Improvement of sustained attention with Cylert¹

GEORGE A. TALLAND

HARVARD UNIVERSITY MEDICAL SCHOOL

Cylert (pemoline with magnesium hydroxide) administered in single doses of 25 mgm improved accuracy in performance of a continuous attention task. This effect was strongest within an hour from oral administration of the drug, and on a task that involved a relatively difficult test in short term memory. The findings are considered as evidence for a non-specific alerting or anti-fatigue effect, as distinct from a specific effect on memory function attributed to Cylert.

Cylert (pemoline with magnesium hydroxide) has recently aroused interest as a drug that enhances learning and memory in persons who are particularly impaired in these functions. This effect has been attributed to the influence the drug exerts on RNA production in the brain (Glasky & Simon, 1966), and has been supported both indirectly by animal experiments (Plotnikoff, 1966), and directly by a report on a clinical study (Cameron, 1966).

While the author's experimental studies with amnesic patients have produced no evidence of improved performance attributable to Cylert, those conducted with healthy student volunteers have shown some gain from treatment with this drug. This gain was more reliable in relearning than in new learning, and seemed consistent with the view that pemoline exerts a general alerting or anti-fatigue effect (Lienert & Janke, 1957). The effect of Cylert on performance was most pronounced in a task that tested sustained attention, although it also demanded proficiency in a short-term memory function.

Design

Twenty-four student volunteers, aged between 21 and 25 years served as Ss on three (eight Ss) or four (16 Ss) occasions, at weekly intervals, for periods of about 3 hr. At the beginning of the experimental session S was administered a tablet of 25 mgm Cylert (C) or lactose placebo (P), and was given a rest period of 70 min. which he spent reading. In the first session the rest period lasted for 90 min., in subsequent sessions the time between min. 70 and 90 was occupied by tests of delayed recall of a narrative text and of a maze learned the previous week. The time between min. 90 and 120 was used for new learning tests; then the S received his second tablet (P or 25 mgm C), and 5 min. later he started a test of sustained attention. This lasted for 50 min., and was followed by tests of recall and relearning. The tablets in which P and C were administered could not be distinguished, and neither S nor E knew the drug schedule, or that one of the drugs was an inert placebo. Every S was tested on schedules P-P, C-P, and P-C in balanced order, and 16 Ss were tested a second time on schedule C-P, the two letters representing the drugs given initially and 2 hr. later.

The test of sustained attention consisted of a continuous series of displays projected on a screen from slides. The content of the display was a pattern of digits, occupying any one or more, up to nine, standard positions: eight at equal distances on the perimeter of a circle, the ninth in its center. The values represented by the digits carried no information for the purpose of the experiment, as the S's task was merely to count the number of digits in view, and to respond by pressing a key each time this number was the same as in the previous display (task I) or the same as two steps back (task II). Displays that qualified on either of these criteria (signals) occurred at the rate of one in 12. Displays changed every 1-1/4 sec. and were in view for 1/2 sec. Responses made within 1-1/2 sec. from the offset of a display were accepted as correct, other responses were scored as incorrect. Task I lasted for a continuous 24 min., and was followed by a break of 2 min. during which S received the new instruction, and then proceeded with task II for another continuous 24 min. Signals and responses were recorded on a punch tape, and the records were analyzed by a computer.

Results

Mean errors of omission and errors by incorrect response are listed in Table 1 according to task and drug treatment. The data are based on N=21, as the records of three Ss were incomplete or faulty for one of the experimental sessions.

Performance evaluated by omission errors on the control treatment (P-P) was compared by analysis of variance separately with performance under immediate (P-C) and under delayed (C-P) drug effect. While both drug schedules resulted in a drop of errors, and in a larger gain in accuracy on task II than on task I, the difference between P-P and C-P, as well as the interaction between treatment and tasks, failed to reach statistical significance. The difference between P-P and P-C, however, was significant, as was also the interaction between treatment and tasks (both $p < .01$). Between-S differences and differences attributable to the two tasks were significant under all treatments. Errors by incorrect response did not differ significantly between

Table 1. Mean errors of omission (percent of signals to which no response was made within 1½ sec. from offset), and false positives on two tasks of sustained attention under three drug schedules, with lactose placebo (P) or Cylert (C) administered 125 and 5 min. before the 50 min. experimental period.

Drug Schedule	Omission Errors			False Responses		
	P - P	C - P	P - C	P - P	C - P	P - C
Task I	39.9	38.7	33.8	13.4	15.9	11.0
Task II	57.2	51.6	49.5	23.5	17.0	22.3

any two treatments, except for task II between P-P and C-P ($p < .05$).

Performance was also evaluated on the more stringent criterion of response made within 1/2 sec. from the offset of the signal. Errors by omission increased by 19 to 26 percent on this criterion, and to the largest extent with the P-C drug schedule. The interactions between treatment schedule and the error increment, however, were not statistically significant.

Discussion

The findings agree with Dureman's (1962) conclusion, from a code tracking experiment, that pemoline enhances performance in tasks requiring continuous attention. Improved efficiency in this type of performance is consistent with a general stimulant or anti-fatigue property attributed to this drug, an interpretation supported by a time sampling analysis of performance in the present experiment. It seems probable that whatever favorable influence Cylert may exert on learning and remembering, reflects an increase in the level of general alertness rather than an effect specific to the processes involved in learning and memory.

The present experiment of continuous attention also involved a test of short term memory, and indeed quite an exacting test in task II. The significant interaction between drug treatment and task could thus reasonably be interpreted as evidence for a stronger Cylert effect when the memory load imposed by the task was heavier. Since, however, task II occupied the second half of the experiment in continuous attention, the larger gain in accuracy with the P-C treatment under its conditions may also be attributable to the time course of the drug effect.

While this latter argument offers a convincing account for the interaction effect observed, the alternate explanation need not be dismissed altogether. Some evidence in support of it can be found in the results obtained with the C-P schedule. Although correct responses were not significantly higher on this than on the control treatment, performance improved especially in task II, and significantly when judged by incorrect

responses. Delay in the drug effect would not account for this finding, since it could hardly be delayed beyond a period of 150 min. when it was in evidence within the first hour on the alternate schedule.

The case for an enhanced effect on performance by Cylert with increased task complexity or retention difficulty needs further experimental evidence. The relation of dose to behavioral effects also needs exploration. The present study has satisfactorily demonstrated that Cylert is capable of improving performance by human operators, though possibly only by mitigating fatigue effects. In the experiment reported the favorable drug effect was fairly instantaneous, and manifest in an increase of correct responses to a class of visual patterns that were specified as signals, without an increase in false positive responses. The gain in performance attributable to the drug was, therefore, not achieved by lowering the criteria for response or by such gambling tactics as would be inferred from a higher incidence of false positives. Nor was it achieved by faster responses; the processes affected were those involved in the perception, short-term retention, and matching of data.

References

- Cameron, D. E. Presidential address, 1966 meeting of the Society of Biological Psychiatry, Washington, D. C.
- Dureman, E. I. Differential patterning of behavioral effects from three types of stimulant drugs. *Clin. Pharmacol. & Therap.*, 1962, 3, 29-33.
- Glasky, A. J., & Simon, L. N. Magnesium pemoline: enhancement of brain RNA polymerases. *Science*, 1966, 151, 702.
- Lienert, G. A., & Janke, W. Pharmacologische Untersuchungen über 5-Phenyl-2-imino 4-oxo-oxazolidine, *Arzneimittel-Forsch.*, 1957, 7, 436-39.
- Plotnikoff, N. Magnesium pemoline: enhancement of learning and memory of a conditioned avoidance response. *Science*, 1966, 151, 703-705.

Note

1. This research was supported by a grant from the Abbott Laboratories, Scientific Divisions, Chicago, Illinois.