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Mouse frontal cortex combines perceptual signals and recent outcomes to compute the expected return of actions

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Abstract:
Making decisions under uncertainty requires estimating the expected return of actions. When the sensory environment is uncertain and action outcomes fluctuate over time, the expected return depends on both immediate perception and recent outcomes. To find neuronal correlates of this computation, we recorded from large populations of neurons in medial prefrontal cortex (mPFC), while mice performed a choice task under perceptual and outcome uncertainty.
We expressed Channelrhodopsin-2 in midbrain dopamine (DA) neurons of DAT-Cre mice, implanted an optical fiber above the ventral tegmental area and trained them in a two-alternative forced choice visual task (Burgess et al, *bioRxiv*, 2016). In each trial, a grating appeared to the left or the right of the monitor, and the mouse turned a steering wheel to indicate the grating's position. We varied stimulus contrast across trials and obtained high-quality psychometric curves. To manipulate choice outcomes, in alternating blocks of trials, we paired correct choices towards one of the two stimuli with brief optogenetic DA stimulation, in addition to the normal water reward. The psychometric curves shifted towards the side paired with DA stimulation,

indicating that mice integrate immediate sensory and past DA reinforcement signals when making decisions. A reinforcement learning (RL) model incorporating perceptual uncertainty and past outcomes into the choice computation (Lak et al, Current Biology, 2017) could account for trial-by-trial choices.
While mice performed the task, mPFC neurons exhibited heterogeneous activity, responding to one or a few task events, such as the trial onset beep, visual stimulus, action onset, or outcome. We quantified these responses by modeling each neuron’s firing rate as a sum of temporal kernels aligned to each task event. For the majority of neurons, the responses observed between the stimulus and action onset could be accounted for by actions. These pre-action responses scaled with the contrast of the visual stimulus, but were almost independent of choice direction (left/right). Moreover, responses varied between blocks, reflecting the upcoming choice outcome (nothing, water, or water + DA stimulation). Finally, correlation of pre-action activity and the value estimates from the RL model showed that ~25% of task-responsive neurons encode the expected return of actions on a trial-by-trial basis.
These results suggest that a subset of mPFC neurons reflect the expected return of actions under perceptual and outcome uncertainty. These signals emerge prior to action onset and could inform downstream structures about the value of ongoing choices.
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