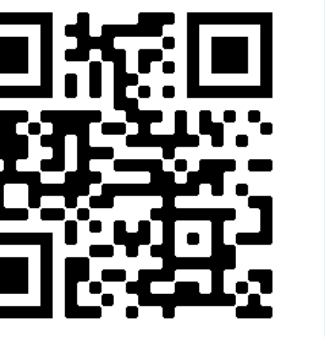


Assessing Anxiety and Affective Bias in Healthy Individuals

Faissal Sharif^{1*}, Haifeng Zhao², Shaoxun Huang¹, Yueting Yang¹, Huiling Tan¹

¹MRC Brain Network Dynamics Unit, Nuffield Department of Clinical Neurosciences, John Radcliffe Hospital (West Wing), Oxford, OX3 9DU (Correspondence: huiling.tan@ndcn.ox.ac.uk)

²Ruijin Hospital, School of Medicine, Shanghai Jiaotong University



Background

- *Fear, anxiety, and negative affective bias* are hallmarks of various psychiatric and neurological conditions.
- Studies have primarily focused on brain regions associated with threat appraisal and experience, but little is known about the evolution of fear memory traces over time and the underlying mechanisms of negative affective bias.
- The investigation of *neuronal, physiological, and behavioural* underpinnings of these mechanisms in healthy participants absent of psychiatric symptoms remains a challenge.
- We modified a *Threat Conditioning and Extinction Task (TCET)* and *Implicit Bias Learning Task (IBLT)* to study threat learning and negative affective bias (win vs. loss), respectively.
- Both paradigms will be paired with high-density electroencephalography (*HD-EEG*), electrooculography (*EOG*), electrocardiography (*ECG*) and galvanic skin response (*GSR*).
- The outcome of this study may aid the development of novel therapeutic targets, e.g. *non-invasive brain stimulation (NIBS)*

Transdiagnostic Approach

- These tasks enable research beyond diagnostic boundaries within the current landscape of psychiatry. Transdiagnostic research seeks to identify common underlying processes and mechanisms shared across different psychological conditions.
- Following the *NIMH Research Domain Criteria (RDoC)* Initiative, which groups these mechanisms into domains, we evaluate both *positive* and *negative* valence systems:

TCET

Acute threat (Fear)
Sustained threat (Anxiety)

IBLT

Reward responsiveness/learning
frustrative non-reward

Further Considerations

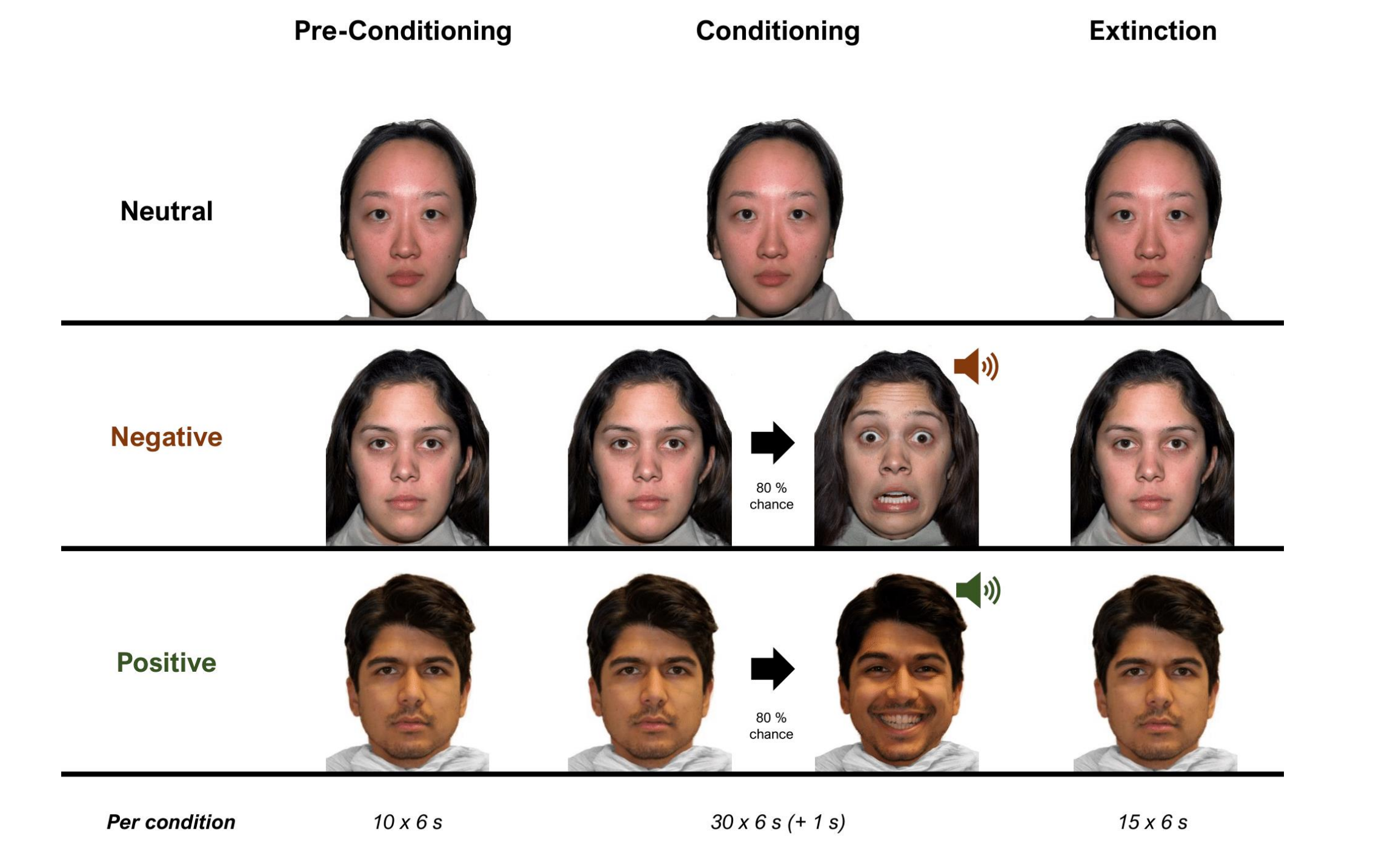
- Eliciting acute fear or negative affective bias in healthy poses challenges, as these experiences entail high *interindividual variability*.
- It is therefore crucial, to validate these paradigms in different populations, especially if they are also used in patients (in this case OCD and Epilepsy).
- A good balance between an adequate number of trials and avoidance of participant fatigue must be ensured.

References

- Abend, R., Gold, A. L., Britton, J. C., Michalska, K. J., Shechner, T., Sachs, J. F., Winkler, A. M., Leibenluft, E., Averbeck, B. B., & Pine, D. S. (2020). Anticipatory Threat Responding: Associations With Anxiety, Development, and Brain Structure. *Biological psychiatry*, 87(10), 916–925.
- Erdem Pulcu, & Browning, M. (2017, October 4). Affective bias as a rational response to the statistics of rewards and punishments. Retrieved June 28, 2023, from eLife website: <https://elifesciences.org/articles/27879#s3>

Threat Conditioning and Extinction Task (TCET)

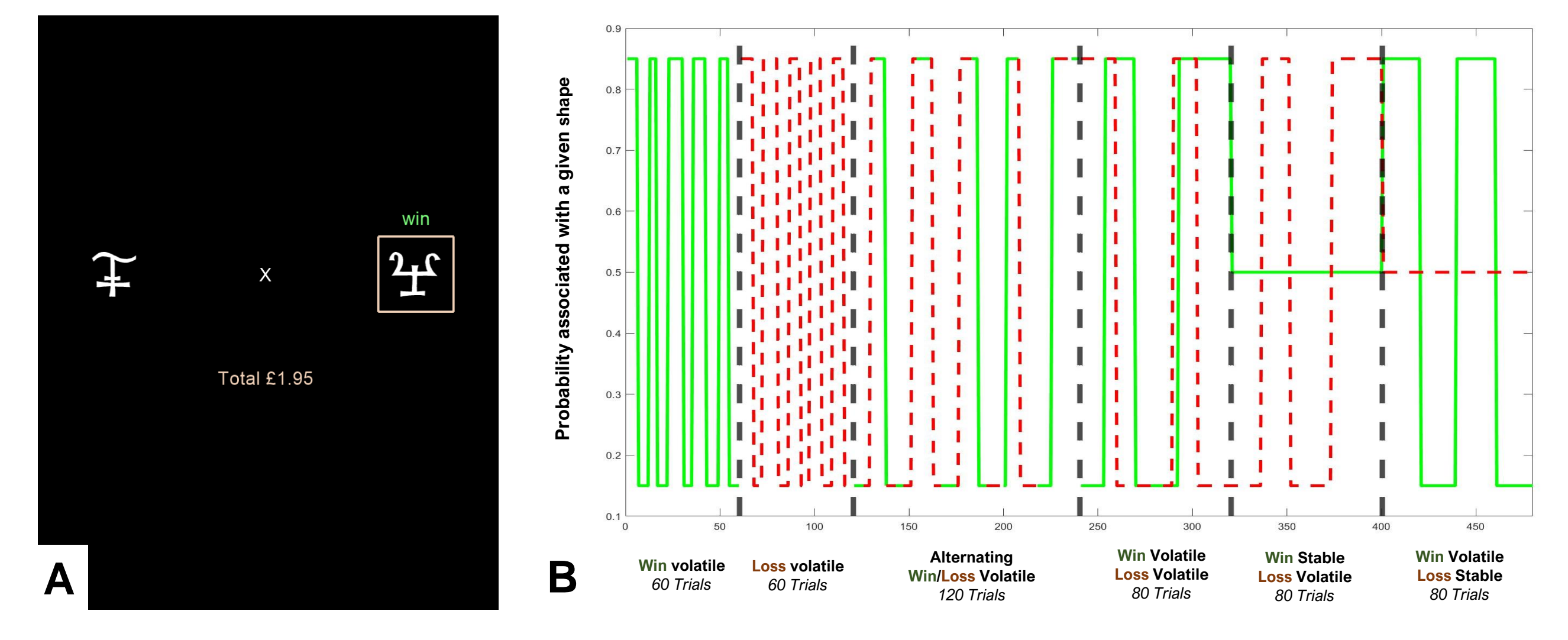
- We modified an established, differential threat learning task that has been tested in healthy and anxious adolescents and adults (Abend et al, 2020).
- The task aims to elicit the learning of the association between a *neutral stimulus* (face with neutral expression) and a negative or positive *unconditioned stimulus* (UCS).
- We, therefore, evaluate *threat learning* as the UCS becomes an anticipated unpleasant stimulus as the task continues.
- As both negative (scream) and positive (laugh) UCS are used, the confounding effect of surprise or e.g., general anticipation can be subtracted from findings.



Threat Conditioning and Extinction Task (TCET). Participants are asked to observe different faces presented in a randomized order over three phases (ITI: 4-6 s). Each face shows a neutral expression and appears for the same number of times in all phases. However, in the conditioning phase, two of the faces may turn into a screaming (negative) or laughing (positive) expression, accompanied by the respective sound. An additional trigger face will be shown randomly on three occasions per phase to which participants need to mouse-click as fast as possible. After each phase, participants rate each face from 0 (negative) to 10 (positive). *Abbreviations: ITI, Inter-trial interval.*

Implicit Bias Learning Task (IBLT)

- The IBLT (Pulcu & Browning, 2017) is at its core a *probabilistic learning task*, i.e. participants learn to associate certain choices with a reward and/or loss.
- We are interested in *reversal learning*, which demands adapting behaviour when previously learned reward patterns are changed.
- This would then lead to *positive* (expected loss) or *negative* (expected win) *prediction error* which may influence the rate of *reward pattern learning*.
- In *negative affective bias*, heightened attention to loss patterns would lead to a higher (i.e. faster) learning rate.



Implicit Bias Learning Task (IBLT). (A) Participants are asked to maximize their monetary wins by selecting one out of two shapes in a self-paced manner. Pairs of shapes will be presented over a total of 480 trials and six phases. Depending on the phase, a shape may lead to either a win (+ 0.15 £), loss (- 0.15 £), neither (+- 0.00 £) or both (+- 0.00 £). Each phase will use different shape pairs which alternate positions (left/right) randomly. The probabilistic characteristics of both wins and losses are manipulated specific to each phase and to elicit reversal learning, negative/positive prediction errors and to assess learning rates for both win and loss probabilities. (B) In each of the six phases, a shape's probability to win or lose may be stable (50 %) or volatile (fluctuating between 15 and 85 %). These sudden switches occur after a min. of 4 trials, maximizing the chances of a learned perceived pattern and subsequent prediction error once a switch occurs.