Computational Studies of the Respiratory Brainstem
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The goal of this collaborative project is to develop a unified network model of the respiratory brainstem, using experiments to test and tune model-based hypotheses. We have generated respiratory-like patterns in simulated networks, reproducing several physiological phenomena and effects of pontomedullary transections. We have modeled responses to hypoxia during sleep and wakefulness, high-frequency oscillations during inspiration, the transition from eupnea to gasping, and neural pacemaker mechanisms. Simulation results, confirmed in isolated pre-Bötzinger complex (pre-BöC) neurons, show that bursting in pacemaker neurons can be induced by a reduction of potassium currents or augmentation of persistent sodium currents. These conditions accompany hypoxia and support hypotheses on central hypoxia chemoreception. Multi-array recordings of respiratory neurons during transient hyperventilatory apnea have revealed distributed circuit dynamics and the dissolution and reemergence of rhythmic respiratory network activity (Figure). We have also explored in intact unanesthetized animals the effects of hypoxia on respiratory neuron discharge patterns during sleep states. Other experimental series show that pontine networks integrate cardiac and respiratory modulated inputs, suggest that pontine and medullary raphe neurons participate in hypoxia-induced gasping, and that pre-BöC neurons are involved in the generation of inspiratory high-frequency oscillations as well as phase timing and pattern generation. Results from the “working heart brainstem preparation” suggest decrementing expiratory neurons prolong expiration following hypoxia. The project is also a catalyst for the development and sharing of multi-array recording technologies and open source software, including a hybrid network simulator, an automatic spike sorting system, and enhanced tools for spike train analyses and data visualization.

Multi-array recordings provide a window on distributed circuit dynamics during the dissolution and reemergence of rhythmic respiratory network activity. Parallel recordings from 61 ventral respiratory column, pontine, and raphe neurons document the first observations of concurrent “up or down” firing rate changes at multiple brainstem sites during hyperventilatory apnea. Extended correlational linkages (e.g., labeled lines, right) support the hypothesis that synaptic interactions among neurons in all three sites contribute to the observed modulation.
PI Website

http://www.hsc.usf.edu/medicine/physiology/blindsey.html

Publications

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