Chronic methylphenidate treatment during adolescence has long-term effects on monoaminergic function

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Abstract

BACKGROUND:
Psychostimulants like methylphenidate or D-amphetamine are often prescribed for attention deficit and hyperactivity disorders in children. Whether such drugs can be administered into a developing brain without consequences in adulthood is still an open question.

METHODS:
Here, using in vivo extracellular electrophysiology in anesthetised preparations, combined with behavioural assays, we have examined the long-term consequences in adulthood of a chronic methylphenidate oral administration (5 mg/kg/day, 15 days) in early adolescent (post-natal day 28) and late adolescent (post-natal day 42) rats, by evaluating body weight change, sucrose preference (indicator of anhedonia), locomotor sensitivity to D-amphetamine and electrical activities of ventral tegmental area dopamine and dorsal raphe nucleus serotonin neurons.

RESULTS:
Chronic methylphenidate treatment during early or late adolescence did not induce weight deficiencies and anhedonia-like behaviours at adulthood. However, it increased bursting activities of dorsal raphe nucleus serotonin neurons. Furthermore, chronic methylphenidate treatment during early but not during late adolescence enhanced D-amphetamine-induced rearing activity, as well as ventral tegmental area dopamine cell excitability (firing, burst and population activity), associated with a partial desensitisation of dopamine D2 auto-receptors.

CONCLUSIONS:
We have demonstrated here that early, but not late, adolescent exposure to oral methylphenidate may induce long-lasting effects on monoamine neurotransmission. The possible clinical implication of these data will be discussed.