



## Effect of chronic administration of fluoxetine on 6-hydroxydopamine-induced catalepsy in rats

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**Background and Aims:** Progressive loss of dopaminergic neurons of the substantia nigra pars compacta (SNc) in Parkinson's disease (PD) leads to impairment of motor skills. Several evidences show that the role of serotonergic system in regulation of normal movement is pivotal and mediates via 5-HT<sub>1A</sub> receptors. Our previous study has shown that fluoxetine in acute injections is able to attenuate catalepsy in 6-hydroxydopamine (6-OHDA)-lesioned rats. Since drugs are used chronically in clinic, in this study we attempted to evaluate effect of chronic administration of fluoxetine on 6-OHDA-induced catalepsy.

**Methods:** Catalepsy was induced by unilateral infusion of 6-OHDA (8 µg/2 µl/rat) into the central region of substantia nigra pars compacta (SNc) and assayed by using bar-test. Fluoxetine (1, 5 and 10 mg/kg) was injected intraperitoneally (ip) for 10 days and its anti-cataleptic effect was assessed at the 10th day.

**Results:** Fluoxetine in higher doses (5 and 10 mg/kg) worsened 6-OHDA-induced catalepsy while it had anti-cataleptic effect at the dose of 1mg/kg. The anti-cataleptic effect of fluoxetine (1mg/kg) was reversed by co-administration with NAN-190, as 5-HT<sub>1A</sub> receptor antagonist.

**Conclusions:** According to the results it can be concluded that fluoxetine has anti-cataleptic effect in parkinsonian rats only at low doses, whereas at higher doses it worsens catalepsy. Its anti-cataleptic effect is exerted through affecting on 5-HT<sub>1A</sub> receptors. However, at high doses other mechanisms may be involved. Further clinical studies are needed to prove its possible clinical application as an adjuvant therapy in reducing catalepsy of PD.

**Keywords:** Fluoxetine; Chronic; 6-Hydroxydopamine; Catalepsy; Rat