already done but not included

done now

still to be decided

hard to address by us now/design critique  
  
Discuss the importance of the research question addressed in the manuscript (e.g., are objectives and justification clearly stated).  
  
Reviewer #1: See review  
  
Reviewer #2: The manuscript addresses an important question about how acute stress affects brain activity in probabilistic reversal learning.  
  
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Discuss the originality (contribution, addition of knowledge to scientific literature or field) of the manuscript.  
  
Reviewer #1: See review  
  
Reviewer #2: The manuscript adds some incremental contributions to the literature of this field.  
  
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Clearly identify the strengths and weaknesses of the method described in the manuscript.  
  
Reviewer #1: See review  
  
Reviewer #2: The within-subject design is powerful to examine the differences between experimental and control groups. The reversal learning task is appropriate to study adaptive learning in a dynamic situation.  
  
However, it is unclear whether the Trier Social Stress Test is an effective and long-lasting induction during the reversal learning task in the scanner.  
  
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Make specific useful comments on the writing of the manuscript (e.g. writing, organization, figures, etc.).  
  
Reviewer #1: See review  
  
Reviewer #2: In the data analysis and results sections, it seems that the authors mainly focus on the computational modeling results of the reversal learning task. A lot of details are missing in the stress response analyses and fMRI results. More detailed analyses should be provided on the effectiveness of stress induction and how it affects brain activations. The label of Figure 3 is missing.  
  
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Make specific comments on the author’s interpretation of the results and conclusions drawn from the results.  
  
Reviewer #1: See review  
  
Reviewer #2: 1. A big concern is that it is unclear whether the stress induction is effective and long-lasting in the learning task. The authors did not provide detailed results on stress response analyses for each time point, but just the average. Cortisol responses (AUC-g) 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. The p value is from a one-tailed t-test and the effect size is relatively small, especially for the cortisol level. Moreover, as shown in Figure 3, the difference of subjective rating between the stress and control group is decrease during the period of reversal learning task in the scanner. There are almost no differences on time point #5 after the learning task.

*From our Supplement: 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).*

2. The fMRI results are too brief. The author only computed contrast images between the experimental and control groups. More analyses can be conducted, such as using cortisol level/subjective stress ratings as regressors, and psychophysiological interaction analysis.  
  
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In case applicable, make specific comments about the statistics. If it is robust and fit-for-purpose and if the controls and sampling mechanisms are sufficient and well described.  
  
Reviewer #1: See review  
  
Reviewer #2: The controls and sampling mechanisms are sufficient and well described. More statistical analysis should be provided in order to examine the robustness of the results.  
  
  
  
Reviewer #1: In this work, the authors studied the impact of stress on the mechanisms underlying behavioural adaptation, using a probabilistic reversal learning task, computational modelling, and fMRI.  
  
The stress induction increased cortisol levels (and subjective ratings) compared with the control condition, but there were no evident effects of stress on choice behaviour. Model comparison tentatively suggested an effect of stress on the inverse temperature parameter, although parameter analyses did not reveal differences between stress and control conditions. Moreover, the authors did not find effects of stress on the neural correlates of PEs.  
  
Although this work is not totally innovative, the research topic is interesting and the combination of computational modelling with fMRI is valuable to probe the effects of stress on the mechanisms of reinforcement learning. However, I found the analyses and data presented in the manuscript underwhelming and with a poor contribution for the current literature on the neurobiology of stress. Specifically, it is unclear what the inverse temperature parameter represents and whether/how it relates to specific cognitive processes of interest and neural mechanisms, and fMRI analyses should be substantially improved.  
  
Below I detail my concerns.  
1) One of my major concerns is the interpretation of the computational modelling data.  
  
\* The current modelling approach assumes that learning in the control and stress conditions is described by the same model (RW-DU-2al), but in the stress condition different weights are given to the parameters of that model. Perhaps it is possible that stress affects neural computations to an extent that the two conditions are better described by different models. Thus, it is unclear why the two conditions were not fitted separately.  
\* A PXP of 0.62 for the RW-DU-2al model is very low for model selection in the control condition.  
\* Further checks, such as simulation of behavioural data and parameter recovery analyses, are needed to validate the selected models (Wilson & Collins, eLife, 2019) in both conditions.  
\* The specific computational meaning and neural correlates (if any) of the inverse temperature parameter need to be clarified, given that the main conclusion focus on this rather tentative finding.  
\* Additionally, individual-specific parameter values could be correlated with individual stress responses (e.g., cortisol AUC, subjective ratings)  
  
2) Other major concern is the lack of in-depth fMRI analyses.  
  
\* The reason to focus only on RPEs in not entirely clear. I understand that the neural correlates of the inverse temperature might be unclear and unspecific, but I recommend rethinking the fMRI analyses as to clarify and enrich the interpretation of the behavioural and computational modelling data. In its current form, model-based fMRI analyses do not seem to add much to the manuscript.  
\* It is unclear why the onsets of the stimuli—parametrically modulated by Q-values—were not included in the GLM. I consider this to be important for two main reasons: i) the authors argue that stress might affect the use of choice values, thus it could be relevant to look into the neural correlates of the Q-values, and ii) there is likely shared variance between BOLD signals at the time of the stimuli and outcomes (these two time points were jittered based on RT, which tend to correlate over time within an individual).  
\* It is unclear why fMRI analyses did not consider the valence of the outcome — wins and losses — given that computational modelling suggested that individuals learned differently across these two valences. This could also help to understand the observed trend in the insula.  
\* Additionally, it would also be interesting to assess whether BOLD estimates of PEs correlated with individual stress responses (e.g., cortisol AUC).  
  
3) Other concerns:  
  
\* To better fit the scope of the Journal, the Introduction could address in more detail the computational and neural mechanisms thought to be implicated in the effects of stress on behavioural adaptation. Also, there are other model-based fMRI studies using within-subject designs to investigate the effects of stress on PEs which could be cited in the last paragraph (e.g., Carvalheiro et al., Neurobiol. Stress, 2021; Robinson et al., PNAS, 2013; Treadway et al., Biol. Psychiatr., 2017). The reasoning for the exploratory analyses should be briefly addressed in the Introduction.  
\* There is no actual stressor during the task. It is possible that this study captures mechanisms implicated in stress recovery rather than acute stress (e.g., Hermans et al., Trends in Neurosciences, 2014; Sapolsky et al., Endocrine Reviews, 2000). Further discussion is needed.  
\* The Discussion should emphasise how the current work contributes for the current literature on the effects of stress on the neurobiological mechanisms of reinforcement learning, and expand on how the null PEs findings disagree with previous fMRI-reinforcement-learning studies (e.g. Carvalheiro et al., Neurobiol. Stress, 2021; Cremer et al., Neuroimage, 2021; Robinson et al., PNAS, 2013; Treadway et al., Biol. Psychiatr., 2017).  
\* Figure 1A does not convey the within-subject nature of the experimental design.  
\* Why 13 subjects in the control condition and 15 in the stress condition? How did the authors deal with this imbalance in all within-subject analyses?  
\* The main text should state the duration of the stress induction. From Figure 3 it seems to last 10 min, but the SI mentions anticipation 5min+spech 5min+arithmetic 5 min  
\* In their exploratory analyses, the authors could correlate WM/chronic stress measures with AUC cortisol.