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EFFECTS OF NEMBUTAL IN BABOONS WITH FRONTAL LESIONS[1]

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STUDIES CONCERNING the effects of barbiturates on the delayed-response and delayed-alternation performance of primates with frontal lesions have yielded discrepant results. An experiment on four monkeys by Blum *et al.* (1) failed to confirm the findings of improvement with sedation obtained on two monkeys by Wade (4) and on two baboons by Pribram (2). Two consistent differences among the experimental conditions employed in these studies have been noted by Blum and co-workers. Their animals were tested late, two at six months and two at two years postoperatively, and all scored significantly above chance prior to injection of the drug. In contrast, Wade's and Pribram's animals were tested early, three months postoperatively, and performed at only a chance level before drug administration. Blum and co-workers suggest that in the latter animals Nembutal may have hastened an improvement which would have occurred without the use of sedatives if sufficient time and training had been allowed following operation.

To test this hypothesis, an experiment on the effects of Nembutal was performed on a group of baboons who had received six months of intensive postoperative training on delayed-response and delayed-alternation problems. At the end of this period, which was comparable to that allowed two of the monkeys studied by Blum and co-workers, the delayed-alternation scores of half the animals were at a chance level and of the other half at a level significantly above chance. A finding of improvement with sedation, particularly in those animals who were already performing reliably better than chance, would be inconsistent with the interpretation advanced by Blum *et al.*

METHODS

Six baboons (*Papio papio*) were used in this experiment. All had been subjects in an earlier study (3). Three animals, DL1, DL2, and DL3, had received bilateral resections of dorsolateral frontal cortex; and three, VM2, VM3, and VM4, had received bilateral resections of ventromedial frontal cortex. The reconstructed lesions and the thalamic degeneration, previously reported in detail (3), are represented diagrammatically in Figure 1.

The testing experience of these animals had consisted of pre- and postoperative training on visual-discrimination and delayed-response problems. The present report deals with their performance on a delayed-alternation test which was administered for the first time early in the sixth postoperative month. Daily sessions on this test consisted of 50 trials, with 5-second delays, presented by the correction technique. Since correction trials were included in the daily total, scores below 50 per cent ordinarily reflected left or right position preferences. A total of 2,000 trials was given on this test: 1,000 before, 500 with, and an

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additional 500 after sedation. Prior to each of the 10 sedation sessions, each animal was given an intramuscular injection of Nembutal of 15 mg./kg. body weight, equal to one half the intraperitoneal anesthetic dose. Animals were tested approximately one hour after injection.

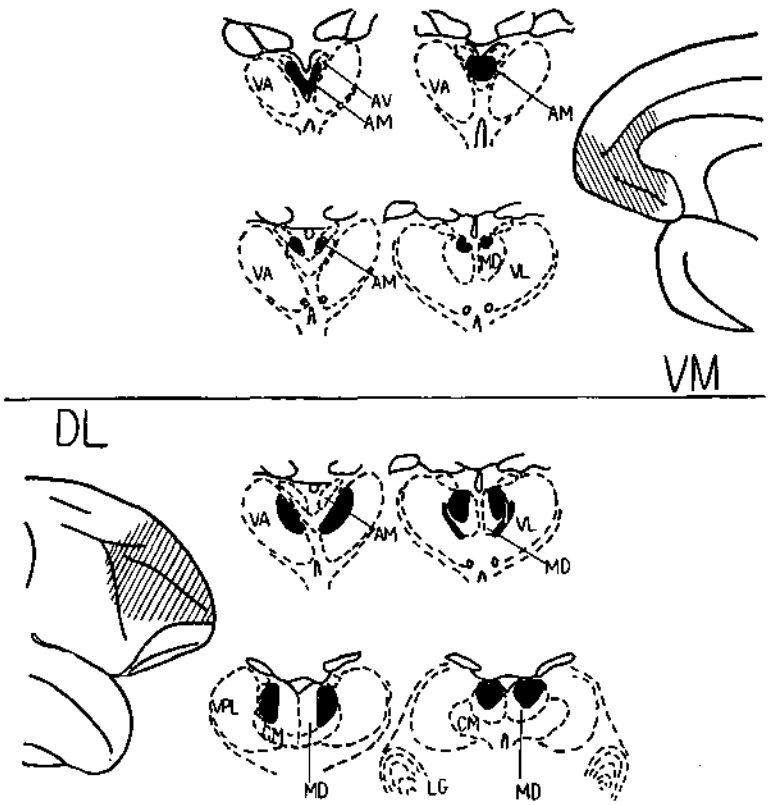

FIG. 1. Diagrammatic representation of cortical damage, indicated by hatching, and of thalamic degeneration, in black. VM, ventromedial lesion; DL, dorsolateral lesion. AM, n. anteromedialis; LG, n. geniculatis lateralis; AV, n. anteroventralis; CM, n. centromedian; MD, n. medialis dorsalis; VA, n. ventralis anterior; VL, n. ventralis lateralis; VPL, n. ventralis posterolateralis.

RESULTS

Performance curves for the six animals are presented in Figure 2.[3] It can be seen that the performance level of the ventromedial operates is consistently superior to that of the dorsolateral operates, with the exception of a single overlap between the scores of DL2 and VM3 on the last 250 trials of the Nembutal period. Table 1 gives the per cent correct achieved by each animal at four different stages of the experiment and presents also those differences between adjacent scores which attain significance. The scores of

[3] Three days before the experiment was concluded DL3 died of a lateral frontal subdural hematoma, caused possibly by an injury sustained while being caught for injections; the final point on her performance curve is based, therefore, on only 100 trials, as against 250 for all others.

all animals showed significant improvement between the early and the late sessions preceding sedation. Nevertheless, the dorsolateral operates were still not performing above chance, indicating that training in 1,000 trials had served only to overcome their strong initial position habits. The late

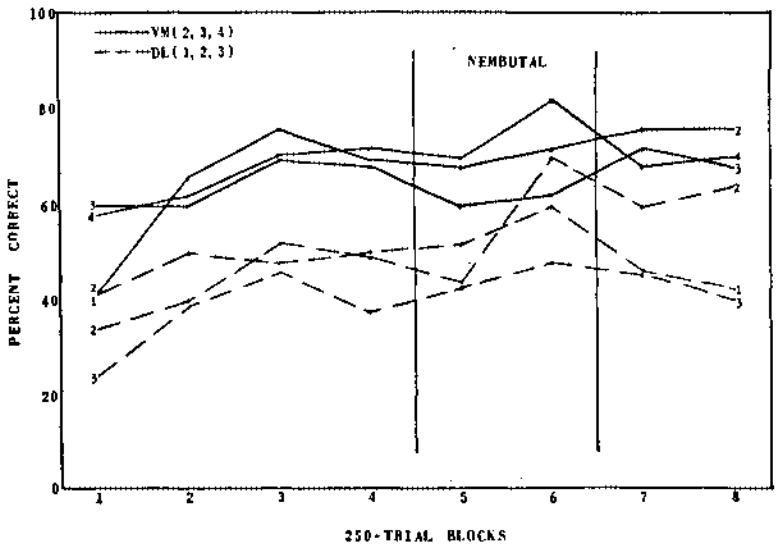

FIG. 2. Per cent correct in eight successive 250-trial blocks of delayed-alternation test.

pre-Nembutal scores of the ventromedial operates, on the other hand, were reliably better than chance.

In the first half of the sedation period only small inconsistent changes were obtained. In the second half, however, the scores of three animals, DL1, DL2, and VM4, improved significantly beyond those they had achieved in the late pre-Nembutal period and then showed a significant drop in the 500 trials after sedation. The scores of the other three animals, DL3, VM2,

*Table 1. Delayed alternation performance: Per cent correct in (A) the first 250 trials and (B) the last 500 trials before Nembutal; (C) the last 250 trials during Nembutal; and (D) the 500 trials following Nembutal injections. The t-tests between adjacent scores which are significant at the 1 and 5 per cent levels of confidence (latter indicated by *) are also given*

Subject	(A) Early Pre-Nembutal	t (B − A)	(B) Late Pre-Nembutal	t (C − B)	(C) Late Nembutal	t (D − C)	(D) Post-Nembutal
VM2	42.4	8.56	73.4	—	72.4	—	75.4
VM3	59.2	2.39*	69.0	—	62.8	—	70.0
VM4	57.2	3.89	71.4	3.28	82.4	3.97	68.8
DL1	41.2	2.02*	49.0	2.94	60.0	3.15	44.6
DL2	34.4	4.83	51.4	4.75	69.6	2.05*	62.0
DL3	24.4	4.68	41.8	—	48.0	—	45.2

and VM4, remained fairly stable throughout the Nembutal and post-Nembutal sessions.

Discussion

These results indicate that Nembutal may produce improvement in delayed-alternation performance, even though animals are tested as late as six months postoperatively (DL1, DL2, and VM4), and have achieved scores significantly better than chance before injections of the drug (VM4). That the improvement in the present study resulted from a variable associated with drug administration and not from additional time and training alone is suggested by the findings that the animals had attained a stable level of performance (see Fig. 2) in the sessions immediately preceding the injections of Nembutal and then approximated this level in the sessions following the injections. Similar results have been reported by Wade (4) and by Pribram (2).

No effects of sedation on delayed-alternation score were osbserved, however, in the first half (250 trials) of the Nembutal period. This finding is in agreement with the observations of Pribram, whose two baboons required approximately 300 trials with sedation before improving, and with the observation of Wade, one of whose monkeys was unaltered when tested with Nembutal, showing improvement only in subsequent tests with Dial. (The number of Nembutal sessions given this monkey was not reported.) Wade's second monkey is the only animal to show an immediate beneficial effect of the drug. In the study by Blum and co-workers (1), consecutive sessions with Nembutal were presented for a total of only 180 trials. This may have been an inadequate number of trials for a cumulative effect of training with the drug to appear. However, merely lengthening the sedation period is apparently insufficient since the scores of half the animals in the present study were unaltered despite an extended period of training with Nembutal. There was no consistent relationship between the effects of the sedative and the locus of lesion or the performance level attained before injections of the drug. Thus, the variable responsible for the improvement in performance observed in half the animals remains to be determined.

Summary

After receiving six months of intensive postoperative training three baboons with dorsolateral frontal lesions and three with ventromedial frontal lesions were trained while under the effects of Nembutal on a delayed-alternation problem. The scores of three animals showed significant improvement, demonstrating that barbiturates may facilitate performance even though prior to sedation animals have been allowed an extended recovery period. It is suggested that prolonged training with sedation is an important though not a sufficient condition for improvement. No consistent relationship appeared, however, either between the locus of lesion or the previous performance level and the effect of the drug.

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