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Serotonin-1A receptor expression in the reinforcing effects of methylphenidate

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Methylphenidate(MPD) is widely prescribed for the treatment of attention deficit hyperactivity disorder(ADHD). Despite its therapeutic importance, there is growing evidence that patients treated with MPD develop an addiction to their therapy. It is therefore important to monitor abuse potential and understanding molecular mechanism involved in cognition enhancing and reinforcing effects of MPD. This experiment is designed to study abuse potential, if any, of clinically relevant doses of MPD. In view of a role of 5-HT(serotonin)1A receptor in cognition as well as addiction, the expression of 5-HT-1A receptors in the prefrontal cortex and nucleus accumbens is monitored in rats repeatedly treated with MPD. We found that lower and clinically relevant doses (0.5 and 2.5 mg/kg) of MPD enhanced learning acquisition and memory retention in a dose dependent manner, but higher doses (5 mg/kg) impaired these. The drug administered repeatedly at a dose of 2.5 mg/kg produced only mild and transient sensitization but was reinforcing. Repeated MPD treated animals exhibited improved memory retention but no effect occurred on learning acquisition. The expression of 5-HT-1A receptor was markedly attenuated in the nucleus accumbens, but not in the prefrontal cortex. The results supporting a role of 5-HT-1A receptors in addiction are of use in improving therapeutics in ADHD.

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