Title: Disinhibitory unmasking of top-down input to sensory cortex by locomotion

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Locomotion has a powerful and diverse influence on neural activity in the sensory cortex. Effects include increasing activity of VIP interneurons, altering levels of 'spontaneous' activity in excitatory neurons, and altering the gain of responses to sensory stimuli[1]. Activation of VIP interneurons is known to inhibit SOM interneurons which themselves preferentially inhibit tuft dendrites of pyramidal neurons[2]. Locomotion is therefore expected to disinhibit tuft dendrites through this VIP-SOM disinhibitory circuit, thus potentially unmasking tuft targeting top-down input. Here we test whether structured patterns of neural activation are unmasked in primary visual cortex when animals initiate movements and how they related to recent visual experience. Mice were presented with videos of natural scenes interspersed with periods of 30 seconds during which no stimulus was presented (blank condition). We analyzed neural activations aligned with locomotion onsets during the blank stimulus periods and found many neurons exhibited elevated neural activity aligned with movement onset. A fraction of these neurons exhibited activity in response to every locomotion onset and had a locomotion correlation of > 0.8 – these most likely constitute VIP interneurons. Finally, locomotion aligned activations were analyzed to determine if they maintain the correlation structure of stimulus evoked activity and the extent to which they are contingent on recent stimulation history.

(1) Vinck, M.; Batista-Brito, R.; Knoblich, U.; Cardin, J. A. Arousal and Locomotion Make Distinct Contributions to Cortical Activity Patterns and Visual Encoding. *Neuron* **2015**, *86* (3), 740–754. https://doi.org/10.1016/j.neuron.2015.03.028.

(2) Huang, S.; Wu, S. J.; Sansone, G.; Ibrahim, L. A.; Fishell, G. Layer 1 Neocortex: Gating and Integrating Multidimensional Signals. *Neuron* **2024**, *112* (2), 184–200. https://doi.org/10.1016/j.neuron.2023.09.041.