Brown, Boston, 1972), pp. 1–41.
73. See P. J. Cook, in *Alcohol and Public Policy: Beyond the Shadow of Prohibition*, M. H. Moore and D. R. Gerstein, Eds. (National Academy Press, Washington, DC, 1981), pp. 255–285; D. Coate and M. Grossman, *J. Law Econ.* **31**, 145 (1988); also see K. E. Warner, in *The Cigarette Excise Tax* (Harvard Univ. Institute for the Study of Smoking Behavior and Policy, Cambridge, MA, 1985), pp. 88–105.
74. J. B. Tye, K. E. Warner, S. A. Glantz, *J. Public Health Policy* **8**, 492 (1987).
75. O. Olsson and P.-O. H. Wikstrom, *Contemp. Drug Probl.* **11**, 325 (fall 1982); M. Terris, *Am. J. Public Health* **57**, 2085 (1967).
76. M. D. Laurence, J. R. Snortum, F. E. Zimring, Eds., *Social Control of the Drinking Driver* (Univ. of Chicago Press, Chicago, IL, 1988).
77. J. M. Polich, P. L. Ellickson, P. Reuter, J. P. Kahan, *Strategies for Controlling Adolescent Drug Use* (RAND, Santa Monica, CA, 1984), pp. 145–152.
78. R. B. Fosdick and A. L. Scott, *Toward Liquor Control* (Harper, New York, 1933).

Organization of the Human Brain

MICHAEL S. GAZZANIGA

Examination of structure-function correlates in the human brain reveals that there is a high degree of functional specificity in the information transmitted over neural systems. It also appears that the human brain has a modular organization consisting of identifiable component processes that participate in the generation of a cognitive state. The effects of isolating entire modular systems or of disconnecting the component parts can be observed. The features of a left hemisphere specialized capacity to interpret the actions of modules are discussed in terms of human consciousness.

THE EXAMINATION OF NEUROLOGIC PATIENTS WITH THE use of experimental methods borrowed from psychology, neuroscience, and medicine yields insights into the cerebral organization of human cognition. An emerging view is that the brain is structurally and functionally organized into discrete units or "modules" and that these components interact to produce mental activities. The idea of modularity is used in several different contexts in the mind sciences. In this article I review the work from my laboratory on patients who have undergone partial or complete brain bisection and address the concept of modularity from three different perspectives.

First, structure-function correlations in the central nervous systems of animals have greatly advanced the understanding of cerebral organization in recent years and continue to represent one of the ways to think about modularity. The clearest instances are in the analysis of sensory systems and, in particular, vision (*1*). Over the past two decades, for example, several anatomically distinct cortical areas have been discovered that are preferentially but not inclusively or exclusively involved in the processing of various dimensions of visual information such as color, motion, and depth perception. Greater specificity in structure-function correlations has also been seen in the monkey for higher order processes such as memory and problem-solving capacity (*2*). Thus, research on animals has led to the belief that there are anatomic modules involved in information processing of all kinds and that they work in parallel and are distributed throughout the brain. Evidence for structure-function correlates in humans is presented.

Second, cognitive science has provided useful and diverse models of mental activity that are based on modular interactions. Particular mental capacities, such as the ability to form visual images, the ability to attend and to remember, the capacity for language, and a host of other cognitive skills, have been analyzed in terms of the "components" or modules that interact to produce what seems to be a unitary skill (*3*). As these models have developed, there have been continuing attempts to test their biologic validity by examining patients with brain damage, or with brain areas disconnected from one another, in order to identify the specific structures involved in particular aspects of a mental activity. Models of human cognition (as opposed to animal cognition) allow for far more extensive examination of modular concepts because more complex mental activities can be studied.

Finally, the idea of modularity is considered at a more integrative level in which mechanisms of consciousness such as human belief formation are investigated (*4*). Here the term modularity refers to the collective action of several subprocesses that produce either overt or covert actions and behaviors. Studies on split-brain patients have revealed the presence of a system in the left hemisphere that interprets these actions, moods, and thought processes that are generated by groups of modules that are acting outside the realm of our conscious awareness. The left-brain "interpreter" constructs theories about these actions and feelings and tries to bring order and unity to our conscious lives. It is a special system that works independently from language processes and appears to be unique to the human brain and related to the singular capacity of the brain to make causal inferences.

Neurologic Correlates of Function

By combining in vivo anatomic data obtained by magnetic resonance (MR) imaging with neuropsychological data, investigators are able to determine some of the effects of brain lesions on human behavior and to evaluate the specificity of the correlations between structure and function. My colleagues and I have seen precise structure-function correlates when the corpus callosum (the structure connecting the two halves of the brain) is surgically cut in an effort to control epilepsy.

In a patient whose corpus callosum is completely transected, there is little or no perceptual or cognitive interaction between the hemispheres (Fig. 1A). Also, contrary to findings in primates and

The author is Andrew W. Thomson, Jr., Professor of Psychiatry, Program in Cognitive Neuroscience, Dartmouth Medical School, Hanover, NH 03756.

cats (*5*), there is no functional overlap at the visual midline after callosal section in humans (*6*). In a study of midline overlap, a double Purkinje image eye tracker was used that permitted the accurate presentation of visual information irrespective of subject's eye movements. This allowed stimuli to be presented to each hemisphere with a positional accuracy of 1 min of arc. Stimuli as close as 15 min of arc were presented to the left or right of the point of fixation. Under these conditions, visual information could be easily used by the hemisphere receiving the stimulus but was not available for the opposite hemisphere. If one assumes that these psychophysical data are a result of anatomical structure, these results emphasize the differences between the brain structures of animals and humans. We have also noted other structure-function differences for the anterior commissure and superior colliculus (7).

In a patient in which a part of the splenium (posterior area of the callosum) was inadvertently spared, there was normal transfer of visual information between the two cerebral hemispheres. In this case, pattern, color, and linguistic information anywhere in either visual field could be matched with information presented to the other half of the brain (Fig. 1B). However, this patient showed no transfer of stereognostic information and also showed a left ear suppression to dichotically presented auditory stimuli. These observations are consistent with other human and animal data (*4*) that show that the major subdivisions of the corpus callosum are organized into functional zones, with the posterior regions more concerned with visual information and the more anterior regions transferring auditory and tactile information.

There are, however, even more compelling examples of specificity of function in discrete callosal regions. The first example reveals the specificity in the domain of elementary cortical-cortical sensory-motor integration. Only the posterior half of the callosum was sectioned in patient E.B. (Fig. 1c). Although the designation "posterior half" is arbitrary, as the surgical section is only an estimate and the extent of the section varies from case to case, the general topology of the callosum would predict that information related to mechanisms of motor control would be affected by the transection.

This issue was examined by using a finger localization task devised for the first split-brain patients (*8*). In brief, a phalanx on one finger is stimulated out of view of the subject and the patient is required to indicate the point of stimulation with the thumb of the same hand. Both normal individuals and partial and complete split-brain patients can easily carry out this task for each hand as long as the stimulus and response are restricted to the same hand. In the second part of the task, after a phalanx is stimulated on one finger, the patient must find the corresponding point on the other hand. In this case a striking difference is seen for the fully split-brain patient. Although a normal individual finds this task easy, patients with a fully sectioned callosum can only perform this task at near chance proficiency.

The ability of E.B. to cross-integrate the needed information was impaired in only one direction. She had no problem integrating the information from right to left, but she failed to integrate information between the hands in the other direction. It would appear that her surgical section included fibers transmitting motor information in one direction but spared those transmitting it in the opposite direction. This condition persists years after the surgery (7).

The second example suggests that even a higher degree of specificity can be observed in these partially disconnected brains. In patient V.P. (Fig. 1D), manipulation of the cognitive content of sensory information critically influenced whether or not spared fibers were activated (*9*). V.P. has been extensively studied and MR imaging revealed spared fibers in both the region of the splenium (posterior) and rostrum (anterior) portion of the callosum. On most tests of perceptual and cognitive function, she showed little or no evidence of interaction between the hemispheres. Even though she has some spared fibers, informational interactions were not detected.

In the course of carrying out a series of electrophysiological studies on V.P., one highly specific stimulus condition that allowed information to pass between her hemispheres was observed. Printed words were presented, one to each half-field, and V.P. was asked to judge whether they rhymed. The word pairs varied along two dimensions. They either looked and sounded alike, looked alike but did not sound alike, sounded alike but did not look alike, or neither looked nor sounded alike. A fully split-brain patient performed at chance in all conditions. However, V.P. performed at chance in all conditions except for the case when the words both looked and sounded alike.

These data suggest there was something about the redundancy of the graphemic and phonemic elements of the stimulus that activated the remaining callosal fibers. It is not possible to say for sure if both remnant fiber groups participated in the communication. However, it is known that the posterior regions serve visual functions and the anterior regions interconnect frontal areas that might be involved in language processes.

The specificity of function indicated by these studies raises the question of how much genetic control there is of the development of a large brain structure such as the callosum. The callosum is far more similar in morphology and area in monozygotic twins than it is in pairs of unrelated controls (*10*) (Fig. 2). Although the results strongly suggest there is a major genetic component to the formation of this structure, they also reveal there are major epigenetic influences as well because the callosa are not completely identical in monozygotic twins. In studies on the cat, such epigenetic factors influence the final formation of the callosum (*11*). Nonetheless, given the known anatomy of the callosum, these data suggest that a callosum of a particular shape and area would be more heavily involved in the projections to one cortical area than would a callosum of another shape and area.

An appreciation of the specificity of interhemispheric connections encourages one to consider a variety of neuropsychological data. Finding specific cognitive loss in a patient with intrahemispheric

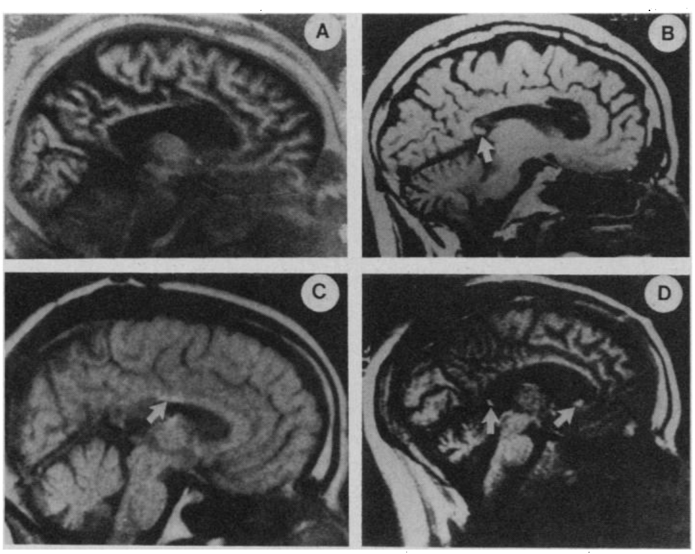

Fig. 1. MR scans of four patients who have undergone callosal section. MR images of four normal intact callosa are shown in Fig. 2. (**A**) Complete transection; (**B**) incomplete transection, splenium (arrow) intact; (**C**) incomplete transection, anterior half (arrow) intact; (**D**) incomplete transection, remnants in splenium and rostrum (arrows). The remaining fibers only transmit specific information from one half of the brain to the other.

lesions requires careful interview and study. After left cerebral stroke, for example, patients can, on superficial examination, appear normal with respect to language function. Yet extended examination of such patients can reveal striking abnormalities that resemble the disconnection effects seen after commissurotomy. One patient, for example, was unable to name the color of fruits that were red. Thus, in response to the question, "What is the color of an apple?" there was a chance performance. Yet, the same patient was easily able to name the color of a banana. Additionally, the same patient was easily able to name the color of fire engines and school houses. It is conceivable that her incapacity to identify the color of red fruits was due to crucial fibers being interrupted within her left hemisphere that connected together the appropriate information sources. Revealing this sort of dissociation is only possible by carefully exploring each patient's psychological condition. Related observations have been made by others where specific categories have been lost after brain damage (*12*). Examination of a patient with a reading disorder revealed the presence of a functional intrahemispheric neural disconnection (*13*). Taken together, the partial disconnection studies argue for the view that specific neuronal systems are selective and specific in the types of information they process.

Modular Components of Cognitive Processes

Disconnecting the cerebral hemispheres has allowed examination of the modular concept as it applies to the study of cognitive processes in two different ways. First, examples are given of the adverse effects of disconnecting processing subunits from one another; that is, disconnected modules cannot interact to produce a cognitive whole. Second, disconnection studies on complex processes such as language and facial recognition provide evidence for the existence of specific whole modular systems and reveal the consequences of their isolation from other cognitive systems.

Disconnecting cooperating modular subprocesses. Most studies on patients in whom the callosum has been sectioned have been carried out with the assumption that each half of the brain is a functioning, independent system that operates no differently when separated than when connected (*14*). New studies are beginning to challenge this original view and suggest a more intricate pattern of cerebral specialization (*15*). The new view is that such classical cognitive activities like those that are assessed by the Block Design subtest of the Wechsler Adult Intelligence Scale are carried out through the interaction of several subprocesses that can be distributed either within or between the cerebral hemispheres.

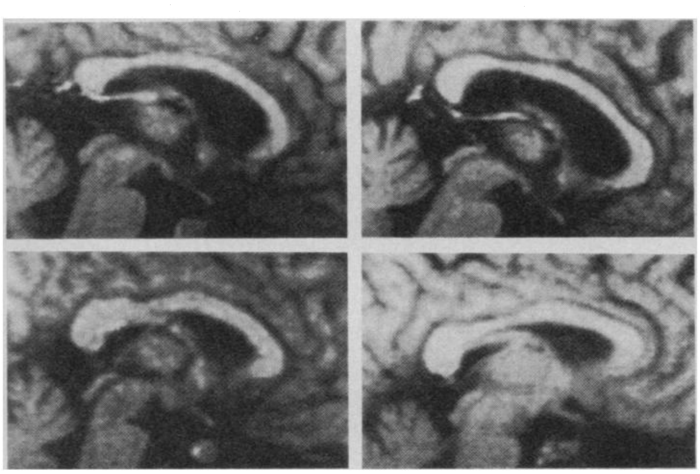

Fig. 2. MR scans of the corpus collosa of monozygotic twins. (Upper) One pair of twins; (bottom) another pair of twins. The great similarity of the twin pairs is seen by visual inspection (*10*).

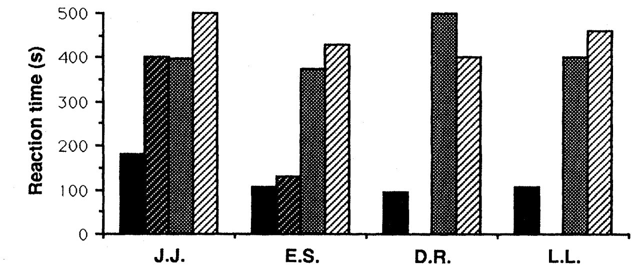

Fig. 3. Comparison of patients in the Block Design test. When the preoperative performance of J.S. and E.S. was compared with their interoperative performance, differences were seen. The surgical section seemed to include fibers that were important for the proper execution of this task in J.J. but not E.S. However, on completion of full surgery, both patients showed impairments when either hand was tested. D.R. and L.L. were also affected after their callosal disconnection. Solid bars indicate preoperative performance; dark hatched bars, interoperative; shaded bars, postoperative, right hand; and light hatched bars, postoperative, left hand.

The first reports on split-brain patients suggested that there were clear right-left dichotomies (*16*). However, in some more recent cases, right hemisphere performance after surgery was poor to nonexistent (*15*). This development raised the question of whether such patients possessed specialized right hemisphere skills at all. Alternatively, it was possible to view the specialized skills as simply "locked in" after disconnection from the dominant left half of the brain, which has verbal ability. That is, if such cerebral skills as performance on the Block Design test were dependent on a number of subprocesses, perhaps the surgery prevented key interactions. For example, before split-brain surgery, E.B. was tested on a number of tests including a nonsense wire figure test that is also believed to depend on right hemisphere specialized systems (*15*). In this test, an irregularly shaped wire figure is palpated out of view and must be subsequently selected from a group of four other wire figures. E.B. was able to perform the task with either hand. Her intact callosum, it would appear, assisted in distributing the information arriving in her left brain from the right hand over to the right hemisphere for specialized processing.

After the posterior half of the callosum was cut, E.B. was unable to name objects placed in the left hand in typical split-brain fashion. The fibers crucial for the interhemispheric transfer of stereognostic information had been severed, and as a result, the left hand–right hemisphere did not know what the right hand–left hemisphere knew. More importantly, however, E.B. could no longer perform the wire figure task with either hand.

Because E.B. could perform the task before surgery, the right hemisphere has the capacity to contribute to solving this kind of task when it is connected to the left. This observation suggests that the left hemisphere normally contributes certain functions to the right brain and vice versa. What was thought to be the product of one integrated system with the capacity to carry out nonverbal tasks is actually the product of the interaction of at least two systems with discrete neural localization.

The same general finding was seen in the scores before and after surgery on the Block Design test for E.B. and four other patients, D.R., L.L., E.S., and J.J. (Fig. 3). This test is generally considered to be a right hemisphere task. Before the callosal surgery, performance on the Block Design test was fast and accurate with the right hand of these four patients. After surgery, neither the left nor right hand of any patient could perform the task with ease. The time to solve the simplest patterns doubled, and completion of the more difficult patterns was usually not possible. Again, these data would suggest that before callosal section, both hemispheres participated in the solving of the block design problem. Because the postoperative reaction times for the left hemisphere were also longer than the preoperative times, the left hemisphere must have benefited from processes located in the right half of the brain.

There are dissociable factors active in what appear to be unified mental activities. In the first patients tested (*16*), the right hemisphere seemed to possess all the subprocesses necessary to perform these visual-spatial tasks. When the early results are considered in light of the present results, it becomes clear that there is wide individual variation in what aspects of a neural system become lateralized in a particular brain. The developmental factors that govern this variation are not known. It also remains to be determined whether the variation seen in the pattern of cerebral specialization correlates with the vast individual differences seen in normal mental functions.

Disconnecting whole modules. When the brain is damaged or surgically disconnected, it is possible to observe other startling dissociations in cognitive function. When such dissociations are revealed, they suggest that the neural architecture honors these functional distinctions and that different brain areas are involved in different aspects of a cognitive ability. Some general aspects of language organization manifested by those rare cases in which the right hemisphere is somewhat language competent should be considered. Additionally, the brain mechanisms involved with face perception can be examined.

1) Studies on language. After hemisphere disconnection the isolated right hemisphere in some patients possesses limited language skills (*17*). In the few patients with right hemisphere language, all of them seem to have an extensive lexicon. Thus, for example, if the word apple is presented only to the right hemisphere, the hand controlled by the right hemisphere can easily point to a picture of an apple. Results from various tests administered to these patients indicate that although the right hemisphere can possess an extensive auditory and visual lexicon that is almost equivalent to the left hemisphere's lexicon, it is severely limited in its capacity to use syntactic information in comprehension (*18*). For example, the right hemisphere has difficulty understanding semantically reversible active and passive sentences and recognizing the differences between phrases like "the flying planes" and "flying the planes."

However, these same right hemispheres are quite capable of judging whether a spoken sentence is grammatical. In short, the right hemisphere can judge the grammaticality of an utterance, but it cannot use syntactic information to place constraints on understanding word strings (*19*). It would be argued from this kind of observation that, not only are there dissociable processes involved in language in the right hemisphere, but that only the left hemisphere has the module for using syntax in a comprehension task.

The foregoing observation is consistent with other clinical studies that aim to determine the exact structures within the left hemisphere that are responsible for syntax. Until recently, accurately specifying the exact location and extent of a human cortical lesion that correlates with a functional disorder has been difficult. By using a new method of unfolding the cortex, the size and spatial relationships of specific cortical areas can be determined (*20*). When the cortex is "flat mapped" in two dimensions, there is what might be called a "language zone" that is contiguous (Fig. 4). This observation contrasts with the traditional views (*21*) of how separate the language centers are from one another and allows for the determination of better structure-function correlates.

2) Studies on face perception. Clinical and split-brain studies suggest that the right hemisphere is specialized for facial recognition. Patients with focal lesions in the right as opposed to the left hemisphere show impairments in recognizing unfamiliar faces (*22*). In split-brain patients, a right hemisphere superiority can also be elicited under special circumstances. Interpretations of the significance of these studies have varied. Some investigators have suggested that the differences reflect differences in cognitive style, that is, processing strategies between the two hemispheres (*23*). Others have suggested that the apparent asymmetry is related to hemispheric differences in processing high- versus low-frequency spatial information (*24*).

My colleagues and I have shown that right hemisphere superiority in split-brain patients can be eliminated when familiar faces are used (*25*). These results suggested that if the stimulus was nameable, there was no apparent superiority. We proposed that the right hemisphere superiority for faces was due to the left hemisphere's tendency to engage in additional processing in the effort to distinguish (name) similar stimuli. Other studies have also shown that there is no consistent hemispheric difference in processing high and low spatial frequencies (*26*).

However, there has been a demonstration that split-brain monkeys are better able to distinguish monkey faces with the right

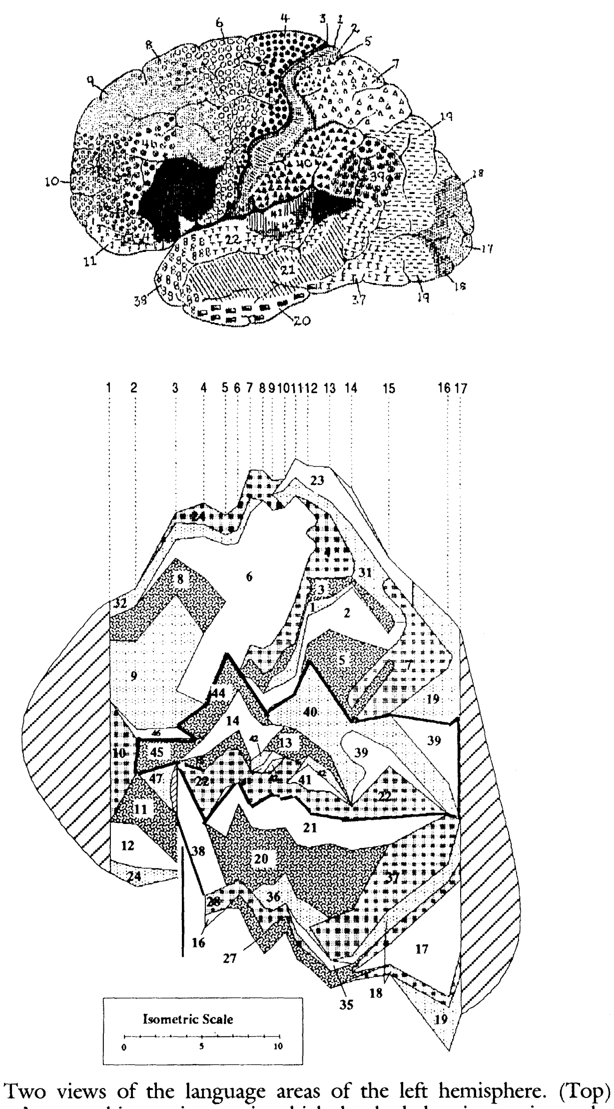

Fig. 4. Two views of the language areas of the left hemisphere. (Top) Brodmann's cytoarchitectonic map, in which the shaded regions estimate the classical speech (Broca's) area anteriorly and the receptive language (Wernicke's) area posteriorly on the visible left lateral surface. (Bottom) A cytoarchitectonic brainprint of the unfolded left hemisphere labeled in accordance with Brodmann's designations by Krieg (*21*). Those Brodmann's areas (13, 14, 15, 22, 41, 42, 39, 40, 44, 45) believed to subserve speech and auditory comprehension on clinical grounds are outlined to illustrate their spatial contiguity within a "language zone" (*21*). In the top illustration these areas appear noncontiguous and are separated by the pre- and post-central gyrus. With the brainprint, they are seen as contiguous.

hemisphere (*27*). This apparent specialization is complementary to a reported left hemisphere specialization for auditory processing in the monkey (*28*). Taken together, the evidence suggests that there are primitive mechanisms established early in primate evolution that are specialized for the important functions of face perception and language processing. Because of this finding and a variety of other experimental studies on the capacity of facial stimuli to evoke specific physiological responses in animals, the issue of facial recognition mechanisms in the disconnected right and left hemisphere of J.W. was reexamined.

Tests examining recognition capacity in humans are easily confounded by intervening and ancillary cognitive and perceptual strategies that could mask underlying specialized systems. Therefore, each hemisphere was required to judge if a series of faces and objects were upside down or right side up. This approach was taken in part because of the apparent importance of viewing faces right side up (*29*). The faces used for this study were taken from the Benton Facial Recognition test. The subject was run on four 50-trial blocks on two separate occasions for a total of 400 trials. On each test day, the four blocks were counterbalanced for response hand. Each block of trials had eight stimulus conditions varying on field of presentation, type of stimuli (face versus non-face), and orientation (upside down versus right side up).

The results of J.W. were clear. For unfamiliar faces, the left hemisphere was significantly inferior to the right in judging whether an unfamiliar face was right side up or upside down [left visual field 0.91 versus right visual field 0.73 ($z = 3.2$, binomial $P < 0.01$)]. The left hemisphere was not significantly different from the right in judging the correct orientations of nonfacial stimuli. By asking the left and right hemisphere about the orientation of a face, a profound difference was revealed. It could be argued that through millions of years of selective pressures a neural circuit has evolved for the fast recognition of upright faces and that it is located in the right hemisphere. Disconnecting the module or circuit from the left hemisphere reveals the specialization. However, the left hemisphere with its vastly superior cognitive structure can also process such stimuli through alternative encoding mechanisms.

The Integration of Modular Processes

In the atomization of cognitive and brain processes, there is a tendency to overlook possible mechanisms related to the truly psychological dimension of human life. In particular, although there is increasing evidence for the idea of modular processes, human beings enjoy what appears to be a unified and unitary experience of conscious awareness. Patients who have undergone brain bisection have the same basic experience of unity even though it is demonstrably the case that each disconnected half-brain can have separate and isolated experiences. Given all the evidence for specialization and specialized subsystems, how is their sense of conscious unity developed and maintained?

A number of years ago my colleagues and I began to make observations on how the left, dominant speaking hemisphere dealt with the behaviors we knew we had elicited from the disconnected right hemisphere (*4*). We revealed the existence of what we call the left brain "interpreter" by using a stimultaneous concept test. The patient was shown two pictures, one exclusively to the left hemisphere and one exclusively to the right, and was asked to choose (from an array of pictures placed in full view in front of him) the ones associated with the pictures lateralized to the left and right brain. In one example of this kind of test, a picture of a chicken claw was flashed to the left hemisphere and a picture of a snow scene to the right hemisphere. Of the array of pictures placed in front of the subject, the obviously correct association is a chicken for the chicken claw and a shovel for the snow scene. P.S. responded by choosing the shovel with the left hand and the chicken with the right. When asked why he chose these items, his left hemisphere replied "Oh, that's simple. The chicken claw goes with the chicken, and you need a shovel to clean out the chicken shed." Here, the left brain, observing the response of the left hand, interprets that response into a context consistent with its sphere of knowledge—one that does not include information about the snow scene presented to the left hemifield.

Hundreds of such observations have now been documented in these cases over the years. When these results are compared to the poor performance the right hemisphere displays (as compared to the left hemisphere) in solving simple problems requiring making inferences and seeing causal relationships (*30*), it is concluded that the left brain interpreter evolved in association with the left hemisphere's specialized capacity in the human brain for such cognitive activities.

This same general result that has been observed when the left brain "interpreter" struggles to deal with overt behaviors has also been seen with more covert responses. Mood shifts, for example, can be produced in an experimental situation by manipulating the disconnected right hemisphere. A positive mood shift triggered by the right hemisphere finds the left interpreting its current experience in a positive way. Similarly, when the right triggers a negative mood state, the left interprets a previously neutral situation in negative terms.

These observations have led to insights into the nature of a variety of psychological disturbances that are initially produced by endogenous errors in cerebral metabolism, such as those known to be associated with panic attacks (*31*). Such biologically driven events produced a different felt state, which in turn must be interpreted (*32*). Each individual's interpretation, unique to their own past and present psychological history, is then stored in memory and becomes powerfully determinant in the content of an individual's ongoing consciousness. If the endogenous events mend through medication or natural events, the interpretations given to the brain's altered mood state remain. In extreme cases such as a panic attack, phobias can develop. The view here would be that the phobia is the interpretation of the altered felt state and can remain long after the precipitous panic attack problem has been medically resolved.

In conclusion, when considering the various observations reported here, it is important to keep in mind the evolutionary history of our species. Over the course of this evolution, efficient systems have been selected for handling critical environmental challenges. In this light, it is no wonder there are specialized systems (modules) that are active in carrying out specific and important assignments. What seems to be unique to the human brain, however, is the interpreter that allows the organism to generate hypotheses about the nature of its responses, and, by doing so, not only presents the human species with a mechanism to both form and modify beliefs, but perhaps also frees the human agent from the shackles of environmental stimuli.

REFERENCES AND NOTES

1. D. H. Hubel and T. N. Weisel, *Proc. R. Soc. London Ser. B.* **198**, 1 (1977); S. M. Zeki, *Nature* **274**, 423 (1978); J. Kass, *Annu. Rev. Psychol.* **38**, 129 (1987); M. Livingstone and D. Hubel, *Science* **240**, 740 (1988).
2. M. Mishkin and T. Appenzeller, *Sci. Am.* **256**, 80 (June 1987); P. S. Goldman-Rakic, in *Neurobiology of Neocortex*, P. Rakic and W. Singer, Eds. (Wiley, New York, 1988), pp. 177–202.
3. S. M. Kosslyn, *Science* **240**, 1621 (1988); D. Swinney, E. Zurif, J. Nicol, *J. Cog. Neurosci.* **1**, 25 (1989); M. I. Posner, S. E. Petersen, P. T. Fox, M. E. Raichle, *Science* **240**, 1627 (1988).
4. M. S. Gazzaniga and J. E. Ledoux, *The Integrated Mind* (Plenum, New York, 1978); M. S. Gazzaniga, *The Social Brain* (Basic Books, New York, 1985).
5. J. Stone, *J. Comp. Neurol.* **136**, 585 (1966); ______, J. Leicester, S. M. Sherman,

ibid. **150**, 333 (1973); A. G. Leventhal, S. J. Ault, D. J. Vitek, *Science* **240**, 66 (1988).
6. R. M. Fendrich and M. S. Gazzaniga, *Neuropsychologia* 27, 273 (1989). A detailed description of the eye tracker is in T. N. Cornsweet and H. D. Crane [*J. Opt. Soc. Am.* **63**, 1192 (1973)].
7. J. D. Holtzman, *Vision Res.* **24**, 801 (1984); M. S. Gazzaniga, in *Neurobiology of Neocortex*, P. Rakic and W. Singer, Eds. (Wiley, New York, 1988), pp. 385–406; B. T. Foxman, J. Oppenheim, C. K. Petito, M. S. Gazzaniga, *Neurology* **36**, 1513 (1986).
8. M. S. Gazzaniga, J. E. Bogen, R. W. Sperry, *Neuropsychologia* **1**, 209 (1963).
9. M. S. Gazzaniga, M. Kutas, C. Van Patten, R. Fendrich, *Neurology* **39**, 942 (1989).
10. J. S. Oppenheim, J. E. Skerry, M. J. Tramo, M. S. Gazzaniga, *Ann. Neurol.* **26**, 100 (1989).
11. D. O. Frost and G. M. Innocenti, in *Two Hemispheres–One Brain*, F. Lepore, M. Ptito, H. H. Jasper, Eds. (Liss, New York, 1986), pp. 255–266.
12. E. Warrington, *Br. J. Psychol.* 72, 175 (1981); ——— and T. Shallice, *Brain* **107**, 829 (1984); J. Hart, Jr., R. S. Berndt, A. Caramazza, *Nature* **316**, 439 (1985).
13. M. J. Tramo, P. Reuter-Lorenz, M. S. Gazzaniga, *Ann. Neurol.* **26**, 126 (1989); P. Reuter-Lorenz and J. Brunn, *Cog. Neuropsychol.*, in press.
14. R. W. Sperry, M. S. Gazzaniga, J. E. Bogen, in *Handbook of Clinical Neurology*, P. J. Vinken and G. W. Bruyn, Eds. (North-Holland, Amsterdam, 1969), vol. 4, pp. 273–290; M. S. Gazzaniga and J. E. Ledoux, *The Integrated Mind* (Plenum, New York, 1978).
15. M. S. Gazzaniga, in *Thought Without Language*, L. Weiskrantz, Ed. (Oxford Univ. Press, New York, 1988), pp. 430–450. For the test used, see B. Milner and L. Taylor [*Neuropsychologia* **10**, 1 (1977)].
16. M. S. Gazzaniga, J. E. Bogen, R. W. Sperry, *Proc. Natl. Acad. Sci. U.S.A.* **48**, 1765 (1962); *Brain* **88**, 221 (1965).
17. M. S. Gazzaniga, *Am. Psychol.* **38**, 525 (1983); M. Kutas, S. A. Hillyard, M. S. Gazzaniga, *Brain* **111**, 553 (1988).
18. M. S. Gazzaniga, *The Bisected Brain* (Appelton Century Crofts, New York, 1970); ———, C. S. Smylie, K. M. Baynes, W. Hirst, C. McCleary, *Brain Lang.* **22**, 206 (1984); E. Zaidel, in *Cerebral Hemisphere Asymmetry: Method, Theory and Application*, J. B. Hellige, Ed. (Praeger, New York, 1983), pp. 95–151.
19. K. M. Baynes and M. S. Gazzaniga, in *Language Communication and the Brain*, F. Plum, Ed. (Raven, New York, 1987), pp. 117–126.
20. M. L. Jouandet *et al.*, *J. Cog. Neurosci.* **1**, 88 (1989).
21. K. Brodman, *Vergleichende Lokalisatonlehre der Grosshirnrinde inihren Prinzipien dargestelt auf Grund des Sellenvaues* (J. A. Barth, Leipzig, 1909); W. J. S. Krieg, *Connections of the Cerebral Cortex* (Brain Books, Evanston, IL, 1963).
22. E. K. Warrington and M. James, *Cortex* **3**, 317 (1967); R. Yin, *Neuropsychologia* **8**, 395 (1970).
23. J. Levy, C. B. Trevarthen, R. W. Sperry, *Brain* **95**, 61 (1972).
24. J. Sergent, *Psychol. Bull.* **93**, 481 (1983).
25. M. S. Gazzaniga and C. S. Smylie, *Ann. Neurol.* **13**, 536 (1983).
26. R. Fendrich and M. S. Gazzaniga, *Soc. Neurosci. Abstr.* **14**, 2 (1988); *Neuropsychologia*, in press.
27. C. R. Hamilton and B. A. Vermeire, *Science* **242**, 1691 (1988).
28. H. E. Heffner and R. S. Heffner, *ibid.* **226**, 75 (1984).
29. P. Thompson, *Perception (London)* **9**, 483 (1980).
30. M. S. Gazzaniga and C. S. Smylie, *Brain* **107**, 145 (1984).
31. F. M. Reiman, M. E. Racihle, F. K. Butler, P. Herscovitch, E. Robins, *Nature* **310**, 683 (1984).
32. M. S. Gazzaniga, *Mind Matters* (Houghton Mifflin, Boston, 1988).
33. I thank all of my colleagues who have made this work possible over the past years. Particular thanks for this article go to K. M. Baynes, R. Fendrich, M. L. Jouandet, W. C. Loftus, P. Reuter-Lorenz, A. G. Reeves, D. W. Roberts, C. S. Smylie, and M. J. Tramo. Supported in part by NIH grant 7P01-NS17778 and Javits Award 4 RO1-NS22626 and the James S. McDonnell Foundation.

Research Articles

Enhancement of Bacteriophage T4 Late Transcription by Components of the T4 DNA Replication Apparatus

DANIEL R. HERENDEEN, GEORGE A. KASSAVETIS, JACK BARRY, BRUCE M. ALBERTS, E. PETER GEIDUSCHEK*

The expression of the late genes in bacteriophage T4 development is closely connected to viral DNA replication. Three T4-encoded DNA polymerase accessory proteins are shown to stimulate transcription at T4 late promoters in an adenosine triphosphate (ATP) hydrolysis-requiring process. The properties of the activation resemble those found for enhancers of eukaryotic transcription. However, the nature of the enhancer of T4 late transcription is novel in that it is a structure—a break in the nontranscribed DNA stand—to which the three replication proteins bind, rather than a sequence. Since the three DNA polymerase accessory proteins are carried on the moving replication fork as part of the replisome, we postulate that viral DNA replication forks act, in vivo, as the mobile enhancers of T4 late gene transcription. Whereas *Escherichia coli* RNA polymerase bearing the T4 gene 55 protein can selectively recognize T4 late promoters, it is only capable of responding to the transcription-enhancing activity of the three replication proteins on acquiring an additional T4-specific modification.

THE CONNECTION BETWEEN DNA REPLICATION AND REGULATED transcription in the development of bacteriophage T4 was established more than 25 years ago by the classic physiological-genetic work of Epstein and collaborators, and later supplemented by a direct analysis of transcription (*1*). One of the

D. R. Herendeen, G. A. Kassavetis, and E. P. Geiduschek are in the Department of Biology and Center for Molecular Genetics, University of California, San Diego, La Jolla, CA 92093. J. Barry and B. M. Alberts are in the Department of Biochemistry and Biophysics, University of California, San Francisco, CA 94143.

*To whom correspondence should be addressed.