Psychopharmacology (1983) 79:367–369

Psychopharmacology

Short Reports

Effects of a 1,5-Benzodiazepine Derivative upon Performance in an Experimental Stress Situation

Andrew C. Parrott* and Sandra Davies

Department of Psychology, University of Leeds, Leeds LS2 9JT, UK

Abstract. Psychological performance tasks were given to normal subjects under different conditions of experimental stress: high stress (being filmed on video), or low stress (tested without filming); and after different pharmacological treatments: clobazam 20 mg (an anxiolytic 1,5-benzodiazepine derivative), or placebo. On all five performance assessments (choice reaction times, serial subtraction times, critical flicker fusion values), there was a consistent tendancy for clobazam performance to be comparatively better under high stress, and for placebo performance to be comparatively better under low stress. From these, and previous similar findings, it seems that the level of experimental "stress" under which subjects are tested, can have important influences upon the psychopharmacological performance levels obtained.

Key words: Benzodiazepine – Clobazam – Performance – Stress – Arousal

Kohnen and Lienert (1980) investigated the effect of cloxazolam upon performance in a memory task, under three levels of experimental stress: high stress – when subjects were filmed on video, medium stress – when tested in the presence of spectators, and low stress – when tested individually. They reported a significant interaction between drug response and stress, with the highest of the three cloxazolam performance values under the high stress condition, and the highest of the three placebo performance values under the low stress condition. Kohnen and Lienert (1980) chose cloxazolam "as a tranquilizer to depress psychoactivity and thus, hopefully influence performance". The present study was undertaken to investigate whether similar effects would occur with the 1,5-benzodiazepine derivative clobazam, an anxiolytic agent with few deleterious effects upon performance (Hindmarch 1979; Steiner-Chaskel and Lader 1981). The high stress and low stress testing conditions described by Kohnen and Lienert (1980) were replicated in the present study. Psychological performance levels were assessed on three separate task: choice reaction time, as an index of psychomotor ability; critical flicker fusion (CFF), as a psychophysical index of alertness; and serial subtraction of numbers, a cognitive processing task.

Offprint requests to: A. C. Parrott

* *Present address:* Institute of Navel Medicine, Alverstoke, Gosport, Hampshire, PO12 2DL, UK

Materials and Methods

Subjects. 24 volunteer students (12 male, 12 female, mean age 22 years) were divided into four groups of six subjects. Each group contained equal numbers of high and low anxiety subjects. This grouping was based upon scores for the Middlesex Hospital Questionnaire (MHQ) anxiety subscale, which provides an index of mixed trait/state anxiety (Crown and Crisp 1970). Speilberger (1966) has shown that high trait anxiety subjects demonstrate more frequent state anxiety (also Clyde 1981). Anxiety levels affect both baseline performance, and performance changes under anxiolytic drug conditions (Janke et al. 1979; Clyde 1981; also Parrott and Kentridge 1983), hence the necessity for controlling baseline anxiety levels across the groups.

Performance Assessments. The performance assessments represent tasks regularly used in psychopharmacological studies. Choice reaction times to one of six randomly occurring stimulus lights were recorded (average of 20 responses). Recognition times (time to lift the finger from the resting template) were separately recorded from the total response times (Hindmarch and Parrott 1979). Serial subtraction of numbers comprised the average time per subtraction, from continuous subtractions over a period of 2 min; two difficulty levels were present, subtraction of 3's and 17's (Parrott and Munton 1981). Critical flicker fusion thresholds were included as a psychopharmacological index of alertness (Smith and Misiac 1976). The average of six thresholds (three ascending, and three descending series) was recorded (Hindmarch and Parrott 1979). Analogue self-ratings (100 mm scales) were also recorded, and are briefly presented.

Procedure. Subjects were tested twice. The first set of data comprised practice familiarisation and was discarded. This practice session was adequate to ensure performance competance on each test. The second session was given 1 week later. The performance assessments were given 90 min after drug administration (clobazam 20 mg or placebo, in matching capsules). Testing was double-blind.

Stress. Stress was induced at two levels: low stress, where subjects were tested individually, and high stress, where a video film of the subjects' performance was taken (Kohnen and Lienert 1980).

Design. Four subject groups were present; placebo low stress, placebo high stress, clobazam low stress, clobazam high stress. Performance was analysed by 2 × 2 factorial analysis of variance (ANOVAR).

Results

The ANOVAR findings are summarised in Table 1. There were no significant drug effects upon any performance measure, confirming previous findings that clobazam 20 mg does not generally lead to performance impairments (Hindmarch 1979; Hindmarch and Parrott 1979; Steiner-Chaskel and Lader 1981). There was a singificant effect of stress upon choice reaction recognition times, which were significantly slower under high stress. There were no significant ANOVAR drug/stress interactions. Group mean performance scores are shown in Table 2. This table also contains high stress/low stress differences scores, and drug/stress difference scores (were positive values indicate higher clobazam scores under the high stress conditions). These performance difference scores indicate faster clobazam performance (low scores) under high stress, and faster placebo performance under low stress. The CFF (alertness) values exhibit a similar trend, with higher clobazam CFF values (higher alertness) under high stress, but higher placebo CFF values (higher alterness) under low stress (Table 2). These performance trends are similar to those reported by Kohnen and Lienert (1980) for cloxazolam. The analogue self-rating questions (for anxiety, relaxedness, tiredness, drowsiness) demonstrated two significant drug effects, with significantly increased relaxedness and drowsiness under clobazam ($P < 0.05$); neither stress effects, nor drug/stress interactions were significant.

Discussion

Kohnen and Lienert (1980) concluded that "the effect of cloxazolam on routine test performance was a function of stress intensity". A similar conclusion can be proposed for the effects of clobazam, since clobazam performance was comparatively better under high stress, and comparatively worse under low stress, for all five performance assessments (Table 2). The ANOVAR interaction effect did not however reach significance (Table 1), possibly because clobazam has comparatively weaker overal effects upon performance than those typically found with the 1,4-benzodiazepine derivatives (Hindmarch 1979; Steiner-Chaskel and Lader 1981). Also, the drug/stress interaction is probably only one of several factors which may influence performance. A number of techniques attempting to induce stress have been used (e.g. threat of electric shock, viewing "stressing" films, loud noises). It is however difficult to define a "stress" or a "stressor", and even more difficult to compare different stressors or performance changes under different stressors. Many findings in the review by Janke et al. (1979) were negative, although with reference to loud noise as a stressor, they concluded: "Performance tests usually reveal slight interactions between stress conditions and drug response". Parrott and Hindmarch (1975, 1977, 1978) reported comparative decrements in choice reaction times under low noise, but not under high noise, with clobazam and other benzodiazepines; this difference was however found only with noise linked to stimulus occurrence, and not with continuous noise (Parrott and Munton 1981).

Stress is a very heterogeneous concept, but it does seem that the level of "stress" under which testing occurs can have important influences upon the nature of the drug response. Noise is "well suited as a stressor" in studies of drug response (Janke et al. 1979). The present study also confirms the practical utility of the procedures described by Kohnen and Lienert (1980), for inducing social stress in psychopharmacological studies.

Table 1. Summary of analysis of variance findings: *F*-values and significance levels

Performance assessments	Drug effect	Stress effect	Drug and stress interaction
Choice reaction time – recognition	0.00	4.80*	1.77
Choice reaction time – total	0.27	2.57	2.43
Serial subtraction of threes	0.34	0.18	0.10
Serial subtraction of seventeens	0.00	0.00	0.38
Critical Flicker Fusion threshold	0.05	0.55	3.47

*$P < 0.05$

References

Clyde CA (1981) The influence of personality on response to low doses of benzodiazepines. R Soc Med Int Symp Series 43:75–86

Crown J, Crisp AH (1970) Manual of the Middlesex Hospital Questionnaire (MHQ). Psychol Test Publications. Barnstable, Devon

Hindmarch I (1979) Some aspects of the effects of clobazam on human psychomotor performance. Br J Clin Pharmacol 7:77S

Hindmarch I, Parrott AC (1979) The effects of repeated nocturnal doses of clobazam, dipotassium clorazepate and placebo on subjective ratings of sleep, and objective measures of performance. Br J Clin Pharmacol 8:325–329

Janke W, Debus G, Longo N (1979) Differential psychopharmacology of tranquilizing and sedating drugs. In: Ban TA (ed) Modern problems in pharmacopsychiatry, vol 14. Karger, Basel

Table 2. Group mean scores for all performance assessments

Performance assessment	Clobazam 20 mg			Placebo			Clobazam/placebo
	High stress	Low stress	Stress difference	High stress	Low stress	Stress difference	Drug stress difference
Choice reaction time – recognition (s)	0.32	0.31	+ 0.01	0.35	0.29	+ 0.06	– 0.05
Choice reaction time – total (s)	0.53	0.54	– 0.01	0.62	0.51	+ 0.11	– 0.12
Serial subtraction of threes (s)	2.53	2.78	– 0.25	2.48	2.52	– 0.04	– 0.21
Serial subtraction of seventeens (s)	7.27	8.16	– 0.89	8.11	7.20	+ 0.91	– 1.80
Critical Flicker Fusion (Hz)	32.50	31.30	+ 1.20	30.20	33.10	– 2.90	+ 4.10

Kohnen R, Lienert GA (1980) Defining tranquilizers operationally by non-additive effect in experimental stress situation. Psychopharmacology 68:291–294

Parrott AC, Hindmarch I (1975) Clobazam a 1,5-benzodiazepine derivative – effects on anxiety, arousal and performance compared with these of CNS stimulants and tranquilisers. IRCS Med Sci 3:177

Parrott AC, Hindmarch I (1977) Comparative effects of three benzodiazepine derivatives – clobazam, nitrazepam, and flurazepam on psychomotor performance under different reinforcement conditions. IRCS Med Sci 5:166

Parrott AC, Hindmarch I (1978) Clobazam: a 1,5-benzodiazepine derivative – effects of human psychomotor performance under different levels of task reinforcement. Arch Int Pharmacodyn 223:261–268

Parrott AC, Kentridge R (1983) Personal constructs of anxiety under the 1,5-benzodiazepine derivative clobazam, related to trait-anxiety levels of the personality. Psychopharmacology (in press)

Parrott AC, Munton A (1981) Comparative effects of clobazam and diazepam on psychological performance under different levels of background noise. R Soc Med Int Symp Series 43:51–57

Smith JM, Misiac H (1976) Critical Flicker Fusion (CFF) and psychotropic drugs in normal human subjects – a review. Psychopharmacology 47:175

Speilberger CD (1966) Anxiety and behaviour. Academic Press, New York

Steiner-Chaskel N, Lader MH (1981) Effects of single doses of clobazam and diazepam on psychological functions in normal subjects. R Soc Med Int Symp Series 43:23–32

Received June 11, 1982; Final version November 30, 1982