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.

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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,

MDMA enhanced emotional empathy. LSD and alcohol enhanced emotional empathy similar to MDMA but only for positive stimuli. Methylphenidate had no effect. MDMA impaired recognition of sad, angry and fearful faces in the FERT [1]. Similarly, LSD impaired decoding of sad and fearful emotions. In contrast, high-dose methylphenidate enhanced recognition of sad and fearful faces, while alcohol facilitated recognition of happy faces. MDMA had no effect on sexual arousal in the SAT, while methylphenidate increased ratings of sexual arousal for explicit sexual stimuli [5]. MDMA and LSD but not the dopaminergic stimulant methylphenidate increased cortisol, prolactin, and oxytocin consistent with their serotonergic action. In conclusion, MDMA and LSD exert emotional and social cognitive effects that may be useful during psychotherapy.

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S.23.04 Bidirectional relations between MDMA and social context: crosstalk between drug response and social interaction

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Many drugs of abuse are used in social settings, i.e., in the presence of others. Yet, little is known about the effects of drugs in social contexts, including how they affect social interactions, or conversely, how social conditions affect responses to drugs. Ecstasy, or methylenedioxymethamphetamine (MDMA), in particular, is known for its prosocial effects, and it is typically used in groups. MDMA is thought to facilitate feelings of social connectedness. However, most controlled studies of the psychopharmacology of this and other abused drugs is that the effects of drugs are typically studied in a socially isolated setting, rather than in a social context. Thus, the full spectrum of drug effects may not be detected. To address this gap, we have conducted controlled, double blind laboratory studies to examine the effects of MDMA on measures of social function, including the ability to detect emotions in others, reactivity to positive and negative social images, and sensitivity to social rejection. We have also studied the effects of social context on responses to the drug, by testing participants in the presence of other subjects, including those who did or did not also receive the drug. Taken together, we have established that MDMA dampens reactivity to negative emotional expressions in others, that it reduces feelings of social rejection, and that its effects are enhanced in the presence of others. This line of research will help to understand the basis of recreational use of MDMA, as well as its potential therapeutic use.

S.25. Emotion recognition in neurodegeneration

S.25.01 Structural and functional brain changes underlying emotion perception in behavioural variant of fronto-temporal dementia

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Impairment in emotion perception is thought to underlie the early socio-emotional symptoms in behavioural variant fronto-temporal dementia (bvFTD). Deficits have mainly been documented through facial expression recognition assessments and are associated with regional atrophy in a distributed network including the amygdala, orbito-frontal cortex, temporal pole and insula.

Extending reports of facial, vocal and musical emotion recognition deficits, we present evidence for impaired recognition of bodily expressions. The absence of differential impairments regarding motion (static vs. dynamic) and category (body vs. face) as well as a significant correlation between bodily and facial expression recognition are in line with a supramodal emotion recognition deficit in bvFTD. Voxel-based morphometry analysis reveals that bodily emotion matching and categorization in bvFTD were positively associated with the inferior frontal gyrus (IFG) whereas emotion detection was associated with the anterior temporal lobe.

Event-related fMRI provides evidence for distant functional effects of anterior temporal atrophy in posterior structurally unaffected areas. In contrast with healthy controls there is no enhanced activation for passive viewing of emotional facial stimuli in ventral and superior temporal cortex in bvFTD, while amygdalar gray matter is positively associated with emotion-specific activation in fusiform face area in bvFTD. This correlation is driven by the superficial and basolateral amygdalar subnuclei consistent with reports of intrinsic amygdalar-cortical networks.

Taken together the data suggests anterior temporal atrophy contributes to a lack of awareness for emotionally relevant stimuli, while integrity of the IFG might contribute to a more detailed description of bodily expressions through involvement of the motor system.

S.25.04 Emotion recognition in Parkinson's disease

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Affective neuroscience is concerned with identifying the neural bases of emotion. For historical and methodological reasons, models describing the brain architecture that supports emotional processes in humans have tended to neglect the basal ganglia, focusing instead on cortical and amygdalar mechanisms. However, Parkinson's disease provides a useful model for studying the functional specialization and integration of the basal ganglia in human