Pharmacology Biochemistry & Behavior, Vol 4, pp 729–730.

BRIEF COMMUNICATION

Noise Stress and the Effects of Viloxazine (Vivalan),[1] a New Antidepressant, on Open Field Activity in Rats[2]

TOM COX AND JANET LEE[3]

Stress Research Group, Department of Psychology, University of Nottingham Nottingham, NG7 2RD, England

(Received 25 November 1975)

COX, T AND J. LEE. *Noise stress and the effects of viloxazine (Vivalan), a new antidepressant, on open field activity in rats.* PHARMAC. BIOCHEM BEHAV 4(6) 729–730, 1976 – The effects of different types and levels of background noise on the response to Viloxazine (Vivalan) were studied in rats. The results showed that increasing the level of noise produced changes in activity which were dependent on its mode of presentation (type). The drug appeared to enhance these changes

Viloxazine Antidepressant Noise stress Stress Vivalan

VILOXAZINE hydrochloride (Vivalan, ICI 58, 834) is a new antidepressant drug [4, 7, 10] developed by Imperial Chemical Industries, which is chemically unrelated to any existing antidepressant agent, and which possesses a novel profile of neuropharmacological activity in animals [2, 6, 8]. The effects of the drug on the behaviour of the rat and the mouse have received attention during its preclinical study, and it has been shown to reduce both activity and defaecation in rats tested in the open field [2]. This has been interpreted as consistent with its clinical effects, and has been shown to be characteristic of the tricyclic antidepressant imipramine, and different from the psychomotor stimulant amphetamine. The open field used in the latter investigations has been described as "novel and stressful", continuous background white noise at a pressure of 70 dB contributing to its stressful nature. Although the effects of such noise on open field behaviour have been studied [1], few studies have examined its effects on the behavioural response to psychoactive drugs. Systematically increasing the intensity of the background noise, and altering its form (continuous or discontinuous) could alter the stressfulness of the test environment [3], and make obvious any interaction existing between the effects of such an environmental stress and the drug under study. Such an interaction would be of particular interest if the drug under test was of clinical significance.

METHOD

The present study investigated the effects of continuous and predictable discontinuous background white noise, at 3 intensities (70, 80 and 90 dB), on the behavioural response to a small dose of viloxazine. The predictable discontinuous noise was repeatedly on for 250 msec, and off for 4750 msec.

Twelve groups of 8 male adult Sprague-Dawley rats were tested in a circular arena, 830 mm in dia. with walls 330 mm high. The inside of the arena was painted white. The floor was sectored radially into 19 approximately equal areas. White noise was imposed on the field (its intensity being measured at floor level), and the background light intensity was adjusted to be moderately bright (5 x 200 watt bulbs, 1.3 m above the floor of the field). The rats under test were placed individually in the centre of the arena, and their activity scored for 2 min. Activity was scored as the number of open field areas entered by the animal. Half of the rats tested had previously been injected with viloxazine (5 mg/kg), and half with saline (0.9% w/v). The drug was dissolved in saline and was injected by the intraperitoneal route in volumes of 1 ml/kg. The saline injections were administered by the same route and in the same volumes. The rats were tested 25 to 35 min after being injected. The small dose of the drug used has been shown to alter the activity of both rats and mice [2, 6, 8].

[1] Trade-mark, the property of Imperial Chemical Industries Limited

[2] This research was supported by a grant from Imperial Chemical Industries Limited, Pharmaceuticals Division, Alderley Park, Macclesfield, England.

[3] Now at Manchester Polytechnic.

The animals were randomly assigned to the 6 drug and 6 control groups, and were designated from 1 through 8 within each group. The order of testing of the first animals (1) from each group was randomized, and so on through (2) to the last animals (8). Testing was spread over 5 days, and took place at midday (11.30 to 12.00 hr).

RESULTS

The results are shown in Fig. 1, and are described below.

An analysis of variance using the obtained activity scores showed a significant difference due to the effects of continuous and discontinuous but predictable noise $F(1,84) = 21.45$, $p = 0.00001$. Activity appeared much reduced by a background of predictable discontinuous noise. Significant interactions existed between the effects of noise level and type of noise $F(2,84) = 7.38$, $p = 0.001$, and between drug and type of noise $F(1,84) = 6.64$, $p = 0.01$. Increasing noise levels appeared to increase activity when the noise was continuous, but decrease it when the noise was discontinuous but predictable. The drug also appeared to increase activity when the noise was continuous but decrease it when the noise was discontinuous but predictable. No other main effects or interactions were significant The effects of the drug at 70 dB continuous noise were consistent with those previously reported by Cox and Tye [2] for that situation (present study: 14% decrease in activity, previous study 27% decrease in activity)

DISCUSSION

The behavioural effects of viloxazine, and possibly other psychoactive drugs, appear to be dependent on the prevailing environmental conditions. Factors, such as loud noise, which have been described as "stressful" [3], can be important determinants of the response to the drug. In the present study the effects of noise on that response are described by an interactive rather than an additive model.

Increasing background noise appears to produce either an increase or a decrease in activity depending on its mode of presentation. These responses may represent changes in flight (or escape) behaviour, in exploration, or in freezing

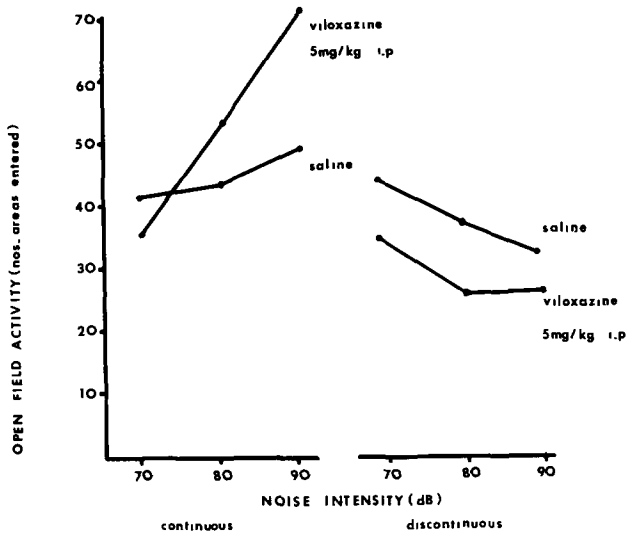

FIG. 1 The effects of noise and viloxazine on open field activity in rats. Group means are shown.

(immobility): the first 2 active patterns of behaviour are not necessarily incompatible. Both the active and passive patterns of stress response (flight and freezing) have been described in a variety of species and it is assumed that, at least in the animals' natural environment, they are adaptive forms of behaviour [5,9].

Although under a low noise level (70 dB) the drug appeared to reduce the level of the animals' activity, irrespective of the mode of noise presentation, at higher levels it appeared to enhance (or mimic in its effects) the behavioural response to that noise. Thus under continuous noise it increased activity, and under discontinuous noise decreased it. Whether or not these effects are adaptive is a matter of debate.

REFERENCES

1. Broadhurst, P L Determinants of emotionality in the rat. I Situational factors *Br J Psychol.* **48**: 1–12, 1957
2. Cox, T and N. Tye The effects of amphetamine, imipramine and ICI 58,834 (Vivalan), a potential antidepressant, on unconditioned behaviour in rats *Psychopharmacologia* **40**: 297–304, 1975
3. Davies, D R Physiological and psychological effects of exposure to high intensity noise. *Appl Acoustics* **1**: 218–233, 1968.
4. Ekdawi, M. Y Viloxazine (Vivalan) comparison with imipramine *J int med Res* **3**: Suppl. 3, 75–78, 1975.
5. Gray, J. Psychology of Fear and Stress, London, Wiedenfeld and Nicolson, 1971.
6. Greenwood, D. T. Animal pharmacology of Viloxazine (Vivalan). *J int med. Res* **3**: Suppl 3, 18–28, 1975.
7. Mahapatra, S B Short term effects of viloxazine (Vivalan) compared with placebo in depression a double blind study *J int. med Res* **3**: Suppl. 3, 70–74, 1975.
8. Mallion, K. B , A H Todd, R W Turner, J. C Bainbridge, D. T Greenwood, J Madinaveita, A R Somerville and B. A. Whittle 2-(2-Ethoxyphenoxymethyl) tetrahydro-1, 4-oxazine hydrochloride, a potential psychotropic agent *Nature, Lond.* **238**: 157–158, 1972.
9. Miller, N E and J. M. Weiss Effects of somatic or visceral response to punishment In *Punishment and Aversive Behaviour*, edited by B. A Campbell and R. M. Church. New York Appleton-Century-Crofts, 1969, pp 343–372
10. Pichot, P., J. Guelfi and J. F. Dreyfus. A controlled multicentre therapeutic trial of Viloxazine (Vivalan) *J. int. med. Res.* **3**: Suppl 3, 80–86, 1975