

Visuomotor Integration in Split-Brain Monkeys with Other Cerebral Lesions

M. S. GAZZANIGA¹

Division of Biology, California Institute of Technology, Pasadena, California

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Split-brain monkeys underwent either deep hemispheric disconnection or unilateral cortical ablations in an attempt to determine the neural mechanisms underlying ipsilateral eye-hand coordination. The results indicate that the responding hand is not in any direct way controlled by visual processes of the ipsilateral hemisphere. Instead, it is suggested that the target information crosses over to the hemisphere in major control of the responding arm through proprioceptive feedback generated during eye, head and neck movements initiated by the hemisphere viewing the target.

Introduction

A split-brain monkey with vision limited to one hemisphere can accurately control the contralateral arm in response to a visual target. Likewise, while early deficits are often observed with the ipsilateral arm (2, 4, 5, 13), after a time good control is usually evident (3, 4, 8, 13). The following studies attempted to analyze the neural mechanisms active in such ipsilateral eye-hand responses in the brain-bisected monkey.

Materials and Methods

Using the surgical techniques developed by Sperry (11), ten anesthetized monkeys (*Macaca nemestrina*) underwent midline section of the corpus callosum, anterior and hippocampal commissures and optic chiasm. In one animal the anterior commissure was left intact. Subsequently, several of the animals were trained to perform visual discriminations before undergoing unilateral cortical lesions. Following this second operation, retesting and training were carried out. Four other animals underwent more extensive midline surgery as described below.

Two behavioral tests were used throughout. Some animals were trained on visual discriminations using the apparatus shown in Fig. 1A. The response panel unit was rigidly mounted on the training apparatus which is part of

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the general testing equipment developed for use in testing and training split-brain monkeys. Simple adjustments make possible the separate testing of any eye-hand combination desired. Criterion was established as 90% correct response in forty consecutive trials.

A second testing procedure required the monkeys to retrieve morsels of food placed in various parts of the available visual field using one eye and

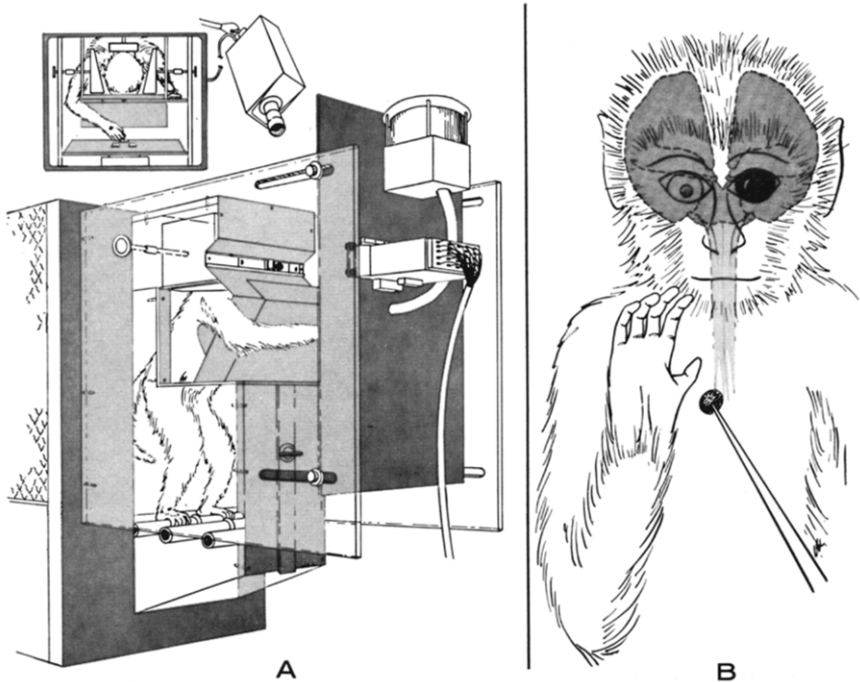


FIG. 1. A. Apparatus used in testing and training of split-brain monkeys. Closed circuit TV allowed for uninterrupted surveillance of monkeys' activity. A complete description is available elsewhere (5). B. A split-brain monkey with occluder in one eye reaching for a grape using an ipsilateral eye-hand combination.

the ipsilateral hand. The animals were free to move around in a large open-faced cage, being restrained only by a waist chain. Vision was limited to one hemisphere by placing an opaque occluder in the opposite eye (Fig. 1B). This procedure proved adequate to show clearly whether or not the animals had the ability to make relatively accurate visuomotor responses. During these tests slow-motion pictures at 64 frame/sec were taken for critical observation and study.

In four animals, midline surgical section was carried down through the pons. In all animals the lower part of the midline surgery was performed first under general anesthesia using either 0.6% halothane or sodium amytal. In

brief, with the animal lying horizontally and the head rigidly placed in a forward position so as to let the chin almost touch the chest, the longitudinal muscles of the neck were exposed and separated away from the midline. A small rectangular flap was then made in the base of the skull over the midline exposing the cerebellum. After cutting back the dura mater a small knife, in combination with some specially made tissue retractors, was used to make the section. Using this general approach, three of the animals underwent midline section of the cerebellum along with midline section of the tegmentum, pons and upper medulla oblongata. In the other animal the midbrain and pons were sectioned from above, thereby leaving the cerebellum intact, but cutting the brachium conjunctivum. After approximately a month a second craniotomy under sodium amytal anesthesia was carried out in all animals to complete the split which included midline section of the forebrain commissures, massa intermedia and optic chiasm. The roof of the midbrain was also sectioned at this stage in the three animals first sectioned from below.

All animals were killed and perfused with 10 per cent formalin. The optic chiasm was found to be completely sectioned in all animals except monkey RVT, where a few extrafoveal fibers remained intact. The degree of deep midline surgery actually accomplished as well as the extent of the cortical ablations is shown for each animal in the various figures.

Results

Role of Direct Ipsilateral Fibers. Four split-brain animals underwent unilateral massive cortical lesions removing almost the entire frontal lobe and usually some parietal cortex. The extent of the lesion for each animal is seen in Figs. 2 and 3. Postoperatively there was a severe contralateral flaccid paralysis of arm and leg; ability to use the affected hand and arm purposefully never returned. Within a week or so, however, and with attentive postoperative care which consisted of placing the animal in a restraining chair, along with needed medication, the animals showed remarkably fast recovery. By the end of a month the paralyzed arm would occasionally move in concert with the opposite unaffected arm. There never appeared to be any individual finger movements of the paralyzed hand.

All animals were able to learn visual discriminations using the lesioned hemisphere and the ipsilateral hand (Figs. 2 and 3). Whether this occipital-temporal system could learn a visual discrimination as fast as the intact hemisphere was not definitely determined. The scores made, however, were no worse than those sometimes seen in split-brain monkeys without cortical lesions (5).

The animals were also able to retrieve very accurately grapes held stationary at various points in the visual field. When the grapes were moved about on a stick, however, reaching accuracy broke down. Again, attempts

by these animals to use the paralyzed hand contralateral to the lesion of the hemisphere with either or both eyes completely failed.

Role of Possible Subcortical Interhemispheric Systems. The extent of the deep midline divisions as determined by postmortem reconstructions of the

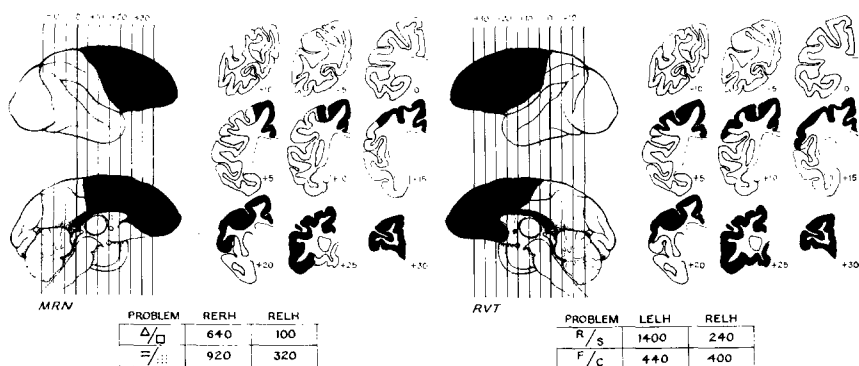


FIG. 2. Following perfusion, each brain was analyzed both grossly and histologically and the lesion reconstructed. The stereotaxic coordinates are indicated and the cross-section outlines are schematic in that they do not show the gross individual variations of cortical topography. Scores refer to number of trials to criterion on discriminations trained postoperatively unless otherwise noted. Eye-hand combinations are indicated as RERH, meaning right eye-right hand, etc.

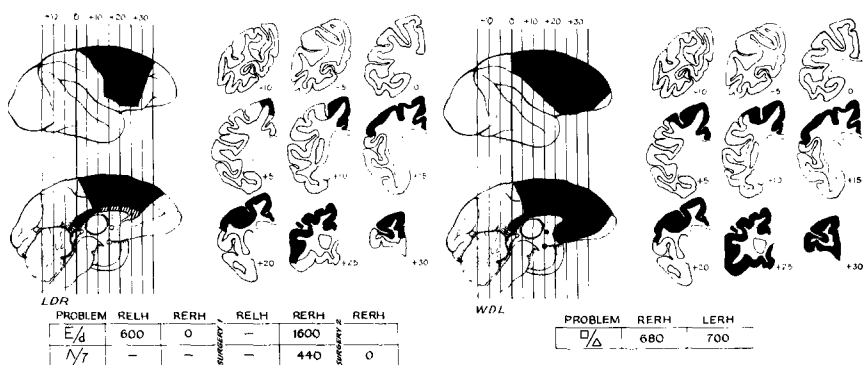


FIG. 3. Same as Fig. 2. On first discrimination monkey LDR had anterior one-half of callosus intact. One second problem effect of its section on ipsilateral performance was tested.

lesions is shown in Fig. 4. In all animals there were remnants of midline structures that remained undivided. Postoperatively there were cerebellar signs in all animals. They suffered from a marked asthenia in the hind limbs and all showed some ataxia when reaching. Asymmetrical facial paralysis was usually present and was presumably due to swelling or midline bruising, or both. With both eyes open conjugate eye movements were observed only

occasionally. Usually the eyes appeared to be moving independently and no discernible pattern was observed. Nevertheless, the animals using one eye, the other being occluded, could at times momentarily fixate on an object. After approximately 3-4 weeks of intensive postoperative care, the animals had recovered to a large degree except for some eyelid droop and there also remained clear signs of postural imbalance, ataxia and oculomotor deficiencies.

In order to test ipsilateral eye-hand combinations, one hand was temporarily taped to the animal's torso, thereby leaving the other free for analysis

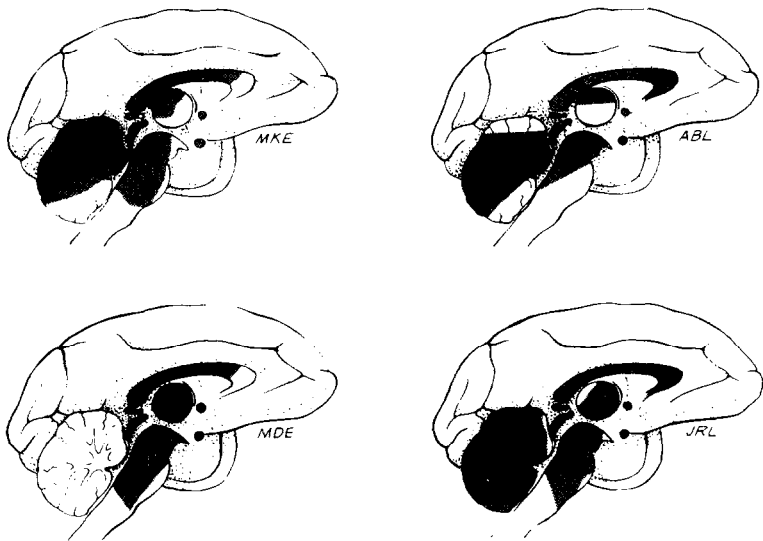


FIG. 4. Reconstitution of deep-split animals showing midline areas unintentionally left intact. The section was sometimes off the midline but other damage was not thoroughly analyzed because of positive nature of findings.

of ipsilateral eye-hand responses. Vision was again limited to one eye by placing a contact occluder in the other. None of the deep-split animals was trained on visual discriminations.

Under these test situations it was clear that animals with this deep midline surgery could also carry off ipsilateral eye-hand responses. They were able to reach out in the correct direction and retrieve grapes placed anywhere in the visual field. In making these observations, however, one had to exclude from consideration blind sweeping movements of the hand which appeared not to be triggered in response to a discrete visual target. Accuracy of response was far better in the second to fourth months after surgery than in the first. Slight errors were frequently made in reaching such that the animal might miss the object by an inch or so on either the horizontal or

vertical plane. However, the response was always in the right general direction and there rarely was a gross error. There appeared to be little appreciation of depth. It was as if only cues on the horizontal and vertical axes were used, and that once these were noted, the hand reached out blindly until it hit the object, whereupon tactile systems initiated appropriate hand movements for retrieving the food morsel.

Under monocular vision, given free hand choice, all deep-split animals almost exclusively used only the contralateral hand. This is not the case in animals with only the forebrain commissure cut.

Analysis of Movements. Slow-motion pictures of both the deep-split and brain-bisected monkeys with cerebral lesions were taken to analyze the sequence of movements. Before the animals reached out for the food, they oriented toward the object to be retrieved, starting with eye, head and neck movements. Following this the responding arm rapidly shot out for the object to be retrieved. It was as if the response of the arm was in itself in no way checked or guided by any visual process. It appeared that the blind hemisphere picked up information as to where the object was in space via peripheral feedback mechanism available to it following the head and neck orientation produced by the visual half-brain. Subsequently, the blind hemisphere, presumably with no further assistance from the other half-brain, followed through with the manual response.

Role of Nonvisual Cortex in Perception. In another series of preliminary and related experiments aimed at determining the amount of cortex necessary in a disconnected hemisphere to demonstrate the presence of pattern vision, two monkeys underwent forebrain commissurotomy plus midline section of the optic chiasm. Massive lesions were then made which included the entire frontal lobe plus varying amounts of parietal and temporal cortex. After recovery both animals were examined on a series of neurological tests. One animal, monkey MRN, was tested on a preoperatively learned visual discrimination. It was killed 26 days after the lesion while the other, monkey GBL, was killed after 30 days. Reconstructions of the lesions are shown in Fig. 5. Histological analysis of the lateral geniculate body of monkey GBL in the hemisphere containing the lesion showed some ipsilateral retrograde degeneration in layers 2, 3 and 5. The majority of cells, however, appeared normal. There was no sign of retrograde degeneration in the geniculate bodies of monkey MRN. Both animals showed transneuronal degeneration in layers 1, 4 and 6 in both geniculate bodies as a result of the chiasm section.

With vision limited to the hemisphere containing the lesion, the animals appeared to be functionally blind. While both had a pupillary response to light, neither could track and neither would react to a threatening gesture. If left alone to move about freely in a large exercise cage, both bumped into obstacles, the walls and the jumping bars. Also, monkey MRN could not

perform a pattern discrimination learned preoperatively. In every behavioral test administered, the animals appeared blind when vision was limited to the half-brain containing the lesion. Tests exclusively administered to the other hemisphere, however, revealed no such deficits in either animal.

From the above it appears that if there is a temporal lobe involvement in addition to frontal and parietal lobe lesions in one hemisphere of a split-brain monkey, the resulting effect is to produce a functional blindness in the half-brain with the lesion. How much recovery would be observed over a longer postoperative course remains to be determined. Also, the possibility remains

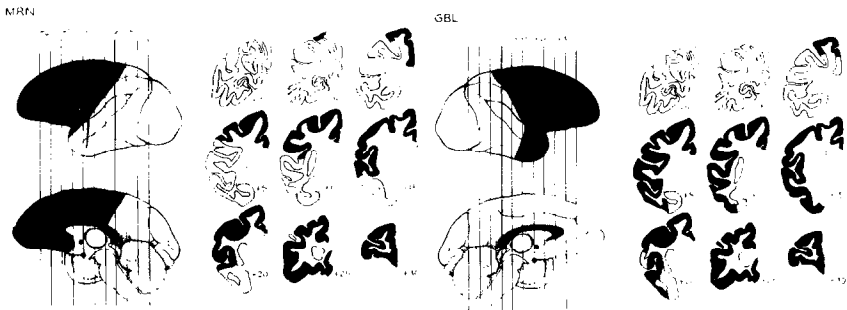


FIG. 5. Extent of lesion in animals appearing to be functionally blind. In monkey MRN a knife stab was made down into temporal lobe beneath the cortical surface.

that the rather dramatic effects seen are due to diaschistic and related factors still active at the end of 4 weeks.

Discussion

The first implication of these experiments is that homolateral corticospinal fibers are not necessary for ipsilateral eye-hand movements. Bucy and Fulton as well as others have shown that ipsilateral corticospinal systems are normally present and are located in the premotor area (1). Inclusion of this area in frontal and parietal ablations resulted in no detectable impairment in ipsilateral eye-hand performance.

It is also concluded that integrity of the contralateral motor cortex is imperative for good ipsilateral eye-hand movements because the unlesioned intact hemisphere could not effect any kind of purposeful control over the ipsilateral paralyzed arm. Additionally, since the hemisphere with the lesion possesses little or no information as to where the ipsilateral arm is at the start of any particular movement, it is difficult to imagine how it alone sets up a meaningful command to the ipsilateral arm. This, plus the foregoing observation suggest, therefore, that the mechanisms of ipsilateral eye-hand movement somehow involve the main sensory-motor mechanisms of the opposite hemisphere.

In an attempt to disconnect subcallosal interhemispheric communicating systems possibly active, deep midline surgery was carried out but failed to interfere with ipsilateral eye-hand control. Errors were seen in reaching but only occasionally of a gross nature. In time, all responses improved and it may well be as the surgical techniques further develop, less and less post-operative deficits will be observed. For example, midline sparing of oculomotor and corticocerebellar systems would probably improve the basic motor picture, but because of the totally crossed nature of these systems would not allow for any additional interhemispheric communication.

The cinematographic studies revealed a strategy the monkeys may have been using to carry out the ipsilateral responses seen in the present study. In short, it appeared as though one hemisphere cross-cued the other on where an object was in space through nonvisual proprioceptive mechanisms resulting from eye, head and neck orientation movements. This cross-cuing mechanism could explain the type of control observed in all previous tests of ipsilateral eye-hand responses reported in the literature.

It is not concluded, however, that the sole mechanism active in ipsilateral movements is of the type just described. Studies on brain-bisected human beings with minimal extracallosal brain damage have shown that sometimes simple finger movements of one hand can be triggered from the ipsilateral hemisphere (Gazzaniga, Bogen and Sperry, unpublished). Likewise with eye, head and neck movements eliminated, accurate ipsilateral eye-hand responses have been observed. These findings suggest that under some conditions, ipsilateral eye-hand responses are triggered and can be controlled through ipsilateral corticospinal systems in combination with the major motor mechanisms of the opposite hemisphere. Or, alternatively, one could imagine that corollary discharge information critical to the visuomotor set of the type described by Sperry (9) and von Holtz (6) could be crossing over in these patients without lesions. It remains to determine experimentally what the effects of fixing head posture would have on normal, split-brain animals and split-brain animals with lesions during ipsilateral eye-hand responses.

The foregoing evidence, as well as electrophysiological studies (7) show that the orientational response, the fixation on the object to be retrieved, can be triggered from the visual associational areas. The implication is that from the occipital areas forward to the frontal lobe, visuomotor integration is constantly taking place and that each level of the motor system involved in a particular movement continually refers to the set and position of the segment preceding it. In other words, the above findings seem to argue for viewing brain processes underlying such behavioral tasks not in the simple sense of how and where visual information gets together with the motor mechanisms of the arm. Rather, the results suggest that multiple interrelated neurological events in the stimulus-response sequence occur on an ever-changing con-

tinuum, from the moment a visual stimulus registers on an animal to the final behavioral response.

The preliminary finding reported above on the effects on visual perception of removal of nonvisual cortical areas confirms in part some earlier findings in the cat (12). In split-brain monkeys it has previously been shown that frontal lobe lesions alone do not lastingly disrupt basic visual processes but tests on the learning capacity of the hemisphere with a lesion were not carried out (8). The present findings suggest that a frontal, parietal and temporal lesion combined produces a functional blindness.

How blind these animals really are remains to be determined. It may well be that the deficits do not lie in the perceptual sphere but involve more the inability of a hemisphere to execute a meaningful behavioral response. If perception is the preparation for response (10), i.e., an animal perceives when it is behaviorally set to respond in a particular fashion to the exclusion of a multitude of other possible responses, then perhaps one could maintain this lesion had interfered with neural systems underlying this more executive function of the perceptual process. Further experimentation is contemplated which would make use of conditioned heart rate to complex visual stimuli. Studies of this kind would help clarify the extent to which the animal "sees" but is incapable of responding.

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