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DIRECTIONAL PERSISTENCE IN THE REWARDED ALTERNATION MODEL OF OBSESSIVE-COMPULSIVE DISORDER IS RESPONSIVE TO BOTH DOPAMINERGIC AND SEROTONERGIC MANIPULATIONS

D. Kontis[1], V. Boulougouris[1], S. Papadopoulos[1], V.-M. Papakosta[1], S. Kalogerakou[1], C. Poulopoulou[1], E. Tsaltas[1], G. Papadimitriou[2]

[1]Experimental Psychology Laboratory, Department of Psychiatry, Eginition Hospital, [2]Department of Psychiatry, Eginition Hospital, Athens University Medical School, Athens, Greece

Rationale: In the rewarded alternation model of obsessive compulsive disorder (OCD), the serotonin agonist m-chlorophenylpiperazine (mCPP) increases persistent behaviour, while chronic pretreatment with selective serotonin reuptake inhibitor (SSRI-fluoxetine) but not benzodiazepine or desipramine abolishes mCPP effects. However, we noted that acute SSRI administration also causes transient persistence increases, counteracted by mCPP pretreatment.

Objectives: This study

a. further explores the apparent cross-tolerance between fluoxetine and mCPP and
b. extends the model by investigating its sensitivity to dopaminergic manipulations ($D^{2,3}$ agonism - quinpirole).

Methods: In both experiments, baseline and drug testing was carried out under daily T-maze alternation training.
Exp.1: Matched group (n=8) pairs of rats received one of the following 20-day pretreatments (daily intraperitoneal administration):

1. saline,
2. low-dose fluoxetine (2.5mg/kg),
3. low-dose mCPP (0.5mg/kg) or
4. combined fluoxetine+mCPP.

One group per pretreatment then received a 4-day challenge with high-dose fluoxetine (10mg/kg), the other with high-dose mCPP (2.5mg/kg).
Exp.2: One group (n=12) of rats received 20-day treatment with saline, another with quinpirole (0.5 mg/kg).

Results:
Exp.1: Saline and low-dose mCPP- or fluoxetine-pretreated animals showed significant persistence increases under both challenges, while combined low-dose fluoxetine+mCPP pretreatment afforded full protection from either challenge.
Exp.2: Quinpirole significantly increased directional persistence after 13 administration days.

Conclusions: These results establish the sensitivity of the rewarded alternation OCD model to $D^{2,3}$ receptor activation, thereby extending its profile of pharmacological isomorphism with OCD. Furthermore, they suggest a common mechanism of action of an SSRI and a serotonin agonist in the control of directional persistence.

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