Methylphenidate Induces Neurons and Astrocytes Loss in Hippocampus and Behavior Changes in Juvenile Rat

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INTRODUCTION. The investigation of the long-term consequences of early treatment with methylphenidate (MPH) on brain and behavior is very important since the abuse of this psychostimulant is rising, particularly during childhood and adolescence. Added to this, little is known about the consequences of chronic use of MPH on the developing brain. **OBJECTIVES:** In the present study, we investigate biochemical and histochemical alterations in the hippocampus, as well as assessment the performance of juvenile rats chronically treated with MPH in behavioral tasks. **MATERIAL AND METHODS**: In this study, Wistar rats received intraperitoneal injections of MPH (2.0 mg/kg) or an equivalent volume of 0.9% saline solution (controls), once a day, from the 15th to the 45th day of age. Twenty-four hours after the last administration of MPH the rats were decapitated (for biochemical studies), or perfused (for histochemical studies) or subjected to the behavioral tasks. Student's t test was used to evaluate the different parameters after the dates presented a normal distribution in Shapiro–Wilk test. **RESULTS AND DISCUSSION**: We showed that chronic MPH treatment promoted a loss of astrocytes and neurons in hippocampus of juvenile rats. BDNF and pTrkB immunocontents, and NGF levels were decreased; while TNF-α and IL-6 levels, Iba-1 and caspase 3 cleaved immunocontents (active microglia marker and active apoptosis marker, respectively) were increased. ERK and PKCaMII signaling pathways, but not Akt and GSK-3β were decreased. We also observed that SNAP-25 was decreased by MPH treatment, while GAP-43 and synaptophisyn were not altered. Exploratory activity and memory of object recognition were impaired by MPH treatment. **CONCLUSION:** These findings provide additional evidence that early-life exposure to MPH can have complex effects, as well as provide new basis for understanding of the biochemical and behavioral consequences associated with chronic use of MPH during the development of central nervous system.

Keywords: Methylphenidate; Neurons and astrocytes cells; Neurotrophins; Cytokines; Cell survival pathways

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