Title: Neural circuits underlying sodium homeostasis

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Abstract: Sodium is the main cation in the extracellular fluid, and it regulates various physiological functions. Depletion of sodium in the body increases the hedonic value of sodium taste, which drives animals towards sodium consumption. By contrast, oral sodium detection rapidly quenches sodium appetite, suggesting that taste signals have a central role in sodium appetite and its satiation. Nevertheless, the neural mechanisms of chemosensory-based appetite regulation remain poorly understood. Here we identify genetically defined neural circuits in mice that control sodium intake by integrating chemosensory and internal depletion signals. We show that a subset of excitatory neurons in the pre-locus coeruleus express prodynorphin, and that these neurons are a critical neural substrate for sodium-intake behavior. Acute stimulation of this population triggered robust ingestion of sodium even from rock salt, while evoking aversive signals. Inhibition of the same neurons reduced sodium consumption selectively. We further demonstrate that the oral detection of sodium rapidly suppresses these sodium-appetite neurons. Simultaneous in vivo optical recording and gastric infusion revealed that sodium taste—but not sodium ingestion per se—is required for the acute modulation of neurons in the pre-locus coeruleus that express prodynorphin, and for satiation of sodium appetite. Moreover, retrograde-virus tracing showed that sensory modulation is in part mediated by specific GABA (γ-aminobutyric acid)-producing neurons in the bed nucleus of the stria terminalis. This inhibitory neural population is activated by sodium ingestion and sends rapid inhibitory signals to sodium-appetite neurons. Together, this study reveals a dynamic neural circuit that integrates chemosensory signals and the internal need to maintain sodium balance.