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Abstract:

Controlling Serotonergic Neuronal Activity: A Strategy to Influence Long-term Mood?

Nicholas J. Penington and Lorin S. Milescu. Downstate Health Sciences University, Dept. of Physiology/Pharmacology and U. Maryland, Dept. Biology.

There are many lines of evidence suggesting that 5-HT release from serotonergic neurons has a long-term modulatory effect on mood. This is the basis for the therapy that utilizes the 5-HT-selective reuptake blockers. We have been probing the gaps in our understanding of the regulation of the firing of these cells in order to comprehend how the activity is regulated in the short and long-term. A small, slowly developing, depolarizing influence is required to maintain slow pace-making in these cells and this was originally modeled with a leak conductance in the inter-spike interval. Fast recovering sodium current (I_{Na}) inactivation occurs for 80% of the sodium current in serotonergic neurons but 20% of it recovers slowly over a period of 1 to 2 seconds; termed long term inactivation (LTI). The recovery from LTI allows for a small, slow, inward current that may fulfill the function of the modeled pacemaker current. The presence of LTI was confirmed in acutely isolated adult dr neurons in both rat and mouse. "Dynamic clamp" was used in post-natal ventral raphe (vr) neurons where the sodium current was blocked with TTX and a model sodium current was injected to replace it. The amount of LTI associated with the injected I_{Na} was varied and the contribution of LTI to firing rate modulation in the control neurons was determined. LTI was shown to regulate the firing of vr neurons and it may also play a role in recovery from the acute inhibitory effects of antidepressant drugs.