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Meeting abstract

Neuromorphological and functional effects of ecstasy during serotonergic damage and recovery

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Background

The ring-substituted amphetamine derivative (±)-3,4-methylendioxymethamphetamine (MDMA; Ecstasy) has become a widely abused psychoactive drug among young people. Studies indicate that MDMA produces long-term alterations of serotonergic parameters in the brain of rodents and primates, and MDMA was also found to be neurotoxic in humans. The aim of our work was to characterize the regional differences of the damage in the terminal and cellular areas, and the alterations during recovery. Serotonin (5-HT) plays a key role in the regulation of sleep, hence we used EEG recordings to measure functional and morphological effects in parallel during partial damage and recovery of brain serotonergic neurons by MDMA.

Methods

Our goal was to investigate the effects of a single dose (15 mg/kg) of MDMA on serotonin transporter and several sleep parameters 7, 21 and 180 days after MDMA administration in the Dark Agouti rat brain. The expression of 5-HT mRNA was compared in MDMA-treated and control animals in the dorsal and median raphe nuclei. The density of immunostained 5-HT fibers was quantified in several brain areas (e.g. cerebral cortex, hippocampus, hypothalamus and brainstem). Immunohistochemical measures and some general parameters (e.g. body weight and food intake) were also determined one year after the treatment.

Results

Seven and 21 days after MDMA treatment we observed significant (20-40%) reductions in 5-HT densities. 5-HT mRNA expressions were significantly elevated 7 days and decreased 21 days after MDMA treatment in the dorsal and median raphe nuclei. We also found alterations in several sleep parameters after drug treatment. Most of the above effects, except the decrease in hippocampal 5-HT densities, were transient; they recovered by 180 days after MDMA administration. One year after MDMA treatment we found some recovery in the hippocampus, but the 5-HT density was still significantly lower in CA2 and CA3 regions.

Conclusion

Our results indicate that a single dose of MDMA causes long-term damage in the terminal regions and also in neural functions of the serotonergic system. Interestingly, although the rate of the axonal damage shows little differences in the regions innervated by ascending axons, the process and speed of recovery differs markedly.

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