Cerebellum-Dependent Learning is Modulated by Cerebellar Secretin

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Eye blink classical conditioning (EBC) is a type of associative learning in which a tone is presented and coterminates with a brief stimulation to the eyelid. The association between the tone and the eyelid stimulation is formed and stored in the cerebellar cortex and the deep cerebellar nuclei (DCN). A previous experiment from our laboratory demonstrated that 1.0 ul infusions of the neuropeptide secretin into the cerebellar cortex facilitated EBC when infusions were over the first 3 days of learning (Williams et al., 2012). Since 1.0 ul of secretin likely reached a fairly large area of cerebellar cortex, the purpose of the present experiment was to determine whether we could replicate these results by limiting our infusions to a sub-area of the region targeted in our initial experiment. The current experiment involved infusions on only the first 2 days of EBC using a smaller volume (0.5 ul) in a slightly more lateral set of coordinates hypothesized to be directly involved in EBC. Rat subjects received infusions of secretin or vehicle immediately prior to the first two days of EBC followed by four more days of EBC without infusions. Each day of EBC consisted of 10 blocks of 10 trials each. Each block of 10 trials consisted of the following trial sequence: 4 tone–eyelid stim trials, 1 tone trial, 4 tone– eyelid stim trials, 1 eyelid stim trial. Following EBC, cerebellar tissue was analyzed to confirm the location of infusions. The results of this experiment supported the hypothesis that fewer infusions are needed with a smaller volume of secretin to facilitate EBC. This suggests that we have found where in the cerebellar cortex secretin has the greatest effect on EBC. We propose a model whereby secretin acts to increase inhibition of inhibitory Purkinje cells, which provide the sole output of the cerebellar cortex to the DCN. Inhibition of Purkinje cells would lead to disinhibition of the DCN, facilitating EBC.