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IMMEDIATE AND SUBSEQUENT EFFECTS OF BRAIN DAMAGE IN RATS[1]

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Small bilateral, parietal lesions were made in 16 rats, and their performances were compared to sham-operated (N = 6) and normal (N = 6) control Ss on "closed-field intelligence test" problems using a repeated-measures design. An immediate deficit was observed in experimental Ss as compared to controls ($p < .025$). Complete recovery in performance of all experimental Ss was seen 1 wk. postoperatively. The results contradicted a previous investigation in which delayed deficits were reported in similarly lesioned Ss under comparable conditions ot behavioral testing.

Forgays (1952a, 1952b) has raised the possibility of delayed loss of behavioral functioning following certain lesions of the brain. Forgays (1952b) observed no difference in maze performance of lesioned *Ss* and sham-operated control *Ss* 2 hr. after lesions of frontal and parietal or parietal neocortex in rats, but 4 hr. postoperatively a significant deficit in lesioned *Ss* was reported. Recovery of function was observed 9–21 days postoperatively. Since Forgays' data were collected almost immediately after operation, the question of delayed loss of function could be raised for any lesion study which did not observe an early and detailed time course for development of behavioral deficit. Forgays' study (1952b) is a potential stumbling block to any claim for localization of function derived from brain ablation unless the immediate effects of ablation are observed. Forgays' behavioral data were given as "control minus experimental mean scores." The scores were number of errors on maze problems standardized by Rabinovitch and Rosvold (1951) for the "closed-field test of rat intelligence." Forgays' report (1952b) did not provide information on the following critical points: (*a*) the actual error scores of the experimental and control *Ss*, (*b*) whether normal (i.e., nontreated) *Ss* would differ from the sham-operated controls under similar conditions of testing, and (*c*) what specific maze problems were used in the immediate postoperative tests.

In view of the potential importance of Forgays' finding, it was felt that the study should be validated under rigorous conditions with a normal control group to assess the effects of anesthesia, etc., on the sham-operated group.

METHOD

Subjects

Twenty-eight male Long-Evans hooded rats, 90–120 days old, were divided into three groups: an experimental group receiving lesions ($N = 16$), a sham-operated control group ($N = 6$), and a normal control group ($N = 6$). Before the treatments were administered, the groups were equated as nearly as possible on the basis of preoperative testing after the manner of Forgays (1952b).

Operative Procedure

All operations were carried out under ether anesthesia. Following a midline incision of the scalp nearly all the dorsal surface of the cranium was exposed. Using sagittal and coronal sutures as points of reference, a hole was drilled bilaterally with a No. 5 dental burr through the dorsal surface of the cranium directly over parietal cortex and the cortical tissue beneath was suctioned through a glass pipette. After the hole was drilled bilaterally partially through the cranium of the sham-operated controls, the scalp was closed with wound clips and the operation terminated. The normal group was not subjected to any part of the operation; however, these *Ss* were maintained on the same testing schedule as the other two groups.

Testing Procedure

The closed-field maze problems standardized by Rabinovitch and Rosvold (1951) were administered as nearly as possible according to the testing program outlined by them. Briefly, this re-

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quired testing *Ss* first on six practice problems, then giving the 12 problems constituting the test proper, one problem per day, 10 trials per problem. The practice procedure described by Rabinovitch and Rosvold which is directed toward adapting *Ss* to the situation is extremely time consuming. Since running each *S* 20 trials or 1 hr. per problem accomplishes the same goal and permits more standardized treatment of *Ss*, this procedure was implemented instead. The standard procedure of administering the problems of the test proper was followed. A 2-day interval was introduced between the practice and test problems.

The groups were matched on the basis of total errors scored on the preoperative tests. The 6 *Ss* of each control group and the first 6 experimental *Ss* were matched individually. It was assumed that the error scores of the last 10 experimental *Ss* would be randomly distributed and would not affect the matching procedure. An error was defined as a crossing of *S*'s thorax of an error boundary (error bounds are shown by Rabinovitch and Rosvold, 1951).

Three mazes, mirror images of the original series, were administered 2 hr. postoperatively; three more were given 4 hr. postoperatively, three more 12 hr. postoperatively, and three more 1 wk. postoperatively. All control *Ss* and the first 6 experimental *Ss* were tested 3 wk. postoperatively with three mazes of the original series. The 3-wk. postoperative test was not given to the remaining 10 experimental *Ss* as it became apparent that the ablated *Ss* were fully recovered 1 wk. postoperatively.

Each of the three-problem groups consisted of one problem from the first four, one from the middle four, and one from the last four mirror images of the original series. The selection of the problems for the postoperative test sessions was random with the restriction that no *S* received the same problem twice in the postoperative tests. No problem groups were used with the experimental *Ss* that had not been used with 1 or more control *Ss*. Since there were more experimental than control *Ss*, the maze sequences used with the first 6 *Ss* of each group were rotated among the extra experimental *Ss*.

All *Ss* were run on similar schedules with respect to morning, afternoon, and evening test periods. Four *Ss* were the maximum that could be run as a group in order to maintain the schedule required on operation day. To assure adherence to all schedules it was necessary to limit the trials to 2 min.; therefore, if an *S* failed to reach the goal box in that interval, the errors made to that point were recorded as the score for that trial.

The *Ss* were deprived of food 48 hr. prior to their introduction to the practice problems. Following each day's session on the practice problems, *Ss* were immediately returned to their home cages and given a maintenance diet of 12–15 gm. of Purina lab chow. They were deprived on the day preceding the test proper, but maintenance rations were given after each day's trials, except the last day which was the day preceding the operations and the three immediate postoperative tests. The *Ss* were given maintenance rations after the 12-hr. postoperative test and daily through 2 days prior to the 1-wk. test. Immediately after the 1-wk. test, *Ss* were given a maintenance ration; this ration was given daily through 2 days prior to the 3-wk. test. The trials on the various tests were rewarded by two .045-gm. food pellets. Water was available at all times, except during testing.

The testing room was maintained at a stable temperature (75–80° F.), and it was illuminated by a 25-w. bulb placed below the level of the table on which the maze was located. Extraneous sounds were masked by a white noise of approximately 70 db. re .0002 dynes/cm^2, measured at the center of the maze.

Anatomical Methods

After the brain had been fixed in formalin, it was placed under an opaque projector and the image projected onto the dorsal view of a Lashley brain diagram. The image was adjusted to correspond in size to the dorsal view of the brain in the diagram, and the extent of the lesion was sketched on the diagram. The percentage of cerebral cortical surface occupied by the lesion was determined by the dot grid method (Thomas & Peacock, 1965).

The brain was embedded in paraffin and sectioned at intervals 25 μ. Each ninth and tenth section was mounted on slides and stained with thionin.

Results

The surface areas of the lesions were 0.5–3.8%; the mean lesion was 1.95%. The *Ss* could be categorized in three groups with respect to depth of the lesion: 5 *Ss* had only neocortical damage, 6 *Ss* had invasion of the corpus callosum, and 5 *Ss* had sub-corpus-callosum damage on at least one side. Since Forgays (1952b) had only neocortical lesions, it was felt that the three groups according to depth of lesion should be treated separately in the analysis of the data.

Analysis of variance showed the treatment groups (i.e., the three groups with respect to depth of lesion and the two control groups) to be significantly different ($p < .025$). Paired comparisons among the lesion groups showed they were not significantly different from each other ($F < 1$). Similarly, the control groups did not differ significantly from each other ($F < 1$). Since there was no suggestion of significant difference between the lesion groups, their data were pooled; similarly, the control groups were pooled. The difference between the treatment groups was the result of lesioned *Ss* making more errors than controls. Figure 1 shows the mean number of errors by the pooled

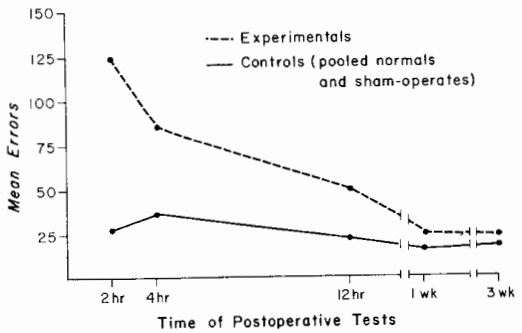

FIG. 1. Mean errors as a function of time of postoperative test.

lesioned *Ss* and the pooled control *Ss* as a function of postoperative test period. The mean number of errors for the experimental *Ss* at the 3-wk. postoperative test was determined from the first 6 experimental *Ss*.

The experimental and control groups were significantly different 2 hr. postoperatively ($p < .01$), but the difference only approached significance at the 4-hr. postoperative test ($p < .10$). The difference in the groups by 12 hr. postoperatively can no longer be considered significant, and it can be seen that recovery is complete in the experimental *Ss* by 1 wk. postoperatively.

The analysis of variance was based on a two-factor design with repeated measures on one factor. Since the group sizes were unequal, Winer's procedures (1962, pp. 374–378) for this case were followed. Winer presented the appropriate F ratios for the specific tests of the main effects. The tests of simple effects were not presented for the case of unequal group sizes, so the tests of simple effects in the two-factor, repeated measures on one-factor analysis of variance with equal group sizes (Winer, 1962, pp. 302–312) were used with one adjustment. When Winer describes a computation with n (i.e., the number of *Ss* per group), the harmonic mean number of *Ss* in the treatment groups of the present experiment was used.

DISCUSSION

The results of the present investigation directly contradict the findings of Forgays (1952b) and, consequently, the delayed loss of function argument. Differences between the present study and Forgays' study must be considered.

Forgays' lesions were larger, on the average. Forgays' parietal lesions averaged 4.9%; the lesions of the present study averaged 1.72% for the *Ss* with neocortical damage only. However, since the greater behavioral decrement was found in the present study, it can scarcely be argued that larger lesions have a lesser effect.

Forgays (1952b) implied that his sham operates were drilled through the cranium, but the cerebral tissue was not damaged. The sham operates of the present study were drilled only partially through the skull. It could be argued that Forgays' *Ss* were not different 2 hr. postoperatively because both groups were displaying a decrement. However, Forgays (1952b) stated, "According to these results, the delayed disturbance of function follows bilateral lesions in a limited area of the brain, that is, in the parietal region [p. 221]." Forgays persistently discussed delayed disturbance, strongly suggesting that there was no disturbance at first.

A third discrepancy must be considered as a possibility only because Forgays (1952b) did not state his procedures explicitly. This possible discrepancy concerns which mazes were administered at what times postoperatively and for how many trials. Since Forgays gave one problem per day and 10 trials per problem preoperatively, it is reasonable to infer that he gave one problem per test session and 10 trials per problem postoperatively. Prior to the operation, he began the problem series with Problem 1 and continued successively through Problem 12. It is reasonable to infer that he began with the mirror image of Problem 1 postoperatively; this would mean that *Ss* got Problem 1 at the 2-hr. postoperative test, the test on which the results of the present study and Forgays' study differ most crucially. If this were the case, the difference in the results of the two studies would be more easily reconciled. Maze 1 is the easiest (as determined empirically) of the series of mazes, and the mirror image of Maze 1 happens to be identical to the original Maze 1. However, more critical is the fact that Maze 1 provides a straight path from the start box to the goal box, a distance of less than 43 in. Robinson and Wever (1930) reported that rats with pigmented eyes (e.g., the hooded rat) can distinguish an open from a closed pathway at a distance of 30 in. It is conceivable that Forgays' rats (1952b) ran the first 13 in. from the start box, saw the goal box, and ran directly to it. It is inferred that Forgays' 2-hr. postoperative test was too easy to provide a basis for discriminating between the performances of the experimental and control *Ss*.

Forgays (1952b) reported that his parietal lesioned *Ss* recovered approximately 9 days postoperatively; whereas the brain-damaged

Ss of the present experiment indicated complete recovery 1 wk. postoperatively. The difference in the two studies with respect to recovery may be attributed to the difference in mean lesion size.

Apparently only three other experimental investigations have been concerned with the immediate (4 hr. postoperatively or less) effects of brain damage (Goddard, 1965; Herschberger, 1960; Rey, 1938). These investigators reported immediate deficits in behavioral performance or no deficit. None of these investigators reported delayed deficits. Forgays' clinical study (1952a) and two other clinical studies (Bucy, 1949; Malmo, 1948) have indicated delayed loss of function following brain damage; consequently, it is believed that further experimental investigations should be conducted.

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