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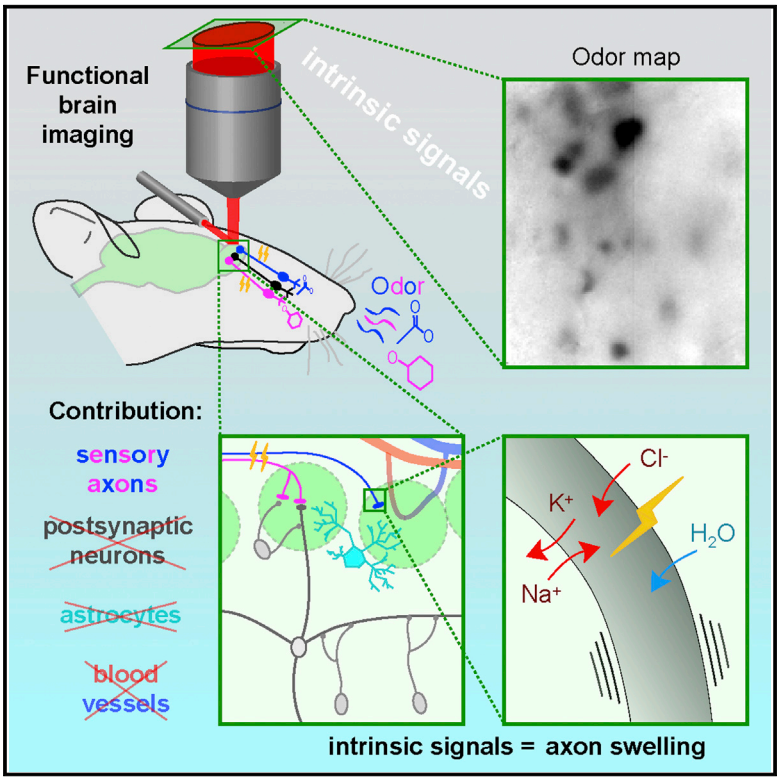
Sensory-Evoked Intrinsic Imaging Signals in the Olfactory Bulb Are Independent of Neurovascular Coupling

Graphical Abstract



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In Brief

In mammalian brains, sensory-evoked intrinsic optical signals are thought to follow hemodynamics through neurovascular coupling. With detailed manipulations of the mouse olfactory bulb circuit, Vincis et al. show that parenchymal intrinsic signals originate from changes in light scattering of sensory neuron axons and are largely independent of neurovascular coupling.

Highlights

- We studied the origin of intrinsic optical signals (IOSs) in the mouse olfactory bulb
- IOSs are independent of neurovascular coupling and astrocyte function
- IOSs are independent of neurotransmitter release and post-synaptic neuronal activity
- IOSs arise from activity-dependent swelling of sensory neuron axons

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Sensory-Evoked Intrinsic Imaging Signals in the Olfactory Bulb Are Independent of Neurovascular Coupling

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SUMMARY

Functional brain-imaging techniques used in humans and animals, such as functional MRI and intrinsic optical signal (IOS) imaging, are thought to largely rely on neurovascular coupling and hemodynamic responses. Here, taking advantage of the well-described micro-architecture of the mouse olfactory bulb, we dissected the nature of odor-evoked IOSs. Using in vivo pharmacology in transgenic mouse lines reporting activity in different cell types, we show that parenchymal IOSs are largely independent of neurotransmitter release and neurovascular coupling. Furthermore, our results suggest that odor-evoked parenchymal IOSs originate from changes in light scattering of olfactory sensory neuron axons, mostly due to water movement following action potential propagation. Our study sheds light on a direct correlate of neuronal activity, which may be used for large-scale functional brain imaging.

INTRODUCTION

In the last decades, imaging techniques have allowed us to watch the brain at work with extraordinary details and have provided an in-depth understanding of how neural networks function. In humans, non-invasive imaging techniques do not directly measure electrical signals but rather measure correlates of neuronal activity. Functional MRI (fMRI) of blood-oxygen-level-dependent (BOLD) contrast relies on changes in blood oxygenation in active brain regions (Logothetis and Wandell, 2004; Logothetis et al., 2001). Intrinsic imaging, either called intrinsic optical signals (IOSs) imaging, near-infrared spectroscopy (NIRS), or 2D optical imaging spectroscopy (2D-OIS), is thought to reflect cerebral blood flow and oxygenation level changes (Grinvald et al., 1999; Martin et al., 2002; Murkin and Arango, 2009), whereas diffusion fMRI measures water diffusion (Le Bihan et al., 2006). Because all these measurements are indirect, it is crucial to understand their relation to neuronal activity to properly interpret functional brain-imaging data.

In animal models, IOSs have been used as a surrogate of BOLD-fMRI to study neurovascular coupling (Berwick et al., 2002; Cardoso et al., 2012; Niessing et al., 2005; Schummers et al., 2008; Sirotin and Das, 2009). Additionally, they have been extensively used for brain mapping in different species and several brain regions: visual, somatosensory, auditory, and gustatory cortices (Accolla et al., 2007; Accolla and Carleton, 2008; Frostig et al., 1990; Grinvald et al., 1986; Harrison et al., 1998), as well as the olfactory bulb (OB) (Abraham et al., 2004, 2014; Meister and Bonhoeffer, 2001; Rubin and Katz, 1999; Vincis et al., 2012). This technique reports changes in brain-tissue reflectance induced by neuronal activity (Grinvald et al., 1999). Such changes depend on incident light absorption by intrinsic chromophores and incident light scattering by the tissue refraction index inhomogeneities (Grinvald et al., 1999; Zepeda et al., 2004). At longer wavelengths (650–850 nm), variations in light scattering are thought to dominate IOS sources (Cohen et al., 1968; Frostig et al., 1990; Grinvald et al., 1999). At shorter wavelengths (450–650 nm), hemoglobin absorbance dominates, with variations in absorbance levels between oxy- and deoxyhemoglobin (Frostig et al., 1990). Both variations in blood flow and oxygenation can contribute to IOSs. It has therefore been proposed that, at shorter wavelengths (450–650 nm), IOSs originate from hemodynamics, following astrocyte-mediated neurovascular coupling (Gurden et al., 2006; Schummers et al., 2008).

In the present study, we unexpectedly found that stimulus-evoked parenchymal IOSs in the OB are independent of neurovascular coupling. We present evidence that parenchymal IOSs in the OB mainly come from the activity of olfactory sensory neuron (OSN) axons and are independent of neurotransmitter release. Our findings represent a significant step forward in understanding the origin of IOSs and provide crucial information about the different physiological correlates of neuronal activity