Multiplexing midbrain neurons entrain movement dependent decision-making

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Abstract

The brain can regulate decision-making by multiplexing information from the internal state and external context. Despite the importance of ongoing motor signals as an internal state, how the movement state dynamically updates the decision process is largely unknown. Here, we designed a novel perceptual decision-making task conducted on a treadmill to investigate the neural correlates associated with movement state-dependent decision-making. We focused on the neural activity of the mesencephalic locomotor region (MLR), a midbrain area involved in movement control. We uncovered that MLR encodes internal kinematic (walk, lick) and external context (reward, sensory stimulus) information concurrently at the single neuron level. In addition, we revealed that the subsets of these multiplexing MLR neurons encode modulation in decision-making associated with different movement states, primarily through alterations in the evidence accumulation phase. Collectively, these findings propose that the multiplexing of MLR neurons is a key regulator for state-dependent decision processes. Our findings will provide insight into the underlying mechanism of cognitive process during perceptual decision-making depending on the movement state.

Keywords: Mesencephalic locomotor region; Movement; Decision-making; Multiplexing; Drift diffusion model

Introduction

While many internal states are known to influence decision-making, the precise mechanisms of how our brain calculates the expected external value based on these internal states remain largely unknown (Flavell, Gogolla, Lovett-Barron, & Zelikowsky, 2022). To integrate external value and internal factors, it has been proposed that the multiplexing ability in an individual neuron, which means a neuron is capable of flexibly encoding multiple types of variables, is one of the key mechanisms for facilitating interaction between two factors (Fusi, Miller, & Rigotti, 2016; Parthasarathy et al., 2017; Raposo, Kaufman, & Churchland, 2014; Rigotti et al., 2013).

Despite the fundamental importance of movement as an internal state, previous works have not much focused on multiplexing in the movement system. Mesencephalic locomotor region (MLR), an evolutionary conserved locomotor center, is one of the key regions in the movement system (Cabelguen, Bourcier-Lucas, & Dubuc, 2003; Grillner, 2018; Ryczko & Dubuc, 2013; Shik, 1966). Recently, several studies have begun to shed light on the higher order cognitive functions of the MLR (Gut & Mena-Segovia, 2019; Mena-Segovia & Bolam, 2017; Thompson, Costabile, & Felsen, 2016; Thompson & Felsen, 2013). With the growing evidence of the concurrent involvement of MLR in reward, and sensory processes as well as locomotor controls, MLR neurons might have multiplexing ability for the decision-making process.

Here, we hypothesized that MLR neurons integrate information from internal kinematic and external context signals to modulate the decision-making process by reflecting internal conditions to make a proper decision.

Results

State-dependent behavior changes in the novel go/no-go auditory discrimination task

To study how our brain controls state-dependent decision processes, we developed a new 'go/no-go' perceptual decision-making task on a treadmill, as in Figure 1. To have the mice perform the task under various movement states, we designed the experiment such that the mice have to voluntarily walk a random distance on the treadmill before each trial.

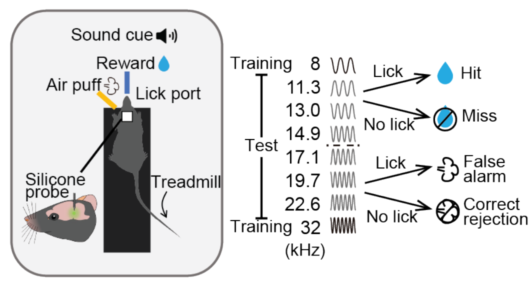

Figure 1: State-dependent auditory discrimination task on a head-fixed wheel

Using this new paradigm, we first examined whether the kinematic state can modulate decision-making behavior. To do that, we separated trials into slow and fast walking trials defined by each mouse's speed distribution in the pre-cue period, as in Figure 2A.

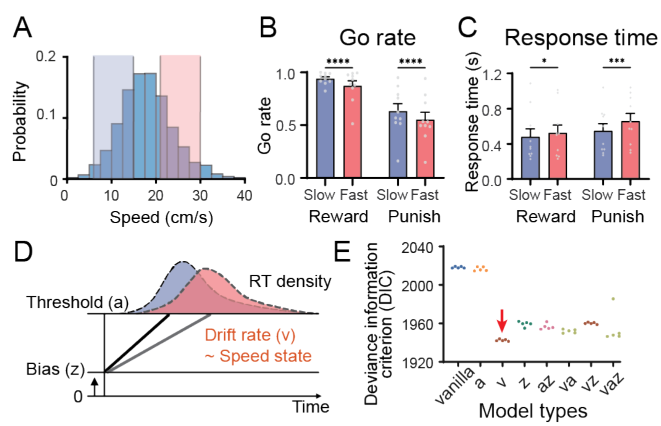

Figure 2: Modulation of decision-making behavior by kinematic states

We revealed that the probability of mice making the 'go' response to each cue type decreased, and their average time to the first lick after the sound cue was slower in fast walking trials, as in Figure 2B and 2C.

To find a latent variable that jointly explains the 'go' rate and response time, we implemented a drift-diffusion model (DDM).

We found that the drift rate, a parameter showing a speed of evidence accumulation for decision, provides the simplest and fundamental explanation for the influence of movement state by the smallest deviance information criterion (DIC), as in Figure 2D and 2E. Thus, we confirmed that the walking speed state at the moment of decision can affect the outcome of decision-making behavior through variation in the evidence accumulation process.

Multiplex encoding exists in MLR neurons

To dissect the multiplexing properties of individual MLR neurons, we next performed in vivo single-unit recording during the task. We applied a general linear model (GLM) to each neuron, which finds the weights of behavioral variables to best predict each neuron's firing rate, as in Figure 3A.

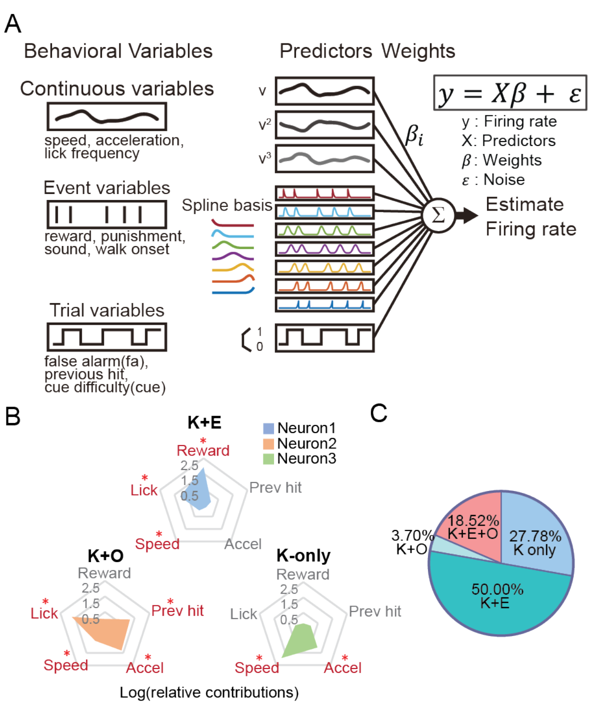

Figure 3: Multiplex encoding of kinematics and task-related context was characterized in MLR neurons

These results highlight that the MLR neurons can encode both **K**inematic (walk, lick) and **E**vent (reward, sound) or **O**utcome (previous hit) information, as K+E and K+O encoding neurons in Figure 3B. The majority of MLR neurons encode more than two variables, and over 70% encode more than two categories at the single cell level, as in Figure 3C.

Modulation of decision-making behavior is linked to multiplexing MLR neuronal activity

Next, we characterized the neural correlates of multiplexing MLR neurons for decision-making. We linked the decision process parameters to the neuronal activity of multiplexing MLR neuron clusters, which were categorized into 10 groups based on their response patterns to reward and punishment. Cluster 1 and 2 especially showed modulated responses to reward or sound by walking speed condition, as in the left panels of Figure 4A and 4B. These clusters are significantly correlated with the drift rate during decision preparation, as in the right panels of Figure 4A and 4B.

We then confirmed whether these multiplexing neurons directly encode decision behavior using a support vector machine (SVM). We calculated the performances of the SVM decoders in predicting trial-by-trial decisions based on each neuron's time-series activity. Individual neurons in cluster 1 encode the expectation of reward by predicting the mouse's 'go' or 'no-go' decision. Neurons in cluster 2 can significantly discriminate between 'Hit' or 'False alarm (FA)' cues, as in Figure 4C.

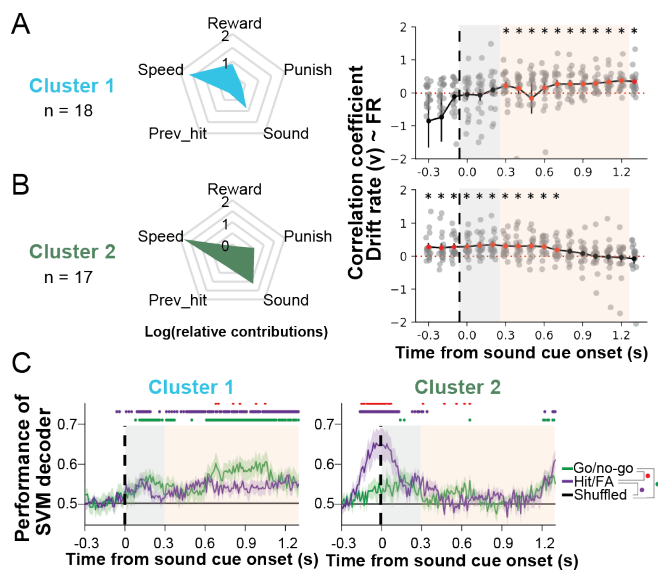

Figure 4: Activity of multiplexing MLR neurons explains state-dependent decision modulation

Conclusion

Collectively, our findings suggest that multiplexing MLR neurons participate in computations to decision-making and are modulated by their movement state, as shown in Figure 5.

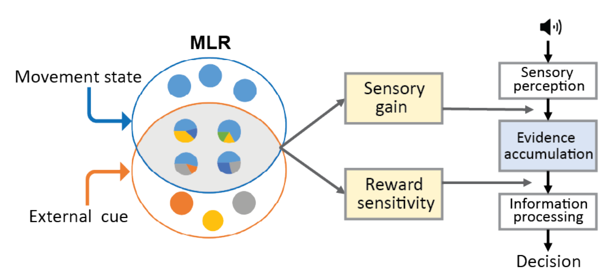

Figure 5: Schematic illustration of hypothesis

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