

FMRI of MDMA Users and Control Subjects During Delayed Memory Task

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The use of the street drug, methylene-dioxymethamphetamine (MDMA, "ecstasy"), is associated with increased impulsivity and working memory deficits in humans, and may cause degeneration of serotonin nerve terminals in animals. Numerous preclinical studies find evidence of long-term changes in serotonergic neurons after MDMA administration. Based on the animal findings of toxic effects of MDMA on serotonin nerve terminals, investigators have attempted to determine the long-term cognitive and behavioral effects of MDMA in humans. The majority of these studies find evidence for long-term effects on working memory, mood, and impulsivity. Because the prefrontal cortex is important both in working memory and in impulse control, and has substantial serotonergic innervation, it is possible that behavioral deficits observed in MDMA users may result from MDMA effects on the prefrontal cortex. To date, there has been only two published studies comparing MDMA abusers and controls using functional magnetic resonance imaging (fMRI), with mixed findings of either no statistically significant differences on random effects after correction (1), or less activation in the temporal cortex, striate cortex, and angular gyrus in MDMA users (2).

In the present study, 15 MDMA using subjects and 19 non-drug using controls underwent BOLD fMRI while performing a working memory task (IMT/DMT). The study was a block design in which the Delayed Memory Task (DMT) alternated with the Immediate Memory Task (IMT), which served as a control condition. The hypothesis was that MDMA users would show differing cortical activation during the working memory condition compared to the controls. Prior to MRI, sessions are conducted with an MRI Simulation Device (mock MRI or MRI Simulator) in the behavioral laboratory. FMRI scans were acquired with a 1.5 GE scanner, using a gradient echo echoplanar pulse sequence, TE 40 ms, TR 2500 ms, FA 90 degrees, FOV 240 mm, matrix 64x64, 24 slices, slice thickness 3 mm, space between slices 1.5 mm, and 250 repetitions. Random effects SPM99 analysis showed significantly greater activation (whole volume corrected cluster $p < 0.05$) in the MDMA subjects compared to the control subjects during DMT relative to IMT in the following areas: medial superior frontal gyrus, the pulvinar in the thalamus extending into the putamen, and in the hippocampal area of the medial temporal lobe.

Since most MDMA users tend to use other drugs, further research on the specificity of MDMA effects on brain function is warranted. Increased BOLD activation in drug users has been interpreted as possibly being due to greater differences between resting blood flow and blood flow during task or inefficient brain processing (3).

Acknowledgments: This study was supported by National Institute on Drug Abuse grants R01-DA15345, R01-DA08425, K02-DA00403 (FGM) and the Charles A. Dana Foundation Clinical Hypothesis in Neuroimaging Grant (JLS).

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