

Effects of recreational use of ecstasy and hallucinogens on the neural circuitry of emotion

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Introduction:

3,4-Methylenedioxymethamphetamine (MDMA, or ecstasy) and hallucinogens (Hal) exert their main psychoactive effects through actions in the serotonin (5-HT) neurotransmitter system, and in particular via the 2A receptor. Furthermore, recreational use of MDMA has been associated with cognitive and affective disturbances. The aim of this study was to assess the effects of MDMA and Hal use on the neural circuitry for emotion processing. In a sample of recreational MDMA/Hal users we have found reductions in cerebral serotonin transporter (SERT) and 5-HT_{2A} receptor binding as well as changes in brain responses to emotional stimuli. We hypothesized that in comparison to age- and gender-matched healthy controls, MDMA/Hal users have structural brain changes in the neural circuitry underlying emotions and control of emotional responses: bilateral orbitofrontal cortex (OfC), insula, amygdala, and anterior cingulate cortex (ACC).

Methods:

Twenty-two current MDMA/Hal users (24.8 ± 4.1, 3 F) and 18 non-using control subjects (23.7 ± 3.6, 3 F) underwent MRI in a Siemens Magnetom Trio 3T MR scanner. Subjects were scanned with 1) a T1-weighted sequence (TR=1550, TE=3.04, voxel size = 1x1x1 mm), and 2) a diffusion weighted sequence (DTI, b=1200, directions=61, voxel size = 2.3 x 2.3 x 2.3 mm). Structural data were analyzed using a voxel-based morphometry (VBM) analysis based on normalization using DARTEL. The DTI data were analyzed using a combined ROI and tract-based spatial statistics approach with focus on the uncinate fasciculi (UF).

Results:

Using an uncorrected threshold of $p < 0.001$, our VBM analysis demonstrated significant structural gray matter reductions in the bilateral medial OfC and ACC, but no changes in the amygdala. A post-hoc analysis revealed additional brain regions with significant volume reductions in the MDMA/Hal users: Paracingulate cortex, frontopolar cortex, lateral prefrontal cortex, cerebellum, red nucleus, middle temporal gyrus, and planum temporale. Our DTI/TBSS analysis showed lower fractional anisotropy values in right UF ($p = 0.023$) and at a lower statistical threshold in the left UF ($p = 0.099$) in MDMA/Hal users compared to controls.

Conclusions:

Our results confirm our hypothesis that recreational use of MDMA is associated with volumetric reductions in regions involved in emotional processing. In addition, the white matter connecting these regions show parallel changes that might reflect axonal damage and gliosis. These results converge with our findings in the same subjects of decline in SERT and 5-HT_{2A} receptor binding, and responses to emotional stimuli.

References

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