Background

Chronic use of serotonergic recreational drugs, such as hallucinogens (Hal) and amphetamines, such as 3,4-Methylenedioxyamphetamine (MDMA, or ecstasy) results in depletion of the neurotransmitter serotonin, and has been reported to cause cognitive and affective deficits.

The exact effects of MDMA and Hal on neural processing of emotional information are not well understood. It is feasible that serotonin depletion following recreational use of drugs may induce changes in processing of faces displaying emotional content, and that such changes may play a part in the neuropsychiatric problems associated with such use.

Aims

To elucidate the effect of current use of MDMA and Hal on responses to emotional stimuli.

To focus particularly on emotional structures, in particular amygdala, orbitofrontal cortex (OFIC), anterior insula (AI), and anterior cingulate cortex (ACC).

To differentiate individual effects based on polydrug profile (Hal vs. MDMA).

Hypotheses

Compared to healthy controls, MDMA/Hal users were expected to show an attenuation of neural responses to aversive stimuli, in particular in the amygdala, OFIC, ACC and AI.

MDMA users were expected to show a differential effect on emotional responses than Hal users.

Methods

21 current MDMA/Hal users (25.2 ± 4.1, 3 females) and 13 non-using control subjects (23.5 ± 3.8, 3 females) were given the covert facial emotion task (CFET, see Figure 1).

Subjects were scanned using BOLD fMRI in a Siemens Magnetom Trio 3T MR scanner with a GE-EPI sequence optimised for the ventromedial prefrontal cortex and medial temporal lobe (TR = 2500 ms, TE = 30 ms, 64x64 matrix), volumes = 192, slices = 38; voxel size = 3 x 3 x 2 mm. Field of view excluded dorsal parietal and prefrontal cortex, temporal lobe (TR = 2500 ms, TE = 30 ms, 64x64 matrix), volumes = 192, slices = 38; voxel size = 3 x 3 x 2 mm.

Onsets for aversive (B, C, D) and neutral (A) faces were used as regressors, and convolved with a hemodynamic response function. The analysis was corrected for onsets for aversive (B, C, D) and neutral (A) faces were used as regressors, and convolved with a hemodynamic response function. The analysis was corrected for.

Task

The CFET task:

Pictures of facial affect were presented for 3s (0.75s ISI), using a sample of subjects from the Ekman facial expression picture set.

Emotions included neutral (A), anger (B), disgust (C), and fear (D), in an ABACADABACAD design (Figure 1).

Total block duration was 30s.

Subjects’ task was to identify the gender of the faces by pressing one of two buttons.

Results

Behavioural results

For the present analysis, we first analysed the difference between MDMA and Hal users on reaction time and performance. We found no significant difference either on reaction time (p=0.9366) or performance (p=0.0876). We therefore chose to collapse the two user groups into one user group, from now called the MDMA/Hal group.

Both MDMA/Hal users (n=21) and control subjects (n=13) responded slower when they saw faces with aversive expressions, compared to neutral face-expressions (MDMA/Hal: F(1,20)=14.61, p=0.005; controls: F(1,12)=6.89, p=0.05, see Figure 2). Further analyses suggest that this effect is mainly driven by significantly slowed responses for faces displaying fear (p=0.005) and aggression (p=0.001), but not disgust and sadness (both n.s).

There were no significant difference between the two groups on reaction time (p=0.9533).

There were no significant difference between the groups on performance. MDMA/Hal users had a mean of 92% correct answers (range: 87%-98%), while controls had a mean of 90% correct (range: 83%-93%).

BOLD fMRI results

The BOLD analysis reported here was done on a smaller subset of the entire sample (8 MDMA/Hal and 12 controls). Further analysis will include all subjects reported in the behavioural data.

Our hypotheses were only partially supported. By using an uncorrected threshold of p<0.001, we found that:

- Compared to controls, MDMA/Hal subjects displayed a lower response to aversive facial expression in the left amygdala (Figure 3).
- Other regions showing reduced activations in MDMA/Hal included left mamilial cortex and left tempopolar cortex (Figure 3).
- No significant changes were apparent in other hypothesised regions such as the anterior insula or the anterior cingulate cortex.

Surprisingly, and counter to our expectations, MDMA/Hal users demonstrated stronger activation of the left medial orbitofrontal cortex to aversive faces (Figure 4).

Conclusions

Our result suggests that serotonin depletion following current use of MDMA and hallucinogens leads to emotional dysfunctions, and that such disruptions may be related to functional changes in structures normally operating in the processing of facial expressions.

In addition, our results may suggest a further impaired function of medial temporal lobe functions in the processing of facial expression.

Surprisingly, increased responses to aversive stimuli in the medial OFIC were unexpected and need further study.

Further analyses are currently comparing these results to changes in brain morphology, SHT1A receptor binding and psychometric factors.