

amygdala is parsed in such a way that CeA- and NAc-projecting neurons in the BLA are preferentially targeted by sensory pathways representing bitter and sweet tastes, respectively. If true, this organization would seem to require a feedback mechanism (perhaps early in development) by which CeA and NAc shape sensory inputs onto BLA neurons in a projection- and valence-specific manner. Because neither the CeA nor NAc projects directly to the BLA, this feedback might be mediated by descending projections to midbrain monoaminergic neurons which, in turn, modulate plasticity in forebrain circuits, including the BLA.

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Inhibition Patterns the Whisking Rhythm

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In this issue of *Neuron*, Deschênes et al. (2016) propose that rhythmic inhibition of whisker motor neurons is a key pattern generator underlying exploratory whisking. The inhibitory premotor neurons located in the brainstem reticular formation are synchronized by breathing-related oscillators.

Rodents actively scan their immediate facial environment through rhythmic forward and backward whisker movements at ~10 Hz. As a moving whisker encounters an object, the whisker bends, causing the opening of mechanogated ion channels depolarizing the nerve endings of sensory trigeminal neurons, which innervate the whisker follicle. Action potential firing in these whisker sensory neurons releases glutamate onto postsynaptic neurons in the trigeminal brainstem, forming the start of diverse sensory signaling pathways to downstream brain areas (Petersen, 2007). Whisker movements provide the drive for active sensing, and thus understanding whisker motor control

is of paramount importance for a mechanistic understanding of whisker sensory perception (Petersen, 2014). In this issue of *Neuron*, Deschênes et al. (2016) report important advances in whisker motor control, unexpectedly finding that rhythmic inhibitory, rather than excitatory, input controls important aspects of whisker motor neuron firing.

Whisker protraction is generated by contraction of intrinsic muscles within the mystacial pad (Dörfl, 1982), controlled by motor neurons located in the ventral lateral facial nucleus (Herfst and Brecht, 2008; Takatoh et al., 2013; Sreenivasan et al., 2015). Deschênes et al. (2016) recorded intracellularly from whisker motor

neurons during kainic acid-induced artificial whisking in anesthetized rats. They found that the whisker motor neurons gradually depolarize and fire action potentials during whisker protraction, and then rapidly hyperpolarize just before the onset of whisker retraction (Figure 1). The membrane potential dynamics of these whisker motor neurons is determined by convergent excitatory and inhibitory synaptic input from premotor neurons. By using transsynaptic rabies virus (Wickersham et al., 2007; Stepien et al., 2010), whisker premotor neurons have been mapped to a large number of brain regions including spinal trigeminal oralis nucleus (Sp5O), the vestibular

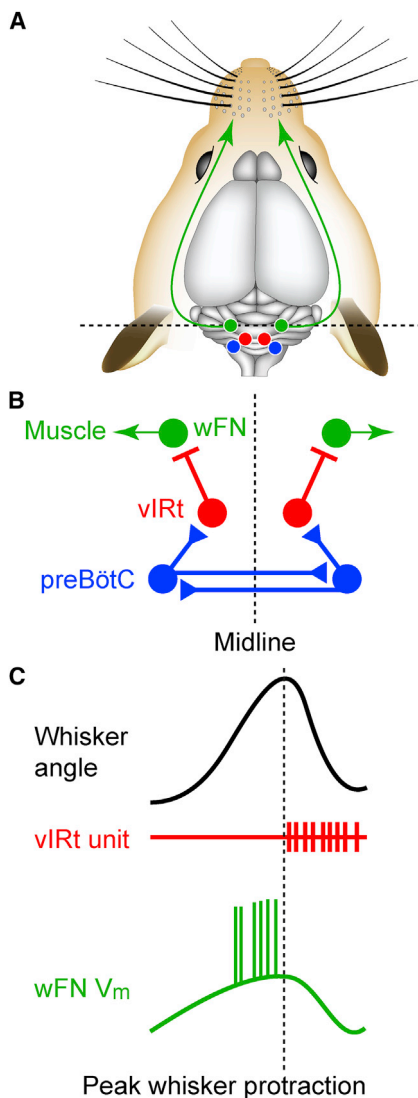


Figure 1. Neurons in vIRt Inhibit Whisker Motor Neurons Leading to Whisker Retraction

(A) Whisker motor neurons in ventral lateral facial nucleus (wFN, green) innervate intrinsic muscle in the mystacial whisker pad, controlling whisker protraction, i.e., forward movement. The vibrissal-related ventral intermediate reticular formation (vIRt, red) is located posterior and medial to wFN. The pre-Bötzing complex (preBötC, blue) is near to vIRt, located slightly more ventral and lateral.

(B) Schematic summary of the most important interactions between neurons in PreBötC, vIRt, and wFN, as proposed by Deschênes et al. (2016). PreBötC excites vIRt, which in turn inhibits wFN. Neither wFN nor vIRt innervate the contralateral brainstem, but PreBötC innervates the contralateral PreBötC. PreBötC can therefore contribute to the bilateral synchronization of whisking.

(C) Schematic summary of the timing relationships of whisker movement, unit firing of inhibitory neurons in vIRt, and membrane potential (V_m) of whisker motor neurons in wFN, as shown in Deschênes et al. (2016). Whisker motor neurons in wFN fire action potentials driving whisker pro-

nuclei (Ve), the lateral paragigantocellular nucleus (LPG), Bötzing/pre-Bötzing complexes, intermediate reticular formation (IRt), gigantocellular reticular formation (GIRt), parvocellular reticular formation (PCrT), medullary dorsal reticular formation (MdD), superior colliculus, the mesencephalic reticular nucleus, and frontal regions of neocortex, i.e., whisker motor cortex (Takato et al., 2013; Sreenivasan et al., 2015). A complete understanding of whisker motor control will require recording and manipulating pre-motor neurons in all these different brain regions. In this study, Deschênes et al. (2016) suggest that the main whisking-related modulation of membrane potential of whisker motor neurons is the rapid hyperpolarization immediately preceding whisker retraction, which they propose to be mediated by inhibitory synaptic input from the vibrissal-related region of ventral IRt (vIRt).

In a previous study by the same group (Moore et al., 2013), the vIRt was proposed to be a key central pattern generator for rhythmic whisker protraction. Injection of the glutamate receptor agonist kainic acid into vIRt was found to induce robust rhythmic whisking for very long periods of time in lightly anesthetized rats. Electrolytic lesion of ipsilateral whisking, whereas contralateral whisking persisted. Recordings of action potential firing of neurons in vIRt revealed that some units were strongly phase-locked to either protraction or retraction of the whisker. Their previous study thus revealed important evidence supporting a profound role for vIRt in regulating whisking (Moore et al., 2013). In this new study (Deschênes et al., 2016), the authors probe synaptic circuits through which vIRt may contribute to whisker motor control.

In technically demanding experiments, Deschênes et al. (2016) carried out juxtacellular recordings of vIRt neurons followed by labeling with Neurobiotin and subsequent *in situ* hybridization to identify the neurotransmitter phenotype of the recorded neurons. Out of five labeled vIRt

traction. During whisker retraction, inhibitory neurons in vIRt fire action potentials hyperpolarizing the whisker motor neurons and thus contributing to patterning the whisking cycle.

units firing on the retraction phase of the whisking cycle, they found that all five contained mRNA coding for the vesicular GABA transporter (VGAT) and were therefore inhibitory neurons. Furthermore, most units in vIRt were found to be retraction units, firing little during protraction and increasing firing rate during retraction. The firing of these neurons will likely release GABA or glycine onto whisker motor neurons in the facial nucleus, thus causing hyperpolarization and preventing action potential firing. Whisker motor neurons in the ventral zone of the lateral facial nucleus drive whisker protraction, and the rhythmic inhibition from vIRt would thus lead to rhythmic retraction of the whisker. The data thus suggest that rhythmic inhibition by vIRt patterns the whisking cycle, at least under the experimental conditions explored in the current study (Deschênes et al., 2016).

Deschênes et al. (2016) further investigate the role of the pre-Bötzing complex (preBötC) in synchronizing whisker movements on both sides of the snout (Figure 1). The pre-Bötzing complex is an important oscillator that generates the inspiratory drive during breathing and sniffing (Feldman and Kam, 2015). Whisking can occur either in tandem with sniffing or on its own (Welker, 1964; Moore et al., 2013). The authors show that when whisking occurs in tandem with sniffing, the whisker movements on either side of the snout are highly synchronized. When whisking occurs in the absence of the inspiratory drive, the whisker movements are bilaterally desynchronized. The authors attribute this effect to the presence of commissural connections between the two pre-Bötzing complexes on either side of the brainstem, each in turn projecting to the ipsilateral vIRt. In the absence of active synchronization by the pre-Bötzing complex, the two vIRts (on either side of the brainstem) operate on their own, and whisker movements on left and right sides drift in phase.

Deschênes et al. (2016) show that vIRt cells can play an important role in patterning the phase of whisking by periodically hyperpolarizing the membrane potential of the motor neurons. However, what causes the motor neurons to depolarize and fire in the first place remains unknown. Transsynaptic rabies

tracing studies have delineated several other structures in the brainstem and midbrain that provide synaptic input to the whisker motor neurons (Takatoh et al., 2013; Sreenivasan et al., 2015). Whisker motor neurons also receive direct excitatory cortical input from upper motor neurons in whisker motor cortex (Grinevich et al., 2005; Sreenivasan et al., 2015), and stimulation of whisker motor cortex causes rhythmic whisker protraction (Matyas et al., 2010; Sreenivasan et al., 2015). In addition, neuromodulators such as serotonin may play an important role (Hattox et al., 2003). The current study (Deschênes et al., 2016) brings us an important step closer to unraveling whisker motor control, but it is clear that there is much further research that needs to be carried out in order to fully understand the neuronal circuits con-

trolling whisker movements, which will likely depend dynamically upon the behavioral context and precise goals of the animal.

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