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Computational Studies of the Respiratory Brainstem

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Current models propose that raphe and pontine neurons modulate the ventrolateral medullary respiratory column of neurons (VRC) considered essential for respiratory rhythm and pattern generation. The aims of this project are to define and model distributed connectivity among neurons in these domains, and the reconfiguration and re-emergence of the respiratory network during and following hypoxia-induced gasps and augmented bursts, coughing, hyperventilation to apnea, and sleep states. 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, a semi-automatic spike sorting system, and enhanced tools for spike train analyses and data visualization.

Short-time scale spike train correlations from multi-site recordings in decerebrate animals suggest and support connections in hybrid network model simulations, including pontine interactions and indirect recurrent VRC-raphe-pontine loops. During severe hypoxia and re-oxygenation, neurons in these regions exhibit bursts correlated with fictive gasping/augmented breath patterns; some show evidence of altered functional connectivity. Gasp-synchronous neuronal discharges, corresponding to both phase shifted and recruited respiratory-modulated and non-respiratory modulated (as identified during baseline conditions) neuronal activities were observed in many pontine neurons and in a small subset of neurons from the caudal medullary raphe. In addition, neurons that discharged tonically and neurons that became silent during hypoxia/re-oxygenation-induced gasping and/or augmented bursts were also encountered.
During hyperventilatory apnea, activities of some neurons increase as others decrease. Extended correlational linkages provide evidence for various interactions between tonic putative modulatory neurons and upon phasic respiratory-modulated neurons. The results suggest that a distributed brainstem network shapes and modulates hypoxic gasps and

augmented burst activity, and reveal distributed circuit dynamics during the dissolution and reemergence of rhythmic respiratory network activity during hyperventilatory apnea.

Single neuron recordings from intact animals during natural sleep have led to a preliminary model of endogenous excitatory effects on medullary respiratory neurons in REM sleep. Results show a complex pattern of excitation of respiratory neurons and muscles during REM sleep. The responsible process begins with a delay after the onset of REM sleep. The result of this process can be disorganization of the output of the central pattern generator, an outcome that can cause hypoventilation and oxygen desaturation in patients with lung disease.

Project (or PI) Websites

http://www.hsc.usf.edu/medicine/physiology/people/lindsey.html

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