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Neurons in the lateral prefrontal cortex (LPFC) exhibit sustained increases in activity during delays in working memory tasks, and this sustained activity is hypothesized to encode information about remembered target stimuli. However, whether this neural code is fixed or changes over time is not clear, and how the code deals with distracting stimuli remains unknown. Now, Yen and colleagues show that the neural code in the LPFC changes when a distractor stimulus is presented during a delay, and that this change is attributable to neurons that show mixed selectivity for stimulus and task features.

The authors recorded from neurons in the LPFC in two monkeys performing a delayed saccade task. In each trial, the monkey was presented with a target square in a certain location for 300 ms. After a 1 s delay (D1), a distractor square was presented in a different location for another 300 ms. Then, after another 1 s delay (D2), the monkey was cued to make a saccade to the remembered location of the target square.

The authors investigated the stability of the codes for the target stimulus in the LPFC. They trained a computational decoder using the recorded population responses from approximately half of the trials, and then tested its ability to

decode the location of the target stimulus using the other half of the recorded responses. Interestingly, the decoder performed well (~35% better than chance) if it was both trained and tested with responses recorded during the same delay period — for example, if it was trained using D1 data and tested using D1 data — meaning that the LPFC accurately encoded the target location. However, the decoder performed poorly if it was trained with D1 responses but tested with D2 responses, or vice versa, suggesting that the LPFC code for the target location changed when the distractor was presented.

Next, the authors investigated the behavioural importance of the neural code transformation in the LPFC. They used principal component analysis to plot, in ‘response space’, the D1 and D2 population responses for each of the target locations, and compared these plots for trials in which the monkeys made the correct response with those for trials in which the monkey made an error. Whereas for correct trials, the clusters of D1 and D2 responses were well separated in response space — reflecting code transformation — the clusters of D1 and D2 responses in error trials overlapped, indicating that in error trials, the code transformation may have been incomplete.

To understand the neuronal basis for the code transformation in the LPFC, the authors classified each of the recorded neurons as showing classical selectivity (that is, selective for the target location or a specific epoch within each trial), linear mixed selectivity (selective for both target location and a task epoch, but with no interaction between these) or nonlinear mixed selectivity (selective for both target location and a task epoch, with an interaction of these factors). Strikingly, when the responses of LPFC neurons with nonlinear mixed selectivity — but not those with linear mixed selectivity or classical selectivity — were omitted from the set of data used to train the decoder, the decoder did not show signs of code changes between D1 and D2, suggesting that nonlinear-mixed-selectivity neurons are necessary for this LPFC code transformation.

Together, these results suggest that LPFC neurons that show nonlinear mixed selectivity encode target features in a flexible manner and transform this code when a distractor is presented, without losing target-related information.

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