health, 3/161 Barry Street, Carlton, VIC 3053, Australia.
E-mail address: andrea.putica@unimelb.edu.au (A. Putica).

https://doi.org/10.1016/j.neubiorev.2022.104704
Received 26 September 2021; Received in revised form 5 April 2022; Accepted 17 May 2022
Available online 21 May 2022
0149-7634/

to a bias in processing present contextual sensory information as dangerous or threatening (e.g. biased processing of outcomes and affective states following a chosen action). The integrated framework of predictive coding and VBDM holds much potential to improve upon prevailing models of PTSD aetiology and treatment.

The fear conditioning model is central in explaining the development of exposure-based treatments for PTSD via habituation and/or inhibitory learning. Although our understanding of the mechanisms responsible for the effects of fear conditioning has evolved over the years (see Craske et al., 2008), the foundational principals are based on Pavlov's (1927) work in classical conditioning, where a learned association between a previously neutral stimulus (conditioned stimulus; CS) and an aversive stimulus (unconditioned stimulus; US), leads to heightened US-expectancy of the CS. After learning, the CS alone generates a conditioned fear response in absence of the US. Within a Pavlovian-conditioning approach, the original CS-US association remains intact while inhibitory learning about the CS-US develops, such that the CS no longer predicts the US (e.g. Bouton, 1993). An example of how this principle has been applied to the experience of a traumatic event follows. An individual involved in an armed robbery (US) is likely to experience a natural response of fear and heightened physiological arousal (the unconditioned response; UCR). Following the robbery, aspects of the trauma that were not associated with the robbery before (e.g. a black-hooded sweatshirt), may act as a trigger to activate the trauma memory, eliciting the CR. For an in-depth review of associative fear learning, please see Li and McNally (2014).

However, the reality outside the laboratory is more complex in a number of ways. While fear conditioning processes can explain the acquisition of conditioned fear, they cannot fully explain the fact that only 20% of those who experience a traumatic event go on to develop PTSD (Bryant, 2003). Naturalistic recovery from traumatic experiences may be attributed to fear extinction learning (Guthrie and Bryant, 2006) – a process of new learning in which repeated exposure to a conditioned stimulus in the absence of an aversive consequence leads to a reduction in conditioned fear responses (Myers et al., 2006). In the context of trauma, this typically involves exposure to trauma reminders without aversive consequences. The prevailing model of PTSD is that the disorder is caused and perpetuated by impaired-fear extinction processes (Zuj and Norrholm, 2019). The prominence of the fear extinction model has led to the development of trauma-focused treatments, such as Prolonged Exposure (PE; Foa and Rothbaum, 1998), which aim to expose patients to trauma cues and memories in order to facilitate extinction learning via emotional processing of these conditioned stimuli. Although fear extinction learning has been paramount in our understanding and treatment of PTSD, it fails to completely predict who will develop PTSD after a traumatic event and is unable to entirely predict who will respond to trauma-focused therapies (Markowitz and Fanselow, 2020). Further, impaired fear extinction learning has been linked to fear-related features of PTSD (re-experiencing, hyperarousal, intrusive memories), but other features may not be well characterised by this approach (guilt, shame, anger).

A number of therapeutic strategies have been found to enhance inhibitory learning and its retrieval (see Craske et al., 2008). One such strategy is to design exposure scenarios that maximally violate expectancies regarding the frequency or intensity of aversive outcomes (Rescorla and Wagner, 1972). This strategy derives from the premise that the mismatch between expectancy and outcome is critical for new learning (i.e. prediction error; Rescorla and Wagner, 1972) and for the development of inhibitory expectancies that will compete with excitatory expectancies. While the concept of prediction errors in fear extinction is akin to prediction errors in predictive coding theories, the latter introduce prediction error signals along a variety of domains (e.g. action values) at multiple levels of processing (hierarchical in nature). In other words, the strength of a belief will effect the strength of the error necessary to update one's internal model. For example, those with a significant trauma history may have prior experiences (referred to as *priors* from this point forward) across multiple domains which are more "ingrained"/ higher in the self-referential hierarchy, requiring self-referential (as opposed to external) anticipatory errors to consolidate adaptive post-trauma learning. Therefore predictive errors must extend beyond a mismatch between anticipated and experienced outcomes (as is the case in inhibitory learning) to include sensory experiences regarding self, world and others. Taking these latter mechanisms into account is paramount; as it is recognised that fear extinction/exposure involves features extending beyond simple fear inhibition learning (as modelled in the standard fear extinction procedure). For example, processes related to early life adversity and ongoing life stress are important individual differences that moderate fear conditioning and extinction (Craske et al., 2018).

The inability of fear extinction learning to fully predict who will respond to treatment (i.e. after cumulative traumatic exposures) may be due an overreliance on the self as object; directly contrasting with the self as an agent (one who generates cognitions, expectations or beliefs, and acts upon the environment to suit its expectations). The self as object develops simple associations (Skinner, 1977) and is incapable of interpreting experiences through the lens of priors in the form of beliefs/ previous experiences. In this context, beliefs, as well as the way that prediction errors influence beliefs, are inconsequential. The self as agent, in contrast, understands experience via an interpretative lens and considers one's role in influencing or changing experience, expanding upon cognitive theories (Beck and Haigh, 2014; Ehlers and Clark, 2000). A hallmark feature of PTSD, consistent with Ehlers and Clark's cognitive model, is negative thoughts about oneself, the world and others (e.g. I'm not competent; the world is unpredictable; others will not protect me (American Psychiatric Association, 2013)). These negative appraisals are not easily explained by traditional learning theories and have been shown to have an independent relationship to PTSD symptomology (not interacting with fear extinction; Zuj et al., 2017). Moreover, numerous studies have shown that post-traumatic negative appraisals significantly predict later PTSD symptomology (e.g. Ehring et al., 2008). To target the impacts of negatively held cognitions, Resick and Schnicke (1992) introduced Cognitive Processing Therapy (CPT) as an alternative treatment for PTSD. CPT consists of two integrated components: cognitive therapy and exposure in the form of writing and reading about the traumatic event. Treatment focuses on distorted and overgeneralised beliefs about oneself and the world. The exposure component in CPT is used to identify "stuck points (i.e. areas of conflicting beliefs, leaps of logic and/or blind assumptions). While CPT, along with contemporary cognitive models, focus on excessively negative appraisals and the autobiographical nature of the self (see e.g. Ehlers and Clark, 2000), they overlook the important role of moment-by-moment affective experience in interpreting and predicting experience.

The recognised importance of self-referential processes in fear learning has been recognised by the foundational contemporary work by LeDoux and Pine (2016). In direct contrast to earlier emphasis on automated physiological responses occurring outside of conscious awareness, the authors highlighted the important role of conscious feeling states reflected in the subjective experience of fear and anxiety. The critical role of subjective experience is supported by research showing that damage to the amygdala, widely thought of as a brain region critical to intense emotion, does not prevent people from experiencing fear and panic after inhaling CO_2 (Feinstein et al., 2013). LeDoux and Pine (2016) speculate that experiences of fear are additionally processed (over and above subcortical regions) by higher-order brain circuits involving the prefrontal cortices. Neural connections within these higher-order networks allow individuals to make sense of a threat in light of memories (emotion schema) and self-reflection (self-schema).

While traditional fear learning models do not account for self-appraisals, predictive coding theories propose an internal working model of an agent which comprises past experiences, current context, and predictions about the future. Consistent with Bayes' theorem, probable causes of experience (posteriors) are estimated as a function of the relationship between probabilities (likelihoods) and prior 'beliefs' about causes. A mismatch between what is expected (predictions), as a function of beliefs (priors), and what happens (posterior) results in a prediction error. Internal states contribute to internal and/or external schemata, the result of which matches or mismatches subsequent experience in the body and the world (Seth, 2013). Prediction errors are weighted by 'precision' which determine the extent to which the prediction error influences prior beliefs; low-precision weighting results in little influence of a prediction error on prior beliefs. Additionally, certain priors (e.g. fundamental threat attributions) are held quite strongly and are resistant to modification (Kube et al., 2020; Linson and Friston, 2019).

Such agentic models nicely explain the subjective experience of negative affect in relation to trauma, something overlooked by contemporary cognitive models. In the context of a traumatic event, a strong prior 'belief' would be generated in response to trauma-related cues and their likelihood to portend danger given the threatening significance of the event and the accompanied physiological reactions. The strong prior is likely to be re-selected in future situations even if it does not match the current, objective sensory input. The agent's experience (or posterior) results from the Bayesian integration between the (strong) prior and the likelihood. The experience then shifts towards the most precise source of information. When the prior for danger is more precise than likelihood (for safety), the agent will experience the situation as being more dangerous than it actually is. The trauma prior is unlikely to be modified despite inaccurate predictions due to the strength of the prior, as strong priors are not easily changed (see Fig. 1). As a result, the prior dominates perception, perpetuating negative emotions such as depressed mood and fear. Given the intensity and regularity of these negative emotions, they can be reinstated and perceived as current, rather than associated with a discrete event in the past (i.e. lack of differentiation between previous danger and current safety). Importantly, the failure to differentiate past from present emotions may be related to a broad deficit of pattern separation (see e.g. Lange et al., 2017).

The present articles outlines how predictive coding models of emotion explain PTSD and its treatment within a value-based decision-making framework. Kube et al. (2020) conceptualised the clinical profile of PTSD using a predictive processing perspective. We offer an extension of this important work by integrating the predictive coding perspective into discrete stages of value-based decision creating a framework of clinical formulation, tailored treatment planning and, research. To our knowledge, this is the first article that integrates advances in affective and computational neuroscience in a value-based decision-making framework to explain mechanisms inhibiting adaptive learning and subsequent treatment response in PTSD. Firstly, we outline that PTSD is a problem within one or more of the following value-based decision-making stages: (1) mental representation; (2) emotional valuation; (3) action selection and, (4) outcome valuation. Finally, we will present clinical and research implications stemming from our hypotheses. It is important to note that not all of the outlined elements are completely unique to predictive coding accounts, however we do posit that our theorised overall formulation model may offer a novel way in formulating individualised treatments (including augmentations of existing treatments), which we outline in the latter part of this manuscript.

1. Predictive coding models of emotion

Predictive coding models can explain much more than just negative cognitions. Models such as the Embodied Predictive Interoception Coding (EPIC; Barrett and Simmons, 2015) and the Predictive Coding Model (PC; Seth et al., 2011), along with the Theory of Constructed Emotion (Barrett, 2017) hypothesise that the brain is constantly generating and updating a mental model of the self, environment and the self-in the environment (Seth et al., 2011). Such models postulate that emotional awareness, a major contributor to representations of the self, is partially based on interoceptive feeling states (i.e. awareness of the bodily state) emerging from the interactions of predictions regarding bodily afferents (signals coming towards the central nervous system; predictions) and the actual experienced afferents (what is actually experienced by the central nervous system) resulting in an internal prediction error (Critchley and Garfinkel, 2017). Notably, similar predictions are made and prediction errors experienced in relation to proprioception (i.e. bodily position/action) and exteroception (i.e. activity in the world and on the body; see Fig. 2; Seth and Friston, 2016). A sense of emotional agency, or emotional presence is achieved when mental representations are successfully matched to experience, resulting in a minimal error signal. However, error signals are not always processed equally and attention to these signals varies as a function of precision weighting. When high, precision weighting results in greater attention to error signals and when low, lesser attention to error signals. A large error signal due to imprecise or misinformed predictions can overwhelm the individual, leading to a reduced sense of presence or agency (Paulus and Stein, 2006).

While fear extinction models posit the importance of prediction errors in learning (see e.g. Rescorla and Wagner, 1972), they largely overlook the possibility of strongly held priors. The updating process of the internal model (i.e. learning) relies on the strength with which prior predictions are held and the extent to which posterior probabilities are integrated. Priors with low-precision (reliability or confidence ascribed to prediction errors at each level of the predictive hierarchy), such as "I'm safe here and now", are more likely to be updated than their stronger, negative counterparts (e.g. "the world is a dangerous place").

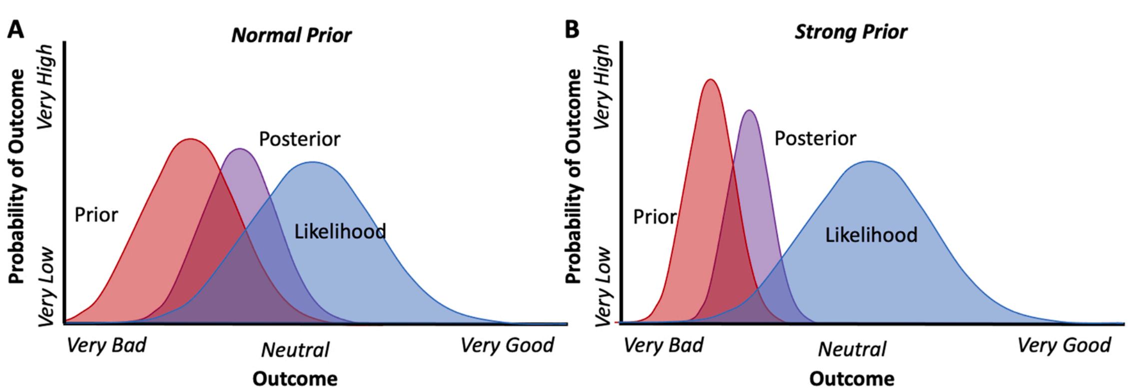

Fig. 1. Panel A represents relationship between prior, posterior, and likelihood with normal priors while Panel B represents the same relationship under strong priors. Per Bayes Theorem, the posterior is generated as a combination of the prior belief (e.g. I'm unsafe) and the likelihood of the outcome given the current information (alternative e.g. I'm safe). Since the posterior shifts towards the most precise source of information, when the prior is strong, the extent of the shift towards the alternative will be smaller than for the normative prior.

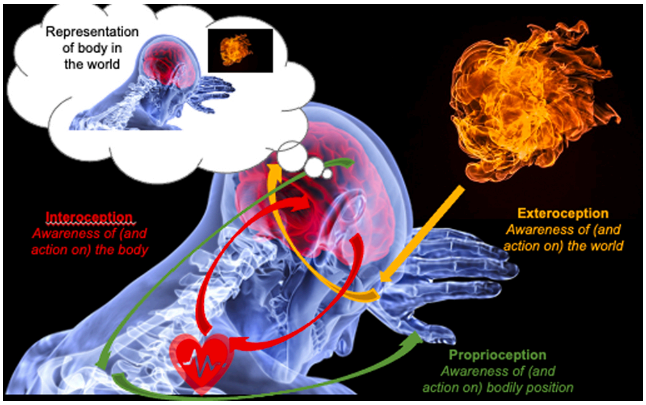

Fig. 2. Inference and perception. The brain is always building and refining its representations or models of the self, internal and external worlds. Green arrows represent proprioceptive predictions underlying action and experience of body ownership. Orange arrows represent exteroceptive predictions underlying perceptual content, such as the visual and tactile experience of fire. Red arrows represent interoceptive predictions underlying mood and autonomic regulation. (For interpretation of the references to colour in this figure, the reader is referred to the web version of this article.)

Similarly, prediction errors may be weighted at multiple levels, increasing or decreasing the influence that they have on the model. Prediction errors in associative learning models are not emphasized or de-emphasized as a function of precision weighting (influenced by conscious awareness; Meijs et al., 2018) nor do they consider the role of beliefs and their potential resistance to change. According to the predictive coding framework, updating of prior beliefs depends in part on the uncertainty of sensory input. The uncertainty, known as inverse precision, is defined by whether the source of error is attributable to irreducible uncertainty (i.e. the complex nature of the world which cannot ever be perfectively predicted) or reducible uncertainty (i.e. an individual lack of knowledge; Kwisthout et al., 2017). Adjusting the internal model in response to prediction errors depends on the error uncertainty of sensory information, with precise sensory data (i.e. more reliable – source of uncertainty is known) having more influence on the updating process than imprecise sensory information (i.e. less reliable – source of uncertainty is unknown and possibly unknowable; Kwisthout et al., 2017).

In PTSD, predictive processing entails a complex interplay between emotion generation and subsequent processing. As we will outline, a number of our concepts are not novel or unique to predictive coding, however, the integration of predictive coding with value-based decision-making offers a parsimonious framework for clinical formulation and treatment planning. Specifically, our model may help understand the effects of cumulative trauma exposure, early life adversity and emotion regulation deficits on the fear conditioning process. Put into the context of decision-making (see Rangel et al., 2008), the dynamic process entails the following: (1) a mental representation of options, along with internal and external states, (2) perceived value associated with action – especially the emotional value, (3) selection of actions based on 1–2, (4) evaluation of the outcome relative to predictions, (5) updating of prior stages via learning processes (see Fig. 3). We hypothesise that PTSD presentations and treatment response will result from one or more problems in value-based decision-making: (1) mental representation; (2) emotional valuation; (3) action selection and (4) outcome evaluation, deficits in one or more of these stages hinder the individual's ability to update perceptions based on new data (i.e. learning). We outline how problems in each of these stages of value-based decision-making presents in PTSD and how it not only perpetuates the disorder but explains heterogeneity in treatment resistance using conceptual, empirical and clinical evidence. Predictive coding models of emotion are also critical here as they situate the process of behaviour within the subjective realm

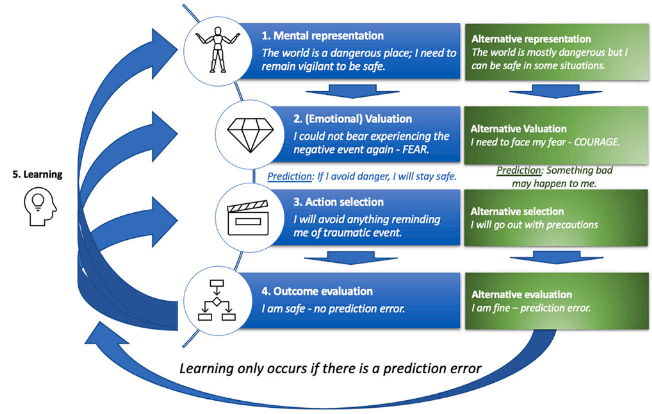

Fig. 3. Proposed predictive coding informed value-based decision-making model, for learning deficits in PTSD. Blue boxes represent maladaptive PTSD related appraisals. Green boxes represent adaptive 'healthy' appraisals. (For interpretation of the references to colour in this figure, the reader is referred to the web version of this article.)

based on information from previous experiences to construct experiences in real time, tinged by emotional experience. Each of these stages can present cumulatively or individually to deficits of safety learning in PTSD. The value of such an approach is that certain stages of the model may be more abnormal for certain individuals, leading to personalised implications. In the next section we outline each of our proposed hypotheses relating to these problems.

2. Mental representation

2.1. Mental representation: conceptual

A predictive coding account of PTSD must first and foremost acknowledge that the prediction model is inefficient, inaccurate, and resistant to change. High allostatic load (i.e. cumulative stress on the body) undermines the efficiency of the brain's internal predictive model by de-coupling affective components from memory and experience, thus impairing emotion processing and predictions. Emerging evidence supports the notion that the brain minimises free-energy by anticipating the content of internal and external events (Chanes and Barrett, 2017). The anticipation is realized via the construction of embodied simulations (full-bodied representations of sensory experience; Barsalou, 2008) which then function as Bayesian filters (Deneve, 2008) for incoming sensory input. Rather than perceiving reality as it is, input is seen through the influence of the simulations which drive action and construct perception. Changes associated with the anticipation of negative outcomes function as plans for ongoing system-wide physiological adjustment to impending physical and emotional challenges. From the external perspective, avoidance behaviour ensures that the prediction of needing to avoid something to stay safe is not challenged, therefore no prediction error is generated and no learning occurs. At a subjective level, certain aspects of the loop can be and often are discounted and/or modified. In PTSD, past experience results in selection and modification of processing by continuously anticipating unpleasant and threatening events in the body (e.g. hyperarousal - interoception) and environment (e.g. hypervigilance - exteroception). In the context of bodily awareness, unanticipated information from both internal and external sensory domains modulates expectations, and perceptions, or bottom-up signals (e.g. increased heartbeat; for a review see Petzschner et al., 2021). Error signals track the difference between the predicted sensations and incoming sensations, identifying discrepancies between the top-down and bottom-up signals (e.g. perceiving no explicit threat but feeling hyper-aroused in the body).

We posit that if internal and external events are processed through embodied simulations, the individual perception may actually be one of continuous danger. Avoidance coping is perceived as effective even if the threat is not real (see e.g. Badour et al., 2012), for reasons mentioned above – avoidance guarantees safety. Alternatively, the individual may use this experience to further reinforce their negative priors for danger, which become even more precise and less malleable to change. Diminution of prediction errors, when they do occur, would result in continued strong prior beliefs about a dangerous world, inhibiting learning and further reinforcing the strength of priors, making them less malleable. While energetically inefficient, it may be experienced as a necessary expenditure, albeit one with serious consequences in the form of allostasis and its associated consequences. We hypothesis that this seemingly perpetual loop of trauma/threat-related prior-driven perception and behaviour reinforcing a continuously stressful embodied simulation of danger (with deleterious secondary multiple-system consequences) interferes with an individual's readiness and ability to engage or even prioritise engagement with treatment. While we acknowledge that negative cognition is not a new concept related to PTSD, it may explain how these cognitions perpetuate PTSD symptomatology and limit treatment response.

2.2. Mental representation: empirical

Many established models of trauma-related psychological sequalae highlight the strength and role of the individual's negative beliefs (priors) about self, others and the world (Ehlers and Clark, 2000; Foa and Rothbaum, 1998; Resick and Schnicke, 1992) in the development and maintenance of PTSD (for a review of literature see Brown et al., 2019). Foa and Rothbaum (1998) emphasise the role of unrealistic appraisals in the development and maintenance of PTSD symptomology, particularly: "the world is dangerous, I am incompetent, and others cannot be trusted". Negative beliefs have been found to discriminate between trauma-exposed individuals with and without PTSD (Zoellner et al., 2011), and to predict the course of chronic PTSD (Dunmore et al., 2001). Consistent with these theories, more severe negative post-traumatic cognitions are associated with more severe PTSD symptoms (e.g. Kleim et al., 2013; Oh et al., 2016; Ter Heide et al., 2017; Tutus and Goldbeck, 2016; Zhou, . et al., 2015) or a greater likelihood of meeting criteria for PTSD (e.g. Dunmore et al., 1999; Jelinek et al., 2013; Karl et al., 2009; Startup et al., 2007). Specifically, individuals whose trauma memories reflected mental defeat (i.e. perception that they gave up, or had no perceived will during the traumatic experience) showed chronic PTSD symptomology (i.e. limited natural fear extinction; Dunmore et al., 2001; Kleim et al., 2007) and little improvement from exposure treatment (i.e. limited therapeutic fear extinction; Ehlers et al., 1998). There are several ways in which mental defeat might impact fear extinction. First, an assault which is experienced within the context of mental defeat is likely to be perceived as more severe. Second, it is generally agreed that it is important to repeatedly revisit the traumatic event in order to promote differentiation between previous danger and current safety. Unfortunately, in cases where mental defeat is prominent, reliving may be less effective, and remind the individual of their perceived incompetence, helplessness or acopia.

The important role of beliefs in PTSD outcomes is further supported by work showing that brief Cognitive Behaviour Therapy produced changes in beliefs regarding oneself and one's safety, and that these changes mediated pre to post symptom changes in PTSD (Zoellner et al., 2011). Furthermore positive shifts in these beliefs have been found to mediate long-term improvement in PTSD symptomatology (Zoellner et al., 2011). Significantly, the impact of PTSD related appraisals has been found to predict later PTSD severity over and above initial post-trauma symptomatology (Dunmore et al., 2001) further adding support for the detrimental role of strong trauma-related priors in PTSD trajectories.

2.3. Mental representation: clinical

Clinically, we hypothesise that patients with biased mental representation may not only possess strong negative beliefs about themselves, others and the world, but also experience greater negative affect. These individuals may find it difficult to integrate new information from exposure activities with their trauma narratives, inhibiting the emotion processing necessary for PTSD treatment response. As a result of this ongoing PTSD symptomology, those with mental representation biases may have poorer quality of life (see Mueser et al., 2015) and engagement in pro-health behaviours, contributing to a heightened allostatic load (see Glover et al., 2006). High allostatic load can also result from or perpetuate health-damaging lifestyle habits such as: lack of physical activity, unhealthy diet, and sleep disturbances (Forrester et al., 2019). Clinically, these markers may serve as functional indicators of mental representation deficits, affording the therapist with interventional targets to 'stabilise' the patient until they are ready to engage in trauma-focused psychotherapy. Our decisional-value model recognises and incorporates the well-established direct relationship between the strength of trauma-related beliefs (priors) and the way in which those beliefs impact individual's evaluations about the world, especially one's emotional experience, a topic to which we will turn to next.

3. Emotional valuation

3.1. Emotional valuation: conceptual

Emotion valuation is the processing of one's internal and external states to assign value to available *actions* (cognitive or behavioural – aimed at altering an emotional state; Ochsner and Gross, 2014). The ability to engage with one's interoceptive and exteroceptive states is paramount in assigning accurate value to all available actions. A discordance between physiological and affective components (i.e. emotion response discordance) and exaggerated threat detection may hinder an individual's sense of emotional presence and emotional agency (see Brown et al., 2020). Specifically if an individual does not have well-integrated emotional awareness, their ability to resolve discrepancies between current and desired emotional states is undermined. Poor emotional valuation impacts an individual's ability to be shaped or modify action based on unfolding emotional experience (Ochsner and Gross, 2014).

Emotion response concordance is characterised by within-individual associations among physiological (arousal) and subjective emotional components (appraisal). We hypothesise that a disconnect between the psychological ("I'm really distressed") and the physiological (no acute change in heart rate) can result from an internally energy inefficient model, which is either insensitive to prediction errors and/or poorly calibrated precision estimates. Such discordance may present in the brain as a lack of confidence understanding and interpreting what is happening in one's experience or "noisy afferent interoceptive inputs" (Paulus and Stein, 2010). Beliefs that interoception is unreliable foster internal predictive uncertainty, resulting in increased attempts to control and predict these inputs (Feldman Barrett and Simmons, 2015). When ascending sensory input is noisy or imprecise - the active inference framework hypothesizes that prediction errors will be resolved not by changing the source of the prediction (i.e. the mental model) but by shifting bodily state and/or perspective to match the error (Feldman Barrett and Simmons, 2015). In other words, the system will reduce attention to the sensory input or actively alter autonomic and metabolic systems in the body to match the sensory prediction.

A lack of confidence in interoceptive signalling may limit an individual's ability to detect salience in the environment, whether it be reward or threat is essential for survival, i.e. when it's important for one to lean into these signals for contextual affective information (e.g. emotion numbing). Conversely, individuals with deficits in emotional valuation may also present with overly sensitive negative salience (or threat) detection. Hypersensitive salience detection could heighten vigilance anxiety sensitivity, and threat reactivity in PTSD – minimizing capacity to detect safety signals, as well as activating fear and protective responses disproportionate to actual threats (Sripada et al., 2012). Exaggerated threat detection or threat-related attentional biases have been proposed as one such potential target in PTSD (Armstrong and Olatunji, 2012). Cognitive models for PTSD have implicated several faulty cognitive processes in the disorder (Brewin and Holmes, 2003), including: attentional biases towards and away from threat (Bar-Haim, 2010), poor attentional control (Lazarov et al., 2019). However, our model while related to the aforementioned perspectives further-expand on them by situating them in relation to psychophysiology and interoceptive processing of current versus desired affective states.

3.2. Emotional valuation: empirical

The importance of situating cognitive affective components within physiology and is evidenced by findings that emotional memory consolidation is directly impacted by interactions of cortisol and noradrenaline in the basolateral amygdala of animals (Roozendaal et al., 2009), and humans (McGaugh, 2004). In the context of processing emotional memory, learning (i.e. consolidation) and/or over-learning (i.e. reconsolidation) is diminished when physiological signalling is attenuated (by administering beta-blockers, for example; Lonergan et al., 2013). While there is some suggestion that such pharmacological agents could be helpful in acute discordance of arousal from trauma memories (see e.g. Giustino et al., 2016), persistent interference with the concordance of somatic and cognitive signals related to emotion may actually interfere with treatment, perpetuating the very discordance that forms part of the aetiology of the condition. While propranolol (a drug that interferes with somatic signals of emotion) can facilitate extinction learning in acute settings (for example see Elsey et al., 2020), it has been shown to be most useful under conditions where stress is high and norepinephrine levels are elevated beyond those optimal for learning (Fitzgerald et al., 2015). In other words, there may be an optimal range of concordance between psycho-physiological components necessary for emotional processing (see e.g. Yerkes Dodson Law; Yerkes and Dodson, 1908) for new learning to occur. In contrast to beta-blockers, which suppress physiological signals, benzodiazepines indiscriminately depress neural functioning across the brain (Guina et al., 2015), which can inhibit the cognitive fear activation necessary for functional exposure (Rosen et al., 2013). Evidence suggests that benzodiazepine use is associated with a poor response to trauma-focused treatments (Guina et al., 2015). Therefore, we hypothesise that a lack of concordance between affective components impacts an individual's ability to fully engage with emotional states to make the (accurate) emotional valuations necessary for learning.

We additionally hypothesise that enhanced threat detection or an attentional bias to threat, associated with increased salience network activation, which has previously been observed in PTSD patients, also impacts one's ability to make accurate emotional valuations (Pannu Hayes et al., 2009). Hypersensitive salience detection could heighten vigilance and threat reactivity in PTSD and activate fear and protective responses disproportionate to actual threats (Liberzon and Abelson, 2016). Excessive activity in the salience network has been found to predict poor treatment response among those with PTSD (van Rooij et al., 2016). Therefore, exaggerated tending to threat may be a further mechanism which limits an individual's ability to be shaped or modify behaviour based on unfolding objective emotional experience.

3.3. Emotional valuation: clinical

The impact of psycho-physiological discordance is clinically exemplified in individuals high in alexithymia, a population associated with PTSD treatment resistance (Kosten et al., 1992). Individuals high in alexithymia tend to report elevated levels of distress (appraisal) despite experiencing minimal autonomic arousal (Eastabrook et al., 2013; Peasley-Miklus et al., 2016). Discordance between arousal and appraisal components may explain why individuals high in alexithymia are able to label basic emotions such as happy or sad but cannot describe the internal states (e.g. increased heart rate) that correspond to these descriptors and instead tend to focus on global states of emotional arousal, misinterpreting bodily sensations (Taylor and Bagby, 2004). Individuals with alexithymia also demonstrate reduced ability to locate affect-related responses in their bodies, reflecting limited awareness of somatic sensations accompanying feelings (Nemiah et al., 1976), and have an increased tendency to report experiencing little to no emotion in response to arousing stimuli (Aaron et al., 2018; Putica et al., 2021). Such lack of emotional awareness is of particular concern in emotional processing as the ability to regulate emotional states (and hence provide an appropriate emotional appraisal of a given situation or behavioural option) arise from the integration of autonomic and cognitive processes (Critchley et al., 2002). The inability to differentiate arousal states can result in restricted response strategies across emotions, as may be evident in the case of anger, wherein any arousal is perceived as reflecting the same emotion and required the same response (see e.g. Harmon-Jones et al., 2009). Deficits of emotional awareness will undoubtedly lead to all states being assigned a comparable subjective label (e.g. "negative" or "bad" or "threatening") and modulate the perceived emotional value of available actions. In the case of exaggerated threat detection commonly observed in PTSD, such atypical salience detection can hinder an individual's ability to assign values to available action. The aforementioned suggests that discordance between affective components or exaggerated pre-occupation with threat detection will impact one's ability to select the most adaptive course of action in bridging the gap between their experienced and desired state. The logical follow-on from such bias in emotional valuation is a bias in the process of selecting behaviours that favour safety.

4. Action selection

4.1. Action selection: conceptual

The third mechanistic deficit of our model as it pertains to PTSD and its treatment is a difficulty in flexibly selecting available actions to resolve discrepancies between desired or expected and sensed emotional states (Paulus and Stein, 2010). Inflexibility in action selection among those with PTSD may be a product of diminished executive function (Liberzon and Abelson, 2016). Executive function is a group of faculties by which we manage cognitive processes, and includes mechanisms of working memory, attention, inhibition, and task shifting (Diamond, 2013). Deficits in these domains impact one's ability to make real-time comparisons between sensed and desired states by impacting contextual processing (Liberzon and Abelson, 2016). The comparison between sensed and expected states serves two major functions: 1. To orient us to the surprising physiological changes that require immediate attention (perceptual inference) and 2. To allow comparison between current and potential future states as a cue to action (active inference). We hypothesise that action-selection inflexibility is caused by individuals with PTSD avoiding engaging in behaviours which are novel or different, and falsely attributing safety to avoidance behaviour despite the absence of any real threat. Specifically, action-selection inflexibility may be a result of heightened distress tolerance and/or anxiety sensitivity, observed among those with PTSD (Marshall-Berenz et al., 2010; Taylor, 2003). This inflexibility may account for the pervasive negative affect (O'Donnell et al., 2004) and reduced quality of life reported by those with PTSD (Vogt et al., 2017). From a learning perspective, inflexibility in action selection inhibits adaptive emotion regulation required for safety learning and even working memory capacity, necessary for overall learning ability (Pe et al., 2013). The pervasive negative and undesired affect observed among those with PTSD, supports our hypothesis that these individuals cannot flexibly select an action to bridge the gap between experienced and desired state.

4.2. Action selection: empirical

Specific to PTSD literature, an inflexibility in action selection may be akin to emotion regulation inflexibility (predisposition to use one strategy to change an internal or external world). Evidence demonstrates that cognitive reappraisal in PTSD is associated with reduced lateral and medial prefrontal activation (Bryant et al., 2020). There is also evidence that treatment with selective serotonin reuptake inhibitors can ameliorate initial deficits in emotion regulation-related prefrontal brain function. Moreover, baseline emotion regulation brain deficits negatively predict treatment-related benefits (MacNamara et al., 2016). It is important to note that flexibility of regulation strategy choice in the context of real-time situational attributes is more critical than use of potentially arbitrary categories of 'adaptive' vs. 'maladaptive' strategies (Aldao et al., 2014). Specific to PTSD, emotion regulation inflexibility has been found to moderate the association between traumatic exposure and PTSD symptomatology (Levy-Gigi et al., 2015). Inflexible emotion response is believed to be a result of an individual being unable to match between core characteristics of regulatory options (actions) and emotional events. Specifically, there are some highly aversive emotional situations, including potentially traumatic events, where choosing to disengage may actually promote adaptation to the stimuli/events (see e.g. Park, 2010). However, applying disengagement regulatory options (e.g. avoidance) to emotional events that are tolerable (high-distress tolerance) may function as a risk factor for the development of anxiety disorders (see, e.g. Campbell-Sills et al., 2006). Flexible real-time action selection is thus critical to PTSD recovery. The relationship of inflexible disengagement and anxiety supports our hypothesis that inflexible action selection hinders learning in PTSD.

4.3. Action selection: clinical

Clinically, patients with action-selection inflexibility are more likely to present with substance-misuse disorders. Drinking alcohol to excess blunts negative affect and may therefore be perceived as an effective or maladaptive action choice (see e.g. Becker, 2008). The importance of assessing for deficits in action selection flexibility is particularly pertinent as approximately half of individuals seeking treatment for substance misuse disorders treatment meet criteria for PTSD (Brady et al., 2004), and individuals with co-occurring PTSD and substance-misuse disorders tend to have poorer treatment outcomes compared to those without this comorbidity (Berenz and Coffey, 2012). It may also be that those who predominately engage in emotional and experiential avoidance may present with high co-morbidities with other emotional disorders (e.g. Major Depressive Disorder; or Generalized Anxiety Disorder; Campbell-Sills. et al., 2006). The over-reliance on avoidance strategies observed among those with PTSD, and indeed other pathologies supports our notion that inflexibility in available action selection perpetuates PTSD pathology. Therefore, those presenting with PTSD and other co-morbidities would benefit from a functional assessment of action-selection flexibility to identify deficits in this stage of value-based decision value which may hinder learning, and subsequent treatment response.

5. Outcome evaluation

5.1. Outcome evaluation: conceptual

The final mechanism of focus is biased processing of outcomes and affective states (internal and external) following a chosen action. Precision signals optimise the sampling of the sensory periphery for allostasis. If a prediction error is anticipated to be relevant for allostasis and therefore worth the metabolic cost of encoding and consolidation, then the gain in these errors is accordingly modulated. These predictions are called precision signals. In predictive coding, precision describes the reliability or confidence ascribed to prediction errors at each level of the predictive hierarchy. Therefore, inaccurate precision signals result in unreliable prediction errors. Precision signals are based on priors developed according to cumulative experience (or in the case of a traumatic experience, a heavily weighted single event or set of cumulative events signalling threat). Precision signals modulate the sampling of contextual sensory experience. Specific to PTSD, the emotionally shocking nature of a traumatic event results in a recalibration of the internal model to sensitise the system to internal and external signals indicating threat (objectively and subjectively), attributing such information the greatest precision weighing. Trauma-weighted sampling of the sensory periphery will prevent the individual from processing real-time objective sensory data. We posit that inaccurate precision signals (heavily weighted towards information signalling danger) inhibit the updating of priors by not providing the individual with real-time, contextual information necessary for outcome evaluation (e.g. "the situation was safe, my chosen actions kept me safe' vs. 'that was a lucky escape, I was fortunate I got out of there when I did"). The role of inaccurate precision signals in outcome evaluation is supported by Kube and colleagues (2020) who theorise that priors at low levels of the predictive hierarchy (objective sensory information which can differentiate between index trauma and current context) are given too little precision, whereas high-level priors are afforded too much precision (anything resembling or activating a fear memory structure). As a result, strong beliefs override sensory information and dominate perception (Benriomoh et al., 2018) inhibiting fear extinction learning by limiting the opportunity to differentiate between index trauma and current contextual information, such as "the world is safe, I was competence at keeping myself safe". The inability to take contextual information into account in favour of anything resembling threat limits the updating of danger-, threat-, and/or trauma-related priors.

5.2. Outcome evaluation: empirical

The implication of problematic precision signal processing (i.e. not giving appropriate weighting to contextual priors and affording too much weighting to historic priors signalling danger is demonstrated; Garfinkel et al. (2014) found that PTSD patients exhibited both abnormally high fear in safety contexts and abnormally low fear in danger contexts. The authors suggest that people with PTSD are characterised by a general deficit in processing contextual information, resulting in the inability to properly modulate brain activity and psycho-physiological responses in accordance to contextual information. Similarly, Jovanovic et al. (2010) found those with PTSD had a higher fear-potentiated startle to safety signals compared to healthy and depressed controls. The PTSD group did not exhibit fear inhibition to safety cues, which was linked to higher PTSD symptom severity (Jovanovic et al., 2009). The significance of contextual information processing on PTSD treatment response was also demonstrated by van Rooij et al. (2014), who compared PTSD patients receiving trauma-focused psychotherapies with combat controls and found that left inferior parietal lobe (IPL) activation during a stop-signal anticipation task at baseline significantly predicted treatment response, as defined by a 30% reduction in clinician-administered PTSD scale scores at post-treatment. The IPL is involved in contextual cue processing, an important component of fear extinction learning, which itself is highly dependent on the context in which it takes place (Shipherd and Salters-Pedneault, 2008). The aforementioned evidence supports our hypothesis that ineffective precision signalling, or inability to accurately identify prediction errors worthy of encoding and consolidation, inhibits processing of contextual information necessary to differentiate between safe and dangerous contexts and outcomes. Individuals with PTSD prioritise sensory information which may indicate threat, dismissing information at lower predictive levels which suggest safety (for a review see Liberzon and Abelson, 2016). Without objective data about the world, individuals with PTSD are not afforded repeated exposure to a CS in the absence of an aversive consequence, which is necessary for a reduction in condition-fear responses. The relationship between contextual information and safety learning among those with PTSD supports the importance of accurate precision signals in updating of priors from threat to relative safety.

5.3. Outcome evaluation: clinical

Magnitude of between session habituation is paramount, as there is mounting evidence that it is the most predictive of treatment outcome in exposure therapy (Sripada and Rauch, 2015). Individuals with inaccurate precision sampling may show limited between session habituation to exposure trials despite their seemingly appropriate emotional engagement. Clinically, such a patient may be observed to discount a successful exposure trial, in which they were able to tolerate distress and habituate within the trial. Instead, the patient may discount this success as specific to the particular session, i.e. behavioural discrimination (Yassa and Stark, 2011). For example, a patient who successfully engages in an exposure trial with a dog, may tell the therapist “I'm only OK, because it was a small white dog on a leash; they are not dangerous, however all other dogs are dangerous”. However, due to this failure of generalization it is not clinically possible to conduct exposure trials targeting each of the potential permutations of exposures with dogs (large white dog on lead, small black dog on lead, etc.) to update a strongly weighted prior, one precision signal at a time. In other words these individuals may demonstrate attenuated pattern completion and enhanced behaviour discrimination. Pattern completion, a process by which partial or degraded cues reinstate previously stored representations, is associated with behavioural generalization (McClelland et al., 1995); while pattern separation, a process by which overlapping representations are made distinct, is associated with behavioural discrimination (Yassa and Stark, 2011). Negative overgeneralisation (commonly observed in PTSD) has also been shown to be rooted in mechanisms of modulation at encoding and pattern completion (McMakin et al., 2020). The association between poor pattern completion and /or exaggerated behavioural discrimination with PTSD supports our hypothesis that unreliable precision signals inhibit an individual ability to evaluate the outcome of a situation (e.g. I was safe, I was able to keep myself safe). Due to the apparent resistance to change across the aforementioned domains, it is recommended that the therapist assess the client for problems in the preceding decisional-value steps. In the following section we outline how our presented hypotheses elaborate on current PTSD treatments.

5.4. Implications for treatment

Although efficacious treatments for PTSD exist (such as Prolonged Exposure Therapy; Foa and Rothbaum, 1998), these treatments (based on fear extinction learning) could fail within the aforementioned stages of decision-making specific to the outlined stages, existing trauma-focused PTSD treatments do not typically target: 1. Biases in mental representation (e.g. perceiving emotions, situations, and trauma memories as inherently dangerous) inhibiting optimal engagement necessary for therapeutic exposures; 2. Difficulties with emotion valuation impacting an individual's sense of emotional presence and agency to move between current and desired emotion states; 3. Inflexibility in action selection which may inhibit therapeutic engagement in novel exposures; and 4. Inaccuracies in outcome evaluation that impact the updating of threat perceived priors. However, we appreciate that existing treatments are largely compatible with parts of the account proposed above (e.g. with respect to the aim of modifying dysfunctional beliefs of PTSD patients; see e.g. Ehlers et al., 2005). Therefore, instead of calling for new treatment approaches per se, we call for the personalisation of clinical formulation and corresponding treatment based on the provided learning framework. Below we present how adjunct could be added to pre-existing PTSD treatments to address deficits across each of afore-outlined stages.

5.5. Mental representation

We recognise that strong priors are often difficult to modulate, however there has been some evidence showing the efficacy in cognitive based approaches, such as Cognitive Processing Therapy (CPT) in successfully modulating strongly held PTSD-related appraisals amongst rape survivors (Iverson et al., 2015) and combat veterans (Monson et al., 2006). Concerningly, treatment non-response rates for CPT have shown to be similar to those of PE (Monson et al., 2006). Therefore, it is not surprising that it has been postulated that individuals who do not benefit from CPT may need to engage in further work challenging and restructuring strongly held priors to successfully ameliorate their symptoms (Stein et al., 2012). Skills Training in Affective and Interpersonal Regulation (STAIR; Cloitre and Schmidt, 2015) is one such phase-based treatment designed to identify core beliefs that are maladaptive and try to moderate these, as well as do emotion regulation (which includes identifying and labelling emotions) prior to engaging the patient in trauma-focused treatments. Furthermore, the role of interoception in modulating strongly held priors is supported by findings showing that changing the bodily milieu via physical activity and/or relaxation might be of benefit (Rosenbaum et al., 2015).

5.6. Emotional valuation

A potential alternative treatment for individuals with aberrations in emotional valuation is the Unified Protocol (UP). UP is an emotion-focused, cognitive-behavioural intervention developed to target core temperamental characteristics underlying emotional disorders. Development of the treatment is based on findings that individuals with emotional disorders not only experience heightened levels of negative affect, but they also find the experience of negative emotions more distressing and are less accepting of their emotional experiences than healthy individuals (Tull and Roemer, 2007). Consequently, they engage in efforts to suppress or avoid the emotional experience, which paradoxically results in the persistence of emotional distress and associated interference (impaired habituation; Abramowitz et al., 2001; Moore et al., 2008). It is the interpretation of emotions as unacceptable or intolerable and subsequent attempts to control the emotional experience that is the proposed mechanism for the maintenance of emotional disorder symptomatology (Barlow et al., 2014). The primary hypothesised mechanism of change in UP is the development of present-focused, non-judgemental emotional awareness to reduce emotional suppression and prolonged reactivity to emotional experiences making it a viable alternative, non-trauma-focused treatment for patients presenting with PTSD and emotional processing deficits (e.g. those high in alexithymia). Difficulties with psycho-physiological discordance are addressed via tracking of the three components of emotional experience (cognitive, physiological and behavioural), therefore increasing attention and concordance between physiological and appraisal components in emotional experiences.

5.7. Action selection

Specifically speaking to our aforementioned biases (active and inference) mindfulness based interventions (e.g. Mindfulness Based Stress Reduction; Kabat-Zinn, 1990) or interoceptive training (Young et al., 2019), or exposures may help increase emotion regulation flexibility, therefore challenging a predisposition to one form of inference (active or perceptual). The exposures used are designed to induce arousal-related but harmless bodily sensations. Examples from Taylor (2000) include: spinning in a chair, hyperventilation, breath holding, breathing through a narrow straw, running up stairs, and staring at a visual grid (which induces visual illusions). These exercises are safe and effective in producing bodily sensations, such as dizziness, dyspnea, faintness, palpitations, paresthesias, and derealisation (Taylor, 2000). The importance of interoception promoting emotional agency is supported by findings demonstrating that awareness of one's bodily feelings seem to be of central importance for the effective regulation of emotional responses (for review, see Pinna and Edwards, 2020). This is supported by several studies exploring benefits of adjunct interoceptive exposures prior to PE and found that interoceptive exposures were associated with decreased PTSD symptomology and improved emotion regulation at post-treatment with further reductions in symptomology reported at three-, six- and, twelve-month follow-up (Wald and Taylor, 2007).

5.8. Outcome evaluation

Sensory discrimination training aimed at improving patients' ability to accurately process sensory information may also be a valuable adjunct to PTSD interventions. Sensory discrimination training addresses the easy triggering of intrusive memories by matching sensory cues. Patients learn to identify the subtle sensory triggers of re-experiencing and learn to realise that they are not responding to objective 'real-time' information. This is achieved by the patient learning to pay close attention to the differences between the trauma-related stimuli and the present context (then vs now). Sensory discrimination training has shown promising results in the treatment of phantom limb pain (Moseley and Wiech, 2009) and is also considered an important part of cognitive treatment approaches for PTSD (Ehlers et al., 2005). Similarly neuro- and bio-feedback training may also be plausible adjuncts. Both of these approaches involve the modulation of either brain activity via fMRI or EEG activity (neurofeedback) or physiological activity such as heart rate (biofeedback). This increased attention to and agency over precision signal to overcome an allostatic challenge may facilitate upgrading of the internal model and generalise into a greater sense of general agency. This is supported by findings demonstrating both approaches to be efficacious in improving PTSD symptomology, reported quality of life and motivations for subsequent trauma-focused treatments (Chiba et al., 2019; Morina et al., 2012; van der Kolk et al., 2016). Treatments could also target circuits that are related to conscious feeling states. For example, some patients may display aberrant stimulus generalization and fail to recognise or appropriately label the boundaries separating different gradations of threat, leading them to inappropriately label ambiguous stimuli as threatening (LeDoux and Pine, 2016). For these patients, treatment may begin by incrementally teaching them to improve their ability to recognize, describe, and label these nuanced boundaries.

5.9. Limitations and future research

In the present article, we aimed to outline mechanisms of maladaptive learning in PTSD and treatment response through the lens of predictive coding. Although we hope that this account may provide useful insights into the understanding of PTSD presentations and treatment, we also recognise that it has some limitations.

Firstly, we acknowledge that while our listed stage-specific interventions are an example of modalities aimed to primarily target stage-specific deficits, they may also equally impact other stages as well. For example, while we indicate that lifestyle medicine approaches for deficits in mental representation (stage 1), these functional indicators may also impact action selection (stage 3) as there is an established interplay between sleep and emotion regulation (Mauss et al., 2013). However, we view these non-discrete secondary effects of proposed interventions as a fortuitous benefit of our approach. Ongoing evaluation of our proposed mechanisms will yield more data about how our interventions effect discrete and all proposed stages.

Further, we acknowledge that predictive coding accounts to psychiatric presentations is not unique to PTSD. Rather these positions may provide a unified framework for deviations in mechanisms which may explain heterogeneity within and between clinical presentations. For example, predictive coding positions have been useful in formulating perceptual disturbance in psychosis as a mismatch between prior beliefs and incoming signals (Fletcher and Frith, 2009). However, in the context of PTSD, higher weighting provided to cues signalling danger and lower weighting (i.e. noise) provided to cues signalling safety prohibit the updating of priors necessary to challenging the beliefs that the world is perpetually dangerous.

Our account does not distinguish explicitly between different trauma types, co-morbidities or clinical subtypes. Several authors have argued that different traumatic events may have differential effects on the course of symptoms and the prognosis of treatment, depending on whether it is a single-incident (Type 1) versus multiple (Type 2) traumas and whether the trauma is interpersonal in nature (Ehring and Quack, 2010). However, previous accounts (Kube et al., 2020; Wilkinson et al., 2017) suggest that the predictive coding framework might be well compatible with trauma types and symptom profiles. However, it is arguable that our account of PTSD and treatment response at the mental representation stage may be attributable to pre-existing psycho-developmental vulnerabilities, such as childhood maltreatment (see e.g. Van Dam et al., 2014).

It is important to note that the predictive coding model does not reduce PTSD to a single cause or treatment to one modality. Rather it is a novel and unified framework which could personalise treatment via combinations of existing approaches. Due to the theoretical nature of our proposed perspective, the integration of these four stages and their corresponding physiological and psychological components within the predictive processing framework does not have any current specific clinical implications. We hope that future additional research will facilitate the discovery of specific clinical uses. However, the hypotheses presented herein need to be tested via empirical work and revised according to those elements that are verified versus disconfirmed. Accordingly, we discuss possible directions for future research into the mechanisms of PTSD treatment that are pressing from a predictive coding perspective. In Table 1, we present additional specific hypotheses derived from our account. We also present some suggestions as to how this could be validated experimentally.

Mental representations provide an individual with information about potential courses of action that need to be evaluated, as well as the internal and external states that inform those evaluations, therefore dysregulations in mechanisms of allostasis may be a proxy for measuring difficulties in this stage. Research exploring whether mental representation problems in PTSD are linked to high allostatic load could explore the link between markers of allostatic load (e.g. cortisol, cumulative trauma/stress measures), psychopathology, and psychosocial difficulties. Secondly, emotional valuation difficulties as characterised by psycho-physiological discordance could use explore intercorrelations of physiological and psychological responding to emotional stimuli such a trauma-script task. Third, to test our hypothesis that problems in the action-selection stage are a result of an inference bias which is operationalised by emotion regulation inflexibility research could utilise Ecological Momentary Analysis (EMA) to assess regulation strategy variance. Further research could also use emotion flexibility paradigm (Sheppes et al., 2014) and assess how closely performance on this is associated with one's interoceptive accuracy which is measured by tasks such as the heartbeat detection task (Schandry, 1981). In regard to our final hypothesis regarding difficulties in outcome evaluation relating to threat, the use of pre-pulse inhibition (PPI) tasks may help assess whether contextual sensory processing deficits are linked to less treatment response in trauma-focused treatments. PPI involves a measure of arousal modulation and orientation to the environment. PPI is an automatic and pre-attentive process, whereby a weak stimulus attenuates responding to a sudden and intense startle stimulus. This weak stimulus reduces interruption of ongoing processing by the startle response and enhances subsequent processing of the most salient aspect

Table 1
Testable Hypotheses for Future Research.

Stage	Hypothesis	Experimental Examination
Mental representation	Predisposition to threat-danger related priors would be linked to greater PTSD symptom severity, general emotion dysregulation (e.g. atypical interoception, emotional clarity, anger) and psychosocial functioning/ decline.	Threat-danger related priors (measured by self-reports, e.g. Posttraumatic Cognitions Inventory or World Assumptions Scale; Personal Beliefs and Reactions Scale) is related psychopathology severity (PTSD and secondary disorders and psychosocial problems) and emotional regulation problems as measured by self-reports.
Emotion valuation	Psycho-physiological discordance will be linked to reduced engagement with trauma-related stimuli.	Concordance between physiological (e.g. HRV; GSR) and psychological (e.g. subjective appraisal) during a trauma-script paradigm.
Action selection	Treatment non-responders will exhibit emotion regulation inflexibility (over-dependence on avoidance) and limited interoceptive awareness.	Ecological Momentary Assessment (EMA) of variability and efficacy in emotion regulation strategy Extinction of avoidance Paradigms (Vervliet and Indekeu, 2015). Impact of Interoceptive awareness (e.g. heartbeat detection; Schandry, 1981) on performance on an emotion-regulation choice paradigm (e.g. Sheppes et al., 2014).
Outcome evaluation	Treatment non-responders will have lower ability to take in contextual information to differentiate between dangerous and safe contexts.	Performance on a Pre-Pulse Inhibition (PPI) task, or the Browning et al. (2015) volatility paradigm; fear-potentiated startle paradigm (Jovanovic et al., 2005).

of the environment (Blumenthal et al., 2015). Therefore, PPI may provide insight into how an individual with PTSD attunes to sensory information of different quality and intensity, i.e. tending to safety- and startle/threat-related contextual sensory information.

6. Conclusion

In this article, we drew on recent advances in predictive coding models of emotion to outline potential difficulties in value-based decision-making for PTSD and related treatment response. This is of particular importance given the high rate of treatment non-response among those with PTSD. Specifically we outlined how PTSD presentations and treatment response may result from one or more problems in stages of value-based decision making: (1) mental representation; (2) emotional valuation; (3) action selection and, (4) outcome evaluation. Given the promising new research directions that were inspired by previous predictive coding accounts of mental disorders, we believe that this perspective can also provide novel insights and research into the understanding of mechanisms of PTSD treatment resistance.

CRediT authorship contribution statement

Development and writing of manuscript: A.P., N.V.D Editing, conceptual/theoretical feedback of manuscript: K.F., M.G, N.V.D. Editing, feedback of manuscript: M.O., K.F, N.V.D Writing, conceptual/ theoretical supervision/ input and editing of manuscript: NVD.

Declarations of interest

None.

References

Aaron, R.V., Snodgress, M.A., Blain, S.D., Park, S., 2018. Affect labelling and other aspects of emotional experiences in relation to alexithymia following standardized emotion inductions. Psychiatry Res. 262, 115–123. https://doi.org/10.1016/j.psychres.2018.02.014.

Abramowitz, J.S., Tolin, D.F., Street, G.P., 2001. Paradoxical effects of thought suppression: a meta-analysis of controlled studies. Clin. Psychol. Rev. 21, 683–703. https://doi.org/10.1016/s0272-7358(00)00057-x.

Aldao, A., Jazaieri, H., Goldin, P.R., Gross, J.J., 2014. Adaptive and maladaptive emotion regulation strategies: interactive effects during CBT for social anxiety disorder. J. Anxiety Disord. 28 (4), 382–389. https://doi.org/10.1016/j.janxdis.2014.03.005.

American Psychiatric Association, 2013. Diagnostic and Statistical Manual of Mental Disorders, fifth ed. American Psychiatric Publishing,, Arlington, VA.

Armstrong, T., Olatunji, B.O., 2012. Eye tracking of attention in the affective disorders: a meta-analytic review and synthesis. Clin. Psychol. Rev. 32 (8), 704–723. https://doi.org/10.1016/j.cpr.2012.09.004.

Badour, C.L., Blonigen, D.M., Boden, M.T., Feldner, M.T., Bonn-Miller, M.O., 2012. A longitudinal test of the bi-directional relations between avoidance coping and PTSD severity during and after PTSD treatment. Behav. Res. Ther. 50 (10), 610–616. https://doi.org/10.1016/j.brat.2012.06.006.

Bar-Haim, Y., 2010. Research review: Attention bias modification (ABM): a novel treatment for anxiety disorders. J. Child Psychol. Psychiatry, Allied Discip. 51 (8), 859–870. https://doi.org/10.1111/j.1469-7610.2010.02251.x.

Barlow, D.H., Sauer-Zavala, S., Carl, J.R., Bullis, J.R., Ellard, K.K., 2014. The nature, diagnosis, and treatment of neuroticism: back to the future. Clin. Psychol. Sci. 2, 344–365. https://doi.org/10.1177/2167702613505532.

Barrett, F.L., 2017. The theory of constructed emotion: An active inference account of interoception and categorization. Soc. Cogn. Affect. Neurosci. 12 (1), 1–23. https://doi.org/10.1093/scan/nsw154.

Barrett, L.F., Simmons, W.K., 2015. Interoceptive predictions in the brain. Nat. Rev. Neurosci. 16, 419–429. https://doi.org/10.1038/nrn3950.

Barsalou, L.W., 2008. Grounded cognition. Annu. Rev. Psychol. 59, 617–645.

Beck, A.T., Haigh, E.A.P., 2014. Advances in cognitive theory and therapy: the generic cognitive model. Annu. Rev. Clin. Psychol. 10, 1–24. ⟨http://10.1146/annurev-clinpsy-032813-153734⟩.

Becker, H.C., 2008. Alcohol dependence, withdrawal, and relapse. Alcohol. Res. Health. J. Natl. Inst. Alcohol. Abus. Alcohol. 31 (4), 348–361.

Benriomoh, D., Parr, T., Vincent, P., Adams, R.A., Friston, K., 2018. Active inference and auditory hallucinations. Comput. Psychiatry 2, 183–204. https://doi.org/10.1162/cpsy_a_00022.

Berenz, E.C., Coffey, S.F., 2012. Treatment of co-occurring posttraumatic stress disorder and substance use disorders. Curr. Psychiatry Rep. 14 (5), 469–477. https://doi.org/10.1007/s11920-012-0300-0.

Blumenthal, T.D., Reynolds, J.Z., Swawapence, T.E., 2015. Support for the interruption and protection hypotheses of prepulse inhibition of startle: Evidence from a modified attention network test. Psychophysiology 52 (3). https://doi.org/10.1111/psyp.12334.

Bouton, M.E., 1993. Context, time, and memory retrieval in the interference paradigms of Pavlovian learning. Psychol. Bull. 114 (1), 80–99. https://doi.org/10.1037/0033-2909.114.1.80.

Brady, K.T., Back, S.E., Coffey, S.F., 2004. Substance abuse and posttraumatic stress disorder. Curr. Dir. Psychol. Sci. 13 (5), 206–209. https://doi.org/10.1111/j.0963-7214.2004.00309.x.

Brewin, C.R., Holmes, E.A., 2003. Psychological theories of posttraumatic stress disorder. Clin. Psychol. Rev. 23 (3), 339–376. https://doi.org/10.1016/s0272-7358(03)00033-3.

Brown, C.L., Van Doren, N., Ford, B.Q., Mauss, I.B., Sze, J.W., Levenson, R.W., 2020. Coherence between subjective experience and physiology in emotion: Individual differences and implications for well-being. Emotion 20 (5), 818–829. https://doi.org/10.1037/emo0000579.

Brown, L.A., Belli, G.M., Asnaani, A., Foa, E.B., 2019. A review of the role of negative cognitions about oneself, others, and the world in the treatment of PTSD. Cogn. Ther. Res. 43 (1), 143–173. https://doi.org/10.1007/s10608-018-9938-1.

Browning, M., Behrens, T.E., Jocham, G., O'Reilly, J.X., Bishop, S.J., 2015. Anxious individuals have difficulty learning the causal statistics of aversive environments. Nat. Neurosci. 18 (4), 590–596. https://doi.org/10.1038/nn.3961.

Bryant, R.A., 2003. Early predictors of posttraumatic stress disorder. Biol. Psychiatry 53, 789–795. https://doi.org/10.1016/s0006-3223(02)01895-4.

Bryant, R.A., Erlinger, M., Felmingham, K., Klimova, A., Williams, L.M., Malhi, G., Forbes, D., Korgaonkar, M.S., 2020. Reappraisal-related neural predictors of treatment response to cognitive behavior therapy for post-traumatic stress disorder. Psychol. Med. 1–11. https://doi.org/10.1017/S0033291720001129 (Advance online publication).

Campbell-Sills, L., Barlow, D.H., Brown, T.A., Hofmann, S.G., 2006. Acceptability and suppression of negative emotion in anxiety and mood disorders. Emotion 6, 587–595. https://doi.org/10.1037/1528-3542.6.4.587.

Chanes, L., Barrett, L.F., 2017. Redefining the role of limbic areas in cortical processing. Trends Cogn. Sci. 20, 96–106. https://doi.org/10.1016/j.tics.2015.11.005.

Chiba, T., Kanazawa, T., Koizumi, A., Ide, K., Taschereau-Dumouchel, V., Boku, S., Hishimoto, A., Shirakawa, M., Sora, I., Lau, H., Yoneda, H., Kawato, M., 2019. Current status of neurofeedback for post-traumatic stress disorder: a systematic review and the possibility of decoded neurofeedback. Front. Hum. Neurosci. 13, 1–13. https://doi.org/10.3389/fnhum.2019.00233.

Cloitre, M., Schmidt, J.A., 2015. STAIR Narrative Therapy. In: Schnyder, U., Cloitre, M. (Eds.), Evidence based treatments for trauma-related psychological disorders: A practical guide for clinicians. Springer International Publishing AG, pp. 277–297. https://doi.org/10.1007/978-3-319-07109-1_14.

Craske, M.G., Kircanski, K., Zelikowsky, M., Mystkowski, J., Chowdhury, N., Baker, A., 2008. Optimizing inhibitory learning during exposure therapy. Behav. Res. Ther. 46 (1), 5–27. https://doi.org/10.1016/j.brat.2007.10.003.

Craske, M.G., Hermans, D., Vervliet, B., 2018. State-of-the-art and future directions for extinction as a translational model for fear and anxiety. Philos. Trans. R. Soc. Lond. Ser. B, Biol. Sci. 373 (1742), 20170025 https://doi.org/10.1098/rstb.2017.0025.

Critchley, H.D., Garfinkel, S.S., 2017. Interoception and emotion. Curr. Opin. Psychol. 17, 7–14. https://doi.org/10.1016/j.copsyc.2017.04.020.

Critchley, H.D., Mathias, C.J., Dolan, R.J., 2002. Fear conditioning in humans: the influence of awareness and autonomic arousal on functional neuroanatomy. Neuron 33 (4), 653–663. https://doi.org/10.1016/s0896-6273(02)00588-3.

Deneve, S., 2008. Bayesian spiking neurons i: inference. Neural Comput. 20 (1), 91–117. https://doi.org/10.1162/neco.2008.20.1.91.

Diamond, A., 2013. Executive functions. Annu. Rev. Psychol. 64, 135–168. https://doi.org/10.1146/annurev-psych-113011-143750.

Dunmore, E., Clark, D.M., Ehlers, A., 1999. Cognitive factors involved in the onset and maintenance of posttraumatic stress disorder (PTSD) after physical or sexual assault. Behav. Res. Ther. 37 (9), 809–829. https://doi.org/10.1016/s0005-7967(98)00181-8.

Dunmore, E., Clark, D.M., Ehlers, A., 2001. A prospective investigation of the role of cognitive factors in persistent posttraumatic stress disorder (PTSD) after physical or sexual assault. Behav. Res. Ther. 39 (9), 1063–1084. https://doi.org/10.1016/s0005-7967(00)00088-7.

Eastabrook, J.M., Lanteigne, D.M., Hollenstein, T., 2013. Decoupling between physiological, self-reported, and expressed emotional responses in alexithymia. Personal. Individ. Differ. 55, 978–982. https://doi.org/10.1016/j.paid.2013.08.001.

Ehlers, A., Clark, D.M., 2000. A cognitive model of posttraumatic stress disorder. Behav. Res. Ther. 38 (4), 319–345. https://doi.org/10.1016/s0005-7967(99)00123-0.

Ehlers, A., Clark, D.M., Dunmore, E., Jaycox, L., Meadows, E., Foa, E.B., 1998. Predicting response to exposure treatment in PTSD: the role of mental defeat and alienation. J. Trauma. Stress 11 (3), 457–471. https://doi.org/10.1023/A:1024448511504.

Ehlers, A., Clark, D.M., Hackmann, A., McManus, F., Fennell, M., 2005. Cognitive therapy for post-traumatic stress disorder: development and evaluation. Behav. Res. Ther. 43, 413–431. 〈http//:10.1016/j.brat.2004.03.006〉.

Ehring, T., Quack, D., 2010. Emotion regulation difficulties in trauma survivors: the role of trauma type and PTSD symptom severity. Behav. Ther. 41 (4), 587–598. https://doi.org/10.1016/j.beth.2010.04.004.

Ehring, T., Ehlers, A., Glucksman, E., 2008. Do cognitive models help in predicting the severity of posttraumatic stress disorder, phobia, and depression after motor vehicle accidents? A prospective longitudinal study. J. Consult. Clin. Psychol. 76 (2), 219–230. 〈http://10.1037/0022-006X.76.2.219〉.

Elsey, J., Filmer, A.I., Galvin, H.R., Kurath, J.D., Vossoughi, L., Thomander, L.S., Zavodnik, M., Kindt, M., 2020. Reconsolidation-based treatment for fear of public speaking: a systematic pilot study using propranolol. Transl. Psychiatry 10 (1), 179. https://doi.org/10.1038/s41398-020-0857-z.

Feinstein, J.S., Buzza, C., Hurlemann, R., Follmer, R.L., Dahdaleh, N.S., Coryell, W.H., Welsh, M.J., Tranel, D., Wemmie, J.A., 2013. Fear and panic in humans with bilateral amygdala damage. Nat. Neurosci. 16 (3), 270–272. https://doi.org/10.1038/nn.3323.

Fitzgerald, P.J., Giustino, T.F., Seemann, J.R., Maren, S., 2015. Noradrenergic blockade stabilizes prefrontal activity and enables fear extinction under stress. Proc. Natl. Acad. Sci. USA 112, E3729–E3737. https://doi.org/10.1073/pnas.1500682112.

Fletcher, P.C., Frith, C.D., 2009. Perceiving is believing: a Bayesian approach to explaining the positive symptoms of schizophrenia. Nat. Rev. Neurosci. 10 (1), 48–58. https://doi.org/10.1038/nrn2536.

Foa, E.B., Rothbaum, B.O., 1998. Treatment Manuals for Practitioners. Treating the Trauma of rape: Cognitive-Behavioral Therapy for PTSD. Guilford Press.

Forrester, S.N., Leoutsakos, J.M., Gallo, J.J., Thorpe, Jr. R.J., Seeman, T.E. , 2019. Association between allostatic load and health behaviours: A latent class approach. *Journal of Epidemiology and Community Health, 73(4),* 340–345. https://doi.org/10.1136/jech-2018–211289.

Garfinkel, S.N., Abelson, J.L., King, A.P., Sripada, R.K., Wang, X., Gaines, L.M., Liberzon, I., 2014. Impaired contextual modulation of memories in PTSD: An fMRI and psychophysiological study of extinction retention and fear renewal. J. Neurosci. 34 (40), 13435–13443. https://doi.org/10.1523/JNEUROSCI.4287-13.2014.

Giustino, T.F., Fitzgerald, P.J., Maren, S., 2016. Revisiting propranolol and PTSD: memory erasure or extinction enhancement? Neurobiol. Learn. Mem. 130, 26–33. https://doi.org/10.1016/j.nlm.2016.01.009.

Glover, D.A., Stuber, M., Poland, R.E., 2006. Allostatic load in women with and without PTSD symptoms. Psychiatry 69 (3), 191–203. https://doi.org/10.1521/psyc.2006.69.3.191.

Guina, J., Rossetter, S.R., DeRhodes, B.J., Nahhas, R.W., Welton, R.S., 2015. Benzodiazepines for PTSD: a systematic review and meta-analysis. J. Psychiatr. Pract. 21, 281–303. https://doi.org/10.1097/pra.0000000000000091.

Guthrie, R.M., Bryant, R.A., 2006. Extinction learning before trauma and subsequent posttraumatic stress. Psychosom. Med. 68 (2), 307–311. https://doi.org/10.1097/01.psy.0000208629.67653.cc.

Harmon-Jones, E., Harmon-Jones, C., Abramson, L., Peterson, C.K., 2009. PANAS positive activation is associated with anger. Emotion 9 (2), 183–196. https://doi.org/10.1037/a0014959.

Iverson, K.M., King, M.W., Cunningham, K.C., Resick, P.A., 2015. Rape survivors' trauma-related beliefs before and after Cognitive processing therapy: associations with PTSD and depression symptoms. Behav. Res. Ther. 66, 49–55. https://doi.org/10.1016/j.brat.2015.01.002.

Jelinek, L., Wittekind, C.E., Kellner, M., Moritz, S., Muhtz, C., 2013. Metacognitive beliefs in posttraumatic stress disorder following forced displacement at the end of the Second World War in older adults and their offspring. Cogn. Neuropsychiatry 18 (5), 452–462. https://doi.org/10.1080/13546805.2012.754749.

Jovanovic, T., Keyes, M., Fiallos, A., Myers, K.M., Davis, M., Duncan, E.J., 2005. Fear potentiation and fear inhibition in a human fear-potentiated startle paradigm. Biol. Psychiatry 57 (12), 1559–1564. https://doi.org/10.1016/j.biopsych.2005.02.025.

Jovanovic, T., Norrholm, S.D., Fennell, J.E., Keyes, M., Fiallos, A.M., Myers, K.M., Davis, M., Duncan, E.J., 2009. Posttraumatic stress disorder may be associated with impaired fear inhibition: relation to symptom severity. Psychiatry Res. 167 (1–2), 151–160. https://doi.org/10.1016/j.psychres.2007.12.014.

Jovanovic, T., Norrholm, S.D., Blanding, N.Q., Davis, M., Duncan, E., Bradley, B., Ressler, K.J., 2010. Impaired fear inhibition is a biomarker of PTSD but not depression. Depress Anxiety 27 (3), 244–251. https://doi.org/10.1002/da.20663.

Kabat-Zinn, J., University of Massachusetts Medical Center/Worcester, 1990. Full Catastrophe Living: Using the Wisdom of your Body and Mind to Face Stress, Pain, and Illness. Delacorte Press, New York, N.Y.

Karl, A., Rabe, S., Zollner, T., Maercker, A., Stopa, L., 2009. Negative self-appraisals in treatment-seeking survivors of motor vehicle accidents. J. Anxiety Disord. 23 (6), 775–781. https://doi.org/10.1016/j.janxdis.2009.03.001.

Kleim, B., Ehlers, A., Glucksman, E., 2007. Early predictors of chronic post-traumatic stress disorder in assault survivors. Psychol. Med. 37 (10), 1457–1467. https://doi.org/10.1017/S0033291707001006.

Kleim, B., Grey, N., Wild, J., Nussbeck, F.W., Stott, R., Hackmann, A., Clark, D.M., Ehlers, A., 2013. Cognitive change predicts symptom reduction with cognitive therapy for posttraumatic stress disorder. J. Consult. Clin. Psychol. 81 (3), 383–393. https://doi.org/10.1037/a0031290.

Kosten, T.R., Krystal, J.H., Giller, E.L., Dan, E., 1992. Alexithymia as a predictor of treatment response in post-traumatic stress disorder. J. Trauma. Stress 5, 41–50. https://doi.org/10.1007/BF00979225.

Kube, T., Berg, M., Kleim, B., Herzog, P., 2020. Rethinking post-traumatic stress disorder – a predictive processing perspective. Neurosci. Biobehav. Rev. 1113, 448–460. https://doi.org/10.1016/j.neubiorev.2020.04.014.

Kwisthout, J., Bekkering, H., van Rooij, I., 2017. To be precise, the details don't matter: on predictive processing, precision, and level of detail of predictions. Brain Cogn. https://doi.org/10.1016/j.bandc.2016.02.008.

Lange, I., Goossens, L., Michielse, S., Bakker, J., Lissek, S., Papalini, S., Verhagen, S., Leibold, N., Marcelis, M., Wichers, M., Lieverse, R., van Os, J., van Amelsvoort, T., Schruers, K., 2017. Behavioral pattern separation and its link to the neural mechanisms of fear generalization. Soc. Cogn. Affect. Neurosci. 12 (11), 1720–1729. https://doi.org/10.1093/scan/nsx104.

Lazarov, A., Suarez-Jimenez, B., Abend, R., Naim, R., Shvil, E., Helpman, L., Zhu, X., Papini, S., Duroski, A., Rom, R., Schneier, F.R., Pine, D.S., Bar-Haim, Y., Neria, Y., 2019. Bias-contingent attention bias modification and attention control training in treatment of PTSD: a randomized control trial. Psychol. Med. 49 (14), 2432–2440. https://doi.org/10.1017/S0033291718003367.

LeDoux, J.E., Pine, D.S., 2016. Using neuroscience to help understand fear and anxiety: a two-system framework. Am. J. Psychiatry 173, 1083–1093. https://doi.org/10.1176/appi.ajp.2016.16030353.

Levy-Gigi, E., Bonanno, G.A., Shapiro, A.R., 2015. Emotion regulation flexibility sheds light on the elusive relationship between repeated traumatic exposure and posttraumatic stress disorder symptoms. Clin. Psychol. Sci. 4, 1–12 https://doi.org/10.1177%2F2167702615577783.

Li, S.S., McNally, G.P., 2014. The conditions that promote fear learning: prediction error and pavlovian fear conditioning. Neurobiol. Learn. Mem. 108, 14–21. https://doi.org/10.1016/j.nlm.2013.05.002.

Liberzon, I., Abelson, J.L., 2016. Context processing and the neurobiology of post-traumatic stress disorder. Neuron 92 (1), 14–30. https://doi.org/10.1016/j.neuron.2016.09.039.

Linson, A., Friston, K.J., 2019. Reframing PTSD for computational psychiatry with the active inference framework. Cogn. Neuropsychiatry 24 (5), 347–368. https://doi.org/10.1080/13546805.2019.1665994.

Lonergan, M.H., Olivera-Figueroa, L.A., Pitman, R.K., Brunet, A., 2013. Propranolol's effects on the consolidation and reconsolidation of long-term emotional memory in healthy participants: a meta-analysis. J. Psychiatry Neurosci. 38 (4), 222–231. https://doi.org/10.1503/jpn.120111.

MacNamara, A., Rabinak, C.A., Kennedy, A.E., Fitzgerald, D.A., Liberzon, I., Stein, M.B., Phan, K.L., 2016. Emotion regulatory brain function and SSRI treatment in PTSD: neural correlates and predictors of change. Neuropsychopharmacol.: Off. Publ. Am. Coll. Neuropsychopharmacol. 41 (2), 611–618. https://doi.org/10.1038/npp.2015.190.

Markowitz, S., Fanselow, M., 2020. Exposure therapy for post-traumatic stress disorder: factors of limited success and possible alternative treatment. Brain Sci. 10 (3), 167. https://doi.org/10.3390/brainsci10030167.

Marshall-Berenz, E.C., Vujanovic, A.A., Bonn-Miller, M.O., Bernstein, A., Zvolensky, M. J., 2010. Multimethod study of distress tolerance and PTSD symptom severity in a trauma-exposed community sample. J. Trauma. Stress 23 (5), 623–630. https://doi.org/10.1002/jts.20568.

Mauss, I.B., Troy, A.S., LeBourgeois, M.K., 2013. Poorer sleep quality is associated with lower emotion-regulation ability in a laboratory paradigm. Cogn. Emot. 27 (3), 567–576. https://doi.org/10.1080/02699931.2012.727783.

McClelland, J.L., McNaughton, B.L., O'Reilly, R.C., 1995. Why there are complementary learning systems in the hippocampus and neocortex: Insights from the successes and failures of connectionist models of learning and memory. Psychol. Rev. 102, 419–457. https://doi.org/10.1037/0033-295X.102.3.419.

McGaugh, J.L., 2004. The amygdala modulates the consolidation of memories of emotionally arousing experiences. Annu. Rev. Neurosci. 27, 1–28. https://doi.org/10.1146/annurev.neuro.27.070203.144157.

McMakin, D.L., Kimbler, A., Tustison, N., Pettit, J., Mattfeld, A., 2020. Negative overgeneralization is associated with anxiety and mechanisms of pattern completion in peripubertal youth. bioRxiv. https://doi.org/10.1101/2020.01.27.921742.

Meijs, E.L., Slagter, H.A., de Lange, F.P., van Gaal, S., 2018. Dynamic interactions between top-down expectations and conscious awareness. J. Neurosci.: Off. J. Soc. Neurosci. 38 (9), 2318–2327. https://doi.org/10.1523/JNEUROSCI.1952-17.2017.

Monson, C.M., Schnurr, P.P., Resick, P.A., Friedman, M.J., Young-Xu, Y., Stevens, S.P., 2006. Cognitive processing therapy for veterans with military-related posttraumatic stress disorder. J. Consult. Clin. Psychol. 74 (5), 898–907. https://doi.org/10.1037/0022-006X.74.5.898.

Moore, S.A., Zoellner, L.A., Mollenholt, N., 2008. Are expressive suppression and cognitive reappraisal associated with stress-related symptoms? Behav. Ther. Res. 46, 993–1000 https://dx.doi.org/10.1016%2Fj.brat.2008.05.001.

Morina, N., Maier, T., Bryant, R., Knaevelsrud, C., Wittmann, L., Rufer, M., Schnyder, U., Müller, J., 2012. Combining biofeedback and narrative exposure therapy for persistent pain and PTSD in refugees: A pilot study. Eur. J. Psychotraumatol. 3, 17660 https://doi.org/10.3402/ejpt.v3i0.17660.

Moseley, G.L., Wiech, K., 2009. The effect of tactile discrimination training is enhanced when patients watch the reflected image of their unaffected limb during training. Pain 144, 314–319. https://doi.org/10.1016/j.pain.2009.04.030.

Mueser, K.T., Gottlieb, J.D., Xie, H., Lu, W., Yanos, P.T., Rosenberg, S.D., Silverstein, S. M., Duva, S.M., Minsky, S., Wolfe, R.S., McHugo, G.J., 2015. Evaluation of cognitive restructuring for post-traumatic stress disorder in people with severe mental illness. Br. J. Psychiatry.: J. Ment. Sci. 206 (6), 501–508. https://doi.org/10.1192/bjp.bp.114.147926.

Myers, K., Ressler, K., Davis, M., 2006. Different mechanisms of fear extinction dependent on length of time since fear acquisition. Learn. Mem. 13 (2), 216–223. ⟨http://www.learnmem.org/cgi/doi/10.1101/NA⟩.

Nemiah, J.C., Freyberger, H., Sifneos, P.E., 1976. Alexithymia: A View of the Psychosomatic Process. Butterworths, London.

Ochsner, K.N., Gross, J.J., 2014. The neural bases of emotion and emotion regulation: a valuation perspective. In: Gross, J.J. (Ed.), Handbook of Emotion Regulation. The Guilford Press, pp. 23–42.

O'Donnell, M.L., Creamer, M., Pattison, P., 2004. Posttraumatic stress disorder and depression following trauma: understanding comorbidity. Am. J. Psychiatry 161 (8), 1390–1396. https://doi.org/10.1176/appi.ajp.161.8.1390.

Oh, W., Muzik, M., McGinnis, E.W., Hamilton, L., Menke, R.A., Rosenblum, K.L., 2016. Comorbid trajectories of postpartum depression and PTSD among mothers with childhood trauma history: course, predictors, processes and child adjustment. J. Affect. Disord. 200, 133–141. https://doi.org/10.1016/j.jad.2016.04.037.

Pannu Hayes, J., Labar, K.S., Petty, C.M., McCarthy, G., Morey, R.A., 2009. Alterations in the neural circuitry for emotion and attention associated with posttraumatic stress symptomatology. Psychiatry Res. 172 (1), 7–15. https://doi.org/10.1016/j.pscychresns.2008.05.005.

Park, C.L., 2010. Making sense of the meaning literature: An integrative review of meaning making and its effects on adjustment to stressful life events. Psychol. Bull. 136 (2), 257–301.

Paulus, M.P., Stein, M.B., 2006. An insular view of anxiety. Biol. Psychiatry 60 (4), 383–387. https://doi.org/10.1016/j.biopsych.2006.03.042.

Paulus, M.P., Stein, M.B., 2010. Interoception in anxiety and depression. Brain Struct. Funct. 214, 451–463. https://doi.org/10.1007/s00429-010-0258-9.

Pavlov, I.P., 1927. Conditioned Reflexes: An Investigation of the Physiological Activity of the Cerebral Cortex. Oxford University Press,, Oxford, England.

Pe, M.L., Raes, F., Kuppens, P., 2013. The cognitive building blocks of emotion regulation: Ability to update working memory moderates the efficacy of rumination and reappraisal on emotion. PloS One 8 (7), e69071. https://doi.org/10.1371/journal.pone.0069071.

Peasley-Miklus, C.E., Panayiotou, G., Vrana, S.R., 2016. Alexithymia predicts arousal-based processing deficits and discordance between emotion response systems during emotional imagery. Emotion 16, 164. https://doi.org/10.1037/emo0000086.

Petzschner, F.H., Garfinkel, S.N., Paulus, M.P., Koch, C., Khalsa, S.S., 2021. Computational models of interoception and body regulation. Trends Neurosci. 44 (1), 63–76. https://doi.org/10.1016/j.tins.2020.09.012.

Pinna, T., Edwards, D.J., 2020. A systematic review of associations between interoception, vagal tone and emotional regulation: Potential applications for mental health, wellbeing, psychological flexibility and chronic conditions. Front. Psychol. 11. https://doi.org/10.3389/fpsyg.2020.01792.

Putica, A., Van Dam, N.T., Steward, T., Agathos, J., Felmingham, K.L., O'Donnell, M.L., 2021. Alexithymia in posttraumatic stress disorder is not just emotion numbing: Systematic review of neural evidence and clinical implications. J. Affect. Disord. 278, 519–527. https://doi.org/10.1016/j.jad.2020.09.100.

Rangel, A., Camerer, C., Montague, P.R., 2008. A framework for studying the neurobiology of value-based decision making. Nat. Rev. Neurosci. 9 (7), 545–556. https://doi.org/10.1038/nrn2357.

Rescorla, R.A., Wagner, A.R., 1972. A theory of pavlovian conditioning: variations in the effectiveness of reinforcement and nonreinforcement. In: Black, A.H., Prokasy, W.F. (Eds.), Classical Conditioning II: Current Research and Theory, 1972. Appleton Century Crofts, New York, pp. 64–99.

Resick, P.A., Schnicke, M.K., 1992. Cognitive processing therapy for sexual assault victims. J. Consult. Clin. Psychol. 60 (5), 748–756. https://doi.org/10.1037/0022-006X.60.5.748.

Roozendaal, B., McEwen, B.S., Chattarji, S., 2009. Stress, memory and the amygdala. Nat. Rev. Neurosci. 10 (6), 423–433. https://doi.org/10.1038/nrn2651.

Rosen, C.S., Greenbaum, M.A., Schnurr, P.P., Holmes, T.H., Brennan, P.L., Friedman, M. J., 2013. Do benzodiazepines reduce the effectiveness of exposure therapy for posttraumatic stress disorder? J. Clin. Psychiatry 74 (12), 1241–1248. https://doi.org/10.4088/JCP.13m08592.

Rosenbaum, S., Vancampfort, D., Steel, Z., Newby, J., Ward, P.B., Stubbs, B., 2015. Physical activity in the treatment of post-traumatic stress disorder: a systematic review and meta-analysis. Psychiatry Res. 230 (2), 130–136. ⟨https://doi.org/10.1016/j.psychres.2015.10.017⟩.

Schandry, R., 1981. Heart beat perception and emotional experience. Psychophysiology 18 (4), 483–488. https://doi.org/10.1111/j.1469-8986.1981.tb02486.x.

Seth, A.K., 2013. Interoceptive inference, emotion, and the embodied self. Trends Cogn. Sci. 17, 565–573. https://doi.org/10.1016/j.tics.2013.09.007.

Seth, A.K., Friston, K.J., 2016. Active interoceptive inference and the emotional brain. Philos. Trans. R. Soc. Lond. Ser. B, Biol. Sci. 371 (1708), 20160007 https://doi.org/10.1098/rstb.2016.0007.

Seth, A.K., Suzuki, K., Critchley, H.D., 2011. An interoceptive predictive coding model of conscious presence. Front. Psychol. 2, 1–16 https://dx.doi.org/10.3389%2Ffpsyg.2011.00395.

Sheppes, G., Scheibe, S., Suri, G., Radu, P., Blechert, J., Gross, J.J., 2014. Emotion regulation choice: a conceptual framework and supporting evidence. J. Exp. Psychol. Gen. 143 (1), 163–181. https://doi.org/10.1037/a0030831.

Shipherd, J.C., Salters-Pedneault, K., 2008. Attention, memory, intrusive thoughts, and acceptance in PTSD: An update on the empirical literature for clinicians. Cogn. Behav. Pract. 15 (4), 349–363. https://doi.org/10.1016/j.cbpra.2008.01.003.

Skinner, B.F., 1977. Why I am not a cognitive psychologist. Behaviorism 5 (2), 1–10.

Sripada, R.K., Rauch, S.A., 2015. Between-session and within-session habituation in prolonged exposure therapy for posttraumatic stress disorder: a hierarchical linear modeling approach. J. Anxiety Disord. 30, 81–87. https://doi.org/10.1016/j.janxdis.2015.01.002.

Sripada, R.K., King, A.P., Welsh, R.C., Garfinkel, S.N., Wang, X., Sripada, C.S., Liberzon, I., 2012. Neural dysregulation in posttraumatic stress disorder: evidence for disrupted equilibrium between salience and default mode brain networks. Psychosom. Med. 74 (9), 904–911. https://doi.org/10.1097/PSY.0b013e318273bf33.

Startup, M., Makgekgenene, L., Webster, R., 2007. The role of self-blame for trauma as assessed by the Posttraumatic Cognitions Inventory (PTCI): A self-protective cognition? Behav. Res. Ther. 45 (2), 395–403. https://doi.org/10.1016/j.brat.2006.02.003.

Stein, N.R., Dickstein, B.D., Schuster, J., Litz, B.T., Resick, P.A., 2012. Trajectories of response to treatment for posttraumatic stress disorder. Behav. Ther. 43 (4), 790–800. https://doi.org/10.1016/j.beth.2012.04.003.

Taylor, G.J., Bagby, R.M., 2004. New trends in alexithymia research. Psychother. Psychosom. 73, 68–77. https://doi.org/10.1159/000075537.

Taylor, S., 2000. Understanding and Treating Panic Disorder. Wiley, New York.

Taylor, S., 2003. Anxiety Sensitivity and Its Implications for Understanding and Treating PTSD. J. Cogn. Psychother. 17 (2), 179–186. https://doi.org/10.1891/jcop.17.2.179.57431.

Ter Heide, F.J.J., Sleijpen, M., van der Aa, N., 2017. Posttraumatic world assumptions among treatment-seeking refugees. Transcult. Psychiatry 54 (5–6), 824–839. https://doi.org/10.1177/1363461517741811.

Tull, M.T., Roemer, L., 2007. Emotion regulation difficulties associated with the experience of uncued panic attacks: Evidence of experiential avoidance, emotional nonacceptance and decreased emotional clarity. Behav. Ther. 38, 378–391. https://doi.org/10.1016/j.beth.2006.10.006.

Tutus, D., Goldbeck, L., 2016. Posttraumatic symptoms and cognitions in parents of children and adolescents with PTSD. Eur. Child Adolesc. Psychiatry 25 (9), 997–1005. https://doi.org/10.1007/s00787-016-0821-x.

Van Dam, N.T., Rando, K., Potenza, M.N., Tuit, K., Sinha, R., 2014. Childhood maltreatment, altered limbic neurobiology, and substance use relapse severity via trauma-specific reductions in limbic gray matter volume. JAMA Psychiatry 71 (8), 917–925. https://doi.org/10.1001/jamapsychiatry.2014.680.

van der Kolk, B.A., Hodgdon, H., Gapen, M., Musicaro, R., Suvak, M.K., Hamlin, E., Spinazzola, J., 2016. A randomized controlled study of neurofeedback for chronic PTSD. PloS One 11 (12), e0166752. https://doi.org/10.1371/journal.pone.0166752.

van Rooij, S.J., Rademaker, A.R., Kennis, M., Vink, M., Kahn, R.S., Geuze, E., 2014. Impaired right inferior frontal gyrus response to contextual cues in male veterans with PTSD during response inhibition. J. Psychiatry Neurosci. 39 (5), 330–339.

van Rooij, S.J., Kennis, M., Vink, M., Geuze, E., 2016. Predicting treatment outcome in PTSD: a longitudinal functional MRI study on trauma-unrelated emotional processing. Neuropsychopharmacol.: Off. Publ. Am. Coll. Neuropsychopharmacol. 41 (4), 1156–1165. https://doi.org/10.1038/npp.2015.257.

Vervliet, B., Indekeu, E., 2015. Low-cost avoidance behaviors are resistant to fear extinction in humans. Front. Behav. Neurosci. 9, 351. https://doi.org/10.3389/fnbeh.2015.00351.

Vogt, D., Smith, B.N., Fox, A.B., Amoroso, T., Taverna, E., Schnurr, P.P., 2017. Consequences of PTSD for the work and family quality of life of female and male U.S. Afghanistan and Iraq War veterans. Soc. Psychiatry Psychiatr. Epidemiol. 52 (3), 341–352. https://doi.org/10.1007/s00127-016-1321-5.

Wald, J., Taylor, S., 2007. Efficacy of interoceptive exposure therapy combined with trauma-related exposure therapy for posttraumatic stress disorder: a pilot study. J. Anxiety Disord. 21, 1050–1060. https://doi.org/10.1016/j.janxdis.2006.10.010.

Wilkinson, S., Dodgson, G., Meares, K., 2017. Predictive processing and the varieties of psychological trauma. Front. Psychol. 8, 1840 https://doi.org/10.3389/fpsyg.2017.01840.

Yassa, M.A., Stark, C.E., 2011. Pattern separation in the hippocampus. Trends Neurosci. 34 (10), 515–525. https://doi.org/10.1016/j.tins.2011.06.006.

Yerkes, R.M., Dodson, J.D., 1908. The relation of strength of stimulus to rapidity of habit-formation. J. Comp. Neurol. Psychol. 18 (5), 459–482. https://doi.org/10.1002/cne.920180503.

Young, H.A., Gaylor, C.M., de Kerckhove, D., Watkins, H., Benton, D., 2019. Interoceptive accuracy moderates the response to a glucose load: a test of the predictive coding framework. Proc. R. Soc. B 286 (1898), 20190244. https://doi.org/10.1098/rspb.2019.0244.

Zhou, X., Wu, X., Fu, F., An, Y., 2015. Core belief challenge and rumination as predictors of PTSD and PTG among adolescent survivors of the Wenchuan earthquake. Psychol. Trauma 7 (4), 391–397. https://doi.org/10.1037/tra0000031.

Zoellner, L.A., Feeny, N.C., Bittinger, J.N., Bedard-Gilligan, M.A., Slagle, D.M., Post, L. M., Chen, J.A., 2011. Teaching trauma-focused exposure therapy for PTSD: Critical clinical lessons for novice exposure therapists. Psychol. Trauma.: Theory, Res. Pract. Policy 3 (3), 300–308. https://doi.org/10.1037/a0024642.

Zuj, D., Palmer, M., Gray, K., Hsu, C., Nicholson, E., Malhi, G., Bryant, R., Felmingham, K., 2017. Negative appraisals and fear extinction are independently related to PTSD symptoms. J. Affect. Disord. 217, 246–251. https://doi.org/10.1016/j.jad.2017.04.016.

Zuj, D.V., Norrholm, S.D., 2019. The clinical applications and practical relevance of human conditioning paradigms for posttraumatic stress disorder. Prog. Neuro Psychopharmacol. Biol. Psychiatry 88, 339–351. https://doi.org/10.1016/j.pnpbp.2018.08.014.