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An Integration Of Preclinical Tests To Assess Acute Anxiolytic And Chronic Antidepressant Effects Of Diazepam And Desipramine In Rats

Although there is a high degree of comorbidity between depression and anxiety, it is not common for antidepressant and anxiolytic effects of drugs to be evaluated in a combined manner. Thus, this study aimed to integrate preclinical tests of anxiety [elevated plus maze (EPM) and open field (OF)] and depression (forced swim test, FST), in a single study design using the standard antidepressant desipramine (DMI) or the anxiolytic diazepam (DZP).

Male Sprague-Dawley rats (7-8 weeks of age) received daily subcutaneous injections of the drugs (DMI, 0, 2.5, 5 and 10 mg/kg; DZP, 0.5, 1 and 1.5 mg/kg); controls received vehicle injections. Thirty minutes after the first injection, rats were assessed in the EPM, followed immediately by the OF. After a further 13 days drug treatment, the antidepressant effects in the FST were examined; home cage locomotor activity (HCA) was measured in the hour preceding the test swim (see (1) for testing protocols). Experimental procedures were carried out in accordance with the guidelines and approval of the Animal Care and Research Ethics Committee, NUI, Galway, Ireland. Data were analysed using One-Way ANOVA, followed where appropriate by *post hoc* SNK test; $p<0.05$ was deemed statistically significant.
DZP had acute anxiolytic effects, and significantly affected ethological parameters in the EPM. DZP decreased distance moved (cm) in the OF. In the FST, chronic DMI significantly decreased immobility and increased climbing in a dose dependent manner. Both DZP and DMI decreased HCA in the hour prior to the FST.

Table 1. Effect of DMI (2.5, 5 or 10 mg/kg) or DZP (0.5, 1, 1.5 mg/kg) on behaviour in the EPM, OF, HCA and FST. Data expressed as Mean ± SD (n=6-8 per group). This study has demonstrated that both antidepressant and anxiolytic effects of drugs can be successfully integrated into a single experimental design, and thus can be proposed as a cost and time-effective approach for assessing these properties for novel compounds.

	EPM	OF	HCA	FST		
	OAE %	DM (cm)	DM (cm)	Immobility (s)	Climbing (s)	Swimming (s)
Control	19±17	2171±638	4794±1217	224±46	59±39	10±4
DMI 2.5 mg/kg	29±20	1665±278	3319±727*	166±52	117±57	12±8
DMI 5 mg/kg	32±12	1801±276	3616±841	126±73**	152±79*	22±13
DMI 10 mg/kg	25±14	1916±317	3867±842	109±53**	169±57**	19±14
Control	21±11	1866±385	5997±1326	187±75	51±21	59±69
DZP 0.5 mg/kg	34±13	2233±533	4826±958	209±24	33±19	59±20
DZP 1 mg/kg	39±15*	1199±484*	4337±1296*	192±54	65±55	43±19
DZP 1.5 mg.kg	41±14*	885±578**	4351±1037*	202±28	38±38	61±34

Simpson J. *et al.* (2012). Prog Neuropsychopharmacol Biol Psychiatry **37(2)**: 227-236.