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Short Reports

Evaluation of the Psychotropic Effect of Etifoxine through Pursuit Rotor Performance and GSR

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Abstract. Six volunteer normal subjects, aged 18–25 years, were selected from a university student population to compare the psychotropic effects of Etifoxine, *d*-amphetamine and placebo. All of them received Etifoxine 300 mg, *d*-amphetamine 5 mg and placebo in a double-blind randomly cross-over design involving a single dose weekly.

The criteria studied were the GSR and performance on the pursuit-rotor. The subjects were tested before (TO), 2 (T2) and 6 (T6) hrs after drug administration. At T2, both the GSR and pursuit-rotor performance obtained with each drug differed significantly from placebo, but not between drugs. The effects of Etifoxine were similar to those of *d*-amphetamine in reducing the GSR and improving pursuit-rotor performance.

Key words: Psychotropic drugs (Etifoxine) – Psychophysiological tests – GSR – Motor tests.

Introduction

Etifoxine (Hoechst 36801) is a new psychotropic agent with a new chemical structure [6-chloro-2-(ethyl-amine)-4-methyl-4-phenyl-4H-3,1-benzoxazine] (Fig. 1) (Hoffmann, 1970).

When administered to animals this compound has tranquilizing effects with an anticonvulsive, spasmolytic and anticholinergic action (Boissier *et al.*, 1972). In a recent pilot study Galeano Muñoz (1972) described Etifoxine as a drug which enhances intellectual and motor performance, without impairing psychomotor coordination, in patients suffering neurosis with asthenic-apathetic components. In a previous pilot trial we found similar results in patients with neurotic depression (unpublished data). On the contrary, Sartory and Rust (1973) reported that Etifoxine reduced the susceptibility of the subjects to extrinsic arousal in galvanic skin response. In view of this, the aim of this study was to define the scope of action of Etifoxine in comparison with a standard central stimulating drug *d*-amphetamine and with placebo, by means of the pursuit-rotor performance and the galvanic skin response, in normal subjects.

Material and Methods

Six volunteer normal subjects (5 males and 1 female), aged 18–25 years, were selected from a University student population by means of individual interviews, the PEN inventory (Eysenck and Eysenck, 1969), and Taylor's manifest anxiety scale (TMAS) (Taylor, 1953). Clinical and laboratory findings showed no evidence of disease in these subjects. None of them had evidence of important psychological disturbances nor were under psychotropic drug therapy during the 6 months prior to the study. Subjects were randomly allocated in a double-blind cross-over balanced design. 300 mg Etifoxine, 5 mg *d*-methyl phenethylamine sulfate or placebo were administered in a single dose, once a week over 3 consecutive weeks. The full dose was taken by all the subjects at 8 a.m., after a cup of milk and a slice of bread and butter. All were tested once a week on the same day, before the experience (T0) and 2 (T2) and 6 hrs (T6) after. At T0, T2 and T6, galvanic skin response (GSR) and pursuit-rotor performance were assessed. 24 hrs before the testing day they went through 7–9 hrs sleep and no alcohol intake. On the day of the experiment the subjects remained at the unit under medical surveillance. Smoking and coffee were not allowed; food intake consisted of a light lunch without alcoholic beverages. The subjects were allowed to remain at the unit, talk and walk between tests.

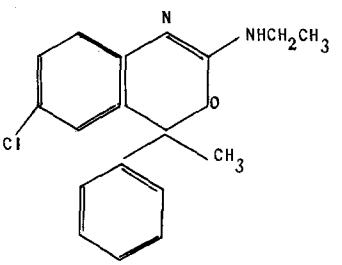


Fig. 1. Chemical structure of Etifoxine (Hoechst 36801)

Apparatus

A pursuit-rotor standardized at 60 rpm, model 5-86 A from Marietta Apparatus Company was used. The rotating base has a diameter of 30 cm. The 2-cm diameter metal disc is placed at 12 cm from the center of the spinning base. The contact head of the floating stylet has a 0.85-cm diameter.

For recording of the galvanic skin response the following equipment was used:

a) a 4-channel Elema Schönander polygraph; b) a dermal resistance amplifier with concentric tetrapolar electrodes (Venables and Martin, 1967; Lader, 1966); c) a Marietta dermal resistance recorder; d) an Akai phonomagnetic tape recorder, 4 channels, professional model; e) a 2-channel oscilloscope for immediate visual control of records; f) 3 programs with 20 auditory stimuli of different duration in each (1, 2 and 3 sec), recorded on phonomagnetic tape, distributed at random intervals of 45–85 sec, preceded by 10 min of pure noise. The remaining characteristics of stimulation were identical in all 3 programs: intensity of 100 db and a frequency of 1000 Hz.

Procedure

Pursuit-Rotor. Each pursuit-rotor test was composed of a series of thirty 10-sec trials. Readings were performed every 10 sec. The results were expressed in seconds as time on target touched by the subjects, and were averaged every 5 trials.

GSR. Each subject was fully informed about the experiment, allowed to be seated on a comfortable chair in a sound-proof room with pleasant and constant temperature and illumination. GSR tetrapolar electrodes were fixed on the thenar and hypothenar eminences of the right hand. After this, the physician placed the headphones on the subject, gave him the directions and turned off the light. The system was operated from a cabin separated from the sound-proof room by a one way mirror, through which the subject was observed. The stimulus-tone sequence was automatically scheduled and fed directly by the tape-recorder. All experiments performed on each subject were recorded on millimetric paper. Results were expressed in millimeters corrected on each pre-stimulation value. The average was calculated for every 4 values.

All data were analyzed by Student's *t* test.

Results

PEN and Taylor's scores in the 6 volunteers who entered into the study did not differ from local norms.

Fig. 2 shows the pursuit-rotor performance measured under the three experimental conditions. The findings in the *d*-amphetamine, placebo and Etifoxine groups were evaluated at times T0, T2 and T6. Each point of the curves represents the average of 5 readings every 10 sec. No significant differences could be found among group performances at T0. At T2 the performance of the placebo group was significantly lower than that of the *d*-amphetamine and Etifoxine groups ($P < 0.01$), which in turn did not differ significantly from each other. Performance at T6 ($P < 0.001$) showed patterns similar to T2.

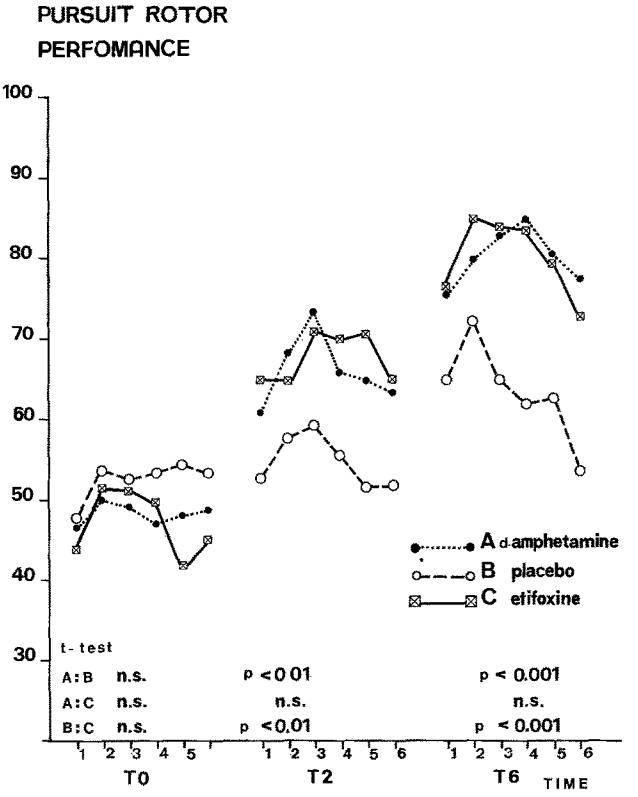
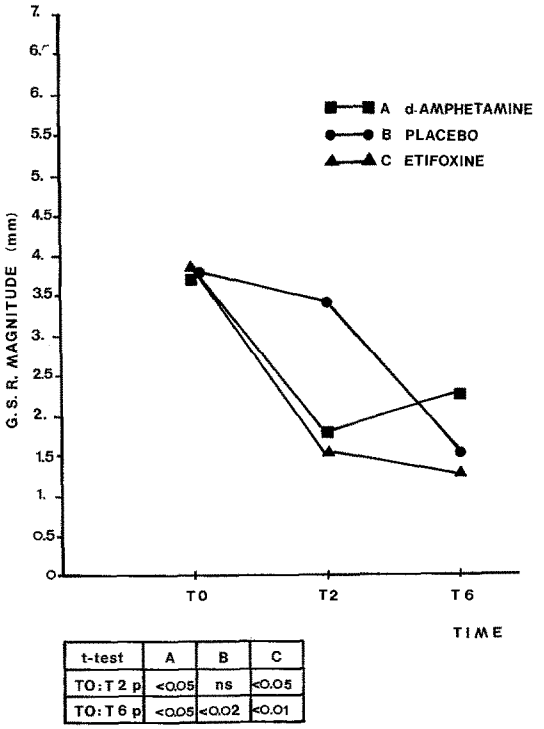


Fig. 2. Pursuit rotor performance before (T0) and after 2 (T2) and 6 hrs (T6) of the administration of *d*-amphetamine Etifoxine and placebo in 6 volunteer man. Each point represents average of 5 readings every 10 sec



t-test	A	B	C
T0:T2 p	<0.05	ns	<0.05
T0:T6 p	<0.05	<0.02	<0.01

Fig. 3. Average of every 4 assessments of the GSR. Before the experience (T0), 2 (T2) and 6 hrs (T6) later

The GSR data from the 3 groups were averaged at T0, T2 and T6 and are shown in Fig. 3. At T0 no significant differences were found. At T2 (time of peak drug effect) the GSR showed significant differences ($P < 0.01$) between placebo and drugs, with no significant difference between *d*-amphetamine and Etifoxine; the GSR is reduced under drug action. The GSR is not reduced by placebo at T6, where no difference occur among the 3 groups.

Discussion

In the selection of patients for this study the PEN inventory scale described by Eysenck and Eysenck (1969) was used. This scale is an inventory containing 20 extroversion, 20 neuroticism and 20 psychoticism questions. The volunteers for this study did not differ, according to this inventory, from local norms (Córsico *et al.*, 1975). None of them had high psychoticism score, and extroversion was found to be within the normal range. The results of this study showed essentially that both Etifoxine and *d*-amphetamine behaved similarly, improving the pursuit-rotor performance and reducing the magnitude of the galvanic skin response. Moreover both of them differ significantly from placebo, which did not produce such results. Since *d*-amphetamine is a well-known psychostimulant agent, the results obtained are compatible with a psychostimulatory pharmacological action of Etifoxine. Previous experimental and clinical studies showed incongruence concerning the pharmacological action of Etifoxine, since some investigators (Boissier *et al.*, 1972) found evidences of a tranquilizing effect, while other studies (Galeano Muñoz, 1972, and Córsico *et al.*, unpublished data) found evidences of a psychostimulatory effect. Furthermore, Sartory and Rust (1973), who studied the same behavioral variables as we did, found Etifoxine to be inactive regarding rotor performance, and interpreted reduced susceptibility to extrinsic arousal as a tranquilizing effect. This lack of correlation between different studies is hard to interpret. Probably differences in the sample and/or certain pharmacological aspects of Etifoxine, at present unknown, could be responsible for this lack of agreement. This indicates the importance of studying homogeneous groups of patients defined by using personality inventory scales. To sum up, our results suggest that Etifoxine could have, at least under some circumstances, a psychostimulatory effect. However, the final psychopharmacological action of the drug seems far from being characterized.

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