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AN INVESTIGATION OF 5-HT2 INVOLVEMENT IN THE ACUTE BEHAVIOURAL EFFECTS OF FLUOXETINE AND MCPP IN AN ANIMAL MODEL OF OCD

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Background: We reported that the non-specific 5HT agonist m-chlorophenylpiperazine (mCPP) and the SSRI fluoxetine (FLX) both cause acute persistence increases in the rewarded alternation (RA) model of OCD. Chronic pretreatment with either substance or their combined subclinical doses protects from this 'pathogenic' effect, so mCPP and fluoxetine exhibit cross-tolerance and synergy.

Aims: Using specific 5HT2A and 5HT2C receptor antagonists we investigated whether these receptors participate in a common mechanism of action mediating the acute mCPP/fluoxetine effect in our model.

Methods: Naïve, male Wistars were used. Drugs used (intraperitoneally): FLX (10mg/kg), mCPP (2.5mg/kg), M100907 (5HT2A antagonist, 0.03mg/kg), SB242084 (5HT2C antagonist, 0.5mg/kg), vehicle. Experiments included a drug-free training/baseline phase in T-maze RA (group-matching for spontaneous persistence: SP).
Experiment 1: Effects of M100907, SB242084, vehicle were assessed on 3 matched low SP and 3 high SP groups.
Experiment 2: The acute effect of FLX, mCPP and saline were examined on RA in 3 SP-matched groups.
Experiment 3: Effects of Vehicle+FLX, M100900+FLX, SB242084+FLX and Vehicle were examined on RA, in 4 SP-matched groups.
Experiment 4: Correspondingly for mCPP.

Results:
Experiment 1: Neither M100907 nor SB242084 affected high or low SP.
Experiment 2 replicated the pathogenic effects of FLX/mCPP.
Experiment 3: Neither M100907 nor SB242084 affected the pathogenic effect of FLX.
Experiment 4: In contrast, SB242084 (but not M100907) significantly reduced the pathogenic mCPP effect.

Conclusions: The acute pathogenic action of mCPP, but not of FLX, involves 5HT2C but not 5HT2A receptors. The similar acute action of mCPP and FLX on persistence cannot be attributed to 5HT2 mediation.

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