Inhibited Enzymes Krebs Cycle in the Brain of Rats After Acute and Chronic Administration of Methylphenidate

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Attention deficit/hyperactivity disorder (ADHD) is a neuropsychiatric syndrome, highly prevalent during childhood, which is characterized by impaired attention, excessive motor activity and impulsivity. Pharmacotherapy using psychostimulant medications, such as methylphenidate, is rigorously the most accepted pharmacological treatment for ADHD patients. Considering that impairment of brain energy metabolism is linked to neuronal death and that mechanisms underlying MPH therapeutic and side effects are poorly known, in the present work we evaluated citrate synthase, malate dehydrogenase and isocitrate dehydrogenase activity in brain of adult rats following acute or chronic administration of MPH. For acute administration, a single injection of methylphenidate (1, 2 or 10 mg/kg) was given to 60-day-old rats. For chronic administration, methylphenidate injections, same concentrations were given to daily for 28 days. Control animals received saline intraperitoneally in the same volumes. Two hours after the last injection, the animals were killed by decapitation, the brain was removed and enzymes activity were measured. Our results demonstrated that methylphenidate acute administration decreased the isocitrate dehydrogenase activity in posterior cortex (10 mg/kg) and cerebellum (2 and 10 mg/kg) of rats. The MPH chronic administration in rats decreased the citrate synthase activity in cerebellum (10 mg/kg) and hippocampus (2 and 10 mg/kg) and decreased isocitrate dehydrogenase in cerebellum (10 mg/kg) and hippocampus (1, 2 and 10 mg/kg). The malate dehydrogenase activity was not altered. Our results demonstrated that some enzymes of Krebs cycle were inhibited after methylphenidate administration, thus contributes understand the mechanisms underlying MPH.

Keywords: Methylphenidate; Krebs cycle; brain.

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