

# International Conference on Parkinson's Disease & Movement Disorders

August 11-13, 2015 Frankfurt, Germany

## Bi-directional modulation by HCN channels on globus pallidus neurons

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**H**yperpolarization-activated Cyclicnucleotide-gated (HCN) channels occupy a critical position in globus pallidus pace-making activity. Morphological studies have shown the expression of HCN channels in the globus pallidus. To investigate the *in vivo* effects of HCN channels in the globus pallidus, extracellular recordings and behavioral tests were performed in the present study. In normal rats, micro-pressure ejection of 0.05 mM ZD7288, the selective HCN channel blocker, decreased the frequency of spontaneous firing in 21 out of the 40 pallidal neurons. The average decrease was  $50.4 \pm 5.4\%$ . Interestingly, in another 18 out of the 40 pallidal neurons, ZD7288 increased the firing rate by  $137.1 \pm 27.6\%$ . Similar bi-directional modulation on the firing rate was observed by a higher concentration of ZD7288 (0.5 mM) as well as another HCN channel blocker, CsCl. Furthermore, activation of HCN channels by 8-Br-cAMP increased the firing rate by  $63.0 \pm 9.3\%$  in 15 out of the 25 pallidal neurons and decreased the firing rate by  $46.9 \pm 9.4\%$  in another 8 out of the 25 pallidal neurons. Further experiments revealed that modulation of glutamatergic but not GABAergic transmission may be involved in ZD7288-induced increase in firing rate. Consistent with electrophysiological results, further studies revealed that modulation of HCN channels also had bi-directional effects on behavior. Taken together, the present studies suggest that HCN channels may modulate the activity of pallidal neurons by different pathways *in vivo*.

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