MBG FOCUS TALK

hosted by Erik Østergaard Jensen

MBG Focus Talks in Molecular Biology

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Science Park, conference room (3130-303)

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Tongue tied and apneic: exploring the premotor circuits that control airway patency

Breathing is extremely reliable, yet adaptable; its output adjusts over orders of magnitude to match changes in metabolic demand and system mechanics that accompany sleep, exercise, disease, and aging. Breathing must also coordinate with other behaviours like sniffing and speaking that use respiratory networks for a different function, and swallowing that shares respiratory network elements but must turn off breathing for it to occur. My research examines the minimal brainstem circuit controlling the upper airway, including the preBötzinger Complex, essential for inspiratory rhythm generation, a premotoneuron population and hypoglossal (XII) motoneurons that innervate muscles of the tongue. Understanding this circuit is of clinical significance because reduced tongue muscle tone is causally related to obstructive sleep apnea (OSA). OSA typically occurs during dreaming sleep, when specific neurochemical systems in the brain that increase motoneuron excitability (i.e. responsiveness) shut down. Loss of this excitation reduces airway muscle activity and during inspiration the airway collapses, blocking airflow. OSA affects 5-15% of the Danish population; it is strongly associated with increased risk of accidental death and cardiovascular disease. Research has focused on XII motoneurons to advance understanding of how reduced motoneuron excitability contributes to OSA, yet pharmacological therapies are still lacking. My attention has turned to XII premotoneurons, which present novel targets for pharmacological intervention. Very little is known about these neurons. They are widely dispersed at low density and have been very hard to locate. My research has discovered a molecular marker for these neurons; using a transgenic mouse model in which these neurons express a fluorescent protein makes them easy to find. Using this model, I discovered that >50% of these neurons are excitatory, and, using selective laser ablation methods, that they relay inspiratory drive from the preBötzinger Complex. These discoveries form the foundation of my future research program that will characterize the cellular and synaptic properties of these neurons, their connectome, and their modulatory control across sleep wake states. Data will inform development of novel therapies for OSA.