Sex difference in the weighting of expected uncertainty under chronic stress

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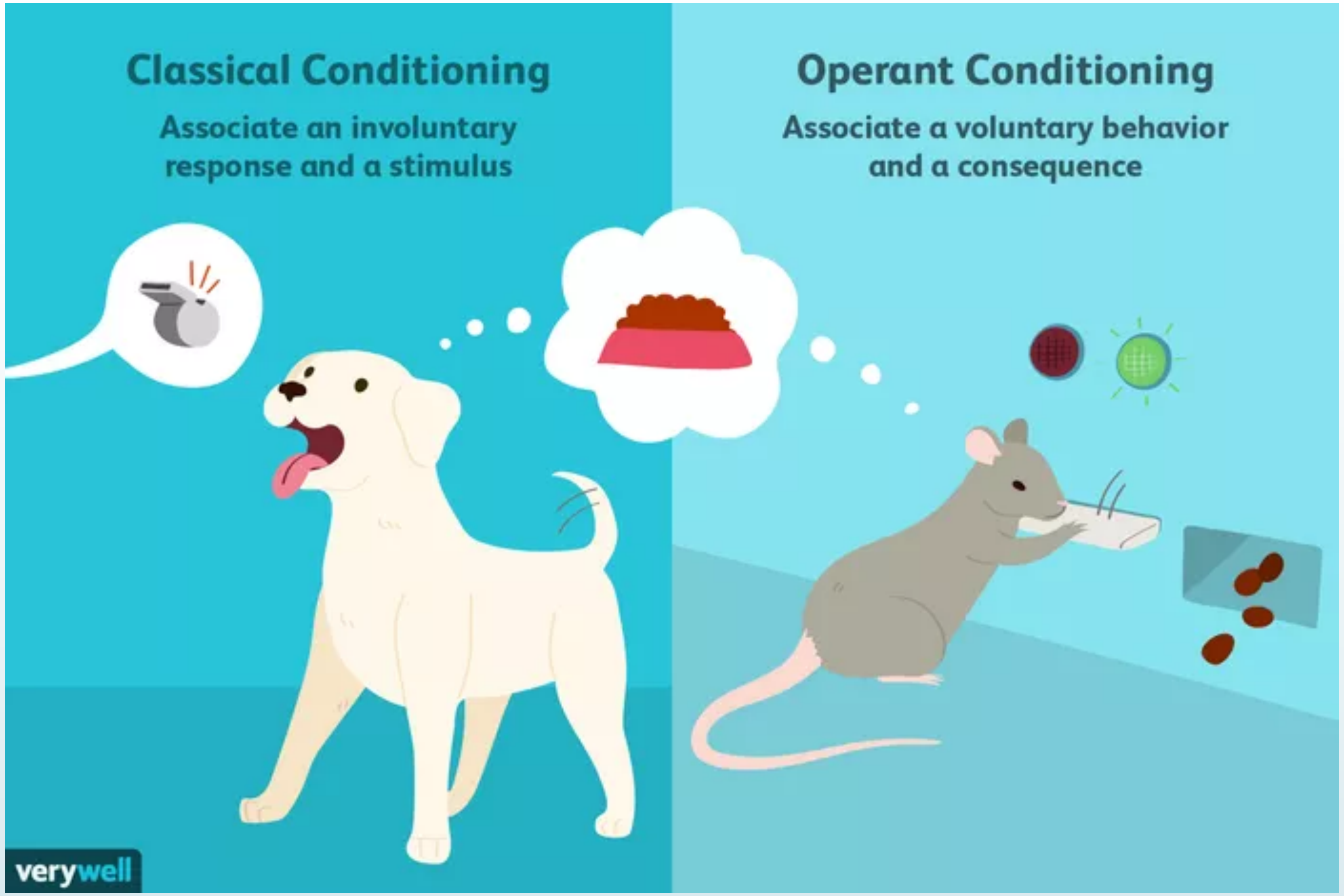
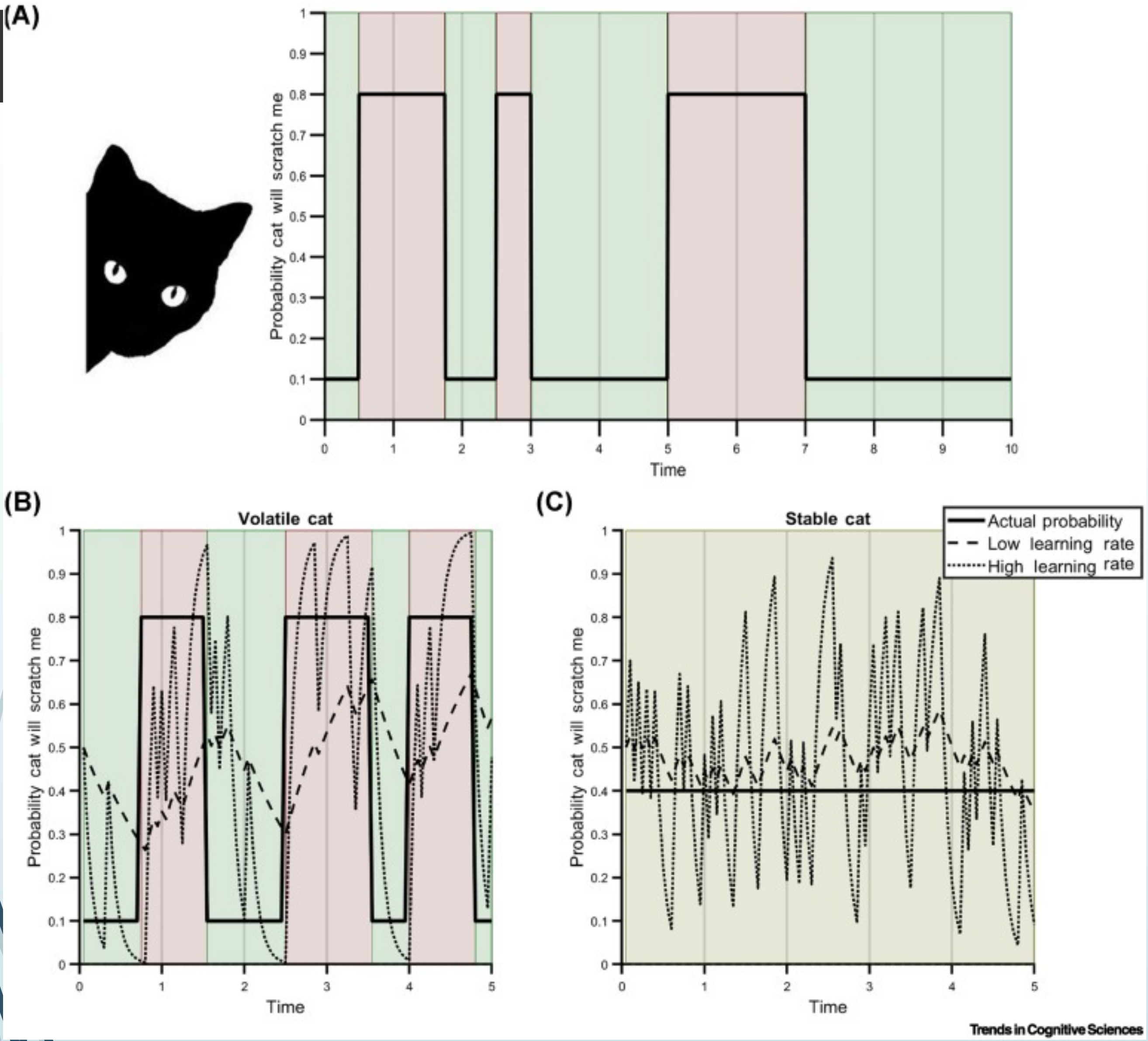


Cherry, 2020. *Verywellmind*

Background

- Previous studies indicated that psychological stress (acute stress) affects decision-making with gender differences [1, 2]. Males and females tend to show different risk attitude [3, 4].
- Chronic stress causes prolonged, maladaptive responses that contribute to depression and anxiety [5] ; Females are twice as likely to develop depression and anxiety compared to males, whether the effects of chronic stress on decision-making is sex-depend remains unclear.
- Reinforcement learning (RL) has been considered a key decision-making mechanism involved in the development and treatment of depression and anxiety [6, 7]. RL-based decision-making involves two independent computational processes, an initial RL of the probabilistic cue-outcome contingencies followed by a subsequent weighting of the learned probability or uncertainty [8, 9].
- In the present study, we set out to investigate the effects of chronic stress on decision-making, by using a RL based decision-making task, in healthy human subjects and sought to identify potential sex differences in these effects.

1. Mather & Lighthall, 2012. *Curr. Dir. Psychol. Sci.*
2. Porcelli & Delgado, 2017. *Curr. Opin. Behav. Sci.*
3. Starcke et al., 2008. *Behav. Neurosci.*
4. van Den Bos et al., 2007. *Behav. Neurosci.*
5. Pizzagalli 2014. *Annu. Rev. Clin. Psychol.*
6. Duits et al., 2015. *Depress. Anxiety*
7. Pittig et al., 2018. *Neurosc. Biobehav. Rev.*
8. *Angela & Dayan, 2005. Neuron*
9. *Pulcu & Browning,2019. Trends. Cogn. Sci.*



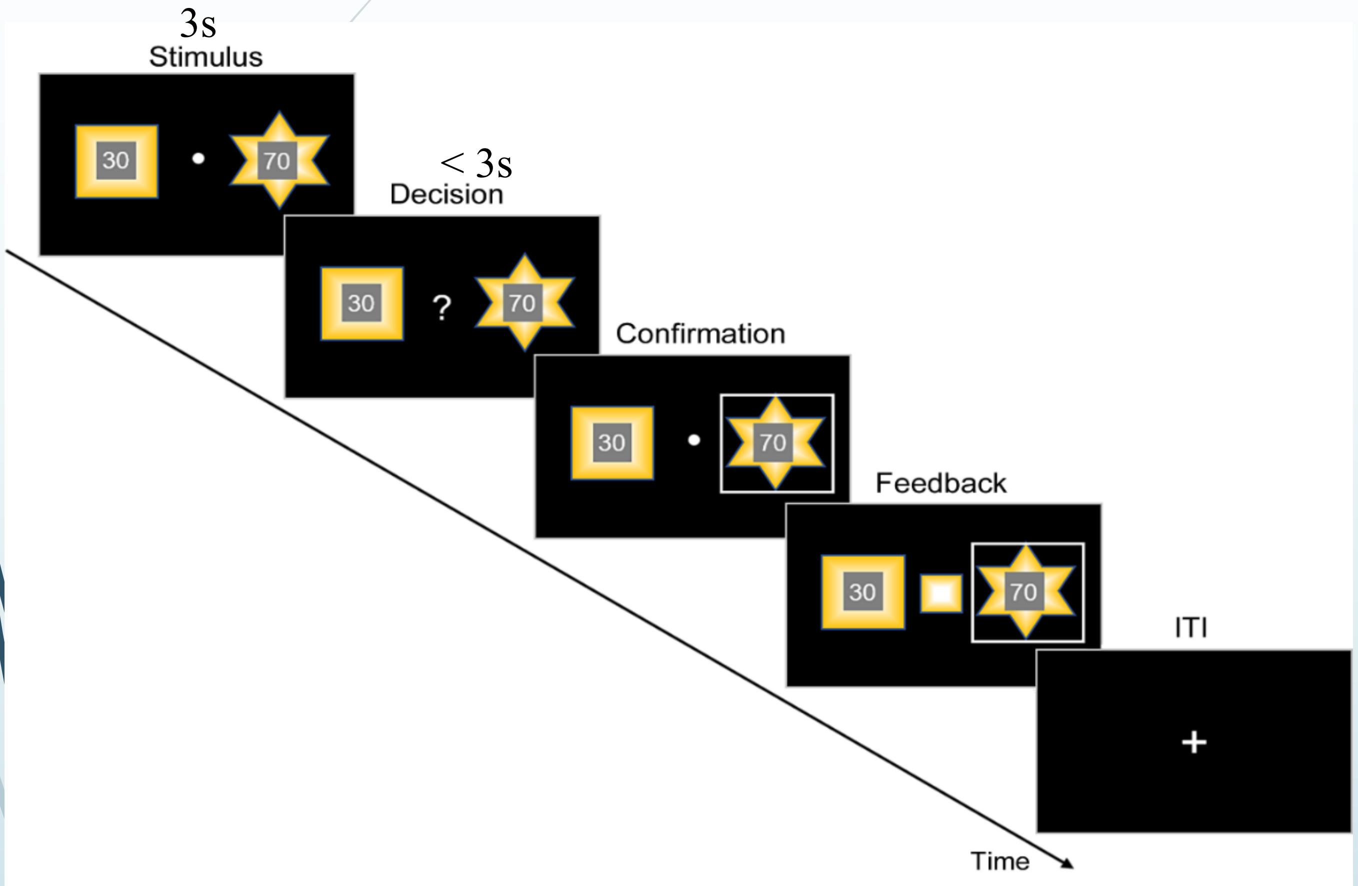
Your cat scratches you on 10% of the times you stroke it when it is in a good mood (**green areas**) and 80% of the time you stroke it when it is in a bad mood (**red areas**).
Expected uncertainty: even if you know exactly what the mood of the cat is, you cannot be certain what its behaviour will be when you stroke it (e.g., even when it is in a good mood, it will scratch you 10% of the time)
Unexpected uncertainty: the mood of the cat changes over time; thus, even if it was in a good mood the last time your stroked it, it might now be in a bad mood. If you stroke the cat and it does something surprising (e.g., scratches you when you thought it was in a good mood), how you should update your belief about its mood depends on what caused the surprising event.

If you think it was **caused by chance** (expected uncertainty, it just happened to scratch you) then you should not change your belief about its mood much (use a low learning rate), whereas if it was caused by **a change in the mood of the cat** (unexpected uncertainty), you need to update your belief quickly (use a high learning rate).

Pulcu & Browning, 2019. *Trends Cogn. Sci.*

Methods

Figure 1Reinforcement Learning Task



60 trials (3 blocks), 10 min

Magnitude (points):

uniform distribution 1-99; with adjustments to balance choices

Probability:

75% vs 25% (not known by participants); with real randomization

Behrens et al., 2007. *Nat. Neurosci.*
Suzuki et al., 2012. *Neuron*

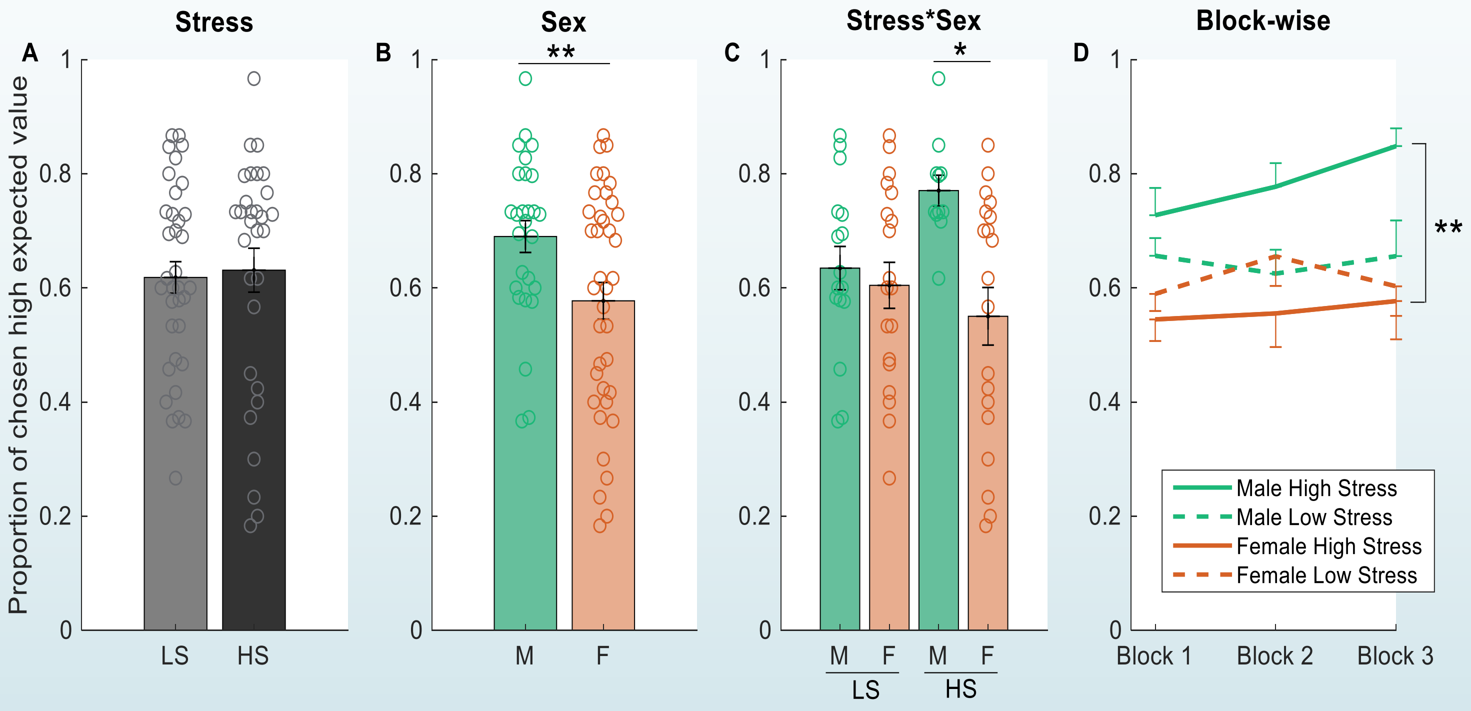
Demographic Information

	Low Stress		High Stress		
	Male (n=16)	Female (n=19)	Male (n=11)	Female (n=19)	Test
Age (years)	22.03±1.02	21.54±1.70	22.19±1.69	23.90±4.64	ns
Father education	4.63±0.86	4.68±1.38	4.60±0.97	4.50±1.15	ns
Mother education	4.63±0.50	4.16±0.77	4.18±0.98	4.00±0.78	ns
Family income	4.45±1.37	3.87±1.46	4.43±1.99	3.88±2.00	ns
Living alone (Y/N)	1/15	4/15	1/10	2/17	ns
Regular social activities (Y/N)	10/6	12/7	9/2	9/10	ns
Perceived stress (PSS)	15.50±2.34	14.37±3.58	22.27±3.20	23.68±3.79	$F_{1,61}$= 85.405, $p<0.001$
Working memory (d_2)	2.60±0.38	2.61±0.29	2.63±0.41	2.51±0.43	ns

Note. Father education missing: n=2, family income missing n=16

Results

Figure 2 Proportion of choosing correct choice



Modeling fitting and selection

	Model name	Free parameters	Mean model evidence
No probability weighting parameter	Static model 1	α, β	-35.8708
	Static model 2	$\alpha_+, \alpha_-, \beta$	-32.8888
	Dynamic model 1	μ, κ, β	-45.4718
	Dynamic model 2	$\alpha_1, \alpha_2, \beta$	-35.6651
Probability weighting parameter	***Static model 1 weighting***	$\boldsymbol{\alpha, \gamma, \beta}$	***-32.2318***
	Static model 2 weighting	$\alpha_+, \alpha_-, \gamma, \beta$	-32.6815
	Dynamic model 1 weight	$\mu, \kappa, \gamma, \beta$	-40.4454
	Dynamic model 2 weight	$\alpha_1, \alpha_2, \gamma, \beta$	-32.6518

Participants were then assumed to choose actions stochastically, according to a sigmoidal probability distribution such that choice probability of stimulus A on trial *t* is given by:

$$p_t(\mathrm{A}) = \frac{1}{1 + e^{-\beta \cdot (Q_t(\mathrm{A}) - Q_t(\mathrm{B}))}} \tag{6}$$

where β is the inverse temperature which adjusts the degree of stochasticity in participants' choices.

Static model 1 (s1)

In this model, after choosing stimulus A on trial t and observing reward r_t (1 if stimulus A is rewarded and 0 otherwise), the predicted probability for stimulus A is updated according to a standard Rescorla–Wagner model with a constant learning rate[16]:

$$p_{t+1}(\mathrm{A}) = p_t(\mathrm{A}) + \alpha \cdot \delta_t \tag{1}$$

$$\delta_t = r_t - p_t(\mathrm{A}) \tag{2}$$

where α is the learning rate and δ_t is the probability prediction error. The predicted probability for stimulus B is modeled as $p_t(\mathrm{B}) = 1 - p_t(\mathrm{A})$. In our implementation, the predicted probability for each stimulus is initialized to 0.5. Then for each trial, the expected value of a stimulus $Q_t(\cdot)$ is computed as the product of the reward magnitude and predicted probability of that stimulus $p_t(\cdot)$.

Static model 2 (s2)

This model is identical to model s1 except that it uses two learning rates, α_+ for positive and α_- for negative prediction errors. This model is incorporated because it has been frequently proposed that people may respond differently to positive versus negative feedback.

Dynamic model 1 (d1)

This model is known as the Pearce–Hall learning model[57] which substitutes associability-gated dynamic learning rate for the constant learning rate in model s1. Unlike model s1, the learning rate in this model changes adaptively in every trial depending on the reliability of prior predictions (i.e., the associability S):

$$\alpha_{t+1} = \kappa \cdot S_{t+1} \tag{3}$$

$$S_{t+1} = (1 - \mu) \cdot S_t + \mu \cdot |\delta_t| \tag{4}$$

where κ is the scale of learning rate, S_{t+1} is the associability on trial $t + 1$, and μ is the step size for updating associability which determines the relative weight of the associability and the absolute value of prediction error on the previous trial t.

Dynamic model 2 (d2)

This simplified dynamic model is identical to model s1 except that it uses two learning rates, one for the first half and the other for the latter half of trials. This model was included to simulate the strategy of fast acquisition at first and subsequent stable choice[33].

Each model described above is then combined with a probability weighting parameter γ that transforms the influence of predicted probability to account for risk-aversive or risk-seeking behaviors[27,28]:

$$\boxed{F(p_t(\cdot), \gamma) = \max\left[\min\left[(\gamma \cdot (p_t(\cdot) - 0.5) + 0.5), 1\right], 0\right]} \tag{5}$$

where $\gamma = 1$, $\gamma > 1$, and $\gamma < 1$ indicate risk-neutral, risk-aversive, and risk-seeking behavior, respectively. This generates models **s1w**, **s2w**, **d1w**, and **d2w**. For these models, the expected value of a stimulus $Q_t(\cdot)$ is computed as the product of the reward magnitude and $F(p_t(\cdot), \gamma)$.

Figure 3 Learning rate and probability weighting parameter across sex and stress groups

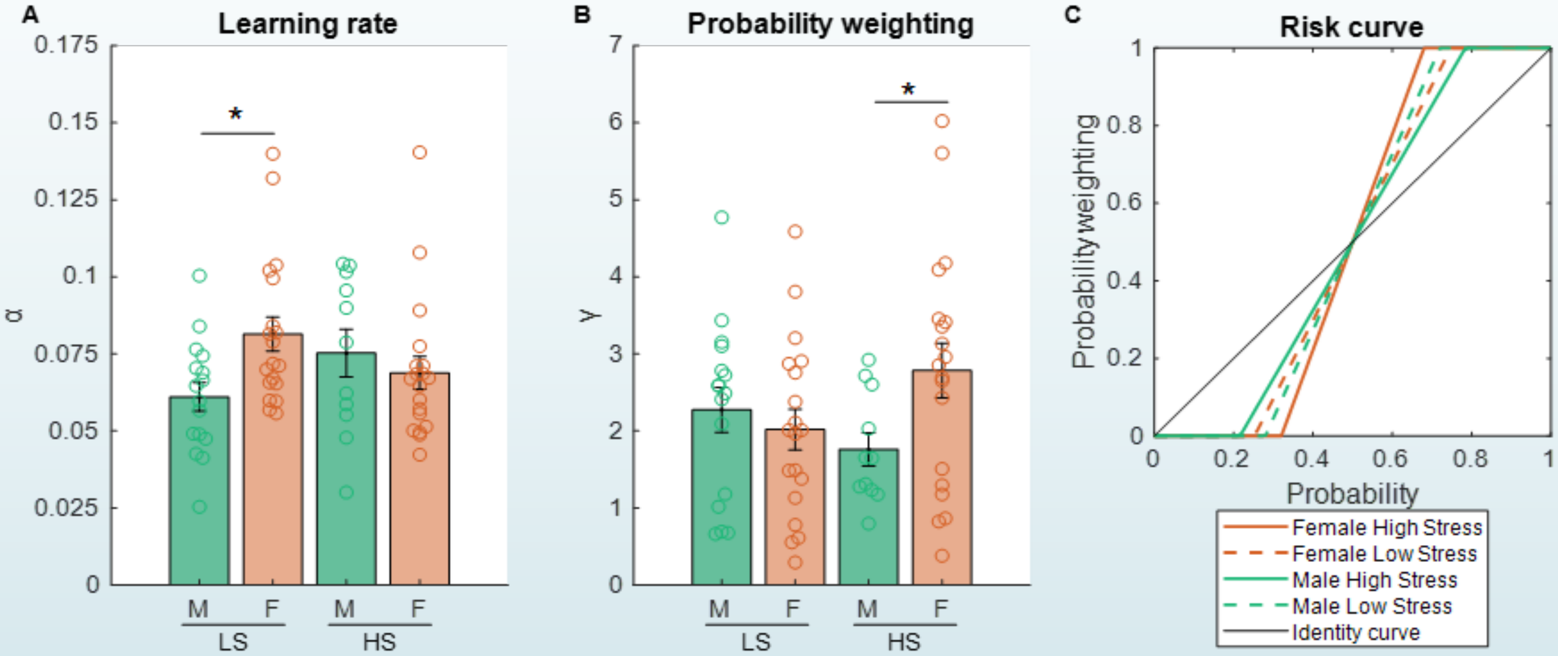


Figure 4 Associations between task performance and model estimated parameters

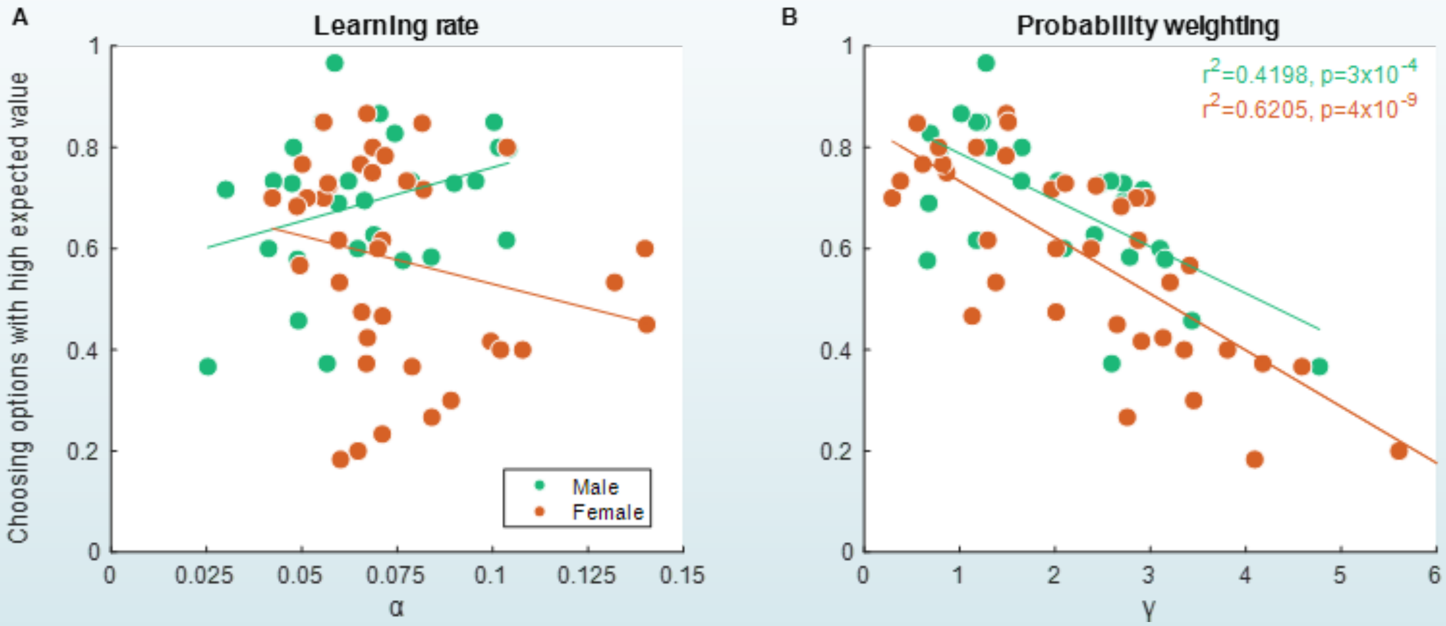
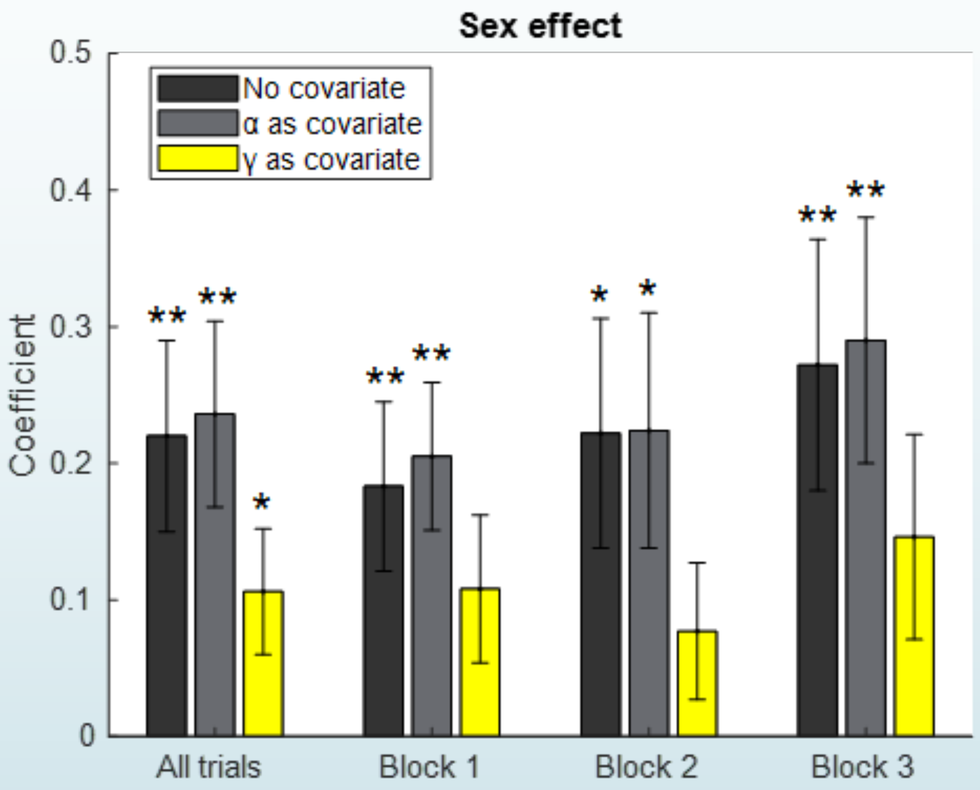


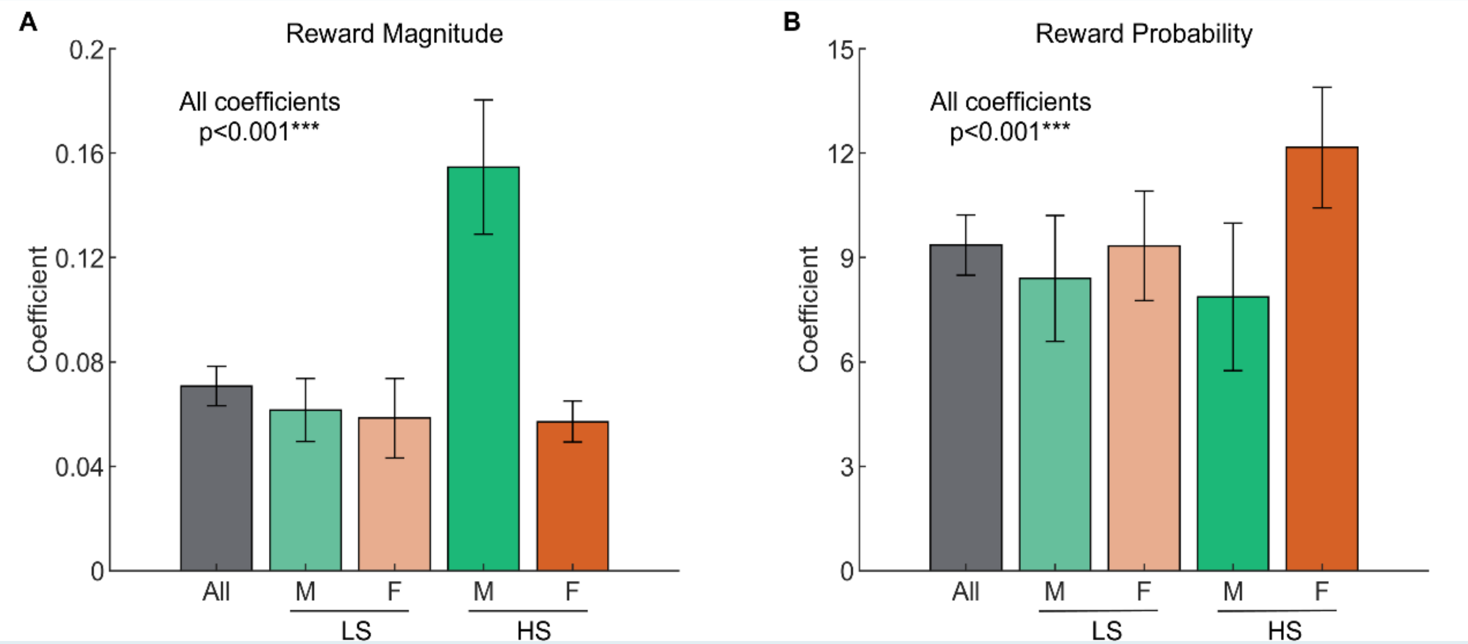
Figure 5 Parameter estimate for the sex difference in task performance under high stress



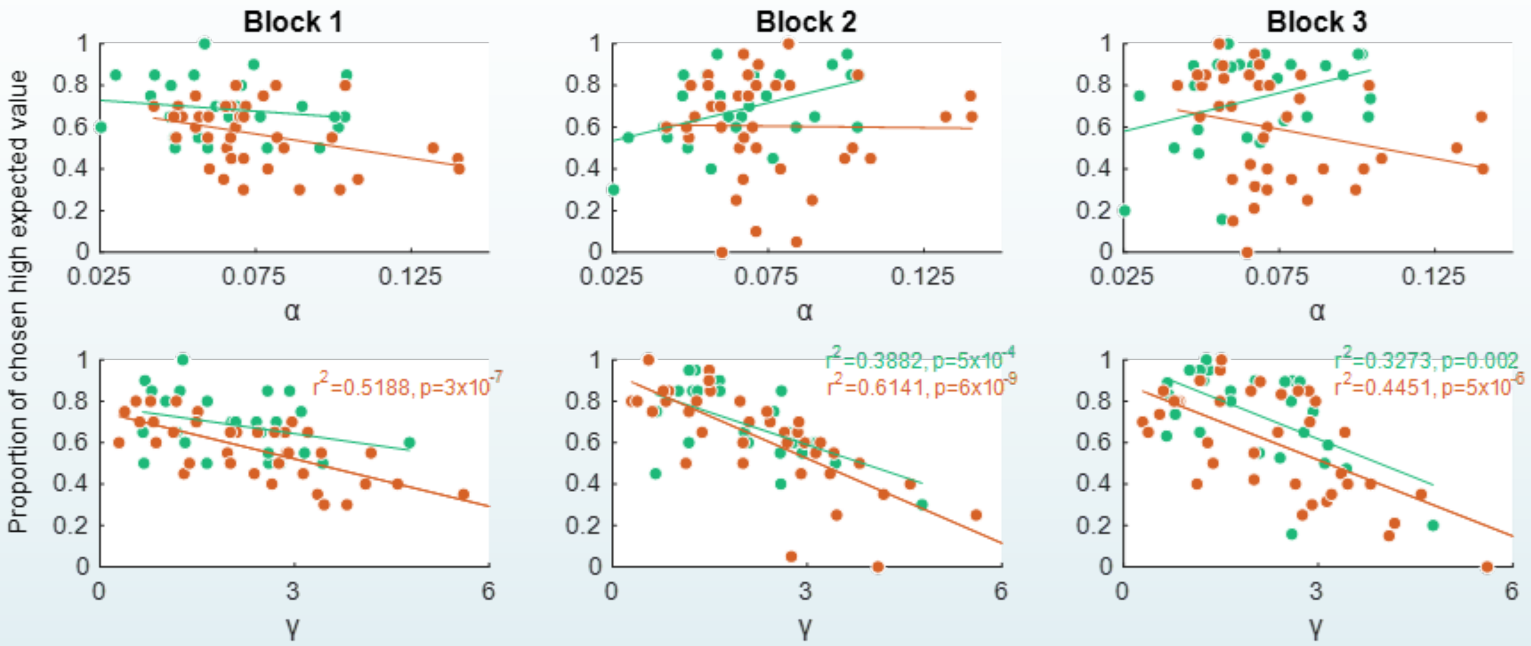
Summary and Discussion

- We found a sex difference in choice performance under high stress that females choose about 20% less correct options compared to males.
- In response to chronic stress, whereas males show a nonsignificant decrease in probability weighting, females show an increase in probability weighting with a trend towards significance. The sex difference in choice performance is explained by different weighting rather than learning of expected uncertainty between sexes under high stress.
- Although we observed a sex difference in probability weighting under high stress, our study had insufficient power to specify if the sex difference was due to a decrease in males or an increase in females due to stress, or both.
- Computational psychiatry may help bridge the explanatory gap between observable behaviors and the underlying specific cognitive computations in the brain.

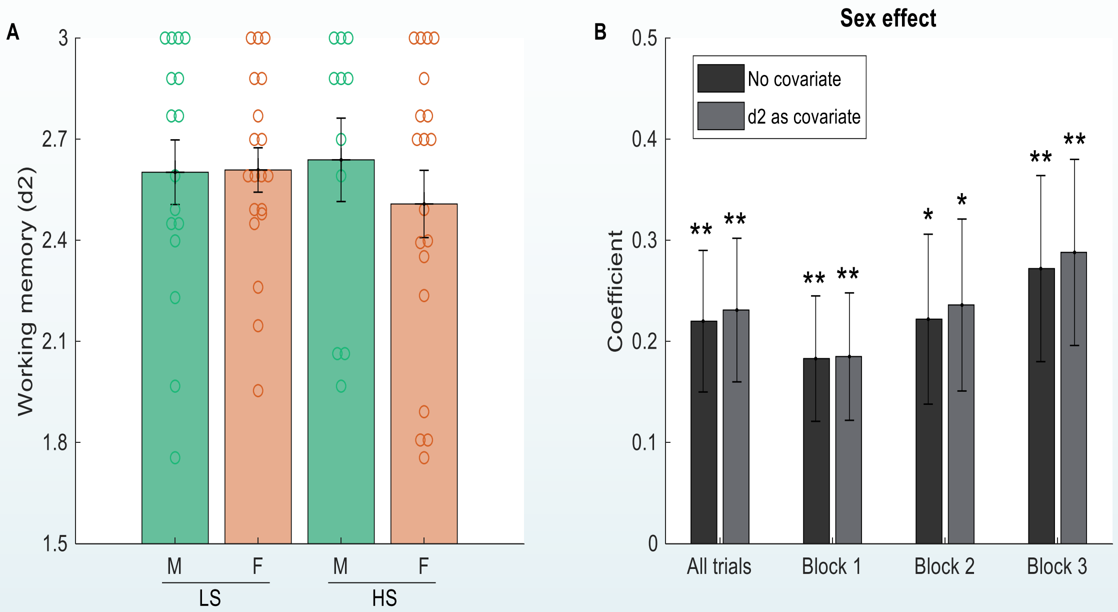
Supplementary



Generalized linear mixed model analysis showing the winning model actually captured participants' behaviors.



Associations between task performance and model estimated parameters across three blocks



The sex difference in task performance was not explained by working memory.

Q & A