Mescaline effects on rat's behaviour and the time profile of mescaline in rat serum and brain tissue after a single subcutaneous dose using GC-MS

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BACKGROUND: The aim of our study was to evaluate behavioural effects and disposition of mescaline (3,4,5-trimethoxyphenethylamine) in rats. We have concentrated on induced changes in locomotor activity and the deficits in sensorimotor gating. In order to verify whether the peak plasma and brain concentrations of mescaline occur and decline in parallel during the behavioural testing period, we have ascertained the disposition and the time course of mescaline in the blood serum related to the brain.

METHODS: All experiments were carried out on male Wistar rats (200 – 250g). In behavioural experiments each animal was tested only once. Sensorimotor gating was tested with Prepulse inhibition of acoustic startle reaction (PPI)(SR-LAB, San Diego Instruments, USA) and the locomotor activity in the open field test (Ethovision Color Pro. V3.1.1, Noldus, NL). Animals were injected with a single subcutaneous dose (10, 20 and 100 mg/kg) of mescaline hydrochloride salt 15 minutes before testing period. Animals were observed for 30 minutes. For statistical analyses ANOVA on ranks was used (SigmaStat v.3.0) with $p<0.05$ considered as significant. Secondly, single subcutaneous bolus doses (20 mg/kg) were administered and rats were sacrificed (in triplicate) after 30, 60, 120 and 480 min. After sampling, blood sera were separated, and sera and whole brains were kept frozen at –20° C until analyses. Mescaline was isolated from sera and brain homogenates after addition of deuterated mescaline as internal standard and using solid phase extraction discs (SPEC-DAU). The analysis was performed after acetylation by GC-MS in SIM mode. Calibration was based on spiked blank rat sera and brain tissues and linearity was verified in the range up to 2000 ng/ml sera or up to 2000 ng/g brain tissue.

RESULTS: Mescaline induced slight but non-significant decrease in both behavioural parameters in all three doses. After the 20 mg/kg dose, the maximum serum level of mescaline was found after 30 min followed by exponential decline. The maximum level in brain was rather delayed in time; it was achieved after 60 min and slowly declined.

CONCLUSION: These findings are in accord with the theory of delayed and hindered transfer of polar mescaline across the blood-brain barrier. Therefore the higher dose of this substance as well as slower onset of its effects is crucial to induce marked behavioural and psychedelic effects relative to other hallucinogens. Further behavioural measurements with mescaline administered 60 minutes before testing rat's behaviour and with higher doses should be accomplished.

KEYWORDS: *Mescaline, Rats, Blood-brain distribution, GC-MS analyses, Locomotion, Sensorimotor gating*

Acknowledgement: Supported by projects IGA MHCR NR8785-3, IGA MHCR NR8332-3 and MŠMT ČR 1M0002375201

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