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1-(m-Chlorophenyl)piperazine induces depressogenic-like behaviour in rodents by stimulating the neuronal 5-HT(2A) receptors: proposal of a modified rodent antidepressant assay.

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Abstract

1-(m-Chlorophenyl)piperazine (**mCPP**) has a fairly complex neuropsychopharmacological profile owing to its affinity to multiple serotonergic receptors. This investigation was designed to establish the effect of **mCPP** on rodent depression-like behaviour. **mCPP** was screened in a rodent behavioural test battery comprising of validated antidepressant assays and interaction studies with conventional antidepressants and ligands were carried out in forced swim and tail suspension test (in mice). **mCPP** (1 mg/kg, i.p.) exhibited depressant-like effects in forced swim and tail suspension test (in mice), without influencing the locomotor status. Potentiation of 5-hydroxytryptophan/pargyline induced head twitches (in mice) and hyperthermic effects (in rats) were observed at the same dose level. Further, the behavioural anomalies of the olfactory bulbectomised (OBX) rats were augmented by chronic **mCPP** (1-2 mg/kg) treatment as observed from the modified open field, elevated plus maze and social interaction paradigms. Interaction studies revealed that the **mCPP** induced depressant-like effects were reversed by ketanserin, escitalopram, amitriptyline, ziprasidone, venlafaxine pretreatments but not by bupropion, harmane, ondansetron, 8-hydroxy-2-(di-n-propylamino) tetralin (8-OH-DPAT) and MK-801. In conclusion, this study provided ample evidence that the stimulation of 5-HT(2A) receptors underlies the depressogenic-like effect of **mCPP**. Finally, the **mCPP** induced depression-like behaviour in rodents is envisaged as a modified antidepressant assay to identify novel serotonergic antidepressants.

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