Effect of Lithium and Valproate on Cerebral Energy Metabolism and Behavior Parameters of Rats Submitted to Animal Model of Mania Induced by Fenproporex

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Introduction: Bipolar disorder (BD) is a devastating major mental illness associated with high rates of suicide and work loss. There is an emerging body of data suggesting that BD is associated with mitochondrial dysfunction. Fenproporex is converted in vivo into amphetamine, which is used to induce animal model of mania. Objectives: In this context, the present study aims to investigate the effects of mood stabilizers lithium (Li) and valproate (VPT) on enzymes of the energy metabolism in brain of rats submitted to animal model of mania with fenproporex. Methods: In the reversal treatment, Wistar rats were first given fenproporex or Tween 2% (control) for 14 days, and then, between days 8-14, rats were treated with Li, VPT or Tween 2%. In the prevention treatment, rats were pretreated with Li, VPT or Tween 2%. Locomotor behavior was assessed using the open-field task and citrate synthase, malate dehydrogenase, succinate dehydrogenase, creatine kinase, mitochondrial chain activity complexes I, II, II-III and IV were measured in brain structures (hippocampus, striatum and prefrontal). Li and VPT reversed and prevented fenproporex-induced hyperactivity. In both experiments, fenproporex inhibited enzymes of the energy metabolism only in the hippocampus. In the reversal treatment, Li and VPT reversed fenproporex-induced mitochondrial dysfunction. In the prevention treatment, Li and VPT prevented fenproporex-induced mitochondrial dysfunction, except the inhibition in the complex IV activity. Conclusions: These findings suggested that dopamine can be an important link for the mitochondrial dysfunction seen in BD and, Li and VPT exert protective effects against this fenproporex-induced mitochondrial dysfunction in the hippocampus.

Word Keys: Behavior activity; Bipolar disorder; Fenproporex; Mitochondrial dysfunction; Mood stabilizers.
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