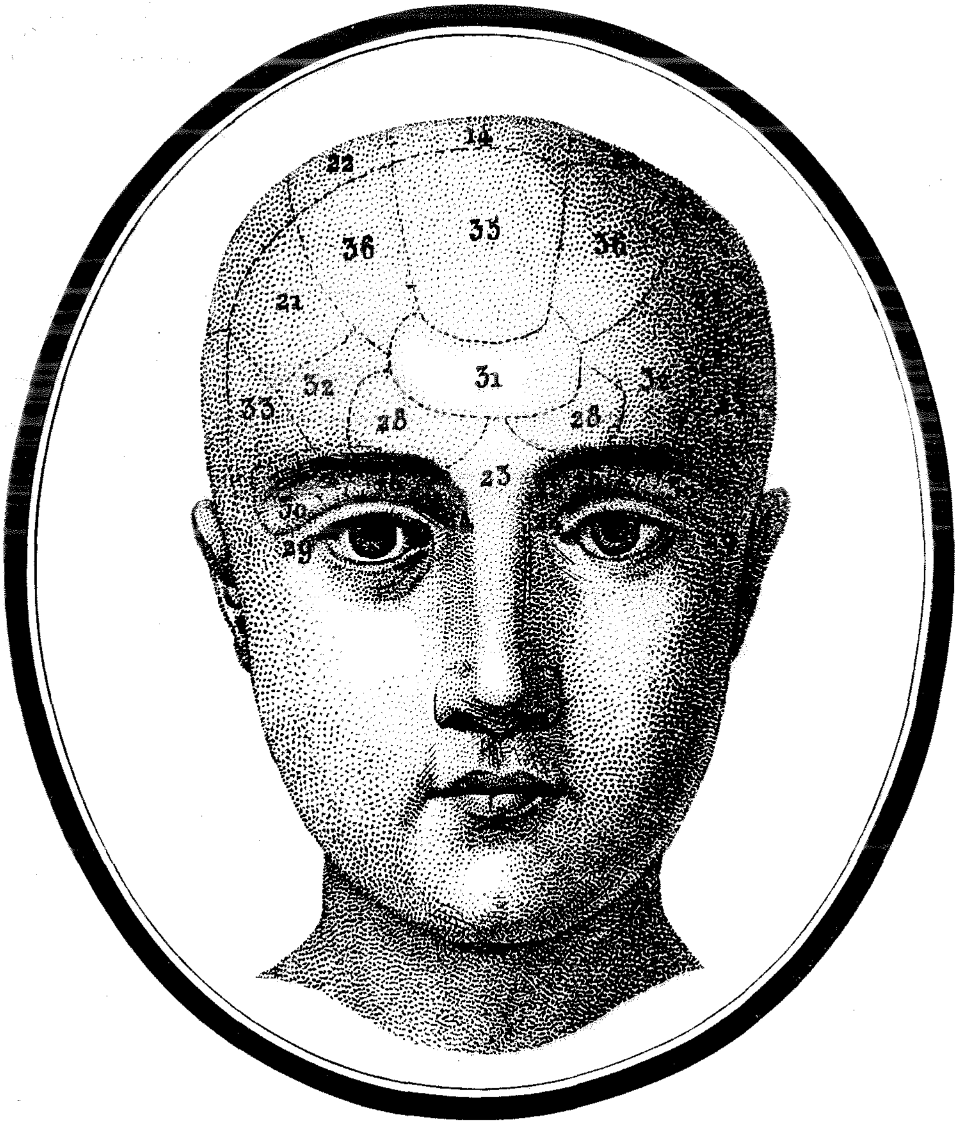


INVESTIGATING THE BRAIN

by Theodore J. Voneida

Consider, if you will, the amount of information to which the brain is exposed at any given moment. As you read this article, for example, the light-sensitive elements in your retina are being bombarded by visual stimuli which are then transformed into electrochemical nerve impulses and carried over highly specific neural pathways to your brain. During their passage and upon their arrival at the final cell station of the visual system — the occipital cortex — they are being processed in such a way that you will be able to recall much of what you read at a later date. The details will fade with time, but even several weeks or months from now you will probably remember something about what you are reading.

Consider also what has been happening to your brain during the past hour. It has received and processed auditory impulses of various sorts, a myriad of odors, great numbers of tactile stimuli, and in all probability some tastes. In addition to these, there are the tremendous number of proprioceptive stimuli which are constantly informing the brain of your postural situation. Information entering the brain over all these sensory systems — just as was the case with vision — is subject to recall at any time. In other words, the brain has the capacity of storing in some manner a great percentage of the information it receives.

This processing and storing of sensory signals is only part of the story, for the brain is also the point of origin for most of the motor information which reaches your muscles. All animals are capable of movement, but among these man alone is capable of

Dr. Voneida gets Vincent, his favorite test subject, ready for a training session in the perceptual integration problem.

the most creative and varied types of motor activity. The ability to play the piano or the violin; to write or speak; the highly individualized facial expressions which result from slight, almost imperceptible contractions of the facial musculature – these are all unique to man, and are based on motor impulses which arise in the highly evolved cortex of the human brain.

The brain is also responsible for your ability to project into the future; you can plan your activity to the finest detail without moving a muscle. You can also reflect on the past, and mentally relive experiences which may have occurred years before.

It is not difficult to understand why so little is known of brain mechanisms when one considers the extreme complexity of this small organ which plays such a critical role in the interaction of each individual with his environment. There are numerous approaches to the study of the brain, and valuable contributions are being made from widely divergent fields of research. Techniques in neurophysiology have evolved to the point where it is possible to record electrical activity from single nerve cells deep in the awake, normally functioning brain. Methods for examining the structure of the central nervous system have been greatly refined, so that it is now possible to examine nerve cells at a molecular level with the electron microscope.

These developments have been accompanied by numerous contributions from disciplines outside the biological sciences, so that we now have a field of study devoted to the mathematical and physical bases of "artificial intelligence." The close working relationship which is developing between the biological, physical, and behavioral sciences in the study of brain mechanisms is exemplified by the Caltech conference of February 1960 on Cerebral Systems and Computer Logic. A few lecture titles from this symposium may serve to illustrate the point: "Mathematical Models of Cerebral Systems;" "Problems of the Visual Physiology and Anatomy of Amphibia;" and "Computing Principles and the Nervous System."

Numerous studies which utilize the biological approach are presently being carried out in our laboratory at Caltech. Two such studies are described here. The first involves primarily those methods which have been developed in the field of behavioral sciences, while the second is concerned more specifically with neuroanatomical techniques.

The two halves of the vertebrate brain are extremely similar, and are connected by numerous neural pathways called commissures. The largest of these, the corpus callosum, has been shown to be responsible for the transmission of highly integrated information from one hemisphere to the other. ("Brain Mechanisms in Behavior" by Roger Sperry – *E&S*, May 1957.)

Some time ago Dr. John Robinson and I became interested in the interaction of the two hemispheres in the performance of a problem involving visual perceptual integration. A training apparatus was used (above) in which cats were taught to push open the brighter of two doors in order to receive a food reward. This comparison of light intensities is a relatively simple task, and a very common one, both for cats and humans. Much of our everyday activity involves a comparison of two or more objects, followed by a choice of the one best suited to our needs at that moment. We have been attempting to investigate the means by which this comparison is made within the central nervous system.

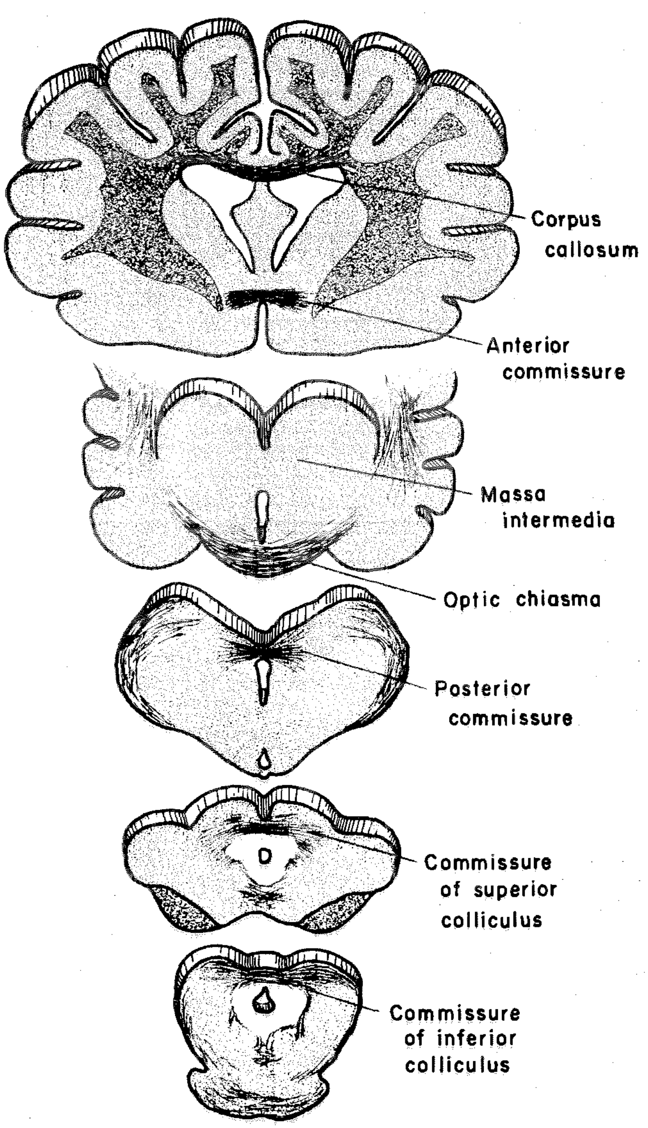
A brief look at the normal anatomy of the cat's visual system shows us that over 50 percent of the nerve fibers from one eye go to the opposite half of the brain; in other words, each hemisphere receives information from both eyes. This means that a normal animal can easily make an *intra*hemispheric comparison between two visual stimuli. What would happen now if an animal were required to make an *inter*hemispheric comparison, first with the commissures intact, then after cutting each of them in a stepwise fashion? Suppose, for example, that the crossed visual fibers were sectioned, and that one of two visual stimuli was presented to the left half of the brain, while the other was presented to the right half. In order to solve the problem, a comparison must still be made between the two, but the comparison must now be made interhemispherically.

The problem of separating the inputs

In the actual experiment, the two visual stimuli were separated by projecting one through a red filter, and the other through a blue filter. The experimental animal wore a mask with a red filter over one eye and a blue filter over the other. The two filters were chosen so that all the light passed by one was completely blocked by the other, and vice-versa. (Color played no part in the training situation – the animals were trained strictly on the basis of a brightness comparison.) Then the optic chiasm, containing the crossed visual fibers, was sectioned. This meant that all visual stimuli from one light source would now go to the right half of the brain, and all from the other would go to the left half. The first commissure to be sectioned was the large corpus callosum, which connects the two cerebral cortices. This resulted in only a very slight, transient drop in performance level.

We continued to surgically separate the two halves of the brain by sectioning each of the remaining commissural connections between the hemispheres. There was no significant loss in the ability to perform this task as long as only cortical commissures were sectioned. As soon as we began to section subcortical connections – specifically, the posterior and tectal commissures – all animals exhibited a severe fluctuation in performance. One day they would perform without making any mistakes, the next day they would perform at a chance level. Even animals with all the commissures sectioned simultaneously were able to perform at high levels of accuracy for short periods of time.

Numerous controls were run, including one animal with all the commissures sectioned, but with the crossed visual fibers intact. This animal showed no fluctuation in performance. When the optic chiasm was finally sectioned, however, the fluctuation appeared.



A diagrammatic series of transverse sections from the front of the brain to the back, showing most of the connections between the two halves of the brain.

The fluctuation in the totally sectioned cases lasted for long periods of time, but eventually – and this is perhaps highly significant – the subjects were once again able to perform consistently at high levels of accuracy. This strongly suggests that areas not normally used for this type of interhemispheric communication are now being called into play, and are indeed capable of functioning very efficiently in the absence of the "proper" cross connections. Experiments are presently being carried out to test these possibilities.

Behavioral studies are of limited use in the overall analysis of brain mechanisms unless we know something as well about the central neural connections. There is a vast anatomical literature pertaining to interhemispheric connections, but surprisingly little is known about the precise connections of the posterior commissure. The general lack of information pertaining to this commissure, plus the specific interest which arose from our behavioral study, provided the

continued on page 22

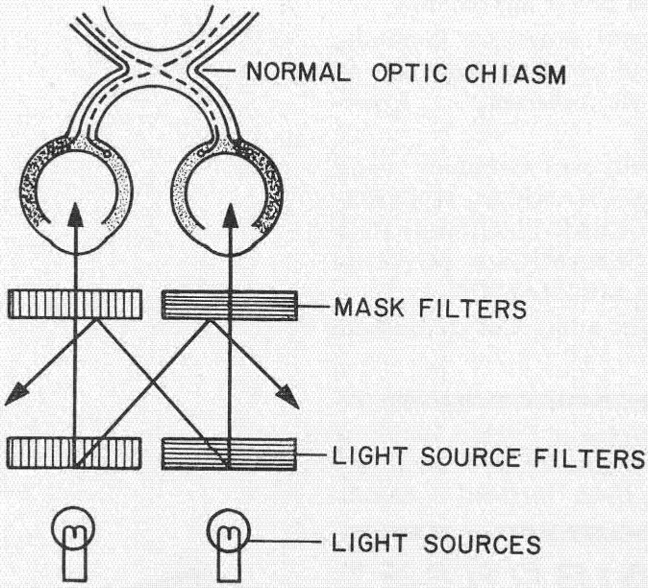
basis for an anatomical investigation of this structure.

Several techniques are available for tracing a highly specific bundle of nerve fibers lying deep in the brain. A great deal can be learned by gross dissection, but this is totally inadequate for describing its structure and location in detail. It becomes necessary to turn to microscopic techniques, all of which have certain procedures in common.

First, the tissue must be sectioned into very thin slices which vary in thickness from five to fifty microns, depending on the technique being used. Next, the tissue must be stained, so that when it is examined under the microscope it will be possible to differentiate the nerve cell bodies from the long fibrous processes called axons which extend out from them. These axons are grouped together into compact bundles called nerve tracts.

The stain which is used depends, of course, on the particular structural elements to be studied. A fiber stain, for example, is the logical choice if one wishes to examine a nerve tract or commissure which is composed of large numbers of tightly packed axons. Indeed, much has been learned about these structures from the study of normal fiber stains. Stains of this type, however, are not adequate to tell us what we need to know about the exact connections which are made by a specific bundle of fibers such as the posterior commissure. It is necessary to do something to that particular group of fibers in order to make it stand out from all the rest.

One approach is based on the fact that damaged nerve fibers will degenerate. Special staining procedures have been developed which make it possible to stain degenerated nerve fibers and nothing else. The remaining problem is that of destroying a specific group of nerve fibers deep in the brain without causing considerable damage to surrounding tissue. If the neighboring tissue is damaged, it too will degenerate, and the results will be greatly obscured. A direct surgical approach is sometimes possible, but this is often undesirable, since some damage to adjacent areas is unavoidable.



A diagrammatic representation of the training apparatus used in the study of brightness comparisons. The two sets of filters are chosen so that all visual stimuli from one light source enter the right eye, while those from the other light source enter the left eye.

Electrolytic lesions

There is a means, however, by which discrete lesions can be placed deep in the brain with a minimum of trauma to surrounding regions. This method involves the use of the Horsley-Clarke stereotaxic instrument. Its design utilizes the constancy of brain-skull relationships in adult animals of the same species. Atlases based on this instrument provide the exact horizontal, vertical and anterior-posterior coordinates for any brain structure. A small, highly localized lesion can be made with this instrument, then after a sufficient period of time is allowed for neuronal degeneration to occur, microscopic sections of the brain are stained specifically for degenerated axons. We are presently tracing some of the unknown connections of the posterior commissure by this method.

I have very briefly outlined two techniques which are presently being used in our laboratory for the study of brain mechanisms. The behavioral approach to the problem of visual perceptual integration has led us into an anatomical investigation of the subcortical interhemispheric connections.

The behavioral study has shown us that interhemispheric brightness comparisons can be made perfectly well in the absence of the crossed optic fibers, plus all the cortical connections between the two halves of the brain. Furthermore, we now know that subcortical connections such as the posterior commissure must play an important role in normal interhemispheric communications of this type. The anatomical data has given us valuable information as to the exact connections of this commissure on each side of the brain. Finally, the ability to perform this integration in the absence of all the commissures strongly suggests that structures not normally used in this capacity can be called into play if needed.

Future investigations have been planned in which the connections of these other areas will be studied, both behaviorally and anatomically. Our understanding of brain mechanisms is gradually increasing — the greatest limitation lies in the ability of the brain to understand its own function.