Some of these studies have been reported in a preliminary communication, Hoffee, P., and E. Englesberg, *Bacteriol. Proc.*, **1962**, p. 120.

Abbreviations: ATP, adenosine triphosphate; αMG, alpha methyl D-glucopyranoside.

† Predoctoral Research Fellow, U.S. Public Health Service.

[1] Rickenberg, H. V., G. N. Cohen, G. Buttin, and J. Monod, *Ann. Inst. Pasteur*, **91**, 829 (1956).

[2] Cohen, G. N., and J. Monod, *Bacteriol. Revs.*, **21**, 169 (1957).

[3] Kepes, A., *Biochim. Biophys. Acta*, **40**, 70 (1960).

[4] Horecker, B. L., J. Thomas, and J. Monod, *J. Biol. Chem.*, **235**, 1580 (1960).

[5] Horecker, B. L., J. Thomas, and J. Monod, *J. Biol. Chem.*, **235**, 1586 (1960).

[6] Osborn, M. J., W. L. McLellan, Jr., and B. L. Horecker, *J. Biol. Chem.*, **236**, 2585 (1961).

[7] Rotman, B., and R. Guzman, *Pathologie-Biologie*, **9**, 806 (1961).

[8] Wiesmeyer, H., and M. Cohn, *Biochim. Biophys. Acta*, **39**, 440 (1960).

[9] Doudoroff, M., W. Z. Hassid, and E. W. Putman, *J. Biol. Chem.*, **179**, 921 (1949).

[10] Englesberg, E., J. A. Watson, and P. A. Hoffee, in *Cellular Regulatory Mechanisms*, Cold Spring Harbor Symposia on Quantitative Biology, vol. 26, (1961) p. 261.

[11] Englesberg, E., these PROCEEDINGS, **45**, 1494 (1959).

[12] Umbreit, W. W., R. H. Burris, and J. F. Stauffer, *Manometric Techniques* (Minneapolis: Burgess Publishing Company, 1957).

[13] Dische, Z., and E. Borenfreund, *J. Biol. Chem.*, **192**, 533 (1951).

[14] Barett, J. T., A. D. Larson, and R. E. Kallio, *J. Bacteriol.*, **65**, 187 (1953).

[15] Davis, B. D., in *Enzymes: Units of Biological Structure and Function*, ed. O. H. Gaebler (New York: Academic Press, 1956), p. 509.

---

*SOME FUNCTIONAL EFFECTS OF SECTIONING THE CEREBRAL COMMISSURES IN MAN**

BY M. S. GAZZANIGA,† J. E. BOGEN,‡ AND R. W. SPERRY†

CALIFORNIA INSTITUTE OF TECHNOLOGY,* PASADENA,
AND LOMA LINDA UNIVERSITY SCHOOL OF MEDICINE, LOS ANGELES

Communicated August 2, 1962

It has been possible in studies of callosum-sectioned cats and monkeys in recent years to obtain consistent demonstration of a variety of interhemispheric integrational functions mediated by the corpus callosum.[1, 2] These animal findings stand in marked contrast to the apparent lack of corresponding functional deficits produced by similar surgery in human patients.[3–9] The general picture of callosal functions based on the animal studies tends to be supported in current early testing of a 48-year-old male war veteran with recent complete section of the corpus callosum, anterior and hippocampal commissures.

The patient (W. J.) had been having grand mal convulsions for fifteen years subsequent to war injuries suffered in 1944. The seizures were refractory to medical management with a frequency, at best, of about 1 per week and, at worst, of 7 to 10 per day culminating in status epilepticus every 2–3 months. The subject was right handed, had an I.Q. of 113, and showed no significant sensory, motor, or associative disturbances in a battery of visual, tactile, and motor tests applied prior to surgery, excepting a mild hypesthesia on the left side.

The commissures were sectioned in a single operation by exposure and retraction of right frontal and occipital lobes. The massa intermedia was judged by the surgeons[10] to be absent and some atrophy of the exposed right frontal pole was ob-

served. Generalized weakness, akinesis, and mutism were evident immediately after surgery but had largely cleared when postoperative testing was started. Anticonvulsant medication was reinstated shortly after surgery. There have since been three brief attacks with loss of consciousness but as yet no major convulsions. Occasional brief episodes of clonic-like tremor confined to the distal portions of the right arm or leg have also been noted. The operation appears to have left no gross changes in temperament or intellect, and the patient has repeatedly remarked that he feels better generally than he has in many years

The tests referred to below were carried out from the 6th to 20th weeks after surgery in weekly 3-hour sessions, mostly in the laboratory but on a few occasions in the patient's home, usually with the patient's physician and wife present. The general test repertoire included a considerable carry-over of items from previous clinical studies plus some new and revised test procedures designed on the basis of observed effects of brain bisection in animals.

Tests involving tactual function have revealed no significant impairments in the right side of the body connected to the dominant left hemisphere. Similar testing of the left hand, however, has indicated a severe agnosia, anomia, and agraphia. For example, in blindfold tests, the patient has regularly been able to manipulate and use correctly most familiar objects such as a pencil, cigarette, ring, pistol, hat, glasses, etc., but has been totally unable to name or to describe any of these. Prior to surgery he could write legibly with the left hand, but afterward has produced only a meaningless scribble.

Also, he locates accurately points of tactile stimulation on the fingers of either hand by touching with the thumb of the same hand, immediately or with a 5-sec delay imposed. He is quite unable, however, under similar conditions to cross-locate with either hand across to the other. Such cross localization is possible for points on the head, face, and upper neck. Taste and touch are both reported correctly from either side of the tongue. When tapped lightly one to four times on one foot or hand, the subject can accurately tap a corresponding number of times with the hand of the same side but is unable to tap the correct number with the opposite hand. Simple jigsaw cutouts could be put together correctly with either hand separately but not when cooperation between both hands was required. In general, when stimulus and response are confined to the same hemisphere in such tests, the performance goes well, but when cross-integration is required, the activity breaks down.

Visual tests were conducted with tachistoscopic presentation of stimuli at $^1/_{10}$ and $^1/_{100}$ sec. The results reveal no marked abnormality in response to stimulation of the right visual half-field, projected to the dominant hemisphere. In the left half-field, however, there is a profound agnosia for all stimuli presented. When very simple geometric designs, or single large numbers or letters are flashed to this half-field, the subject can retrieve the corresponding figure at a level 30 per cent above chance from among a series of five or more patterns on cards placed within easy reach of the left hand. He is unable to perform above chance, however, when colors are used, or when he is obliged to select the same cards with the opposite hand. Also, he has been unable to name, draw a rough semblance, or to otherwise describe the left field figures with either hand or verbally. More complicated written material is read easily in the right half-field but evokes only a blank response from the left field. In visuomotor studies with the right hand working a push but-

ton, he responds to the simple on-flash of a small light when it appears in the right half-field only, while with the left hand he is able to respond to the light signal in either field. When a choice between red and green lights was required, the reaction was correct only for responses of the right hand to stimuli in the right half field. In simple visual constructional tests, as in copying a sketch of a Necker cube, the drawings of the left hand were less defective than those of the right.

With respect to motor function no special coordinative difficulty has been observed in tests involving independent use of the right hand. The left hand also is capable of refined individuated finger movements and generally is adept and dextrous enough in the performance of familiar automatic activities such as handling and smoking a cigarette, lifting a coffee cup, putting on glasses, and the like. The left hand also works well along with the right in other habitual tasks such as tying a knot in the belt of his robe, folding towels, putting on and removing clothes. In other respects, however, the use of the left hand is obviously impaired. For example, if the patient is interrupted in any of the foregoing activities and asked to repeat on command with his left hand any of these motor performances or even to make much simpler movements, the left arm and hand may fail to respond at all or the response may be spasmodic and grossly inadequate. Much as in a stammerer's block, the more intense the effort, the more difficult to achieve the movement. In the early tests especially, a profound apraxia was apparent with respect to any independent movements of the left hand in response to a purely verbal command. Beginning with the 3rd month, however, if the test was presented with nonverbal aids, i.e., if the experimenter said, "Do this" and demonstrated the requested movement, then the patient with the left hand was usually able to follow very simple actions like writing a T or an L and lifting individual fingers as in a piano exercise.

Movements like lifting the left hand and placing it behind the head or using it to point to something, i.e., responses that could not be carried out by the left hand alone to a verbal command, were achieved readily when he was directed to use both hands to make the same or symmetrical movements. Frequently, when his left hand had been fumbling ineffectively at some task, he would become exasperated and reach across with the right hand to grab the left and place it in the proper position.

None of these apraxic difficulties was apparent in the use of the dominant right hand during the regular testing sessions. However, transient difficulty with the right hand was reportedly seen on a few occasions by the patient's wife. She has also noted antagonism between the actions of the right and left hands, e.g., the patient would pick up the evening paper with the right hand, but put it down abruptly with the left and then have to pick it up again with the right. Similar contradictory movements were observed occasionally in the course of dressing and undressing, and in other daily activities, at times on a scale sufficient to be distinctly bothersome. It was as if the control of the left hand were strongly centered in the minor hemisphere at such times and hence isolated from the main intent and prevailing directorship of the dominant hemisphere.

There were further indications that the separated hemispheres were each unaware of activity going on in the other in the case of those functions that are highly lateralized, e.g., visual perception within right or left half-field, language functions, or tactile and motor functions of the extremities. For example, the patient often

retrieved a correct visual stimulus card with the left hand after exposure to the left visual half-field, but after the card had been turned over he was completely unable, on request, to describe or to otherwise use the major hemisphere to identify the figure he had chosen. Or, after responding intently with the correct count by the left hand to a series of tactile stimuli applied to the left leg or hand, it was often clear from his reply to question that in his literate hemisphere he had been totally unaware of having either felt the stimuli or made the response. In a few tests involving the learning of simple tactile discriminations with right or left hand, the learning did not carry over to the opposite hand.

The severe left apraxia following callosal section may have been exaggerated in this patient by an unnatural potentiation of cerebral dominance and the lateralization of volitional control as a result of the damage to the non-dominant cortex incurred in his injuries of 1944. On the other hand, since pre-operative studies suggested a focus in the left parietal lobe,[10] it is also possible that damage to the left hemisphere may have impaired its ipsilateral motor control thus leading to exaggeration of the left apraxia after commissurotomy. The extent to which visual perception is intact in the left half-field still remains something of a problem that it may be possible to settle with further tests that combine half-field presentation with nonverbal responses.

The question of how typical the findings in this case may be is complicated by the unknown amount and nature of the pre-existent cerebral damage. Nevertheless the marked differences between the pre- and post-operative results and most of the other impairments observed seem best ascribed to interruption of the commissural connections particularly those linking the sensory and motor areas of the right cerebral cortex with the speech and related centers of the dominant left hemisphere. The results are in line with the picture of callosal function obtained from recent animal studies and with certain minority interpretations of callosal lesions in man as reviewed by Sweet[11] and amplified recently by Geschwind.[12] They appear to favor the existence of a genuine callosal or cerebral deconnection syndrome in human adult subjects who have been free of childhood cerebral complications, and have the normal lateralization of language.

With regard to the discrepancy between the foregoing and the apparent absence of similar disconnection impairments in the majority of callosum-sectioned patients previously described, the following are of interest: Visual testing without tachistoscopic control in the present patient failed to demonstrate satisfactorily his left hemiagnosia. His depth perception and stereoscopic vision are preserved. Blindfold learning of part of a stylus maze of the same type used in the earlier studies[8] transferred at a high level in this patient also from either hand to the other. Further, the first author had earlier applied a number of the same visual and tactile tests to a nine-year-old boy of above-average intelligence with reported congenital agenesis of the corpus callosum complicated by postnatal hydrocephalus. This boy performed close to the level of normal control children with almost no indication of the disconnection effects observed in the adult surgical patient. Bilateralization of cortical speech centers and other compensatory developmental effects are presumed to be present in the boy with agenesis. On the other hand, the normal right-handedness of the surgical patient and correlated lateralization of speech, the development of which took a normal course to well beyond 30 years of age is

considered important to the observed impairments. By contrast, many of the earlier cases studied had childhood neurological complications. Finally, it is entirely possible that a significant range of variability is normal in the development of callosal functions in different individuals, and that a corresponding spectrum is therefore to be expected in the syndrome of the corpus callosum. Even so, there remain some puzzling inconsistencies not satisfactorily resolved as yet. Testing is still in progress and more thorough detailed reports are contemplated.

The authors wish to express their regard and thanks to the patient and his wife for the invaluable cooperation throughout.

* Aided by the F. P. Hixon Fund of the California Institute of Technology and by grants to the Institute, No. M3372 and No. 2G86, from the U.S. Public Health Service.

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

‡ Loma Linda University School of Medicine, Department of Neurosurgery, Los Angeles, California.

[1] Sperry, R. W., *Fed. Proc.*, **20**, 609 (1961).

[2] Sperry, R. W., *Science*, **133**, 1749 (1961).

[3] Akelaitis, A. J., *Arch. Neurol. Psychiat.*, **45**, 788 (1941).

[4] Akelaitis, A. J., *J. Neuropath. Exp. Neurol.*, **2**, 226 (1943).

[5] Akelaitis, A. J., *J. Neurosurg.*, **1**, 94 (1944).

[6] Bremer, F., J. Brihaye, and G. Andre-Balisaux, *Schweiz. Arch. Neurol. Psychiat.*, **78**, 31–87 (1956).

[7] Bridgman, C. S., and K. U. Smith, *J. Comp. Neurol.*, **83**, 57–68 (1945).

[8] Smith, K. U., *Science*, **114**, 117 (1951).

[9] Smith, K. U., and A. J. Akelaitis, *Arch. Neurol. Psychiat.*, **47**, 519–543 (1942).

[10] Bogen, J. E., and P. J. Vogel, *Bull. Los Angeles Neurol. Soc.* (in press).

[11] Sweet, W. H., *Arch. Neurol. Psychiat.*, **45**, 86–104 (1941).

[12] Geschwind, N., *New Engl. J. Med.* (in press).

---

*ON THE MECHANISM OF TISSUE RECONSTRUCTION BY DISSOCIATED CELLS, III. FREE ENERGY RELATIONS AND THE REORGANIZATION OF FUSED, HETERONOMIC TISSUE FRAGMENTS**

BY MALCOLM S. STEINBERG†

DEPARTMENT OF BIOLOGY, THE JOHNS HOPKINS UNIVERSITY

Communicated by Dietrich Bodenstein, August 15, 1962

In the previous papers of this series, we have reported observations on the mutual segregation of mixed populations of chick embryonic cells within aggregates *in vitro*. It was found that the establishment of internal and external tissues within such aggregates proceeds in the absence of directed centripetal or centrifugal migration of the component cells.[1] When cells of the potential internal component are sparse, they remain distributed in all nonsurface locations within the aggregates. When such cells are numerous, those which occupy surface sites rapidly withdraw, while random collisions potentiate a process of aggregation of the cells of this kind within each mixed aggregate. Clusters of cells of the internally segregating type are produced: these fuse with one another; and by this process, one or more co-