S.23. Ecstasy, the love drug: acute effects of MDMA on psychosocial processes

S.23.01 Recent insights into the psychopharmacology of MDMA

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MDMA is the chemical name for the recreational drug ecstasy. Originally developed in the early 1900s as a possible antidepressant it was re-discovered by Schulgin in the 1960s. When the drug became popular on the "rave" scene it was banned and put into Schedule 1 so that research effectively stopped [1]. In recent years however several groups have begun to explore its value as a part of psychotherapeutic treatments particularly in PTSD [2].

How MDMA might be effective is of great interest. The pro-empathy effect will aid trust and bonding in therapy and is probably mediated by central 5HT stimulatory actions and possibly by oxytocin release. MDMA has been shown to reduce threat-induced activation of the amygdala [3]. We have conducted the first whole-brain analysis of the effects of MDMA [100 mg of the HCl salt] using 3T fMRI and found a distinct pattern of reduced activation in brain without any increases being seen. These reductions in activity were most prominent in the stress-related amygdala and hippocampus that was associated with a decrease in the magnitude of negative personal memories [4,5]. These changes may underpin its therapeutic effects as they would allow re-engagement and with and then control of the trauma memories with less interference from emotional centres. The drug was well tolerated with little physiological impact and so in this dose it could be a viable pharmacological intervention in a number of different stress-and trauma related disorders.

References

[1] Sessa B and Nutt D (2015) Making a medicine out of MDMA. Brit J Psychiatry 206, 4–6. doi: 10.1192/bjp.bp.114.152751.
[2] Mithoefer MC, Wagner MT, Mithoefer AT, Jerome L, Martin SF, Yazar-Klosinski B, et al. Durability of improvement in PTSD symptoms and absence of harmful effects or drug dependency after MDM-assisted psychotherapy: a prospective long-term follow-up study. J Psychopharmacol 2013; 27: 28–39.
[3] Wardle MC, de Wit H. MDMA alters emotional processing and facilitates positive social interaction. Psychopharmacology (Berl) 2014; 231: 4219–29.
[4] Carhart-Harris RL, Erritzoe D, Williams LTJ, Erritzoe D, Wall MB, Ferguson B, et al. The effects of acutely administered 3,4-methylenedioxymethamphetamine on spontaneous brain function in healthy volunteers measured with arterial spin labeling and blood oxygen level-dependent resting state functional connectivity. Biol Psychiatry 2014; 10 Jan (Epub ahead of print) 5.
[5] Carhart-Harris RL, Wall MB, Erritzoe D, Kaelen M, Ferguson B, De Meer I, Tanner M3 Bloomfield M, Williams TM, Bolstridge M, Stewart L, Morgan C, Newbould RD, Feilding A, Curran HV, Nutt DJ (2013) The effect of acutely administered MDMA on subjective and BOLD fMRI responses to favourite and worst autobiographical memories. Int J of Neuropsychopharmacology 17: 527–40 http://www.ncbi.nlm.nih.gov/pubmed/24345398.

S.23.02 Effects of ecstasy on autobiographical memories: implications for MDMA assisted psychotherapy

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Preliminary clinical research suggests that 3,4-methylenedioxymethamphetamine (MDMA) may boost the effectiveness of psychotherapy for post-traumatic stress disorder (PTSD). As psychotherapy for PTSD generally involves revisiting traumatic memories, we set out to determine how MDMA affects encoding and recall of emotional memories. Effects of 100 mg of MDMA-HCl were compared with placebo in a double-blind, repeated-measures design. We used functional magnetic resonance imaging (fMRI) and self-referent encoding (SRE) of positive and negative adjectives in relation to oneself, or another person or a neutral condition. The placebo condition replicated typical SRE effects in both behavioural and fMRI data. When processing words in relation to oneself, MDMA significantly reduced activation in the medial prefrontal cortex and left insula; behaviourally it decreased recognition accuracy and response bias overall but did not influence the self-positivity bias even though ratings of compassion showed marked MDMA-increases. A second task in the same study – recollection of each participant's favourite and worst autobiographical memories – showed a significant effect of memory valence: hippocampal regions showed preferential activations to favourite memories and executive regions to worst memories. Favourite memories were rated as significantly more vivid, emotionally intense and positive after MDMA than placebo and worst memories were rated as less negative. These findings suggest a mechanism through which MDMA might enhance psychological therapy via reducing self-referential processing and inducing a positive emotional-bias.

S.23.03 Effects of MDMA on social cognition

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There is limited data on MDMA's effects on social cognition. We investigated acute effects of MDMA (75 and 125 mg) on aspects of social cognition in healthy subjects. We also tested other psychoactive substances including methylphenidate (40 and 60 mg), LSD (0.1 and 0.2 mg), and alcohol (target blood concentration 0.4 g/L). Outcome measures included visual analog scales (VASs) for subjective effects, a face emotion recognition task (FERT), the multifaceted empathy test (MET), and a sexual arousal task (SAT). Additionally, we measured plasma concentrations of oxytocin, cortisol, and prolactin. In the VASs, MDMA increased ratings for well-being, happy, open, closeness, trust, and extroversion [1–3]. LSD produced similar MDMA-like subjective effects [4]. Alcohol slightly increased ratings for happy, open, and trust while methylphenidate had no such empathogenic effects. In the MET,