EXPERIMENTAL NEUROLOGY 56, 323–333 (1977)

Processing Difficulties Following Commissurotomy in the Monkey

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Received January 10, 1977

Split-brain, partial-split, and normal monkeys were trained to perform a nested match-to-sample task. Results showed that split-brain monkeys with visual information limited to one hemisphere performed more poorly than partial-split and normal animals. At the same time, when the split-brain animals used both hemispheres their performances were the same as controls. These groups were then compared on a color discrimination reversal task and similar results were found. Taken together, these findings suggest that the processing difficulties seen in one half of a split-brain animal are frequently more apparent than real. These studies rule out earlier interpretations that such defects are due to mass action effects. Rather, the poor performance by one-half brain is due to the interfering response made by the opposite hemisphere.

INTRODUCTION

The split-brain preparation, in which the anterior commissure, corpus callosum, and optic chiasm are divided midsagittally, was used to study hemispheric function in the absence of direct interhemispheric communication [for reviews see (3, 4, 13)].

Several authors have shown that split-brain cats using a single hemisphere suffer deficits on discrimination and discrimination reversal learning. As a result, it has been concluded that a single hemisphere is inferior to the whole brain on those tasks, and the deficit has been attributed to loss of cortical mass action (7, 12, 14). In contrast, and except for Hamilton's report (5), split-brain primates using a single hemisphere did not show

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[1] This research was supported by U.S. Public Health Service Grant MH-25643. The authors would like to thank Morton Mendelson, Mortimer Mishkin, Nicholas Brecha, and Joseph LeDoux for their helpful comments on the manuscript. Dr. Nakamura's current address is National Institute of Mental Health, Laboratory of Neuropsychology, Building 9 Room 1N107, Bethesda, Maryland 20014.

ISSN 0014–4886

learning losses. Myers (8) found overlapping tactile discrimination learning curves for split-brain and normal monkeys, even though split-brain animals showed learning in only one hemisphere. Butler (2) failed to find losses on color, brightness, or pattern discrimination after forebrain commissurotomy, and Noble's (11) split-brain and partial-split monkeys did not show significant differences from normal monkeys in learning rate on an object learning set when vision was restricted to a single hemisphere. Although these studies did not specifically address the question of unihemispheric–bihemispheric differences, the data failed to replicate the large differences found in cats.

To resolve an inexplicable discrepancy between cat and monkey data, we analyzed central processing abilities in the single hemisphere of the split-brain monkey (9). We took several precautions to obviate artifacts due to reduced perceptual abilities or surgical trauma. First, the tasks were designed to minimize sensory demands while maximizing demands on central processing. Second, subjects were highly overtrained to discriminate test stimuli. Third, no postoperative testing was done for at least 3 months after surgery. Finally, emphasis was placed on performance rather than on acquisition; that is, the animals were tested until performance no longer improved rather than until a preset level of acquisition was reached. Using these precautions, split-brain monkeys were compared to normal controls on a multiple delay match-to-sample task using one or both hemispheres. This task is a red–green automated match-to-sample with randomized delays of 0, 2, 6, or 8 s interposed between the sample and matching lights. On this task, split-brain monkeys were found to be equal to normal animals at all delays and under all eye conditions, apparently supporting earlier findings in monkeys.

In the two studies reported here, we continued our investigation of the possibility that commissurotomy does indeed affect central processing in monkeys. Because of the likelihood that the task used in our previous research was too simple to reveal processing losses, we conducted experiment 1 using a more difficult task. In experiment 2 we investigated the effect of commissurotomy on an acquisition task to enable us to compare results with previous cat studies.

EXPERIMENT 1

In order to be able to show central processing deficits due to forebrain commissurotomy, a task which significantly taxes normal animals was designed. The nested match-to-sample task is based on the match-to-sample, but demands simultaneous storage of two bits of information rather than one for successful performance.

TABLE 1

Experimental Conditions for Each Monkey

Animal and surgical group	Preoperative experiments			Postoperative experiments		
	MDMTS[a]	1	2	MDMTS[a]	1	2
Normal only						
NG			×			
UT			×			
WT		×	×			
Partial split						
BL					×	×
HR					×	
SR					×	×
CR					×	×
Split						
CH	×	×		×	×	×
MR	×	×		×	×	×
PR[b]	×	×			×	
SC[c]				×	×	×

[a] Multiple Delay Match-to-Sample (9).

[b] PR would not do the MDMTS after surgery and was dropped from the study after experiment 1 when it became too aggressive.

[c] SC was fully split after completing the MDMTS on which it was run as a partial split.

Methods

Subjects. Nine monkeys (seven *Macaca mulatta* and two *Macaca nemestrina*) served as subjects. Three monkeys (CH, MR, and PR) were tested as normals and as full splits. One monkey (WT) was tested as a normal only, and one monkey (SC) was tested only as a full split. Four animals (BL, CR, SR, and HR) were tested only as partial splits. Four animals (SC, CH, MR, and PR) were tested earlier on the multiple delay match-to-sample task (9). See Table 1 for a summary of the experimental conditions for each monkey.

Surgery. A detailed description of the split-brain operation may be found elsewhere (4, 13). Briefly, the anterior commissure and corpus callosum were divided at the midline by aspiration under visual control; the optic chiasm was divided at midline using a special knife. Inevitably, the hippocampal commissure was also divided. The operation was done using aseptic procedures in a single stage except for SC which had the anterior commissure divided in a second operation. Surgery on the partial-split animals was identical because although it was intended that they be completely split, histology demonstrated the surgery to be incomplete as follows: BL

TABLE 2

Summary of Histological Results: Extent of Commissural Division and Unintended Damage

Animal	Corpus callosum	Anterior commissure	Optic chiasm	Unintended damage
CH	Complete	Complete	Complete	Fornix, septum, left cingulate heavily damaged
MR	Complete	Complete	Complete	Right fornix slightly damaged
PR	Complete	Complete	Complete	Left fornix heavily damaged
SC	Complete	Complete	Complete	Right fornix slightly damaged; Left ventricle enlarged
BL	Partial[a]	Complete	Posterior only	None
CR	Partial[a]	Intact	Complete	Cortical damage left hemisphere near midline
HR	Partial[a]	Complete	Complete	Fornix and left cingulate slightly damaged
SR	Complete	Complete	Posterior only	Left fornix slightly damaged

[a] See text for description.

had the anterior portion of the optic chiasm and about 8 mm of the corpus callosum anterior to the last 6 mm of the splenium intact; SR had the anterior portion of the optic chiasm intact; HR had the anterior 5 mm of the rostrum of the corpus callosum intact. The fourth partial-split animal, CR, had the optic chiasm completely divided and the anterior commissure and the corpus callosum were deliberately left intact except for about 8 mm of the body of the corpus callosum which was divided to permit access to the optic chiasm.

All operated animals were autopsied. See Table 2 for a summary of histological results including unintended damage.

Apparatus. The monkeys were tested in a sound-attenuated isolation booth. They were seated in a restraining transport case and their heads were placed inside a restrainer that permitted restriction of vision to one eye by insertion of a metal eyehole occluder. The animals sat facing a black acrylic panel which had three 3.8-cm-square translucent screens. Colors or simple patterns were rear-projected onto the screens using IEE projectors (model 0010). The animals responded by pressing the screens which activated a microswitch to record the response. The reward for a correct response was 0.5 ml water delivered via a metal tube directly to the mouth. Animals were water-deprived for 20 hours before testing and given supplementary water after completion of testing. All stimulus presentations, response records, and rewards were controlled by a PDP 8-I computer.

Pretraining. All animals were first trained to a 90% criterion on color (red–green) and pattern (8–1) match-to-sample problems. In the match-

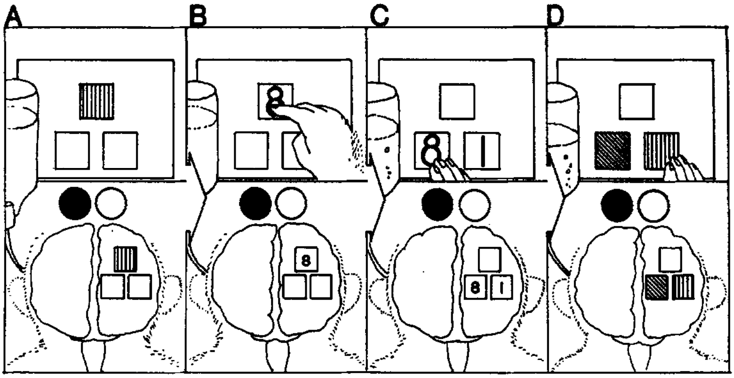

FIG. 1. Experiment 1. Nested match-to-sample task. This diagram illustrates the sequence for one representative trial on the nested match-to-sample task.

to-sample task the animals faced three screens. The sample appeared on the top screen and the monkey responded to the sample by pushing the screen. Then, the sample disappeared and was replaced by two stimuli on the bottom two screens. If the monkey selected the previously seen stimulus he received a water reward.

Testing. The nested match-to-sample task intermixes the pattern and color match-to-sample problems such that one (color) starts before and ends after the other (pattern), thus nesting the pattern problem inside the color problem.

A trial went as follows (see Fig. 1): A color sample appeared on the top screen (Fig. 1a); the animal pressed the screen to turn off the color. A pattern sample appeared on the top screen (Fig. 1b); the animal pressed the screen again to turn off the pattern. Immediately, both patterns were presented on the bottom screens. If and only if the animal correctly selected the pattern matching the sample, a water reward was delivered (Fig. 1c). Whether or not the monkey was correct, both colors appeared on the bottom screens. If the monkey correctly selected the color matching the earlier color sample, a water reward was delivered (Fig. 1d). A blankout intertrial interval of 4 s followed the monkey's response to the color problem. Eighty trials were given each day and all sample presentations and matching stimuli positions were determined randomly.

A monkey was tested with the right eye open until performance ceased to improve for 10 consecutive days; it was then tested with both eyes open, again until performance did not improve for 10 consecutive days. The right eye (hemisphere) was selected for the single-eye condition because surgery always involved retraction of the left hemisphere, and incidental damage was more likely to affect left than right hemisphere function. Animal HR (while partially split) and PR (while normal) were tested only under the

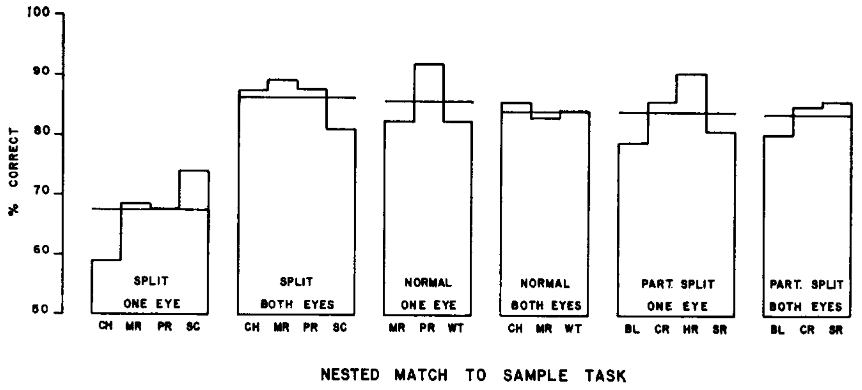

FIG. 2. Experiment 1. Nested match-to-sample task. The mean of the best three consecutive days' performances of each monkey grouped by eye and surgical condition is illustrated. The straight line through each group shows the mean performance for the group.

single-eye condition and animal CH (while normal) was tested only under the both-eyes-open condition. Best performances for three consecutive days on the single-eye and both-eyes conditions were averaged and graphed. After completion of testing as normal animals, monkeys CH, MR, and PR were fully split and retested with the same schedule of pretraining and testing.

Results and Discussion

Figure 2 shows the mean percentage correct for all animals. The results from the pattern problem were averaged with the color problem as both showed the same trends. The animals are grouped by surgical and eye conditions. Clearly, the split-brain animals in the single-eye condition are worse than all other animals ($P < 0.025$). Monkeys in other conditions do not differ from each other. Although the fully split animals perform worse in the single-eye condition ($P < 0.025$), they are in the normal range in the both-eyes condition. Partially split animals are not impaired on any condition.

The nested match-to-sample problem reveals a deficit attributable to forebrain commissure and optic chiasm transection. With one eye open the split-brain animals are severely retarded compared to the normal controls. The normal performance of the partial-split controls makes it unlikely that less than full commissurotomy and optic chiasm transections could produce these results. This outcome is in accord with earlier demonstrations that split-brain cats using one eye learn more slowly than normal cats (7, 12, 14). At the same time, split-brain monkeys using both eyes do as well as normal animals, a result which is in accord with the cat study of Voneida and Robinson (14).

EXPERIMENT 2

Introduction

We demonstrated deficits in split-brain monkeys using one hemisphere on the nested match-to-sample, which was a performance rather than an acquisition task. Other investigators, however, using cats, have examined single hemisphere performance using exclusively acquisition measures. To ensure that our results for monkeys were comparable to the findings of those other studies, we tested the monkeys on a learning task on which sensory and surgical artifacts could be minimized. The color discrimination reversal task appeared to be appropriate because repeated testing was possible using the highly familiar red and green stimuli.

Voneida and Robinson (14) compared the performance of split-brain cats with split-chiasm and normal controls on a brightness discrimination reversal task. They found that split-brain cats were slower than normal cats in learning the reversal in monocular conditions and unimpaired in binocular conditions.

In an attempt to examine the effects of commissurotomy on long-term memory, our monkeys were given 40 retention trials before each reversal on the day after reaching criterion. This was done because Sechzer (12) suggested that split-brain cats show long-term memory deficits compared to controls.

Methods

Subjects. Ten monkeys (nine *Macaca mulatta* and one *Macaca nemestrina*) served as subjects. Three animals (NG, UT, and WT) were normal controls; three animals (BL, SR, and CR) were partial-split controls; and four animals (CH, JS, MR, and SC) were completely split. See Table 1 for the details of each monkey's experimental history.

Surgery, Histology, and Apparatus. Surgical procedures were the same as in the preceding experiment. All operated animals (with the exception of JS, which has not yet undergone autopsy) have had their lesions confirmed to be as stated (see Table 2).

The apparatus used was the same as described in the preceeding experiment.

Pretraining. Animals trained previously on color match-to-sample problems were given no pretraining on this task. The remaining three subjects, NG, JS, and UT, were trained on the red–green match-to-sample problem with no delay for 200 trials per day until they reached a criterion of 90%

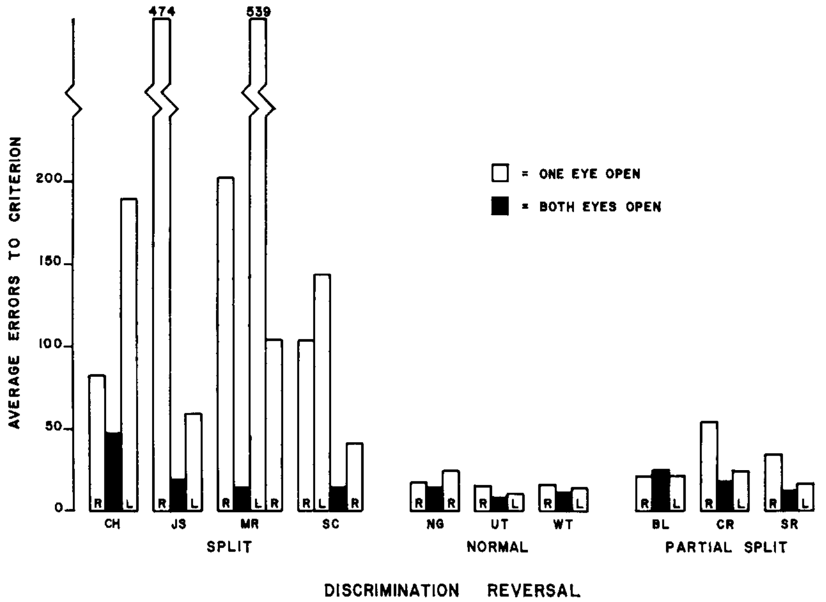

FIG. 3. Experiment 2. Discrimination reversal task. Each bar represents reversal acquisition means on each eye condition for each monkey grouped by surgical condition. Letters R and L on the open bars indicate the eye open.

correct for 200 trials. This was done to ensure that all animals were thoroughly familiar with the testing chamber and stimuli without biasing the reward significance of the stimuli.

Testing. The task was a red–green discrimination reversal. A monkey was shown a red light and a green light on the lower two screens, the position being randomly determined. On a set of trials, the animal always had to select the same color for a water reward. Trials were presented, 200 per day, with 3-s intertrial intervals until a criterion of 95% for 40 trials was achieved. On the day after reaching criterion, the monkey was first given 40 retention trials on the same discrimination. Then the discrimination was reversed and the animal was given 200 trials per day until criterion was achieved. Errors to criterion averaged for each eye condition was the basic measure used for comparison of the results.

All animals except two were tested according to the following schedule: Six reversals were given to the right eye, then four reversals with both eyes open, then four reversals with the left eye open. To avoid overlaps in the effects of the eye conditions, the initial discrimination to criterion was considered a practice set and was never counted as a reversal. The two exceptions (split-brain monkeys MR and SC) received six reversals with the right eye, four reversals with the left eye, four reversals with both eyes open, and finally four more reversals with the better single eye open. This was done to control for the fact that the normal animals would receive more experience in each hemisphere under the single-eye conditions than the splits because of interhemisphere transfer.

Results

Average errors to criterion for each eye condition have been graphed in Fig. 3. Split-brain monkeys using one eye learned the reversals more slowly than normals, but with both eyes open performed at normal levels. These results confirm the findings from the nested match-to-sample task and increase their generalizability. Mean performance on the retention trials for the split, partial split, and normal groups are shown in Fig. 4. These data have been calculated for the last two eye conditions—the both-eyes-open and the subsequent single-eye-open conditions (see Fig. 3). The split-brain animals perform significantly worse under the single-eye condition compared to the both-eyes condition ($P < 0.025$), and eye condition does not make a significant difference for the partial-split and normal groups. This suggests a long-term memory deficit for split-brain monkeys using a single hemisphere.

GENERAL DISCUSSION

The experiments reported here are in accord with and extend the generality of the facts from studies using cats. They support the view that a split-brain animal using a single hemisphere learns, performs, and remem-

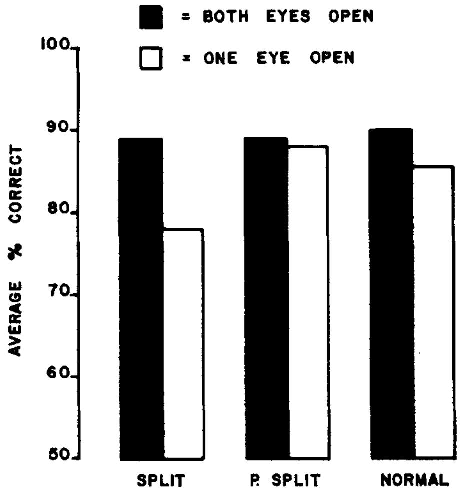

FIG. 4. Experiment 2. Retention trials. This graph illustrates mean performance on the retention trials of the split, partial-split, and normal groups with both eyes open and also with one eye open. Only the split-brain monkeys showed a significant reduction in the single-eye-open condition.

bers worse than does a normal animal. In addition, as Voneida and Robinson found in cats (14), we showed that split-brain monkeys using both hemispheres perform normally on visual tasks.

Previous investigators have cited cortical mass to explain their results (7, 12, 14). In contrast, we offer a new interpretation of the mechanisms underlying the deficits shown by split-brain animals. A new formulation is necessary because mass action theory is inconsistent with the fact that split-brain cats and monkeys using both hemispheres perform normally. Attempting to deal with this phenomenon, Voneida and Robinson (14) argued that the two hemispheres in a cat with commissurotomy of the forebrain can combine to form a larger cortical mass when both hemispheres receive the same visual input. However, it is important to remember that separated hemispheres do not exchange information about either visual stimuli or problem solving strategies (3, 4, 11, 13). Thus Voneida and Robinson's argument is seriously weakened because cortical mass action in the absence of direct interactions is an explanation without logical foundation.

A better explanation of the data can be derived from our proposal that the seeing hemisphere in a split-brain animal using one eye undergoes nonvisual interference from the unseeing hemisphere. A possible source of such interference could be conflicting demands on the common motor and attentional apparatus of the organism. Both hemispheres have access to the motor apparatus of most of the body (1). If both hemispheres are independently placing demands on this apparatus while only one hemisphere has the information necessary to do the task, then a performance loss must appear [see also (6)]. Improvement to normal levels occurs with both eyes open because both hemispheres can focus on the task, either one of which can do the task alone as long as there is no interference. This suggests that although a split-brain animal using one eye shows poor performance, the information processing ability on long-term memory of the single hemisphere may not have been reduced by forebrain commissurotomy.

This interference hypothesis is given added weight by the results of the partial-split animals. In all these animals, performance appears normal despite drastically different degrees of brain bisection. One animal, HR, is of particular interest because its performance was the best among the partial-split animals although it had only a small portion of the anterior (nonvisual) corpus callosum intact. It is more reasonable to assume that this small area of interhemispheric communication is preventing interference than that it provides a bridge for cortical mass action.

Support for this hypothesis can be derived also from preliminary results of a monkey with hemispherectomy (one cerebral hemisphere removed to the level of the thalamus) on the nested match-to-sample task (10). Unlike the split-brain monkeys, this animal shows normal performance using one or both eyes despite a 50% reduction of cortical mass. Though uncertainty remains due to lack of autopsy and need for replication, the contrast of hemispherectomy with commissurotomy strongly suggests that it is interference rather than loss of brain mass which is the critical factor in reduced performance by split-brain animals.

We conclude that our findings show a reduction in behavioral performance when visual information is confined to a single hemisphere in a split-brain animal. We suggest that the effect is not due to a change in cortical mass, but to the creation of interhemispheric interference.

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