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Series: Graduate and CTN

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Topic: Dissertation Defense: Glutamatergic Fast Synaptic Neurotransmission in the Pedunculopontine and Dorsal Subcoeruleus Nuclei: Implications for Arousal

Abstract:

The pedunculopontine nucleus (PPN) is involved in the generation and maintenance of the cortically activated states of waking and rapid eye movement (REM) sleep, forming part of the brainstem reticular activating system (RAS). The dorsal subcoeruleus nucleus (SubCD) is a descending target of the PPN involved in the generation of REM sleep, muscle atonia, and ponto-geniculo-occipital (PGO) waves. The PPN and SubCD receive glutamatergic afferents from other mesopontine nuclei, and glutamatergic input has been proposed to be involved in the generation of arousal states. Injections of specific glutamate (Glu) receptor agonists into the PPN of the rat increased waking or REM sleep, while injections into the SubCD induced a REM sleep-like state with muscle atonia. Whole-cell patch clamp recordings were performed on brainstem slices from 9 to 17 day-old rat pups to test the effects of glutamatergic input to the PPN and SubCD *in vitro*. This age range was selected because it spans the developmental decrease in REM sleep that occurs in the rat from birth to postnatal day 30. Pharmacological and electrical stimulation were used to measure glutamatergic responses of PPN and SubCD neurons. These studies revealed that 1) all cells in the PPN and SubCD are excited by the Glu receptor agonists N-methyl-D-aspartic acid (NMDA) and kainic acid (KA). 2) In the PPN, a developmental decrease in the contribution of the NMDA receptor and developmental increase in the contribution of the KA receptor was observed following local stimulation and agonist exposure in different cell types. 3) In the SubCD, no developmental changes were observed in the relative contribution of KA and NMDA receptors to the response following local stimulation. However, there was a developmental decrease in the half-width duration of evoked responses and a decrease in the response following agonist exposure. 4) PPN afferents contain presynaptic KA receptors located on axon terminals that function to decrease Glu release. 5) Glutamatergic inputs induce membrane oscillations in PPN and SubCD neurons, which may underlie the repetitive AP firing properties of these neurons. Together, these studies provide novel information about the role of Glu in the RAS.