Value Estimation and Latent-State Update-Related Neural Activity During Fear Conditioning
Predict Posttraumatic Stress Disorder Symptom Severity

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Abstract

Learning theories of posttraumatic stress disorder (PTSD) purport that fear learning processes, such as those that support fear acquisition and extinction, are impaired. Computational models that aim to capture specific processes involved in fear learning have primarily assessed model free, or trial-and-error, reinforcement learning (RL). Although prior research indicates that aspects of model-free RL are disrupted among individuals with PTSD, models have yet to quantify and identify whether more nuanced, contextually driven learning is also disrupted. Given empirical evidence of aberrant contextual modulation of fear in PTSD, the present study sought to identify whether model-based RL processes are altered during fear conditioning among women with interpersonal violence (IPV)-related PTSD (n=85) using computational modeling. Several traditional models and a latent-state model that captured model-based RL were applied to skin conductance responses (SCR) collected during fear acquisition and extinction, and the latent-state model was identified as the best fitting model. Model-derived parameters from the latent-state model were carried forward to neuroimaging analyses (voxel-wise and independent component analysis) and results revealed that reduced latent-state related activity within visual processing regions uniquely predicted higher PTSD symptoms. Additionally, after controlling for latent-state update-related encoding, greater value estimation encoding within the left frontoparietal network during fear acquisition and reduced value estimation encoding within the dorsomedial prefrontal cortex during fear extinction predicted greater PTSD symptoms. Results provide evidence of disrupted model-based RL processes in women with IPV-related PTSD, which may contribute to difficulties revising fear and safety information. Future work should further assess model-based RL in PTSD.

1. Introduction

Posttraumatic stress disorder (PTSD) is an impairing anxiety-related disorder that is marked by deficits in several aspects of learning (Jovanovic et al., 2010; Jovanovic, Kazama, Bachevalier, & Davis, 2012; Pacella, Hruska, & Delahanty, 2013). For example, individuals with PTSD overgeneralize conditioned fear, which is characterized by greater fear to fear-related stimuli than healthy controls (Kaczurkin et al., 2017; Lopresto, Schipper, & Homberg, 2016), impaired inhibition of previously learned fear associations, and impaired recall of extinction learning (for a review, see Lissek & van Meurs, 2015). Given the ubiquity of learning deficits in PTSD, identifying specific learning-related processes that are disrupted is an important research endeavor.

Computational methods have enhanced researchers' ability to circumscribe cognitive processes with greater sensitivity and precision (Stephan & Mathys, 2014; Price, Brown, & Siegle, 2019). The progression of reinforcement learning (RL) models has been particularly successful, with computational models increasingly capturing behavior and learning phenomena not well explained by prior models (Le Pelly, 2004; Mihatsch & Neuneier, 2002; Cochran & Cisler, 2019; Redish, Jensen, Johnson, & Kurth-Nelson, 2007). For example, whereas the standard Rescorla-Wagner (RW) model, which was developed to quantitatively formalize Pavlovian RL, models simple trial-and-error learning, it does not capture more dynamic processes that occur during conditioning and extinction. Indeed, hybrid Pearce-Hall/RW learning models, which track trial-by-trial associability (i.e., the salience of a cue), provide a better fit for probabilistic (Brown et al., 2018) and fear-related learning (Homan et al., 2019; Li, Schiller,

Schoenbaum, Phelps, & Daw, 2011) than the standard RW model among healthy controls and individuals with PTSD.

In addition to data-driven model development, alignment of computational models with psychological theory is paramount (Huys, Maia, & Frank, 2016), as this will allow for the testing and refinement of current hypotheses regarding the role of learning in disorders, such as PTSD. Whereas prior research has primarily assessed relatively simple trial-and-error learning in PTSD (Brown et al., 2018; Cisler et al., 2015; Cisler et al., 2019; Ross et al., 2018), few have included models that capture higher-level cognitive processes. Importantly, theories of anxiety and PTSD implicate abstract, higher-order cognition in fear learning and extinction (Dunsmoor & Murphy, 2015). For example, the degree to which learned fear is generalized may depend on individuals' reasoning about internal conceptual representations (Dunsmoor & Murphy, 2015). In addition to the ability to reason about, integrate, and abstract categorical representations, which is facilitated by the anterior prefrontal cortex (Davis, Goldwater, Giron, 2016), the abstraction of rules and contextual information is mediated by prefrontal regions (Cools, Clark, & Robbins, 2004; Fogelson, Shah, Scabini, & Knight, 2009). Evidence of impaired contextual modulation of fear learning among individuals with PTSD further suggests a potentially important role of complex cognitive functions in the acquisition and revision of fear (Steiger, Nees, Wicking, Lang, & Flor, 2015).

Unlike model-free (e.g., RW) and hybrid models, which capture trial-and-error revisions of cue-outcome associations, model-based RL models can capture structured and dynamically shifting “rules” of learning (Daw et al., 2005; Redish et al., 2007). Model-based RL is theorized to support the development of complex cognitive maps that contain hypotheses about different task conditions to allow a learner to make predictions about future actions (Daw et al., 2005;

Gläscher, Daw, Dayan, & O'Doherty, 2010). Whereas model-free and hybrid RL are primarily implemented within regions of the ventral striatum, amygdala, and the salience network (Beierholm, Anen, Quartz, & Bossaerts, 2011; Brown et al., 2018; Cisler et al., 2019; Daw, Gershman, Seymour, Dayan, & Dolan, 2011; Gläscher et al., 2010; Ross et al., 2018), model-based RL is primarily implemented within regions of the prefrontal cortex and frontoparietal network (FPN; Beierholm et al., 2011; Gläscher, et al., 2010). Despite these distinctions, RL processes do not reflect completely separate learning systems. Rather, they are implemented via hierarchical corticostriatal circuits that support higher levels of abstract learning (Frank & Badre, 2012), with model-based processes capturing abstract aspects of RL.

The primary goal of the present study was to build on previous work assessing model-based RL during acquisition and extinction of fear among women with assault-related PTSD. It was hypothesized that the model-based RL model would provide a better fit for participants' behavior than the model-free and hybrid models, which do not allow a learner to develop sets of cue-outcome associations that are differentially applied and updated based on inferences about task rules (e.g., rules that differ for the acquisition and extinction context). It was further hypothesized that FPN encoding of trial-by-trial updates of current beliefs about task conditions, which are specific to the model-based model and contribute to differential weighting of cue value expectations based on a learner's hypotheses, would predict PTSD symptom severity. Specifically, it was anticipated that reduced FPN encoding would predict greater PTSD symptom severity, reflecting poorer contextually derived learning. Because PTSD is related to difficulties with fear extinction/safety learning (Jovanovic et al., 2009; Jovanovic et al., 2012), potential differences in the encoding of model-belief updates during acquisition versus extinction were explored. Due to high overlap between belief update and prediction error parameters during

extinction, the acquisition versus extinction analyses focused on value expectations while controlling for belief updates.

2. Methods

2.1 Participants

One hundred and three women were enrolled in as part of a larger study (Cisler et al., 2020) across two study sites: 1) University of Arkansas Medical Sciences and 2) University of Wisconsin-Madison. Primary inclusion criteria included female sex, age between 21 and 50 years old, and a current diagnosis of PTSD related to sexual or physical assault. Primary exclusion criteria included psychotic symptoms, pregnancy, learning disability, and medication or MRI contraindications. Twelve women were excluded due to task visit no show, claustrophobia, or a positive drug screen, yielding 91 subjects. Of these 91 subjects, a total of 85 had either viable skin conductance responses or neuroimaging data (see Computational Modeling and Neuroimaging sections below).

2.2 Clinical Interview and Measures

The past month version of the Clinician Administered PTSD Scale for DSM-5 (CAPS-5) was used to assess for the presence of current PTSD (Weathers et al., 2018). The CAPS-5 is a 30-item structured clinical interview that assesses for PTSD symptoms across four clusters: reexperiencing, avoidance, negative cognitions and mood, and hyperarousal. Symptoms are rated on a scale from 0 (absent) to 4 (extreme/incapacitating). To meet criteria for current PTSD, individuals must endorse a score of 2 or above for at least one reexperiencing symptom, one avoidance symptom, two negative cognitions/mood symptoms, and two hyperarousal symptoms. In addition to providing a categorical diagnosis, total symptom scores provided a dimensional measure of current PTSD symptoms. Although all participants had a diagnosis of PTSD, there

was substantial variation in the CAPS-5 symptom severity scores (see distribution of scores in Supplemental Figure S1). Participants' verbal intelligence quotient (IQ) was estimated using the Receptive One-Word Picture Vocabulary Test, Fourth Edition (ROWPVT-4). During this test, participants match vocabulary words that are administered verbally to illustrations that are presented in a book (Brownell, 2000). Scores were normed according to chronological age.

2.3 Fear Conditioning and Fear Extinction Task

Participants completed four task blocks that alternated between fear acquisition and fear extinction (see Figure 1A). During each fear acquisition block, 18 conditioned safety cues (CS-) and 18 conditioned danger/threat cues (CS+) were presented for 3 seconds, with an intertrial interval of 2-6 seconds. During acquisition, the presentation of the CS+ was followed by an electrotactile stimulation (UCS) on 50% of trials, which occurred 2.5 seconds after the CS+ onset for duration of 500 msec. During each fear extinction block, there were 18 trials each of the CS- and CS+ cues, which were presented for 3 seconds, with an intertrial interval of 2-6 seconds. During extinction, no electrotactile stimulations occurred following the presentation of the CS+. The CS- and CS+ stimuli were pseudorandomly presented during each block, and participants completed a total of 156 task trials (see Supplement for additional task details).

2.4 Skin Conductance Response Acquisition

Skin conductance response (SCR) data were acquired from participants' left hand with the BIOPAC MP150 Data Acquisition System using the EDA100C module with the MECMRI-TRANS (MRI compatible) cable system. BIOPAC AcqKnowledge 4.3 software recorded SCR data at a rate of 2000 Hz at the Arkansas site and 1000 Hz at the Wisconsin site (see Supplement for preprocessing details).

2.5 Computational Models

To identify whether a model-free, hybrid, or model-based model derived parameters provided a better fit to participants' SCR data, several models were tested. The primary set of models that were tested against the model-based model included a standard RW model and a hybrid model, both of which have previously been used to estimate learning parameters from SCR data during fear conditioning tasks and the latter of which has been found to provide a better fit than the standard RW model (Li et al., 2011). Additional versions of the standard RW model were tested for completeness (see Supplement).

2.5.1 Model-free Models

The standard version of the Rescorla-Wagner (RW) model was the primary model that was used to assess model-free RL. The standard RW model updates parameters as follows: $V_{t+1,c} = V_{t,c} + \alpha \times \delta_t$, where $V_{t,c}$ is the value expectation (i.e., associative strength) of cue (c) on the current trial (t), α is the learning rate, and δ_t is the prediction error (PE; $outcome_t - V_{t,c}$). The PE captures the difference between what was expected to occur and what occurred on a given trial. The $outcome_t$ variable can either be binary or scalar and was set to 0 if no shock occurred and 1 if a shock occurred in the present study.

2.5.2 Hybrid Model

The hybrid model builds on the RW model: $V_{t+1,c} = V_{t,c} + \kappa \alpha_t \times \delta_t$, where $V_{t,c}$ is the value expectation of cue (c) on the current trial (t), κ is a learning rate, α_t is the associability for the current trial, and δ_t is the PE for the current trial (Le Pelley, 2004; Li et al., 2011). As with the RW model, $\delta_t = outcome_t - V_{t,c}$. Unlike the RW model, a constant learning rate (κ) scales an associability parameter that changes from trial to trial and is defined as $\alpha_{t+1} = \eta |\delta_t| + (1-\eta)\alpha_t$. The free parameter, η , scales the prior magnitude of PE and its additive inverse scales the prior

associability (i.e., weighted PE). A higher η reflects greater weighting of the prior PE relative to the prior associability.

2.5.3 Model-based Model

A latent state (LS) model was used to capture model-based RL (Cochran & Cisler, 2019; Letkiewicz, Cochran, & Cisler, 2020). This model was previously found to explain learning phenomena characterized by contextually based learning better than other widely used models (e.g., renewal, spontaneous recovery). Latent states are unobserved task rules/conditions that, in aggregate, define a learning environment. Each latent state contains sets of associations between cues and outcomes and a learner must infer which associations are currently most applicable. The LS model builds on the RW model by using integer l (i.e., the latent state) to index these sets of associations, where $V_{t,c,l}$ is the current value strength of option c for latent state l : $V_{t+1,c,l} = V_{t,c,l} + \alpha_{t,c,l} \times \delta_{t,l}$. For the LS model, the learning rate ($\alpha_{t,c,l}$) is specific to the cue (c) on the current trial (t) for latent state l . The learning rate is proportional to a quantity that captures the degree to which a learner believes that the current task conditions are captured by a given latent state, referred to as latent-state beliefs, $p_{l,t}$. The PE is specific to the latent state, whereby $\delta_{t,l} = outcome_t - V_{t,c,l}$ for cue c on trial t for latent state l . Trial-by-trial expectations $V_{t,c}$ of cue c are computed by taking a weighted average of $V_{t,c,l}$ with weights $p_{l,t}$. Following an outcome on a given trial, beliefs about current task conditions are updated (*delta* beliefs, dB). Larger updates in latent-state beliefs reflect larger changes in a learner's internal model of the current task rules.

Additional LS model information is included in the Supplement.

2.6 Analyses

2.6.1 Computational Modeling

Skin conductance responses that were acquired during the Fear Conditioning and Extinction Task were used to identify optimal participant model parameter estimates. For each participant, model parameters were estimated by fitting computational models to SCR data from participants without any missing data ($n=74$) via maximum likelihood estimation. Following convention, a square root transformation was applied the SCR (prior to the transformation, SCR values were rescaled between 0 and 1). Normalized, square root transformed SCR values were regressed onto trial-by-trial linear value estimation terms ($V_{t,c}$). Skin conductance responses were also regressed onto associability (α_t) for the hybrid model and onto updates in latent state beliefs (δB_t) for the LS model. Regression error was assumed to follow a normal distribution with mean zero and unknown variance. Maximum likelihood estimation was performed by minimizing squared regression error summed only over trials in which a shock was omitted (Li et al., 2011) using `fmincon` in MATLAB (The MathWorks, Inc., Natick, MA). For each participant and RL model, estimation yielded regression coefficients and RL model parameters. Resulting log-likelihood values were compared to identify the best-fitting model. Additional regression parameters were included in exploratory analyses to identify whether the inclusion of non-linear terms would capture large trial-by-trial changes in SCR not readily captured by linear terms, thereby yielding better model fit (results provided in the Supplement).

2.6.2 Neuroimaging

All neuroimaging analyses focused on the LS model parameters (see Supplement for neuroimaging acquisition and preprocessing details). Trial-by-trial δB_t s, which characterize model-based RL updates, were carried forward to voxelwise and independent component analysis (ICA) to identify brain regions and networks that support implementation/encoding of latent-state updates among women with PTSD. Additionally, analyses focused on identifying

whether PTSD symptom severity modulated dB-related encoding. Because individual-level parameters have previously been shown to be too noisy to yield reliable neuroimaging results (i.e., they exhibit high levels of error variance), learning parameters (e.g., V , PE, dB) were averaged across participants and the resulting trial-by-trial mean parameters were used in the neuroimaging analyses in accordance with previous research (Daw et al., 2005; Daw, Gershman, Seymour, Dayan, & Dolan, 2011; Li et al., 2011; Schönberg et al., 2007; Schönberg, Daw, Joel, & O'Doherty, 2010). Of the 91 participants who were eligible for the present study, seventy-seven participants had viable neuroimaging data. However, one participant was excluded due to missing clinical variables (final sample: $n=76$; see the Supplement for information regarding the overlap between the computational modeling and neuroimaging samples). See Table 1 for demographic and clinical characteristics of participants included in the computational modeling and/or neuroimaging analyses ($n=85$).

2.6.2.1 Voxelwise Analyses

Participants' voxelwise time courses were regressed onto the design matrix using AFNI (3dREML; Cox, 1996). The design matrix included the stimulus onset and outcome phases of the task. The onset phase was parametrically modulated by trial-by-trial value expectation ($V_{t,c}$) from the LS model, and the outcome phase was parametrically modulated by trial-by-trial PE (positive and negative; $PE_{t,c}$) and latent-state belief updates ($dB_{t,c}$) from the LS model (see Figure 1B). To account for the potential impact of the electrotactile stimulation on neural activity, the design matrix also included a "shock" regressor. Because PE and the occurrence of the shock are highly correlated (Erdeniz, Rohe, Done, & Seidler, 2013), PE-related neural activity was not interpreted. Beta coefficients for the onset phase modulated by V and the outcome phase modulated by dB were included in the second-level analyses. Linear mixed effects models

(LMEs) were implemented using MATLAB (fitlme; The MathWorks, Inc., Natick, MA) to test for main effects of neural activity during dB and V, controlling for age, IQ, and study site:

1. $\text{dB } \beta \sim \text{age} + \text{IQ} + \text{study site} + (1|\text{subject})$
2. $\text{V } \beta \sim \text{age} + \text{IQ} + \text{study site} + (1|\text{subject})$

Additionally, a model tested for potential unique effects of dB and V-related neural activity on CAPS-5 symptom severity. PE was included as a predictor, but PE results were not interpreted (for the reasons stated above):

3. $\text{CAPS} \sim \text{V } \beta + \text{dB } \beta + \text{PE } \beta + \text{age} + \text{IQ} + \text{study site} + (1|\text{subject})$

A set of follow-up analyses assessed for differential effects of acquisition versus extinction on the results of models 2 and 3. The design matrix included separate regressors for trial onset modulated by value expectation during acquisition ($V_{\text{ta,c}}$) and extinction ($V_{\text{te,c}}$), and separate regressors for outcome modulated by dB during acquisition ($\text{dB}_{\text{ta,c}}$) and extinction ($\text{dB}_{\text{te,c}}$).

Because correlations between PE during extinction ($\text{PE}_{\text{te,c}}$) and $V_{\text{te,c}}$ and between $\text{PE}_{\text{te,c}}$ and $\text{dB}_{\text{te,c}}$ were highly correlated ($|r| > .70$), PE was not included in these analyses. Additionally, given that outcome-related neural activity associated with PE could not be separated from that of dB, LME tests focused on whether neural activity during V significantly differed during acquisition versus extinction (contrast coded: acquisition=1, extinction=-1), controlling for age, IQ, and study site:

1. $\text{V } \beta \sim \text{contrast} + \text{age} + \text{IQ} + \text{study site} + (1|\text{subject})$

Separate models tested for potential unique effects of V and dB-related neural activity on CAPS symptom severity during acquisition and extinction.

2. $\text{CAPS} \sim \text{V } \beta_{\text{acquisition}} + \text{dB } \beta_{\text{acquisition}} + \text{age} + \text{IQ} + \text{study site} + (1|\text{subject})$
3. $\text{CAPS} \sim \text{V } \beta_{\text{extinction}} + \text{dB } \beta_{\text{extinction}} + \text{age} + \text{IQ} + \text{study site} + (1|\text{subject})$

Voxelwise comparisons were implemented within a sample specific grey matter mask and controlled for by using an uncorrected $p < .001$ and cluster size $k \geq 18$ (identified using AFNIs 3dClustSim).

2.6.2.2 Independent Component Analysis

An ICA identified temporally coactivated spatially distributed neural networks. Thirty-five components were identified and 13 of these components were identified as functional networks, including a left and right FPN that were of primary interest. Additionally, follow-up analyses were implemented with the remaining eleven networks (see Supplemental Figure S2). ICA timecourses were regressed onto the same design matrices described above using AFNI (3dREML; Cox, 1996) and resulting beta coefficients were included in the second-level analyses. The same series of LMEs described above were implemented for 1) each FPN and 2) follow-up networks using MATLAB (fitlme; The MathWorks, Inc., Natick, MA). Bonferroni correction was applied for the two FPN networks ($p < .025$) and for the post-hoc analyses across the eleven additional networks ($p < .005$). Additionally, following an approach used by Erdeniz et al. (2013), several GLMs were fitted to participants' ICA time courses to identify whether the inclusion or removal of the PE and/or shock regressors altered the main effects of dB and/or V (see Supplement).

3. Results

3.1 Model Fit

The standard RW and hybrid models, which are nested models, were formally tested using a log-likelihood ratio test. Similar to previous studies (Boll et al., 2013; Homan et al., 2019; Li et al., 2011), the hybrid model outperformed the standard RW model, $\chi^2=515.43$, $df=148$, $p < .001$. It also outperformed the additional RW models that were tested (see

Supplement). Because the LS model does not contain the terms included in the hybrid model, a log-likelihood ratio test was not performed to compare these models. A comparison between Akaike Information Criterion values, which were summed across participants, revealed that the LS model provided a better fit than the standard RW and hybrid models (see Figure 2), as well as the additional RW models that were tested (see Supplemental Figure S2).

3.2 Main Effects

3.2.1 Voxelwise Analyses

Table 2 lists the brain regions in which neural activation predicted latent-state belief updates. Greater activity emerged in the left inferior frontal gyrus, left and right insula, right paracentral lobule, left and right calcarine gyrus, left postcentral/precentral gyrus, cerebellum, and right cuneus (see Figure 3A). Lower activity emerged in left and right inferior occipital gyrus, superior orbital gyrus, left superior frontal gyrus, precuneus, left middle frontal gyrus, and left angular gyrus. Table 3 lists the brain regions in which neural activation predicted value expectation. Greater activity emerged in the paracentral lobule, right middle frontal gyrus, and left thalamus (see Figure 3B). Lower activity emerged in the left precuneus.

Table 4 lists the brain regions in which the parameter-related neural activity uniquely predicted PTSD symptom severity. Figure 3C shows that lower latent state update-related activation within the right calcarine gyrus/right posterior cingulate cortex predicted higher CAPS scores. As shown in Figure 3D, greater value expectation-related activation within the left angular gyrus/inferior parietal lobule predicted higher CAPS scores.

3.2.2 ICA

Table 5 lists the ICA networks that predicted trial-by-trial latent-state belief update encoding. Reduced encoding was evident in the left frontoparietal network (FPN), as well as the

limbic, dorsomedial prefrontal cortex/posterior cingulate cortex, and hippocampal networks (see Figure 4A). Increased encoding was evident in the pre-supplementary motor area and striatal networks. Table 5 lists the ICA networks that predicted trial-by-trial value estimation encoding. Increased encoding emerged in the pre-supplementary motor area and striatal networks (see Figure 4B). Results for all networks are provided in the Supplement. A similar pattern of results emerged across study sites (see Figure S5 in the Supplement).

Table 6 lists the networks in which parameter-related encoding uniquely predicted PTSD symptom severity on the CAPS. Increased encoding of value expectation within the left FPN predicted greater PTSD symptom severity, $t(68)=3.58$, $p<.001$. No other results held above correction.

3.3 Task Phase Effects (Acquisition versus Extinction)

3.3.1 Voxelwise Analyses

Table 7 lists the brain regions in which neural activation differentially predicted value expectation during the acquisition versus extinction task phases. Greater activity during extinction than acquisition emerged in the middle cingulate cortex, thalamus, left fusiform gyrus, right lingual gyrus, left calcarine gyrus, left middle occipital gyrus, cuneus, and right lingual gyrus.

3.3.2 ICA

Table 8 lists the ICA networks that exhibited differential value expectation encoding during the acquisition versus extinction task phases. A significant effect of task phase emerged for value expectation encoding within both FPNs. Specifically, greater value expectation encoding was evident in the left and right FPN during acquisition relative to extinction, $t(146)=2.53$, $p=.013$ and $t(146)=2.62$, $p<.010$, respectively (see Figure 5). Significantly greater

value expectation encoding was also evident in medial/lateral prefrontal cortex network during acquisition versus extinction, $t(146)=3.38, p<.001$, whereas lower value estimation encoding was evident in hippocampal network during acquisition versus extinction, $t(146)=-2.92, p<.004$.

Results followed a similar pattern across study site (see Figure S6 in the Supplement).

Table 9 lists the networks in which value expectation-related encoding uniquely predicted PTSD symptom severity on the CAPS during acquisition and extinction. As shown in Figure 6A, during acquisition, but not extinction, greater value expectation encoding in the left FPN uniquely predicted higher PTSD symptom severity, $t(69)=2.99, p=.004$. As shown in Figure 6B, during extinction, but not acquisition, lower value expectation encoding in the dorsomedial prefrontal cortex/posterior cingulate cortex network uniquely predicted higher PTSD symptom severity, $t(69)=-4.05, p<.001$. A similar pattern of results was evident across study site (see Figure S7 in the Supplement).

4. Discussion

Results in this sample of adult women with IPV-PTSD revealed that the latent-state model provided a better fit for participants' physiological responses during the fear conditioning task than the standard RW and hybrid models. Notably, the latter model is considered a gold-standard for modeling fear conditioning responses, as it has been found to fit fear conditioning responsivity better than standard RW models in several previous studies (Homan et al., 2019; Li et al., 2011), which was replicated in the current study. However, it was outperformed by the latent-state model in the present study. This suggests that the latent-state model captures learning dynamics during fear conditioning and extinction that are not readily measured by the hybrid model, such as learning that varies as a function of task conditions.

Contrary to predictions, latent-state updates were associated with reduced activity in regions previously associated with model-based RL and cognitive control, including the left FPN and left superior frontal gyrus. In contrast, latent-state belief updates were related to increased encoding within the striatal network, activity of which has previously been found to be associated with model-based encoding (Daw, Gershman, Seymour, Dayan, & Dolan, 2011; McDannald, Lucantonio, Burke, Niv, & Schoenbaum, 2011; but also see Gläscher et al., 2010). Latent-state belief updates were also related to increased activity of the left and right insula, which are implicated in punishment and loss-related learning (Palmentari et al., 2012). Although the bilateral anterior insula are components of the salience network, which is associated with model-free PE encoding (Cisler et al., 2019; Preuschoff, Quartz, & Bossaerts, 2008), this is not the first study to identify insula activation during model-based RL (Lee et al., 2014). In the present study, heightened insula activity during updates to latent-state beliefs may reflect sensitivity to unexpected and changing environmental demands that signal increased need for cognitive control processes during learning (Jiang, Beck, Heller, & Egner, 2015).

Despite providing a better overall fit than the other computational models, highlighting a role of model-based processes in fear learning, PTSD symptom severity was not predicted by FPN-related encoding of latent-state belief updates. Instead, higher PTSD symptom severity was uniquely related to reduced activity during latent-state updates in the right calcarine gyrus/posterior cingulate cortex, which are implicated in visual processing, visual imagery, and the focus of attention (Klein, Paradis, Poline, Kosslyn, & Le Bihan, 2000; Leech & Sharp, 2014). By contrast, increased value estimation-related encoding in the left FPN and activity of the angular gyrus/intraparietal lobule uniquely predicted greater PTSD symptom severity. It was further revealed that increased encoding within the left FPN during acquisition predicted greater

PTSD symptom severity during acquisition, whereas reduced encoding within the dorsomedial prefrontal cortex (dmPFC) predicted greater PTSD symptom severity during extinction.

Heightened encoding of value estimation during the acquisition blocks (i.e., when threat expectancies are high) among cognitive control regions may contribute to enhanced representation of fear, while reduced encoding of value estimation during the extinction blocks (i.e., when threat expectancies are low) of the dmPFC may contribute to reduced valuation and representation of safety information (Wang et al., 2014).

A notable limitation of the present study is the lack of a control comparison group. Although altered neural activity during latent-state belief updates did not emerge within cognitive control regions or networks in relation to PTSD symptoms, we did not test whether individuals with PTSD exhibit poorer encoding of latent-state belief updates within FPNs relative to individuals without PTSD. It is possible that PTSD symptoms scaled with value expectations, rather than latent-state belief updates, within the left FPN because overall individuals with PTSD generally had difficulty engaging contextual learning processes during fear conditioning. It will be important to establish the typical pattern of neural activity and encoding of value expectations and latent-state belief updates to further contextualize the meaning of present results.

Overall, results provide some evidence that model-based RL processes that are altered during fear conditioning are related to PTSD symptoms among women with IPV-related PTSD. While research has primarily been devoted to examining relatively simplistic learning processes, model-free and hybrid models do not capture higher-level, nuanced fear and safety learning, the latter of which may be particularly important in the acquisition and revision of human fear. Although disruptions in model-based processes that scaled with PTSD symptoms occurred

within brain regions or networks that were not anticipated (e.g., reduced encoding within visual processing regions during latent-state belief updates), our results provide preliminary evidence of model-based RL-related impairments in PTSD that are separate from other learning processes (e.g., value estimation). Our latent-state model also identified a pattern of value estimation encoding that is distinct from latent-state update encoding that may disrupt normative fear and safety learning among individuals with PTSD. Given the significant impact of PTSD on functioning and the need to enhance treatment outcomes, it is proposed that future research further examine fear acquisition and extinction among individuals with PTSD using a model-based framework (e.g., by implementing computational models that can capture model-based RL processes).

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Tables

Table 1. Participant Demographic and Clinical Characteristics

	Participants	Arkansas Site	Wisconsin Site
n	85	39	46
Age, Mean (SD)	33.7 (8.7)	36.1 (8.4)*	31.6 (8.5)
Race/Ethnicity (%)			
White	74	69	78
Black/African American	17	23	11
Asian	0	0	0
Hispanic, Latina	4	0	7
Pacific Islander	0	0	0
Native American	0	0	0
Other	5	8	4
IQ, Mean (SD)	98.8 (20.6)	88.1 (21.6)*	107.5 (15.0)
CAPS Symptom Severity, Mean (SD)	42.4 (11.2)	42.2 (11.5)	40.9 (10.9)
CAPS Current # Symptoms	14.3 (2.8)	13.8 (2.7)	14 (2.9)
PCL-C	43.6 (13.8)	45.6 (13.7)	41.9 (14.7)
*IQ=Intelligence Quotient, One-Word Receptive Vocabulary Test; CAPS=Clinician-Administered PTSD Scale; PCL-C=PTSD Checklist - Civilian Version			

Table 2. Regions Associated with Trial-by-Trial Changes in Latent-State Beliefs (dB) during Outcome

Region	Cluster Size in mm³	Peak t-value	Center of Mass Coordinates		
			X	Y	Z
R. IFG/Insula	1664	11.60	42	-8	16
R. Paracentral Lobule	1600	9.53	1	-23	59
L. Insula Lobe	1132	12.81	-34	-6	10
R. Calcarine Gyrus	153	6.81	18	-60	7
L. Postcentral/Precentral Gyrus	149	7.13	-43	-7	48
R. Inferior Occipital Gyrus	135	-5.51	41	-75	-3
L. Cerebellum	125	6.74	-5	-38	-20
Superior Orbital Gyrus	103	-6.89	-4	59	-21
L. Calcarine Gyrus	70	6.09	-15	-68	7
L. Superior Frontal Gyrus	63	-5.43	-14	39	47
Precuneus	57	-6.15	-2	-56	27
Cerebellum	34	5.47	1	-58	-36
L. Cerebellum	31	5.18	-31	-53	-28
R. Cuneus	29	4.61	13	-77	33
L. Inferior Occipital Gyrus	24	-6.48	-46	-70	-9
L. Middle Frontal Gyrus	23	-4.58	-33	15	47
L. Angular Gyrus	23	-4.72	-46	-66	29
L. Postcentral Gyrus	18	-4.60	-38	-28	53

Table 3. Regions Associated with Trial-by-Trial Associative Strength (V) during Stimulus Onset

Region	Cluster Size in mm³	Peak t-value	Center of Mass Coordinates		
			X	Y	Z
Paracentral Lobule	252	6.64	4	-23	66
R. Middle Frontal Gyrus	29	4.99	43	-3	50
L. Thalamus	26	5.42	-6	-19	7
L. Precuneus	21	-5.16	-7	-65	44

Table 4. Parameter-Related Activity Uniquely Predictive of Clinician-Administered PTSD Scale Severity

Region	Parameter	Cluster Size in mm³	Peak t- value	Center of Mass Coordinates		
				X	Y	Z
Left Angular Gyrus/IPL	V	27	4.68	-46	-66	36
Right Calcarine Gyrus/Right PCC	dB	22	-3.75	8	-62	15

Table 5. Networks Associated with Trial-by-Trial Encoding of Latent-State Updates (dB) and Value Estimation (V)

Parameter	ICA Network	t-value	p-value
dB	L. Frontoparietal	-3.64	<.001
	Pre-Supplementary Motor Area	6.70	<.001
	Limbic	-7.44	<.001
	Hippocampus	-3.14	.003
	Dorsomedial PFC/Posterior Cingulate Cortex	-6.26	.001
	Insula/Middle Frontal Gyrus	2.45	.017
	Striatum	10.66	<.001
V	Pre-Supplementary Motor Area	4.28	<.001
	Limbic	-2.24	.029
	Striatum	3.86	p<.001

Note: Networks in gray font did not survive Bonferroni correction.

Table 6. Parameter-Related Activity Uniquely Predictive of Clinician-Administered PTSD Scale Severity

ICA Network	Parameter	t-value	<i>p</i>-value
L. Frontoparietal	V	3.58	.0007
Default Mode	V	2.01	.049
Dorsomedial PFC/Posterior Cingulate Cortex	V	2.02	.048
Inferior Frontotemporal	V	-2.37	.021

Note: Networks in gray font did not survive Bonferroni correction.

Table 7. Regions Associated with Trial-by-Trial Value Expectation (V) During Stimulus Onset, Acquisition versus Extinction

Region	Cluster Size in mm³	Peak t-value	Center of Mass Coordinates		
			X	Y	Z
Middle Cingulate Cortex	107	-5.68	-1	-40	35
Thalamus	62	-5.05	-1	-21	9
L. Fusiform Gyrus	60	-4.56	-40	-51	-14
R. Lingual Gyrus	49	-5.13	9	-44	3
L. Calcarine Gyrus	47	-4.45	-18	-64	9
L. Middle Occipital Gyrus	36	-5.27	-31	-84	5
Cuneus	28	-4.53	6	-67	24
R. Lingual Gyrus	27	-3.89	17	-58	3

Table 8. Networks Associated with Trial-by-Trial Encoding of Value Estimation (V) during Acquisition versus Extinction

Parameter	ICA Network	t-value	p-value
V	L. Frontoparietal	2.53	.013
	R. Frontoparietal	2.62	.010
	Medial/Lateral PFC	3.38	<.001
	Medial PFC/Striatum	-2.44	.016
	Limbic	2.78	.006
	Hippocampus	-2.92	.004
	Dorsomedial PFC/Posterior Cingulate Cortex	2.51	.013

Note: Regions in gray font did not hold above Bonferroni correction.

Table 9. V-Related Activity Uniquely Predictive of Clinician-Administered PTSD Scale Severity

ICA Network	t-value	p-value
<i>Acquisition</i>		
L. Frontoparietal	3.45	.001
<i>Extinction</i>		
Dorsomedial PFC/PCC	-4.05	<.001

Figures

Figure 1. **A.** Schematic representation of the acquisition and extinction blocks of the Fear Conditioning and Fear Extinction Task. **B.** Representation showing the temporal mapping of value estimations (V), prediction errors (PE), and latent state belief updates (dB) during the no shock and shock trials. For the neuroimaging analyses, the onset phase was parametrically modulated by trial-by-trial value expectations ($V_{t,c}$) and the outcome phase was parametrically modulated by trial-by-trial PEs (positive and negative; $PE_{t,c}$) and latent-state belief updates ($dB_{t,c}$).

Figure 2. Summed Akaike Information Criterion (AIC) values across participants showing that the Latent State model outperformed the Rescorla Wagner and Hybrid models (note: lower AIC values reflect better model fit).

Figure 3. Brain regions associated with **A.** latent-state belief updates and **B.** value estimations. Parameter-related neural activity that uniquely predicted PTSD symptom severity for **C.** latent-state updates and **D.** value estimations. L = left. Warm colors = positive z-values.

Figure 4. Depiction of the main effects of encoding during trial-by-trial changes in **A.** latent-state beliefs (dB) and **B.** value estimation (V) for GLM model 1 (full model: dB, PE, V, and shock regressor included).

Figure 5. Depiction of the effects of acquisition versus extinction on encoding during trial-by-trial changes in value estimation (V).

Figure 6. **A.** Scatterplots depicting relationships between left frontoparietal network encoding and PTSD symptom severity during (1) acquisition and (2) extinction, and a graphical depiction of the left frontoparietal ICA network. **B.** Scatterplots depicting relationships between dorsomedial prefrontal cortex network encoding and PTSD symptom severity during (1) acquisition and (2) extinction, and a graphical depiction of the dorsomedial prefrontal cortex network ICA network.