Dopamine 2016
Vienna, 5–8 September 2016

MEETING ABSTRACT

A13.1
The role of striatal adenosine A2A—dopamine D2 interactions in cocaine addiction
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Cocaine is one of the most addictive substances in humans and its dependence is characterized by high risk of relapse following periods of abstinence. Cocaine is accepted as to its rewarding properties resulting from the activation of the mesolimbic dopamine (DA) system including DA neuron projections from ventral tegmental area to the nucleus accumbens (NAc) and prefrontal cortex (PFC) [1]. Recent studies indicate that adenosine (ADO) may influence DA neurotransmission through A2A receptors antagonistically interacting with D2 receptors [2]. In the present study we examined the effects of selective A2A receptor ligands (the agonist CGS 21680 and the antagonists KW 6002 or SCH 58261) as well as of the D2-like receptor ligands (the agonist quinpirole and antagonist raclopride) in cocaine self-administration and reinstatement procedures in rats. For comparison, effects of the A2A receptor ligands on rewarding effects of food and food seeking were also analyzed. The obtained results demonstrate the lack of tonic A2A receptor activation in rewarding effects of artificial and natural rewards because none of the tested A2A antagonists affected their behaviors in rats. On the other hand, the selective A2A receptor agonist CGS 21680 reduced both rewarding effects of intravenous cocaine and food. A2A receptors are also implicated in relapses to cocaine behavior since their blockade induced cocaine and food seeking, while their stimulation inhibited not only cocaine and food seeking but also reinstatement induced by conditioned cue. A potent reduction toward the cocaine-, quinpirole-, cue- or A2A receptor antagonist-induced reinstatement of cocaine seeking was seen after raclopride administration. The results indicate that A2A activation and D2-like receptor blockade counteract cocaine and food relapse. As shown by using microinjection technique, CGS 21680-mediated inhibitory actions towards cocaine reward and seeking effects depend on stimulation of A2A receptors localized in the NAc. In conclusion, our results indicate the significance of agonist induced A2A receptor stimulation in counteracting the rewarding actions of artificial and/or natural rewards. The study points to A2A receptors as a new drug target in cocaine abuse treatment strategies.

Supported by the Polish National Science Centre in Kraków (grant no. 2011/03/N/NZ7/06294).

Reference

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