A PASSIVE AVOIDANCE RESPONSE IN MICE - THE EFFECTS OF PHASE-SHIFT AND CHLORDIAZEPOXIDE

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It has previously been shown that passive avoidance responding in rats is disrupted by phase-shift (the sudden alteration of external time-cues) and that this disruption is prevented by pretreatment with chlordiazepoxide (CDZ) (Librium) (Davies & others 1974). This test appeared to provide a rapid and sensitive method of detecting anxiolytic activity; our observations have therefore been extended to mice, and to the use of a single-trial passive avoidance test, as opposed to the two-trial procedure previously used.

Groups of 10 male CFLP mice, weighing 35-50g, were housed under constant conditions of 12h light (0600-1800h), 12h dark (1800-0600h), and with free access to food and water. The passive avoidance response (PAR) was measured over 1 minute using manually-controlled apparatus based on that of Boissier & others (1968), and giving a shock of 0·2mA constant current for 0·5s.

The results are summarised in Table 1. PAR showed a significant variation over 24h, being lowest at the end of the light phase, and rising to a peak in the dark phase. A 6h phase-shift, (prolonging the dark phase by 6h, so that subsequent light-dark cycles were 1200-0000h light, 0000-1200 dark), produced a dual effect on PAR. After 3 days, PAR at 1200h was significantly decreased, the behaviour characterised by 'freezing' and signs of stress, eg piloerection, defaecation, tachycardia. On days 4 and 5 the PAR was increased, and the expected scores were not obtained until 6 or more days after phase shift.

Table 1 Passive avoidance response (PAR) in mice

24h variation in PAR

	n	PAR (mean ± s.e.)
1200h	20	5·1 ± 0·3
1800h	20	4·0 ± 0·3
2400h	20	6·0 ± 0·7
0600h	20	5·2 ± 0·5

Effect of 6h phase-shift

days after phase-shift	n	PAR (mean ± s.e.)
3	20	3·3 ± 0·4*
4	10	7·2 ± 0·9*
5	10	8·6 ± 0·9*
6	10	6·7 ± 1·0

Effect of CDZ on PAR

	Dose (CDZ μg ml^{-1})	n	PAR (mean ± s.e.)
Expected control value		20	5·2 ± 0·5
Phase-shifted	0	20	3·3 ± 0·4*
	50	20	6·1 ± 0·8
	100	20	6·1 ± 0·7
	200	10	11·5 ± 0·6*
Controls	50	20	5·0 ± 0·9
	100	20	4·8 ± 0·8
	200	10	7·7 ± 0·8*

*significant difference from expected control value $p < 0·05$

Drug-treated animals were presented with chlordiazepoxide, 50, 100 or 200 μg ml^{-1} in the drinking water. Although chlordiazepoxide 50 μg ml^{-1} given to control animals for 3 days produced no measurable effect, in phase-shifted animals a significant increase in PAR was seen, so that the 'freezing' behaviour was abolished, and scores were not significantly different from the expected control values.

These results confirm the earlier findings in rats that phase-shift induces inhibition of the PAR and further suggest that since this is a one-trial procedure, the deficit is one of acquisition or short term memory rather than retention or recall. It has also been confirmed that this effect can be inhibited by chlordiazepoxide in doses significantly lower than those required to produce a measurable effect in normal animals.

Boissier, J. R., Simon, P. & Avon, C. (1968). Eur.J.Pharmac, 4, 145-151.
Davies, J. A., Navaratnam, V. & Redfern, P. H. (1974). Br.J.Pharmac, 51, 441-451.