Editorial

Making a medicine out of MDMA

Ben Sessa and David Nutt

Summary

From its first use 3,4-methylenedioxymethamphetamine (MDMA) has been recognised as a drug with therapeutic potential. Research on its clinical utility stopped when it entered the recreational drug scene but has slowly resurrected in the past decade. Currently there is enough evidence for MDMA to be removed from its Schedule 1 status of ‘no medical use’ and moved into Schedule 2 (alongside other misused but useful medicines such as heroin and amphetamine). Such a regulatory move would liberate its use as a medicine for patients experiencing severe mental illnesses such as treatment-resistant post-traumatic stress disorder.

Declaration of interest

None.

For those of us researching the development of 3,4-methylenedioxymethamphetamine (MDMA) therapy for patients with post-traumatic stress disorder (PTSD) the drug’s historical association with recreational ecstasy is a hindrance. Although clinical use precedes recreational ecstasy the media focuses primarily on the rare incidences of harm associated with misuses of the latter. After a quarter of a century of epidemiological evidence of MDMA’s low rates of morbidity and mortality (even when used recreationally as ecstasy), as well as mounting data supporting clinical MDMA as a therapeutic agent, we feel it is time to concentrate on the objective evidence-based research. Otherwise, we risk denying a population of needy patients a potentially important treatment. An important step towards recognising MDMA as a medicine is to move it from Schedule 1 to Schedule 2 of the UK’s drug classification system.

A brief history of MDMA in medicine

First synthesised in 1912 by the German pharmaceutical company Merck as a chemical precursor, MDMA failed to make an impact on the 1960s drug scene. In the 1970s a few psychotherapists were using it legally as a tool in couples therapy, where it was seen to help traumatised clients address repressed emotional memories without being overwhelmed by the negative affect that usually accompanies such memories. It was then banned in the mid-1980s in the wake of growing recreational use. No placebo-controlled studies were conducted with MDMA in the 1980s, but case–control studies showed MDMA could be used without adverse effects to produce qualitative improvements in psychological functioning and resolution of relationship difficulties.

Controlled clinical trials

A recent placebo-controlled study of participants with treatment-resistant PTSD showed that 85% of those in the MDMA group (compared with 15% in the placebo group) no longer had a diagnosis of PTSD after three sessions of MDMA-assisted psychotherapy. These results were sustained at 3.5 years long-term follow-up, with no further MDMA interventions required and many patients reducing or stopping their regular psychiatric medications. A subsequent Swiss MDMA study demonstrated substantial improvements for treatment-resistant PTSD.4

MDMA exerts its effects through 5-hydroxytryptamine (5-HT)1A, 5-HT1D, 5-HT2A, dopamine and alpha-2 receptors. It also produces oxytocin release, which improves bonding and raises levels of empathy. Its multiple and varied effects make the drug a good candidate for facilitating psychotherapy – especially for patients with post-traumatic symptoms, in which helping the patient to reach a position of empathic understanding and compassionate regard is part of their resolution and remittance of symptoms.5

Participants given MDMA are more likely to use words relating to friendship, support and intimacy, in comparison to the drug methamphetamine, which by contrast reduced participants’ discussions about compassion.6 MDMA appears to enhance the quality of social interactions and thereby improve relationships, recently tested using a simulated experimental paradigm of social exclusion by Frye et al, showing how participants taking MDMA exhibited reduced social exclusion phenomena.7 Similarly, MDMA enhances levels of shared empathy and prosocial behaviour compared with placebo.8 Furthermore, Wardle et al showed how MDMA can facilitate a faster detection of happy faces, and reduces the detection of negative facial expressions, which leads participants to view their social interaction partner as more caring.9 A recent study by Kirkpatrick et al comparing MDMA against intranasal oxytocin demonstrated the former produced greater improvements in prosocial communication.10 And the positive effects of MDMA appear consistent across different environments, with participants examined in San Francisco, Chicago and Basel demonstrating broadly similar prosocial outcomes.11

Recently, several groups have used neuroimaging to explore the actions of MDMA in the brain. For example, Carhart-Harris et al, using magnetic resonance imaging blood oxygen level-dependent and arterial spin labelling techniques, showed that MDMA reduced amygdala and hippocampus activity and selectively attenuated the magnitude of negative memories.
the UK government advisory body on drugs, the Advisory Council on the Misuse of Drugs, recommends this to the Home Secretary, regulations can then be amended within weeks. It is important to note that the UK is not legally obliged to adopt the UN structure for scheduling drugs; and based on medical advice put heroin in Schedule 2 against the UN recommendation. Similarly, in another example the UN placed tetrahydrocanabinol in Schedule 1 in 1971, but in the UK it is available (in the form of the drug sativex) and placed in Schedule 4. Moreover there is no reason to suppose putting MDMA into Schedule 2 would have any impact on illicit use of ecstasy, just as pharmaceutical heroin in Schedule 2 is almost never diverted into criminal hands.

We call on the Advisory Council on the Misuse of Drugs to recommend MDMA become a Schedule 2 drug. This will allow medical research to explore the full potential of MDMA as a medicine for treatment-resistant PTSD and other possible brain disorders.

**Conclusion**

MDMA has been subjected to inappropriate, non-evidence-based, legislative restrictions. These have not effectively reduced the harm or burden of recreational ecstasy use on society but they have effectively held back research on clinical MDMA. We urge the regulatory authorities to consider whether a move from Schedule 1 to Schedule 2 might more accurately reflect MDMA's relative harms and safety, while also facilitating greater research of the substance for possible therapeutic uses within psychiatry.

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**References**


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