LITHIUM EFFECT ON PURINERGIC RECEPTORS AND ECTONUCLEOTIDASES GENE EXPRESSION IN RAT PREFRONTAL CORTEX AND HIPPOCAMPUS

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Introduction and objectives: From the last decades, lithium is being largely used for reversing and avoiding recurrent manic crisis in patients with Bipolar Disorder (BD). Even though, little is known about the etiology of BD or about the mechanisms involved on lithium (and others mood stabilizers) use for treating/preventing mania. The physiopathology of BD shows the involvement of different signaling pathways, including the purinergic system. The role of purinergic system in BD is still debatable. The presented work evaluated the gene expression of purinergic receptors and ectonucleotidases in hippocampus and prefrontal cortex of healthy rats after intraperitoneal administration of lithium chloride.

Materials and methods: Purinergic receptors and ectonucleotidases expression was analyzed in prefrontal cortex and hippocampus of adult rat on day 7 following treatment with lithium chloride (LiCl) compared to saline control (NaCl). Adult Sprague-Dawley rats (age 100-120 days; weight 450-550g) were subjected to repeated intraperitoneal (I.P.) injections twice per day for a period of 7 days with 47.5 mg/kg LiCl (n=7) or 0.9% NaCl (n=7). Prefrontal cortex (PFC) and hippocampus (HC) of treated adult rats were collected two hours after the last treatment and RNA was isolated followed by cDNA synthesis for RT-qPCR analysis.

Results and conclusions: Gene expression analysis of P1(A1, A2a, A3), P2X(2-7) and P2Y(4, 12, 13, 14) purinergic receptors were significantly downregulated in the PFC but not in HC of rats after LiCl administration. In addition, ectonucleotidases ENTPD(1, 2, 3, 5 6, 8) and CD73 were downregulated in both CPF and HC. The results show that the purinergic system in the prefrontal cortex is part of the mechanism of action of Lithium due to the downregulation of the gene expression of its receptors and metabolic enzymes. Further studies are necessary for elucidating the underlying mechanisms.

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