Serotonergic Challenge of Cognitive Functions in Ecstasy Users

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Background

Alterations to the serotonin (5-HT) system induced by the consumption of ±3,4-methylenedioxy-methamphetamine (MDMA, ‘ecstasy’) have been documented in animals [1] and humans [2]. Moreover, memory deficits have been demonstrated by current and recently abstinent MDMA users [3]. Pharmacological challenge studies offer an effective way to disclose the relation between the 5-HT system and cognitive impairments shown by MDMA users, mainly because this method provides potential to detect subclinical changes in central 5-HT function. Furthermore, little is known about the reversibility of memory deficits once consumers quit using MDMA. We therefore measured memory performance under the influence of the 5-HT releaser dexfenfluramine in comparison to placebo in current and former MDMA users and control subjects.

Methods

Dexfenfluramine and placebo were administered double-blind, randomized, and counter-balanced on two test days with an interval of 14 days. Memory functioning was measured in 15 abstinent current MDMA users, 12 former MDMA users, and 13 drug-naïve controls. All participants were male and matched for age, education, and verbal IQ. Subjects completed various verbal and visuo-spatial mnemonic tasks (Rey Auditory Verbal Learning Test [RAVLT] and tasks from the Cambridge Neuro-psychological Test Automated Battery [CANTAB]). Subtests were grouped into three memory domains and a memory index including all variables (see Tab. 1). Mean values were z-transformed for each individual on the mean of the control group. Memory scores were subjected to a 3 x 2 (group x treatment) repeated-measures ANOVA, with treatment as within-subject and group as between-subject factor.

Results

The dexfenfluramine challenge exerted significant group x treatment interactions in two out of four memory domains on a significance level of p ≤ 0.05 after controlling for dexfenfluramine blood level: declarative memory (F = 3.87; p = 0.03) and the memory index (F = 3.45; p = 0.05). Current MDMA users, former MDMA users and controls did not respond significantly different to the pharmacological challenge in working memory (F = 1.58; p = 0.22) and recognition (F = 1.32; p = 0.28) (see Fig. 2). Furthermore, current MDMA users showed significant deficits in verbal and visuo-spatial memory, whereas former MDMA users only performed worse in specific subtests related to visuo-spatial memory when compared to controls (see Tab. 2).

Discussion

Group differences in response to the pharmacological challenge with dexfenfluramine were found for declarative memory and the total memory index. In contrast to drug-naïve controls, MDMA users seem to benefit from the administration of dexfenfluramine. As mnemonic abilities of current and former MDMA users were sensitive to the serotonergic challenge, these results support previous findings, which indicate long-term changes of the 5-HT system of MDMA users. The present data further suggest that these alterations of the 5-HT system are primarily impairing declarative memory function. Further analyses revealed that current MDMA users showed marked verbal and visuo-spatial memory deficits, whereas former MDMA users only exhibited deficits in visuo-spatial memory. These results indicate that memory deficits in MDMA users show greater reversibility for verbal than for visuo-spatial memory after consumers quit using MDMA.

Conclusion

Verbal and visuo-spatial memory deficits persist in MDMA users seem to be related to alterations of the 5-HT system. Verbal deficits diminish more strongly than visuo-spatial deficits after MDMA consumption is stopped.

Disclosure

The authors declare no conflict of interests.

References


Fig. 1: Sagittal plane, dark field photomicrograph of 5-HT immunoreactive axons in the frontal cortex of a control monkey (a), a monkey treated with Sigma MDMA (2 times a day for 4 days) (b) and a monkey treated with MDMA 7 years previously (c) (from Halász et al., 1999).

Fig. 2: Memory performance for current and former MDMA users and drug-naïve controls in baseline and dexfenfluramine condition (means and standard deviations). * indicates significant difference in memory score compared to the control group.

Table 1: Configuration of memory domains, defined by factor analysis.

Table 2: Results of neuropsychological test scores for current and former MDMA users and drug-naïve controls (means and standard deviations). Turkey HSD Posthoc test: *p<.05, **p<.01.

Fig. 2: Memory performance for current and former MDMA users and drug-naïve controls in baseline and dexfenfluramine condition (means and standard deviations). * indicates significant difference in memory score compared to the control group.

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