Abstract View

LONG-TERM EFFECTS OF (+)-MDMA ON STRIATAL DA AND METABOLITES IN MICE

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3,4-Methylenedioxymethamphetamine (MDMA) is an illegal amphetamine derivative that is widely consumed among young people at all-night dancing parties called " raves".

In rats and monkeys, systemic administration of MDMA causes long-term depletion of serotonin in various brain regions. However, in mice, MDMA administration results in long-lasting changes to the dopaminergic system. The current work quantified effects of (+)-MDMA in C57Bl/6J male mice (10-11 weeks old) using in vivo microdialysis and immunoblotting procedures. A single (20 mg/kg, s.c.) dose of (+)- MDMA increased striatal DA levels approximately 6-fold, peaking two hours after administration and remaining elevated four hours post-injection. A neurotoxic administration regimen (e.g., (+)-MDMA, 20 mg/kg every 2 hrs X 4) resulted in striatal MDMA levels ranging from 3.0 - 16.4 µM over an 8-hour period. Seven days after (+)-MDMA exposure, significant reductions were observed in striatal levels of DA, DOPAC and HVA (decreased by 61.6%, 46.4% and 30.8%, respectively, compared to control animals). Striatal 5-HT levels were also reduced a week after treatment (13.7% reduction), though hippocampal 5-HT and 5-HIAA remained unchanged. Western blot analyses of striatal DAT, VMAT2, and TH also revealed significant reductions one week after (+)-MDMA treatment (70%, 37%, and 58% respectively). These data show that systemic MDMA exposure targets several regulatory processes in the dopaminergic system, causing long-term neurotoxicity in mice.

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