

A Comparison of the Effects of Varying Dose Levels of Oxypertine on Mood and Physical Performance of Trained Athletes

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Oxypertine (also known as Win. 18,501 -2) is a member of a series of alkyl indolyl-4-phenyl piperazines (Archer *et al.*, 1962), and is 1-[2-(5,6-Dimethoxy-2-methyl-3-indolyl) ethyl]-4-phenylpiperazine.

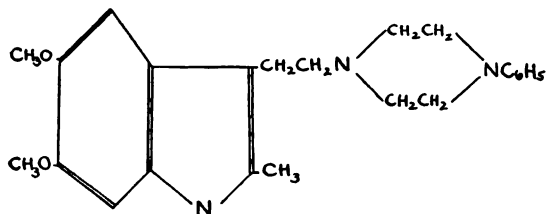


FIG. 1.

Clinical evaluation of this compound has suggested that, in contrast to its tranquilizing effects at high dose levels, in lower doses it may have stimulant properties (Durell and Pollin, 1963; Friedhoff and Hekimian, 1963; Hollister *et al.*, 1963; Flament, Lofft and von Mendelssohn, 1964). This has been supported by the results of animal experiments, in which the stimulant effects of dexamphetamine have been potentiated by low doses, and inhibited by high doses of oxypertine (Cole and Edwards, 1964; Randrup and Munkvad, 1964).

Studies by Smith and Beecher (1960) and Adamson and Finlay (1965) on the effects of psycho-stimulant drugs on muscular performance have suggested that the alteration of mood produced by compounds of the amphetamine group can be correlated with the performance of physical tasks.

The object of the present study was to discover the effect of different doses of oxypertine on the mood of five trained athletes, and to

assess any concomitant improvement or impairment of physical performance.

METHOD

The double-blind trial involved a within-subject comparison of five dose levels of oxypertine: 0, 5, 10, 20 and 40 mg., in the five subjects, with each dose repeated twice. The medicaments were presented as single tablets, identical in appearance.

The five volunteers were trained university athletes, ranging in age from 20 to 30 years. Each subject reported to the Department of Student Health at a specific time on each of ten days. The allocation of treatment on these ten occasions was randomized. After receiving the appropriate tablet, the subject rested for two hours. Ten minutes before undergoing a series of physical tests in the gymnasium each subject completed a feeling and attitude scale questionnaire, based on that designed by Lasagna, von Felsing and Beecher (1955). This comprised 32 items, each of which consisted of a pair of opposing feelings, e.g. "sad-happy", with a scale of seven possible degrees, i.e. a central zero point, and three points on either side. The subjects were asked to circle the number which described their feelings at that moment. The numbers were allotted positive or negative signs for the purpose of scoring for psycho-stimulant effect, but these signs were not included in the forms presented to the athletes.

The subjects performed four types of physical test on each occasion. Simple reaction time was estimated by measuring response to visual stimulus preceded at varying intervals by a warning buzzer. The mean of nine scores was taken. The procedures for determining muscular force (grip strength and lumbar strength) and

muscular endurance ("chinning the beam") were as described previously (Adamson and Finlay, 1965).

RESULTS

The results of the mood scale scores were analysed by the usual method of analysis of variance, as a three-factorial experiment with the factors: subjects, treatments and occasions. The analysis of the physical test scores was four-factorial, the readings being treated as a factor rather than as a simple replicate, since in all tests there is likely to be a fatigue element. In the case of reaction time especially, it is important to seek changes in the rapidity of onset of fatigue with different doses of the test drug.

There were five possible mood responses to increasing doses of the drug:

- (i) No response
- (ii) Depression
- (iii) Stimulation followed by depression
- (iv) Depression followed by stimulation, or
- (v) Stimulation

(a) Effect on Mood

Table I shows the individual mood scale scores after the administration of five dose levels of oxypertine. Analysis of these results shows

that the effect of different doses of oxypertine on the mood of the five subjects is significant. Examination of these scores by the method of orthogonal contrasts shows that, although the linear fit is better than the quadratic, the best result is obtained from the "a priori" contrast comparing 5 mg. and 10 mg. doses with the rest. Thus, according to the mood scale used, there is evidence of a psycho-stimulant effect at the 5 mg. and 10 mg. dose levels.

(b) Effect on Physical Performance

The means of the scores obtained by the five athletes after the five different treatments, for each of the four physical tests, are shown in Table II. Analysis of variance reveals that, in the case of the grip strength and lumbar pull tests, the response to different doses was not the same for all the subjects, although there was a consistent drug response at each level on different occasions. The results show a deterioration of physical performance with increasing dose of oxypertine. Examination of linear and quadratic trends confirms the absence of any stimulation at low dosage. Inspection of the means shows a downward trend from the first to last reading on any occasion; this is clearly a fatigue effect.

TABLE I
Mood Scale Scores

	Treatment						Subject Number					Total Score
							1	2	3	4	5	
P	+1	-6	+27	+3	-24	+1
5	+2	+27	+9	+2	+2	+42
10	+21	+15	+15	+9	-1	+59
20	-11	-8	-18	-50	-23	-110
40	-19	-37	-49	+12	-22	-115
Total	-6	-9	-16	-24	-68	-123

Mean of 2 scores after: P - Placebo

- 5 - Win. 18,501, 5 mg.
- 10 - Win. 18,501, 10 mg.
- 20 - Win. 18,501, 20 mg.
- 40 - Win. 18,501, 40 mg.

TABLE II

Factor	Mean Result For				
	(1) Grip strength lb	(2) Lumber Pull lb	(3) Reaction Time milli-seconds	(4) Chinning number	
Subject No.	1	140·47	619·33	317·87	18·93
	2	125·47	609·27	319·93	21·80
	3	109·50	604·53	318·72	10·23
	4	114·23	652·57	293·40	13·75
	5	128·97	644·20	310·41	11·60
Dose of oxypertine (mg.)	0	129·47	637·57	308·70	15·71
	5	124·80	648·83	309·14	15·09
	10	125·03	624·47	313·97	15·35
	20	121·20	613·40	315·40	15·18
	40	118·13	605·63	313·12	14·98
Occasion	First	122·11	624·03	313·63	14·51
	Second	125·35	627·93	310·50	16·01
Reading	(1)	127·06	643·76	318·42	16·60
	(2)	122·66	617·52	313·88	13·92
	(3)	121·46	616·66	315·64	
	(4)			309·98	
	(5)			312·30	
	(6)			310·12	
	(7)			310·72	
	(8)			306·90	
	(9)			310·64	

When the results of the muscular endurance test are analysed, the subjects vary in their response to the different treatments. In this case, however, the effect of the drug is not significant. The second effort on each occasion is, on average, poorer than the first, and this difference is significant.

Analysis of the reaction time test scores reveals that the only significant effect is that of differences between subjects. The differences between doses, between occasions and between readings are not significant. This indicates that the drug has no effect on the reaction time, and that there is no fatigue or learning effect demonstrable.

DISCUSSION

Analysis of the scores of the mental attitude questionnaire suggests that 5 mg. and 10 mg. doses of oxypertine brought about a definite enhancement of mood in the five subjects examined. This supports the hypothesis that, in

contrast with its tranquillizing effects at high dose levels, oxypertine has a mentally stimulating action at lower dosages. However, statistical analysis of the results of the physical tests carried out in this trial indicates that this action of low doses of oxypertine cannot be correlated with a significant improvement of muscular force in any of the five subjects examined. There was, in fact, a gradual impairment as the dose level was increased from 5 to 40 mg. Muscular endurance and reaction time were unaffected.

In these experiments it was hoped to provide objective tests of the effects of psycho-stimulant or psycho-depressant drugs, the change in mood being reflected in enhancement or impairment of muscular force. This has not happened in the present trial. The important question now is whether the subjective responses to the mood questionnaire are more or less reliable than the objective findings of the alteration in muscular force.

SUMMARY

The effects of placebo and four dose levels of oxypertine on mood and physical performance of five trained athletes were evaluated in a within-subject comparative trial.

Low dosages of oxypertine were found to bring about a definite enhancement of mood. This could not be correlated with physical performance, which showed no evidence of stimulation at lower dose levels, and declined progressively as the dosage was increased. Reaction time, however, was unimpaired.

Side effects were minimal and in no case necessitated withdrawal from the trial.

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