Posttraumatic Stress Symptoms are Associated with Diminished Learning from Reward

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Abstract

Posttraumatic stress disorder (PTSD) and subthreshold posttraumatic stress symptoms (PTSS) are associated with differences related to learning, particularly impaired fear extinction. The extinction of learned fear responses relies on neural mechanisms of reward learning, in that the absence of the expected aversive event triggers unexpected relief, which is a form of reward. Impaired learning from reward may therefore be important in the aetiology and maintenance of PTSS. PTSS have been linked to reduced reward responsiveness, but evidence regarding learning from reward is limited. This study examined whether reward learning is associated with PTSS. Participants (N = 150, 110 female) completed the Life Events Checklist and the PTSD Checklist for *DSM-5* to indicate their trauma history and current PTSS. The mean PCL-5 score was 14.82, and 14 participants also reported having PTSD. Participants' learning from reward and from punishment were derived from their performance on a probabilistic reinforcement learning task. In a linear regression model, lower reward learning, more directly experienced traumatic events, and lower age were all associated with more severe PCL-5 scores. The relationship between PTSS and reward learning appeared to be driven by the *DSM-5* symptom cluster of intrusive re-experiencing, for which reward learning predicted 4.2% of the variance. Participants who reported having PTSD had poorer reward learning than those who did not. These results provide evidence for ties between poor reward learning and PTSS. This contributes to potential therapeutic approaches to the disorder, as reward learning deficits may contribute to the severity and longevity of PTSS.

Keywords: posttraumatic stress disorder, posttraumatic stress symptoms, associative learning, reward learning

Declaration

This thesis contains no material which has been accepted for the award of any other degree or diploma in any University, and, to the best of my knowledge, this thesis contains no material previously published except where due reference is made. I give permission for the digital version of this thesis to be made available on the web, via the University of Adelaide's digital thesis repository, the Library Search and through web search engines, unless permission has been granted by the School to restrict access for a period of time.

Veronica Wagner

September 2021

Contribution Statement

In writing this thesis, my supervisor and I collaborated to develop the research questions and design the methodology. The data collected and used in this project is part of a larger study; the overall design of this study, the ethics application, and participant recruitment were completed by my supervisor in collaboration with other researchers. My supervisor coded the learning task. I completed the literature review. I contributed to the testing of participants along with other research assistants. My supervisor and I collaborated in the analysis of the data. I wrote this thesis.

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Posttraumatic Stress Symptoms are Associated with Diminished Learning from Reward

1.1 Posttraumatic Stress Disorder

Posttraumatic stress disorder (PTSD) is a serious and sometimes debilitating trauma-related disorder, which places a high burden on both individuals and populations and entails substantial personal and economic costs (Kessler, 2000; Kessler et al., 2017; Sabes-Figuera et al., 2012). As outlined in the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; *DSM-5*; American Psychological Association, 2013), the first criterion (Criterion A) for a diagnosis of PTSD requires a specific stressor event that involves exposure to actual or threatened death, serious injury, or sexual violence. A person can experience a potentially traumatic event directly, or indirectly through witnessing it, learning about it occurring to someone close to them, or being exposed to it in the course of their work.

Posttraumatic stress symptoms (PTSS) given in the *DSM-5* are divided into four clusters: intrusive re-experiencing symptoms related to the traumatic event, avoidance of thoughts about the event or external reminders of it, negative alterations in cognition and mood, and alterations in arousal and reactivity. The diagnostic criteria for PTSD require at least one symptom from each of the intrusion and avoidance clusters and at least two symptoms from each of the cognition and mood and arousal clusters, resulting in a flexible array of potential symptom profiles reflecting the heterogeneity of the disorder (Friedman, 2013; Galatzer-Levy & Bryant, 2013). To qualify for PTSD diagnosis, these symptoms must occur more than a month after the event, cause significant distress or impairment, and not be attributable to the effects of a substance or medical condition.

In PTSD, comorbidities and adverse psychosocial outcomes are the rule rather than the exception (Brady et al., 2000). Common comorbid psychopathology includes depressive and anxiety disorders, substance use disorders, dissociative disorders, and personality

disorders (Brady et al., 2000; Kessler et al., 2005; Mills et al., 2006). Comorbid depressive or anxiety disorders are more common than PTSD alone, and entail more functional impairment (Chapman et al., 2012; Ginzburg et al., 2010; Rytwinski et al., 2013). PTSD is also associated with poorer physical health outcomes and disability, suicidality, aggressive behaviour, unemployment, poverty, and homelessness (Blankenship, 2018; Davidson et al., 1991; Davis et al., 2019; LeBouthillier et al., 2015; Mills et al., 2006; Ryder et al., 2018; Smith et al., 2005).

Intrusive re-experiencing of a past traumatic experience forms a core part of PTSD symptomatology. This thesis investigates learning mechanisms that could contribute to the development and maintenance of these symptoms, and in doing so, it seeks to further our understanding of the aetiology of the disorder.

1.1.1 Subthreshold Posttraumatic Stress Symptoms

Subthreshold PTSS refer to symptoms that are present but do not meet the full criteria for PTSD. Such symptoms are common and can entail serious psychosocial dysfunction and distress, as well as being a risk factor for later PTSD (Brancu et al., 2016; McLaughlin et al., 2015; Pietrzak et al., 2014; Zlotnick et al., 2002). Rather than a binary perspective of the disorder, it may be more accurate to consider posttraumatic stress reactions as a continuum from milder subthreshold symptoms to full PTSD at the severe end, a conceptualisation supported by neurobiological evidence (McFarlane et al., 2017; Steudte-Schmiedgen et al., 2015). Subthreshold PTSS are associated with significantly elevated depressive symptomatology and other psychopathological comorbidities, which occur in the same pattern as in the full disorder (Brancu et al., 2016; Marshall et al., 2001; McLaughlin et al., 2015; Muller et al., 2014). They are also associated with other adverse outcomes such as suicidality, substance abuse, and physical health problems, although these outcomes are less

consistent than with a full diagnosis of PTSD (Brancu et al., 2016; Fetzner et al., 2012; Marshall et al., 2001).

1.1.2 Prevalence of Trauma and PTSD

Most people experience at least one traumatic event during their lifetime. An estimated 70.4% of people worldwide and 74.9% in Australia experience such an event (Kessler et al., 2017; Mills et al., 2011). Post-trauma reactions are common, but persist longer than a month in only a minority of people (Nugent et al., 2009; Shalev et al., 1998). Fewer than 10% of those who experience a traumatic event develop PTSD (Breslau, 2009). The overall risk per event of developing PTSD is estimated at 4%, varying widely by trauma type (Breslau et al., 2004; Kessler et al., 2017).

In Australia, projected lifetime risk of PTSD is 9.7%, and 12-month prevalence is estimated at 4.4% (Chapman et al., 2012; McEvoy et al., 2011). Of those who develop PTSD, 25-50% remit within two years, while over a third have symptoms for 30 years or longer (Chapman et al., 2012; Kessler et al., 2017). PTSD prevalence and risk per trauma both tend to be higher among women, and prevalence and severity generally decrease with age, although these findings are not consistent across populations (Brewin et al., 2000; Kessler et al., 2017; Koenen et al., 2017; Norris et al., 2002).

Only 1.5% of respondents to the 2017-18 National Health Survey reported having been told by a health professional that they had PTSD (Australian Bureau of Statistics, 2018). However, measuring PTSD prevalence by existing medical diagnosis risks greatly under-detecting the disorder (Liebschutz et al., 2007). Help-seeking and diagnosis for PTSD can be hindered by factors including the avoidance that is characteristic of the disorder, lack of awareness of or insight into the symptoms, and stigma about the disorder or a traumatic event that precipitated it (Phoenix Australia, 2020; Smith et al., 2020). This highlights the need to better understand PTSS outside the context of people diagnosed with PTSD.

1.2 Trauma and Individual Differences in Posttraumatic Stress Symptoms

An individual's risk of developing PTSS, as well as their severity and longevity, is greatly associated with the amount, kind, and severity of trauma they experience in their life (Courtois, 2008; Dohrenwend et al., 2006). Previous traumatic experiences that may not have triggered PTSS become risk factors for future PTSS, as does exposure to chronic or prolonged non-traumatic stress (Kessler et al., 2017; Kessler et al., 2018; Liu et al., 2018; McKeever & Huff, 2003). Exposure to traumatic stressors cumulatively enhances both PTSD risk and PTSS severity, such that PTSD prevalence approaches 100% at sufficiently extreme trauma exposure levels (Karam et al., 2014; Schauer et al., 2003). The endorsement of higher numbers of types of trauma is associated with greater functional impairment, more psychopathological comorbidities, and longer duration of PTSS (Karam et al., 2014). Greater risk of PTSD is also associated with traumatic events that are experienced first-hand as opposed to those experienced indirectly, whether witnessed or learned about occurring to a loved one (Breslau, 2009; Chapman et al., 2012; Kessler et al., 2017). In light of this, when investigating PTSS, it is important to ascertain trauma history in more detail than a binary measure of the presence or absence of exposure to a traumatic event (Kolassa et al., 2010; McFarlane et al., 2017).

Experiencing a traumatic event is necessary but not sufficient for the development of PTSD (Bowman, 1999). The aetiology of PTSD, by a diathesis-stress model, involves the contribution of both the external stressors an individual undergoes, that is, the trauma they experience, and their vulnerability to the disorder. At low levels of traumatic exposure, individual differences are critical in understanding PTSD risk and predict symptoms more reliably than features of the traumatic event (Bowman & Yehuda, 2004; Brewin et al., 2000; McFarlane et al., 2017; Rubin et al., 2008). Environmental, biophysiological, and psychological variables can play a major role and have additive or interactional relationships

between them (Gil & Caspi, 2006; Gil & Weinberg, 2015; McKeever & Huff, 2003; Paris, 2000). The consideration of individual differences can improve research on PTSD-related outcomes, such as in studies on treatment efficacy (Bowman & Yehuda, 2004) and in animal stress paradigms (Bush et al., 2007; Holly & Miczek, 2015).

1.3 Learning and Posttraumatic Stress Symptoms

PTSD can be conceptualised as a disorder of learning and memory. A conditioning model of PTSD holds that the disorder involves abnormalities in learning, as its symptoms stem from associations with a particular event (Lissek et al., 2005; Lissek & van Meurs, 2015; Pitman, 1988; Pitman et al., 2012). Considerable research has examined possible differences in learning and memory in PTSD, particularly related to learned fear associations. A key factor in the development and maintenance of PTSS is an impaired ability to extinguish a learned fear association in the aftermath of trauma (Rothbaum & Davis, 2003; VanElzakker et al., 2014; Zuj & Norrholm, 2019; Zuj et al., 2016). In this sense, PTSS are framed as a failure to recover from a normal short-term reaction following trauma (Holmes & Singewald, 2013; Pitman, 1988; Rothbaum & Davis, 2003). An innocuous stimulus that was present during a traumatic experience can serve as a reminder of that event and trigger fear responses long afterwards. In healthy individuals, fear extinction should occur, that is, fear responses should gradually diminish as the stimulus is no longer accompanied by the traumatic aspects of the original experience. Fear extinction can be measured experimentally by pairing a neutral cue with an aversive event, then presenting the cue on its own, and measuring the rate at which the fear response evoked by the cue diminishes. This can yield a measure of individual differences in fear extinction (Zeidan et al., 2012).

Most previous studies have demonstrated an association between PTSS and deficits in fear extinction learning (Lissek & van Meurs, 2015; VanElzakker et al., 2014). This may be in either the initial extinction of learned fear or in the retention of that extinction over time

(Guthrie & Bryant, 2006; Milad et al., 2008; Milad et al., 2009; Norrholm et al., 2011). Further evidence comes from the efficacy of exposure therapy in treating PTSD, as the process of exposure is presumed to operate through the associative learning process of extinction (Lissek & van Meurs, 2015; Rothbaum & Davis, 2003). The efficacy of exposure therapy for anxiety is also associated with individual differences in fear extinction learning (Ball et al., 2017; Forcadell et al., 2017; Waters & Pine, 2016).

Several mechanisms have been proposed to underlie the failure to extinguish conditioned fear in PTSS (Lissek & van Meurs, 2015). One such mechanism is the facilitated acquisition of fear associations in PTSD, related to an exaggerated response to threat or trauma cues (Brown et al., 2018; Handy et al., 2018; Pitman, 1988). However, overall, most research has found that the acquisition of fear in PTSD is normal (Lissek & van Meurs, 2015; VanElzakker et al., 2014). Conversely, there is some evidence that PTSD is associated with deficits in associative learning in general, including in neutral, non-fear-based paradigms (Ayers et al., 2003; Lambert & McLaughlin, 2019; Zuj et al., 2016). Again, however, evidence is mixed, and while PTSD is associated with general cognitive deficits, the effects are generally subtle (Aupperle et al., 2012; Lissek & van Meurs, 2015; Scott et al., 2015).

1.3.1 Fear Extinction and Reward Learning

The process of extinction does not appear to involve the erasure of the initially learned fear association, but rather competition between the original association and new learning (Bouton, 2004; Lissek & van Meurs, 2015; Manning et al., 2021; Myers & Davis, 2007). This competition reflects more general theories concerning appetitive and aversive processes which mutually inhibit each other, in that fear extinction operates through an appetitive learning process, such as the feeling of relief when the aversive event does not occur (Konorski, 1967; Nasser & McNally, 2012; Raczka et al., 2011). Neurobiological evidence for this model suggests that fear extinction learning is derived from the same neural

circuitry and dopaminergic neurons that signal reward learning (Felsenberg et al., 2018; Raczka et al., 2011; Salinas-Hernández et al., 2018; Thiele et al., 2021; Zhang et al., 2020). If reward learning processes drive the fear extinction process, we might expect that impaired reward learning would be associated with PTSS.

1.3.2 Reward Learning and Posttraumatic Stress Symptoms

Past studies have found limited behavioural evidence of impaired reward learning in relation to PTSD. In some cases, patients with PTSD were slower than healthy controls to learn a rewarded response sequence (Koenen et al., 2001; Sailer et al., 2008), which may reflect reduced reward-motivated learning, among other explanations (Aupperle et al., 2012). Studies using probabilistic reinforcement learning tasks found no association between reward learning and diagnosed PTSD or PTSS severity (Howlett et al., 2021; Ross et al., 2018). PTSD has also been linked to hypoactivation of relevant neural networks during reward learning tasks (Ross et al., 2018; Sailer et al., 2008), although not consistently (Howlett et al., 2021).

Myers et al. (2013) found that, in a sample of veterans, those with more severe PTSS achieved better results on reward-based trials of a probabilistic classification task. Crucially, in that study, veterans with higher PTSS weighed the positive feedback outcome as preferable to the no-feedback outcome, while those with lower PTSS weighed the no-feedback and positive feedback outcomes the same. This suggests reward-related differences in PTSS, and may indicate that veterans resilient against PTSS tended to interpret neutral stimuli as rewarding. Similarly, soldiers resilient against PTSS after severe trauma did not differentiate between large and small rewards in levels of neural activation, in comparison to civilians whose neural activation differed by reward size (Vythilingam et al., 2009). There is also evidence that reward learning mediates the relationship between childhood adversity, including trauma, and ongoing psychosocial problems, where diminished learning from

reward predicts more psychopathology or other difficulties while stronger reward learning predicts resilience (Hanson et al., 2017; Pechtel & Pizzagalli, 2013; Sheridan et al., 2018; Wismer Fries & Pollak, 2017). Overall, the evidence for reduced reward learning associated with PTSS is suggestive, but neither consistent nor conclusive.

1.3.3 Other Reward Functioning and Posttraumatic Stress Symptoms

Learning from reward, in terms of predictive associations, is one distinct part of broader reward functioning, which also includes motivation ("wanting") and hedonic impact ("liking") (Berridge et al., 2009; Olino, 2016). PTSD is associated with deficits in reward functioning, in reduced anticipation, approach, and response to rewarding stimuli, across self-report, behavioural, physiological, and neural evidence (Fonzo, 2018; Nawijn et al., 2015; Seidemann et al., 2021). Individuals with PTSD demonstrated lower motivation to engage in an enjoyable activity (Elman et al., 2005) and a bias towards avoiding positive affective stimuli (Clausen et al., 2016). In an animal model of PTSD, traumatised rats displayed reduced hedonic behaviours and pursuit of pleasurable experiences (Enman et al., 2015). PTSS were associated with lower self-reported expectation of reward and lower self-reported satisfaction with reward when received (Hopper et al., 2008). PTSD and higher PTSS have been associated with lower self-reported subjective ratings of positive emotions, of the pleasantness of visual stimuli, and of the intensity of happy faces (Elman et al., 2018; Felmingham et al., 2014; Frewen et al., 2012). Differences in neural activation accompanying the receipt of reward or pleasant stimuli have also been associated with PTSD and higher PTSS, both in support of and in the absence of behavioural differences (Boukezzi et al., 2020; Fonzo, 2018; Nawijn et al., 2015). These differences in neural activation have most commonly involved hypoactivation of areas within the striatum and prefrontal cortex (Admon, Lubin, et al., 2013; Ben-Zion et al., 2021; Elman et al., 2009; Elman et al., 2018; Felmingham et al., 2014; Frewen et al., 2012). Higher PTSS have also been associated with

blunted electrophysiological responses to correct feedback (Lieberman et al., 2017). In a non-clinical sample, PTSS severity was related to lower environmental access to rewards (Acuff et al., 2018).

1.3.4 Reward and Posttraumatic Stress Symptom Clusters

PTSS are heterogeneous, and it is possible that reward functioning relates differently to the different symptom clusters. The bulk of previous research about general reward functioning in PTSD has considered this a relevant consideration in relation to the symptoms of anhedonia or emotional numbing (Fonzo, 2018; Nawijn et al., 2015; Seidemann et al., 2021). Several studies have found that diminished responsiveness to rewards relates specifically to the negative alterations in cognition and mood symptom cluster or particular symptoms within it (Elman et al., 2009; Felmingham et al., 2014; Frewen et al., 2012; Lieberman et al., 2017). Anhedonia has also been linked to reward-related neural hypoactivation in PTSD patients, in a study where anhedonia was assessed separately from PTSS (Pessin et al., 2021). By contrast, low neural reward responsiveness a month after a potentially traumatic event predicted only avoidance symptoms (Ben-Zion et al., 2021). From an associative learning perspective, the intrusion symptom cluster is thought to result from deficits in fear extinction, in that these symptoms involve a failure to extinguish the conditioned fear response and reduce the persistent memory of the traumatic event (Norrholm et al., 2011; Zuj et al., 2016). Poor reward learning may therefore be associated with intrusion symptoms, through the reward-driven neural mechanisms thought to underlie fear extinction. It is possible that abnormalities in dopaminergic functioning and poor reward sensitivity underpin and connect all of the different symptoms of PTSD (Ney et al., 2021; Torrisi et al., 2019). This issue, however, requires further investigation.

1.4 The Current Study

The aim of the current study is to investigate whether there is a relationship between learning from reward and PTSS. Existing scholarship supports the notion of reduced reward functioning and reactivity associated with PTSS, but evidence of behavioural differences in reward learning specifically is scarce. Furthermore, there is a lacuna in research investigating reward learning in relation to PTSS measured as a continuous variable, including at subthreshold levels, and accounting for cumulative trauma exposure. Controlling for trauma exposure is important given the evidence linking trauma exposure levels and PTSS risk. It is also important to control for sex and age because of potential confounding relationships with PTSD (Section 1.1).

This study's primary hypothesis is that lower reward learning will predict higher PTSS, after controlling for age, sex, and trauma history. It is also hypothesised that higher punishment learning will be associated with PTSS, in light of evidence linking PTSD with more effective learning from punishment (Sawyer et al., 2016) and increased sensitivity to punishment (Dretsch et al., 2013). However, existing research provides a greater basis to expect differences in reward learning than punishment learning.

This study will also assess reward learning between groups of participants with and without possible PTSD. Although we are most interested in PTSS as a continuous variable, the categorisation of participants into groups will allow us to compare the results obtained through different methods of defining possible PTSD: by self-reported diagnosis and by applying diagnostic criteria to self-reported PTSS. If enough participants report a prior diagnosis of PTSD to make the analysis viable, it is hypothesised that this group will also show significantly lower reward learning than those without diagnosis. Reward learning will also be compared across groups divided by a PTSS cut-off score indicating possible PTSD

and by PTSS endorsement in accordance with the symptom criteria for PTSD in the *DSM-5* (Section 2.2.3).

Reward learning may relate differently to symptoms from the four *DSM-5* clusters: intrusive re-experiencing, avoidance, negative alterations in cognition and mood, and arousal. Previous studies have demonstrated an association between reward functioning and cognition and mood symptoms, but intrusion symptoms may also be closely related to learning from reward, which is thought to underlie fear extinction at a neural level. This will be investigated as an exploratory aim.

Chapter 2: Method

2.1 Participants

Participants (N = 150) were aged between 18 and 81 (M = 45.69, SD = 19.06); 110 were female and 40 were male. Fourteen participants (9.3%) self-reported having PTSD.[1] These participants were aged between 19 and 73 (M = 52.93, SD = 16.52), and 12 were female.

These data were collected as part of a broader study on cognitive function across the lifespan. Participants were recruited through online advertisements on Facebook, Gumtree, and personal contacts of the researchers. All participants were provided with information sheets (reproduced in Appendix A) and gave informed consent. The Adelaide University Human Research Ethics Committee approved the study (ethics approval number H-2020-017). Data were collected between May and August 2021. Participants received a $50 Coles/Myer gift card as compensation.

[1] Of these 14 participants, 11 identified their PTSD as diagnosed, two not diagnosed, and one not sure. As participants' diagnostic status was not externally verified, this distinction was not considered in the analysis.

Participant inclusion criteria were that they were over 18 and fluent English speakers; exclusion criteria are given in Appendix B. The sample size was determined by the time available to collect data in the timely completion of this thesis. No effect size could be estimated from the existing literature, as previous studies using similar designs did not find behavioural effects. According to an a priori power analysis, a minimum sample size of N = 92 is required for a multiple linear regression with five predictors (reward and punishment learning variables, and controlling for age, sex, and trauma history) to detect an effect size of $f^2 = 0.15$ with a statistical power of .8.

2.2 Materials

2.2.1 Demographic Information

Participants provided demographic information including their age, sex assigned at birth (from options "Male", "Female", and "Intersex"), and medical histories for specific conditions, of which only PTSD was included in this study.

2.2.2 The Life Events Checklist for DSM-5

Exposure to traumatic events was measured with the Life Events Checklist for *DSM-5* (LEC-5; Weathers, Blake, et al., 2013b). The checklist is a self-report measure, developed by the US National Center for PTSD to screen for potentially traumatic events that a person has experienced. It contains 17 items, 16 of which list specific events (for example, "Fire or explosion"), as well as one non-specific item ("Any other very stressful event or experience"). For each event, the LEC-5 enquires about multiple types of exposure (*Happened to me*, *Witnessed it*, *Learned about it*, *Part of my job*, *Not sure*, and *Doesn't apply*). Participants are instructed to indicate if they have experienced the event during their life, including in childhood, and if so in what way, and can endorse multiple types of exposure to the same event.

In this study, only events endorsed as having been experienced directly were used as a measure of trauma history; this scoring protocol has demonstrated superior test-retest reliability and external validity through its relationship with PTSS levels, in comparison to the full scale (Pugach et al., 2021; Reger et al., 2019; Weis et al., 2021). Directly experienced events were measured by the number of different event types for which participants endorsed *Happened to me*. For items 14 and 15, which refer to death, and item 16 ("Serious injury, harm, or death you caused to someone else"), *Witnessed it* was also considered direct experience, similar to the scoring used by Bae et al. (2008).

This study employed the standard version of the LEC-5. This does not include an additional measure of Criterion A, which requires the participant to identify and describe the most traumatic event experienced. This decision was the result of multiple considerations. The study's aim was not diagnostic, and so participants' endorsement of Criterion A was not pertinent. The judgement of whether a participant's stated worst event meets *DSM-5* Criterion A requirements is subjective and cannot be quantified in a way that coheres with this study's quantitative analysis. Furthermore, PTSS can occur with comparable severity regardless of whether the symptoms are associated with a Criterion A event (Bardeen & Benfer, 2019; Heir et al., 2019; Lansing et al., 2017; Zelazny & Simms, 2015). Finally, obtaining Criterion A information in this study would not justify the burden on the participant, given the potential discomfort of providing details about traumatic experiences.

2.2.3 The Posttraumatic Stress Disorder Checklist for DSM-5

The Posttraumatic Stress Disorder Checklist for *DSM-5* (PCL-5; Weathers, Litz, et al., 2013) is a well-validated and widely used self-report measure of the symptoms of PTSD in the *DSM-5*. The PCL-5 contains 20 items, corresponding to the 20 symptoms of PTSD in the *DSM-5*. The scale was developed at the US National Center for PTSD and was designed to maximise content validity, in the sense that the PCL-5 items should faithfully reflect *DSM-*

5 PTSD symptoms (Blevins et al., 2015; Friedman, 2013). For each item, participants are asked to report how much each symptom has bothered them in the past month (for example, "Repeated, disturbing dreams of the stressful experience?"). The items are presented on a 5-point Likert scale (0 = *Not at all*, 1 = *A little bit*, 2 = *Moderately*, 3 = *Quite a bit*, 4 = *Extremely*), giving possible scores of 0–80, with higher scores indicating more severe PTSD symptoms. The PCL-5's items correspond to the four *DSM-5* symptom clusters: intrusive re-experiencing of the traumatic event (items 1–5), avoidance (items 6–7), negative alterations in cognition and mood (items 8–14), and arousal (items 15–20; Blevins et al., 2015).

The PCL-5 has demonstrated robust psychometric properties (Blevins et al., 2015; Cohen et al., 2014). The scale has exhibited high internal reliability in numerous studies (Blevins et al., 2015; Roberts et al., 2021); in the present sample, Cronbach's $\alpha = .96$. It has demonstrated excellent or moderate test-retest reliability in a variety of populations (Roberts et al., 2021). The scale is efficient and convenient, and correlates strongly with gold standard diagnostic interviews, as well as other self-report measures of PTSD symptomatology (Blevins et al., 2015; Bovin et al., 2016; Geier et al., 2019; Krüger-Gottschalk et al., 2017; Roberts et al., 2021; Ruggiero et al., 2003).

The PCL-5 has strong convergent and divergent validity, indicated by relationships with measures of a wide range of constructs, including strong positive correlations with depression and anxiety, positive correlations with stress, avoidance, disability, and functional impairment, and weaker relationships with comparatively unrelated constructs (Blevins et al., 2015; Bovin et al., 2016; Roberts et al., 2021). It has good external validity, demonstrating strong psychometric properties in a wide variety of contexts, including military, student, and community samples, adolescents, refugees, and survivors of traumatic events, in a variety of languages (see, for example, Ibrahim et al., 2018; Liu et al., 2014; Murphy et al., 2018).

Treating the PCL-5 as a continuous symptom measure rather than obtaining binary diagnostic information confers some advantages. PTSS can occur on a spectrum, entailing distress and dysfunction even at subthreshold levels (Section 1.1.1). Continuous measures also avoid the attenuating and potentially misleading effects of grouping, and can thus strengthen statistical power and increase insight into relationships with other variables (Brewin et al., 2000; Galatzer-Levy & Bryant, 2013; MacCallum et al., 2002).

As a symptom checklist, the measure does not assess all *DSM-5* diagnostic requirements for PTSD. Nevertheless, the identification of participants with clinically relevant symptoms or possible PTSD can be obtained from the scale in two ways. One is division by a cut-off score. The optimal cut-off scores in agreement with diagnostic interviews are generally found to be 31-33 (Blevins et al., 2015; McDonald & Calhoun, 2010). Alternatively, the PCL-5 can indicate a possible PTSD diagnosis by treating items rated 2 (*Moderately*) or higher as an endorsement of a symptom, and then following the *DSM-5* diagnostic rule: at least one symptom from each of the intrusion and avoidance clusters and two from each of the cognition and mood and arousal clusters (Blevins et al., 2015). In terms of agreement with diagnostic interviews, this method is generally inferior to assessment by cut-off score (Bovin et al., 2016; Geier et al., 2019; Roberts et al., 2021).

2.2.4 Probabilistic Reinforcement Learning Task

The probabilistic reinforcement learning task (Cavanagh et al., 2011) was programmed using Xojo software (Xojo Inc., version 3, 2019, Austin, Texas, USA) and performed by participants on a 10.2-inch iPad Pro (Apple Inc., Cupertino, California, USA). This task measured learning from reward and punishment using participants' responses to the positive and negative feedback they received (Frank et al., 2004). The task assessed learning in a neutral, non-fear-based way, which was appropriate to capture potentially subtle individual differences, whereas a fear-based learning paradigm might flatten individual

differences in responses (Lissek & van Meurs, 2015). Reward and punishment, and opportunities for learning from both, were presented with equivalent stimuli differing only in valence, so as to enable comparison between the learning variables.

The task comprised six sets of forced choice trials in which participants choose between a pair of different cue pictures (Figure 1). Each cue was associated with a set chance of eliciting positive feedback if chosen. Each set of trials contained a training phase followed by a test phase. Participants were guided by written instructions (reproduced in Appendix C) as well as pre-recorded verbal instructions and animations at the beginning of the task, before each of the six sets, and before each test phase.

The training phase for each set contained 16 trials. One pair of cues, denoted as A and B, had a 100% and 0% chance respectively of triggering correct feedback, and the other, C and D, had a 75% and 25% chance respectively of being correct. The probability of receiving correct feedback on CD trials was stochastic, that is, generated independently on each trial. Each of the two pairs was presented on eight of the 16 trials, with the cues in each pair presented on the left and right side for four trials each. The trials within each training phase were randomly intermixed.

Participants responded by tapping one of the cues within 4 s. Their choice was emphasised by a darkened border for 300 ms, followed by feedback displayed for 1 s. Correct feedback consisted of the word “Correct!”, in blue font; incorrect feedback consisted of the word “Incorrect” is displayed in red. If the participant did not respond within 4 s, “No response detected” appeared in red for 1 s and then the next trial began. Trials were separated by an inter-trial interval consisting of a blank screen for 1.5 s.

Participants had the opportunity to learn the optimal response by selecting the cue for which they received the most positive feedback or by avoiding the cue that produced the most negative feedback, or both. Measures of participants’ learning from reward and punishment

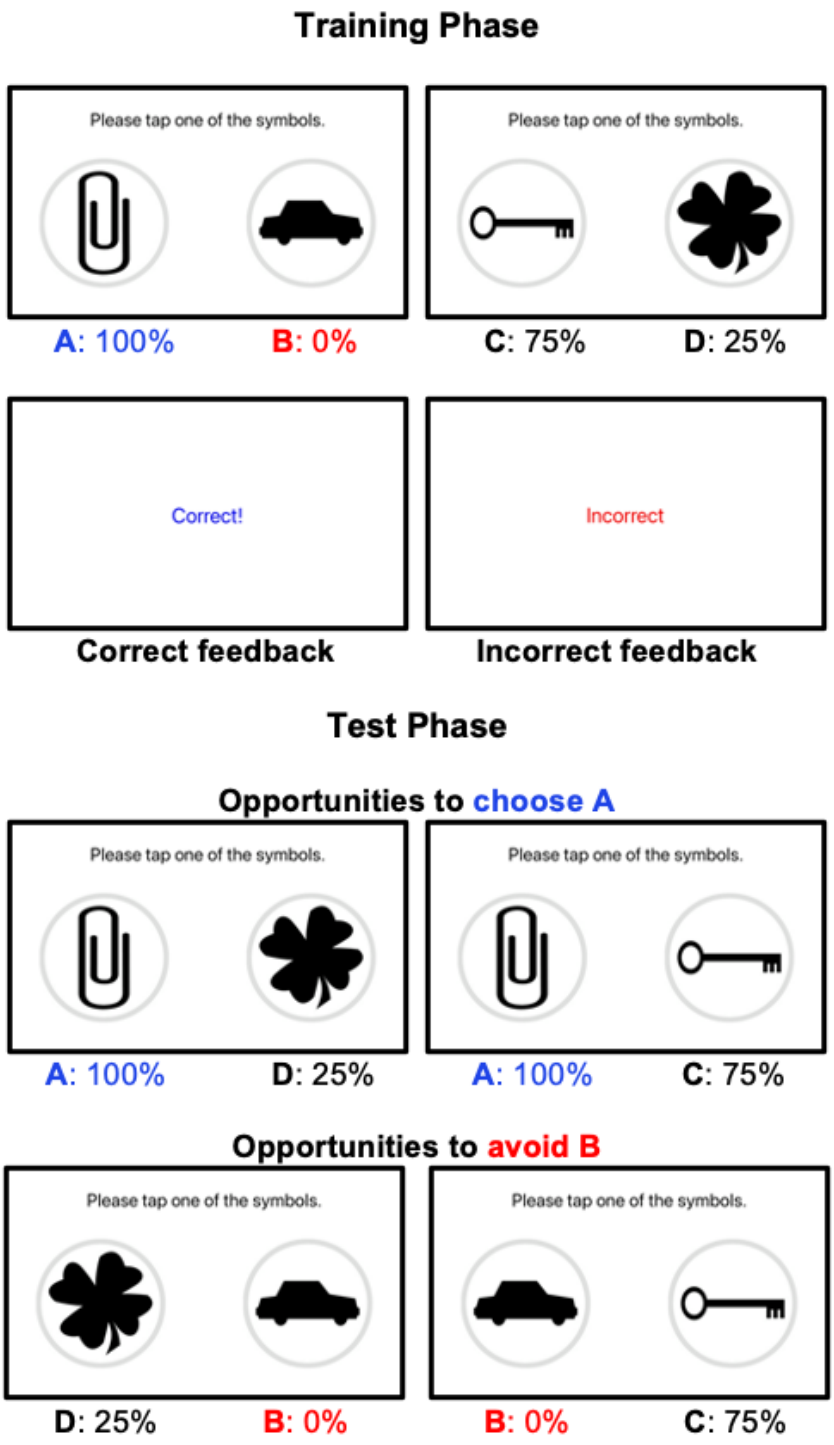
were derived from their responses in the training phase. *Win-stay* scores refer to the proportion of opportunities that participants took to repeat the preceding successful choice, reflecting their ability to learn to repeat rewarded choices. *Lose-shift* scores refer to the proportion of the opportunities that participants took to not repeat the preceding unsuccessful choice, that is, to shift their choice after negative feedback, reflecting their ability to learn to avoid punished choices.

Test phases also consisted of 16 randomly intermixed trials, in which participants were presented with the previously unused cue pairs AC, AD, BC, and BD four times each. Each cue was again shown on the left and right sides for half of the trials. Trials proceeded with the same format and timing as in the training phase, except that no feedback was given following their choice.

Participants' responses in the test phase provided a second pair of measures of their learning in the task. Successfully choosing A (the cue with a 100% chance of being correct) was considered to result from learning from the reward of positive feedback, and avoiding B (the cue with a 0% chance of being correct) was considered to result from learning from the punishment of negative feedback. The *choose-A* and *avoid-B* variables refer, respectively, to the proportion of opportunities that participants took to choose A and avoid B in the test phase.

Figure 1

Probabilistic Reinforcement Learning Task



Note. During the training phase, participants were presented with two pairs of cues, each associated with a different chance of eliciting correct feedback. Upon selecting a cue, they received correct or incorrect feedback for 1 s. This phase lasted for 16 trials, with equal trials

for each cue pair and their positions on the left or right. When participants received correct feedback following their selection of a cue, the next time this cue recurred, they may or may not take the opportunity to repeat their previously rewarded choice; the proportion of opportunities a participant took to do so produced their win-stay score. Similarly, following incorrect feedback to a particular cue, a participant's lose-shift score was the proportion of opportunities they took to avoid choosing that cue the next time they were presented with it. During the test phase, participants were presented with the unused combinations of cues. Regardless of their choice, they did not receive feedback. This phase also lasts for 16 trials, with the four trials of each pair, positioned equally on the left or right. Half of these trials included cue A, here represented by the paperclip, which was associated with a 100% chance of being correct in the training phase, and the other half included cue B, here represented by the car, which was associated with a 0% chance of correct feedback. The proportion of trials that included cue A where participants chose A produced their choose-A score, while the proportion of trials that included cue B where participants did not choose B produced their avoid-B score.

2.3 Procedure

After viewing the information sheet and providing informed consent, participants provided their age and completed the LEC-5 and PCL-5 as part of a battery of online surveys, collected through REDCap (Research Electronic Data Capture; Harris et al., 2009). This battery took approximately 30 minutes. At the subsequent in-person session, which lasted approximately 2.5–3 hours, participants provided additional demographic information, including sex assigned at birth and medical history, and completed the probabilistic reinforcement learning task as part of series of other tasks not analysed here. The study also

included verbally administered measures, motor tasks, and the collection of saliva samples. All analyses were conducted using R software (R Core Team, 2020).

Chapter 3: Results

3.1 Descriptive Statistics

Table 1 presents descriptive statistics and Shapiro-Wilk tests for normality for age, participants' scores on the self-report measures, and the four measures of learning derived from the learning task. Among these variables, only the lose-shift scores were normally distributed.

Table 1

Descriptive Statistics and Shapiro-Wilk Tests for Study Variables

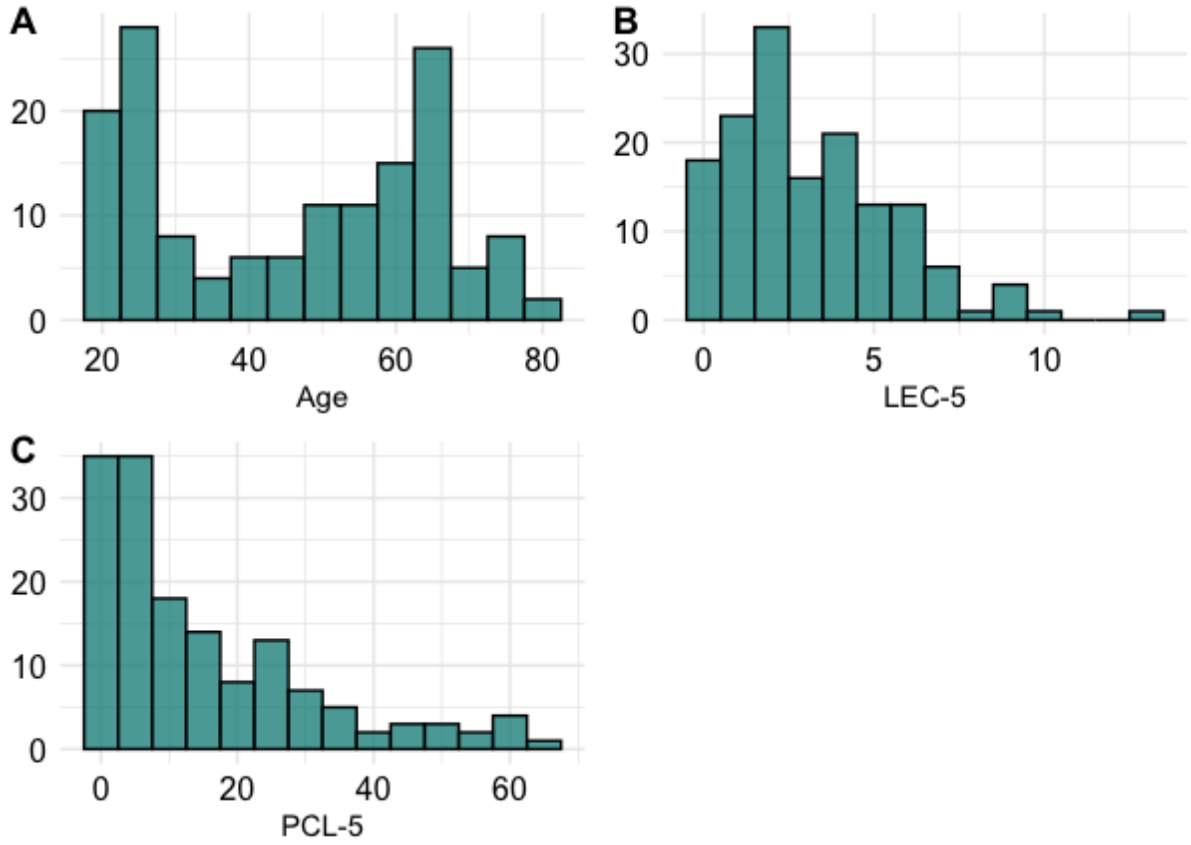
Variable	*M*	*SD*	Range	Skew	Kurtosis	*W*	*p*
Age	45.69	19.06	18–81	-0.03	-1.52	.90	<.001
LEC-5	3.15	2.44	0–13	0.95	1.04	.92	<.001
PCL-5	14.82	16.07	0–66	1.35	1.18	.83	<.001
Learning measures							
Training phase							
Win-stay	.87	.12	.34–1	-1.98	4.87	.81	<.001
Lose-shift	.63	.12	.39–.91	0.10	-0.65	.99	.198
Test phase							
Choose-A	.76	.15	.27–1	-0.49	-0.20	.97	.003
Avoid-B	.78	.14	.44–1	-0.34	-0.92	.96	<.001

Note. LEC-5 = Life Events Checklist for *DSM-5*, possible scores 0–17; PCL-5 = Posttraumatic Stress Disorder Checklist for *DSM-5*, possible scores 0–80.

The majority of participants (88%) endorsed at least one directly experienced traumatic event on the LEC-5. Figure 2 shows histograms of participants' age and scores on the LEC-5 and the PCL-5.

Figure 2

Histograms of Age, LEC-5 Scores, and PCL-5 Scores



Note. LEC-5 = Lifetime Events Checklist for *DSM-5*, possible scores 0–17; PCL-5 = Posttraumatic Stress Disorder Checklist for *DSM-5*, possible scores 0–80.

3.2 Primary Analyses

The primary hypothesis of the current study was that higher posttraumatic stress symptoms would be associated with lower reward learning, after controlling for the potentially confounding effects of age, sex, and trauma history.

3.2.1 Relationships between Variables

None of the variables differed significantly by participants' sex (smallest $p = .298$; Appendix D). Table 2 presents correlation coefficients for participants' age, scale scores, and learning scores. As most variables were not normally distributed, the table shows Spearman correlation coefficients. LEC-5 and PCL-5 scores were significantly positively correlated. Age positively correlated with LEC-5 but not PCL-5 scores. All of the learning measures had significant positive correlations with each other, most strongly between choose-A and avoid-B, and between both of those and win-stay. Neither LEC-5 nor PCL-5 scores correlated significantly with any learning measures; age correlated negatively with the choose-A measure only.

Table 2

Spearman Correlation Coefficients for Study Variables

Variable	Age	LEC-5	PCL-5	Win-stay	Lose-shift	Choose-A	Avoid-B
Age	–						
LEC-5	.24**	–					
PCL-5	-.13	.32***	–				
Win-stay	-.11	-.06	-.08	–			
Lose-shift	.04	.05	-.04	.17*	–		
Choose-A	-.32***	.01	-.04	.46***	.19*	–	
Avoid-B	-.10	.14	-.03	.38***	.17*	.50***	–

Note. LEC-5 = Life Events Checklist for *DSM-5*; PCL-5 = Posttraumatic Stress Disorder Checklist for *DSM-5*. Correlations with $p < .001$ were significant after the application of a Bonferroni correction.

*$p < .05$. **$p < .01$. ***$p < .001$.

3.2.2 Principal Components Analyses

In order to reduce the measures of learning from reward and from punishment into a single variable each, two principal components analyses were conducted. For the measures of learning from reward (win-stay and choose-A), the first unrotated component had an eigenvalue of 1.51 and accounted for 76% of the variance; both measures loaded .87 onto this component. For the punishment learning scores (lose-shift and avoid-B), the first unrotated component had an eigenvalue of 1.16 and accounted for 58% of the variance, and both measures loaded .76 onto this component. These two variables are henceforth referred to as reward learning and punishment learning scores.

Table 3 presents the descriptive statistics and Shapiro-Wilk tests for normality for these variables. Punishment learning scores were normally distributed, while reward learning scores were negatively skewed.

Table 3

Descriptive Statistics and Shapiro-Wilk Tests for Learning Scores

Variable	*M*	*SD*	Range	Skew	Kurtosis	*W*	*p*
Reward learning	0	1	-3.57–1.55	-1.21	1.79	.91	<.001
Punishment learning	0	1	-2.62–2.40	-0.10	-0.39	.99	.801

Table 4 shows the Spearman correlation coefficients for reward and punishment learning scores with participants' age, LEC-5 scores, and PCL-5 scores. The two learning scores had a strong positive relationship, and reward learning had a negative correlation with age. Neither learning score had a significant relationship with the LEC-5 or PCL-5 scores.

Table 4

Spearman Correlation Coefficients for Learning Scores

Variable	Reward Learning	Punishment Learning
Reward learning	–	
Punishment learning	.45***	–
Age	-.29***	-.03
LEC-5	-.03	-.14
PCL-5	-.05	-.05

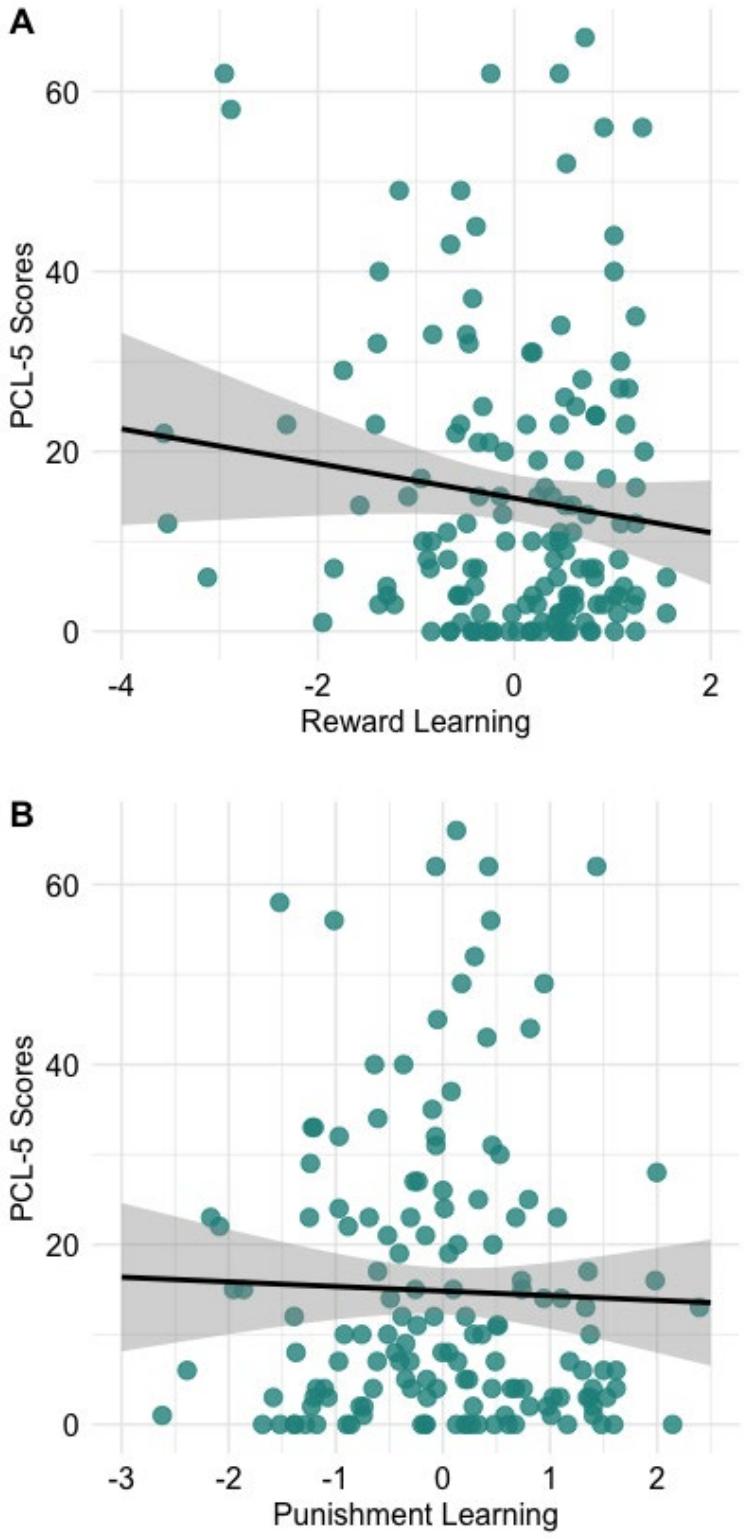
Note. LEC-5 = Life Events Checklist for *DSM-5*; PCL-5 = Posttraumatic Stress Disorder Checklist for *DSM-5*.

***$p < .001$.

Figure 3 illustrates the relationship between participants' reward and punishment learning scores and their PCL-5 scores.

Figure 3

PCL-5 Scores and Reward Learning and Punishment Learning Scores



Note. PCL-5 = Posttraumatic Stress Disorder Checklist for *DSM-5*. Shaded areas indicate 95% confidence intervals.

Female participants had lower reward learning scores (M = -0.03, SD = 1.02) than male participants (M = 0.09, SD = 0.96); however, this difference was not significant (t(73.4) = -0.70, p = .485). Punishment learning scores among female participants (M = 0.01, SD = 0.96) and male participants (M = -0.03, SD = 1.11) were also not significantly different (t(61.5) = 0.19, p = .854).

3.2.3 Regression Analyses

To test the relationship between reward learning and PTSS while controlling for other variables, we first ran a multiple linear regression with age, sex, and LEC-5 scores as predictors of PCL-5 scores. The model was significant (F(3, 146) = 10.21, p < .001), and captured 17.34% of the variance. We ran a second regression model which included the reward and punishment learning variables as predictors of PCL-5 scores, alongside age, sex, and LEC-5 scores. This second model was also significant (F(5, 144) = 7.61, p < .001). The introduction of the two learning scores explained an additional 3.56% of the variance beyond that predicted by the first model, to a total of 20.90% of the variance, and this increase was statistically significant (F(2, 144) = 3.24, p = .042). Reward learning was a significant predictor in the second model, as were age and LEC-5 scores, while sex and punishment learning were not (Table 5).

Table 5

Regression Models Predicting Posttraumatic Stress Symptoms

Variable	R^2	*B*	*SE B*	*β*	*t*	*p*
Model 1	.17					
Constant		18.61	3.46		5.38	<.001
Age		0.24	0.07	-0.28	-3.62	<.001
Sex (male)		-2.73	2.75	-0.08	-0.99	.323
LEC-5		2.47	0.51	0.38	4.86	<.001
Model 2	.21					
Constant		20.48	3.50		5.85	<.001
Age		-0.28	0.07	-0.34	-4.20	<.001
Sex (male)		-2.55	2.71	-0.07	-0.94	.349
LEC-5		2.51	0.50	0.38	4.98	<.001
Reward learning		-3.34	1.45	-0.21	-2.31	.022
Punishment learning		0.42	1.41	0.03	0.30	.768

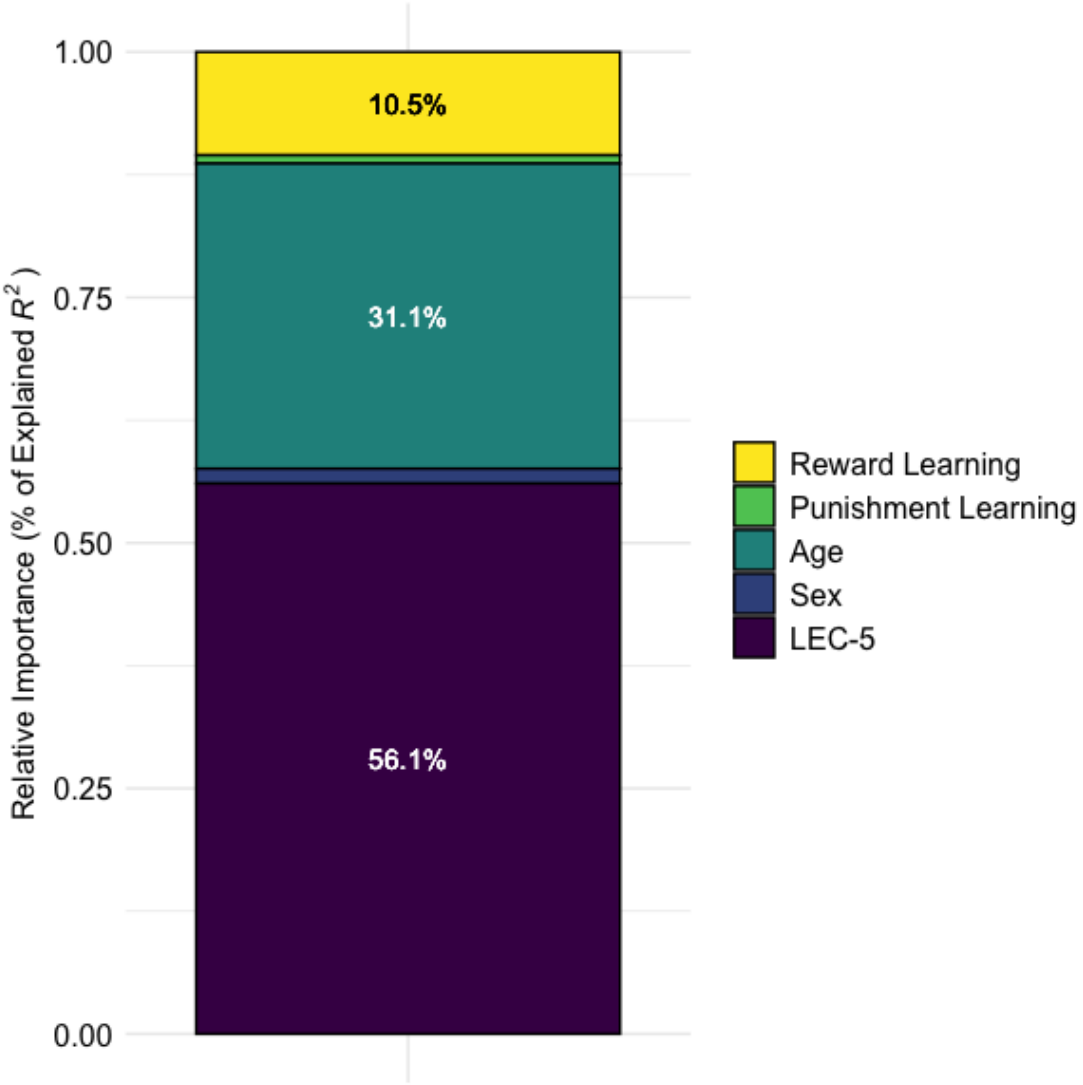
Note. For Model 1 *t*-statistic, *df* = 146; for Model 2, *df* = 144. LEC-5 = Life Events Checklist for *DSM-5*.

Due to the skewed distribution of the outcome variable, these results were verified with a robust regression. This analysis confirmed the pattern of statistical significance of predictors in the model (Appendix E).

The relative contributions of the variables to the total variance explained by this regression model are visualised in Figure 4, which shows the results of a relative importance regression (Grömping, 2007).

Figure 4

Relative Contribution of Variables in Predicting Posttraumatic Stress Symptoms



Note. The relative contribution of each predictor to the variance explained by the model predicting scores on the Posttraumatic Stress Symptom Checklist for *DSM-5*. LEC-5 = Life Events Checklist for *DSM-5*. Sex accounted for 1.5% of the explained variance, and punishment learning 0.8%.

3.3 Secondary Analyses

Fourteen participants (9.3%) reported having PTSD. We hypothesised that self-reported PTSD would be associated with lower reward learning scores. Twelve of these 14 participants were female and two were male; a chi-squared test of association confirmed that the sex distribution was not significantly different between the two groups ($\chi^2(1) = 0.61$, $p = .434$). Table 6 shows how these participants compare with the others on the study variables. Participants with self-reported PTSD did not differ significantly on age or punishment learning, but had significantly higher scores on the LEC-5 and PCL-5, and, in support of the hypothesis, significantly lower reward learning scores. We further tested two other ways of grouping participants: by the conventional PCL-5 cut-off score of 31, and by endorsement of the pattern of symptoms required for PTSD diagnosis in the *DSM-5* (Blevins et al., 2015). Neither analysis produced significant differences in learning variables between the groups (Appendix F).

Table 6

Comparison of Variables by Self-Reported PTSD

Variable	PTSD+		PTSD-		*t*(*df*)	*p*	Cohen's *d*
	M	*SD*	*M*	*SD*			
Age	52.93	16.52	44.94	19.20	-1.69 (16.8)	.109	–
LEC-5	5.86	2.82	2.88	2.23	-3.83 (14.7)	.002	1.30
PCL-5	31.93	18.40	13.06	14.80	-3.72 (14.8)	.002	1.26
Reward learning	-0.63	1.06	0.06	0.97	2.33 (15.3)	.034	0.70
Punishment learning	-0.20	0.77	0.02	1.02	0.97 (18.1)	.346	–

Note. PTSD = posttraumatic stress disorder; PTSD+ = participants who self-reported having PTSD ($n = 14$); PTSD- = participants who did not self-report having PTSD ($n = 136$); LEC-5

= Life Events Checklist for *DSM-5*; PCL-5 = Posttraumatic Stress Disorder Checklist for *DSM-5*.

3.4 Exploratory Analyses: Posttraumatic Stress Symptom Clusters

3.4.1 Descriptive Statistics

The four symptom clusters that comprise PTSD in the *DSM-5* are represented through their corresponding items on the PCL-5: intrusion symptoms by items 1–5, avoidance symptoms by items 6–7, negative alterations in cognition and mood symptoms by items 8–14, and arousal symptoms by items 15–20. Descriptive statistics and Shapiro-Wilk tests for normality for these four scores are shown in Table 7. All four symptom cluster scores were positively skewed and non-normally distributed (see Appendix G for histograms depicting their distributions).

Table 7

Descriptive Statistics and Shapiro-Wilk Tests for Symptom Clusters

Variable	*M*	*SD*	Range	Skew	Kurtosis	*W*	*p*
Intrusion	3.88	4.30	0–19	1.36	1.44	.83	<.001
Avoidance	1.89	2.09	0–8	1.03	0.12	.83	<.001
Cognition and mood	5.28	6.35	0–24	1.28	0.65	.81	<.001
Arousal	3.77	4.74	0–20	1.48	1.36	.78	<.001

Note. Highest possible score for each cluster: intrusion = 20; avoidance = 8; negative alterations in cognition and mood = 28; arousal = 24.

3.4.2 Relationships Between Symptom Cluster Scores and Other Variables

None of the symptom cluster scores differed significantly by sex (smallest $p = .242$; Appendix H). Table 8 shows Spearman correlation coefficients among the four symptom clusters and the study's other variables. All four symptom clusters had significant positive correlations with each other and with the LEC-5. Age had small negative correlations with each symptom cluster, although only the correlation with arousal symptoms reached significance. Neither learning variable significantly correlated with any symptom cluster.

Table 8

Spearman Correlation Coefficients for Symptom Cluster Scores

Variable	Intrusion	Avoidance	Cognition and mood	Arousal
Intrusion	–			
Avoidance	.82***	–		
Cognition and mood	.76***	.72***	–	
Arousal	.80***	.73***	.84***	–
Age	-.07	-.07	-.13	-.19*
LEC-5	.30***	.27**	.29***	.28***
Reward learning	-.10	-.06	-.03	.02
Punishment learning	-.05	.00	-.04	-.04

Note. LEC-5 = Life Events Checklist for *DSM-5*. Correlations with $p < .01$ were significant after the application of a Bonferroni correction.

*$p < .05$. **$p < .01$. ***$p < .001$.

3.4.3 Regression Analyses

To test the association of reward learning with each symptom cluster, we ran multiple linear regressions predicting each symptom cluster in turn, with age, sex, LEC-5 scores as predictors, followed by a second model with the addition of reward and punishment learning scores as predictors. The first model predicting intrusion symptoms was significant ($F(3, 146) = 6.13$, $p < .001$) and explained 11.18% of the variance. The second model with the learning scores included was also significant ($F(5, 144) = 5.76$, $p < .001$) and explained 16.67% of the variance, and reward learning was a significant predictor (Table 9). The difference between these models was significant ($F(2, 146) = 4.74$, $p = .010$). The inclusion of the learning scores explained an additional 5.49% of variance, a greater increase than the inclusion of learning scores brought to the regression model predicting total PTSS symptoms (Section 3.2.3). Reward learning accounted for 25.2% of the variance explained by the model, according to a relative importance regression (Figure 5).

Table 9

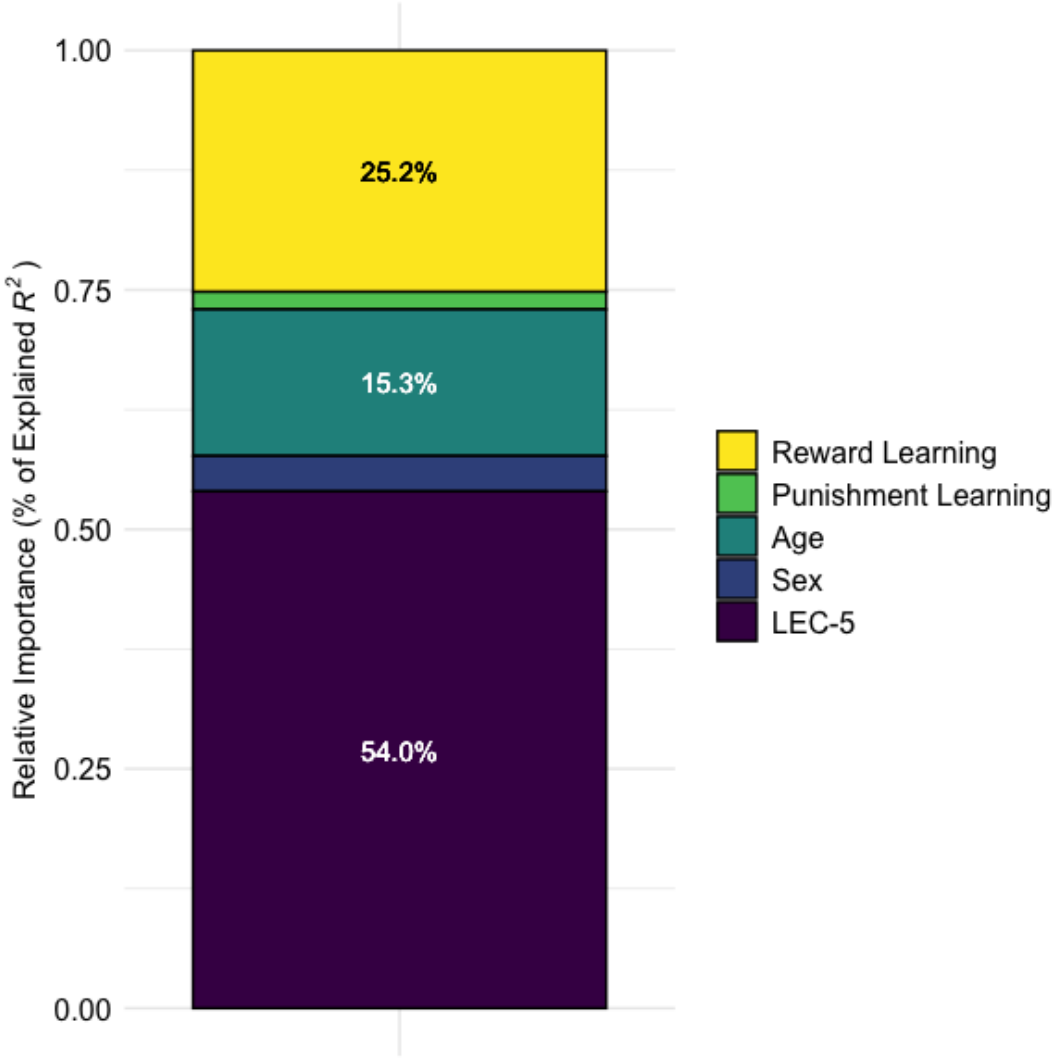
Regression Models Predicting Intrusion Symptom Cluster Scores

Variable	R^2	*B*	*SE B*	*β*	*t*	*p*
Model 1	.11					
Constant		4.07	0.96		4.24	<.001
Age		-0.04	0.02	-0.17	-2.07	.040
Sex (male)		-0.90	0.76	-0.09	-1.18	.239
LEC-5		0.56	0.14	0.32	4.00	<.001
Model 2	.17					
Constant		4.71	0.96		4.90	<.001
Age		0.05	0.02	-0.23	-2.86	.005
Sex (male)		-0.84	0.75	-0.09	-1.12	.264
LEC-5		0.57	0.14	0.33	4.15	<.001
Reward learning		-1.15	0.40	-0.27	-2.88	.005
Punishment learning		0.23	0.39	0.05	0.59	.560

Note. For Model 1 *t*-statistic, *df* = 146; for Model 2, *t*(*df*) = 144. LEC-5 = Life Events Checklist for *DSM-5*.

Figure 5

Relative Contribution of Variables in Predicting the Intrusion Symptom Cluster



Note. The relative contribution of each predictor to the variance explained by the regression model predicting intrusion symptom cluster scores on the Posttraumatic Stress Symptom Checklist for *DSM-5*. LEC-5 = Life Events Checklist for *DSM-5*. Sex accounted for 3.7% of the explained variance and punishment learning accounted for 1.8%.

A model predicting avoidance symptoms with age, sex, and LEC-5 scores was significant ($F(3, 146) = 6.64$, $p < .001$, $R^2 = .12$), as was a second model including learning scores as predictors ($F(5, 144) = 5.01$, $p < .001$, $R^2 = .15$), in which reward learning was a

significant predictor ($t(144) = -2.08$, $p = .039$). However, the addition of the learning scores did not significantly increase the amount of explained variance ($F(2, 146) = 2.37$, $p = .097$). Reward learning was not a significant predictor in regressions predicting negative alterations in cognition and mood or arousal symptoms. The full results of the regressions for these three clusters are given in Appendix I. Reduced reward learning was thus a significant predictor only for the intrusion symptoms, and this relationship was significant even after correcting for the fact that four exploratory regression models were run on the four symptom clusters.

Chapter 4: Discussion

4.1 The Current Study

The aim of this study was to investigate the relationship between PTSS and reward learning. It was hoped that we would be able to clarify this relationship through methodological choices that differentiated this study from previous research. Specifically, the central hypothesis was that poorer reward learning would be predictive of higher PTSS, measured on a spectrum including subthreshold levels. The data supported this hypothesis, both in an analysis controlling for trauma history, age, and sex, and also in the comparison of participants who did and did not report having PTSD. PTSS appears to relate specifically to poorer reward-based learning, not a general deficit in associative learning, as we did not find similar results in relation to learning from punishment. It is notable that the present study reports behavioural evidence of impaired reward learning associated with PTSS, which other studies have not found. There are a number of methodological factors which may have contributed to this, discussed below in Section 4.3.

These results extend the body of evidence that links PTSS to abnormalities in learning. PTSD is associated with poor fear extinction learning, as the failure of fear extinction is thought to maintain symptoms over time and prevent recovery (Rothbaum & Davis, 2003; VanElzakker et al., 2014). Learning from reward, as was measured in this study,

is generally thought to occur in the brain through the activity of dopaminergic neurons in a network of reciprocally connected areas including the ventral tegmental area, striatum, and prefrontal cortex (Cox et al., 2015; Der-Avakian & Markou, 2012; Pessiglione et al., 2006; Schultz, 2016). Research in various species, including humans, suggests that learning to extinguish fear operates through similar activity of dopaminergic neurons in the same or equivalent neural network (Abraham et al., 2014; Gerlicher et al., 2018; Kalisch et al., 2019; Thiele et al., 2021; Zhang et al., 2020). Some studies have identified fear extinction learning as specifically occurring in reward-responsive neurons (Felsenberg et al., 2018; Josselyn & Frankland, 2018; Zhang et al., 2020). In light of this apparent neural overlap, our results suggest that the recognised deficit in fear extinction learning in PTSD may be accompanied by a deficit in learning from reward. This also lends support to future investigations for the underexplored and potentially central role of dopamine in PTSS (Ney et al., 2021; Torrisi et al., 2019).

4.2 Exploratory Analyses: Posttraumatic Stress Symptom Clusters

As an exploratory analysis, this study investigated the relationship between reward learning and the four symptom clusters of PTSD in the *DSM-5*: intrusion, avoidance, negative alterations in cognition and mood, and arousal. Reward learning significantly predicted both intrusion and avoidance symptom scores, although only in the case of intrusion symptoms did the learning scores produce a significant increase in the variance explained by the model and remain significant after correcting for multiple comparisons. Reward learning was more predictive of the intrusion symptoms than it was of overall PTSS. These results suggest that, in the present study, the relationship between PTSS and reward learning was driven by the intrusion symptoms, and perhaps to a lesser extent by the avoidance symptoms, and not by the cognition and mood or arousal symptoms. This raises a number of interesting considerations.

In the *DSM-5*, the intrusion symptoms of PTSD involve persistently re-experiencing the traumatic event, such as through upsetting memories, nightmares, and flashbacks, or emotional distress or physical reactivity after exposure to reminders of the event (American Psychological Association, 2013). Many researchers consider these symptoms to be the core element of PTSD, as opposed to symptoms like anhedonia that may also be associated with other disorders (Bryant, 2019; Norrholm et al., 2011; Pitman et al., 2012; Rasmussen et al., 2018). Intrusion symptoms have been particularly linked to fear learning and fear extinction, such as in their association with a failure to regain physiological homeostasis after trauma-related cues (Norrholm et al., 2011; Norte et al., 2013; Zuj et al., 2016). The association found between higher intrusion symptoms and lower reward learning lends theoretical support to this model, in that intrusion symptoms represent the ongoing failure of fear extinction, and fear extinction is facilitated by reward learning.

As reviewed in Section 1.3.4, several studies have linked diminished reward responsiveness, in the sense of hedonic impact, to the symptom cluster of negative alterations in cognition and mood (Elman et al., 2009; Felmingham et al., 2014; Frewen et al., 2012; Lieberman et al., 2017). In the present study, however, this cluster was not significantly associated with reward learning. This suggests that different facets of reward functioning, or different neural abnormalities, may relate separately to different clusters of PTSS (Berridge et al., 2009; Der-Avakian & Markou, 2012; Ney et al., 2021; Torrisi et al., 2019). To further investigate this, it would be valuable to directly compare PTSS clusters with individual differences in the hedonic enjoyment of reward and in learning to predict future reward.

4.3 Methodological Factors: Strengths and Weaknesses

4.3.1 Study Sample

The sample size of the present study was substantially larger than those of previous studies of reward learning in PTSD as reviewed in Section 1.3.2, the largest of which was 87

(Myers et al., 2013). Given the apparent subtlety of the learning differences in question, having adequate power to detect such differences is vital (Lissek & van Meurs, 2015).

However, the characteristics of the present sample may compromise the generalisability of the findings. Participants self-selected in response to advertisements, and the resultant age and sex distributions were not representative of the general population. Participants were also subject to a number of exclusion criteria required by the larger study of which this research was a small part; these may have influenced the makeup of this study's sample. One such exclusion criterion was a current or past alcohol or drug dependency, both of which have high comorbidity with PTSD (Grant et al., 2015; Grant et al., 2016). This exclusion criterion was designed to remove the confounding effect of drug or alcohol dependency on learning tasks, but may also have prevented the participation of a particular subset of individuals with PTSD.

The use of a non-clinical, general population sample was a strength of the study. As described in Section 1.1.2, there are a number of barriers to the diagnosis of PTSD. For example, Liebschutz et al. (2007) found that only 11% of patients in primary care who met the full criteria for PTSD had it noted on their medical record. Samples comprised of individuals with known PTSD may therefore be non-representative of PTSS in the population. The use of a general population sample may have facilitated the examination of PTSS across a spectrum, regardless of fulfilment of the other criteria for PTSD.

4.3.2 Measurement of Posttraumatic Stress Symptoms

The inclusion of PCL-5 scores as a continuous variable was a strength of this study. The division of participants into groups for analysis, based on a cut-off of a continuous variable, is unfortunately common in PTSD research and weakens the analysis without any meaningful advantages (MacCallum et al., 2002). In this study, grouping by such a division did not reveal a significant relationship between PTSS and reward learning. Additionally,

while cut-off scores of the PCL-5 can achieve excellent sensitivity and specificity in specific populations, optimal cut-off scores vary greatly between populations (Geier et al., 2019; McDonald & Calhoun, 2010).

The measurement of PTSS could be improved by the administration of a clinical assessment by interview, such as the Clinician-Administered PTSD Scale for *DSM-5* (Weathers, Blake, et al., 2013a). The PCL-5 is a well-validated measure and was practical in the context of this study, but a clinical assessment could ensure more accurate and consistent interpretation of symptoms.

The measurement of PTSS could also be improved with the addition of information over time. The PCL-5 captured PTSS over the previous month, and did not include any other information about the timing of symptoms, whether they were recent or persistent, or whether they related to a recent or distant past event. This study therefore cannot shed light on how reward learning may relate to PTSS over time. This question is particularly important as PTSD may not follow a straightforward course to recovery, but can increase or fluctuate over time, along with unstable patterns of comorbid disorders (Kenardy et al., 2018; Solomon & Mikulincer, 2006). Symptoms can fluctuate above and below the threshold of diagnosis over time and as a result of varying life stress (Bryant et al., 2015; McFarlane et al., 2017). Approximately 40% of people with PTSD do not follow a trajectory of recovery, instead displaying symptoms with a delayed onset or at a high level chronically (Galatzer-Levy et al., 2018). Reduced reward learning may relate to present PTSS symptom levels or to lifetime PTSD. Remitted PTSD has been linked to blunted reward responsiveness (Kalebasi et al., 2015). By contrast, the self-reported PTSD variable referred to the condition over the lifetime. This variable may have therefore captured people with remitted PTSD. This ambiguity requires longitudinal studies or studies with more time-specific information in order to investigate these possibilities.

This study also measured PTSD by participants' report. This variable only captured participants who were aware of having or having had PTSD, which is not necessarily an accurate measure of lifetime PTSD. Additionally, their self-report was not externally verified, and three participants indicated that they were not diagnosed or unsure. The validity of the variable and the conclusions that can be derived from it are therefore limited.

4.3.3 Measurement of Trauma Exposure

In this study, the measurement of trauma exposure as a continuous variable was a strength. Although a single event can trigger PTSS, there is a well-established relationship between PTSS severity and the cumulative effect of multiple traumatic experiences over time (Section 1.2). It is common for studies on PTSD to analyse participants by group: those with PTSD and controls, who may be trauma-exposed, without a history of trauma, or separate groups of both. This has the advantage of theoretically being able to distinguish differences associated with trauma history and with PTSS, but could still be improved by the consideration of cumulative trauma exposure. Trauma history, as a continuous variable, should have provided this study with more sensitive and accurate information for analysis than is captured by the categorisation of participants (MacCallum et al., 2002).

Future research could include still more information regarding the level of risk of PTSS to which an individual's experiences have exposed them. In this vein, estimates of exposure to PTSS risk would ideally take into account the greater risk associated with events involving interpersonal or intimate partner violence (Breslau et al., 2004; Do et al., 2019; Forbes et al., 2014; Kessler et al., 2017). Additionally, traumatic events can be experienced directly or indirectly, through an individual witnessing them, learning about them occurring to a close loved one, or being exposed to them regularly in the course of work. This study used only directly experienced events, but indirectly experienced events also confer risk of PTSS and contribute to lifetime cumulative trauma exposure (Breslau, 2009; Chapman et al.,

2012; Kessler et al., 2017). Weis et al. (2021) have proposed a weighted scoring system as a compromise to reflect the risk levels associated with different types of exposure. The inclusion of information about the frequency with which individual events occurred might also increase the measure's power to predict PTSS (Wilker et al., 2015). Finally, evidence suggests that PTSS can also be triggered or worsened by non-traumatic stressors, including chronic stress and non-traumatic childhood adversity, which were not addressed in this study (Long et al., 2008; McLaughlin et al., 2017).

In this study, we did not hypothesise a relationship between trauma history and reward learning. There is mixed evidence regarding whether other differences in cognitive functioning in PTSD, including fear extinction learning, are a pre-trauma risk factor or acquired after trauma (Gurvits et al., 2006; Guthrie & Bryant, 2006; Lommen et al., 2013; Milad et al., 2008). There is some evidence that dampened reward functioning is linked to trauma in early life (Hanson et al., 2017; Harms et al., 2018) as well as other forms of early life stress (Sheridan et al., 2018; Wismer Fries & Pollak, 2017). However, in general, deficient reward functioning does not appear to be strongly acquired from trauma where PTSS do not develop (Nawijn et al., 2015). As covered in the introduction, reward learning may mediate the relationship between trauma or adversity in childhood and subsequent psychosocial difficulties (Section 1.3.2). General reward functioning may be a mechanism by which individuals are vulnerable to or resilient against PTSS following trauma (Charney, 2004). Elevated sensitivity to reward has been shown to buffer against the development of psychopathology following childhood maltreatment and traumatic experiences (Dennison et al., 2016; Kasparek et al., 2020). The regression models in this study did not test for a possible interaction or mediating relationship between trauma history and reward learning. It is likely that pre-existing neurocognitive qualities that act as risk factors for PTSD and those that develop as consequences of trauma or of the disorder interact and mutually influence

each other (Admon, Milad, et al., 2013; Jacob et al., 2019). Longitudinal data would be necessary to assess whether reward learning deficits precede trauma as a vulnerability factor for PTSS; in the absence of such data, our understanding of the relationships between these variables is limited.

4.3.4 Age

In this study's sample, the negative correlation between PTSS and age did not reach significance, but age was significantly predictive of PTSS in regression analyses. As covered in the introduction, older age is generally associated with lower PTSS, although this differs between samples and may interact with other factors (Section 1.1.2).

The relationship between these variables may be affected by the tendency among older adults to report less overall negative affect (Spaniol et al., 2008). Age might also interact with PTSS due to the time elapsed since the experience of traumatic events. For example, sexual assault is associated with a high risk for the development of PTSS (Breslau et al., 2004) and is more commonly experienced by younger than older adults (Cox, 2016). We might therefore expect that the relationship of trauma history and PTSS could be complicated by the passage of time, as the majority of individuals who develop PTSS after trauma recover over time (Chapman et al., 2012). As well as the general tendency for recovery from PTSS, symptoms may be affected by the fading affect bias, in which negative events are remembered with less specificity and less negative emotion over time (Walker et al., 2003).

Although possible interactions between age, trauma history, and reward learning were not analysed in this study, they may be important in future research. Age is logically related to measures of cumulative trauma history, as they encompass the whole lifespan. There is also a well-established relationship between lower reward learning and older age (Eppinger et

al., 2011). It is therefore important that this variable be taken into account in analyses on this subject.

4.3.5 Other Improvements and Future Directions

Alongside the possible improvements outlined above, the conclusions drawn in this study would also have been illuminated by the inclusion of other variables, such as substance use, prescription medications, and other psychopathologies such as depression and anxiety disorders. These variables may interact with the variables of interest in this study and provide a greater understanding of the factors involved. The measurement of reward learning could also be improved by incorporating a variety of learning tasks. To further validate the theoretical connection between reward learning and fear extinction learning, future research could compare individual performance on measures of both, with the caveat that a fear-based extinction learning task would entail a different motivational state from the neutral reward and punishment learning task used here.

4.4 Practical Implications

Front-line therapies for PTSD typically involve exposure, in the sense of direct engagement with the memory of trauma, which is theoretically based in fear extinction learning (Bryant, 2019; McLean & Foa, 2011). However, these therapies are generally ineffective for approximately a third of patients, and so there is a distinct need for the development of novel therapeutic approaches for PTSD (Bradley et al., 2005).

Given the research on the reward-related, dopaminergic basis of fear extinction, pharmacological approaches that enhance reward learning may be useful in treating PTSD (Craske et al., 2018; Raczka et al., 2011; Salinas-Hernández et al., 2018). Studies have found support for the treatment of PTSS with drugs that enhance dopamine release, which is necessary for reward learning, including L-Dopa (Gerlicher et al., 2019; Whittle et al., 2016), methylphenidate (Houlihan, 2011; McAllister et al., 2016), and 3,4-

methylenedioxymethamphetamine (MDMA), the latter of which has shown effectiveness in otherwise treatment-resistant PTSD and with lower dropout rates than exposure-base psychotherapy (Amoroso & Workman, 2016; Mithoefer et al., 2018). Such pharmacological therapies may translate to early interventions with the potential to prevent PTSS following trauma and interventions for populations at risk for psychopathology following early life stress (Bryant, 2021; Novick et al., 2018). This may also contribute to treatments for other disorders that have been associated with impairments in fear extinction, such as obsessive compulsive disorder, phobias, and schizophrenia (Holt et al., 2009; Milad et al., 2013; Ressler & Mayberg, 2007).

4.5 Conclusion

In summary, the current study sought to investigate the relationship between PTSS and reward learning, and found that higher PTSS were associated with lower learning from reward. This study employed methodological choices that may have allowed greater sensitivity to detect subtle individual differences than previous similar work. Additionally, this relationship was strongest with symptoms of intrusive re-experiencing, which previous research has linked to deficits in fear extinction learning. These results suggest a relationship between extinction learning and reward learning in PTSS, which may contribute to both further research and developments in treatment in the future.

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Appendix A

Information Sheets and Consent Forms

Cognitive function across the lifespan
Participant Information Sheet

Investigators	Dr Irina Baetu, Dr Lyndsey Collins-Praino, A/Prof Sarah Cohen-Woods, Dr Ahmed Moustafa, Prof Nicholas Burns
Human Research Ethics Committee Approval Number	H-2020-017
Location	The University of Adelaide, North Terrace Campus / Western Sydney University

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project. Please read the information contained in this document carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor.

Participation in this research is voluntary. If you don't wish to take part, you don't have to.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:
• Understand what you have read
• Consent to take part in the research project
• Consent to have the tests that are described
• Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

2 What is the purpose of this research?

This project will examine how general cognitive function (for example, decision-making, reasoning ability, working memory, processing speed) changes with age. We know that many aspects of cognitive function are to some extent genetically determined. Genes (DNA) that affect the expression of certain chemicals and receptors in the brain seem to influence the ability to perceive and process information in our environment, form new memories, and make decisions. This project will try to understand genetic influences on cognitive performance across the lifespan. This project could lead to a deeper understanding of how cognitive function evolves in healthy ageing, and could provide a tool based on genetic

scores to predict an individual's trajectory of cognitive function. This could help identify individuals who are at risk for cognitive decline, which could then inform better interventions.

In addition, depending on your demographics, your results may also be used in a study investigating genetic predictors of cognitive performance in patients with Parkinson's disease (University of Adelaide ethics approval number H-2016-219). Given that we need to compare the patients' performance to that of healthy individuals, your results may be included in this study's healthy control group. Given that we need to ensure that our patient and healthy control groups are similar in terms of age, gender distribution and education levels, the inclusion of your data in the healthy control group will depend on the demographics of our recruited patient groups.

3 What does participation in this research involve?

For this study, we are seeking participants who are:

1. aged 18-80 years
2. native English speakers (This is because we will employ a vocabulary test, and interpreting the results of individuals whose native language is not English is difficult)
3. not suffering from a neurological disorder and no history of brain injury
4. not suffering from a drug or alcohol dependency, either a current or previous condition
5. not smoking more than 5 cigarettes per day
6. not using medication that affects neurological function (e.g., sedatives, antipsychotics)
7. not suffering from an uncorrected visual disorder
8. not diagnosed with a learning disability.

You will be asked to attend a testing session, which will take approximately 2.5-3 hours in total, with breaks given as required. Refreshments will be available during needed breaks. The testing session will take place at the University of Adelaide, North Terrace Campus or Western Sydney University. You will also be asked to complete a series of surveys using an online link that will be sent to you via email or text message. If you are having difficulty accessing or completing the surveys online, please let us know and we will organise for you to complete them in person during the testing session.

Questions and tests will include:

1. Questions regarding demographic information (age, gender, disease history)
2. Questions regarding vascular risk factors (high blood pressure, tobacco use, weight, history of diabetes, physical inactivity, poor diet, history of high cholesterol/lipids)
3. The Montreal Cognitive Assessment
4. Short questionnaires that assess mood, personality, and history of adverse life events
5. A series of tests that assess your reasoning ability, processing speed, working memory, executive function, and general vocabulary.
6. Tests that assess your ability to learn to select correct actions and inhibit incorrect actions.
7. Short tests that assess motor function (for example, tremor).

In order to investigate whether there is a relationship between target genotypes and cognitive performance, we will ask you to provide a saliva sample from which your DNA will be analysed. The genetic code of our DNA varies between people, with these changes called a variant, or a mutation. This variation exists for a number of reasons and can contribute to the many things that make us different from one another. In addition to physical factors such as hair, and eye colour, they can contribute to behaviour and how we learn and make decisions. We know that different DNA variants affect cognitive performance, and we

would like to compare your DNA with that of other participants, to identify potential genetic pathways that are related to differences in cognitive performance. The genetic variation we will investigate is likely to have small effects on performance. This could, nevertheless, be useful in the future for developing more accurate diagnoses for a number of disorders that are characterised by loss of cognitive function, along with other pieces of information, such as motor, cognitive and mood assessments.

We wish to store your DNA and collected data in a biobank, a database that contains your de-identified information (preserving your anonymity) so that other researchers could use this data to answer other research questions. Please see the attached Biobank Information Sheet and Consent Form for more information about this.

To thank you for your participation in the study, you will receive a $50 Coles/Myer gift card at the end of the testing session.

4 Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign, as well as the Biobank Information Sheet and Consent Form, and you will be given a copy to keep.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your opportunity to take part in future studies.

5 What are the possible benefits of taking part?

The results of this research project will not provide you with any direct benefit. However, the current study will advance our understanding of brain functions, which has potential implications for detection and treatment of cognitive impairment in a number of disorders, including Parkinson's disease.

6 What are the possible risks and disadvantages of taking part?

Mood questionnaires
You will be asked to complete questionnaires that assess levels of depression, anxiety and stress. The questionnaires are not diagnostic tools and cannot be used to diagnose depression or anxiety. However, you may be contacted (via e-mail and telephone) for follow-up based on your scores. The purpose of this follow-up is to provide you with information about available resources for coping with psychological problems should you need them.

Montreal Cognitive Assessment
We will use the Montreal Cognitive Assessment to screen for possible cognitive impairment. Scores below 26/30 are considered abnormal, and we may contact you if your score is below 26 to inform you of the outcome of the test, as an early diagnosis of cognitive impairment could help planning treatment. Please note that this is not a diagnostic test. Mild cognitive impairment is not dementia, and it does not always lead to dementia. It is defined as a noted problem with cognition or brain processing that is unusual for a person's age or education. Mild cognitive impairment does not usually cause any interference with the person's daily level of activities. Although the cause of the syndrome is not fully known, it is possible that it could be triggered by stress or illness. So someone can score below the cutoff score because of temporary illness, fatigue, or other reasons. Furthermore, a good

number of people who score below the cutoff at some point seem to recover their cognitive function and score in the normal range when retested. For these reasons, this test cannot be used to diagnose an illness such as dementia. Such a diagnosis would require further testing.

Genetic analyses
Finally, even though results do not have clinical utility at this stage and individual results will not be returned, statutory or contractual duties may require us or you to disclose the results of genetic tests or analysis to third parties (for example, insurance companies, employers, financial and educational institutions), particularly where results provide information about health prospects.

7 Will I be given the results of the research project?

We have developed new cognitive tests to assess cognitive performance more precisely. However, because these tests are novel, they have not been standardised. This means although one can compare scores of different individuals, it is difficult to interpret these differences in a meaningful way (for example, a given score on a test does not necessarily indicate cognitive decline). For this reason, we will not give you feedback on your results on the cognitive tests. We can only give you feedback on the Montreal Cognitive Assessment and the mood questionnaires, which are standardised tests.

Part 2 How is the research project being conducted?

8 What will happen to information about me?

A unique ID number will be given to all your samples and data in place of your name, in order to prevent anyone from identifying you from your samples or data. These ID numbers **will not** correspond to any names, emails, addresses or phone numbers that may be used to identify you. A document linking your name to your unique ID will be kept by the Principal Investigator, Dr Irina Baetu, who will store this securely on a computer at the University of Adelaide. In general, your samples and data will not be released for any use without your prior consent, unless required by law or by the ethics committee that approved this project. It may also be used to re-contact you in the future to ask for your participation in a follow-up study if you have consented to be re-contacted for that purpose, or to convey the results of mood questionnaires and the Montreal Cognitive Assessment, as explained in Section 6.

Only average results from all participants will be reported in future publications and presentations. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, maintaining your confidentiality.

Please note that publication and funding requirements may require submission of data or information to controlled access repositories that meet international security and safety standards for sharing with researchers globally. Any data (including genetic and cognitive testing data) shared via such repositories will be de-identified, protecting your anonymity.

In accordance with relevant Australian privacy and other relevant laws, you have the right to request access to your information collected and stored by the study team. You also have the right to request that any information with which you disagree be corrected. Please contact a study team member named at the end of this document if you would like to access your information.

9 Who is organising and funding the research?

This project is funded by the Australian Research Council, and is being conducted by Dr Irina Baetu, Dr Lyndsey Collins-Praino and Professor Nicholas Burns of the University of Adelaide, A/Prof. Sarah Cohen-Woods of Flinders University, and Dr Ahmed Moustafa of Western Sydney University.

Please note that you will not benefit financially from your involvement in this research project even if, for example, knowledge acquired from analysis of your saliva sample and other information collected from you prove to be of commercial value to the institutions with which the investigators are affiliated.

No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

10 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of the University of Adelaide.

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2018)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

11 Further information and who to contact

The person you may need to contact will depend on the nature of your query.
If you want any further information concerning this project, you can contact the principal Investigator, Dr Irina Baetu, or any of the following people:

Dr Irina Baetu
Phone: (08) 8313 6102
Email: irina.baetu@adelaide.edu.au

Dr Lyndsey Collins-Praino
Phone: (08) 8313 5488
Email: lyndsey.collins-praino@adelaide.edu.au

A/Prof Sarah Cohen-Woods
Phone: (08) 8201 2722 / (08) 8404 2803
Email: sarah.cohenwoods@flinders.edu.au

Dr Ahmed Moustafa
Phone: (02) 9772 6847
Email: a.moustafa@westernsydney.edu.au

Prof Nicholas Burns
Phone: (08) 8313 3965
Email: nicholas.burns@adelaide.edu.au

The study has been approved by the Human Research Ethics Committee at the University of Adelaide (approval number H-2020-017). Please contact the Human Research Ethics Committee's Secretariat on phone +61 8 8313 6028 or by email to hrec@adelaide.edu.au if you wish to speak with an independent person regarding concerns or a complaint, the University's policy on research involving human participants, or your rights as a participant. Any complaint or concern will be treated in confidence and fully investigated. You will be informed of the outcome.

12 If I want to participate, what do I do?

Following your reading of this Participant Information sheet, if you wish to participate, please contact cognitive_study@adelaide.edu.au or (08) 8313 0012.

Mental Health Resources

We understand that some of the questionnaires included in this study might cause feelings of distress or might remind you of events or circumstances that cause you to feel anxious. Should you need to speak to someone immediately regarding your psychological difficulties, please contact your GP or health professional. There are also a number of services that you can access to help you with any difficulties you might experience.

The Australian Government provides access to information and digital resources, as well as information about other free or low-cost counselling and support services for mental health. Please visit www.headtohealth.gov.au for more information. In particular, please take note of the following services:

Mental Health Assessment and Crisis Intervention Service: provides immediate help in regard to a crisis in your health or living circumstances.
13 14 65 *[Note that this number is for South Australia; participants recruited in Sydney will be given the New South Whales contact number: Mental Health Line 1800 011 511]*

Lifeline Australia: a crisis support service that provides short-term support at any time for people who are having difficulty coping or staying safe.
www.lifeline.org.au
13 11 14

Beyond Blue: provides support on a range of mental health issues and is available by phone, online chat or email.
www.beyondblue.org.au
1300 22 4636

Suicide Call-Back Service: anyone considering suicide, living with someone who is considering suicide, or bereaved by suicide, can access the Suicide Call-Back Service.
www.suicidecallbackservice.org.au
1300 659 467

MensLine Australia: a telephone and online counselling service for men.
www.mensline.org.au
1300 78 99 78

Open Arms – Veterans and Families Counselling: provides current serving armed forces personnel, veterans and their families free and confidential counselling, group treatment programs, and community and peer networks.
www.openarms.gov.au
1800 011 046

Kids Helpline: a free, private and confidential phone and online counselling service for young people aged 5 to 25 years old.
www.kidshelpline.com.au
1800 55 1800

eheadspace: free online and telephone support and counselling for young people aged 12 to 25 years old, their families and friends.
headspace.org.au/eheadspace
1800 650 890

ID: _____

Cognitive function across the lifespan
Participant Consent Form

Investigators	Dr Irina Baetu, Dr Lyndsey Collins-Praino, A/Prof Sarah Cohen-Woods, Dr Ahmed Moustafa, Prof Nicholas Burns
Human Research Ethics Committee Approval Number	H-2020-017
Location	The University of Adelaide, North Terrace Campus / Western Sydney University

Declaration by Participant

- I have read the Participant Information Sheet.
- I understand the purposes, procedures and risks of the research described in the project.
- I have had an opportunity to ask questions and I am satisfied with any answers I have received.
- I understand that I will be given a signed copy of this document to keep.

I consent to being recontacted in the future if I am eligible to participate in other studies and/or to provide further biological samples: **Yes** ☐ **No** ☐

I wish my treating health professional to be notified if my scores on the mood questionnaires indicate that I may be suffering from depression, anxiety, or stress (if you tick yes, please provide his or her name and contact information): **Yes** ☐ **No** ☐

Name_____ Contact Information:_____

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the project by contacting the researchers listed in the information sheet, and that withdrawal will not affect my future health care.

I understand that should I choose to withdraw, I can request for my data (including questionnaire answers and genetic information) be omitted from research, and my biological samples destroyed.

Name of Participant (please print): _____

Signature: _____ Date: _____

Declaration by Researcher

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood all the necessary information contained in the information sheet required for their informed consent.

Name of Researcher (please print): _____

Signature: _____ Date: _____

Note: All parties signing the consent section must date their own signatures.

A biobank for genomic, cognitive and motor function data
Participant Information Sheet

Investigators	Dr Irina Baetu, Dr Lyndsey Collins-Praino, A/Prof Sarah Cohen-Woods, Dr Ahmed Moustafa, Prof Nicholas Burns, Dr Oren Griffiths
Human Research Ethics Committee Approval Number	H-2020-016
Location	The University of Adelaide, North Terrace Campus / Western Sydney University

Part 1 What does my participation involve?

1 Introduction

You will be asked to donate a sample of saliva which will be used for genetic research. Please read the information contained in this document carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor.

Participation in this research is voluntary. If you don't wish to take part, you don't have to.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:
• Understand what you have read
• Consent to take part in the research project
• Consent to have the tests that are described
• Consent to the use of your personal and health information as described.

You will be given a copy of this Biobank Information Sheet and Consent Form to keep.

2 What is genetic research?

Genes are made of DNA – the chemical structure carrying your genetic information that determines many human characteristics such as the colour of your eyes and hair. Researchers study genes in order to understand the link between our biological makeup and our behaviour, or our risk for different diseases. For example, genetic research can be used to understand why some people have a certain condition, such as Parkinson's disease, or why some people's cognitive function is better preserved as they age.

3 What is the purpose of this research?

We know that many aspects of motor and cognitive function are to some extent genetically determined. Genes (DNA) that affect the expression of certain chemicals and receptors in the brain seem to influence the ability to perceive and process information in our

environment, form new memories, and make decisions. This biobank will provide a tool to help us understand genetic influences on behaviour. This could help identify individuals who are at risk for cognitive decline, which could then inform better interventions.

4 What does participation in this research involve?

In order to investigate whether there is a relationship between target genotypes and behaviour, we will ask you to provide a saliva sample from which your DNA will be analysed. The genetic code of our DNA varies between people, with these changes called a variant, or a mutation. This variation exists for a number of reasons and can contribute to the many things that make us different from one another. In addition to physical factors such as hair, and eye colour, they can contribute to behaviour and how we learn and make decisions. We know that different DNA variants affect cognitive performance, and we would like to compare your DNA with that of other participants, to identify potential genetic pathways that are related to differences in cognitive performance. The genetic variation we will investigate is likely to have small effects on performance. This could, nevertheless, be useful in the future for developing more accurate diagnoses for a number of disorders that are characterised by loss of cognitive function, along with other pieces of information, such as motor, cognitive and mood assessments.

5 What are the possible risks and disadvantages of taking part?

Genetic testing involves the study of genetic material (typically DNA), which you share with your blood relatives. Genetic research is undertaken for many reasons, including discovering more accurate ways of predicting disease within a group of people. It is important to note the current study **is not** employing genetic testing. That is, we will not intentionally test whether you carry genetic material that is known to cause a disease. Instead, we will perform genetic analyses that identify patterns in the DNA that are linked to small differences in brain function and behaviour between individuals. Although these genetic differences may cause changes in behaviour, they are not currently used to diagnose disorders. Our primary analyses focus on single point mutations in the genome. So given that we are not screening for clinical disorders in this study, we will not return your individual genetic results.

Please be aware that the impact of genomic information may change over time as new knowledge is gained. We will not be revisiting your genomic data in the context of medical advancements as this is indefinite.

6 What will happen to my test samples?

We would like to store your saliva sample in a biobank for use in any future research studies that may or may not be related to the original research project. Further information can be found in this document's section on banking. Any such studies would require additional ethical clearances through our ethics committees.

7 Will I be given the results of the research project?

If you wish to find out the aggregate results of the study as they might appear in professional publications, please feel free to follow A/Prof. Cohen-Woods' laboratory's official Facebook page linked below. Please note that these publications will not include any information that can identify any individual.
Behavioural GEMs Facebook page: https://www.facebook.com/bGEMslab/

8 Banking (long term storage of samples and data)

“Banking” is storing health information and biological samples for future research studies. A “bank” is the place where the health information and samples are stored. Your saliva will be securely stored as re-identifiable specimen(s) by A/Prof. Cohen-Woods, currently at the Flinders Centre for Innovation in Cancer (FCIC). The health information will be the responses to the questionnaires and your performance on the cognitive and motor function tests, as well as your diagnosis, and will be stored securely on computers at the University of Adelaide and Flinders University. New information is constantly being published in relevant scientific fields, and we would like to take the opportunity to contribute to future research where relevant with your samples. We are not currently able to specify what these studies in the future may be, however we seek permission to store and analyse your samples in the future for such analyses. We request you to consider taking part in this bank due to the potential benefits of ongoing research in this area. Other researchers may also have access to a de-identified database including your saliva, DNA and cognitive test results, which may allow them to answer research questions that we have or could not answer. When data and samples are shared with other researchers and/or deposited in a repository, the data and samples are de-identified.

Your saliva, DNA, and data will be stored in the bank using a means that ensures your confidentiality and anonymity. The only people with access to identifying information are the professionals who need to check the project data. These people are limited supervisors of the project and/or inspectors from the ethics committee. They may view your name and other collected information but have no right to reveal this information to anyone else.

Your saliva sample will be stored to be re-identifiable. This means that your identity is not linked within the bank, data, or in analyses, however it can be re-linked for purposes of follow-up studies. Therefore it is re-identifiable. You can have your sample removed and destroyed from the bank at any point by contacting the principal investigator, Dr Irina Baetu, via email (irina.baetu@adelaide.edu.au) or by writing at the following address:

Dr Irina Baetu
School of Psychology
The University of Adelaide
North Terrace Campus
Hughes Building, level 5
Adelaide, SA 5005

Please note that if you choose to withdraw your data, including your saliva sample, your saliva sample and/or DNA will be disposed of according to biohazard management policies of the University, but this will not affect any de-identified (i.e., anonymous) data already shared with other researchers, or data previously analysed. This will result in your data being deleted and excluded in future analyses, but will not influence analyses and/or data sharing retrospectively.

9 What are the possible benefits of banking my saliva?

There is no direct benefit to you. Other people might benefit if researchers learn more by using your banked saliva sample and other information collected during this study.

10 What are the possible risks and disadvantages of banking?

This procedure forms part of the main research project. There is no extra physical risk to you as part of the research.

Your saliva will be stored in the bank using a means that ensures your confidentiality and anonymity. The only people with access to identifying information are professionals who need to check the project data. These people are limited to the research team and/or inspectors from the ethics committee. They may view your name and associated information but have no right to reveal this information to anyone else.

11 Will I be informed of results of future research using my biospecimen?

The aggregate results of this and other studies that have used your saliva sample and other data will likely appear on A/Prof. Cohen-Woods' laboratory's official Facebook page (https://www.facebook.com/bGEMslab/). Please note that these publications will not include any information that can identify any individual.

Although genomic information may change over time as new knowledge is gained, we will not be revisiting your genomic data in the context of medical advancements as this is indefinite. Therefore, you will not be informed of the results of future research.

12 Banking of Health Information

The health information we will collect and store in a bank for this research project consists of your responses to the questionnaires and your performance on the cognitive and motor function tests, as well as your answers to the demographic and health-related questions.

We will not use your personal health information for a different research project without the permission of a Human Research Ethics Committee. Once all personal identification is removed, the information might be used or released for other purposes without asking you. Results of the research project may be presented in public talks or written articles, but information will not be presented that identifies any participant.

Part 2 How is the research project being conducted?

13 What will happen to information about me?

All genetic and other biological samples will be de-identified; a unique ID number will be given to all your samples in place of your name, in order to prevent anyone from identifying you from your samples. These ID numbers **will not** correspond to any names, emails, addresses or phone numbers that may be used to identify you. A document linking your name to your unique ID will be kept by the Principal Investigator, Dr Irina Baetu, who will store this securely on a computer at the University of Adelaide. She will be the only one able to access this information. This information will only be accessed in the case that a) we find medically significant information, and b) you have requested that we inform you of said information. In general, your samples and data will not be released for any use without your prior consent, unless required by law, by an insurance agency, or by the ethics committee that approved this project. It may also be used to re-contact you in the future to ask for your participation in a follow up study if you have consented to be re-contacted for that purpose.

Only average results from all participants will be reported in future publications and presentations. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, maintaining your confidentiality.

Please note that publication and funding requirements may require submission of data or information to controlled access repositories that meet international security and safety standards for sharing with researchers globally. Any data (including genetic and cognitive testing data) shared via such repositories will be de-identified, protecting your anonymity.

In accordance with relevant Australian privacy and other relevant laws, you have the right to request access to your information collected and stored by the study team. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your information.

Please note that you will not benefit financially from your involvement in this research project even if, for example, knowledge acquired from analysis of your saliva sample and other information collected from you prove to be of commercial value to the institutions with which the investigators are affiliated.

14 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of the University of Adelaide.

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2018)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

15 Further information and who to contact

The person you may need to contact will depend on the nature of your query.
If you want any further information concerning this project, you can contact the principal investigator, Dr Irina Baetu, or any of the following people:

Dr Irina Baetu
Phone: (08) 8313 6102
Email: irina.baetu@adelaide.edu.au

Dr Lyndsey Collins-Praino
Phone: (08) 8313 5488
Email: lyndsey.collins-praino@adelaide.edu.au

A/Prof Sarah Cohen-Woods
Phone: (08) 8201 2722 / (08) 8404 2803
Email: sarah.cohenwoods@flinders.edu.au

Dr Ahmed Moustafa
Phone: (02) 9772 6847
Email: a.moustafa@westernsydney.edu.au

Prof Nicholas Burns
Phone: (08) 8313 3965
Email: nicholas.burns@adelaide.edu.au

Dr Oren Griffiths
Phone: (08) 8201 7567
Email: oren.griffiths@flinders.edu.au

The study has been approved by the Human Research Ethics Committee at the University of Adelaide (approval number H-2020-016). Please contact the Human Research Ethics Committee's Secretariat on phone +61 8 8313 6028 or by email to hrec@adelaide.edu.au if you wish to speak with an independent person regarding concerns or a complaint, the University's policy on research involving human participants, or your rights as a participant. Any complaint or concern will be treated in confidence and fully investigated. You will be informed of the outcome.

ID: _____

A biobank for genomic, cognitive and motor function data

Participant Consent Form

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Human Research Ethics Committee Approval Number	H-2020-016
Location	The University of Adelaide, North Terrace Campus / Western Sydney University

Declaration by Participant

I have read the Participant Information Sheet
I understand the purposes, procedures and risks of the research described in the project.
I have had an opportunity to ask questions and I am satisfied with any answers I have received.
I understand that I will be given a signed copy of this document to keep.
I give permission for the use of my data and DNA and/or tissue for the purposes of **(choose one)**:

The research project associated with this study only ☐

This research project associated with this study, and any future research projects that may or may not be related to the aims of this research project ☐

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the project by contacting the researchers listed in the information sheet, and that withdrawal will not affect my future health care.

I understand that should I choose to withdraw, I can request for my data (including questionnaire answers and genetic information) be omitted from research, and my biological samples destroyed.

Name of Participant (please print): _____

Signature: _____ Date: _____

Declaration by Researcher

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood all the necessary information contained in the information sheet required for their informed consent.

Name of Researcher (please print): _____

Signature: _____ Date: _____

Note: All parties signing the consent section must date their own signatures.

Appendix B

Exclusion Criteria

Exclusion criteria comprised of the following:

- suffering from a neurological disorder;
- history of brain injury;
- suffering from a drug or alcohol dependency, either a current or previous condition;
- smoking more than 5 cigarettes per day;
- using medication that affects neurological function (e.g. sedatives, antipsychotics);
- suffering from an uncorrected visual disorder;
- diagnosed with a learning disability.

Appendix C

Learning Task Instructions

Initial task instructions:

"In this task, you'll be presented with different pairs of pictures. For every pair you're presented with, you'll need to tap one of the two pictures, like this. Once you do, you'll find out whether your response was correct or incorrect. This feedback will help you make the right choices more often. You'll only have 4 seconds to make a response, so don't waste too much time making a decision.

Remember, your task is to discover which pictures are more likely to be correct, and to maximise how many correct choices you make. Tap the 'Replay' button to watch these instructions again, or tap the 'Start' button to begin."

Instructions before each test phase:

"It's time to test what you've learnt! During this set of trials you will NOT receive feedback ('Correct!' or 'Incorrect') to your responses. If you see new combinations of pictures, please choose the picture that 'feels' more correct based on what you have learnt so far. If you're not sure which one to pick, just go with your gut instinct. Please remember to continue responding even though you will no longer receive feedback. Tap the 'Start' button to begin."

Instructions before each new set:

"In the next phase of this task, you will be presented with entirely new pairs of pictures. On every trial you will have to choose one of the pictures by tapping it. Like before, you will be informed whether your response was correct or incorrect. Your task is to discover which pictures are more likely to be correct and to maximise how many correct choices you make. Tap the 'Start' button to begin."

Appendix D

Comparison of Variables by Sex

Table D1

Comparison of Variables by Sex

Variable	Female (n = 110)		Male (n = 40)		$t(df)$	p
	M	*SD*	*M*	*SD*		
Age	47.24	18.99	41.42	18.83	1.67 (69.8)	.100
LEC-5	3.17	2.30	3.10	2.82	0.15 (59)	.884
PCL-5	15.23	16.85	13.70	13.85	0.56 (83.6)	.575
Win-stay	.87	.13	.87	.10	-0.18 (83.3)	.860
Lose-shift	.63	.11	.62	.13	0.61 (61.1)	.547
Choose-A	.75	.15	.78	.15	-1.05 (72.4)	.298
Avoid-B	.78	.14	.79	.16	-0.32 (60.1)	.750

Note. LEC-5 = Life Events Checklist for *DSM-5*; PCL-5 = Posttraumatic Stress Disorder Checklist for *DSM-5*.

Appendix E

Robust Regression Model Predicting Posttraumatic Stress Symptoms

Table E1

Robust Regression Model Predicting Posttraumatic Stress Symptoms

Variable	*B*	*SE B*	*t*(144)	*p*
Constant	17.19	3.12	5.52	<.001
Age	-0.25	0.06	-4.13	<.001
Sex (Male)	-1.93	2.41	-0.80	.426
LEC-5	2.50	0.45	5.58	<.001
Reward learning	-3.19	1.29	-2.47	.015
Punishment learning	0.04	1.25	0.03	.974

Note. LEC-5 = Life Events Checklist for *DSM-5*. The robust regression was performed using the `rlm` function of the MASS package in R (R Core Team, 2020; Venables & Ripley, 2002).

Appendix F

Comparison of Variables by Possible PTSD

The PCL-5 scores of 24 participants (16%) were over the conventional cut-off score of 31, indicating possible PTSD (Blevins et al., 2015). Of these participants, 19 were female and five male, while of participants under the cut-off, 91 were female and 35 male; this distribution was not significantly different between the two groups ($\chi^2(1) = 0.21$, $p = .650$). Table F1 shows the comparison of participants by cut-off score across the study's main variables; those above the cut-off score were significantly younger than those below, while LEC-5 scores and both learning variables were not significantly different.

Table F1

Comparison of Variables by PCL-5 Cut-Off Score

Variable	PTSD+		PTSD-		*t*(*df*)	*p*	Cohen's *d*
	M	*SD*	*M*	*SD*			
Age	35.55	16.17	47.66	18.98	3.32 (36.2)	.002	0.66
LEC-5	4.33	3.34	2.93	2.17	-1.98 (26.8)	.058	–
Reward Learning	-0.24	1.15	0.05	0.97	1.15 (29.5)	.261	–
Punishment Learning	-0.10	0.74	0.02	1.04	-0.64 (42.8)	.523	–

Note. PTSD = posttraumatic stress disorder; PCL-5 = PTSD Checklist for *DSM-5*; PTSD+ = participants scoring 31 or higher on the PCL-5 ($n = 24$); PTSD- = participants who scored below 31 on the PCL-5 ($n = 126$); LEC-5 = Life Events Checklist for *DSM-5*.

Twenty-three participants (15.3%) met the *DSM-5* symptom pattern across clusters, indicated by endorsing a 2 (*Moderately*) or higher on the relevant symptoms: one symptom in each of the intrusion and avoidance clusters, and two in each of the negative alterations in

cognition and mood and arousal clusters. Of these participants, 17 were female and six were male. A chi-square test of association confirmed that this distribution did not differ significantly ($\chi^2(1) < .001$, $p = 1$). Table F2 shows the comparison of participants by cut-off score across the study's main variables. Those who endorsed the *DSM-5* symptom pattern had significantly younger age and greater PCL-5 scores than those who did not, and did not differ significantly in the other variables.

Table F2

Comparison of Variables by DSM-5 *PTSD Symptom Pattern*

Variable	PTSD+		PTSD-		*t*(*df*)	*p*	Cohen's *d*
	M	*SD*	*M*	*SD*			
Age	33.91	16.30	47.82	18.80	3.67 (33.5)	<.001	0.75
LEC-5	3.78	2.84	3.04	2.36	-1.18 (27.7)	.247	–
PCL-5	44.65	12.68	9.42	9.25	-12.7 (26.4)	<.001	3.58
Reward Learning	-0.08	1.19	0.01	0.97	.341 (27.5)	.736	–
Punishment Learning	0.05	0.82	-0.01	1.03	-0.32 (35.9)	.749	–

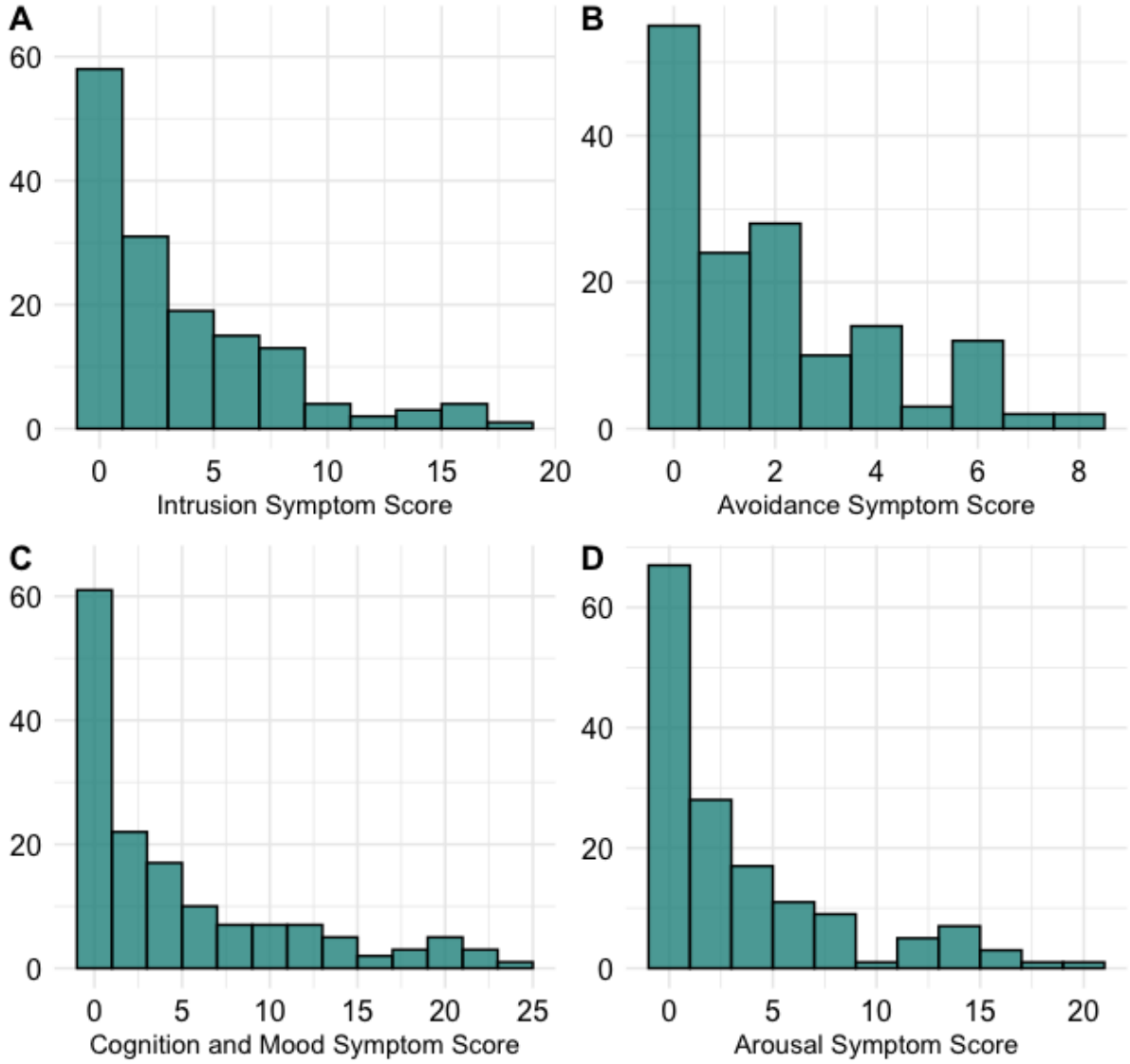
Note. PTSD = posttraumatic stress disorder; PTSD+ = participants who endorsed a symptom pattern required for PTSD by the *DSM-5* ($n = 23$); PTSD- = participants who did not endorse this pattern ($n = 127$); LEC-5 = Life Events Checklist for *DSM-5*; PCL-5 = PTSD Checklist for *DSM-5*.

Appendix G

Posttraumatic Stress Symptoms by Cluster

Figure G1

Histograms of Posttraumatic Stress Symptoms by Cluster



Appendix H

Comparison of Symptom Cluster Scores by Sex

Table H1

Comparison of Symptom Cluster Scores by Sex

Variable	Female (n = 110)		Male (n = 40)		$t(df)$	p
	M	*SD*	*M*	*SD*		
Intrusion	4.07	4.48	3.35	3.77	0.987 (81.6)	.327
Avoidance	1.99	2.23	1.60	1.61	1.18 (95.6)	.242
Cognition and mood	5.28	6.49	5.28	6.01	0.006 (74.3)	.995
Arousal	3.88	4.94	3.48	4.19	0.501 (61.5)	.854

Appendix I

Regression Models Predicting Clusters of Posttraumatic Stress Symptoms

Table I1

Regression Models Predicting Clusters of Posttraumatic Stress Symptoms

Variable	*B*	*SE B*	*β*	*t*	*p*
Model 1: Avoidance ($F(3, 146) = 6.64$, $p < .001$, $R^2 = .12$)					
Constant	2.22	0.46		4.79	<.001
Age	-0.02	0.09	-0.21	-2.61	.010
Sex (Male)	-0.51	0.37	-0.11	-1.37	.173
LEC-5	0.27	0.07	0.32	3.96	<.001
Model 2: Avoidance ($F(5, 144) = 5.01$, $p < .001$, $R^2 = .15$)					
Constant	2.45	0.47		5.19	<.001
Age	-0.03	0.01	-0.26	-3.12	.002
Sex (Male)	-0.48	0.37	-0.10	-1.31	.191
LEC-5	0.27	0.07	0.32	4.01	<.001
Reward learning	-0.41	0.20	-0.19	-2.08	.039
Punishment learning	0.10	0.19	0.05	0.54	.588
Model 1: Cognition and mood ($F(3, 146) = 9.41$, $p < .001$, $R^2 = .16$)					
Constant	6.94	1.38		5.05	<.001
Age	-0.10	0.03	-0.29	-3.71	<.001
Sex (Male)	-0.50	1.98	-0.04	-0.46	.646
LEC-5	0.92	0.20	0.35	4.55	<.001
Model 2: Cognition and mood ($F(5, 144) = 6.76$, $p < .001$, $R^2 = .19$)					
Constant	7.56	1.40		5.41	<.001

Variable	*B*	*SE B*	*β*	*t*	*p*
Age	-0.11	0.03	-0.34	-4.17	<.001
Sex (Male)	-0.45	1.08	-0.03	-0.42	.678
LEC-5	0.94	0.20	0.36	4.66	<.001
Reward learning	-1.10	0.58	-0.17	-1.91	.058
Punishment learning	0.01	0.56	<0.01	0.01	.992
Model 1: Arousal ($F(3, 146) = 11.18$, $p < .001$, $R^2 = .19$)					
Constant	5.38	1.01		5.35	<.001
Age	-0.09	0.02	-0.32	-4.16	<.001
Sex (Male)	-0.82	0.81	-0.08	-1.02	.310
LEC-5	0.72	0.15	0.37	4.83	<.001
Model 2: Arousal ($F(5, 144) = 7.39$, $p < .001$, $R^2 = .20$)					
Constant	5.76	1.04		5.56	<.001
Age	-0.09	0.02	-0.36	-4.49	<.001
Sex (Male)	-0.78	0.80	-0.07	-0.98	.331
LEC-5	0.73	0.15	0.37	4.88	<.001
Reward learning	-0.69	0.43	-0.15	-1.61	.110
Punishment learning	0.08	0.42	0.02	0.20	.843

Note. For all Model 1 *t*-statistics, $df = 146$; for all Model 2 *t*-statistics, $t(df) = 144$. LEC-5 = Life Events Checklist for *DSM-5*.