

Thesis Title	Behavioural and Neurochemical Characteristics of Pseudoephedrine in Rats
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### Abstract

The structural and pharmacological similarity of pseudoephedrine to amphetamine has led to evaluation of its psychomotor stimulant properties. The present investigation was carried out using operant drug discrimination assays and also an *in vitro* dopamine uptake experiment. The drug discrimination technique has been used to examine whether the internal cues arising from pseudoephedrine resemble those of amphetamine. Rats were trained to discriminate amphetamine 1 mg/kg given intraperitoneally from saline injection in a two-lever operant drug discrimination task. Pseudoephedrine (a sympathomimetic drug with central and peripheral actions) at doses of 10 mg/kg failed to substitute for amphetamine, at 20 mg/kg partial substitution occurred, while at 40 mg/kg full substitution was seen. The high degree of specificity of the amphetamine cue at the training dose studied (amphetamine 1mg/kg) was shown by the finding that the nonstimulant drug diazepam (1mg/kg) and a peripherally acting sympathomimetic drug phenylephrine at doses from 0.2 to 0.8 mg/kg failed to substitute for amphetamine. The dopamine D<sub>1</sub> antagonist SCH23390

(0.3 mg/kg) produced disruption of behaviour by causing the rats to become immobile and no lever presses occurred. It is difficult to interpret this result which may involve pharmacological antagonism of dopaminergic mechanisms or the SCH23390 may have produced a non-specific disruption of the operant behaviour. The present studies have shown that pseudoephedrine induces, in a dose-dependent manner, an interoceptive cue similar to that of amphetamine. The uptake experiment clearly demonstrates that pseudoephedrine inhibits the [<sup>3</sup>H] dopamine uptake in striatal and nucleus accumbens synaptosomal preparations. The inhibitory effect when compared with amphetamine, was less potent in both brain tissues (156 and 180 folds less potent than amphetamine in inhibiting the [<sup>3</sup>H] dopamine uptake in striatal and nucleus accumbens synaptosomes, respectively). The data from the drug discrimination assay and the *in vitro* dopamine uptake experiment, indicate that pseudoephedrine has some degree of abuse potential as it produces a discriminative stimulus similar to that of amphetamine and its mechanism of action is via the blockade of dopamine uptake.