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Cell-Type-Specific Activity in Prefrontal Cortex during Goal-Directed Behavior

Highlights

- Sensory, motor, outcome signals are found in mouse PFC during goal-directed behavior
- Inhibitory neurons of the same subtype show similar functional properties
- Different subtypes of PFC inhibitory neurons encode different task-related signals
- Excitatory neurons are diverse and their task-related activity varies across layers

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In Brief

Cellular-resolution Ca^{2+} imaging from the mouse PFC during goal-directed behavior reveals sensory, motor, and outcome signals. Interneurons of the same subtype are functionally similar, but different subtypes encode different task-related signals. Excitatory neurons have diverse properties that vary across layers.

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Cell-Type-Specific Activity in Prefrontal Cortex during Goal-Directed Behavior

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SUMMARY

The prefrontal cortex (PFC) plays a key role in controlling goal-directed behavior. Although a variety of task-related signals have been observed in the PFC, whether they are differentially encoded by various cell types remains unclear. Here we performed cellular-resolution microendoscopic Ca^{2+} imaging from genetically defined cell types in the dorsomedial PFC of mice performing a PFC-dependent sensory discrimination task. We found that inhibitory interneurons of the same subtype were similar to each other, but different subtypes preferentially signaled different task-related events: somatostatin-positive neurons primarily signaled motor action (licking), vasoactive intestinal peptide-positive neurons responded strongly to action outcomes, whereas parvalbumin-positive neurons were less selective, responding to sensory cues, motor action, and trial outcomes. Compared to each interneuron subtype, pyramidal neurons showed much greater functional heterogeneity, and their responses varied across cortical layers. Such cell-type and laminar differences in neuronal functional properties may be crucial for local computation within the PFC microcircuit.

INTRODUCTION

Goal-directed behavior involves multiple sensory, motor, and cognitive processes. When engaged in a task, the animal must attend to task-relevant sensory cues, control the initiation and termination of appropriate motor actions, and monitor the outcome of each action in order to adjust future behavioral strategies. The prefrontal cortex (PFC) plays a crucial role in coordinating these processes through its long-range connections with many other brain areas (Desimone and Duncan, 1995; Euston et al., 2012; Fuster, 2008; Gabbott et al., 2005; Heidbreder and Groenewegen, 2003; Miller and Cohen, 2001; Squire et al., 2013). Electrophysiological recordings from both primates and rodents have shown that a variety of task-related signals are encoded in the spiking activity of PFC neurons (Euston et al., 2012; Miller and Cohen, 2001). In addition to sensory stimuli and impending motor actions, many neurons respond to expected or actual action outcomes (reward and punishment), thus allowing the PFC to orchestrate sensory and motor processes for the current task and to improve future behavioral performance (Hayden et al., 2008; Hyman et al., 2013; Insel and Barnes, 2014; Ito et al., 2003; Matsumoto et al., 2007; Narayanan et al., 2013; Ridderinkhof et al., 2004; Schall et al., 2002; Wallis and Kennerley, 2010; Watanabe, 1996).

Individual PFC neurons encode various combinations of task-related variables (Hyman et al., 2013; Machens et al., 2010; Mante et al., 2013; Rigotti et al., 2013), exhibiting a high degree of complexity and heterogeneity. How these functional properties are organized and computed within the PFC microcircuit remains largely unknown. In well-studied sensory cortical areas, glutamatergic neurons and subtypes of GABAergic interneurons exhibit different stimulus selectivity (Kerlin et al., 2010), and they are differentially influenced by brain state and neuromodulatory inputs (Alitto and Dan, 2012; Fu et al., 2014; Gentet et al., 2012; Lee et al., 2013; Pi et al., 2013; Zhang et al., 2014), suggesting separate roles in local computation. However, how different types of neurons in the PFC respond to task-related events is only beginning to be investigated (Courtin et al., 2014; Kvitsiani et al., 2013; Sparta et al., 2014). Furthermore, a prominent feature of the neocortex is its laminar organization. Neurons in different layers receive different inputs and project to distinct targets, and their interconnections play crucial roles in intracortical processing (Douglas and Martin, 2004; Harris and Mrsic-Flogel, 2013). Characterizing the laminar organization of neuronal response properties is thus a critical step in understanding how the PFC circuit operates in cognitive control.

In this study, we characterized PFC activity while the mouse performed a simple go/no-go sensory discrimination task, which has been used extensively to study PFC functions (Fuster, 2008). The use of microendoscopes (Ghosh et al., 2011) allowed optical access to the dorsomedial PFC (dmPFC), a region important for cognitive control of behavior (Bissonette et al., 2008; Euston et al., 2012; Hanks et al., 2015; Matsumoto et al., 2007; Narayanan et al., 2013; Ridderinkhof et al., 2004) but inaccessible to conventional imaging techniques. Using several Cre mouse lines, we performed cellular-resolution Ca^{2+} imaging from excitatory pyramidal (PYR) neurons as well as three distinct subtypes of inhibitory interneurons: parvalbumin-positive (PV^+), somatostatin-positive (SST^+), and vasoactive intestinal peptide-positive (VIP^+) neurons, which together comprise 85% of all GABAergic neurons in the cortex (Rudy et al., 2011; Xu et al.,