Exploring the dynamics of choice ensembles in the frontal cortex during a multiple-choice delayed-response task

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During perceptual decision-making, sensory information is transformed into decisions through the recruitment of specific neural ensembles that represent the subsequent choice. Previous studies in mice highlight the role of the Anterolateral Motor cortex (ALM), an area showing a significant proportion of neurons selectively encoding the upcoming choice (choice-ensembles) and whose photo-suppression causes pronounced deficits in choice performance (Guo et al. 2014; Pinto et al 2022). Moreover, modeling work has proposed that ALM choice-ensembles operate in a winner-take-all regime implying that one and only one ensemble is active during the choice maintenance period (Inagaki et al 2019).

To characterize the dynamics of ALM ensembles involved in choice selection and maintenance, we developed a multiple-choice delayed-response task (nDRT) for freely moving mice, where a brief stimulus is presented at one of three possible locations on a touchscreen. Animals had to retain the information during a short variable delay (~1s), after which they must respond by poking at the remembered stimulus location. We found that errors increased as a function of delay, indicating that mice made memory maintenance errors. In addition, we found a consistent dependence on previous responses (i.e. win-stay-lose-switch pattern) that remained unaffected by delay. Pharmacological ALM inactivation using GABA receptor agonists resulted in a decrease in choice accuracy, confirming the involvement of the area in the task.

We then aimed to characterize the interaction between ALM neural ensembles representing choice. We used a c-fos-driven tagging method (TRAP2 system) for the permanent expression of channelrhodopsin in ALM choice-ensembles. We TRAPed a neural ensemble specific to one choice by performing a behavioral session with a single choice. In subsequent sessions, photoactivation of the TRAPed ensemble did not bias task behavior towards the labeled choice. Instead, when stimulating at 5Hz, but not at 20Hz, it specifically impaired the accuracy for the labeled choice. These results suggest that the photostimulation of a specific choice ensemble in ALM does not interfere with the activation of other choice ensembles, but rather has a frequency-dependent choice-specific deleterious effect. Our findings provide important constraints on the network dynamics governing frontal cortex circuits during choice selection and maintenance.