

Cortical and Subcortical Interhemispheric Interactions Following Partial and Complete Callosotomy

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The corpus callosum is the largest fiber tract in the human brain, and plays a critical role in many aspects of interhemispheric integration. Much has been learned about the structure and connectivity of this fiber tract through anatomical studies on a variety of species. The functional implications of these anatomical findings are supported by behavioral studies on monkeys and humans with lesions of the corpus callosum.

Much of the behavioral data in humans is derived from studies on patients who have undergone callosotomy for the control of intractable epilepsy. Surgical section of the corpus callosum results in a classic disconnection syndrome characterized by a breakdown in communication between the 2 hemispheres. In the early stages of recovery from callosotomy, this communication failure can be manifested in startling ways. For example, some patients have exhibited the “alien hand” syndrome after surgery, in which the left hand appears to behave as if it were controlled by some other person. As recovery progresses, the overt symptoms tend to abate, and these “split-brain” patients are remarkably unaffected in daily living. Despite the appearance of normal cerebral function, many signs of hemispheric disconnection persist and can be revealed through specialized testing procedures. The chronic disconnection of the cerebral hemispheres has made patients with callosotomy an invaluable population for the study of the specialized capabilities of each hemisphere in isolation. Comparisons between patients with callosotomy and those with localized lesions involving different portions of the corpus callosum also provide a powerful method of investigating the functional capacities of callosal regions.

THE ROLE OF THE CORPUS CALLOSUM

Postmortem research on human and monkey brains has revealed that the corpus cal-

losum is topographically organized with anterior fibers connecting frontal regions of the 2 hemispheres and posterior fibers connecting posterior cortical structures. Specifically, fibers from the superior parietal lobule and the occipital cortex pass exclusively through the splenium, while frontal fibers pass through the rostral half of the corpus callosum, including the genu.¹ This anterior-to-posterior organization results in modality-specific regions of the corpus callosum (**Figure 1**). For example, the anterior midbody transfers motoric information; the posterior midbody transfers somatosensory information; and the isthmus transfers auditory information. Because of this topographic organization, lesions of specific callosal regions result in predictable deficits in interhemispheric transfer of information.

In patients who have undergone complete callosotomy, all callosal connections are severed. With the hemispheres surgically disconnected, information can be presented to each hemisphere in isolation by taking advantage of the contralateral organization of the nervous system. To lateralize visual stimuli, for example, subjects are asked to fixate on a central crosshair. Stimuli are briefly flashed to one side of the crosshair or the other. Because of the anatomy of the visual system, each stimulus will be processed exclusively by the contralateral hemisphere. Thus, stimuli presented to the left of fixation are processed in the right hemisphere, and vice versa. More recently, a technique has been developed for stabilizing stimuli on the retina so that presen-

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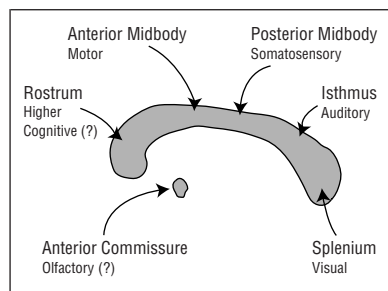


Figure 1. Functional topography of the corpus callosum. Different regions of the corpus callosum connect different regions of the 2 cerebral hemispheres. This topographic organization is reflected in the functional deficits that result from lesions to different callosal regions.

tation times can be increased while maintaining lateralization. This is accomplished by monitoring the patient's eye movements with a dual-Purkinje-image eye tracker and deflecting the retinal image to compensate for changes in visual fixation. Using this type of testing, it has been demonstrated that information presented to one hemisphere is unable to transfer to the other hemisphere. For example, if the right hemisphere is presented with a picture of a common object, the patient is unable to name the object because the right hemisphere cannot produce speech, and the language-dominant left hemisphere has no knowledge of the presented object. The right hemisphere can express its response, however, by pointing to the correct picture with the left hand. This type of finding initially led to the conclusion that interhemispheric transfer does not occur in patients with complete callosotomy.

In contrast to complete callosotomy, patients with incomplete lesions of the corpus callosum do not exhibit the classic disconnection syndrome. Behavioral testing has revealed subtle deficits, and the pattern of deficits observed in these patients provides further evidence for regional specificity of the corpus callosum. Risse et al² report that patients who had the anterior two thirds of the corpus callosum sectioned, sparing the splenium, did not show any discernible disruption of interhemispheric transfer except in a dichotic listening task and some somatosensory tasks. Patients who underwent a more complete anterior

callosal section that spared only one third of the splenium demonstrated intact visual transfer but lack of interhemispheric transfer in all other modalities. Surgical resection of the posterior corpus callosum, preserving the anterior regions but lesioning the splenium, results in lack of interhemispheric visual transfer.³ These results confirm that regions of the corpus callosum have specific functional roles and that the type of callosal lesion in a given patient can be inferred from performance on tests of interhemispheric transfer.

SUBCORTICAL INFORMATION TRANSFER IN PATIENTS WITH CALLOSOTOMY

Patients who have undergone full callosotomy are described as split-brained, but possible conduits of interhemispheric transfer remain. Subcortical connections are presumably unaffected by callosotomy, and the search for subcortical information transfer between the hemispheres has been a major focus of research with callosotomy patients. This research has been contentious, with some investigators reporting evidence of limited transfer of information and others disputing these claims. Some of the literature in support of interhemispheric transfer has reported transfer of perceptual information.⁴ Other researchers have reported evidence for transfer of higher-level cognitive information but not of perceptual information.⁵ Corballis⁶ reviewed much of this literature and concluded that the evidence for subcortical transfer of higher-level perceptual or cognitive information was not convincing and that many of the findings could be explained by information available to one hemisphere rather than to subcortical transfer. There is, however, some evidence for subcortical transfer of coarse perceptual information (eg, large vs small). Transfer of this type of information could facilitate above-chance guessing in some paradigms and produce the appearance of subcortical information transfer. Gazzaniga et al⁷ provided an elegant demonstration of this type of transfer in a patient

with a complete callosotomy verified by magnetic resonance imaging (MRI) studies. When the right hemisphere was presented with 1 of 2 digits (1 or 2), the left hemisphere was able to name the digit under certain conditions. The response had to be binary, and the left hemisphere had to be aware of what the 2 response choices were. Interestingly, although the left hemisphere was able to verbally identify the stimulus presented to the right hemisphere, the patient was unable to match stimuli across visual fields. This indicates that, although there is limited subcortical information transfer, this transfer is only capable of supporting certain types of responses.

Kingstone and Gazzaniga⁸ investigated the issue of subcortical transfer of higher-level information in patient 1, who had a complete callosotomy verified by postsurgical MRI findings. They presented pairs of words simultaneously with 1 word in each visual field (eg, tooth + brush). After each word pair was presented, patient 1 was given a pad of paper and a pen and asked to draw a picture of what he had seen; he drew a substantial number of pictures that combined the words presented to the 2 visual fields. From this, it could be concluded that there was interhemispheric transfer of information. However, patient 1 drew many more of these compound words when he was able to see the paper on which he was drawing than when it was hidden from view. This raises the possibility that the integration occurred on the paper rather than in the brain. The authors therefore designed a second experiment in which the word pairs were constructed such that the pair formed a compound word that was not suggested by either of the individual words in the pair (eg, break + fast). In this task, patient 1 never drew pictures combining the information from both visual fields. They concluded that the evidence from the first experiment suggesting transfer of semantic information in this patient was illusory and could be attributed to bilateral control of the same hand. Thus there was no evidence for the transfer of higher-order information between the 2 hemispheres.

CORTICAL INFORMATION TRANSFER IN PATIENTS WITH CALLOSOTOMY

In addition to preserved subcortical pathways in patients with callosotomy, other cortical commissures may remain intact because the extent of the surgical section varies by patient and by surgeon. These preserved cortical pathways may be capable of supporting interhemispheric information transfer. In addition, postsurgical MRI findings in patients who were reported to have full callosotomies have occasionally revealed unintentional sparing of callosal fibers. As the research from patients with partial callosotomy suggests, these intentionally or unintentionally spared fibers may provide a pathway for the interhemispheric transfer of information.

Sparing of fibers in some patients may account for the incompatible findings reported in the literature on interhemispheric transfer. Some evidence of this comes from the authors' patient 2. Previous research with patient 2 consistently failed to show any interhemispheric transfer of perceptual information. Despite this, results of MRI studies performed 5 years after surgery revealed spared callosal fibers in both the splenium and the rostrum.⁹ It is possible that these spared fibers could potentially support interhemispheric transfer. Although there has been no evidence for this in purely perceptual tasks, some evidence for limited interhemispheric transfer of information in patient 2 has been demonstrated.¹⁰ In this study, patient 2 was able to make reasonably accurate judgments about whether words simultaneously presented to opposite visual fields rhymed in some conditions but not others. She was able to make these judgments with 77% accuracy when the words both looked alike and sounded alike (eg, look/book), but her performance was at chance when the words looked alike but did not sound alike (eg, cough/dough) and when the words sounded alike but did not look alike (eg, rule/tool). The authors concluded that patient 2 was able to transfer weak or degraded phonologic and orthographic infor-

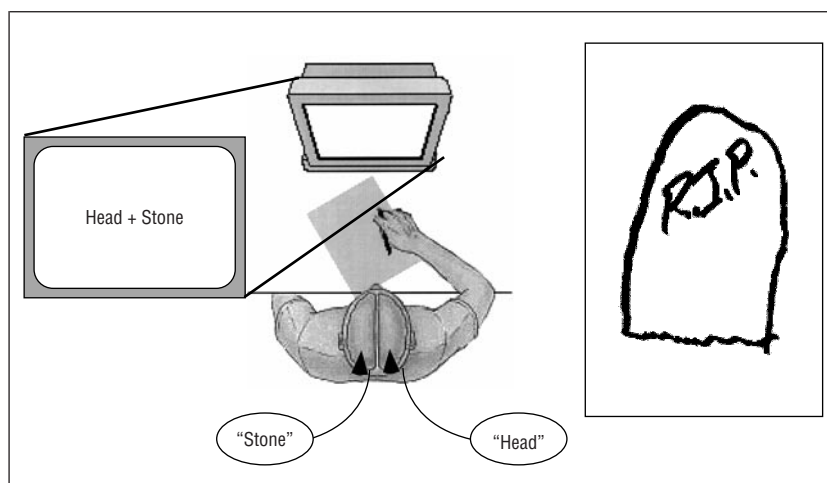


Figure 2. Paradigm for assessing interhemispheric transfer of semantic information in a patient with a callosotomy. A single word is presented to each side of visual fixation for 150 milliseconds so that each word is only "visible" to one hemisphere. The patient is asked to draw a picture that represents the word(s). Patient 2 frequently drew pictures that reflected a compound of the 2 words that was not suggested by either of the words in isolation (right).

mation between hemispheres and that this transfer seemed to occur via spared callosal fibers.

To further investigate the role of spared callosal fibers, we tested patient 2 in a number of paradigms that could potentially reveal interhemispheric transfer. In the first experiment, she was presented with word pairs that were constructed such that the pair formed a compound word that was not suggested by either of the individual words in the pair, as in the study reported by Kingstone and Gazzaniga.⁸ Presentation of the 2 words in each pair was simultaneous with 1 word in each word pair appearing in each visual field. Patient 2's eye movements were monitored to ensure that each hemisphere had access to only 1 word in the pair. Patient 2 drew the emergent object suggested by the combination of the 2 words in every trial (eg, breakfast, cockpit, home run). These results indicate that there is transfer of information between hemispheres (**Figure 2**). It is unlikely that this transfer is occurring subcortically since there was no evidence of transfer in this task with patient 1.⁸ We suggest, therefore, that the interhemispheric transfer observed in patient 2 is via the spared callosal fibers revealed by postsurgical MRI findings.

Further experiments were designed to determine the basis of this transfer. To assess visual transfer, patient 2 was asked to compare objects

presented simultaneously in both visual fields. The objects differed in either color, size, shape, or number. Patient 2's performance was at chance for all comparisons, suggesting that there is little or no interhemispheric transfer of visual information. A subsequent experiment explored transfer of phonological information. It is possible that visually presented words can be translated into phonological code within each hemisphere and that this representation is then transferred from one hemisphere to the other. If the phonological code of the word is transferred but not the visual word form, then patient 2 might be able to differentiate between words that are phonologically different, but would make errors on word pairs that are homophones (eg, toe and tow). In these word pairs, the visual word form would be different, but the phonological code would be identical. When these word pairs were presented with 1 word in each visual field, patient 2's performance was at chance for all word types, suggesting that she was unable to transfer either the visual word form or the phonological code of words between hemispheres.

THE ROLE OF SPARED CALLOSAL FIBERS IN INTERHEMISPHERIC TRANSFER

These 2 experiments provide no evidence for interhemispheric transfer related to the physical coding of

the stimulus. This is not entirely consistent with the data reported by Gazzaniga et al¹⁰ from which they concluded that there was evidence for transfer of weak or degraded phonologic and orthographic information. In addition, the results of the drawing experiment also demonstrate transfer of information between the hemispheres. Although it is clear that there is interhemispheric transfer in this patient, there are clearly discrepancies among the experimental findings. This gives rise to a number of questions: What pathways are mediating this transfer? What type of information is being transferred, and why is transfer seen in some experiments and not others? Do the findings from this patient have implications for studies with other patients?

First, since there is interhemispheric transfer of information in patient 2, it is likely to be occurring via subcortical pathways or via the spared callosal fibers in the rostrum and splenium. Patient 1 had a complete callosotomy with no evidence of any fiber sparing, so only subcortical pathways were available for interhemispheric transfer. In the drawing experiment, he showed no evidence of any transfer between hemispheres. This suggests that subcortical pathways are not capable of supporting this type of information transfer. It is therefore unlikely that the information transfer demonstrated by patient 2 in this experiment is occurring via subcortical pathways. A second possibility is that the transfer is not occurring via cortical or subcortical connections, but rather by more peripheral mechanisms such as subvocal speech. If the right hemisphere is able to program the speech apparatus, this could account for patient 2's ability to make rhyming judgments about word pairs that look and sound like rhymes (eg, look/book). If this were the case, however, then patient 2 should also have been able to make rhyming judgments about words that sounded alike but did not look like rhymes (eg, rule/tool) because the visual word form should not influence subvocal speech mechanisms. However, since her performance was at chance on these word pairs, subvocal speech cannot ac-

count for the data. This suggests that any transfer of information is not likely to be occurring via the speech apparatus. Because the data are not consistent with subcortical or peripheral mechanisms, interhemispheric information transfer is likely to be occurring via the spared callosal fibers.

If these spared fibers are capable of supporting interhemispheric transfer, the question then is what type of information is being transferred. The results of the rhyming experiment suggest that there is transfer of weak or degraded orthographic and phonological information. Other findings do not support this conclusion, but if the transferred information is truly degraded, it may be sufficient for making some types of judgments but not others. There is also evidence for transfer of higher-level information in the drawing experiment. It is not likely, however, that higher-level information alone would provide sufficient information for making judgments about rhyming. We conclude, therefore, that there is some transfer of higher-level information, probably via the spared rostral fibers, and some transfer of degraded perceptual information via the sparing in the splenium. The fact that some types of information are transferred and some are not, and that some of the transferred information is likely to be in a degraded form, accounts for why information transfer is seen in some experiments with patient 2 but not in others.

The findings from patient 2 may have implications for studies with other patients. The literature on subcortical information transfer in patients with callosotomy is rife with inconsistencies. Because the extent of the cortical separation in these patients has not always been confirmed by brain imaging techniques, it is possible that some of these patients have spared callosal fibers. This sparing may be sufficient to support some types of information transfer. Differences in the extent of cortical separation among patients may account for the discrepancies in the literature.

CONCLUSIONS

Patients with callosotomy provide a unique opportunity to study the functions of the 2 hemispheres in isolation. Much has been learned from these patients about hemispheric specialization in visual perception, imagery, language, and memory, as well as in other areas of perception and cognition. In addition to insights into hemispheric specialization, the deficits in cognitive processing demonstrated by patients with callosotomy provide clues about the integrative function of the corpus callosum in the intact brain. Although some issues of hemispheric specialization and integration can be studied in normal subjects, many of these issues can only be studied in patients with callosotomy because the presence of an intact corpus callosum masks the specific contributions of each hemisphere and of any subcortical pathways. Therefore, split-brain patients provide a valuable way, and in some cases the only way, of studying hemispheric specialization and integration.

Although there is relatively little controversy about hemispheric specialization of function, there has been a great deal of controversy about the extent of subcortical information transfer in patients with complete callosotomy. Research on interhemispheric transfer in split-brain patients has produced discrepant results in both perceptual and higher-level domains. We suggest that the apparent inconsistencies in the literature may be the result of different degrees of callosal sparing. In most if not all split-brain patients, there are cortical commissures or callosal fibers that are spared either intentionally or unintentionally.

Prior to the advent of MRI, there was no way to confirm the extent of surgical section. Even with the availability of MRI, there are few reports in the literature on imaging studies of patients with callosotomy. Behavioral studies investigating interhemispheric transfer have generally assumed that any callosal sparing is not sufficient to support functional interhemispheric transfer. The case of patient 2, however, lends a cautionary note to such con-

clusions. While some studies of perceptual function make her look fully split, there is evidence for transfer of both degraded perceptual and of some higher-level information by spared callosal fibers. This raises the possibility that studies showing transfer in some patients and in some paradigms, but not in other patients or other paradigms, may be the result of different degrees of callosal disconnection. We suggest that when the corpus callosum is fully transected, there is little or no transfer of higher-order perceptual or semantic information. Studies on split-brain patients who show transfer of more complex perceptual and cognitive information may be contami-

nated by the presence of spared callosal fibers.

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