

# 5-HT<sub>1A</sub> receptors in the reinforcing effects of methylphenidate and its modulation with buspirone

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## Abstract

Accumulating studies consistently show that methylphenidate (MPD), the first line drug for treating Attention-Deficit Hyperactivity Disorder (ADHD), is abused by patients to whom the drug is prescribed. Like other psychostimulants, only low doses of MPD improve cognitive performance while higher doses can impair it. Preventing the use of high doses of MPD is important for preventing its overuse and for retaining its therapeutic efficacy. Previously, we have shown that performance in Morris water test was improved in rats treated, orally, with MPD in doses of 2.5 mg/kg; but higher doses (5 mg/kg) impaired it. The present study concerns rewarding/reinforcing effects of 2.5 mg/kg MPD in conditioned place preference (CPP) paradigm and its modulation with buspirone. Our results show that rewarding effects of MPD in CPP test are prevented in rats co-treated with buspirone in doses of 0.1 and 0.3 mg/kg. Animals treated with MPD exhibit a down regulation of 5-HT<sub>1A</sub> receptor in the nucleus accumbens which is reversed in rats co-treated with 0.1 and 0.3 mg/kg buspirone. Administration of buspirone in these doses is not rewarding in CPP test and produces an upregulation of 5-HT<sub>1A</sub> receptor in the nucleus accumbens. The findings suggesting an important role of 5-HT<sub>1A</sub> receptor in the rewarding effects of MPD, open a gateway for improving therapeutic use of MPD.

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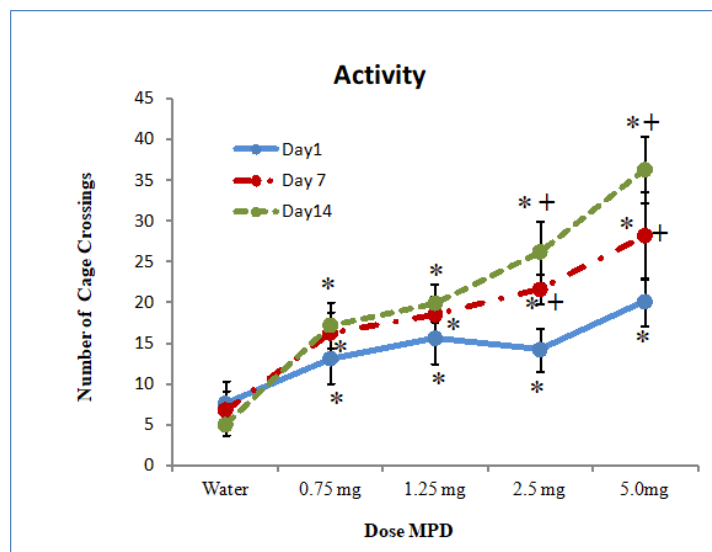


Figure 1

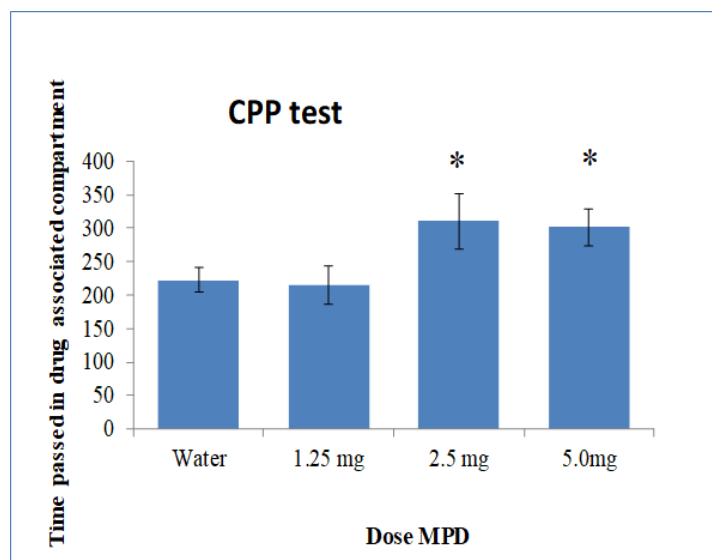


Figure 2

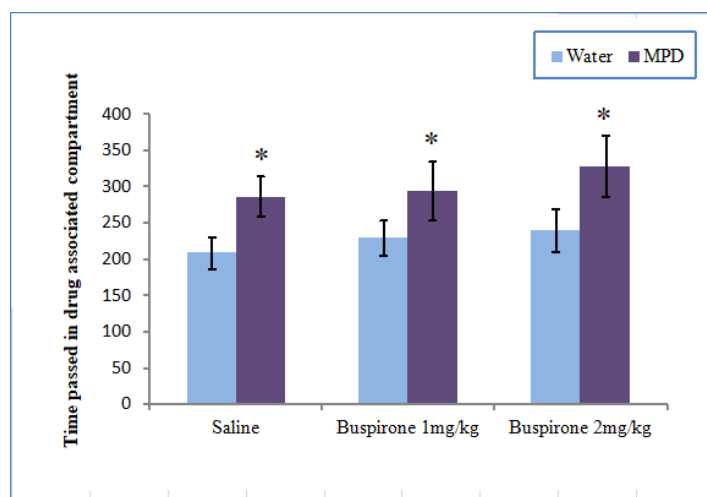


Figure 3

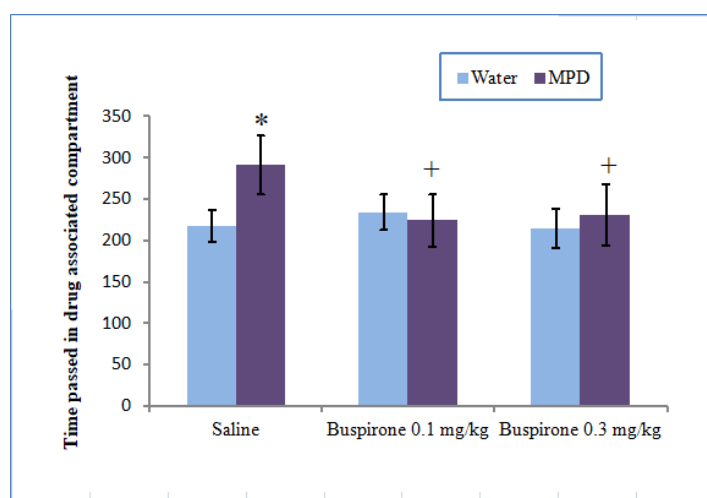


Figure 4

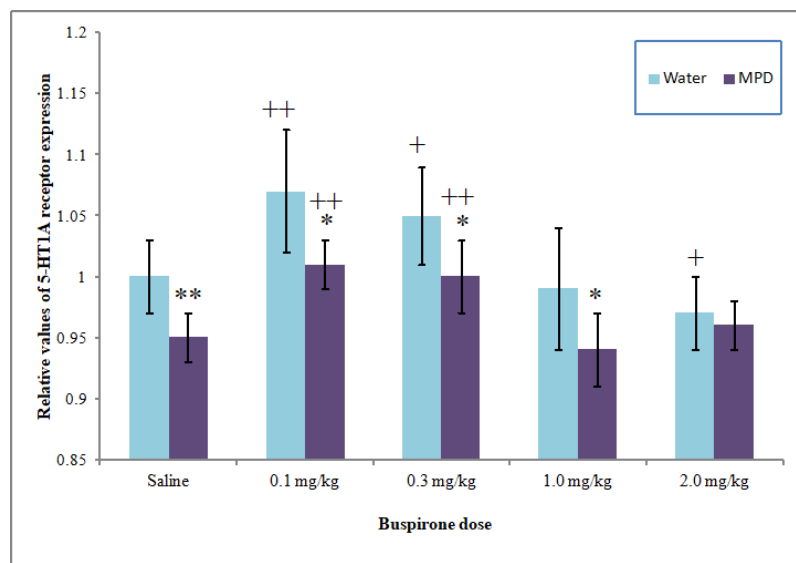


Figure 5

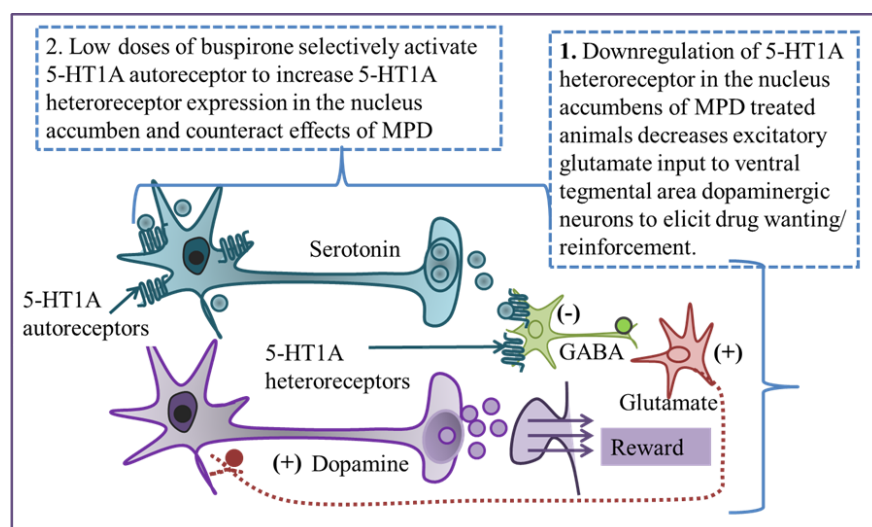


Figure 6