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A neurocomputational account of how inflammation differentially modulates learning to punishments versus rewards

Inflammation rapidly impairs mood and cognition and, when severe, can appear indistinguishable from major depression. These sickness responses are characterized by an acute reorientation of motivational state; pleasurable activities are avoided, and sensitivity to negative stimuli is enhanced. However, it remains unclear how these rapid shifts in behavior are mediated within the brain. In this talk I will present data from a study combining computational modeling of choice behavior, experimentally induced inflammation, and functional brain imaging (functional magnetic resonance imaging). In this double-blind, randomized crossover study, 24 healthy volunteers completed a probabilistic instrumental learning task on two separate occasions, one 3 hours after typhoid vaccination and one 3 hours after saline (placebo) injection. Participants learned to select high probability reward (win £1) and avoid high probability punishment (lose £1) stimuli. An action-value learning algorithm was fit to the observed behavior, then used within functional magnetic resonance imaging analyses to identify neural coding of prediction error signals driving motivational learning. Results demonstrate that inflammation acutely biased behavior, enhancing punishment compared with reward sensitivity, through distinct actions on neural representations of reward and punishment prediction errors within the ventral striatum and anterior insula. Consequently, choice options leading to potential rewards were less behaviorally attractive, and those leading to punishments more aversive. This suggests that inflammation induces a state-dependent reorientation of reward versus punishment sensitivity. This mechanism may aid the adaptive reallocation of metabolic resources during acute sickness but might also account for maladaptive, motivational changes that underpin the association between chronic inflammation and depression.