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Assessing psychoactivity of the MDMA analogue 6-F-MDMA as potential medicinal agent

Rationale and hypothesis: Sensorimotor gating is the ability of one stimulus to modify a motor response to another stimulus. A typical measure of sensorimotor gating is prepulse inhibition (PPI) of the acoustic startle reflex, where a weak, non-startling stimulus reduces the startle response to a second intense acoustic startling stimulus. MDMA (3,4 methylenedioxymethamphetamine) reverses the vesicular monoamine transporter type 2 (VMAT-2), the serotonin transporter (SERT), and, to lesser extent, the dopamine transporter (DAT) resulting in elevated levels of serotonin and dopamine in of the extracellular space of experimental animals and thereby impairs sensorimotor gating. PPI is also disrupted in schizophrenia and other psychiatric illnesses. In these conditions PPI has been proposed to reflect an inability to inhibit irrelevant sensory information, which would be the prepulse in this case.

Objectives: The first objective of the present study was to examine the effect of MDMA on different parameters of the startle-intensity response magnitude (SIRM) function – a new method of PPI characterization. The second objective was to examine the effect of different doses of an MDMA analogue, i.e. 6-F-MDMA on PPI.

Methods: 72 male Wistar rats were exposed to PPI experiments in this study. Drugs were administered intraperitoneally in a fully-balanced design. MDMA was used as a positive control in order to distinguish which parameters of the SIRM function belong to which neurotransmitter system. To examine the way of action of MDMA we have used haloperidol – a dopamine D₂ receptor antagonist. A dose-response classification of an analogue of MDMA, 6-F-MDMA, was done to assess potential psychoactivity of the drug. MDMA was administered at doses of 5 mg/kg and 6-F-MDMA at doses of 0.2, 0.5, 2 and 5 mg/kg.

Results: By blocking the D₂ receptors with haloperidol, we found a decrease in the SIRM parameter Rₘₐₓ as well as a decrease in general motor activity, but no effect on ES₅₀. The dose-response of 6-F-MDMA did not show any significant effects on PPI measures.

Conclusion: Rₘₐₓ belongs to the motor component of the acoustic startle response and ES₅₀ to the sensory unit. The effect of haloperidol on Rₘₐₓ implies that dopamine is involved, therefore, it seems reasonable to claim that Rₘₐₓ is controlled by the dopaminergic system and we hypothesized that ES₅₀ correlates to serotonergic activity since MDMA also has strong effects on serotonin concentrations. There was no similarity found between MDMA and 6-F-MDMA on parameters like Rₘₐₓ and ES₅₀ as well as general motor activity. At the doses used, we found 6-F-MDMA to show no psychoactive symptoms in rats.