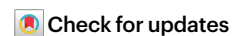# Correspondence

Reply to 'Post-encounter freezing during approach–avoidance conflict: the role of the hippocampus'

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We thank Fernández-Teruel and McNaughton for their correspondence on our Perspective article (Roelofs, K. & Dayan, P. Freezing revisited: coordinated autonomic and central optimization of threat coping. *Nat. Rev. Neurosci.* 23, 568–580; 2022)[1], which raises interesting issues about the role of the hippocampus in defensive freezing (Fernández-Teruel, A. & McNaughton, N. Post-encounter freezing during approach–avoidance conflict: the role of the hippocampus. *Nat. Rev. Neurosci.* https://doi.org/10.1038/s41583-023-00703-y; 2023)[2]. They provide an insightful analysis of two-way active avoidance (TWAA), showing hippocampal involvement in a form of approach–avoidance conflict that evolves over hundreds of trials. TWAA is an important paradigm in which Pavlovian 'misbehaviour' readily corrupts necessary instrumental actions[3]. How, though, does it relate to the focus of our Perspective[1]: single-trial, circumstance-specific, information gathering and action preparation in post-encounter threat states? Here, it is less clear that freezing depends on hippocampal involvement[4] or that the approach–avoidance conflict is always the central problem to be resolved.

In line with animal work, human studies show that freezing (immobility and bradycardia) does not occur only as a function of approach–avoidance conflict[5]. A recent study examined the effects of threat value, reward value and conflict (the interaction between
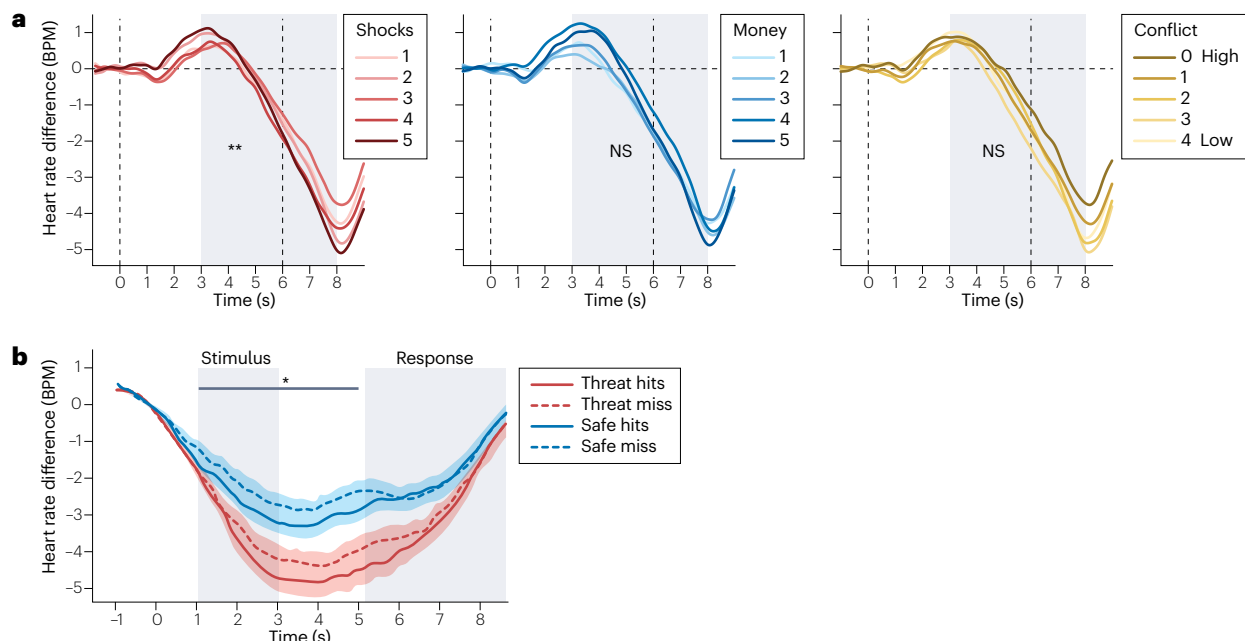

Fig. 1 | Examples of freezing-related bradycardia, independent of approach–avoid conflict. a, Freezing-related bradycardia scales to anticipated threat level, not to reward or conflict level, during approach–avoid decisions. The panels show average time course of baseline-corrected heart rate (BPM, beats per minute) across trials in a human approach–avoidance conflict task in which the amounts of reward (money) and punishment (electric shocks) varied[6]. A mixed effects model was used to examine the effects of reward value, punishment value and the conflict between reward and punishment on the rate of bradycardia-related freezing during decision making. The steepness of the heart rate slope (within the grey area: 3–8 s after stimulus onset at 0 s) increased significantly as a function of varying shock (left), but not as a function of the amount of money (middle) or of conflict (right; conflict is defined as the difference between reward and punishment levels, with distance 0 indicating that conflict is high and distance 4 indicating that conflict is low)[6]. Shock level therefore affects freezing-related bradycardia under approach–avoidance conflict, but this effect is independent of reward value and of the conflict between shock and reward (**Bayesian posterior probability < 0.025; NS, not significant)[6]. **b**, Bradycardia under threat of shock versus safety in a perceptual task without approach–avoid conflict, showing average time course of baseline-corrected HR across trials[7]. Heart rate is lower under threat of shock (red lines) than during safety (blue lines) *P < 0.05; shaded area represents standard error of the mean. Bradycardia was also linked to upregulated sensory sensitivity, as shown by the fact that it was stronger preceding correct detection of visual stimuli (hits, solid lines) than incorrect trials (misses, dashed lines)[7]. The left image in part **a** is adapted from ref. 6, Springer Nature Limited. Data shown in the right two images in part **a** are from ref. 6. Part **b** is adapted from ref. 7, Springer Nature Limited.

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reward and threat) on freezing during an approach–avoidance task. Only threat value significantly affected the magnitude of heart rate deceleration during decision anticipation, suggesting that freezing can scale with threat value, independently of reward value and conflict[6] (Fig. 1). Freezing can also be elicited during simple threat cue exposures and threat of shock paradigms (reviewed elsewhere[5]), where it facilitates sensory processing[7]. In both of these examples, dependence on the hippocampus is less clear, with a predominant role indicated for amygdala–periaqueductal grey–medulla–spinal cord projections[4].

This is not to deny the important roles of the hippocampus in threat processing. Take the phenomenon of hippocampal replay and preplay — the reactivation or preactivation of activity patterns associated with actual or imagined states of the world[8]. Replay during safe and pre-encounter states can create effective defensive policies[9]. This can benefit all three stages of post-encounter threat outlined in our Perspective[1]. In phase 1, detection of potential danger, animals need effective policies to scan the environment for threats (and to track potential forms of escape). Habitized methods for this would limit the burden on more taxing forms of processing. In phase 2, sensory processing and planning, preplay might allow online pre-visioning of the consequences of courses of action. Depending on the nature of the potential danger and the affordances of the environment for escape, approach–avoidance conflicts

may arise that this preplay could help to resolve. Defensive policies compiled by replay during safer states could also be very helpful. In phase 3, switch to action, fight or flight is engendered by sensory cues associated with the more proximal approach of danger, and is mediated via the central amygdala, anterior cingulate cortex and periaqueductal grey[4,10]. Here again, precompiled policies would be of great value, although they may be more generic and less situation-specific.

In summary, we value the notion that the hippocampus plays a prominent role in post-encounter threat freezing during approach–avoidance conflicts and particularly during active avoidance learning. However, active freezing can also occur outside these conditions, during acute decision making[1]. Here, the hippocampus can also be important, but, we argue, may not even be first among equals.

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Competing interests

The authors declare no competing interests.