Investigating a Model System of Learning and Memory:

The Role of Secretin in Different Regions of Cerebellar Cortex

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Abstract

A novel cellular mechanism that may underlie mammalian learning and memory has been investigated using the model of cerebellar voltage-gated ion channel regulation and eyeblink conditioning (EBC). The learned response is an eyeblink conditioned response (CR) to a tone that precedes an eyelid stimulation. Secretin is a neuropeptide released from depolarized Purkinje cells in the cerebellar cortex that may modulate EBC by downregulating Kv1.2 potassium channels. Our laboratory has previously shown that infusions of either the Kv1.2 blocker tityustoxin or the Kv1.2 down-regulator secretin into the cortex of the cerebellum facilitates conditioning of EBC. However, these infusions were relatively large (1.0 μL), so it is difficult to know exactly which region of cerebellar cortex mediates this effect. With smaller volume, more localized infusions, we hypothesized that secretin infused into the lobulus simplex of the cerebellar cortex would facilitate acquisition of CRs, while secretin infusion into the anterior lobe of the cerebellar cortex would cause CRs to occur sooner after tone CS onset. This was tested by surgically implanting a cannula with its tip either in the lobulus simplex or anterior lobe of the cerebellar cortex of rats, then infusing a small volume (0.25 μL) of either secretin (1 μg/μL) or vehicle into said cannula prior to the first two days of EBC. The rats were run through a total of six days of EBC, with one 100-trial session per day. In each trial, a tone was paired with an eyelid stimulation. The rate of acquisition of the tone-eyelid stimulation association as well as the latency of conditioned responses were analyzed statistically. No differences were found between groups. We are continuing to try to identify small areas of cerebellar cortex that mediate the effects of secretin on EBC. Localization of a precise area will help us in identifying the role of voltage-gated ion channel regulation in learning.