LITHIUM REGULATES NEURONAL EXCITABILITY IN RAT HIPPOCAMPUS

Luca Murru, M. Carta, S. Pitzianti. G. Corda, E. Sanna and G. Biggio.

Dept. Experimental Biology, Sect of Neuroscience, and Center of Excellence for the Neurobiology of Dependence. Cittadella Universitaria, SS 554 Km 4,500, 09042, Monserrato, Cagliari, Italy

Lithium (Li^+) has been prescribed for many years in the psychiatric domain as mood-stabilizer to treat manic-depressive disorders. However, despite its wide use its precise molecular mechanism of action is still not completely clear. In the hippocampus the functioning of the entire network is tightly regulated by GABA released from local inhibitory interneurons. Recent postmortem studies have provided consistent evidence that a defect of the GABAergic neurotransmission probably plays a role in bipolar disorder.
In the present study, using electrophysiological techniques, we investigated the possibility that Li^+ may alter the GABAergic inhibition. We prepared coronal hippocampal slices from 30-40 day old Sprague-Dawley male rats. Whole-cell patch clamp recording of pharmacologically isolated spontaneous inhibitory post synaptic currents (sIPSCs) were performed from granule cells of the dentate gyrus (DGGCs) of the hippocampus. After a baseline period of 5 minutes, application of Li^+ (25 mM) for 10 minutes induced a reversible increase of the frequency, but not amplitude, of sIPSCs. We tested the same concentration of Li^+ in other 8 neurons and we found a significant enhancement ($p< 0.01$, $n=7$) of 88.1 ± 20.1 % from baseline level in the frequency of sIPSCs.
These preliminary data clearly suggest that Li^+ may act by enhancing GABAergic inhibition to physiological levels. Further experiments are currently in progress in order to understand the mechanism that leads to an increased GABA release and how this enhanced inhibition can regulate the excitability of the hippocampal circuit.