Reports

Interocular Transfer of Brightness Discrimination in "Split-Brain" Cats

Abstract. "Split-brain" cats with midsagittal section of the optic chiasm and the corpus callosum are able to transfer interocularly a simple brightness discrimination although they are unable to transfer a pattern discrimination. This strongly suggests that the interocular transfer of a simple brightness discrimination is mediated subcallosally.

Recent experimental work by Sperry *et al.*, by Myers, and by Downer (*1*) has demonstrated that cats and monkeys that have had the optic chiasm and the corpus callosum sagittally sectioned in the midline fail to transfer to the untrained eye visual pattern discriminations learned with the other eye. These experiments implicate the corpus callosum as the interhemispheric commissure important for the interocular transfer of pattern discriminations. No systematic observations, however, have been reported on the interocular transfer of brightness discrimination or other types of visual discriminations in the "split-brain" cat, although Schrier and Sperry (*2*) have suggested that the transfer of brightness discrimination might be different from pattern discrimination. The present experiment was designed to determine if a simple, suprathreshold visual brightness discrimination would transfer interocularly in "split-brain" cats that failed in the interocular transfer of a visual pattern discrimination.

Six experimentally naive cats were used. Prior to all training, each animal had the optic chiasm sectioned sagittally by the transbuccal approach, followed in 14 to 35 days by section of the corpus callosum. The right cerebral hemisphere was retracted during callosal surgery in all animals. All abnormal postoperative neurological signs were transitory and abated within one week. A 2 to 4 week postoperative period intervened before training and testing were begun.

All training and testing were performed in a semidarkened, food-approach discrimination apparatus. The animals were trained to select the correct one of two adjacent, translucent, plastic panels illuminated from the rear and hung at the end of an alley 2½ feet long. Correct responses were rewarded with a small piece of meat, and the animal was permitted to correct errors. All training and testing, after initial shaping in the discrimination apparatus, were performed with one of the cat's eyes covered by a mask of the type devised by Myers (*3*).

During pattern-discrimination training and testing, both plastic doors to which the stimuli were affixed were illuminated to the same intensity. To minimize differences in brightness cues between the patterns used, the positive and the negative stimuli were respectively black upright and inverted equilateral triangles of the same area. During brightness discrimination training and testing, one plastic door remained dark, while the other door was illuminated from the rear by a 40-watt incandescent bulb producing a brightness of 3.27 ca/ft.^{2} at the surface of the door. The brightness at the surface of the nonilluminated door was 0.24 ca/ft.^{2} In both brightness and pattern discrimination trials, the positive and negative stimuli were alternated from right to left according to the Gellerman sequence (*4*).

Four cats were trained and tested first in the brightness discrimination and then in the pattern discrimination, and two cats were trained and tested in the reverse order. The training schedule consisted of 5 to 7 daily sessions each week with 30 to 50 trials daily. With three cats the upright triangle was the positive stimulus, and with the other three cats the inverted triangle was positive. Because cats generally prefer the illuminated door in this brightness discrimination procedure, all animals were tested for interocular transfer with the darker door as the positive stimulus. Three of the animals were initially trained with the illuminated door as the positive stimulus and were then subjected to stimulus-reversal training before interocular transfer was tested.

The criterion for successful initial learning and for successful interocular transfer was designated as 18 or more correct choices among the final 20 trials on one day and 18 or more correct choices among the initial 20 trials on the next succeeding day, the total over-all percentage of correct responses on both days being 90 percent or better. No overtraining beyond criterion was carried out in either testing procedure.

Of the six cats prepared for this experiment, two transferred the pattern as well as the brightness discrimination at or near criterion levels, and gross inspection of their brains revealed incomplete chiasmal sections although the corpus callosum was completely sectioned in both of these brains. The data on these two animals are not reported here.

The four remaining animals satisfied our behavioral criterion by failing in the interocular transfer of a pattern discrimination. Each of these four cats, however, transferred the bright-

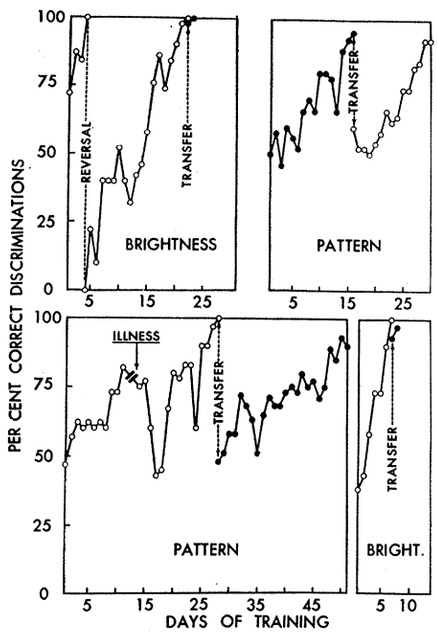

Fig. 1. Brightness- and pattern-discrimination learning curves for two "split-brain" cats. Upper two graphs, animal No. 1; lower two graphs, animal No. 2. Open circles indicate left eye training; closed circles indicate right eye training.

Instructions for preparing reports. Begin the report with an abstract of from 45 to 55 words. The abstract should *not* repeat phrases employed in the title. It should work with the title to give the reader a summary of the results presented in the report proper.

Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to *one* 2-column figure (that is, a figure whose width equals two columns of text) or to *one* 2-column table or to *two* 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to Contributors" [*Science* **125**, 16 (1957)].

ness discrimination at or above criterion levels, regardless of whether the brightness discrimination testing was conducted before or after the pattern discrimination testing and regardless of the order in which the eyes were trained and tested in the two discriminations.

These results are shown in Fig. 1. Inspection of the learning curves for pattern discrimination with each eye shows that the "split-brain" cat essentially relearns with the untrained eye. Furthermore, the course and rate of the learning with the untrained eye closely approximates that of the initially trained eye. Pattern-discrimination learning is impaired in both eyes, however, for when compared to the monocular learning of the unoperated cat, the "split-brain" cat requires 2 to 5 times more trials to reach criterion. Brightness discrimination, on the other hand, not only transfers completely from one eye to the other in the "split-brain" cat, but learning of the discrimination proceeds about as rapidly in this cat as in the normal cat restricted to monocular vision.

Because the four animals reported in this experiment are still being tested in other visual problems, the extent of their lesions has not yet been determined. Nevertheless, these results demonstrate that in cats with mid-sagittal section (of undetermined completeness) of the optic chiasm and the corpus callosum, a simple, suprathreshold brightness discrimination will transfer interocularly whereas a pattern discrimination will not. This suggests either that in cats the corpus callosum is not essential in mediating the transfer of a simple brightness discrimination or that less functional corpus callosum is necessary for brightness transfer than for pattern transfer.

Smith (*5*) has reported that simple brightness discriminations can be performed in the cat after ablations of the striate cortex; this indicates the capabilities of undetermined other cortical or subcortical structures in visual discriminations. Bridgman and Smith (*6*), however, have shown that with brightness discriminations at or near threshold levels in the cat, the striate cortex is involved and thus is essential for critical performance at these levels. Hence, if the chiasmal and callosal sections are complete in the animals reported here, the present results indicate that a simple, suprathreshold brightness discrimination is transferred by undetermined subcallosal commissures. Therefore, the corpus callosum may be essential only for the transfer of brightness discriminations at or near threshold, a cortically dependent visual function.

These interpretations suggest two sequel experiments which are now in progress utilizing "split-brain" cats: (i) testing interocular brightness discrimination transfer near threshold levels, and (ii) testing interocular brightness discrimination transfer after additional subcallosal midline-sections of other commissures (*7*).

THOMAS H. MEIKLE
JERI A. SECHZER
Institute of Neurological Sciences, University of Pennsylvania, Philadelphia

References and Notes

1. R. W. Sperry, J. S. Stamm, N. Miner, *J. Comp. and Physiol. Psychol.* **49**, 529 (1956); R. E. Myers, *Brain* **79**, 358 (1956); ———, *Arch. Neurol.* **1**, 74 (1959); J. L. deC. Downer, *Federation Proc.* **17**, 37 (1958).
2. A. M. Schrier and R. W. Sperry, *Science* **129**, 1275 (1959).
3. R. E. Myers, *J. Comp. and Physiol. Psychol.* **48**, 470 (1955).
4. L. W. Gellerman, *J. Genet. Psychol.* **42**, 206 (1933).
5. K. U. Smith, *ibid.* **51**, 329 (1937).
6. C. S. Bridgman and K. U. Smith, *Am. J. Physiol.* **136**, 463 (1942).

7. This work was supported by U.S. Public Health Service grant 2B-5273. The authors are indebted to Dr. Eliot Stellar for his advice throughout this experiment.

17 June 1960

On the Reported Inhibition of Monoamine Oxidase by an Agent with Sedative Properties

Abstract. 1-Benzyl-2-methyl-5-methoxytryptamine has been reported, on the basis of indirect evidence, to inhibit monoamine oxidase. More direct experiments, however, demonstrate that the drug is devoid of the ability to block monoamine oxidase in brain in vitro or in vivo.

Considerable evidence supports the hypothesis that the antidepressant action of monoamine oxidase inhibitors is associated with their ability to inhibit the enzyme in brain (*1*). Based on this hypothesis there have been developed a number of potent monoamine oxidase inhibitors (for example, iproniazid, phenylisopropylhydrazine, phenelzine, nialamide) for the treatment of depressed mental conditions. Feldstein *et al.*, in a recent report (*2*), question whether the antidepressant effect produced by such compounds is related to inhibition of monoamine oxidase. Their objection to this view is based on evidence that 1-benzyl-2-methyl-5-methoxytryptamine (BAS), though a sedative agent, blocks monoamine oxidase. As evidence that this sedative agent inhibits monoamine oxidase they reported that the pretreatment of schizophrenic patients for 1 to 2 weeks with about 1.5 mg of the drug per kilogram per day prevented the expected rise in urinary 5-hydroxyindoleacetic acid after the administration of DL-5-hydroxytryptophan. They concluded that their data cast doubt upon the hypothesis that there is an association between the central stimulatory effects of monoamine oxidase inhibitors and their ability to inhibit monoamine oxidase. However, they also reported that BAS did not reduce the excretion of endogenously formed 5-hydroxyindoleacetic acid. In view of the nature of their indirect and contradictory evidence we undertook to determine by direct means whether the sedative blocks the activity of brain monoamine oxidase.

Previous studies have shown that iproniazid and other potent monoamine oxidase inhibitors interfere with the destruction of serotonin and norepinephrine in rabbit brain, thereby causing a two- to threefold elevation in the levels of these amines (*1*). 1-Benzyl-2-methyl-5-methoxytryptamine was given intravenously to rabbits in daily doses of 1 to 2 mg/kg for 10 days. The levels of the brain amines, as measured by previously described techniques (*3*), were not increased over the normal values during the 10 days of drug administration. Increasing the daily dose of the sedative to 25 mg/kg also failed to elevate the levels of these brain amines.

The inhibitory action of BAS on monoamine oxidase in vitro was assayed by its effect on the metabolism of serotonin added to rabbit brain homogenates (*4*). At concentrations as high as $10^{-4}M$ BAS failed to inhibit monoamine oxidase; contrastingly, iproniazid at $10^{-4}M$ or β-phenylisopropylhydrazine at $10^{-6}M$ completely suppressed the activity.

These results indicate that 1-benzyl-2-methyl-5-methoxytryptamine has little or no activity as an inhibitor of brain monoamine oxidase in vitro or in vivo. It is not surprising, therefore, that the compound does not show antidepressant properties (*5*).

SYDNEY SPECTOR
PARKHURST A. SHORE
BERNARD B. BRODIE
National Heart Institute, Bethesda, Maryland

References and Notes

1. "Symposium on amine oxidase inhibitors," *Ann. N.Y. Acad. Sci.* **80**, 551 (1959).
2. A. Feldstein, H. Hoagland, H. Freeman, *Science* **130**, 500 (1959).
3. D. F. Bogdanski, A. Pletscher, B. B. Brodie, S. Udenfriend, *J. Pharmacol. Exptl. Therap.* **117**, 82 (1956); P. A. Shore and J. S. Olin, *ibid.* **122**, 158 (1958).
4. A. Sjoerdsma, T. E. Smith, T. D. Stevenson, S. Udenfriend, *Proc. Soc. Exptl. Biol. Med.* **89**, 36 (1955).

5. We are grateful to Dr. D. W. Woolley, Rockefeller Institute, and to Dr. Gilbert M. Bayne, Merck Sharp & Dohme Research Laboratories, for supplying us with samples of BAS.

2 June 1960