

MDMA neurotoxicity discussed

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There are several issues related to MDMA neurotoxicity:

1. Do persistent reductions in serotonin levels in humans result from taking MDMA? If so, from what doses and frequency?
2. If there are persistent reductions, are they temporary or permanent?
3. If there are persistent reductions in serotonin levels in humans under any circumstances, do these reductions have any functional or behavioral consequences?

In other words, does MDMA cause lowered serotonin levels and, if so, does it matter?

The answer to the first question is that there is some suggestive evidence that there are serotonin reductions in a group of people who have taken MDMA an average of 90 or more times.^{1,2,3}

HOWEVER, this evidence is not conclusive, since MDMA users were compared to matched control groups, which may or may not be matched on all factors that impact on serotonin levels. The most persuasive evidence would come from studies in which MDMA-naive subjects were tested, then given multiple exposures to MDMA, then tested again. Unfortunately, no studies of this sort have been conducted. MAPS recently donated \$6,000 toward the costs of a pilot study being conducted under the direction of Dr. Franz Vollenweider, University of Zürich. In this study one dose of MDMA was given to several MDMA-naive subjects, who were evaluated with PET scans before and after the MDMA. The results should be available in a few months.

It is also as yet unknown whether the reductions in serotonin as suggested in some MDMA human studies are linked to damage or to down-regulation, in which neurons adapt to lower levels of serotonin, or to some other factor unrelated to MDMA.⁴

The extent of MDMA-related "damage" would depend—among other factors—on

the frequency of use and the doses used. The present state of knowledge does not allow us to tell at which frequency and dosage to draw the line between non-neurotoxic and neurotoxic use in humans. The line would certainly have to be individually drawn at different dosages and frequencies in different users, due to individual variability. Of course, the best way to avoid the risk of MDMA-related neurotoxicity is to avoid MDMA. The balancing of risk and benefit is a decision that each individual must make for themselves.

An unpublished MAPS-funded study by Ricaurte, in which oral 2.5 mg/kg MDMA was administered to non-human primates once every two weeks for four months (8 administrations) showed no effect in levels of serotonin. This is at or above the normal therapeutic or recreational dose level. However, the relative sensitivity to MDMA's effects on serotonin of non-human primates as compared to human beings is unknown.

In animal studies, there is evidence that an SSRI taken acutely (once) even a few hours after MDMA will provide

“neuroprotection” against the possibility of toxicity to serotonin neurons. This suggests that a person who ingests MDMA could take a Prozac for neuroprotection within six hours after ingestion. It is obviously not clear if this holds true for humans, not only because a prospective study has not been done, but also because it is still controversial whether MDMA induces structural changes which can be considered “neurotoxic.”⁵

As to the second question, whether reductions are temporary or permanent, there is clear evidence of regeneration of serotonin neurons. However, this regeneration pattern does not restore the pattern exactly to the original state.⁶

The answer to the third question is that there is a lot of circumstantial evidence, and no convincing evidence to the contrary, that serotonin reductions, if there are any, make no difference. There is a frequently repeated claim that MDMA users may show no problems at present but will show such problems in the future, as they age. This delayed effect will supposedly take place when the combination of MDMA and the normal aging process has reduced serotonin levels below a certain threshold. This hypothetical time bomb theory ignores that fact that there are already quite a few people over 60 or 70 who have taken substantial amounts of MDMA and seem fine. Furthermore, the serotonin system does not decline much with age, certainly not as much as the dopamine system, the decline of which can contribute to Parkinsonism.

One should certainly note from the analyses of “Ecstasy” tabs conducted by Nicholas Saunders that most MDMA tablets are not pure and can easily contain drugs which are harmful when taken acutely or on a chronic basis (e.g. atropine, ephedrine). These drugs may be harmful but there is no evidence they reduce serotonin levels. MAPS sponsored an MDMA Analysis Project of U.S. samples in 1996.

Finally, fenfluramine, a drug with actions identical to those of MDMA with respect to effects on serotonergic neurons, does not appear to have toxic effects on these neurons in humans taking the drug twice daily for several years, nor is there evidence of functional or behavioral problems in fenfluramine users. However,

no thorough studies have been conducted searching for such effects. Nevertheless, the absence of reported neurotoxic effects from fenfluramine suggests that such effects, if any exist, are likely to be subtle. For example, the dramatic neurotoxic effects of MPTP, the synthetic heroin that caused Parkinson's-like symptoms and for which the term “designer drug” was originally used, were noticed after only a handful of people had taken the drug. In contrast, MDMA has been used for over two decades and millions of people have taken it, some excessively so. Some people have had problematic psychological reactions but there is still no clear evidence of any functional or behavioral consequences linked to MDMA neurotoxicity. While subtle changes can still be important, perhaps crucially so to what it means to be fully human, no such changes have yet been demonstrated from the yet unproven mechanism of MDMA neurotoxicity. At the same time, many people report long-term benefits from their use of MDMA. As a result of these reports of long-term benefits, MAPS focuses on the development of clinical studies designed to scientifically investigate the therapeutic applications of MDMA. •

References:

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(MAPS played a major role in recruiting volunteers for the first two of the studies referenced above and in covering travel expenses involved in bringing many of the volunteers to be tested in the study referenced as #2.)
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