Inferring Cognitive Components by Behavioural Analysis and Computational Modelling in Novel Rule Switching Task for Head-Fixed Mice in a Virtual Reality Environment

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1 Introduction

Cognitive flexibility, the capacity to adaptively adjust behaviour in response to changing environmental demands, is a core executive function also implicated in neuropsychiatric disorders such as schizophrenia and autism spectrum disorder (Uddin, 2021). The circuit mechanisms by which the medial prefrontal cortex (mPFC) orchestrates hippocampal computations to enable cognitive flexibility remain largely unknown. It is hypothesized that when changes in outcome contingencies are detected, the mPFC projects top-down executive signals to various brain areas. These signals are relayed via the thalamic nucleus reuniens (RE) to the dorsal CA1 hippocampus, where they precisely adjust local circuit operations to facilitate behavioural adaptation (Cassel et al., 2021). Crucially, it is proposed that the timing of these signals is coordinated with hippocampal theta oscillations, which is essential for their effective integration (Fries, 2005). To investigate these mechanisms, a novel virtual reality (VR)-based rule-switching task for head-fixed mice was employed, enabling high-temporal-resolution analysis of behavioural changes during trials. My role in this project is to conduct behavioural analysis and computational modelling to identify cognitive processes underlying rule switching, including behavioural inhibition (the suppression of previously rewarded responses following a rule change) and reward expectation updating. Ultimately, the goal is to link the findings to neural correlates recorded by the research group.

2 Methods

A novel virtual reality-based spatial navigation task paired with auditory cues for head-fixed mice was designed by the research group. Mice run along a virtual corridor and must switch between a spatial strategy (fixed reward location) and a cue-guided strategy (reward location signaled by an auditory cue). Orofacial movements and licking are captured by a high-speed infrared camera during task performance. To characterize firing correlates of cognitive flexibility and their phase-coupling to hippocampal oscillations, high-density silicon probe and Neuropixels recordings were applied simultaneously in the mPFC and dorsal CA1. To functionally isolate neurons within the mPFC–RE–dCA1 pathway, the research group employs optogenetics, with inhibition of this pathway during strategy switching used to establish its causal role in adaptive behaviour.

3 Analysis

Data obtained from the experimental trials is used for behavioural analysis. Orofacial video data are analysed using DeepLabCut (DLC), an open-source animal pose estimation toolbox employing deep neural networks. Facial keypoints including tongue tip, lickport contact, lip margins, whisker positions, and eye centre are tracked frame-by-frame to extract quantitative behavioural metrics: tongue-to-lickport distance, mouth opening amplitude, composite licking intensity index, and orofacial motion index. Lick events are detected automatically from local minima in tongue-to-lickport distance. These metrics provide continuous, high-resolution readouts of anticipatory licking and orofacial activity across trials.

Subsequently, computational modelling will be applied to the behavioural data to quantify the cognitive components of rule switching. A Rescorla–Wagner reinforcement learning model estimates trial-by-trial reward expectations, capturing how mice update outcome predictions following reward or omission. A Bayesian inference model then tracks rule inference and strategy weighting across trials, estimating the probability that the animal has identified the currently active rule. Together, these models will provide latent variables such as reward expectation, prediction error, and rule posterior that can be directly aligned with the neural recordings obtained by the research group.

4 Outlook

The combined behavioural, computational, and neural approach aims to elucidate how top-down prefrontal control signals dynamically reconfigure hippocampal information processing to support cognitive flexibility, advancing understanding at circuit-level relevant for dysfunctional behaviour in neuropsychiatric diseases.

References

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