PSYCHOBIOLOGY AND VICE VERSA

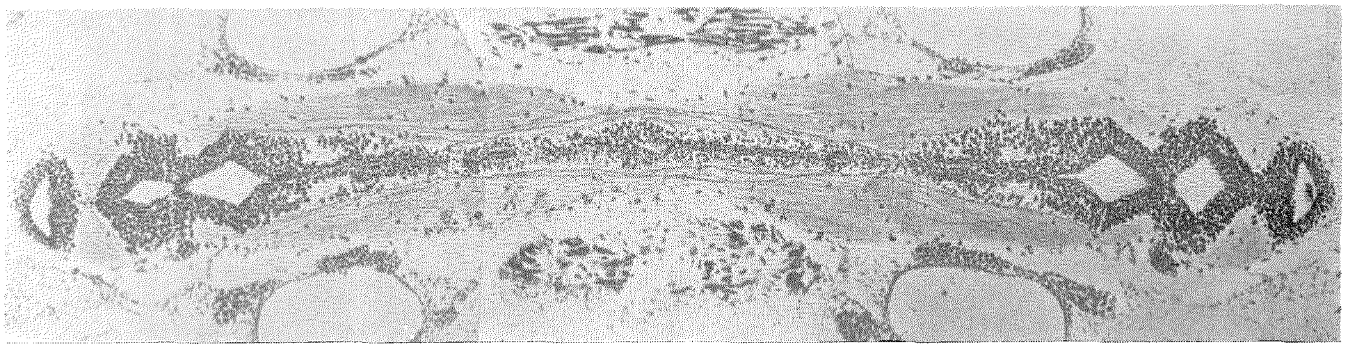
By ROGER W. SPERRY

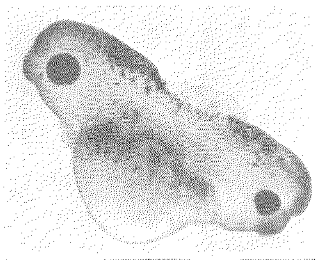
In which the human brain seeks within itself the structural bases, inherited and learned, of psychic function— for the essence of memory and sensation, speech and thought. Can we shape a mirror to the mind?

Psychobiology, like its synonyms biopsychology, psychophysiology, physiological psychology, neuropsychology, neurobiology, behavioral biology, behavioral science, neuroscience, etc., is a term that is rather loosely defined and means different things in different places. Regardless of the name of the game, our research strategy is to keep our biological sights trained on the higher functions of the nervous system—the mental, cerebral, or psychic activities for which brains are particularly noted. This concern for the higher or mental functions separates psychobiology somewhat from the more broadly defined "neuro" sciences. If some of our projects deal with subjects like "the cytochemical basis of morphogenetic gradients regulating selective interneuronal adhesivity," it is not because of any prime interest in the molecular phenomena as such, but because some general principle of cerebral integration is at issue. The direct bearing on questions of higher mental function makes the difference.

In modern biology few problem areas remain where one can point to phenomena that are still genuinely mysterious—phenomena for which science cannot as yet even conceive, in principle, a satisfactory explanation—but the higher functions of the brain clearly qualify in this category. We lack even a reasonable hypothesis for the way in which cerebral tissue generates conscious awareness or any form of mental experience. Mind/brain relations continue to offer a challenging frontier with plenty of room at both top and bottom for new discoveries and some major conceptual breakthroughs.

A general idea of where we stand in the field today may be inferred from a quick sampling of some of the changes that have taken place in psychobiol-





To test the influence of body gradients in nerve growth, frog embryos (left) are joined surgically at the point where the tails would normally develop. (The black spots are the eyes, the bulge is the yolk sac of the joined embryos.) The stained microscopic section of the same embryos (above) shows how the spinal fibers of one embryo (hairlike strands on either side of the spinal cord), that normally grow head-to-tail, cross the junction and then grow tail-to-head in the spinal cord of the other embryo.

ogy in the last several decades and of some of the kinds of problems currently under investigation. Only 30 years ago it was generally believed, largely on the basis of dozens of nerve transplantation studies, that the machinery of the brain was so designed that one could interchange its fiber connections—disarrange its basic wiring diagram—without causing more than a transitory disturbance in function. Having its wires crossed seemed to be no problem for a brain. It was believed that the functional plasticity in the learning process and the very nature of cerebral control could transcend the specifics of brain connections. Neurosurgeons were treating various forms of motor paralysis by cross-connecting shoulder nerves to face nerves, for example, or even arm nerves to leg nerves; while less distant nerve-muscle substitutions were being performed routinely, all on the assumption that somehow orderly function would prevail in the face of the disordered structure.

This concept of a wholesale dynamic plasticity in the organization of brain circuitry was contradicted in some of our early experiments. When more careful experimental controls were instituted, it was found that surgical disarrangements in nerve connections do in fact cause directly corresponding disturbances of sensory and motor function. The disfunction had been missed earlier because the remaining intact portion of the nervous system does everything possible to compensate for the local malfunction of the interchanged parts.

The outcome of the later experiments led shortly to a complete reversal of doctrine. It meant that we no longer had to imagine elusive dynamic properties of cerebral control that were independent of the brain's wiring diagram. Cerebral function can now be seen to be much more closely tied to brain structure and hence much more accessible to scientific investigation.

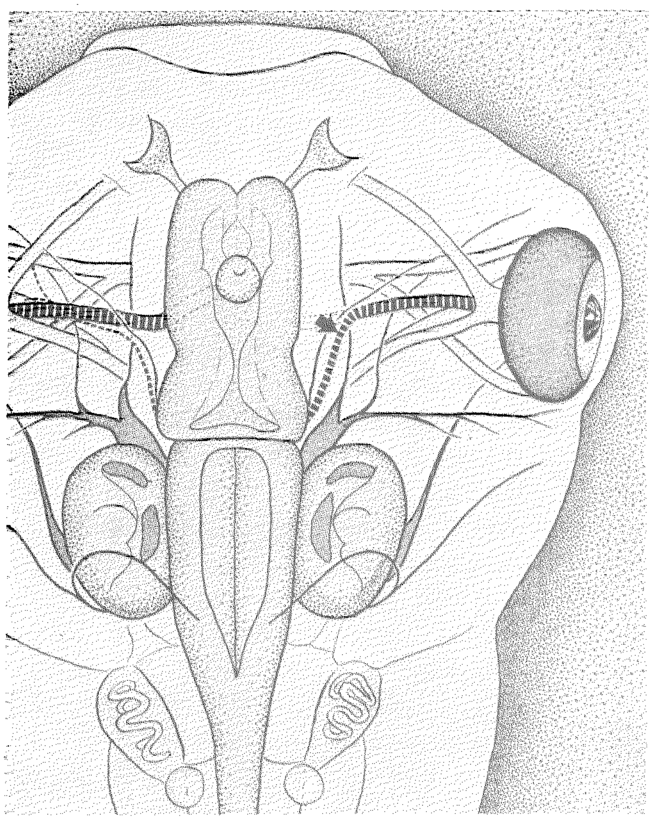
The idea that our behavior might be partly instinctive or inherited was considered quite intolerable by the majority of psychologists 30 years ago. The very word "instinct" could not be used in professional circles in psychology except in a derisive context. Experiments on nerve development seemed to show that the growth and connection of developing nerve fibers are entirely diffuse and nonselective. Thus, no conceivable means could be imagined by which an inherited behavior pattern could be directly grown into a brain. Extreme, and today laughable, efforts were resorted to in order to show that what seemed to be inherited in behavior was actually a result of experience, environment, and a series of conditioned reflexes and training extending back into fetal development.

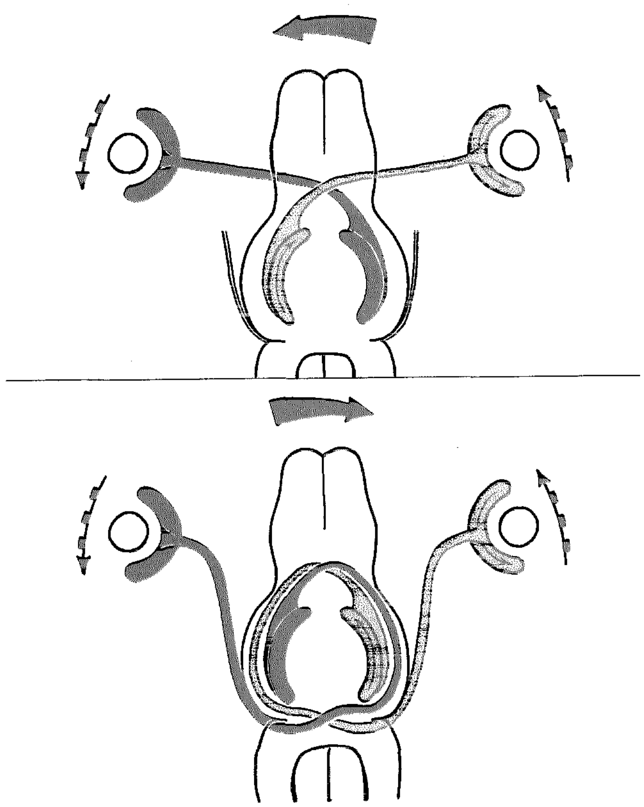
Subsequent experiments have now contradicted the earlier results to show that nerve fibers do indeed grow and connect with the utmost precision within the brain centers, in contrast to what had been seen earlier in the peripheral nervous system and in tissue-culture studies. It is now widely accepted, on the basis of our newer evidence, that each brain cell is specifically tagged with identifying chemical labels bound to the surface of the cell and that an elaborate chemical guidance system operates in development to insure that each of the millions of brain fibers grows along the proper pathway to reach the proper relay centers to connect with just the proper nerve cells to form adaptive behavior patterns. Some of the most highly intricate and precisely organized connection systems of the brain, like the central pathways and connections that subserve vision, have been found to be laid down in the normal predetermined order by the growth process itself—without aid of function.

The balance of the evidence brings us far from the extreme environmentalist bias of 30 years ago to a position close to the general impressions that prevailed before 20th-century science discovered the "conditioned reflex," "behaviorism," and "nonselectivity in nerve growth." Modern biology now routinely accepts the position of ethology that an entire evolutionary tree can be built in terms of inherited behavior traits just as it can on morphological traits. Psychology and the social sciences, with a somewhat heavier investment in learning and environment, have been slower to relinquish the older environmentalist views.

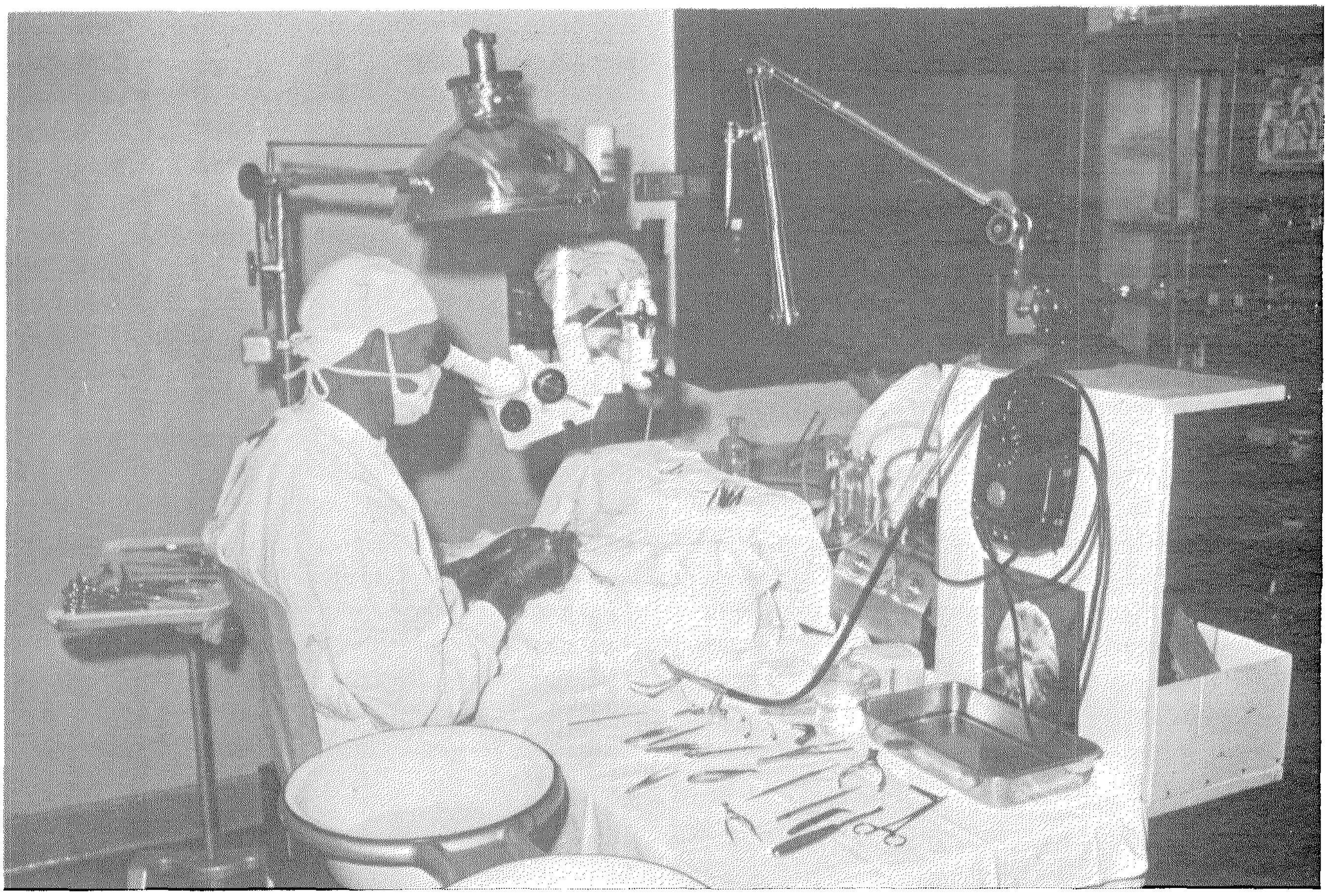
A substantial part of our research in psychobiology is still concerned today with further study of the nature of the developmental mechanisms by which the growing brain gets itself prewired for adaptive function. These studies center around the role of neurospecificity in growth and appear to be headed toward the biochemistry and specificity of macromolecules.

In efforts to account for some of the more challenging of the higher properties of brains, many hypotheses have been proposed regarding the basic nature of the underlying cerebral activity. Some examples are electric field theory to account for Gestalt phenomena in perception; specific nerve energies to account for different qualities in sensation; and reduplicated interference patterns to explain cortical equipotentiality in memory storage. Thus far, however, no single general theory that





Growth properties of the optic nerves are studied in the frog tadpole brain after optic nerves have been cut and deflected into foreign brain pathways (above). Deflected optic fibers methodically grow through roundabout routes to find their appropriate central connection zone in the optic lobe (above). The right and left sides of the brain are not chemically distinct; hence, the deflected nerves often form connections on the wrong side. Visual responses then show right-left reversal (large arrows) to outside movement (small arrows).



Surgical disconnection of the cerebral hemispheres (areas disconnected are shown on the page opposite) and related brain operations are performed on laboratory animals with special surgical procedures that involve use of a high-power stereomicroscope and special instruments, along with standard aseptic precautions.

would much simplify an understanding of the complexities of brain action has survived experimental test. When we attempted to check a proposed role of electric field forces in cortical organization by implantation into the brain of dielectric plates and metallic conductors, the results failed to indicate anything above and beyond the classical type of fiber conduction of nerve impulses. We seem to be forced more and more to think in terms of highly complex, intricate, and precisely organized communication circuits in which neural excitations are generated, rise and fall, and are passed along at high speed from cell to cell within the microscopic fiber networks of the brain.

Persisting holdouts for some kind of unknown controlling forces in the brain that operate independently of discrete fibers and their connections found support in a longstanding observation that the largest and most central cable of fiber connections in the mammalian brain, the *corpus callosum* (once designated as the seat of the soul), could be completely severed in surgery without disturbing mental or physical functions. The *corpus callosum,* containing in man some 200 million fibers, forms a rich system of reciprocal cross-connections between right and left halves of the brain and is the principal channel for communication between the cerebral hemispheres. Even so, people with congenital absence or complete surgical section of the *corpus callosum* were found, most surprisingly, to be quite free of any distinct functional deficits.

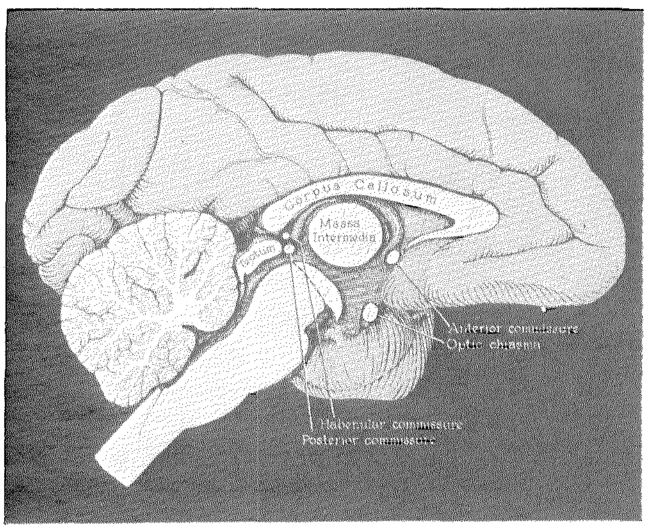
This enigma of the *corpus callosum* has been largely resolved in studies of the past ten years—first with animals and later with human patients—in which we have succeeded in demonstrating that a whole series of distinct functional symptoms are indeed produced by section of the *corpus callosum.*

In brief, we find that, although the surgically separated hemispheres do indeed continue to function at high level for most ordinary behavior, they operate independently to a large degree with respect to the higher cerebral activities. In effect, each hemisphere has a separate mind of its own. Each separated hemisphere, that is, can be shown to have its own private sensations, perceptions, feelings, ideas, memories, and related mental experiences, all of which are out of contact with the corresponding experiences of the other hemisphere. Breakdown in right-left integration, though not apparent in ordinary behavior nor in routine neurological tests, can be demonstrated for a host of sensory-motor performances with tests of appropriate design. Other types of deficits result from the loss of cooperation between the more specialized functions of right and left hemispheres, as in tasks involving language and spatial perception. With the important functional role of this strategic fiber system finally clarified, the close correlation between cerebral function and the underlying fiber pattern seems more firmly established than ever.

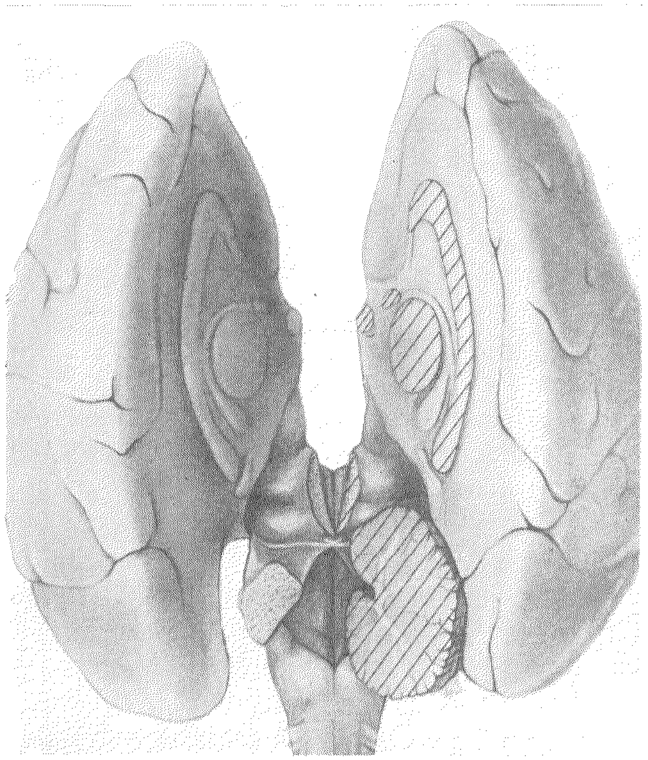
Much of the research of our Caltech laboratory has been centered in recent years around this intriguing twin-brain situation. The two half-brains are mirror images in their anatomy and largely reduplicate each other in activity as well. Each contains most of the main cerebral functions, and each is self-sufficient to a large extent. Accordingly, it becomes feasible, with the hemispheres disconnected, to carry out research with surgical and other analytic procedures in a single hemisphere, leaving the other hemisphere intact for the use of the animal. This approach offers a number of technical advantages and provides as well many new research possibilities. The work is supported by grants from the National Institutes of Health and by the Frank P. Hixon Fund.

In collaboration with Philip J. Vogel of the Neurological Medical Group and Joseph E. Bogen of the Ross-Loos Medical Group in Los Angeles we have been able to study a number of human patients with related neurosurgical operations. These studies lead into complexities involving cerebral dominance and the lateral specialization of function in the human hemispheres.

Recently Ronald Saul of the USC School of Medicine and I did a study on a woman patient in whom the *corpus callosum* was discovered to be totally missing as an anomaly of development. This patient was a 19-year-old college sophomore at the time, with an average scholastic record of B's and C's. Prior to the x-ray diagnosis of her condition she had been considered to be entirely normal. It seemed quite possible that in this person, as in the surgical patients earlier, the symptoms of hemisphere deconnection might have actually been present but had gone undetected. Accordingly, for a year we put her through our entire battery of tests using the same procedures as with the surgical patients. Her



Right and left hemispheres of the brain, largely separate in the natural state, may be completely disconnected by strategic surgical sections through the structures labeled above. The extent of the anatomical separation achieved as seen in the monkey brain is illustrated schematically at the right.



Newly hatched chicks are given electroshock treatment to test for memory consolidation. A mild subconvulsive current applied for only 0.25 seconds will disrupt memory for preceding events up to 30 seconds. After that the memory traces become sufficiently "consolidated" in brain tissue to survive.

performance throughout was quite comparable to that of normal subjects and showed none of the cross-communication deficits that are still pronounced five years after operation in the surgical cases.

The striking difference between the effects of congenital and of surgical separation of the hemispheres is attributed to the special functional plasticity of the developing brain. During that long period from birth to adolescence while the brain is still growing and at the same time learning and remembering, the human brain in particular possesses an enhanced plasticity and a special potency for the shaping of cerebral organization and behavioral patterns that is no longer present after maturation.

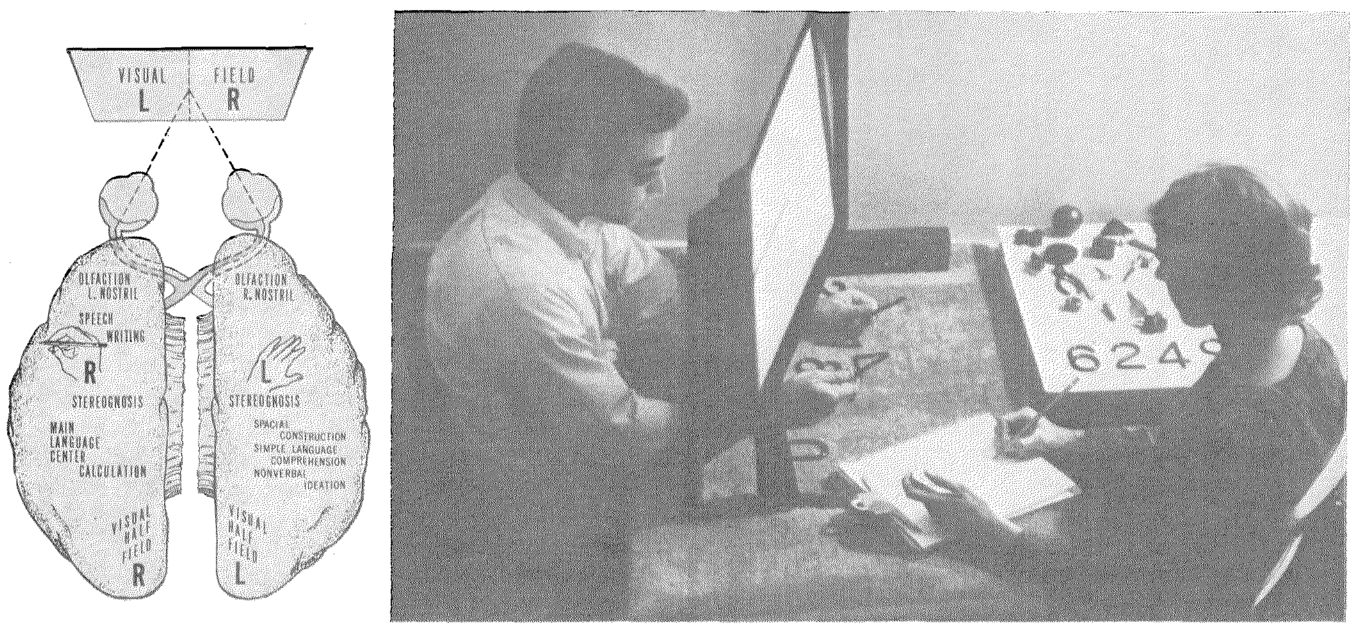
The underlying cellular mechanisms responsible for this special plasticity of the still-growing brain remain unknown. On the one hand they would appear to be related to the processes of learning and memory and on the other to those of growth and neural maturation—the two processes overlapping and interacting in some unknown fashion. It is of critical importance to learn more about these underlying mechanisms and their potentialities and limitations because of the direct bearing on problems concerning the effects of early experience on adult behavior—the plasticity of human nature, Head Start programs, and early enrichment of experience.

The age-old problem of the memory trace still remains unsolved. In recent years there has been a great flurry of studies aimed at the "chemistry of the memory" and the "memory molecule." The answer to the question of the nature of the molecular changes that underlie long-term memory should not be far away. It is important to recognize, however, that any molecular answer promises to leave unexplained many of the phenomena of memory as we think of memory at the behavioral level. It would be like discovering the chemistry of the ink in which a coded message or secret map is inscribed. Many of the more remarkable and intriguing features of memory, such as the orderly filing, the selective retrieval, the information content, etc., seem likely to require an understanding of the broader and more involved complexities of cerebral organization.

Considerable publicity has been directed recently to reports that chemical extracts of trained brains injected into the blood stream, body cavity, or brain ventricles of a naive animal may carry the mnemonic information directly to the naive brain in molecular form where it may serve in place of actual training to guide behavior. Transfer of memory in chemical form has been reported to occur also via cannibalism in flatworm studies. None of these experiments, however, has been confirmed to a point where one can feel any assurance about the phenomenon itself, much less the interpretation.

Clues to the nature of the underlying process by which memory traces are formed in the central nervous system can be obtained by measuring the kinetics for the consolidation of the memory trace. Electroconvulsive shock, brain concussion, or other trauma seem to wipe the brain clean of memories for the immediately preceding experiences, leaving only the more firmly established, better consolidated traces of long-term memory. When electroconvulsive shock is applied at increasingly long intervals after a learning experience, one can determine how long it takes for the particular memory trace to become sufficiently consolidated to resist erasure. This "consolidation time" has recently been measured with new precision by Evelyn Lee-Teng at Caltech. Applying a statistical approach with large numbers of newly hatched chicks she finds the critical time for the chick brain to be about 30 seconds.

As we look ahead in psychobiology, it is difficult to imagine any quick solution to an understanding of the cerebral events that underlie even the simplest mental experience. An understanding of the

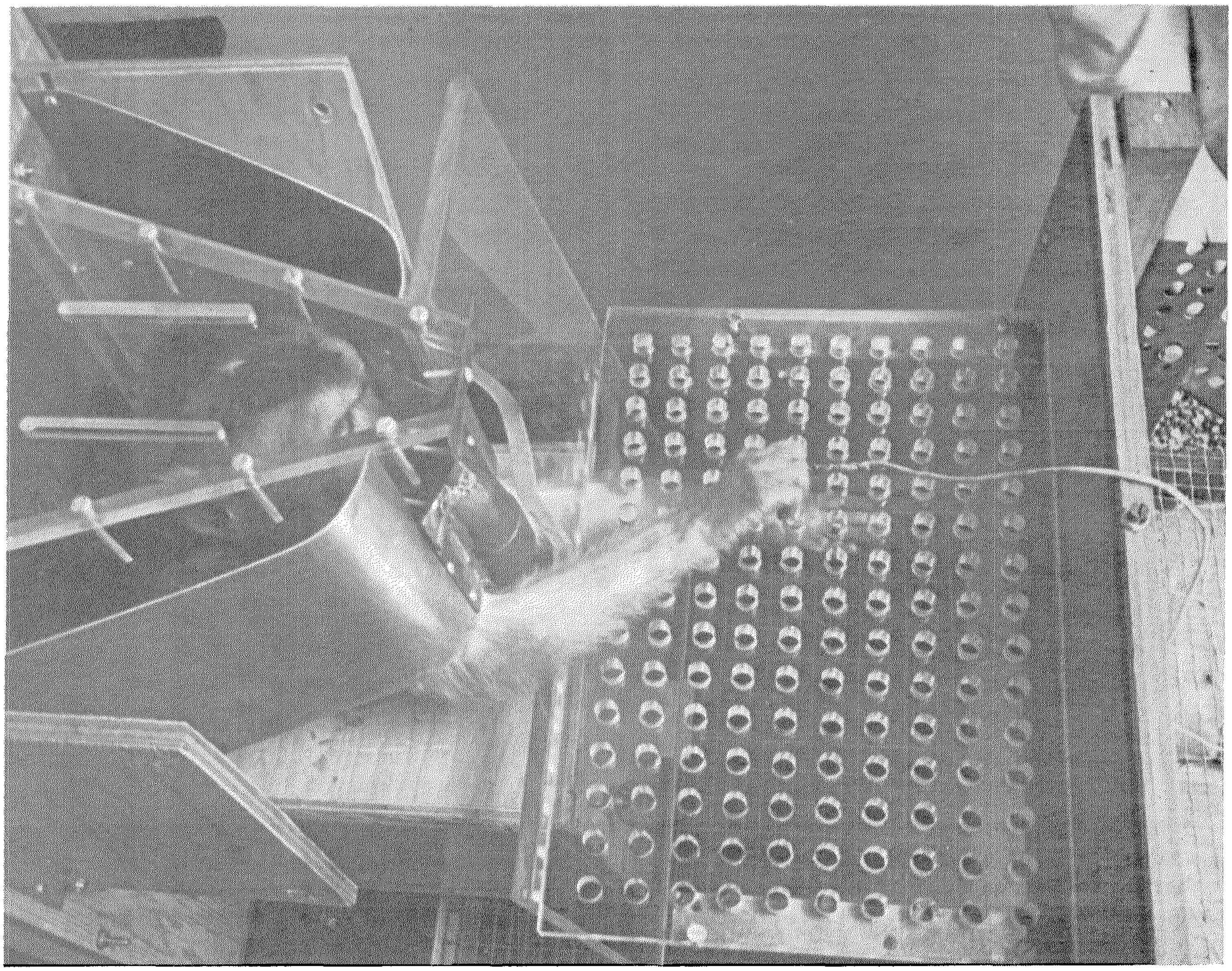


Tests for differential function of right and left hemispheres in human subjects are carried out with strict controls for lateralized sensory input. An upright screen serves for back-projection of visual material and keeps the subject from seeing the test items, his own hands, and the examiner. Diagram at left indicates some of the lateral specialization in cerebral function found in patients whose brain hemispheres have been surgically disconnected (for control of intractable epilepsy). Each hemisphere is simultaneously aware of activities in its own hemisphere but lacks conscious contact with the other hemisphere. Only the left hemisphere can talk or write in most right-handers. Thus the patient can describe what he sees in the right half of his visual field, but not what he sees in the left.

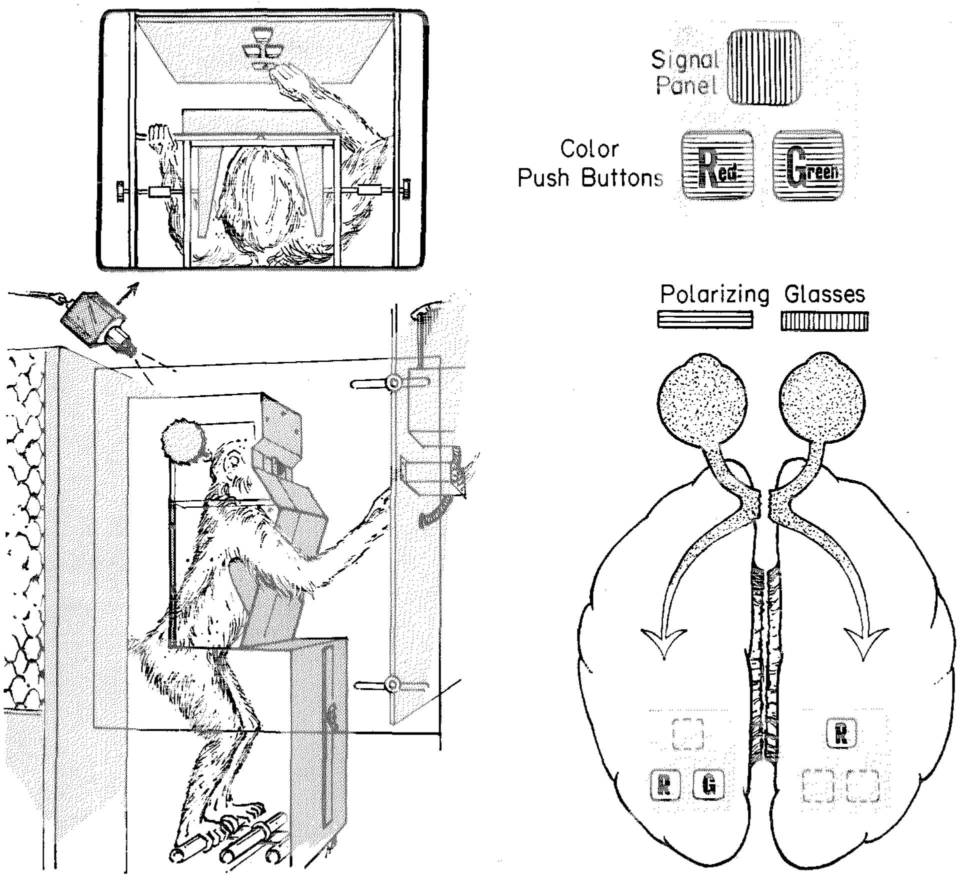
central mechanisms responsible for the subjective perception of color, for example, would seem to require an extensive analysis of highly complex and intricately organized circuitry of microscopic dimensions—attainable, with present methods, only one slow, small step at a time. Even the basic principle by which these circuits produce conscious color sensations remains far out of sight.

Aside from their overwhelming complexity, brains have two properties in particular that make it difficult for many persons to accept behavioral science as a true science: consciousness and free will. What kind of a science can be built around a subjective, will-o-the-wisp-like consciousness that seems to resist even a satisfactory definition? And, equally disturbing, how can one construct scientific laws for the kind of system that, under the most controlled laboratory conditions, reacts to a given invariant stimulus according to its whim of the moment?

The answer of psychology and the behavorial sciences in general has simply been to deny the existence of both consciousness and free will. A purely objective approach is adhered to, with subjective introspective description being strictly excluded. The working premise holds that a complete conceptual model of brain function is possible in purely mechanistic physical and chemical terms without any reference to consciousness. Every choice we make is assumed to have its causes, like



Split-brain monkeys are used to study coordination between right and left hands. This monkey attempts to catch with the lower hand a falling peanut that has been found by touch and poked loose with the upper hand. The two hands are prevented from making any contact. With vision excluded, the location of the target is known only from position-sense in the other hand. The cerebral pathways involved are determined by selective surgery.



In automated experiments to test cerebral processing of color, a monkey presses a red or green push button to match the color flashed on a signal panel. The colors on the panel change at random. The color information received by the monkey, split and projected in the visual pathways partly to one hemisphere and partly to the other by means of polarizing light filters, must be put together centrally for a correct response.

all behavior, in the preceding brain states and surrounding circumstances.

I subscribe to the view that each mental choice is causally determined, but on condition that the phenomena of consciousness are not excluded from the causal sequence. It is my contention that the kind of causality that prevails in brain function must be extended to include mental forces, these being defined as either "emergent" or "entitive" properties of the living, alert brain in action. Like the roundness of a sphere or like the weight, speed, or design of an airplane, these overall "boundary" properties of the brain circuits in action largely control the course and the fate of their inner molecular and other constituents. Similarly these pattern properties of the brain circuitry are subject in principle to objective scientific investigation; it only remains to develop a technology to record them.

Philosophic but not idle, such matters carry important implications for the future place of psychology in scientific institutions. If it proves true that mental phenomena (ideas, sensations, feelings, etc.) are real entities and are potent as controlling factors in the objective chain of command in the brain, it would restore mind and mental phenomena to the domain of experimental science from which they have been largely excluded by the behaviorist movement for over half a century. This change of position would also resolve some of the longstanding disparities between the objective analytic approaches in psychology and the more subjective humanistic and clinical approaches that deal with inner experience and the whole person. Extensive fallout can be seen also with reference to questions concerning human values.

It is apparent that our current thinking on the mind/brain (psycho-biologic) relationship has not advanced beyond a hypothetical answer posed in abstract principle only. The explicit engineering trick by which brain circuits generate conscious properties remains a major guideline problem for the future. The trick may be of such nature that it is impossible to replicate except with living hardware in living brains. On the other hand, it remains possible that conscious awareness is essentially a property of communication networks, in which case consciousness might some day be simulated in the growing technology of artificial intellect. □