Cellular and Synaptic Mechanisms that Underlie Eupnea and Sigh Rhythms for Breathing Behavior in Mice

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Abstract

Breathing is a lifelong activity that involves the coordination of several rhythmic behaviors. This dissertation investigates the neural origins of two of these breathing rhythms: eupnea and sighing. Eupnea, or regular unlabored breathing, occurs on the order of seconds and serves to drive the exchange of oxygen and carbon dioxide between the circulatory system and the environment. Sighs, deep breaths that are typically 2-5 times the volume of a eupneic breath, occur on the order of minutes and are critical in maintaining pulmonary function. Understanding how these rhythms are generated on a cellular and synaptic level is an essential step in preventing numerous pathologies, such as sudden infant death syndrome and respiratory depression and failure as a consequence of opioids in a clinical setting or as drugs of abuse. First, I uncover the cellular and synaptic mechanisms that couple these two rhythms using electrophysiology and an in vitro breathing model from neonatal mice. Next, using mathematical modeling techniques, I explore how topology of the neural circuitry could be driving the eupnea rhythm. Finally, I layout my framework for how intracellular calcium oscillations are driving the sigh rhythm with electrophysiology and an in vitro breathing model combined with mathematical modeling. Unraveling the mechanisms that generate the eupnea and sigh rhythms reveals deeper insights into rhythms throughout the brain.