Functional connectivity between neuronal partners according to cortical brain states

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Synaptic inhibition orchestrates both spontaneous and sensory-driven activity in the cerebral cortex, and it's generated by interneurons reciprocally connected to other cortical neurons. Neurons expressing parvalbumin (PV), somatostatin (SOM) and vasoactive intestinal peptide (VIP) are the three largest and non-overlapping classes of interneurons in the mouse cortex. Several studies have shown cortical interactions between these groups of interneurons and their excitatory partners, but the functional meaning of the connections are poorly understood. An important question in systems neuroscience is how behavioral state modulates the processing of sensory signals. To gain further insights into the impact of behavioral state on local cortical circuitry, we employ a novel approach based on resonant scanning 2-photon imaging of large populations of identified cortical neurons in frontal cortex of behaving mice. GCAMP6 calcium sensors were used to image activity of excitatory and inhibitory neurons, using cell type specific CRE-driver lines that also expressed a red fluorescent protein. Our data identify a novel dual role of VIP interneurons to modulate the gain of excitatory neurons. During arousal, pyramidal neurons receive both indirect VIP→SOM cell-mediated disinhibition and direct VIP cell-mediated inhibition. An expected outcome from this circuitry is that variability in the net balance of inhibition and disinhibition generates a heterogeneous response of excitatory neurons, some of which are enhanced during arousal as others are suppressed. The net effect on individual cells is expected to shift their operating point, modulating the gain of pyramidal neurons during arousal.

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