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DELAYED-RESPONSE IMPROVEMENT IN FRONTAL RATS AFTER ELECTROCONVULSIVE SHOCK TREATMENTS AND SPACING OF TRIALS

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Abstract. Frontal rats, subjected to electroconvulsive shock (ECS) after each experimental session, performed better than they did before ECS treatment. The other subjects, which were treated with ECS after every third session, showed lower error scores on days immediately following ECS administration that 2 or 3 days later. When only one trial was applied every 3–4 days, the performance of the frontal rat did not differ significantly from that of normal rats. It is concluded that in both experiments improvement resulted from the decrease of retention of the returning route from previous sessions.

INTRODUCTION

It was found in previous studies (Łukaszewska 1968, 1971) that frontal lesion affects the performance in the returning behavior test which was essentially a version of delayed responses. Returning behavior was tested in an inverted T maze; the subjects went for food from one maze arm to the end of the maze stem and returned to the place of start along the same route. Under the conditions in which the subjects started from the same maze arm in all daily trials (the place of start varied between maze arms in alternative sequence from day to day), the incorrect response of frontal rats appeared mainly in the first trial of each experimental session. Therefore, the frontal deficit might be attributed to the deleterious effect of retention of the returning route from the previous day.

In the present paper it was attempted to decrease this effect by administration of electroconvulsive shocks (ECS) immediately after experimental training. It was also desirable to test returning behavior of fron-

tal operates employing widely spaced trials since previous experiments (Gleitman et al. 1963) pointed to the considerable importance of distribution of trials in delayed-response performance.

METHOD

Subjects. The *S*s were 45 naive male albino rats of Wistar strain approximately 120 days old at the start of the experiments. Thirty three animals were subjected to bilateral frontal lesions. The operation was performed by suction under Nembutal anesthesia, 3 weeks before the experiments. Typical examples of frontal lesions are presented in Fig. 1. In most cases the lesions were placed on the dorsolateral convexity of the hemisphere, sparing the medial wall, except its very tip.

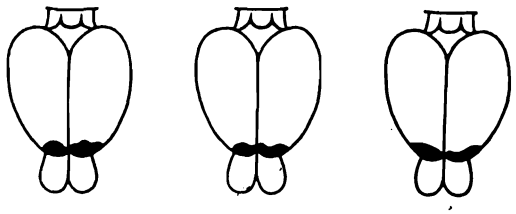

Fig. 1. Examples of frontal lesions.

Apparatus. An elevated T maze with a stem 40 cm long, 13 cm wide, and each arm 70 cm long and 13 cm wide was used (Fig. 2). The rat had to leave the starting box which was placed on one of the two starting platforms (S_1 or S_2), then reach the cup on the maze stem, take the reward and return to the box where he was allowed to eat. As a reward small pieces of cookies were used. While returning, the rat did not respond

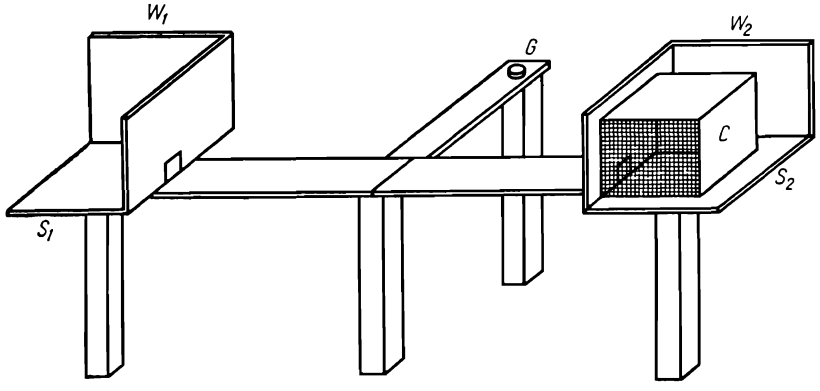

Fig. 2. An inverted T maze. S_1, S_2, starting platforms; C, box; W_1, W_2, wooden screens; G, cup with food.

to actual stimuli since both platforms were screened, but to the traces of kinesthetic stimuli acting several seconds earlier, when he turned from the maze arm to the maze stem. Time elapsed between this turn and the choice of the return route constituted the delay; it varied from 2 to 4 sec in different subjects and trials. After finishing one food portion the rat immediately went for another one, starting the next trial. Thus the inter-trial intervals also varied, being on the average 30–40 sec. The subject approaching the incorrect platform on his way back found the screen door locked, but was permitted to go to the other platform (self correction).

Procedure: *Experiment I.* Two groups of frontal rats were used. In both groups three daily trials were carried out in which the subjects started from the same platform; the position of start changed from day to day in alternative sequence. Group I was tested for 10 days without ECS and then, during the next 10 days treatment was applied after each experimental session. Group II was tested for 30 days; after every third experimental session the subjects received ECS treatment. Within 60 sec following the last trial each subject was removed from the apparatus, transferred to the next room and firmly grasped. Earclip electrodes wrapped with cotton and dipped in 0.9% NaCl solution were attached and approximately 150 ma a-c current was applied for 0.5 sec producing full tonic seizures. Following ECS the subject was returned to this home cage.

Experiment II. The effect of spacing of trials was studied on 12 normal and 12 frontal subjects which were given only one trial a day. Both groups were tested for 10 experimental sessions separated by 3–4 days. Similarly as in Experiment I the position of start varied from session to session in alternative sequence.

RESULTS

Experiment I

Group I. The difference in performance of frontal subjects during the 10 day period before ECS treatments and in the next 10 days with ECS administration after each session, was confined only to the first trial in the session (Trial I). ECS treatments resulted in a decrease of error scores in 7 out of 10 subjects (Table I). Analysis of variance with row data transformed according to $y = \sqrt{x+1}$ revealed the significant effect of ECS treatment ($p < 0.01$).

Although subjects, when treated with ECS improved from 72 to 83% of correct responses, they did not reach the level of performance observed

TABLE I

The number of errors in Trial I scored by each subject in 10 day blocks before and during ECS treatments

Rat	Before	During	Rat	Before	During
1	5	4	6	3	1
2	3	1	7	2	3
3	5	2	8	2	1
4	2	3	9	3	0
5	1	1	10	2	1

previously in normal rats which showed above 90% of correct responses (Łukaszewska 1968).

In Trials II and III the subjects performed correctly in both situations. Probably one trial was sufficient for them to learn where the box was placed, thus they did not respond necessarily to the predelay cue.

Group II. Subjects of this group received ECS treatment every third session, therefore it was possible to compare their performance on days immediately following the ECS treatment (Day 1) and the performance in the sessions 1 and 2 days after ECS (Days 2 and 3). Differences between Days are apparent in the correct responses data for Trial I (Fig. 3). Ana-

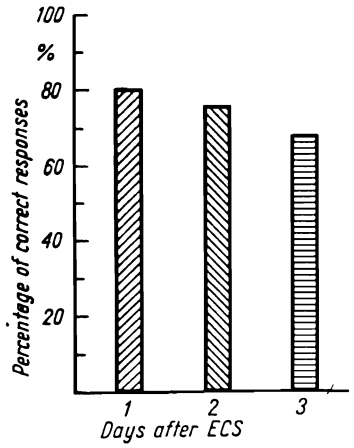

Fig. 3. The percentage of correct responses in Trial I in blocks of sessions after ECS treatment.

lysis of variance of repeated measures type with row data transformed according to $y = \sqrt{x+1}$ yielded a significant Days effect ($p < 0.05$). Student's test indicated that subjects performed better on Day 1 than on Day 3. No differences were found between Day 1 and Day 2 or between Day 2 and Day 3.

As in the previous group in Trials II and III the subjects performed correctly irrespectively of the Days.

Experiment II

When experimental sessions were separated by 3 or 4 days and consisted of only one trial, the performance of frontal subjects did not differ significantly from that of unoperated controls (Mann–Whitney *U* test, two tailed). Comparison of error scores by these two groups and by the frontal group given three trials a day (Experiment I, Group I) presented in Fig. 4 indicate that under conditions of spaced trials the data of frontal

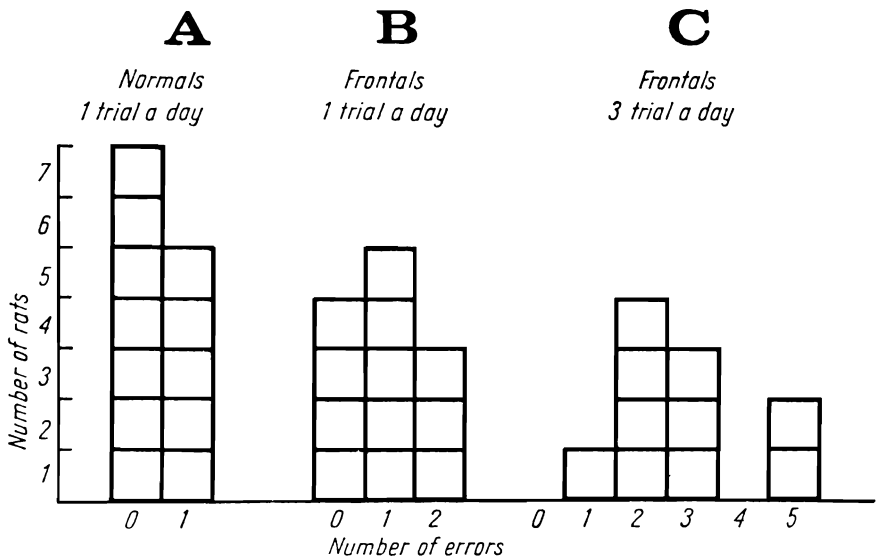

Fig. 4. The number of rats with different error scores in Trial I in blocks of 10 sessions. *A* and *B*, the sessions were separated by 3–4 days and only trial a day was employed. *C*, the sessions were separated by 24 hr and consisted of three trials.

subjects closely resemble those of normal rats. In contrast, the shape of diagram of errors scored by frontal subjects given three trials a day differs considerably.

DISCUSSION

The result obtained on Group I in Experiment I indicates the facilitating effect of ECS treatments on returning behavior in frontal rats. Since frontal rats not treated with ECS did not show any improvement in performance in the course of experimental training (Łukaszewska 1971) the

observed increase in percentage of correct responses during the period of ECS administration cannot be attributed to the experimental training which preceded the ECS treatments.

The most plausible interpretation of the improvement of frontal subjects during ECS treatments is that ECS rules some factors interferring with the animals' performance on the next day. Since according to experimental design of this study on one day the subjects returned to the starting place along the one maze arm, and on the next day — along the other one, the interference with performance seems to be due to retention of the returning route from the preceding day. However, the result on Group II indicates that the interfering factor in question is not exactly the retention from the preceding day only. If so, the percentage of correct responses on Day 2 should be the same as on Day 3, whereas it was higher. The difference is not statistically significant, but the difference between Day 1 and Day 2 is also not significant; the accepted 0.05 level of significance was found only between Day 1 and Day 3. It seems then, that not excluding the possibility of influence of the preceding session on the following one, there must exist some cumulative effect of several previous sessions regardless of the direction of returning route.

It should be stressed that ECS treatments attenuated the interferring effect of previous sessions rather than abolish it entirely. It was probably due to employing massed trials as here the engram formed by the first and second trials must surely be consolidated to some degree before ECS administration.

Although numerous studies indicate that ECS results in some impairment of a previously learned response, considerable controversy still surrounds the question of whether such impairments are due to retrograde amnesia (Duncan 1949) or other disruptive effects such as development of fear (Coons and Miller 1960) or competing conditioned responses produced by ECS (Levis and Adams 1963). Thus one may doubt whether the facilitating effect of ECS on returning behavior in frontal rats may be attributed to the decrease in retention, particularly since experiments in which repeated treatments were employed, as was the case in the present study, are considered in general to support the "fear" or "competing response" hypotheses. However, the only way which fear could affect the performance in returning behavior, was caused by the refusal of the animal to leave the starting box. In fact the subjects went readilly for food and returned thus, the result of the present study cannot be ascribed to aversive effect of ECS.

Another objection might be derived from the finding that rats can learn to avoid going to a place in a maze where they received several

ECS treatments (Hayes 1948). In the present experiment the ECS was applied not only outside the maze but also outside the experimental room. It seems unlikely then, that the subjects could associate the response in the maze (returning along e. g. the left maze arm) with ECS which they received 1 min later in an entirely different situation.

There is a general agreement that the degree of ECS induced effect varies inversely with the duration of time elapsed between training and ECS administration. Some authors (Chorover and Schiller 1965, Quartermain et al. 1965) conclude however, that retrograde amnesia may be responsible for impaired retention only when the ECS treatment is given within a few seconds after a learning trial. It is obvious that the length of posttraining interval during which the ECS will produce some degree of amnesia is a function of many variables such as task complexity, procedural variables and so on. 60-sec intervals applied in the present experiment seems to be short enough to attribute the observed ECS effect to impairment of retention rather than to other disruptive influences. However, it is possible that with shorter intervals the ECS effect would be more pronounced.

Experiment II showed that spacing of trials is much more effective in the decrease of interference of the returning route from previous sessions than ECS applied after three daily trials. Subjects given only one trial a day with 3–4 day intervals performed almost as well as unoperated controls. This result is not consonant with the finding of Wilson et al. (1963) on frontal monkeys. In this experiment frontal monkeys were still deficient when only one trial was given per day. However, the subjects were tested at 24 hr intervals, thus it seems likely that even a single trial might interfere with performance, particularly in view of the fact that on the first postoperative trial (i.e. 20 days after the last preoperative trial) all frontals responded to the side that had been last baited preoperatively.

Although in the present study lesions did not cover the projection field of nucleus medialis dorsalis (Leonard 1969) they affected the test which may be viewed as a delayed response test which is a typical effect of lateral frontal cortex lesions in higher mammals. The finding that procedural variables such as ECS treatments and spacing of trials attenuated or even prevented the impairment of delayed-response tests in frontal rats is of considerable importance for frontal deficit interpretation.

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