A neural circuit that responds to threats and controls appetite

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Both visceral and somatosensory neuronal information is relayed to higher brain regions by glutamatergic neurons that reside in the parabrachial nucleus (PBN) that express calcitonin gene-related peptide (CGRP) and several other neuropeptides. Activation of these CGRP-expressing neurons either by photo-activation of channelrhodopsin (ChR2) or CNO activation of hM3Dq DREADD receptors inhibits feeding and chronic activation of these neurons would lead to starvation. Additional experiments demonstrate that a relevant output of these CGRP-expressing neurons that mediates anorexia is a projection to the lateral capsule region of the central nucleus of the amygdala onto neurons that express the receptor for CGRP. Pairing artificial activation of CGRP-expressing neurons with either a novel taste or a novel tone/context is sufficient to establish conditioned taste aversion or fear behaviors (freezing), respectively. Inactivation of CGRP neurons ameliorates taste or fear conditioning, indicating that they transmit the classical unconditioned stimulus for both of these learning paradigms. Calcium imaging reveals that virtually CGRP neurons are activated by all threats that have been examined; thus, they serve as a general alarm system. These neurons respond to potential threats and cues that have been associated with harm in the past. Different threats are presumably distinguished by the intensity of the stimulations and where conditioned stimuli (sensory cues) and unconditioned stimuli (pain) converge in the brain.