Psychoneuroendocrinology

Acute stress alters probabilistic reversal learning in healthy participants

--Manuscript Draft--

Manuscript Number:	
Article Type:	Research Paper
Section/Category:	Clinical science (in human)
Keywords:	stress; fMRI; reversal learning; Decision-making; modeling; cognitive flexibility
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Abstract:	Behavioral adaptation is a fundamental cognitive ability, ensuring an organism's survival by allowing for flexible adjustment to changing environmental conditions. In laboratory settings, these adaptive abilities can be measured with reversal learning paradigms requiring agents to adjust their reward learning to sudden changes in stimulus-action-outcome contingencies. Stressful situations have been found to alter flexibility of reward learning, but directionality of effects has been mixed across studies. Here, we used functional MRI (fMRI) informed by computational modeling in a within-subjects design with healthy male human volunteers to investigate the effect of acute psychosocial stress on flexible behavioral adaptation. Participants (n=28) underwent fMRI during a reversal learning task, once after the Trier Social Stress Test (TSST), a validated psychosocial stress induction method, and once after a control condition, in two separate sessions. Effects of stress on choice behavior were investigated using multilevel generalized linear models and a set of computational models describing different learning processes that might have generated the data. Computational models were fitted using a hierarchical Bayesian approach, and model-derived reward prediction errors (RPE) were used as regressors for fMRI analyses. We found that acute psychosocial stress slightly increased correct response rates in our participants. Model comparison revealed that double-update learning with stress-specific scaling of the inverse decision temperature parameter best explained the observed behavior under stress. On the neural level, model-derived RPEs were correlated with BOLD signals in striatum and ventromedial prefrontal cortex (vmPFC). The striatal RPE signal for win trials was stronger during the stress compared to the control condition. Our study suggests that acute psychosocial stress can enhance reversal learning and neural representation of RPE in healthy participants.
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To
Editor-in-chief of *Psychoneuroendocrinology*
Robert Dantzer, DVM, PhD, Houston, Texas

20 April, 2022

Dear Dr. Dantzer,

We herewith submit our manuscript entitled **Acute stress alters probabilistic reversal learning in healthy participants**, which we would kindly ask you to consider for publication in *Psychoneuroendocrinology*.

We used functional MRI (fMRI) informed by computational modeling in a within-subjects design of n = 28 healthy male human volunteers to investigate the effect of acute psychosocial stress on flexible behavioral adaptation. In our probabilistic reversal learning paradigm we found a slight increase of correct response rates in our participants under acute psychosocial stress, reflected in altered choice stochasticity and a whole-brain-correctable neural effect of stress in win trials.

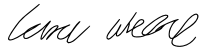
Previous studies found that acute stress can have beneficial as well as detrimental effects on decision-making, depending on type of stressor, paradigm and study sample. For the first time, our study design allows for a fine-grained computational analysis of intra- and interindividual differences in reversal learning under stress and its neural correlates. Understanding the effects of stress on decision-making is crucial to improve our mechanistic understanding of healthy behavioral adaptation and lays the foundation to investigate how maladaptive behavior in psychiatric illness is developed and maintained.

We are confident that the current study significantly contributes to the understanding of learning under acute stress. We believe that the results are of great interest for readers of *Psychoneuroendocrinology*.

No work resembling the enclosed article has been published or is being submitted for publication elsewhere. We have each made a substantial contribution to qualify for authorship. We have disclosed all financial support for our work and declare that there are no conflicts of interest for any of the authors.

We hope that you will find the manuscript suitable for publication in *Psychoneuroendocrinology*.

Sincerely on behalf of all authors,



Lara Wieland

Highlights

Flexibly adjusting reward learning to changing environmental conditions is crucial for an organism.

Acute stress can have beneficial as well as detrimental effects on reward learning.

Specifically, we investigated probabilistic reversal learning in n = 28 healthy male participants.

We found an increase of correct responses under acute psychosocial stress in our participants.

Correspondingly, we observed altered choice stochasticity and neural effect of stress in win trials.

Acute stress alters probabilistic reversal learning in healthy participants

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Keywords: Stress, fMRI, reversal learning, decision-making, modeling, cognitive flexibility

Text no. of words: 7556 (5931 without references and abstract)

no. of references: 50

Abstract

Behavioral adaptation is a fundamental cognitive ability, ensuring an organism's survival by allowing for flexible adjustment to changing environmental conditions. In laboratory settings, these adaptive abilities can be measured with reversal learning paradigms requiring agents to adjust their reward learning to sudden changes in stimulus-action-outcome contingencies. Stressful situations have been found to alter flexibility of reward learning, but directionality of effects has been mixed across studies. Here, we used functional MRI (fMRI) informed by computational modeling in a within-subjects design with healthy male human volunteers to investigate the effect of acute psychosocial stress on flexible behavioral adaptation. Participants (n=28) underwent fMRI during a reversal learning task, once after the Trier Social Stress Test (TSST), a validated psychosocial stress induction method, and once after a control condition, in two separate sessions. Effects of stress on choice behavior were investigated using multilevel generalized linear models and a set of computational models describing different learning processes that might have generated the data. Computational models were fitted using a hierarchical Bayesian approach, and model-derived reward prediction errors (RPE) were used as regressors for fMRI analyses. We found that acute psychosocial stress slightly increased correct response rates in our participants. Model comparison revealed that double-update learning with stress-specific scaling of the inverse decision temperature parameter best explained the observed behavior under stress. On the neural level, model-derived RPEs were correlated with BOLD signals in striatum and ventromedial prefrontal cortex (vmPFC). The striatal RPE signal for win trials was stronger during the stress compared to the control condition. Our study suggests that acute psychosocial stress can enhance reversal learning and neural representation of RPE in healthy participants.

1. Background

Humans and other agents are routinely confronted with decision-making situations under stress, for example when choosing an efficient and cheap way of commuting to work, despite running late. Different choice options, such as taking the car, bike or train, are associated with relatively stable and predictable levels of cost and reward. In contrast, the weather forecast of the day, a congestion on the preferred route or a train delay, are more uncertain, less predictable factors. Both, stable and uncertain factors interact, in that cycling to work may be rewarding in sunny weather but not on a rainy day. Stress impacts individuals' emotions, mood, physiological responses and may affect their cognitive processing resources, influencing their decision-making strategies (Lupien et al., 2007). This might be especially relevant in situations that afford high behavioral flexibility, for instance in constantly changing environments. Stress is also an important factor in causing and maintaining psychiatric conditions (McEwen, 2004) and strongly influences health-related behavior in general (Cohen et al., 2016).

Flexible decision-making requires one to learn what is most rewarding in the current environment and adapt one's decision-making to that. Studies have found mixed results for the influence of stress on decision-making, ranging from beneficial to detrimental effects across paradigms (Goldfarb et al., 2015; Plessow et al., 2012, 2011). In a meta-analysis, acute stress showed a small negative impact for tasks in which reward seeking and risk taking is disadvantageous (d = .26 and d = .44), but showed no effect if this was not the case (Starcke and Brand, 2016). Similarly, a meta-analysis over a small number of studies investigating the effects of acute stress on cognitive flexibility concluded that stress had a small impairing effect (Hedges' g= -.30) (Shields et al., 2016). Different processes involved in decision-making are presumably differentially prone to interruption by stress (Schwabe and Wolf, 2011, 2009). Whereas habitual decision-making relies on simple stimulus-related associations, goal-directed decision-making associates actions with a motivational value and is therefore more flexible but also computationally more costly. It has been found that acute and chronic stress

disrupt goal-directed decision-making, while habitual decision-making appears unaffected at the behavioral as well as neural level (Schwabe et al., 2013, 2008). One possible explanation for the variable findings are different types of standardized stressors, which are commonly used in behavioral experiments. They can be physiological as in the Cold Pressor Task, psychosocial as in the Trier Social Stress Test (TSST) or both as in the Socially Evaluated Cold Pressor Test (Starcke and Brand, 2016). The physiological paradigms lead to more immediate stress during learning, whereas the psychosocial paradigms release their full physiological effect 10-20 mins after stress induction. Another source of variability for meta-analytical findings lies in in how cognitive flexibility was measured. Both meta-analyses predominantly focused on classical paradigms such as the Wisconsin card sorting test or task-switching tests. While providing valuable insight into overall cognitive flexibility, these paradigms mostly rely on averaged outcome measures. In contrast, tasks designed for computational modeling may provide a more fine-grained measure of behavioral adaptation.

An understudied subject remains how the brain adapts to learning from rewards in a changing environment under stress. Probabilistic reversal learning requires participants to choose between stimuli with varying reward contingencies. In these paradigms contingencies are reversed several times throughout the task unannounced and therefore demand behavioral adaptation to a changing environment. A computational mechanism underlying the putative learning process can be formalized by the reward prediction error (RPE), a computational quantity derived from the reinforcement learning (RL) framework. RPE signal the difference between an observed and expected reward (Dolan and Dayan, 2013) and are used to update the value of a stimulus, a state, or an action. The neural signature of RPE during reversal learning is reliably found in the human ventral frontostriatal circuitry (Doherty et al., 2003).

So far, small sample sizes, heterogenous subdomains in the operationalization of decision-making, and methodological differences regarding the type of stressor have complicated the picture (Porcelli and Delgado, 2017). Most previous studies on stress effects on decision-making have employed between-subject designs – but subjects vary drastically in

both individual stress responses, choice behavior and how stress affects performance. In the previously used between-subject designs it thus remains unclear, how much of stress-related changes to the neural correlates of probabilistic reversal learning can be attributed to the stressor and how much may be related to interindividual differences in stress reactivity. Stress reactivity may also differ, depending on long-term stress exposure (Radenbach et al., 2015) or cognitive (Otto et al., 2013) and personality trait (Raio et al., 2020) variables. The few studies using within-subjects designs to investigate learning are either purely behavioral (Radenbach et al., 2015) focused on psychoimmunological measures (Treadway et al., 2017) or neuroimaging methods such as electroencephalography (Cavanagh et al., 2011), which lacks the possibility of precise spatial signal localization and anatomical specificity with respect to the neural representation of RPE signals. To our knowledge, only two studies combine a within-subject design with computational modeling and functional neuroimaging (fMRI) to elucidate underlying cognitive mechanisms (Carvalheiro et al., 2021; Robinson et al., 2013). However, type of stressor and reward-learning paradigm differ from our study design. Here, we used a psychosocial stress intervention and fMRI to study probabilistic reversal learning in healthy male participants employing a within-subjects design. Applying a state-of-the-art hierarchical Bayesian modeling approach (Piray et al., 2019) allowed us to model the impact of stress on behavioral adaptation, quantified in a reinforcement learning framework.

2. Methods

2.1. Study Design:

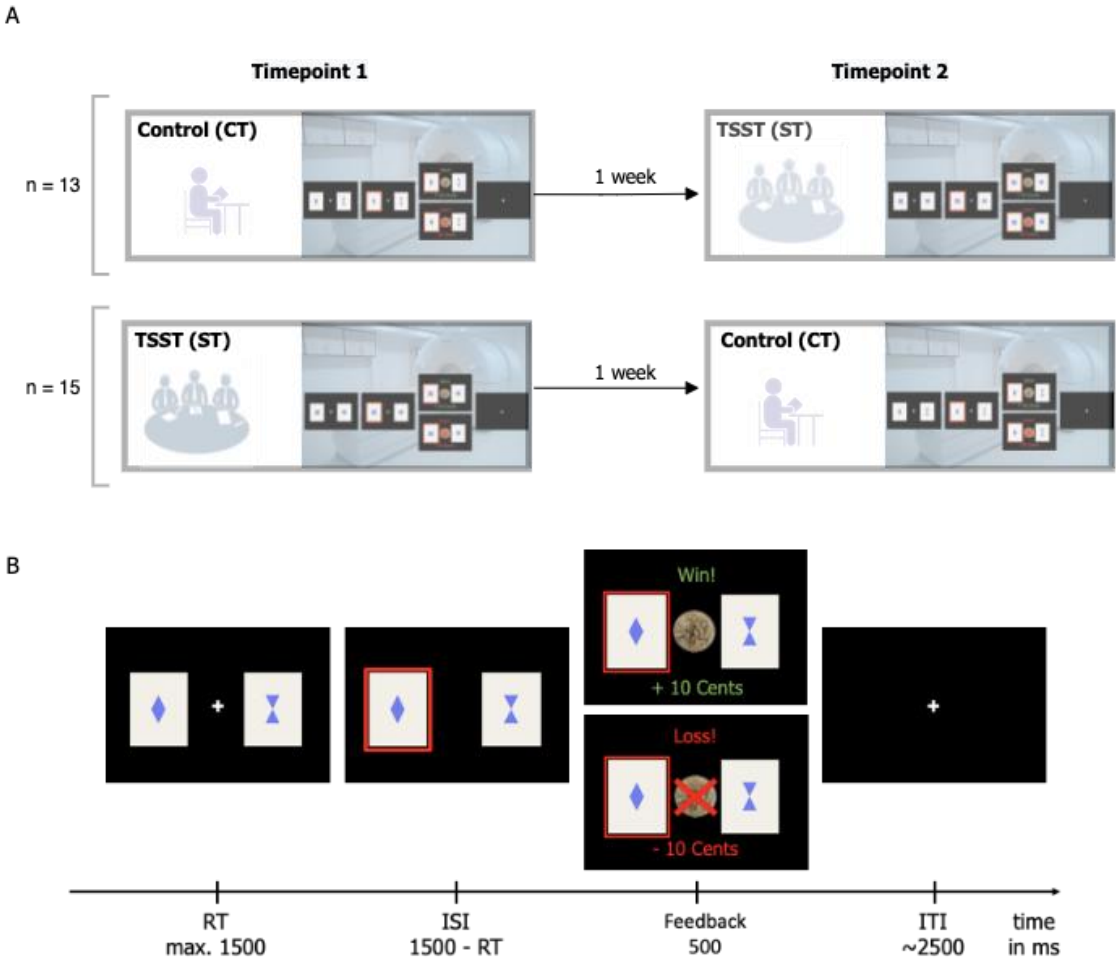

Figure 1. Study design (A) and task design (B)

Employing a within-subjects design, 38 healthy male adult participants (n=28 in the final analyzed sample, all right-handed) performed a probabilistic reversal learning task during fMRI in two separate sessions seven days apart (Figure 1). Procedures and materials are identical with a previous study from our laboratory using another paradigm (Luettgau et al., 2018). The study was approved by the ethics committee of the medical faculty at the University of Leipzig, including informed consent prior to inclusion and a full debriefing about the aims of the study after the entire protocol. During the stress condition, participants were exposed to a mock

interview and calculus in front of a socially unresponsive committee in white lab coats, following the standardized Trier Social Stress Test (TSST) protocol (Kirschbaum et al., 1993). During the control condition, participants read a neutral text in absence of the committee (see Supplement). Order of session type (stress vs. control) was counter-balanced across participants. In order to prevent confounding effects of circadian rhythm on cortisol levels (Kudielka et al., 2004), both experimental sessions were scheduled at the same time of the day. Acute stress responses were assessed at physiological (cortisol) and subjective (self-report) levels at six time points throughout the session (Figure 2).

2.2. Physiological stress response:

We assessed physiological stress response via salivary cortisol, measured six times throughout the experiment at the following time points relative to the start of intervention (stress or control): t1: -30 minutes; t2: -2 minutes; t3: +10 minutes; t4: +15 minutes; t5: +30 minutes; t6: +45 minutes (Luettgau et al., 2018). For collection and extraction of saliva we used Salivette saliva sampling tubes (SalivetteCortisol®, Sarstedt, Nuembrecht, Germany) (see Supplement). Individual cortisol reactivity was determined by calculating the area under the curve (AUC) with respect to ground (AUCg-stress and AUCg-control, see Pruessner et al., 2003) separately for both conditions and subtracting AUCg-control from AUCg-stress. The AUC was calculated based on individual subject-wise time points, to account for slight temporal dispersion in the testing protocol. For an additional analysis to confirm stress reactivity please refer to Supplement.

2.3. Subjective stress response:

Three different visual analogue scales (VAS) ranging from 0 to 100 were used to assess subjective arousal, valence and stress at all time points (T1-T6). Participants were asked to rate how they felt, regarding arousal on a scale "Please rate your current state" from 0 (sleepy) to 100 (active), valence on a scale from 0 (unhappy) to 100 (happy) and stress on a scale from 0 (not stressed) to 100 (stressed). Analogue to cortisol values this was determined by calculating the area under the curve with respect to ground (AUCg-stress and AUCg-control;

Pruessner et al., 2003) separately for both conditions and subtracting AUCg-control from AUCg-stress.

2.4. Working memory capacity:

Participants also performed the digit span backwards task from the test battery Hamburg-Wechsler-Intelligenztest HAWIK (Tewes and Wechsler, 1991) to assess working memory capacity.

2.5. Past subjective stress response:

Furthermore, participants filled in a German version of the Perceived Stress Scale (PSS-10; Cohen et al., 1983), at home via an internet-based survey (Limesurvey, www.limesurvey.org). They evaluated potential situations in their life, with regard to their respective stressfulness during the last 30 days.

2.6. Task design

Participants performed a probabilistic reversal learning task, which included 160 trials and comprised around 15 minutes. The task (Boehme et al., 2015; Reiter et al., 2016a) was programmed in Matlab (The MathWorks, Natick, MA) with Psychtoolbox (Brainard, 1997). On every trial, participants chose between two cards, each depicting a different geometric figure. The underlying reward structure was not explicitly instructed but had to be inferred: reward probabilities associated with the two choice options were anti-correlated (i.e. when card A had a reward probability of 80% and therefore a punishment probability of 20%, card B had a reward probability of 20% and a punishment probability of 80% and vice versa). Furthermore, participants were informed of the probabilistic nature of the task but not on the actual probabilities: the currently “better” card was only rewarded in 80% of all trials with 10 Cent. After a fixed number of 55 trials, contingencies reversed and these reversals repeated several times over the middle experimental phase, followed by another stable phase in the end starting at trial 126 (see Supplementary Figure S1). Participants were instructed to win as much money as possible and received the winnings at the end of the experiment.

Because feedback was drawn probabilistically on each trial, and we wanted to ensure that the number of probabilistic events was matched between the control and the stress condition six participants had to be excluded from the final sample to avoid confounds due to different task environments. Additionally, two participants had to be excluded due to technical failure and two additional participants had to be excluded because they performed the task below chance level, leaving a total of 28 participants for final analyses.

2.7. Analyses

2.7.1. Stress response analyses

Cortisol responses (AUCg) and the three subjective VAS scales were compared across conditions (stress vs control) using one-tailed paired-sample *t*-tests at a significance level of $p < .05$.

2.7.2. Behavioral data

Single-trial multilevel generalized linear models (logistic regressions) were conducted using the lme4 package (Bates et al., 2015) in R (Version 4.0.3). Parameter estimates were considered significant at p≤.05. We analyzed trial-by-trial correct responses (choose better option), win-stay (select same stimulus after win) and lose-switch (switch stimulus after loss) behavior with the factors *stress condition* (CT vs. ST, effect coding as -0.5 and 0.5) and *experimental phase* (pre, reversal, post) as fixed effects and subject as a random effect, allowing for an individually varying intercept per subject. For the factor *experimental phase* we specified a custom centered contrast, testing the null hypothesis of performance differences between first stable vs. reversal and late stable vs. reversal phase using the hypr package (Rabe et al., 2020). Main effects of condition and phase, as well as an interaction effect were added incrementally in two steps. We used χ^2-tests based on log-likelihood changes to compare a null model, which predicted outcome variables with the individually varying intercept per subject to a model including varying intercepts and all main effects. If this showed a significant better fit, we compared the main effect model to an interaction effect model. For the best-fitting model, the parameter estimates' odd's ratio was computed to assess effect size. Additionally, we performed the same analysis using the cortisol AUCg values instead of condition labels as predictor. Participants were excluded when their performance was below chance (correct responses < 50%), as described in the methods section 2.6. Across all trials, participants missed a relatively low number of trials (0.71%).

Furthermore, to explore the potential moderating impact of past stress exposure as well as working memory capacity on stress-related learning (Otto et al., 2013; Radenbach et al., 2015) we associated these with the stress effect on task performance (based on total correct responses in the stress condition – total correct responses in the control condition). We correlated this value with past subjective stress (PSS-10), as well as working memory performance (digit span backwards task). Due to missing values for four participants, regarding the PSS-10, the former analysis was conducted with a reduced sample of 24 participants.

2.7.3 Computational models

We set up the following model space to describe different learning processes that might have generated the data. It comprised Rescorla-Wagner (RW), Pearce-Hall (PH; (Pearce and Hall, 1980) models and a null model (no-learning). In the RW and PH models, the expected value $Q_{a,t}$ of an action a at trial t is updated via the RPE $\delta_{Q_{a,t}}$ (eq. 1), which is defined as the difference between received reward R_t and previously expected reward value for the chosen stimulus $Q_{a,t}$(eq. 2):

(1) $\delta_{Q_{a,t}} = R_t - Q_{a,t}$

(2) $Q_{a,t+1} = Q_{a,t} + \alpha_{\text{win/loss}}\delta_{Q_{a,t}}$

(3) $Q_{ua,t+1} = Q_{ua,t} + \kappa * \alpha_{\text{win/loss}} * \delta_{Q_{ua,t}}$

In RW models, we accounted for learning about the unchosen option as indicated by the implicit anti-correlated task structure in different sub-models (eq. 3, $\kappa = 0$ for single update (SU), $\kappa = 1$ for full double update (DU) and freely fitted κ for individually weighted double update (iDU)). We further varied whether learning rates α differed for wins and losses. The PH model encompasses eq. 1 and 2 with a dynamic learning rate depending on a decay over time as and the absolute prediction error (see Supplement or Pearce and Hall, 1980). In the no-learning model, a stable bias towards one of the stimuli was implemented. For all learning models, trial-wise Q-action values are transformed into choice probabilities by a softmax response model with different inverse decision noise temperatures β following wins and losses:

(4) $\mathrm{p}(a_i) = \frac{exp\left(\beta_{\text{win/loss}} Q_{a_i}\right)}{\sum_{j=1}^{K} exp\left(\beta_{\text{win/loss}} Q_{a_j}\right)}$

The softmax temperature parameter β reflects choice stochasticity with higher values equating more deterministic and lower values equating more stochastic choices.

We followed a two-step procedure: First, we fit our model space to the behavioral data of the control condition. Then, the best fitting model from the control condition was used for modelling behavior under stress now with additional 'stress weights' on the free parameters. Taken together, the 'step 1 model space' consisted of 8 models for learning under the control condition: RW-SU-1al, RW-SU-2al, RW-DU-1al, RW-DU-2al, RW-iDU-1al, RW-iDU-1al, PH and no-learning. We applied Bayesian model comparison (Piray et al., 2020) to find out which of these models explained the data best (see protected exceedance probabilities (PXP) in Figure 4).

To model learning under the stress condition, we added stress weights to the free parameters of the best-fitting model from the first step (RW-DU-2al). The 'step 2 model space' included the DU-2al model without stress effects (RW-DU-2al-NoStress), one with stress weights affecting only the learning parameters α_{win} and α_{loss} (RW-DU-2al-StressLearning) one model with stress only affecting the temperature parameters β_{win} and β_{loss}, (RW-DU-2al-StressBetas) and a full model with stress affecting all free parameter (RW-DU-2al-StressAll). This model space was fitted to combined data from both conditions: trials were concatenated across control and stress conditions within subjects, with the free stress parameters quantifying the additive effect on the respective parameters for the trials of the stress condition. As in step 1, model fits were then compared between models.

2.7.4. Model fitting

Models from both steps were fitted under the hierarchical Bayesian inference approach as implemented in the cbm toolbox (Piray et al., 2020) run in in Matlab R2018a. This procedure allowed for concurrent model comparison and parameter estimation. Thereby, the latter also followed a multilevel modelling approach: the group mean parameter affects individual parameter estimation and vice versa, but the relationship is scaled by how (relatively) well the model explains the individual subject's behavior.

2.7.5. fMRI data

Scans were acquired on a Siemens 3 T high-resolution PRISMA MR-System with a 20-channel head coil (Siemens, Erlangen, Germany). Covering the whole brain, 40 slices were acquired in oblique orientation at 20° to the anterior commissure-posterior commissure line and in ascending order with the following parameters: T2*-weighted gradient-echo echo-planar imaging (EPI) (TR: 2.09 s; TE: 22 ms; flip angle: 90°; 3 × 3 mm^2 in-plane voxel resolution, 0.5 mm gap between slices, voxel size: 3 × 3 × 4 mm). After preprocessing (see Supplement) fMRI data was analyzed within SPM12. On the first level individual subject level the feedback onsets were modeled with the reward prediction errors (RPE) included as parametric modulator for the control and stress condition. The six realignment parameters were added as nuisance regressors. Contrast images were computed for the RPE for the control and stress condition and subsequently submitted to random-effects group statistics (second level) using a paired t-test to compare activation between conditions (stress/control). To control for multiple comparisons, family-wise error correction (p_{FWE}) was applied at the whole-brain level at $p_{FWE}<0.05$. For testing the condition effect, a mask of the RPE main effect over both conditions were used at $p_{FWE}<0.05$. In order to differentiate RPE signals for win and loss trials (similar to xxx) we modeled those trial types separately introducing the RPE as parametric modulator, which results in two contrast images (RPE win and RPE loss) subjected to similar second level analyses.

3. Results

3.1. Sample characteristics

The final sample consisted of n = 28 healthy male adult human participants with a mean age of 26.9 (*SD* = 5.7; range: 18-41) years, a mean of 12.2 (*SD* = 1.2) educational years, and a mean verbal intelligence of 103.8 (*SD* = 10.1).

3.2. Stress response analyses

The stress intervention significantly increased subjective stress responses (arousal, valence and subjective stress), as well as physiological responses (cortisol levels). For detailed statistics refer to the Supplement and Figure 2.

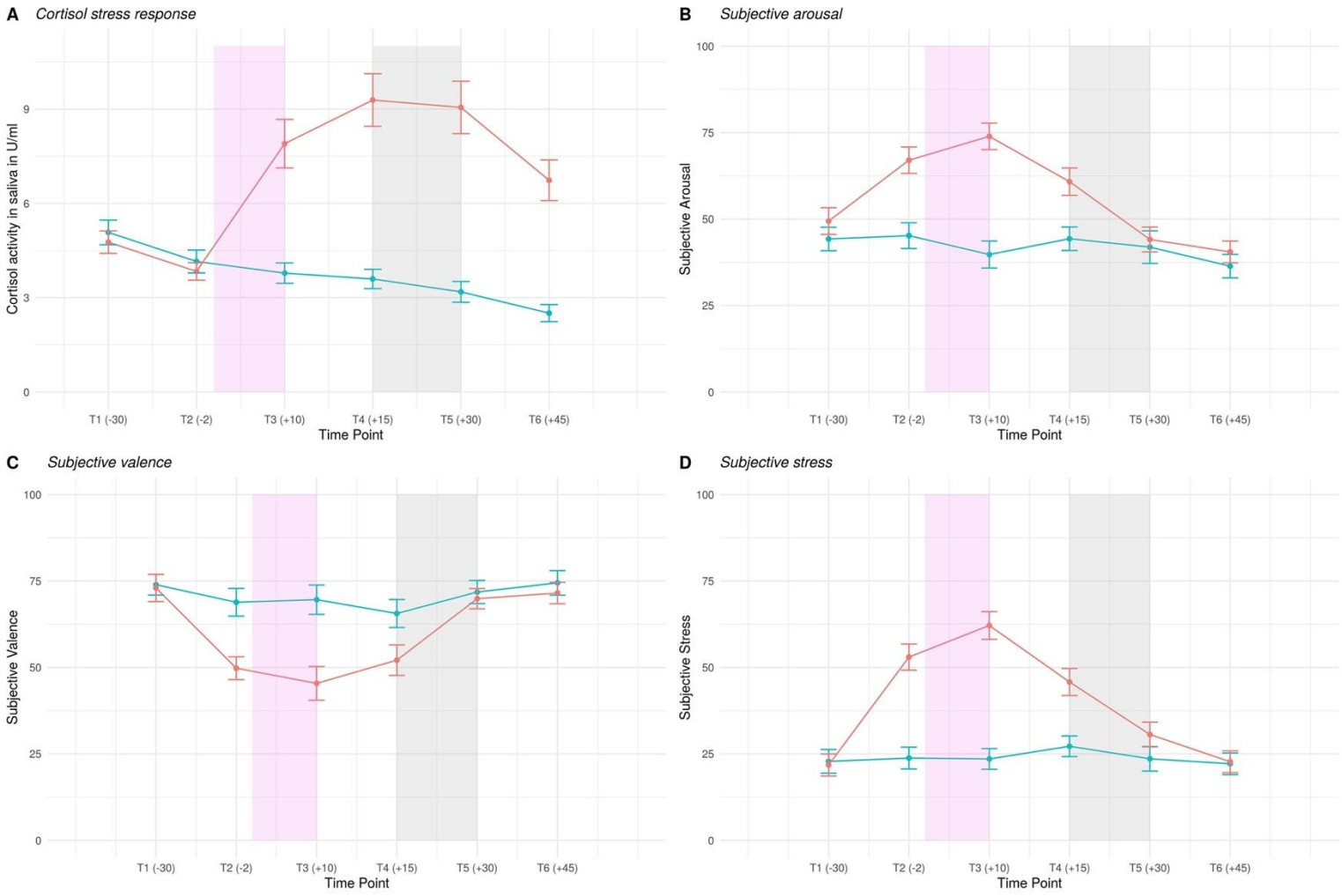

Figure 2 Physiological (cortisol) (A) and subjective stress response (B-D) over the course of the session. Violet shaded area: period of intervention (either stress induction (TSST) or control intervention), grey shaded area: reversal learning task was administered in the MR scanner.

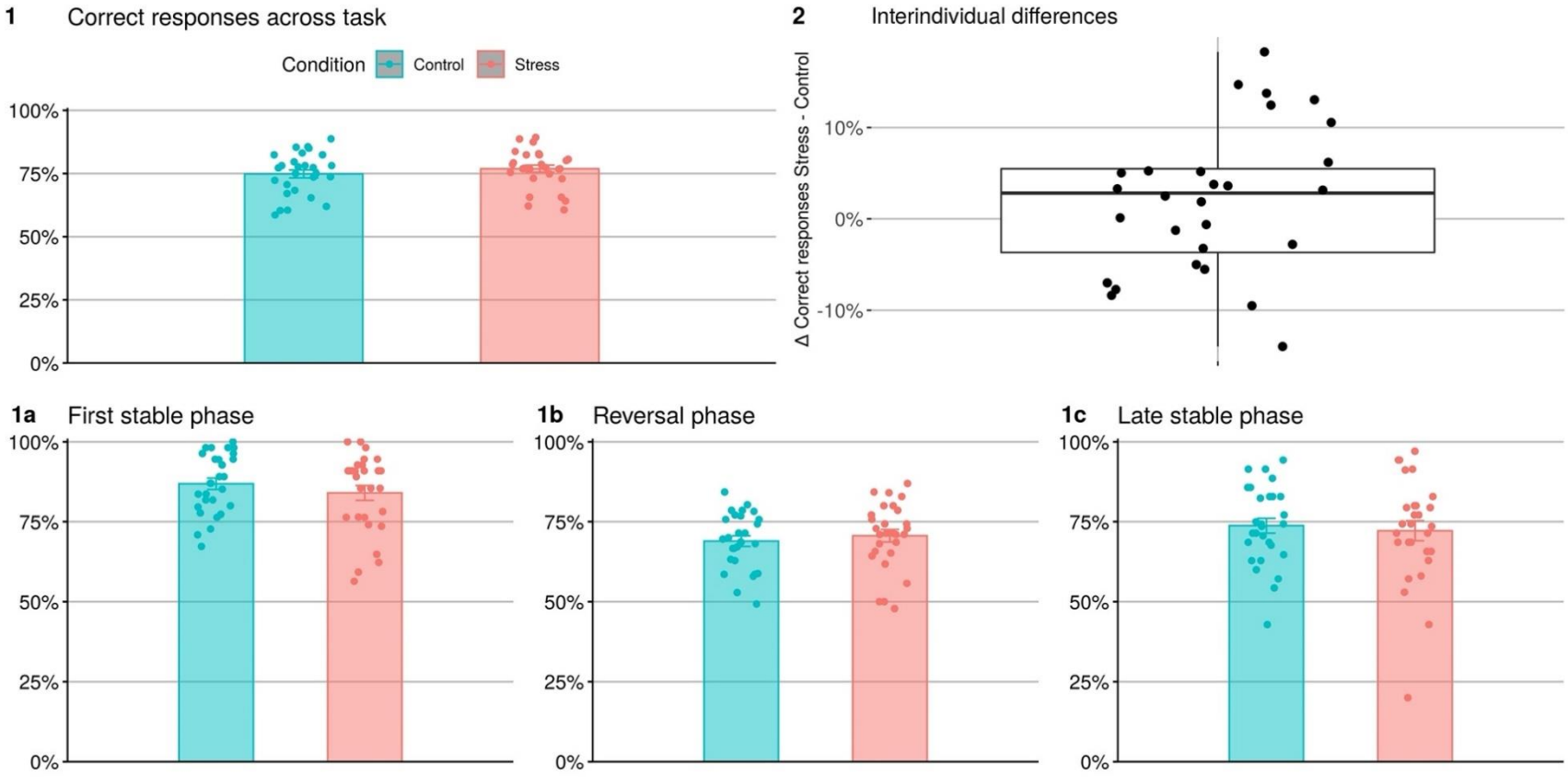

Figure 3 Correct responses during stress (turquoise) and control condition (red) across task (1), as well as phases (1a-c) and interindividual differences between conditions (2).

3.3. Behavioral results

Best-fitting multilevel linear modeling included a subject-specific intercept, as well as main effects of condition and phase. Predicting correct responses on a single-trial basis with multilevel linear modeling indicated the expected task effect in the reversal ($p < 0.001$) and in the last stable phase ($p < 0.001$). For both phases, correct responses decreased with respect to the first reference phase. Furthermore, there was a main effect of condition ($p = 0.020$), suggesting that participants' correct responses subtly increased with a 1.13 higher chance (odds ratio, OR = 1.13) for correct responses under stress (see Table 1 and Supplement: Figure S1). As shown in Figure 3.2, the effects of stress on correct responses were quite heterogenous with high interindividual variability. The findings on correct responses were supported by a significant main effect ($p = 0.030$) of stress when the physiological stress level (AUC) was used as a continuous predictor instead of experimental condition (see Supplementary Figure S2b and Table S-A). In this model, task effects were again significant for the reversal phase ($p < 0.001$) as well as the last stable phase ($p < 0.001$). Regarding win-stay behavior, best-fitting multilevel linear modeling included a subject-specific intercept, as well as a main effect of condition and phase. Task effects of the reversal phase ($p < 0.001$) and the last stable phase ($p < 0.001$) were significant, but not the experimental condition ($p = 0.22$). Similarly, lose-switch behavior resulted in significant task effects of reversal phase ($p < 0.001$) and last stable phase ($p < 0.001$), but not experimental condition ($p = 0.73$) (see Supplementary Tables S-B and S-C).

Exploratory behavioral analysis of moderator variables:

The impact of stress on behavioral performance (Δ correct responses) did not correlate with working memory capacity ($r(26) = 0.16$, $p = 0.42$) nor with our measure of past subjective stress ($r(22)=-0.19$, $p = 0.37$).

Table 1 Multilevel generalized linear modeling results of the best-fitting model predicting correct responses

	Correct Responses				
Predictors	*Estimate (SE)*	*CI*	*Z*	*p*	*OR*
Intercept	1.23 (0.07)	1.08-1.38	17.13	< 0.001	
Condition	0.12 (0.05)	0.01-0.22	2.32	0.020	1.13
Reversal Phase	0.96 (0.06)	0.83-1.07	15.27	< 0.001	2.6
Last Stable Phase	0.8 (0.07)	0.65-0.94	10.89	< 0.001	2.22
ICC	0.04				
$N_{subject}$	28				
Observations	8893				
Marginal R^2 / Conditional R^2	0.053/0.08 8				

3.4. Computational modeling results

Behavior in the control condition ('step 1 model space') was best explained by a Rescorla-Wagner model with full double update and two learning rates (the RW-DU-2al) across all participants with a PXP = 0.62 (see Figure 6). This indicates that most participants used the anticorrelated task structure and updated the chosen and the unchosen choice option to a similar extent (full double update model, DU). Although there is some evidence for use of an individual double update (iDU) we decided to focus on DU-learning, as present in the majority of participants. Furthermore, the learning rate in win trials was lower than in loss trials (paired

t-test on alpha win vs alpha loss: $t(27) = -6.7$, $p < 0.001$), resulting in stronger updates after loss compared to win feedback. In a next step, additional free parameters for potential stress effects were entered for this winning model (the 'step 2 model space'). This resulted in a best fit for RW-DU-2al-StressBetas (PXP = 0.92), indicating that only the temperature parameters β_{win} and β_{loss} were different between control and stress condition but not the learning rates (see Supplementary Table S-D for parameter estimates). Model comparison resulted in lower protected exceedance probabilities (PXP < 0.1) for all other models (see Figure 6). Choice temperature parameters were significantly higher after win trials compared to loss trials ($F(1,27)= 22.77$, $p < .001$) and numerically higher during the control compared to the stress condition, although the latter effect was not significant ($F(1, 27) = 0.25$, $p = .623$). We observed a large interindividual variance for the temperature parameters (see Supplementary Figures S3 and S4 for violin plots of parameter distributions and Supplementary Table S-D for parameter mean estimates of the winning model of 'step 2 model space').

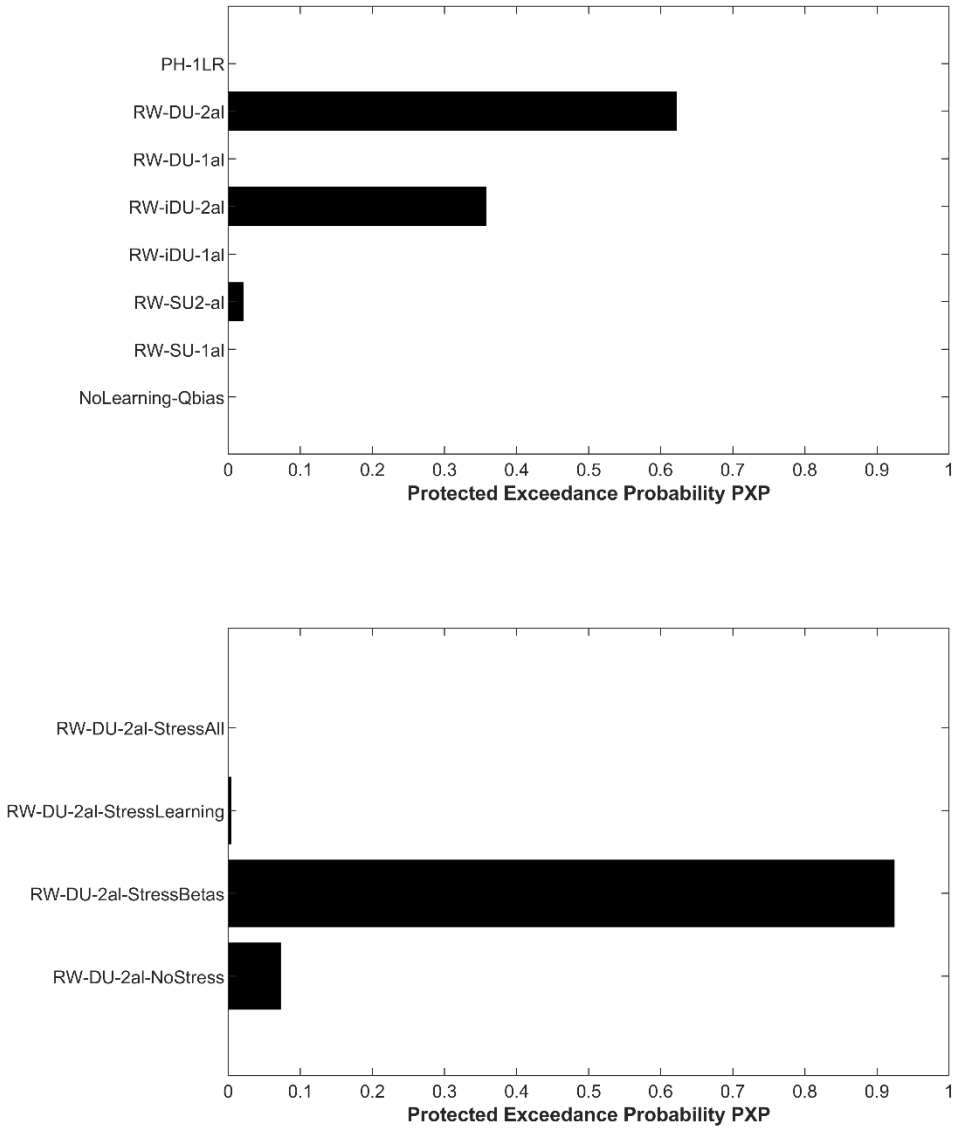

Figure 4 Protected exceedance probability: (a) 'step 1' model space explaining behavior in the control condition (top), (b) 'step 2' model space with added free stress parameters to the best fitting model of the control condition, in order to detect stress-related parameter differences between control and stress condition (bottom).

fMRI results

We found a main effect of RPE combined over both conditions in the vmPFC, bilateral ventral striatum, posterior cingulate cortex (PCC) and bilateral insula (p_{FWE}< .05 for the whole brain, see Figure 5 and Supplementary Table S-E). We did not observe significant RPE-related activation differences between control and stress condition, when modeling win and loss trials together. On an uncorrected level, there was higher activation in the right insula during stress compared to the control condition, but this did not entirely survive multiple comparison correction ([46 4 10], t = 4.02, $p_{FWE\ SVC\ main\ effect}$ = .068, $p_{uncorrected}$ < 0.001; see Supplementary Figure S7).

Exploratory analysis of moderator variables

Parallel to our exploratory behavioral analysis we assessed potential associations between past subjective stress (PSS) and working memory capacity (WM) with changes in RPE signal induced by acute stress (Δ RPE stress – control). We computed new first level statistics combining stress and control condition into one model and generated a contrast image with the difference between stress and control condition. These contrast images were then entered into separate second level models with PSS and WM as covariates, respectively. We did not find significant effects of PSS nor WM on the changes in RPE activation.

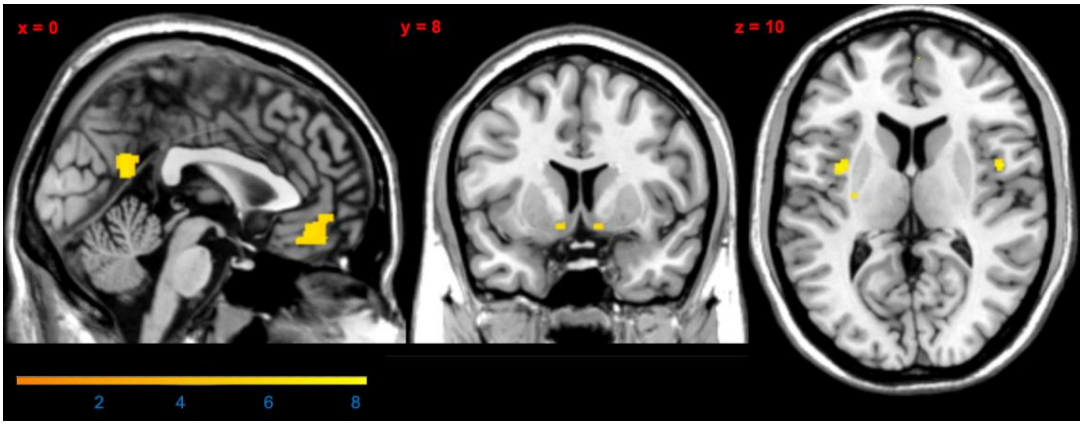

Figure 5: Neural activation related to reward prediction error across both conditions. Displayed are clusters showing significant RPE coding in vmPFC, ventral striatum and insula at $p_{\text{FWE whole brain corrected}} < 0.05$ combining stress and control conditions (main effect of task).

Furthermore, modeling win and loss trials separately, yielded a main effect of condition for win trials in the left striatum ([-10 10 2], t = 6.43, $p_{FWE\ whole\ brain\ corrected}$ = .041, see Figure 6). Compared to the control condition participants under stress exhibited stronger signaling of RPE for win trials in a reward-related brain region. No significant difference between stress and control condition was observed for RPE in loss trials.

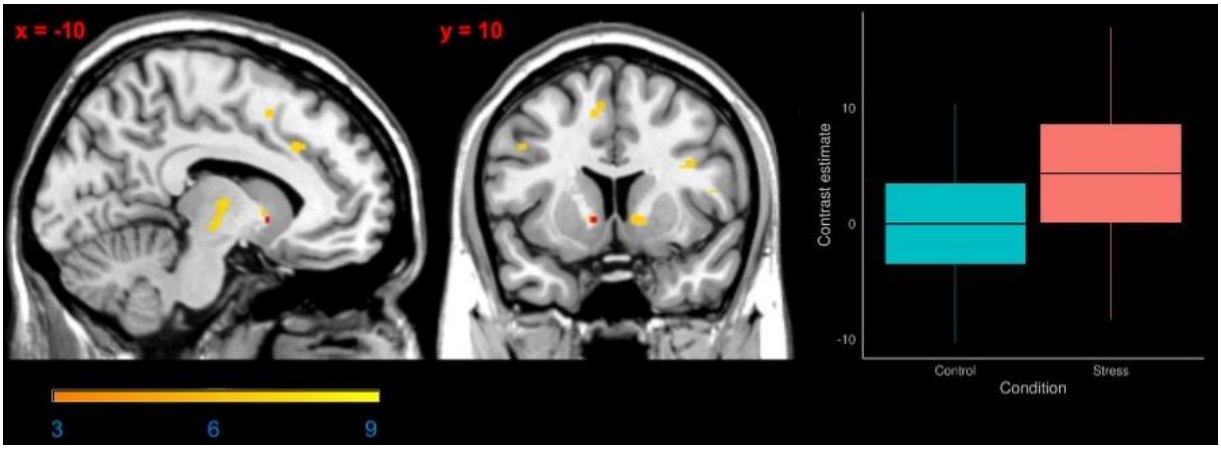

Figure 6: Neural activation related to reward prediction error (RPE) when modeling win and loss trials separately. Lefthand side and middle: main effect RPE during win trials across conditions (yellow-orange gradient) and the stress effect (stress condition > control condition;

red) in the ventral striatum at $p_{\text{FWE whole brain corrected}} < 0.05$. Righthand side: Box plot of contrast estimates for RPE win for control and stress condition at the peak voxel (x = 10, y= -10, z=-2).

Discussion

The present study investigated the behavioral and neural effects of acute psychosocial stress on reversal learning in healthy male human participants. Participants were slightly more accurate under acute stress. Additionally, the neural representation of RPE signals was significantly higher during acute stress for win trials in our sample. Computational modelling of choice behavior showed no stress effect on learning rates, but high stress-related interindividual variability in the use of learned values.

On the behavioral level, participants learned to choose the correct (i.e. more often rewarded) stimulus and adapted their choices after changes in reward contingencies (reversals) during both the control as well as the stress condition. Unlike previous studies (Shields et al., 2016), we observed more correct responses during the stress compared to the control condition in our analysis, but the effect size was small (OR = 1.13) and other behavioral measures such as win-stay or lose-switch behavior were not affected. Furthermore, participants displayed substantial interindividual variability including better, worse, or non-different performance under acute stress in our within-subjects design.

Computational modelling of choice behavior showed that participant's behavior was best explained by a RL model using reward prediction errors to update the expected values of both the chosen and the unchosen choice option, indicating that participants considered the anticorrelated task structure. Acute stress did not affect the learning rate, which scales the influence of the RPE in updating of the expected values. Therefore, within our model space there was no evidence that stress affected the updating speed of learned expected values itself. However, our modeling analysis suggests that the degree to which participants used the learned values (temperature parameter) differed between the stress and control condition. Interestingly, there was no overall condition effect, but model comparison showed that introducing different temperature parameters for the control and the stress condition

individually explained the observed behavior best. The absence of a significant condition effect on the temperature parameter together with the model selection result indicates meaningful interindividual variability of choice behavior in response to acute stress. Two studies using cognitive computational modeling during learning tasks also observed effects of acute stress on choice temperature, mostly higher stochasticity (Cremer et al., 2021; Radenbach et al., 2015) while other studies observed attenuation of model-based behavior (Otto et al., 2013) or an increased tendency for win-stay behavior (Raio et al., 2020). However, comparability is limited due to the different tasks used, mainly focusing on the balance between model-free and model-based learning (Cremer et al., 2021; Otto et al., 2013; Radenbach et al., 2015; Raio et al., 2020), which was not the focus of the present study.

On the neural level, RPE signals were correlated with neural activation in a network comprising vmPFC, bilateral ventral striatum, posterior cingulate cortex and insula across both conditions, in line with previous studies using the same paradigm (Boehme et al., 2015; Katthagen et al., 2020; Reiter et al., 2017, 2016) and with meta-analytic findings of RPE fMRI studies (Fouragnan et al., 2018). No whole-brain correctable stress effects on RPE representation were observed when assessing win and loss trials together. No whole-brain correctable stress effects on RPE representation were observed when assessing win and loss trials together. The trendwise increase of RPE-related activation in the insula during the stress compared to the control condition, might contribute to the behavioral effect as the insula has been implicated in error processing, mainly interpreted to code salience signals (Fouragnan et al., 2018). However, this finding did not survive stringent correction for multiple testing and therefore needs to be interpreted with caution.

When differentiating RPE signals during win and loss trials, we found stronger coding of positive RPEs in the ventral striatum during the stress compared to the control condition in our sample of healthy male participants. This increased neural activation following acute social stress corresponded to better performance in the stress condition. Stress has been shown to affect the mesolimbic dopaminergic system although both increasing and inhibiting effects

have been described depending on the intensity, duration, and controllability of the stressor (Baik, 2020). In line with our finding, stressful experience in rodents has been found to increase reward-evoked dopamine release in the ventral lateral striatum (Stelly et al., 2020). Another study found an increase of negative (unexpected aversive face stimuli) but not of positive (appetitive) prediction error signals in the ventral striatum in a condition of threat (potential of electric shock) while no difference between positive and negative PE signals were observed in the safe condition in a condition of threat (potential of electric shock) while no difference between positive and negative PE signals were observed in the safe condition (Robinson et al., 2013). While we did not differentiate between threatening and safe context, this finding suggests that RPE signals are highly context-sensitive. In contrast to our finding, another study observed a blunted positive prediction error signal in the dorsal striatum with impaired performance in win-trials (Carvalheiro et al., 2021). In our study acute social stress was induced using the TSST before scanning, while Carvalheiro et al. used aversive sounds inside the scanner to induce stress. Therefore, differences in stress induction likely contribute to the different findings.

In rodents acute stress improved reversal learning whereas chronic stress impaired reversal learning (Bryce and Howland, 2015; Hurtubise and Howland, 2017). Differential long-term stress exposure may have led to the heterogenous effects of stress on reversal learning in our sample. In humans, chronic stress increased the detrimental influence of acute stress on model-based learning (Radenbach et al., 2015). Apart from chronic stress exposure, cognitive capacities or personality traits are further potential explanations for the inconsistent impact of acute stress on learning. A high working memory capacity seems to hold a protective function against the attenuation of model-based learning (Otto et al., 2013), while trait impulsivity interacts with different aspects of learning differentially, but particularly seems to increase perseveration (Raio et al., 2017). As probabilistic reversal learning does not disentangle model-based and model-free learning these effects of moderators were impossible to replicate here. Exploratory analyses on working memory capacity and past subjective stress did not reveal any respective effects on stress in our sample.

Our findings are limited by some of the following factors. Considering the gender differences in decision-making (Shields et al., 2016) which may be amplified by stress (Mather and Lighthall, 2012) and potential impact of cyclical changes in female individuals we decided to investigate an exclusively male sample. Furthermore, our sample was homogenously young and highly educated. Therefore, our findings cannot be generalized to the general population or patient samples. Our task does not allow to temporally disentangle value and RPE representations in the brain. Stress effects may be related to the value representation and utilizing of those values during the decision process as indicated by our modeling findings. Although speculative at this point, our finding of altered choice stochasticity parameters may hint towards this and aligns with recent findings on the importance of computational noise directly affecting value representation (Findling et al., 2019). Dissociating these computations might be a promising avenue for future studies to determine the neurocomputational processes underlying reversal learning performance increases under acute stress.

While our relatively young and healthy study sample has shown slight beneficial effects of acute stress, other more vulnerable populations may show different patterns. Stress, especially when long-term or chronic, is an important factor in causing and maintaining psychiatric illness (McEwen, 2004). While healthy individuals can adapt to a certain level of stress and even find it beneficial (Lighthall et al., 2013), decision-making frequently goes awry in psychiatric disorders (Cáceda et al., 2014). Our results suggest that it might be worthwhile assessing decision-making under acute stress in populations at risk of developing psychiatric conditions to reveal how stress is involved in maladaptive decision-making. Identification of altered choice behavior and relevant neural networks in healthy individuals make it possible to disentangle how stress affects healthy decision-making and what might be a maladaptive psychiatric alteration. As an operationalization of cognitive flexibility, reversal learning is a construct with high relevance for several psychiatric disorders. For instance, cognitive flexibility and its neural correlates are impaired in patients with alcohol use disorder (Reiter et al., 2016), anorexia nervosa (Bernardoni et al., 2017), binge-eating disorder (Reiter et al., 2017), ADHD (Hauser et al., 2021) or schizophrenia (Schlagenhauf et al., 2014).

Conclusion

Our study combines the advantages of a within-subjects design and fine-grained computational measures to investigate the effect of acute psychosocial stress on healthy male adults. Several lines of analysis showed slightly improved performance, reflected in altered choice stochasticity, with whole-brain-correctable neural effects of increased RPE signaling for win trials under stress.

Funding

This work was supported by the Rubicon award granted to ZS by the Netherlands Organization for Scientific Research (NWO, Rubicon 2014/05563/ALW), by the Einstein Center for Neurosciences (LW), and by the Heisenberg program from the German Research Foundation (grant number SCHL 1969/5-1), as well as the Max Planck Society and grants from the German Research Foundation awarded to FS (DFG SCHL 1969/2-2 as part of FOR1617 and SCHL1969/1-2 and 402170461 as part of TRR265).

Acknowledgements

We thank all the authors contacted who provided additional information. The authors would like to thank all volunteers who participated in this study. The authors would also like to thank C. Edwards, K. Hudl, L. Golz, M. Jochemko, A. Kummer, N. Pampus, J. Lepsien, A. Pampel, T. Schlumm, S. Thiers, C. Backhauß, M. Falk, and L. Fisher for their valuable assistance in recruitment and data acquisition throughout the study.

Disclosure Statement

The authors have declared that there are no conflicts of interest in relation to the subject of this study.

Data availability

Data and analysis scripts are available via https://github.com/agschlagenhauf/SALAD

Author Contributions

ZS, FS; Conceptualization.

LL, ZS; Data curation.

LW, CE, TK, FS; Formal analysis.

LW; Writing - original draft.

CE, TK, ZS, FS, LL, MP, AH; Writing - review & editing.

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Supplementary material

Acute stress alters probabilistic reversal learning in healthy participants

Wieland et al.

Study design: Within seven days prior to the first intervention participants performed a verbal intelligence assessment (Schmidt and Metzler, 1992) and a high-resolution structural MR scan, which was used for coregistration of fMRI data. After arrival on the intervention day participants rested for 10 minutes and practiced the reversal learning task outside of the MR scanner before the stress or control intervention. After the intervention, participants were led to the MR scanner. For further details see Luettgau et al. (2018).

Stress/control intervention: After arrival, participants were able to accommodate to the environment by relaxing for about 10 minutes. During the anticipation period (5 mins) of the TSST stress condition participants were instructed to prepare for a job interview. They were allowed to take notes in preparation but not to use them afterwards in a free speech for 5 mins in front of a mock committee explaining why they would be suitable candidates. The committee acted in an emotionally and socially non-responsive manner and wore white laboratory coats to heighten stress response. The committee consisted of an actor and a trained psychologist student who were introduced as specializing in the analysis of non-verbal behavior. As a second part of the stress intervention participants were asked to perform a mental arithmetic task (5 minutes) in front of the committee. They had to perform a serial substraction of the number 17 starting at 2043 verbally as fast and accurately as possible. During both parts participants were supposedly video- and audiorecorded, which was enhanced by a microphone and a video camera (turned off unknown to the participants). In the debriefing after finishing the study participants were told about the purpose of the stress intervention by a psychologist. They were told that they had not been video- or audio-recorded and that the interview would not be relevant for the remaining parts of the study. In the anticipation phase of the control condition, participants were instructed that they would read a piece of text and could relax. Afterwards, they read a neutral non-fiction text about the Mesozoic era for 10 minutes.

Power analysis:
We calculated an a priori power analysis in G*Power 3.1(Faul et al., 2007). Expecting an impairing effect of stress on cognitive flexibility with an effect size of Hedge's g = -0.3 (Shields et al., 2016), for a paired t-test with given significance threshold $\alpha = .05$ indicates a sample of $n = 71$ participants would be necessary to achieve a power $(1 - \beta) = .80$ and reject the null hypothesis of no differences between the stress and control conditions. Due to external contraints we were only able to include $n = 28$ participants in the final sample and thereby could only achieve a power = 0.46.

Task design:
Right-side versus left-side location of the stimulus was randomized on each trial. Participants had to choose one card by button press within 1.5 s, whereafter the feedback (in case of monetary win a 10 Eurocent coin and in case of monetary loss a crossed 10 Eurocent coin) was displayed for 0.5 s. A fixation cross was shown during inter-trial interval with a variable duration (jittered and exponentially distributed, range 1-12.5 s, mean 3.5 s). This resulted in an average trial length of 4 s

fMRI:
Field maps were acquired after the task to account for individual homogeneity differences of the magnetic field (TR = 488 ms, TE = 4.92 ms, flip angle = 60°, matrix = 192 × 192 mm). The scanning procedure further comprised a three-dimensional T1-weighted images (TR: 0.5 s, TE: 2.03 ms, FoV = 256 × 240 × 176, voxel size: 1 × 1 × 1 mm) with a magnetization-prepared two rapid acquisition gradient echoes (MP2RAGE) and 32-channel head coil recorded within seven days before the first test session. fMRI data were preprocessed and analyzed using SPM8 (http://www.fil.ion.ucl.ac.uk/spm/) in Matlab. The first 5 volumes of each functional time series were discarded. Before preprocessing, the origins of

the functional imaging series were reoriented to the anterior–posterior commissure plane in native space. Preprocessing included slicetiming, realignment, coregistration, and warping to Montreal Neurological Institute (MNI) space. The obtained normalization parameters were applied to the realigned images, which were resliced with a voxel size of 3 x 3 x 4 mm. All images were smoothed with a Gaussian kernel of 6 mm full width at half-maximum (FWHM).

Computational modeling:

Pearce-Hall model

We implemented a Pearce-Hall model, where $|\delta|$ denotes the absolute RPE, C is an arbitrary scaling coefficient and γ is a decay constant. The learning rate depends on the absolute RPE on previous trials, the learning rate on previous trials, and the decay constant γ (Pearce-Hall, 1980).

$$\alpha_n = \gamma C|\delta_{n-1}| + (1-\gamma)\alpha_{n-1}$$

Stress response analyses:

Our analyses resulted in a significant difference between ST and CT condition with regard to subjective arousal ($t(27) = -4.9$, $p < .001$), subjective valence ($t(27) = 4.2$, $p < .001$), and subjective stress ($t(27) = -6.7$, $p < .001$). Furthermore, we found a significant difference between ST and CT for cortisol AUC-G ($t(26) = -2.6$, $p = .02$).

Supplementary Figures

Choice behavior in both conditions

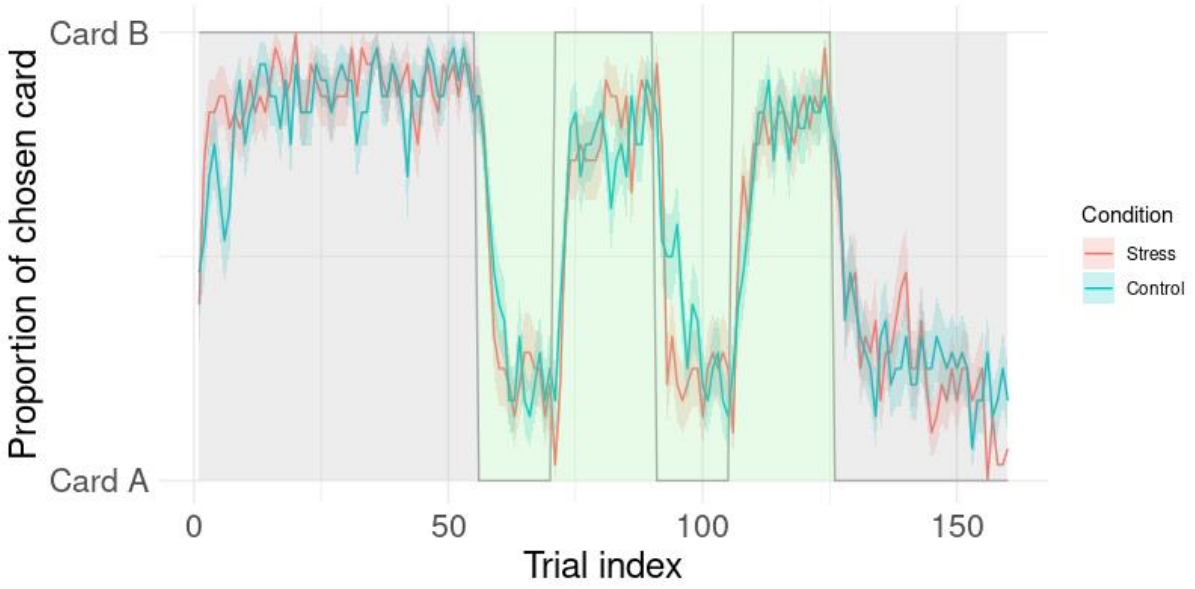

Figure S1. Empirical choice behavior in both conditions (lines showing the mean percentage of chosen card for stress (ST) in red and control (CT) in blue and shaded red and blue areas showing standard errors) with underlying task structure in grey line and shaded areas in grey for stable and light green for volatile phases.

Generalized mixed effects modeling: Odd's ratio

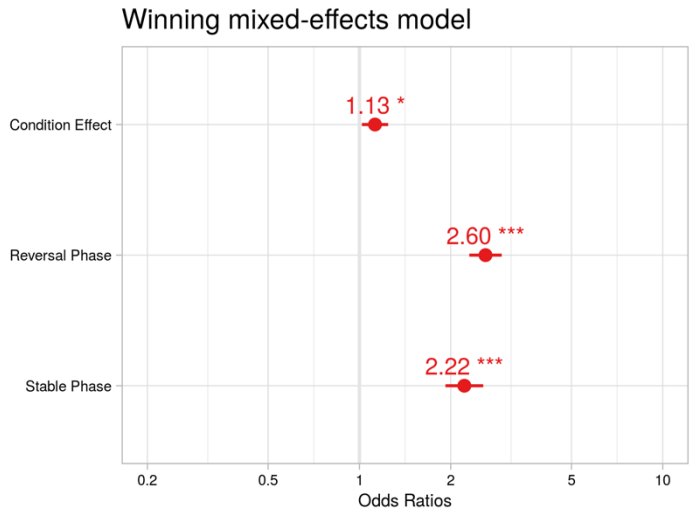

Figure S2a. Odd's Ratio of condition (1.13, CI: 1.02-1.24), reversal phase (2.60, CI: 2.30-2.94) and stable phase (2.22, CI:1.92-2.56) contrasts from fixed-effects model.

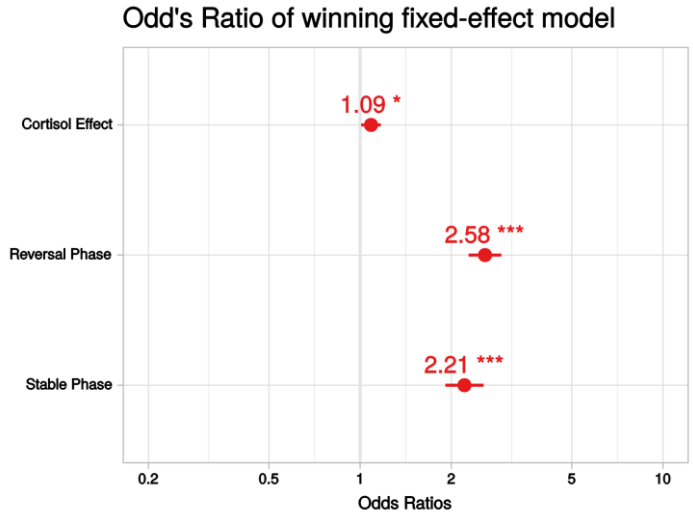

Figure S2b. Odd's Ratio of cortisol (1.09, CI: 1.01-1.17), reversal phase (2.58 CI: 2.28-2.93) and stable phase (2.21, CI:1.91-2.56) contrasts from fixed-effects model.

Computational modeling: parameter distribution

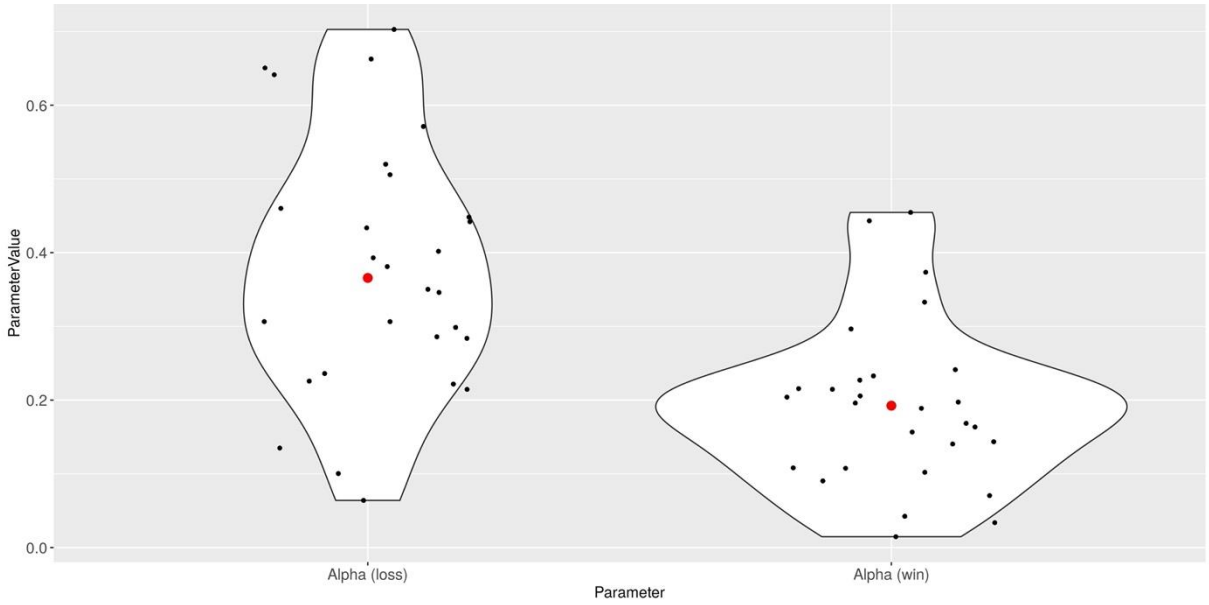

Figure S3. Learning parameter values across all participants (median in red).

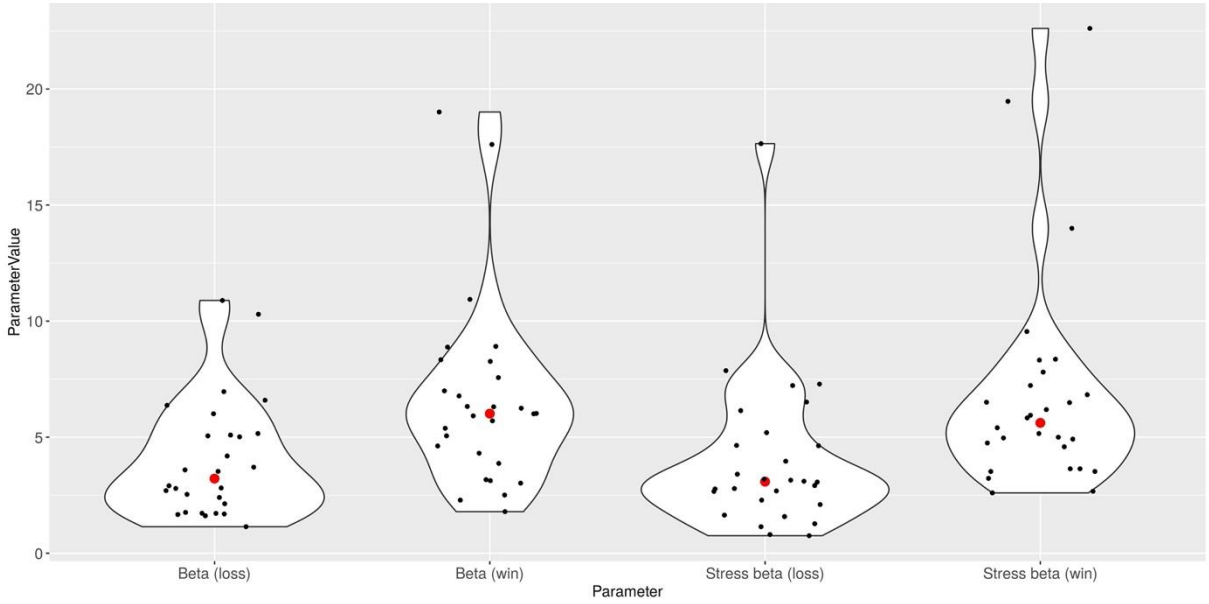

Figure S4. Choice stochasticity parameter values across all participants (median in red).

Computational modeling: choice stochasticity and behavioral results

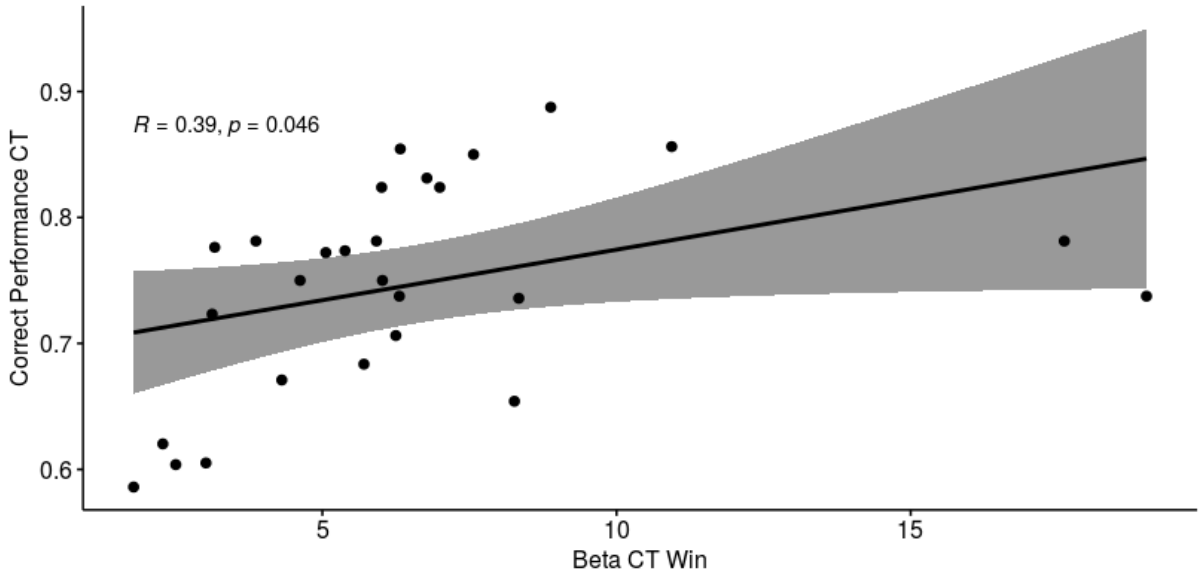

Figure S5. Correlation of $\beta_{\text{control win}}$ and correct performance (%) in the control condition.

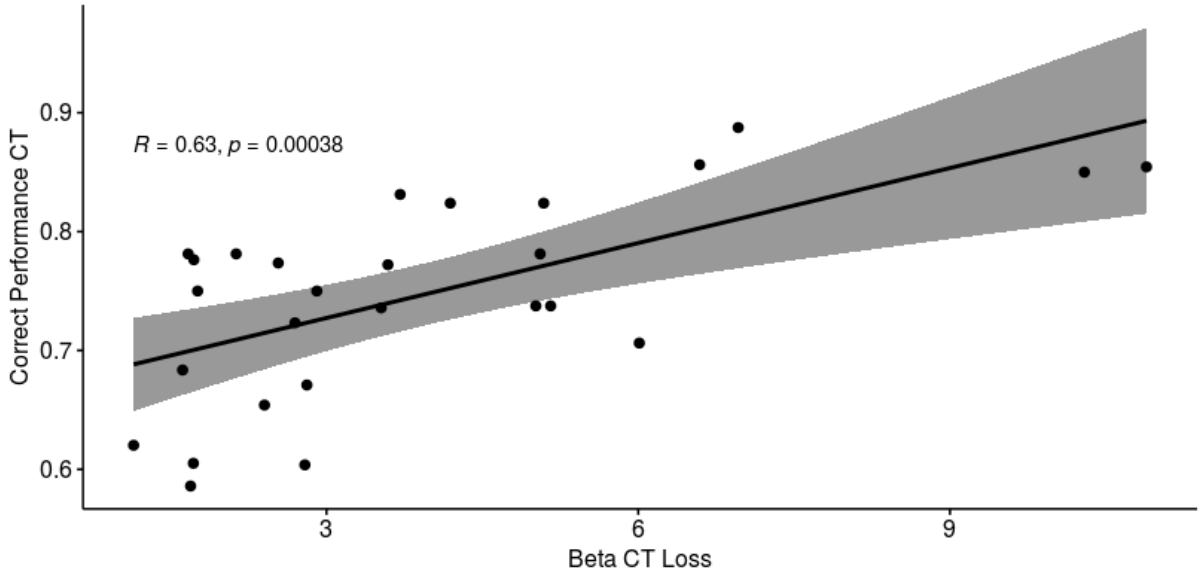

Figure S6. Correlation of $\beta_{\text{control loss}}$ and correct performance (%) in the control condition.

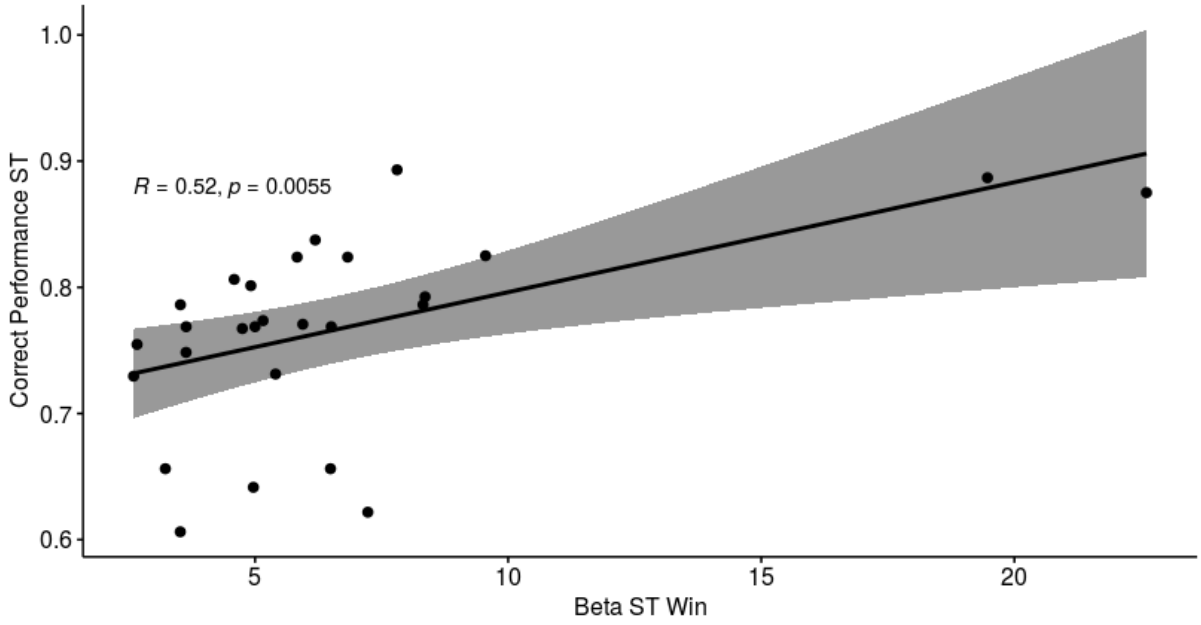

Figure S7. Correlation of $\beta_{\text{stress win}}$ and correct performance (%) in the stress condition.

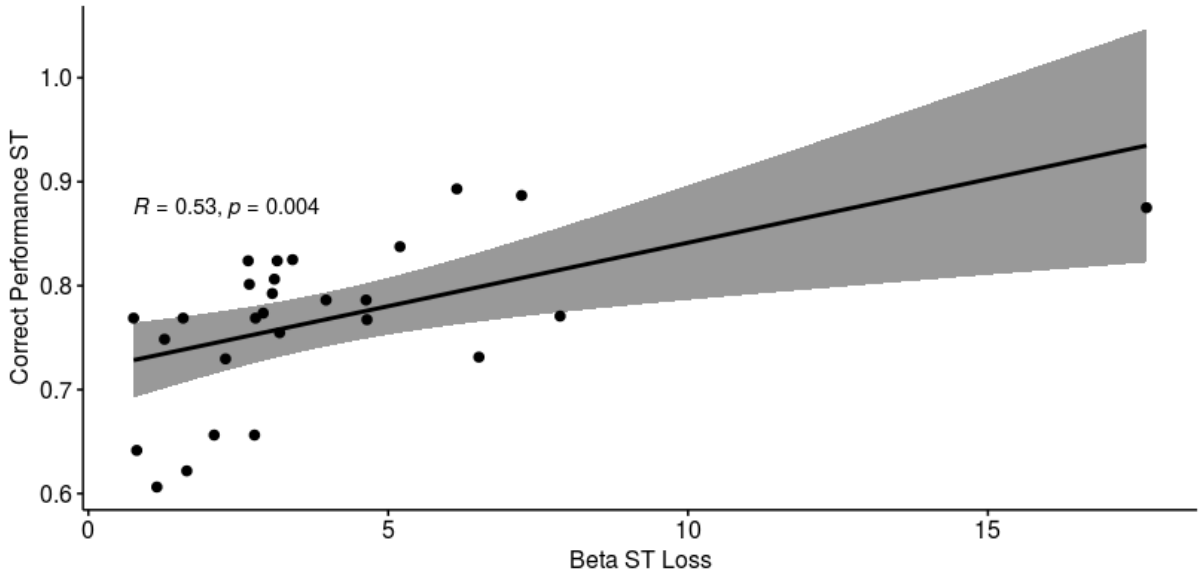

Figure S8. Correlation of $\beta_{\text{stress loss}}$ and correct performance (%) in the stress condition.

fMRI Analyses

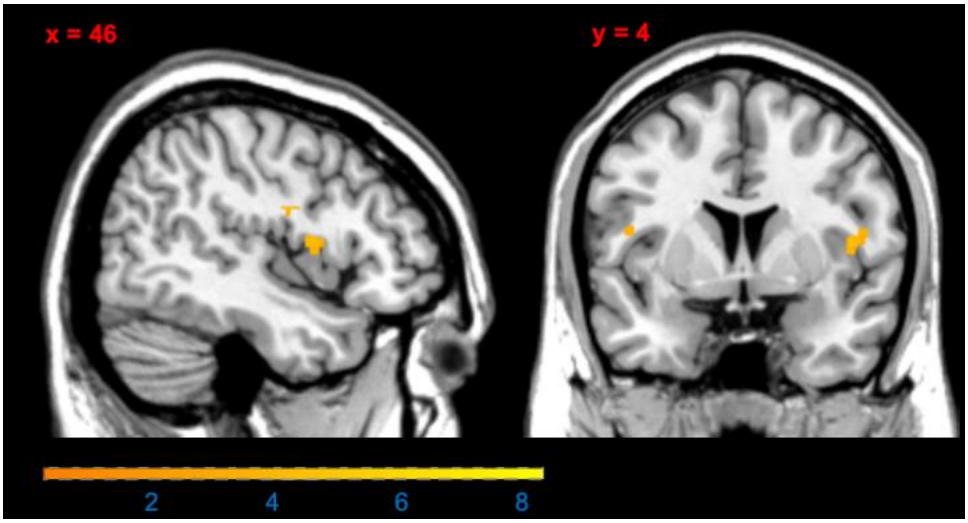

Figure 9: Stronger coding of RPE in right insula during stress compared to control condition (t=4.02, $p_{FWE\ SVC\ for\ task\ main\ effect}$ = 0.068; displayed at t>3 with cluster extent of 20 voxels for display purposes).

Supplementary Tables

Table S-A Multilevel linear modeling results predicting correct responses of the winning model: random-subject intercept, main effect of continuous cortisol response (AUC-G) and phase

	Correct Responses				
Predictors	*Estimate (SE)*	*CI*	*Z*	*p*	*OR*
Intercept	1.22 (0.07)	1.07-1.37	16.54	< 0.001	3.39
Cortisol Level	0.08 (0.04)	0.01-0.16	2.16	0.030	1.09
Reversal Phase	0.95 (0.06)	0.83-1.07	14.94	< 0.001	2.58
Last Stable Phase	0.79 (0.07)	0.65-0.94	10.70	< 0.001	2.21
ICC	0.04				
$N_{subject}$	27				
Observations	8578				
Marginal R^2 / Conditional R^2	0.053/0.088				

Note. Sample of *n* = 27 due to a missing AUC-G value for one subject.

Table S-B Multilevel linear modeling results predicting win-stay behavior of the winning model: random-subject intercept, main effect of condition and phase

	Win-stay behavior				
Predictors	*Estimate (SE)*	*CI*	*Z*	*p*	*OR*
Intercept	0.44 (0.07)	0.30 – 0.59	6.23	< 0.001	1.56
Condition	0.05 (0.04)	-0.03 – 0.14	1.23	0.220	1.06
Reversal Phase	0.47 (0.05)	0.37 – 0.57	9.14	< 0.001	1.59
Last Stable Phase	0.36 (0.06)	0.23 – 0.48	5.81	< 0.001	1.43
ICC	0.04				
$N_{subject}$	28				
Observations	8837				
Marginal R^2 / Conditional R^2	0.013/0.050				

Table S-C Multilevel linear modeling results predicting lose-switch behavior of the winning model: (random-subject intercept, main effect of condition and phase)

	Lose-switch behavior				
Predictors	*Estimate (SE)*	*CI*	*Z*	*p*	*OR*
Intercept	-1.74 (0.1)	-1.95 – -1.55	-17.75	< 0.001	0.17
Condition	-0.02 (0.06)	-0.14 – 0.1	-0.34	0.734	0.98
Reversal Phase	-0.45 (0.07)	-0.58 – -0.31	-6.45	< 0.001	0.64
Last Stable Phase	-0.41 (0.08)	-0.57 – -0.25	-5.01	< 0.001	0.66
ICC	0.04				
$N_{subject}$	28				
Observations	8837				
Marginal R^2 / Conditional R^2	0.012/0.079				

Table S-D Parameter mean estimates of the winning model of ‘step 2 model space’.

Variable	*M*	*SD*
win	0.19	0.11
loss	0.36	0.17
control win	6.01	3.99
control loss	3.21	2.52
stress−win	5.61	4.68
stress−loss	3.08	3.33

Table S-E Main effects of task on RPE representation across conditions

Region	Cluster size	Side	$P_{FWE\ corrected}$	t-value	$P_{uncorrected}$	x	y	z
Middle frontal gyrus	401	L	0.000	9.48	< .001	10	42	-12
Middle frontal gyrus		R	0.001	8.12	< .001	4	40	-12
ACC pregenual		L	0.004	7.44	< .001	-2	48	-4
Posterior cingulate cortex	222	L	0.000	9.05	< .001	-8	-52	32
Precuneus		L	0.001	8.27	< .001	-2	-56	26
Precuneus		L	0.001	8.04	< .001	0	-56	18
Ventral striatum	16	R	0.000	8.62	< .001	10	2	-12
Ventral striatum		R	0.005	7.29	< .001	10	10	-10
Insula	56	L	0.001	8.08	< .001	-36	2	12
Insula		L	0.009	7.05	< .001	-36	-6	18
IFG pars orbitalis	39	L	0.001	8.05	< .001	-22	32	-12
Precentral gyrus		R	0.002	7.69	< .001	32	-20	58
Superior frontal gyrus		L	0.003	7.59	< .001	-18	38	44
Postcentral gyrus	75	R	0.003	7.56	< .001	38	-26	46
Postcentral gyrus		R	0.007	7.19	< .001	48	-22	60
Postcentral gyrus		R	0.007	7.16	< .001	42	-26	54
Rolandic operculum	11	R	0.005	7.35	< .001	46	2	10
Middle cingulate	11	R	0.007	7.17	< .001	16	-14	46
Paracentral lobule	12	L	0.010	7.00	< .001	-4	-26	50
Ventral striatum	9	L	0.010	7.00	< .001	-10	-6	-10
Putamen	7	L	0.010	6.99	< .001	-32	-12	2
Rolandic operculum	8	R	0.015	6.82	< .001	54	-18	20
Postcentral gyrus	21	L	0.015	6.81	< .001	-34	-30	48
Postcentral gyrus		L	0.022	6.62	< .001	-44	-24	58
Superior frontal gyrus medial	7	L	0.020	6.68	< .001	-10	60	28
Insula	2	R	0.024	6.59	< .001	38	6	12
Postcentral gyrus	4	L	0.024	6.57	< .001	-46	-24	40
Anterior orbital gyrus	6	L	0.025	6.57	< .001	-34	36	-14
Precentral gyrus	9	L	0.027	6.53	< .001	-34	-18	52
SupraMarginal gyrus	1	L	0.035	6.40	< .001	-60	-26	24
Middle temporal gyrus	7	L	0.036	6.39	< .001	-58	-50	-6
Putamen	2	L	0.037	6.38	< .001	-30	-14	10
Precentral gyrus	5	L	0.038	6.36	< .001	-42	-16	56
IFG pars orbitalis	1	L	0.038	6.36	< .001	-42	40	-12
Postcentral gyrus	2	L	0.046	6.27	< .001	-54	-20	52
Superior frontal gyrus, medial	1	R	0.047	6.27	< .001	4	58	10
Precentral gyrus	1	R	0.047	6.27	< .001	48	-14	54
Posterior orbital gyrus	1	R	0.047	6.27	< .001	24	32	-14

Note. Uncorrected as well as whole-brain corrected fMRI results from the main task effect across conditions in n = 28 participants are illustrated above. Abbreviations: ACC = Anterior cingulate cortex, fMRI = functional magnetic resonance imaging, FWE = family-wise error correction, IFG = inferior frontal gyrus, L = left, MNI = Montreal Neurological Institute, R = right.

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Disclosure Statement

The authors have declared that there are no conflicts of interest in relation to the subject of this study.

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- The standard reporting guidelines appropriate to the studies reported to the manuscript have been followed
- All precautions have been taken to ensure that the studies described in the manuscript are not underpowered and appropriate power analyses have been conducted
- Guidelines for specific types of studies have been followed
- Care has been taken to ensure the manuscript is written in clear scientific English

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Acute stress alters probabilistic reversal learning in healthy participants

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Keywords: Stress, fMRI, reversal learning, decision-making, modeling, cognitive flexibility

Text no. of words: 7556 (5931 without references and abstract)

no. of references: 50