



Oscillations trumped by behavior: a link between sensory and direct electrical stimulation of cortical activity

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A commentary on

Behavioral modulation of stimulus-evoked oscillations in barrel cortex of alert rats

by Venkatraman, S., and Carmena, J. M. (2009). *Front. Integr. Neurosci.* 3:10. doi:10.3389/neuro.07.010.2009.

Behavior is well known to influence spiking responses in both thalamus and cortex to either sensory stimuli or electrical stimulation of afferent nerves (Chapin and Woodward, 1981; Fanselow and Nicolelis, 1999; Fontanini and Katz, 2009). This fact has been particularly well documented in the rodent somatosensory system, where whisking behavior tends to decrease the initial response of thalamic and cortical neurons to activation of the trigeminal nerve, as well as the prolonged suppression of activity that commonly follows this initial response (Fanselow and Nicolelis, 1999).

In a largely unconnected set of experiments, sensory cortices have been shown to exhibit oscillations at particular frequencies following direct or sensory stimulation, as measured in field potentials (Contreras and Steriade, 1996; Muthuswamy et al., 1999). The fact that these phenomena are more commonly observed under systemic anesthesia (e.g., Derdikman et al., 2003) than in awake animals (but see Kay, 2005; Tort et al., 2010), makes it tempting to conclude, in light of the above-described work, that awake behavior might suppress both neuronal responses and oscillatory activity. Now, in *Frontiers*, Venkatraman and Carmena (2009) employ direct cortical recording and stimulation techniques that they have recently developed (Venkatraman et al., 2009) to provide evidence that this is indeed the case. These findings also suggest, for the first time, common cellular and network mechanisms underlying the cortical response to direct electrical activation and peripheral sensory stimulation.

Working with awake, whisking rats, Venkatraman and Carmena (2009) start with the observation that direct electrical microstimulation of the barrel cortex induces oscillations in the 15–18 Hz range, but that this induction is far from 100% reliable. An important factor underlying this variability, they suggest, is the behavioral state of the rat, as relates to whisking behavior: prominent oscillations are induced when stimulation is delivered to an animal exhibiting quiet immobility, but much less rhythmic activity is induced during active whisking. In fact, the authors show a direct, inverse correlation between the amplitude of the stimulation-induced oscillations and the strength of whisking during stimulation; they also demonstrate that this inverse relation with behavior occurs very precisely in time, and rule out potentially confounding variables such as the level of attention. These results effectively bring together the previous findings described above, showing that motor behavior similarly affects induced spiking responses and network oscillations. In fact, Venkatraman and Carmena make this similarity explicit, showing that the strength of spike inhibition following the immediate burst of stimulation-induced spikes also exhibits a negative dependence on whisking behavior.

Venkatraman and Carmena go on to simulate a feasible biophysical substrate for the observed dynamics. Making clever use of previous modeling work (Suffczynski et al., 2004), they show how strong feedforward inhibition (possibly involving GABA_B) could play a chief role in inducing thalamic neurons to burst (this thalamic bursting would be transmitted to cortical neurons as the observed oscillations), and suggest that the deinactivation of thalamic I_T currents promoted by strong hyperpolarization is crucial to rebound excitation and beginning of bursting activity in these cells (I_T currents are inactivated during excitation, and are set to deinactivate during prolonged inhibition;

for reviews on this mechanism of bursting generation, see Sherman, 2001; Steriade, 2005; Huguenard and McCormick, 2007). According to this model, whisking would likely provide a greater level of excitation to thalamic neurons (e.g., by increased sensory inputs or by a greater action of neuromodulators such as acetylcholine), which would counteract hyperpolarization, keeping I_T inactivated and decreasing the likelihood of bursts and oscillations. Responses are thus governed by an appealing balance between corticothalamic feedforward inhibition and behaviorally induced thalamic excitation. The authors' demonstration that they could induce cortical oscillations even in the presence of active whisking behavior by increasing the intensity of the stimulation is compatible with their model, assuming that the generation of oscillations is dependent on the number of cortical neurons recruited.

The functional consequences of these observations remain to be explored. It has been suggested that thalamocortical network settings in “quiet” animals are optimized for stimulus detection (such that spiking responses are large and bursting). During active exploration, neurons are tonically active, such that they are better prepared to perform a more fine-grained analysis of stimulus dynamics (Nicolelis and Fanselow, 2002). It may well be that the differences in oscillatory power observed in response to cortical stimulation are a slightly more direct assay of these differences in network settings, rather than being the purpose of the network settings *per se*.

This is a particularly pertinent issue given that multiple distinct but overlapping rhythms can be observed in cortical circuits (Tort et al., 2010). That is, the function of the induced rhythm may be a subtle function of precisely *what* rhythm is induced. The authors specifically suggest that their observed oscillations more closely resemble the spindles observed under ketamine–xylazine anesthesia than

the spontaneous spike-and-wave shaped “ μ ” rhythm that induces whisker twitching, and show that a blockade of GABA_A can conceivably participate in making their thalamocortical network model transition from one of these rhythms to the other. With this combination of behavior, oscillation induction, and modeling, Venkatraman and Carmena are therefore poised to integrate a disparate body of results, and provide us with a uniquely wholistic explanation of thalamocortical function in awake rats.

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