372 P AN INVESTIGATION OF THE ANTIDEPRESSANT PROPERTIES OF 8-OH-DPAT AND IPSAPIRONE IN RATS

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Evidence is accumulating that 5-HT_{1A} receptor ligands, such as ipsapirone may represent a new class of mixed anxiolytics/antidepressants (Stahl *et al.*, 1992). The purpose of this study was to compare the properties of ipsapirone with those of the full 5-HT_{1A} agonist 8-OH-DPAT, in animal models indicative of antidepressant potential (Kelly & Leonard, 1994).

Male Sprague Dawley rats (250-280g, n = 8-10 per group) were housed 4 per cage, under a 12 h light cycle, (lights on; 0800 h), with free access to food and water. Bilateral olfactory bulbectomy (OB) was performed under tribromoethanol anaesthesia (2.5% w/v; 10 ml/kg, i.p.) (Cairncross *et al.*, 1977). Animals were allowed 14 days to recover after surgery. Both 8-OH-DPAT (hydrobromide; 1 mg/kg, i.p. twice daily) and ipsapirone (3 and 10 mg/kg, i.p. once daily) were administered for a period of 16 days. Controls received injections of saline vehicle alone. Immobility time in the forced swim test was recorded over 5 min following the third injection. Hyperactivity of the OB rat was assessed on the morning of the 15th day of the study and prior to drug treatment on that day. The effect of a challenge dose of 8-OH-DPAT (0.15 mg/kg, s.c.) on rectal temperature was determined on day 16, 2 h following treatment with the test substance. Results were expressed as group means ± s.e.means and a two-way analysis of variance was performed, followed by a posteriori least significant difference test.

In conclusion, 8-OH-DPAT and ipsapirone display antidepressant-like activity in all 3 tests and these changes could be due to 5-HT_{1A} autoreceptor desensitization, which might implicate 5-HT_{1A} receptor modulation in the mode of action of antidepressants (Goodwin, 1989).

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Table 1. The effect of 8-OH-DPAT and ipsapirone in animal models indicative of antidepressant potential

	8-OH-DPAT				Ipsapirone		
	Forced Swim (Immobility s)	'Open field' (Ambulation)	8-OH-DPAT challenge (°C at 30 min)		Forced Swim (Immobility s)	'Open field' (Ambulation)	8-OH-DPAT challenge (°C at 30 min)
Sham				Sham			
Vehicle	238 ± 8	69 ± 4	35.5 ± 0.3	Vehicle	213 ± 11	59 ± 6	36.3 ± 0.1
1 mg/kg	115 ± 14*	59 ± 7	36.9 ± 0.1*	3 mg/kg	150 ± 15*	59 ± 5	36.8 ± 0.1*
				10 mg/kg	121 ± 8*	56 ± 6	37.1 ± 0.1*
OB				OB			
Vehicle	241 ± 7	107 ± 8*	34.9 ± 0.1	Vehicle	244 ± 8	98 ± 7*	36.1 ± 0.2
1 mg/kg	123 ± 24+	79 ± 8+	37.2 ± 0.2+	3 mg/kg	180 ± 12+	84 ± 5	36.9 ± 0.3+
				10 mg/kg	117 ± 18+	72 ± 4+	36.6 ± 0.1

* $p<0.05$ versus vehicle-treated sham animals. + $p<0.05$ versus vehicle-treated OB animals.

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373 P A CAL SYSTEM FOR TEACHING ELEMENTARY DRUG DISPOSITION AND PHARMACOKINETICS: VERSION 2

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This program is the first part of a second version of a previous CAL package on Drug Disposition and Pharmacokinetics (Ogg and Stevenson, 1993). Although this package is incomplete according to the original remit, it does cover a large section of basic drug disposition and pharmacokinetics and may be considered as a stand-alone package. The revision was thought desirable due to the perceived design criteria adopted by the PharmaCALogy and the PCCAL consortia. A consistent, well evaluated, user interface should eliminate the students' need to learn how to navigate and use the material presented. The original package did not allow any interaction and animations had to be produced in a different package. Animations are very important in order to stimulate student learning and to allow them to conceptualise the more difficult material. In many ways this is the most important point of any CAL system, to avoid the "text-book on screen". The objective here therefore was to change student perception and use of the material to one of "use" rather than "avoid" This new version has been re-written in Authorware (Macromedia) which allowed an integrated development of the original material with the specific inclusion of student-machine interaction. The program was produced as an Honours B.Sc. Student project in 10 weeks. This was possible since many of the original text and diagrams from the earlier program were retained. Due to time constraints, however, it was not possible to include as much interactive material as desired. Over the next year this package will be completed to cover the rest of version one.

The PCCAL consortium has produced some good CAL software in pharmacokinetics, especially the pharmacokinetics workshop package. The main pharmacokinetics package we felt was rather weak in some areas, in comparison to our original coverage in version one. This version two of our package integrates well with the PCCAL software and therefore complements it to a great extent. The software therefore keeps true to version one's premise of not just telling, "why" but also the "how".

Student evaluation of this version revealed a strong preference for the new design but indicated that there was not enough interaction (based on other pharmaCALogy & PCCAL packages). There is therefore a strong case for modifying this program in light of these comments in order that a richer more fulfilling experience of CAL can be achieved.

Ogg G.D.and I.H. Stevenson (1993) A CAL System for Teaching Elementary Drug Disposition and Pharmacokinetics. Br. J. Pharmacol. 108 311P.