Abstract View

BEHAVIORAL AND NEUROCHEMICAL CHANGES ASSOCIATED WITH (+/-)-MDMA SELF-ADMINISTRATION IN RATS

M.E.Reveron*; C.L.Duvauchelle

Div. of Pharm./Tox., The Univ. of Texas, Austin, TX, USA

(+/-)3,4-Methylene-dioxymethamphetamine ((+/-)-MDMA) is an amphetamine analogue that affects serotonin (5-HT) neurotransmission in humans and experimental animals. MDMA administration causes 5-HT and dopamine (DA) release from nerve terminals such as the nucleus accumbens (NAcc). Though several studies have investigated the neurotoxic outcome of experimenter-administered MDMA in high dosages, few studies have examined the neurochemical and rewarding effects of MDMA through voluntary intake (e.g., self-administration). In the present study, behavioral, NAcc DA and 5-HT changes associated with MDMA self-administration were assessed in male Sprague Dawley rats. MDMA was self-administered during twenty daily 2-hr sessions (0.5 and 1.0 mg/kg/infusion). During initial sessions, rats exhibited flattened body postures, low levels of MDMA self-administration and locomotor activity. However, as MDMA self-administration sessions progressed, body position normalized, MDMA intake increased and locomotor activity was enhanced. In vivo microdialysis in both MDMA-naive and experienced animals revealed that (+/-)-MDMA (3.0 mg/kg, i.v.) had greater effects on basal NAcc 5-HT levels (~500-fold) compared to NAcc DA changes (~200-fold). Tissue analyses of hippocampal and prefrontal cortex 5-HT and 5-hydroxyindole acetic acid (5-HIAA) in rats that had self-administered MDMA over 20 sessions (cumulative intake approx. 50-149 mg/kg, i.v.), revealed 5-HT and 5-HIAA levels to be comparable to MDMA-naive controls. These findings seem at odds with toxicology studies showing profound hippocampal and cortical 5-HT and 5-HIAA depletions in rats seven days after a single experimenter-administered injection of (+/-)-MDMA (10 and 15 mg/kg, i.p.). Such disparities support the notion that the presence of neurotoxic intermediates during MDMA metabolism are dose-dependent.

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