Possible Effects of I_h on Locomotor Networks in the Lamprey Spinal Cord

Dana Watt
Carthage College
Program Mentor: Dr. James Buchanan

Cyclic locomotion is generated by neuronal networks in the spinal cord called central pattern generators (CPGs) that provide rhythmic excitation and inhibition of motor neurons. The rhythmic output of CPGs can be modified by altering the intrinsic firing properties of their individual cells. The firing properties of the cells are the product of many interacting ionic currents, one of which may be I_h. When a cell becomes hyperpolarized, I_h channels will open and allow a depolarizing cation current to flow. Although well characterized in cardiac cells, the role of I_h in the generation and maintenance of vertebrate locomotor activity has yet to be addressed. The purpose of the present study was to determine whether I_h contributes to the generation and maintenance of vertebrate locomotion by studying its effects on locomotor activity in the isolated spinal cord preparation of the lamprey. The spinal cord of the lamprey, a lower vertebrate, exhibits the neural correlate of locomotion *in vitro* ("fictive swimming") and the underlying central pattern generator is better understood than those of higher vertebrates.

Fictive swimming is induced by bath application of D-glutamate (0.5 mM) to the isolated spinal cord and the rhythmic activity of swimming is monitored with extracellular suction electrodes placed on the ventral roots. The I_h current can be blocked using ZD7288. Effects of ZD7288 on fictive swimming were statistically significant at 10 μM. We found that bath application of ZD7288 to fictively swimming spinal cord preparations had two effects. First, the cycle period of ventral root bursting significantly increased across preparations. In individual preparations, an increase in cycle period was first observed within 15 minutes of the onset of ZD7288 perfusion. A gradual increase in cycle period continued for about 60 minutes with normal variability of cycle periods. Second, the cycle period began to exhibit variability after 60 minutes. We measured this variability or "quality of rhythmic activity" using an autocorrelation technique. The quality of rhythmic activity of ventral root bursting significantly decreased across preparations and was associated with the onset of a slow modulation of cycle period with periods of slow and fast swimming alternating. Experiments were performed using intracellular recording techniques to attempt to characterize the underlying cellular mechanism of the effects. Application of ZD7288 to motor neurons during fictive swimming tended to hyperpolarize the membrane potential but had little or no effect on the rate of depolarization. In motor neurons exhibiting NMDA-induced, TTX-resistant oscillations, application of ZD7288 both hyperpolarized the cell and increased the oscillatory cycle period. The increase in cycle period of fictive swimming suggests that I_h contributes to rhythm generation by the locomotor central pattern generator. While the effects of I_h in motor neurons appear small, it is possible that a small I_h is sufficient to account for the network effects. Alternatively, it is possible that interneurons of the network may have stronger I_h currents.