Nonmotoric influences of meprobamate on established shuttle shock-avoidance performance

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Meprobamate has been shown to effect shock avoidance in two detrimental ways. Trained rats under drug influence show agitated disorientation and avoid less frequently than placebo controls. These effects remain for 30 min. to an hr. after motor complications characteristic of the drug are no longer measured.

Early research with meprobamate seemed consistent with clinical reports claiming tension-reducing actions without complicating side-effects. Several studies indicated that meprobamate could be used in clinical dosages which did not interfere with various psychomotor task performances including driving skills (Kelly, Miller, Marquis, Gerard, & Uhr, 1958; Reitan, 1957). Now, not only has enthusiasm for the drug's potential as a tension-reducing panacea waned, but the degree of its innocuousness in experimental procedures has been reappraised and revised (Uhr & Miller, 1960; Upton & Chambers, 1959).

Beyond its muscle-relaxant, sedative mode of action meprobamate is now conceded to have more complex effects which may be facilitatory or inhibitory depending on Ss and test circumstances (Uhr & Miller, 1960; Khenseval, 1964). These data support the opinion that meprobamate acts centrally on perceptual and/or dispositional processes. For this reason it seemed appropriate to reopen the question of meprobamate's action on avoidance tasks, for tension and attention both contribute importantly to adequate performance in such problems. In previous reports, meprobamate has not been shown to influence avoidance performance in the shuttle-box (Berger, Hendley, & Lynes, 1954; Jacobsen, 1957), pole-climbing (Pfeiffer, Riopelle, Smith, Jenny, & Williams, 1957), wheel-turning (Verhave, Owen, & Slater, 1958) or lever-pressing (Hunt, 1957; Gatti, 1957; Boren, 1961).

Subjects

Ten adult female Wistar rats were selected from an original group of 40 on the basis of early performance in a shuttle-avoidance problem.

Apparatus

The training apparatus was a 10-tier shuttle-avoidance box. Each tier consisted of two 6 in. square cells separated by a common wall with a small tunnel. Grid floors were wired to provide scrambled, constant-current (2 mA) foot-shock. Flashlight bulbs protruding from the rear cell wall provided the means for presenting photic conditioning cues.

Procedure

Forty rats began training in groups of 10. After tests for response predisposition to light and a session of

response shaping trials, training to light-shock pairings was given a 50 trial per day basis. The CS of fixed 10 sec. duration was overlapped in the last 2 sec. by grid shock. After 300-500 trials the 10 most efficient Ss were picked and over-trained 400-600 trials past a criterion performance series of nine avoidances in 10 trials. Therefore, total experience for experimental Ss ranged close to 1000 trials prior to the test series.

Four sessions spaced 48 hr. apart were programmed to test avoidance performance under counterbalanced conditions of drug and placebo treatment, i.e., an ECCE or CEEC program. The meprobamate was dissolved in a minimal amount of 30% ethanol and introduced via IP injection. Placebo treatments were equivalent amounts of the vehicle alone. Treatment on a body weight basis (100 mg/kg) called for injection volumes of 0.3 to 0.5 ml. Alcohol by itself in such amounts does not interfere with established avoidance responses (Reynolds & Van Sommers, 1960).

Because of differences in S drug reactions experimental sessions were not equally successful for all Ss or for both drug treatments with individual Ss. Depending on S behavior in the first drug session, dosage was modified slightly in the second session. Despite such adjustments, problems with over-sedation required the adoption of a motor rehabilitation criterion of five consecutive short latency (< 2 sec.) escape reactions before scoring test performance. Fifteen min. were allowed for drug (and placebo) induction prior to test trials. After the last test session drugged Ss were rested an hour then run an extra 30 trials to investigate characteristics of post-treatment recovery. A final session was run two days after all procedures with Ss free of treatment.

Results

When experimental sessions were begun, response rates of superior performance Ss had stabilized sufficiently to provide a performance baseline. Although all Ss gave criterion performance on repeated occasions only three or four demonstrated consistent 90% avoidance. Average performance for the last three pre-test runs is indicated by the first column in Table 1 (only the last 40 trials per session are counted to allow for warm-up effects). Data from the experimental series, the placebo series and the post-test session complete the table. Performance was scored as the proportion of avoidances for trials during the test period after motor rehabilitation. An acceptable session was one in which at least 10 trials were run under this stipulation. Clearly, even when motor effects are taken into consideration by this reservation, an action of meprobamate

Table 1. Proportion of avoidance responses for last 40 of 50 trial sessions (10 trials "warm-up" allowed). Number of post-rehabilitation meprobamate trials indicated in parentheses.

	Pretraining Sessions-3	Meprobamate Tests-2	Placebo Tests-2	Post Session
1.	.53	.35 (62)	.63	.88
2.	.70	.31 (39)*	.46	.58
3.	.75	.44 (77)	.74	.93
4.	.58	.05 (65)	.75	.68
5.	1.00	.68 (40)*	.95	1.00
6.	.90	.22 (63)	.78	.90
7.	.75	.25 (63)	.70	.88
8.	.55	0 (35)	.45	.70
9.	.68	.39 (61)	.46	.60
10.	.90	.60 (62)	.83	.73

*Only one session with more than ten acceptable trials.

is demonstrable on the performance of well established avoidance skills in the shuttle-box. All Ss show impaired performance under drug treatment. No S was either unaffected or aided by meprobamate. This influence is transient, as shown by the recovery of avoidance performance in post-test sessions, and seems to bear full effect for 30 min. to an hour. Plots of escape latency decrease to asymptote for this period of time before the frequency of avoidances begins to rise towards normal levels.

Besides the failure to avoid another phenomenon was noted. At a certain point in testing a short latency escape signalled that an S had sufficient ambulatory control to make the required operant response, but neither avoidance nor short latency escape responses were made on a consistent basis. Since the criterion for motor rehabilitation was the more stringent five successive short latency trials, a number of disorderly trials might be registered during this transitory period.

The behavior of Ss during this stage was quite unique. Normally Ss would respond to either the light or shock by precise transit of the dividing tunnel followed by reorientation for the next trial. During the disorderly trials period, Ss were not at all tranquilized but tense and agitated. Trials were usually begun with Ss facing the rear wall, i.e., they did not reorient to face the tunnel after escaping the previous trial's shock. When shocked again they struggled vigorously to the rear and not until they chanced to face the tunnel did they bolt through to safety. Also, during this period affected Ss showed a tendency to return to the active grid before the signal for the next trial, usually re-experiencing difficulty in shock escape. Failure to reorient and "returns" are ordinarily seen only during early phases of training and very rarely in a skilled S.

Discussion

Perhaps the present results bring meprobamate back into line with other "tranquilizers" regarding an anticipated influence on "fear" motivated behavior. However, there is question as to the significance of such a dynamism in the satisfactorily performed, well established avoidance habit. Signs of fear are not characteristic of adequately performing Ss. In a more obvious way neither do the data support any "anxiety" reduction-performance improvement hypothesis.

On the other hand, signal response cuing remains a critical event in both acquisition and performance of avoidance skills. Adequate thruput of signal information is essential; blocked pathways mean responses conditioned to a specific sensory input must fail. With meprobamate the problem may be once removed from sensory input, for there is no evidence that the drug acts on sensory processes per se. Motor processes are directly affected, but in the present investigation these actions have been taken into consideration. An additional effect of the drug remains in the nature of a disturbance in orientation and attention. The affected S fails to respond appropriately with respect to previous training experience. He fails as well to adjust his behavior to his immediate physical situation, i.e., he may persist in frenetic, unproductive behavior. Furthermore, the appearance of "returns" after successful escapes may reflect a disruption of the time sense as suggested by Xhenseval (1964).

A number of reports indicate that meprobamate may act in the thalamus (Kajtor, Veress, & Kocsar, 1961). The present observations of disoriented, agitated behavior without motor debility are consistent with such an opinion, if the thalamus is correctly viewed as a locus for various coordinating functions. Perhaps in addition to its demonstrated clinical usefulness as a sedative, meprobamate may be an effective tool for the investigation of perceptual integration processes especially as carried out in the thalamus.

References

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Note

- References not listed may be found in Uhr and Miller.