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Presentation Abstract

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Presentation Title:	Automated multiple-cell patch clamp assessment of multineuron subthreshold dynamics in waking and anesthetized states
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Topic:	++G.04.b. Optogenetics
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Abstract:	We are developing a robot capable of patch-clamp whole cell neural recording of many cells at once (the “multipatcher”), in the waking and anesthetized brain, in order to reveal the synaptic and ion channel conductances that generate neural dynamics that support different brain states. Building from our

past work (Kodandaramaiah et al., Nature Methods, 2012), we are both perfecting the technology and applying it to a major question: investigating the cellular mechanisms of general anesthesia. Despite its clinical importance, as well as its importance in basic-science studies of consciousness, perception, awareness, arousal, and other brain functions, little is known about how anesthetics act on specific cell types in the live brain, despite overt similarities in anesthetized behavioral states arrived at through administration of different drugs. In this study we are using our multipatching robot to study neural responses to multiple kinds of anesthetic drug: ketamine, an NMDA receptor antagonist; dexmedetomidine, an alpha-2 adrenoceptor agonist; and propofol, a GABA-A receptor agonist. We have performed single and multiple whole-cell patch clamp recordings in the somatosensory cortex of awake head-fixed mice, while tracking the changes in membrane potential and spiking activity as the awake animals transition into sedated states. We observe that the membrane potential of both inhibitory and excitatory cortical neurons in awake animals are characterized by slow oscillations during quiet wakefulness, interspersed by persistent depolarization during movement. Systemic infusion of both ketamine and dexmedetomidine results in the abolishment of the persistent depolarization, with the slow oscillation remaining. These membrane potential slow oscillations are highly coherent across nearby (<200 microns) and more distant neuron pairs (200-500 microns). However, infusion of propofol produces a strong, constant hyperpolarization of the membrane potential. Our results indicate that ketamine and dexmedetomidine which are two very different drug classes have similar effects on the membrane potential of cortical neurons, possibly through their actions in brainstem arousal nuclei; whereas propofol might be inducing inhibition, perhaps in part by enhancing GABA-mediated chloride currents in pyramidal neurons in the cortex.

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