

Recent Advances in Network Electrophysiology Using Multi-Electrode Arrays

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Convention Center, Room 3, San Diego, CA

Actions of Serotonin (5-HT) in the Arcuate Nucleus.

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Introduction: The neuronal systems regulating food intake and body weight control include several hypothalamic nuclei. The arcuate (ARC) nucleus is thought to regulate food intake with neurons providing both anorexic and orexic signals. Although a balance between these competing signals likely determines the ultimate drive, the mechanisms and pathway of cross talk between these regions are unknown. 5-HT has been demonstrated to inhibit food intake via activation its receptors in VMH and ARC. We sought to simultaneously determine the localization and response of ARC neurons to serotonin, an anorexic-inducing agent, in the presence of intake and block synaptic transmission, to assess the pathways of orexic regulation.

Methods: Adult rats (n=13) maintained on ad lib diets were sacrificed and hypothalamic brain slices (375 μm) freshly prepared. Slices were positioned to simultaneously measure up to 64 neuronal sites, within the ARC using the MED-64 system (Alpha MED Sciences, Japan). During a stabilization period (20 min), active neurons were defined as a firing rate 2.84 ± 0.21 spikes/s. Neuronal responses to 5-HT (30 μM) (n=42) were quantified as firing rates increases or decreases (20% change). Effects of 5-HT during synaptic blockade (n=56) were examined in a low Ca^{2+} /high Mg^{2+} solution (0.25 mM Ca^{2+} /4.7 mM Mg^{2+}). Electrical activities were recorded and analyzed in customized software.

Results: During the stabilization period, 42 ARC neurons demonstrated a stable basal activity (2.84 ± 0.21 spikes/s) with localization in both medial and lateral regions. 5-HT administration significantly reduced firing rates in 45%, increased firing in 31%, and did not change firing in 24% of neurons. Inhibited neurons localized primarily to the medial region, with stimulated cells localized to the lateral region. Under conditions of synaptic blockade, there was an increase in basal neuronal activity (3.60 ± 0.32 spikes/s; $p < 0.05$). The response to 5-HT was significantly different with reduced firing rates in only 25% ($p < 0.05$), similar increased firing in 21 cells (38%), and no change in four neurons. The reduction in firing rates was focused on the medial region.

Conclusions: These electrophysiological responses demonstrate region specific responses of the ARC. Responses to the anorexic agent 5-HT suggest that the medial region produces primarily orexic signals and a lateral region anorexic signals. The blunting of the inhibition of medial (orexic responses) in the presence of synaptic blockade suggests that basal anorexic pathways from the lateral to medial regions regulate both basal orexic drive and 5-HT induced anorexia.