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FORTY-FOURTH JAMES ARTHUR LECTURE ON THE EVOLUTION OF THE HUMAN BRAIN 1974

# PERSISTENT PROBLEMS IN THE PHYSICAL CONTROL OF THE BRAIN

ELLIOT S. VALENSTEIN

THE AMERICAN MUSEUM OF NATURAL HISTORY NEW YORK : 1975

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## PERSISTENT PROBLEMS IN THE PHYSICAL CONTROL OF THE BRAIN

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#### JAMES ARTHUR LECTURES ON THE EVOLUTION OF THE HUMAN BRAIN

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Frederick Tilney, The Brain in Relation to Behavior; March 15, 1932

- C. Judson Herrick, Brains as Instruments of Biological Values; April 6, 1933
- D. M. S. Watson, The Story of Fossil Brains from Fish to Man; April 24, 1934
- C. U. Atiens Kappers, Structural Principles in the Nervous System; The Development of the Forebrain in Animals and Prehistoric Human Races; April 25, 1935
- Samuel T. Orton, The Language Area of the Human Brain and Some of its Disorders; May 15, 1936
- R. W. Gerard, Dynamic Neural Patterns; April 15, 1937
- Franz Weidenreich, The Phylogenetic Development of the Hominid Brain and its Connection with the Transformation of the Skull; May 5, 1938
- G. Kingsley Noble, The Neural Basis of Social Behavior of Vertebrates; May 11, 1939
- John F. Fulton, A Functional Approach to the Evolution of the Primate Brain; May 2, 1940.
- Frank A. Beach, Central Nervous Mechanisms Involved in the Reproductive Behavior of Vertebrates; May 8, 1941
- George Pinkley, A History of the Human Brain; May 14, 1942
- James W. Papez, Ancient Landmarks of the Human Brain and Their Origin; May 27, 1943
- James Howard McGregor, The Brain of Primates; May 11, 1944
- K. S. Lashley, Neural Correlates of Intellect; April 30, 1945
- Warren S. McCulloch, Finality and Form in Nervous Activity; May 2, 1946
- S. R. Detwiler, Structure-Function Correlations in the Developing Nervous System as Studied by Experimental Methods; May 8, 1947
- Tilly Edinger, The Evolution of the Brain; May 20, 1948
- Donald O. Hebb, Evolution of Thought and Emotion; April 20, 1949
- Ward Campbell Halstead, Brain and Intelligence; April 26, 1950
- Harry F. Harlow, The Brain and Learned Behavior; May 10, 1951
- Clinton N. Woolsey, Sensory and Motor Systems of the Cerebral Cortex; May 7, 1952
- Alfred S. Romer, Brain Evolution in the Light of Vertebrate History; May 21, 1953
- Horace W. Magoun, Regulatory Functions of the Brain Stem; May 5, 1954

- \*Fred A. Mettler, Culture and the Structural Evolution of the Neural System; April 21, 1955
- \*Pinckney J. Harman, Paleoneurologic, Neoneurologic, and Ontogenetic Aspects of Brain Phylogeny; April 26, 1956
- \*Davenport Hooker, Evidence of Prenatal Function of the Central Nervous System in Man; April 25, 1957
- \*David P. C. Lloyd, The Discrete and the Diffuse in Nervous Action; May 8, 1958
- \*Charles R. Noback, The Heritage of the Human Brain; May 6, 1959
- \*Ernst Scharrer, Brain Function and the Evolution of Cerebral Vascularization; May 26, 1960
- Paul I. Yakovlev, Brain, Body and Behavior. Stereodynamic Organization of the Brain and of the Motility-Experience in Man Envisaged as a Biological Action System; May 16, 1961
- H. K. Hartline, Principles of Neural Interaction in the Retina; May 29, 1962
- Harry Grundfest, Specialization and Evolution of Bioelectric Activity; May 28, 1963
- \*Roger W. Sperry, Problems Outstanding in the Evolution of Brain Function; June 3, 1964
- \*José M. R. Delgado, Evolution of Physical Control of the Brain; May 6, 1965
- Seymour S. Kety, Adaptive Functions and the Biochemistry of the Brain; May 19, 1966
- Dominick P. Purpura, Ontogenesis of Neuronal Organizations in the Mammalian Brain; May 25, 1967
- \*Kenneth D. Roeder, Three Views of the Nervous System; April 2, 1968
- <sup>†</sup>Phillip V. Tobias, Some Aspects of the Fossil Evidence on the Evolution of the Hominid Brain; April 2, 1969
- \*Karl H. Pribram, What Makes Man Human; April 23, 1970
- Walle J. H. Nauta, A New View of the Evolution of the Cerebral Cortex of Mammals; May 5, 1971
- David H. Hubel, Organization of the Monkey Visual Cortex; May 11, 1972
- János Szentágothai, The World of Nerve Nets; January 16, 1973
- Ralph L. Holloway, The Role of Human Social Behavior in the Evolution of the Brain; May 1, 1973

<sup>\*</sup>Published versions of these lectures can be obtained from The American Museum of Natural History, Central Park West at 79th St., New York, N.Y. 10024.

<sup>&</sup>lt;sup>†</sup>Published version: *The Brain in Hominid Evolution*, New York: Columbia University Press, 1971.

### PERSISTENT PROBLEMS IN THE PHYSICAL CONTROL OF THE BRAIN<sup>1</sup>

#### INTELLECTUAL AND SOCIAL CLIMATE AND SCIENTIFIC DISCOVERY

There is great temptation to dramatize scientific discoveries by picturing them as the result of sudden insights or lucky accidents. In actuality, this is seldom the entire story since most discoveries also reflect the intellectual and social climate of their time. The many potentially significant observations that were neglected or misinterpreted attest to the importance of a prepared mind. It is true, for example, that Luigi Galvani observed a suspended frog twitch in synchrony with flashes of lightning, but this event was significant because it occurred at a time of increasing interest in the relation of physical and biological phenomena. Galvani's observation occurred only a short time after Mesmer's suggestion that "animal magnetism" was the basis of what is now called hypnotism. Not very many years earlier, the Scottish anatomist John Hunter and the English physicist Henry Cavendish speculated that the study of such electric fish as the eel and torpedo (an electric ray fish) might help to explain the action of nerves in general. In fact, the part played by electric fish in the early history of bioelectricity and electrotherapy has been the subject of an interesting essay by Kellaway (1946).

Galvani's observations, therefore, were not entirely accidental. It is certain that Galvani did not suspend a frog between a wire attached to a lightning rod and a rod immersed in a well by mere chance. He was very much aware of Benjamin Franklin's demonstration that atmospheric electricity could be

<sup>&</sup>lt;sup>1</sup>A comprehensive discussion of the historical, scientific, and ethical considerations related to the physical control of the brain was presented by Valenstein (1973). The research reported in the present paper was supported by NIMH Research Grant 2 RO1 MH20811-03.

tapped in a harmless manner. This particular frog experiment was clearly only one of many Galvani designed to study the role of electricity in biological phenomena. Many of these experiments involved the observation that a frog's muscle would twitch when touched with metal probes. The lively dispute between Galvani and the physicist Allesandro Volta that took place between 1790 and 1798 was over interpretation. Galvani argued for the existence of "animal electricity," whereas Volta argued for "metallic electricity" and claimed that the dissimilar metals used in most of Galvani's experiments produced an electric force that caused the muscles to contract. This controversy shaped much of the research on the nervous system during the early part of the nineteenth century. By 1848 when du Bois-Reymond published his book, Investigations of Animal *Electricity*, and Helmholtz had shown that the speed of nerve conduction was very different from that of electric current, the controversy had disappeared.

The value of electrical stimulation to study the nervous system, however, increased in importance with the passage of time. The technique, which had been applied primarily to the crural nerve and gastrocnemius muscle of the frog, began to be applied directly to mammal brains. Legend has it that while dressing the head wounds of soldiers, Eduard Hitzig observed that their muscles twitched on the side of the body opposite the injury. The 1870 report by Fritsch and Hitzig describing the frontal lobe regions of dogs from which electrical stimulation could evoke bodily movement is traditionally attributed to this accidental observation. As Doty pointed out, there is no truth in this legend despite the number of writers who delight in repeating it. Fritsch and Hitzig had become embroiled in the controversy over specific versus holistic representation of functions within the brain, particularly the cerebral cortex. Many investigators were using electrical stimulation to settle the issue but the results were often confusing because it was not yet appreciated that Galvanic (direct) current destroyed nerve tissue. (Du Bois-Reymond had already developed an inductorium for providing alternating or faradic current, but it was not universally used.)

Fritsch and Hitzig concluded that their results showed clearly that "some pyschological functions and perhaps all of them . . . need certain circumspect centers of the cortex." David Ferrier reached the same conclusion a few years later as a result of his electrical stimulation of the monkey cortex. Friedrich Goltz, on the other hand, argued for holism by describing dogs that were still capable of moving all their limbs after removal of virtually half the brain. The literature of the period provides much support for the statement attributed to Alfred Binet, "Tell me what you are looking for and I'll tell you what you will find."

Even the first known attempt at psychosurgery must be examined against the background of the localization controversy. In 1891, Gottlieb Burckhardt, the director of the insane asylum at Prefargier, Switzerland, reported the results of removing part of the cortex of six "demented" patients. He said: "Who sees in psychoses only diffuse illness of the cortex . . . for him it will naturally be useless to remove small parts of the cortex in the hope to influence a psychosis beneficially by this means. One has to be as I am, of a different opinion. That is, our psychological existence is composed of single elements, which are localized in separate areas of the brain .... Based on these considerations and theories expressed earlier, I believe one has the right to excise such parts of the cortex, which one can consider starting points and centers of psychological malfunctions and furthermore, to interrupt connections whose existence is an important part of pathological processes."

Controversies about localization are still with us, but of course at a more sophisticated level. Stereotaxic techniques and reliable methods for permanently implanting electrodes have made it possible to undertake behavioral (psychological) studies over long periods of time. Earlier controversy was about simple motor responses; current arguments often focus on the localization of relatively complex motivational states. The intellectual and social climate also influences contemporary research, but it is difficult to achieve adequate perspective when one is very close to a scene. Nevertheless, it is helpful to try. I believe I can discern two major influences that have shaped brain stimulation studies from 1950 to the present. One of these involves the attempt to accumulate evidence demonstrating that electrical stimulation of discrete subcortical brain areas can evoke natural drive states. The other influence, which stems directly from the first, has been the preoccupation with brain stimulation as a technique for controlling behavior.

For psychologists interested in studying the process of learning, the early 1950s was a time of increasing disillusionment with theories based on changes in hypothetical drive states assumed to take place in the brain. (Indeed, this was a period when it was often maintained that CNS, the common abbreviation for the central nervous system, in reality meant the "conceptual nervous system.") These drive-reduction learning theories, as they are called, emphasized that we learn only (or in the weaker versions of the theory, we learn best) those stimulus-response connections that are associated with changes in level of drive state. Although it was recognized that peripheral body factors may contribute to drive state, a number of experiments had made it evident that drives such as hunger and thirst did not depend upon intensity of stomach contractions, dryness of mouth, or other obvious bodily cues. Drive states, therefore, were presumed to be represented mainly by the level of activity in functionally specific neural systems within the brain. However, this conclusion was inferential, and therefore the properties of drive, the major variable in the theory, had to be inferred and could not be measured. The field was rapidly degenerating into unresolvable arguments of little interest to anyone not indoctrinated into this specialty.

Drive-reduction theorists desperately needed some new input into their system. Although the Swiss physiologist Walter Hess had received a Nobel prize by this time, the details of his German publications were not well known in the United States. Hess had been stimulating the diencephalon in cats, using a technique that permitted him to study the responses evoked in awake, relatively unrestrained animals. Most of his observations were directed toward understanding the regulation of so-called autonomic responses such as changes in pupil size, blood pressure, heart rate, respiration, and the like. When Hess was invited to speak at Harvard in 1952, a number of people became aware for the first time that some of his studies seemed to demonstrate that electrical stimulation of certain areas in the diencephalon could suddenly make peaceful cats aggressive or satiated cats hungry. These reports were seized upon, for they seemed to provide a means to manipulate drives and to measure them directly.

Neal Miller (1973, pp. 54-55) reflected on his initial interest in brain stimulation studies and described it as follows:

"If I could find an area of the brain where electrical stimulation has the other properties of normal hunger, would the sudden termination of that stimulation function as a reward? If I could find such an area, perhaps recording from it would provide a way of measuring hunger which would allow me to see the effects of a small nibble of food that is large enough to serve as a reward, but not large enough to produce complete satiation. Would such a nibble produce a prompt, appreciable reduction in hunger, as demanded by the drivereduction hypothesis?"

This certainly does not reflect the sophistication of Miller's current thinking on the problem, but it does illustrate the earlier intellectual climate that produced a need to find similarities between such behaviors as eating, drinking, and aggression when elicited by brain stimulation, and the same behaviors when motivated by natural internal states. What was found was that eating, drinking, grooming, gnawing, aggression, foot-thumping, copulation, carrying of young, and many other behaviors could be triggered by brain stimulation. What was claimed was that discrete brain centers were identified which. when stimulated electrically, would evoke specific and natural states such as hunger, thirst, sexual appetite, and maternal drives. Tests were designed to emphasize the naturalness of the evoked states and dissimilarities were disregarded or dismissed as experimental noise. A personal experience illustrates the influence of the prevailing bias. When reporting at a meeting

that the same brain stimulus frequently evoked eating, drinking, and other behaviors, I noted that these and other observations raised some serious questions about the belief that natural drive states were evoked. A colleague attending the session told me that he had made similar observations several years earlier, but as they interfered with the planned experiments, the testing conditions were arranged so that the stimulated animals had no chance to express these "irrelevant" behaviors.

In addition to overlooking behavioral observations inconsistent with the assumption that natural drive states could be duplicated by stimulating single points in the brain, several other trends characterized the period from 1955 to 1970. There was a tendency to rush into print with every new observation of a different behavior that could be evoked by brain stimulation. The competition for priority of discovery and the need to demonstrate progress to the granting agencies often interfered with any serious attempt to understand the relation between brain stimulation and behavior change. One active researcher remarked to me that he would not be "scooped" again, bemoaning the fact that someone had published an article describing a new behavior that could be evoked by brain stimulation before he had. The list of such behaviors kept growing. One other factor that had a major impact was the belief that each evoked behavior was triggered from different and discrete brain sites. In some cases, reports encouraging the growth of this belief actually presented no anatomical information, but despite this deficiency, there was little hesitancy in using loosely defined anatomical terms (really pseudoanatomical) such as the "perifornical drinking area." Some reports presented very complete histological data, but where the authors emphasized the separateness of brain areas eliciting different behaviors, others with a different bias could just as readily see diffuse localization and considerable overlap. In total, the impression was created that a large number of natural motivational states could be reliably controlled by "tapping into" discrete brain sites.

#### POPULARIZATION OF RESEARCH

As the reports of these experiments began to be disseminated, a number of other distortions were introduced. These accounts fed the growing fear that this new brain technology might be used to control human behavior. The emphasis on control, by numerous demonstrations of behavior being turned "on and off" and by selective and oversimplified descriptions of these demonstrations in the popular press, has had the predictable effect. The possibility of behavior control by various brain interventions has become a popular topic for novels, television shows, movies, magazines, feature articles in newspapers, and even essays purporting to describe life in the not too distant future. Michael Crichton's The Terminal Man is only one of many novels that have used this theme. It may be no exaggeration to say that this story may have a greater impact (because it is believed by more people) than Mary Shelley's Frankenstein. Taking a different tack, an article that appeared in Esquire magazine described a government of the future, an "electroligarchy," where everyone is controlled by electrodes (Rorvik, 1969). It is not necessary to demonstrate that all this material is believed by everyone, or even by most people, in order to recognize that the virtual bombardment from the media has had a profound effect.

Even the material meant only for amusement, and not intended to be taken seriously, gradually begins to become a part of our serious thinking and influences our perception of interpersonal relations. A *New York Times* article dated September 12, 1971, described the scientists who: "have been learning to tinker with the brains of animals and men and to manipulate their thoughts and behaviors. Though their methods are still crude and not always predictable, there can remain little doubt that the next few years will bring a frightening array of refined techniques for making human beings act according to the will of the psychotechnologist."

With more drama and expressing less reservation, Perry London (1969, p. 37) a professional psychologist, stated that

All the ancient dreams of mastery over man and all the tales of zombies, golems, and Frankensteins involved some magic formula, or ritual, or incantation that would magically yield the key to dominion. But no one could be sure, from the old Greeks down to Mrs. Shelley, either by speculation or vivisection, whether there was any door for which to find that key ... This has been changing gradually, as knowledge of the brain has grown and been compounded since the nineteenth century, until today a whole technology exists for physically penetrating and controlling the brain's own mechanisms of control. It is sometimes called "brain implantation," which means placing electrical or chemical stimulating devices in strategic brain tissues ... These methods have been used experimentally on myriad aspects of animal behavior, and clinically on a growing number of people . . . The number of activities connected to specific places and processes in the brain and aroused, excited, augmented, inhibited, or suppressed at will by stimulation of the proper site is simply huge. Animals and men can be oriented toward each other with emotions ranging from stark terror or morbidity to passionate affection and sexual desire ... Eating, drinking, sleeping, moving of bowels or limbs or organs of sensation gracefully or in spastic comedy, can all be managed on electrical demand by puppeteers whose flawless strings are pulled from miles away by the unseen call of radio and whose puppets made of flesh and blood, look "like electronic toys," so little self-direction do they seem to have.

It is little wonder that the feeling of being controlled by surreptitiously implanted brain devices has become an increasingly common delusion in paranoia.

While many people emphasize the potential misuse of these new brain-manipulating techniques, there are some who have stressed what they believe is their positive potential. They see in them a possible cure not only for intractable psychiatric disorders, but for intractable social problems as well-particularly those related to violent crimes and wars. This potential of brain intervention to achieve desirable ends has been expressed by Kenneth Clark in his presidential address to the 1971 convention of the American Psychological Association: Clark suggested that "we might be on the threshold of that type of scientific biochemical intervention which could stabilize and make dominant the moral and ethical propensities of man and subordinate, if not eliminate, his negative and primitive behavioral tendencies."

Proposals of this type can best be discussed after a more

realistic foundation is prepared for critically examining the capacity of physical techniques to modify brain-behavior relationships.

#### A CRITICAL EXAMINATION OF THE EVIDENCE

It should be recognized from the outset that evidence limited to the demonstration of inhibition or evocation of some behavior pattern can be very misleading. Such demonstrations convey the impression that there is a simple and predictable relationship between specific brain sites and complex behavior patterns. Also, the implication that only one behavior is influenced by the electrical stimulation encourages the inference that the control is very precise and selective.

It might not be inappropriate to begin the critical examination with a demonstration that is familiar to most people, Delgado's (1969) purported demonstration of brain stimulation inhibiting aggressiveness in a bull. An article in the *New York Times* (September 12, 1971) described the event as it is typically reported: "Dr. Delgado implanted a radio-controlled electrode deep within the brain of a *brave* bull, a variety bred to respond with a raging charge when it sees any human being. But when Dr. Delgado pressed a button on a transmitter, sending a signal to a battery-powered receiver attached to the bull's horns, an impulse went into the bull's brain and the animal would cease his charge. After several stimulations, the bull's naturally aggressive behavior disappeared. It was as placid as Ferdinand."

Although this interpretation is commonly accepted, there is actually little evidence supporting the conclusion that the stimulation had a specific effect on the bull's aggressive tendencies. A viewing of the film record of this demonstration should make it apparent to all but the most uncritical observer that the stimulation forced the bull to turn in circles in a very stereotyped fashion. This should not surprise anyone familiar with the brain, as the stimulating electrode was situated in the caudate nucleus, a structure known to play an important role in regulating bodily movements. It is true that the bull's aggressive

charges were stopped for a short period, but there is no evidence that it was because aggression was inhibited. Rather, because it was forced to turn in circles every time it came close to its target, the confused bull eventually stopped charging. Patients receiving caudate nucleus stimulation also display various types of stereotyped motor responses. Sometimes all movement is stopped in an "arrest response," so that a person instructed to continue tapping a table may be immobilized by the stimulation with his hand in midair (Van Buren, 1966). Destruction of the caudate nucleus in cats and other animals has been reported to produce a syndrome called obstinate progression, a curious phenomenon characterized by persistent walking movements even when an animal's head may be wedged into a corner (Mettler and Mettler, 1942). In humans, movement disorders such as the spasticity and tremors seen in Parkinson's disease have frequently been linked to caudate nucleus pathology.1

Caudate stimulation has also been reported to cause confusion and to interfere with speech (Van Buren, 1963). There are several animal studies indicating that caudate stimulation interferes with the normal habituation of responses to novel stimuli when they are presented repeatedly, e.g., Deadwyler and Wyers (1972), and Luria (1973) have suggested that in humans the caudate nucleus is important for focusing attention because of its role in selectively `inhibiting responses to irrelevant stimuli. Kirkby and Kimble (1968) reported that rats have difficulty inhibiting responses in passive avoidance tests following damage to the caudate nucleus, and Rosvold, Mishkin, and Szwarcbart (1958) have concluded that this structure is

<sup>1</sup>Plotnik and Delgado (1970) have presented evidence that stimulation of the caudate nucleus, putamen, gyrus pyriformis, and gyrus rectus may inhibit the threatening grimaces in monkeys that normally followed tail shock. Although only a minimum amount of data were presented, these changes in the monkeys' behavior did not seem to be accompanied by motor disturbances or general disorientation. Although the report suggests that stimulation of some structures may inhibit the expression of aggressive displays at current intensities that do not produce gross motor disturbances, there is no reason to assume that the large number of other functions believed to be regulated by these brain areas were unaffected. involved in delayed alternation and visual discrimination performance of monkeys.

Many more functions of the caudate nucleus are described in the scientific literature, but a cataloguing of them all is not necessary for our present purpose. It should be clear, however, that we will not advance very far in our attempt to analyze the contribution of the caudate nucleus to behavior if we restrict ourselves to listing the complex behaviors affected by electrical stimulation. What is needed is a testing program designed to characterize functional changes with increasing precision by dissecting out the elements common to behaviors appearing to be very different.

The fact that it is possible to inhibit or evoke different complex behaviors by electrical stimulation has led some people to conclude that specific behaviors might be modified by destroying the neural area around the tip of the stimulating electrode. Thus, using the electrode implanted in the bull's caudate nucleus to destroy a portion of this structure would be expected to alter the aggressive temperament of that animal. Although the specific experiment has not been done, there is no reason to believe that this would be the case. Destruction of the caudate nucleus does not change the aggressive tendencies of other animals, but it may produce various movement deficits or impairments on tasks requiring a selective inhibition of sensory and motor processes and the connections between them.<sup>1</sup> Similarly, if one destroys the hypothalamic area that evokes aggressive behavior in a cat or rat, under an electrode, no change in natural aggressivity is induced unless the area destroyed is so extensive that the animal is incapable of any behavior at all. Even after surgical isolation of the entire hypothalamus, a cat is still able to display integrated attack and rage responses when

<sup>&</sup>lt;sup>1</sup>None of this evidence is meant to argue against the possibility that parts of the caudate nucleus may be more involved in one type of process than in another. It has been shown that specific parts of the caudate nucleus receive input from the orbital frontal, the dorsolateral frontal, or the inferotemporal cortex, and the deficits that follow selective destruction of portions of this complex structure differ accordingly (Divac, Rosvold, and Szwarcbart, 1967). The behavioral manifestations of these deficits, however, vary with the demands of the situation.

provoked, as Ellison and Flynn (1968) have demonstrated. Earlier, Hess described his disappointment at not being able to modify a behavior elicited by stimulation even after destroying the tissue around the electrode. He said:

"This step, involving the use of the same electrodes, seemed to be most promising, inasmuch as we expected that a comparison of stimulation and destruction effects would provide us with a reciprocal confirmation in the sense of a plus or minus effect. In reality, however, the results were disappointing. Today we know why. Since our procedure aimed for the greatest possible precision, we often produced only corresponding small foci of coagulation. As is shown by the stimulation study, however, even the best demarcated 'foci' are relatively diffuse" (Hess, 1957, p. 43).

Luria (1973, pp. 33-34) commented that localization of complex functions in specific regions of the brain is always misleading. What is needed, he said is to "ascertain by careful analysis which groups of concertedly working zones of the brain are responsible for the performance of complex mental activity; what contribution is made by each of these zones to the complex functional system."

Luria also noted that though it is appropriate to speak of the secretion of bile as a function of the liver, insulin secretion as a function of certain cells in the pancreas, and the transduction of light by photosensitive elements in the retina, when we speak of such functions as digestion or perception, "it is abundantly clear that [they] cannot be understood as a function of a particular tissue." Similarly, Luria (1973) quoted Pavlov on the question of a "respiratory center." "Whereas at the beginning we thought that this was something the size of a pinhead in the medulla . . . now it has proved to be extremely elusive, climbing up into the brain and down into the spinal cord, and at present nobody can draw its boundaries at all accurately."

The idea that the brain is organized into discrete compartments whose function corresponds to our social needs is simply not in accord with reality. The brain does not work that way. A concept such as aggression is a man-made abstraction and it

therefore should not be expected to exist as a separate entity in the nervous system. Many parts of the nervous system play roles in regulating what most of us would label aggressive behavior and each of these parts also plays a role in regulating other aggression, and copulation. Even though all of these behaviors point. These investigators destroyed a small amount of the hypothalamic tissue in a rat by means of a specially designed knife and reported changes in eating, drinking, irritability, aggression, and copulation. Even though all of these behaviors were not affected equally, the possibility of modifying a large number of behaviors by destroying even a small amount of brain tissue is quite clear. In drawing conclusions from brain stimulation experiments, what is almost invariably overlooked is that just about every area of the brain is involved in many different functions and all but the simplest functions have multiple representation in the brain.

The eagerness to believe that discrete and natural motivational states such as hunger can be manipulated by brain stimulation has resulted in a selective perception of even some of the pioneering work in this field. For example, although Hess is consistently mentioned as having produced bulimia by hypothalamic stimulation, it sometimes seems that his classic papers are not read so often as they are cited. Hess (1957, p. 25) actually said the following: "Stimulation here produces bulimia. If the animal has previously taken neither milk nor meat, it now devours or drinks greedily. As a matter of fact, *that animal may even take into its mouth or gnaw on objects that are unsuitable as food, such as forceps, keys, or sticks.*" (Italics mine.)

It must be recognized that most hungry cats are more discriminating than Hess's brain-stimulated animals.

In the studies from my own laboratory, it has been shown that the behavior evoked by brain stimulation is very different from behavior motivated by natural states. A stimulated animal may eat one type of food, but not the food it normally eats in its home cage (fig. 1), or it may not eat even the same food if it is changed in texture, as when food pellets are offered as a ground mash. Stimulated animals may drink water from a drinking tube, but not from an open dish (fig. 2), and the taste preferences of an animal drinking in response to stimulation differ from those of a thirsty animal (fig. 3). Most important from the point of view of behavior control (or lack of it), the elicited behavior may change even in response to identical brain stimulation. A rat that drinks only in response to stimulation, for example, may start to eat when stimulated at a later time (figs. 4, 5). Moreover, the brain sites from which eating and drinking may be evoked are much more widespread than is usually implied. There is no anatomically discrete focus for this phenomenon, although there are brain areas where the probability of evoking eating and drinking is very low (Cox and Valenstein, 1969). In 1973 Reis, Doba, and Nathan reached a similar conclusion. These investigators found that they could evoke grooming, eating, and predatory behavior (depending on the intensity of the stimulating current) from almost all electrodes placed in the fastigial nucleus of the cat's cerebellum. Since the behaviors invariably appeared in the same order as the stimulus intensity was increased, regardless of the electrode placement within the fastigial nucleus, the investigators concluded (op. cit., p. 847): "Thus, it is the intensity of the stimulus and not the location of the electrode which is one of the determinants of the identity of the behavior. Second, the observation that the nature of the behavior evoked from a single electrode at a fixed stimulus intensity could be changed by altering the availability of goal objects (such as food or prey) is another demonstration that the locus of the electrode is not critical. Thus, our findings suggest that the behavioral responses from fastigial stimulation are probably not due to excitation of discretely organized neural pathways."

The conclusion to be drawn from these experiments is certainly not that stimulation at any brain sites can evoke any behavior if the contingencies are arranged appropriately or that stimulation at different sites all evoke the same general state. These misinterpretations continue to appear in print although we have made an effort to be clear on these points. Valenstein,

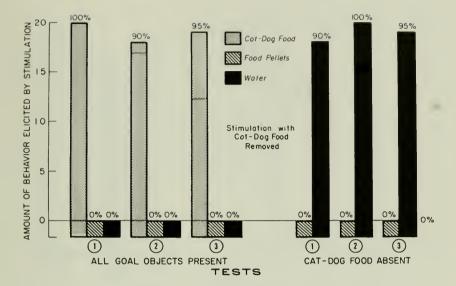


FIG. 1. Behavior evoked by brain stimulation in a testing situation involving choices. During initial 3 tests, rats received brain stimulation in the presence of commercial cat-dog food, their regular food pellets, and a water bottle. Stimulation evoked eating cat-dog food only. Then cat-dog food was removed. We assumed that if stimulation evoked a hunger state animals would readily switch to eating food pellets. Instead, stimulation gradually evoked drinking with increasing regularity (see fig. 5). After stimulation evoked regular drinking three additional tests with food pellets and a water bottle were administered. Animals drank almost every time stimulation was given. Stimulus parameters were invariably the same. Each test consisted of 20 stimulations (20 sec. duration). Maximum score for any one behavior was 20, but animals could display more than one behavior during a single 20-second stimulation period. (Data from Valenstein, Cox, and Kakolewski, 1968b.)

Cox, and Kakolewski (1970, p. 30) said: "We are not suggesting that any elicited response may substitute for any other, but rather that the states induced by hypothalamic stimulation are not sufficiently specified to exclude the possibility of response substitution." And Valenstein (1969, p. 300) said, "[it] is not meant to imply that it will not be possible to differentiate the effects of stimulation at different hypothalamic regions, but rather that the application of specific terms such as hunger, thirst and sex may not be justified."

It seems clear that some behaviors are more likely to be

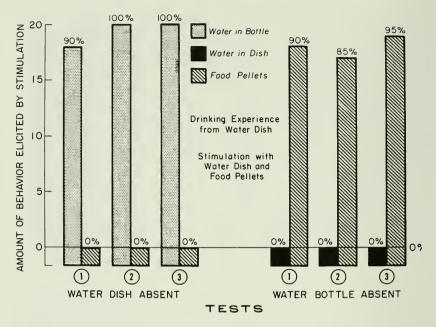


FIG. 2. Behavior evoked by brain stimulation in a testing situation. During initial tests, rat drank from water almost every time stimulation was administered, but did not drink water from a dish or eat food pellets. Afterward, the animal drank all the water from a dish for three days (this was natural drinking; no brain stimulation was administered) before periodic stimulation in the presence of the water dish and food pellets were initiated. It was assumed that if thirst had been induced by stimulation during initial tests, rat would rapidly switch to drinking water from dish when stimulated. Instead, stimulation gradually evoked eating of food pellets. During three stimulation tests with water dish and food pellets available, rat did not drink, but ate food pellets during most of stimulation trials. Stimulus parameters were invariably the same. Each test consisted of 20 stimulations (20-sec. duration). Maximum score for any one behavior was 20, but animals could display more than one behavior during a single 20-second stimulation period. (Data from Valenstein, Kakolewski, and Cox, 1968.)

interchangeable than others. This probably reflects the role of the sensory, motor, and visceral changes induced by the stimulation in channeling behavior in certain directions. Although these bodily changes do not duplicate natural motivational states, they do play an important role in determining the types of behavior that will or will not be seen during stimulation.

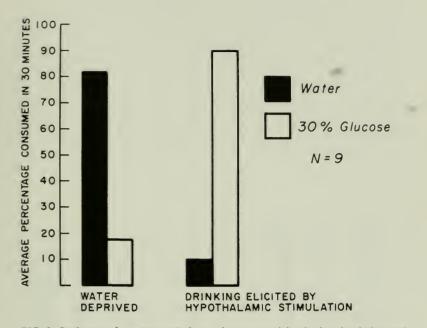


FIG. 3. Preference for water and glucose by rats receiving brain stimulation and the same animals being deprived of water for 48 hours. All rats initially drank water when stimulated but did not eat. In a two-bottle choice test, they preferred glucose during brain stimulation, but water when thirsty. (Data from Valenstein, Kakolewski, and Cox. 1968.)

To date, the direct effects of stimulation have been relatively neglected. Although it is often stated that stimulation does not produce behavior changes unless the appropriate stimulus is available, such changes are actually often neglected even when the data suggest their importance. For example, the first description of drinking evoked by brain stimulation contained a strong suggestion that motor responses may have been more important in directing behavior than any presumed thirst state. In his report, Greer (1955, pp. 60-61) said:

Stimulation of the animal began 24 hours after the electrodes were implanted. It was immediately apparent that the animal was under great compulsion to perform violent "licking" activity when a current was passed between the hypothalamic electrodes. In response to stimulation, it would stand on its hind legs and run vigorously around the glass enclosed circular cage, licking wildly at the glass wall. This behavior would cease immediately upon shutting off the current. If the voltage were slowly increased, licking would gradually become more vigorous. With stimulation continuing by timer control, the reaction of the animal changed during the first night. The water bottle containing 200 ml was found completely empty at 9 a.m. even though it had been filled at 6 p.m. the previous evening. It was now found that stimulation would result in violent drinking activity. The non-specific licking response had been lost. As soon as the current was turned on, the animal would jump for the water bottle and continue to drink avidly until the switch was turned off. If the water bottle was removed and the current then turned on, the rat would go back to its "licking" behavior of the previous day, but would immediately transfer it to drinking behavior when the water bottle was replaced.

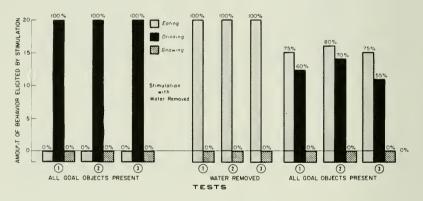


FIG. 4. Behavior evoked by brain stimulation in a choice situation. Initially, animal drank only when stimulation was given (first 3 tests). After periodical stimulation in the presence of food and a wooden block (for gnawing), but without water bottle, rat gradually began to eat food pellets. Next three tests demonstrated that stimulation evoked regular eating. Last 3 tests demonstrated that even when tested with water bottle present, stimulation elicited eating as well as drinking. Stimulus parameters were invariably the same. Each test consisted of 20 stimulations (20-sec. duration). Maximum score for any one behavior was 20, but animals could display more than one behavior during a single 20-second stimulation period. (Data from Valenstein, Kakolewski, and Cox, 1968a).

Visceral changes produced by the stimulation may also play a role in determining the behavior evoked by brain stimulation. For example, Folkow and Rubinstein (1965) contrasted the visceral changes produced by hypothalamic stimulation that evokes eating with those changes produced by electrodes evoking rage reactions. Among the prominent bodily changes

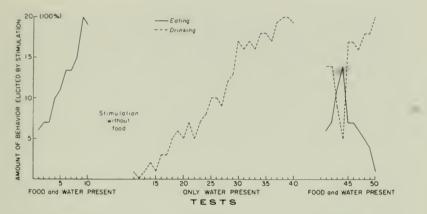


FIG. 5. Gradual development of behavior evoked by brain stimulation. Rat was tested shortly after first demonstration of eating in response to stimulation. In more than 10 successive tests, eating was evoked by brain stimulation with increasing regularity. Although water was available, stimulation never evoked drinking. Animal was then given periodic stimulation for one-week period until it started to drink in response to stimulation. In more than 40 tests, rat drank in response to stimulation with increasing regularity. During last 10 tests, both food and water were present. During most tests rat ate and drank when stimulation was administered, although drinking gradually became dominant evoked response. Stimulus parameters were invariably the same. Each test consisted of 20 stimulations (20-sec. duration). Maximum score for any one behavior was 20, but animals could display more than one behavior during a single 20-second stimulation period. (Data from Valenstein, 1971.)

produced by stimulation that caused rats to eat were a marked increase of intestinal motility and change in stomach volume plus mild increases in blood pressure and heart rate. The pattern was different when rage was evoked; intestinal and gastric motility were inhibited, and the blood pressure and blood distribution patterns differed from those produced by electrodes that evoked eating.

Ball (1974) also stressed the importance of visceral changes for evoked eating. In rats displaying this response, Ball sectioned the vagus nerve at a point close to where it innervates the stomach. He reported that the stimulus threshold for elicitation of eating was raised significantly even after the animals recovered from surgery and were eating the normal amount of food in their home cage. Even though the thresholds increased, it was clear that the visceral changes controlled by

this branch of the vagus nerve were not necessary for the evoked behavior, as stimulation continued to evoke eating. Similarly, as noted earlier, Reis, Doba, and Nathan (1973) reported that electrical stimulation of the rostral fastigial nucleus of the cat's cerebellum elicited either grooming, feeding, or killing of a rat, depending on the intensity of stimulation used. The magnitude of the cardiovascular responses (heart rate and blood pressure) differed for each of the three behaviors evoked, but the behaviors were still displayed after these visceral responses were blocked by an injection of phentolamine. It is evident from the many important studies by Flynn and his colleagues (see Flynn, Edwards, and Bandler, 1971) that brain stimulation produces many different sensory, motor, and visceral changes. Apparently the blocking of one or two of these changes is not likely to be very disruptive once an elicited behavior has become established. These bodily changes, however, may play an important role in channeling behavior during the initial brain stimulation experience.

In addition to producing bodily changes, the positive or aversive motivational effects evoked by brain stimulation may also serve to channel behavior and determine which behaviors are interchangeable. Plotnik (1974) summarized the motivational consequences of 174 brain stimulation sites in monkeys. The motivational effects were determined by tests that measured whether an animal sought out escaped from or was indifferent to the brain stimulation. It was found that 117 sites were neutral, 22 were positive or rewarding, and 35 were aversive or negative. All 14 points that elicited aggressive behavior directed at other monkeys had aversive motivational properties, although the converse was not true. Plotnik views the elicited aggression as "secondary aggression" produced by reaction to an aversive stimulus. In such cases, it would be as misleading to conclude that there was a direct relationship between natural aggression and the brain site stimulated as there would be to conclude the same about the soles of the feet because an electric shock delivered to them produces fighting between animals caged together. The point is well illustrated by

Black and Vanderwolf (1969, p. 448), who reported that a foot-thumping response could be evoked in the rabbit by stimulation of diverse brain sites (in the hypothalamus, thalamus, central gray, septum, reticular formation and fornix-fimbria). Rather than postulate the existence of a complex "thumping circuit" in the rabbit brain, they noted that thumping could be elicited by foot shock and concluded that "thumping behavior in the rabbit is a fear or pain response."

The significance of the motivational properties of brain stimulation is made clearer by distinguishing predatory from aggressive behaviors. In cats and rats, hypothalamic stimulation has evoked both types of behaviors. In these animals, a predatory, stalking behavior (called "quiet biting attack" in the rat), which is well directed at an appropriate prey, has been distinguished from a diffusely directed "affective rage attack" (Wasman and Flynn, 1962; Panksepp, 1971). Stimulation at sites that evoke the predatory (or appetitive) behavior has been shown to also evoke positive or rewarding effects (Panksepp, 1971), whereas stimulation at sites evoking "affective attack" has been demonstrated to be aversive (Adams and Flynn, 1966). In primates, the elicited aggression is intraspecific, resembling fighting rather than predatory behavior, and is evoked primarily, if not exclusively, by stimulation having aversive motivational properties.<sup>1</sup> Although the evidence is inadequate, aggression provoked by brain stimulation in humans also seems to occur only in cases of stimulation having aversive consequences (see Valenstein, 1973, for a review of this literature). Considerations such as these, suggesting that certain behaviors are compatible with aversive and others with positive states, may set limits on the behaviors that can be evoked by a particular brain electrode.

Although the somatic and motivational effects produced by

<sup>1</sup> Robinson, Alexander, and Browne (1969) reported one instance where stimulation elicited aggressive attacks on another monkey and also supported self-stimulation behavior. This suggests that brain stimulation that elicits intraspecies aggression may be motivationally positive. However, as self-stimulation was tested with brief (0.5 sec.) stimulus trains and aggression was elicited by relatively long (10-40 sec.) stimulus trains, this exception may be more apparent than real. brain stimulation make it more likely that one group of behaviors will be evoked rather than another, these factors are by no means sufficient to determine completely the specific behavior displayed or the motivational states induced. Environmental factors and individual or species characteristics can also be very important determinants. An experiment from my own laboratory demonstrates this point and also illustrates how easily one can be misled by first impressions in brain stimulation experiments.

Figure 6 illustrates a two-compartment chamber used to test the behavior of rats receiving rewarding hypothalamic stimulation (Phillips et al., 1969). The equipment was so arranged that when the rat interrupted the photo cells on the right side of the chamber, brain stimulation is turned on and remained on until the animal interrupted the photo cell in the left compartment. In an amazingly short time, the rat learned to play the game, running to the right side and turning the stimulation on for a period, then running to the opposite side and turning the stimulation off. This behavior was repeated rapidly over and over again. The rat was stimulating its own brain and apparently enjoying it—at least it continued doing it.

At this point, we placed food pellets on the right, the stimulation side. After a brief period, the rat started to pick up the pellets when stimulated and carry them (as pictured in fig. 6) to the opposite side of the chamber, where they were dropped as soon as the brain stimulation was turned off. We were fascinated by this unexpected turn of events, as it seemed possible that we had stumbled on a region of the rat's brain that regulated food-hoarding behavior. At least that is what we were thinking until we investigated a little further. When we substituted rubber erasers and pieces of dowel sticks, the rat carried them just as readily. If we mixed the edible and inedible objects together, the rat did not discriminate between them. It carried both. This was a very strange type of food-hoarding behavior! Next we placed some rat pups on the right side and found that these also were carried to the other side. It dawned on us that had we started with the rat pups and gone no farther, we would have been convinced that we were activating the brain structures that controlled the pup-retrieval component of maternal behavior. Probably we would have found it difficult to resist speculating about the significance of the fact that males carried pups as readily as females.

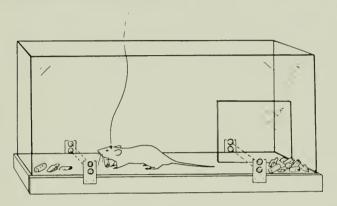


FIG. 6. Rat carrying wooden dowel stock from stimulation (right) to nonstimulation (left) side of test chamber. (In this variation of the basic experiment, animals were given a choice between receiving hypothalamic stimulation with or without the opportunity to carry objects; they chose the former.) (Data from Phillips et al., 1969; figure reproduced from Valenstein, Cox, and Kakolewski, 1970.)

Once the rats started carrying objects regularly, they would pick up and carry almost anything in response to the stimulation. When stimulated, the compulsion to carry became so strong that the rats carried parts of their own bodies when all the objects were removed. A rat picked up its tail or a front leg with its mouth and carried it over to the other side where it was "deposited" as soon as the stimulation was turned off.

Finally, we found that if the very same stimulation was delivered to the rat's brain under different conditions, objects were no longer carried. We programmed the equipment to deliver the same temporal pattern of stimulation the rat had previously self-administered, controlled now by a clock rather than by the rat's position. This procedural change resulted in the possibility that the animal could be stimulated any place in the test chamber rather than the stimulation being turned on and off consistently in different parts of the chamber. Under these conditions the identical electric stimulus, delivered to the same brain site through the same electrode, no longer evoked object-carrying even if the animal was directly over several of the objects when the stimulation was turned on.

We believe that the answer to this puzzling phenomenon lies partly in the rat's tendency to carry objects (food, pups, even shiny objects) from an open field, where the rat is vulnerable and therefore highly aroused, back to the relatively secure and calming environment of the nest site. When stimulation is delivered regularly in certain parts of the rat's life space and turned off regularly in other parts, it not only produces alternating arousal and calming states, but links these states to specific parts of the environment. In addition, because rats prefer to turn off even rewarding brain stimuli after a period of time (Valenstein and Valenstein, 1964), they are forced to move back and forth in the test chamber. Taken all together, we may have inadvertently duplicated all the internal and external conditions that exist when a rat makes repeated forays from its nest site to the outside world.

Admittedly, this explanation is speculative. It is clear, however, that the behavior produced by stimulation is not determined in any simple fashion by the location of the electrode in the brain. (Actually, we achieved the same results with electrodes in different rewarding sites.) The behavior produced by the stimulation can only be understood by considering the natural propensities of the rat in the environmental conditions in which it is tested.

### BRAIN STIMULATION IN HUMANS AND OTHER PRIMATES

If the response to brain stimulation is variable in inbred rats, it is certainly much more variable in monkeys and humans. In monkeys, for example, brain stimulation may initiate drinking when the animal is confined to a restraining chair. However, when the stimulation is administered when the monkeys are in a cage and not restrained, they do not drink, even though they

may be sitting within inches of the water dispenser when the stimulation is administered (Bowden, Galkin, and Rosvold, In press). In humans, brain stimulation may evoke general emotional states that are somewhat predictable in the sense that certain areas tend to produce unpleasant feelings and other areas tend to produce positive emotional states. Patients may report feeling tension, agitation, anxiety, fear, or anger, or they may describe their feelings as being very pleasant or relaxed. Different patients report different feelings from stimulation of what is presumed to be the same brain area, and the same person may have very different experiences from identical stimulation administered at different times (see Valenstein, 1973, for a review of this literature). The impression that brain stimulation can evoke the identical emotional state repeatedly in humans is simply a myth, perhaps perpetuated in part because of its dramatic impact. Janice Stevens et al. (1969, p. 164) stressed this variability: "Subjective changes were elicitable in similar but not identical form repeatedly on the same day, but often were altered when stimulation was carried out at the same point on different days."

Many people have the impression that the results of brain stimulation are predictable because of the reports that the same visual hallucinations and memories can be evoked repeatedly by brain stimulation. It is true that Wilder Penfield, who operated on the temporal lobes of patients suffering from intractable epilepsy, had emphasized that electrical stimulation of this brain region may repeatedly evoke the same memory. Considerable excitement was generated by reports that these evoked memories had the fidelity of tape recording playbacks of past, forgotten experiences. Indeed, on the basis of these reports, a few psychoanalysts began to speculate about the neural basis of repressed memories (Kubie, 1953). What was generally overlooked, however, was that Penfield had reported that the same response could be evoked within a minute or two, but a different response was obtained after a longer period (see Penfield and Perot, 1963). The similarity of this conclusion to that of Stevens et al. (1969) is apparent. Moreover, recent

studies have made it clear that the occurrence of these evoked memories is rare and when they do occur it can usually be shown that they were determined by what was on the patient's mind or some other aspect of the situation when stimulation was administered (Van Buren, 1961; Mahl et al., 1964).

Even relatively simple motor and sensory responses to stimulation of specific areas of the cerebral cortex of primates may vary with time and individuals. When Leyton and Sherrington (1917) reported their observations following cortical stimulation of the chimpanzee, orang-utan, and gorilla, they noted considerable evidence of "functional instability of cortical motor points." Not only did thresholds vary and stimulation of a particular brain site produce either extension or at other times flexion of the same joint, but the muscles involved sometimes also changed. Levton and Sherrington reported that often a particular response became dominant and was elicited from a variety of cortical points that had previously given very different responses. They also observed that stimulation of the same cortical points produced different responses from different individuals and even from opposite hemispheres within the same individual. This is not to deny that there was general agreement as to the parts of the frontal cortex most likely to produce movement of some kind in specific muscle groups, but Levton and Sherrington emphasized that the details of the movements would not be the same if the experiment were repeated. Observations of this type have also been made following stimulation of the human cortex. Penfield and Boldrey (1937, p. 402) noted that stimulation at a point on the post-central gyrus, which does not elicit a particular response, may gain this capability if it is tested after stimulating a brain point that does evoke the response. Similar observations of variation of responses have been reported following electrical stimulation of sensory cortical areas in humans. Penfield and Welch (1949), for example, noted that if a brain site evoked sensations seeming to originate in the thumb, the same stimulation might later evoke sensations experienced as coming from the lips if the stimulation had been preceded by activation of another site that evoked lip sensations. These authors have called such variability "deviation of sensory response." Libet (1973) discussed the variability in human response to electrical stimulation in more detail.

It is totally unrealistic to believe that stimulation of a discrete point in the brain will invariably elicit the same memory, emotional state, or behavior. The changes produced by the stimulation depend upon what is going on in the rest of the brain and in the environment at the time. The understandable need in science to eliminate variability and demonstrate control over phenomena may, when applied to the study of the brain, distort reality by concealing the very plasticity that is an essential aspect of adaptive behavior.

#### CONTROL OF HUMAN BEHAVIOR: FACT AND FANTASY

No discussion of electrical brain stimulation and behavior control would be complete without considering the existence of rewarding brain stimulation. As everyone surely knows by now, Olds and Milner (1954) accidentally discovered about 20 years ago that electrical stimulation of certain brain structures can serve as an effective reward for rats. Subsequent studies of the behavior of rats and other animals indicated, in many different ways, that pleasurable sensations can be evoked by brain stimulation (see Olds, 1973). No other single discovery in the brain-behavior field has produced more theoretical speculation than the phenomenon that animals are highly motivated to stimulate their own brains. Clarke's reaction (1964, pp. 200-201) to this discovery is representative:

Perhaps the most sensational results of this experimentation, which may be fraught with more social consequences than the early work of the nuclear physicists, is the discovery of the so-called pleasure or rewarding centers in the brain. Animals with electrodes implanted in these areas quickly learn to operate the switch controlling the immensely enjoyable electrical stimulus, and develop such an addiction that nothing else interests them. Monkeys have been known to press the reward button three times a second for eighteen hours on end, completely undistracted either by food or sex. There are also pain and punishment areas of the brain; an animal will work with equal singlemindedness to switch off any current fed into these.

The possibilities here, for good and evil, are so obvious that there is no point in exaggerating or discounting them. Electronic possession of human robots controlled from a central broadcasting station is something that even George Orwell never thought of, but it may be technically possible long before 1984.

In part, because the pleasurable reactions have been produced by direct stimulation of the brain and involve electronic gadgetry, there is a tendency to conjure up images of "pure pleasure" that are completely irresistible. It should surprise no one that science fiction writers have seized this phenomenon as a theme for their stories. In Larry Niven's story (1970), for example, the presumed omnipotence of rewarding brain stimulation is at the very center of the "perfect crime." The story takes place in the year 2123 and Owen Jennison's body has just been discovered under conditions that appear to indicate a suicide, but the death actually was the result of a carefully planned murder:

Owen Jennison sat grinning in a water stained silk dressing gown. A month's growth of untended beard covered half his face. A small black cylinder protruded from the top of his head. An electric cord trailed from the top of the cylinder and ran to a small wall socket.

The cylinder was a droud, a current addict's transformer.

It was a standard surgical job. Owen could have had it done anywhere. A hole in his scalp, invisible under the hair, nearly impossible to find even if you knew what you were looking for. Even your best friends wouldn't know, unless they caught you and the droud plugged in. But the tiny hole marked a bigger plug set in the bone of the skull. I touched the ecstasy plug with my imaginary fingertips, then ran them down the hair-fine wire going deep into Owen's brain, down into the pleasure center.

He had starved to death sitting in that chair.

Consider the details of the hypothetical murder. Owen Jennison is drugged no doubt-an ecstasy plug is attached-He is tied up and allowed to waken. The killer then plugs Mr. Jennison into a wall. A current trickles through his brain, and Owen Jennison knows pure pleasure for the first time in his life. He is left tied up for, let us say, three hours. In the first few minutes he would be a hopeless addict.

No more than three hours by our hypothesis. They would cut the ropes and leave Owen Jennison to starve to death. In the space of a month the evidence of his drugging would vanish, as would any abrasions left by ropes, lumps on his head, mercy needle punctures, and the like. A carefully detailed, well thought out plan, don't you agree?

The readiness to believe that artificial stimulation of the brain can evoke such intense and irresistible pleasures reveals more about our desires than about our brain. Routtenberg and Lindy (1965) did demonstrate that some rats actually starved themselves to death because they continued to stimulate their brains rather than eat. However, one can be terribly misled by the popular accounts of this experiment. In the actual experiment, rats with electrodes implanted in rewarding brain structures were given only one hour a day to press a lever for food. It was necessary for them to eat during that hour in order to stay alive. After the rats were on this feeding schedule for a period, they were given a second lever that offered brain stimulation as a reward. Some of them spent so much time on this second lever that they did not receive sufficient food to keep them alive until the next day's hourly session. This is quite different from the picture most people have in mind about what took place. In the special conditions of a brief test designed to emphasize the controlling power of brain stimulation, some of the rats were apparently not able to anticipate the consequences of choosing the brain stimulation lever. Under conditions providing rats with free access to brain stimulation and food, they never starve themselves. In fact, they eat their usual amount of food (Valenstein and Beer, 1964).

Rewarding brain stimulation is not equally compelling for all species. In humans, it does not seem capable of inducing an irresistible, pleasurable experience. Robert Heath, who is probably more experienced than anyone else with the pleasurable reactions brain stimulation can evoke in humans, has commented that it does not seem able to induce a euphoria equal to that produced by drugs (personal commun.). This is not to deny that patients have reported feeling considerable pleasure during brain stimulation or that they were willing to repeat the experience, particularly after receiving the impression that this was part of the therapeutic program. (See Valenstein, 1973, for a review of the reports of pleasure evoked by brain stimulation in humans.) Brain stimulation has evoked orgasms, but there is a tendency to attach too much significance to this. It is usually overlooked that, as with masturbation, brain stimulation that produces an orgasm does not continue to be as pleasurable afterward.

The emotional state induced in humans by brain stimulation varies with the emotional and physical condition of the patient. (Heath, John, and Fontana, 1968, p. 168) stated that "When the same stimulus was repeated in the same patient, responses varied. The most intense pleasurable responses occurred in patients stimulated while they were suffering from intense pain, whether emotional and reflected by despair, anguish, intense fear or rage, or physical, such as that caused by carcinoma. The feelings induced by stimulation of pleasure sites obliterated these patients' awareness of physical pain. *Patients who felt well at the time of stimulation, on the other hand, experienced only slight pleasure*." (Italics mine.)

The existence of circuits in the brain that can induce both pleasure and arousal may be telling us something important about neural mechanisms that have evolved to help focus attention, to increase involvement in a task, and to facilitate the consolidation of memories (see discussion in Valenstein, 1973, pp. 40-44). There are speculations that malfunctioning of these reward circuits is responsible for such psychiatric conditions as depression and schizophrenia (see Stein, 1971). Such speculation leads to more research that ultimately will increase our understanding of how the brain regulates behavior. This is very unlikely to be the consequence of the proposals to use brain stimulation to control behavior.

It would be difficult to fabricate a better example of the distortions that can result from a preoccupation with behavior control than that contained in a proposal, apparently seriously advanced, by Ingraham and Smith (1972). These two criminologists suggested that techniques are available for maintaining a surveillance on paroled prisoners and for controlling their behavior. They propose that implanted devices could be used to keep track of the location of the parolee and his physiological state while remotely operated brain stimulation could deliver either rewards or punishments or it could control behavior in other ways. For example, Ingraham and Smith (1972, p. 42) suggested the following scenario.

"A parolee with a past record of burglaries is tracked to a downtown shopping district (in fact, is exactly placed in a store known to be locked up for the night) and the physiological data reveals an increased respiration rate, a tension in the musculature and an increased flow of adrenalin. It would be a safe guess, certainly, that he was up to no good. The computer in this case, *weighing the probabilities*, would come to a decision and alert the police or parole officer so that they could hasten to the scene; or, if the subject were equipped with an implanted radiotelemeter, it could transmit an electrical signal which could block further action by the subject by causing him to forget or abandon his project."

It is impossible to be certain, but it seems unlikely that anyone would approve such a plan. The more serious problem is the amount of creative energy diverted from the search for realistic solutions to important social problems by this type of thinking. It sometimes seems that difficulties in implementing necessary social changes encourage people to search for solutions in a fantasy world.

Hopefully, it is clear by now that the responses that can be evoked from stimulating discrete brain areas are too variable and affect too many different functions to be useful in behavior-control schemes. The evoked behavior depends on what is going on elsewhere in the brain, individual and species characteristics, and is very much influenced by situational factors. Those who prefer to think only in terms of control may be very disappointed to learn this. Those who think that the basic concern of science is understanding may find it useful to be reminded of the complex relationship between brain and behavior.

It is not surprising that biological solutions to social problems have been discussed most frequently in the context of controlling violence. This discussion, and some actual proposals, have taken very different forms. In his address to the American Psychological Association mentioned earlier, Kenneth Clark also stated:

Given the urgency of the immediate survival problem, the psychological and social sciences must enable us to control the animalistic, barbaric and primitive propensities in man and subordinate these negatives to the uniquely human moral and ethical characteristics of love, kindness and empathy. We can no longer afford to rely solely on the traditional prescientific attempts to contain human cruelty and destructiveness.

Given these contemporary facts, it would seem that a requirement imposed on all power-controlling leaders, and those who aspire to such leadership, would be that they accept and use the earliest perfected form of psychotechnological, biochemical intervention which would assure their positive use of power and reduce or block the possibility of using power destructively. It would assure that there would be no absurd or barbaric use of power. It would provide the masses of human beings with the security that their leaders would not sacrifice them on the altars of their personal ego (Presidential Address, American Psychological Association, 1971).

Undoubtedly Kenneth Clark is seriously concerned about possible misuse of the enormous capabilities for destruction that exist. His speech and the types of solutions he proposes make it apparent that he has been greatly influenced by the experiments interpreted as revealing discrete neural circuits regulating aggression. Stripped to its essentials, his proposal appears as a modern variant of phrenology, a belief that the brain is organized into convenient functional systems that conform to our value-laden categories of behavior. Clark seems to believe that we need only to exorcise those critical regions of the brain that are responsible for undesirable behavior, or to suppress them biochemically, and goodness will dominate. Mankind will be saved by a "goodness pill." The great impact of the many distorted descriptions of the power of brain control techniques becomes especially evident when even social scientists accept the questionable hypotheses that wars are mainly caused by man's animal-like aggressive tendencies and that biological intervention offers a practical way to prevent them. Clark has not suggested any specific biological intervention, so it is not possible to discuss his proposal in any detail. The situation is different with the proposal advanced by Vernon Mark and Frank Ervin.

Mark and Ervin (1970) stressed the magnitude of the problem of violence in the United States and the belief that a biological approach can make a significant contribution toward finding a solution. The following are typical of a number of statements from their book.

"Violence is, without question, both prominent and prevalent in American life. In 1968 more Americans were the victims of murder and aggravated assault in the United States than were killed and wounded in seven-and-one-half years of the Vietnam War; and altogether almost half a million of us were the victims of homicide, rape, and assault."

They introduced their book (1970) with the Preface that "We have written this book to stimulate a new and biologically oriented approach to the problem of human violence." In the foreword to the book, William Sweet, a neurosurgeon affiliated with Harvard University and the Massachusetts General Hospital and a frequent collaborator of Mark and Ervin, expressed "the hope that knowledge gained about emotional brain function in violent persons with brain disease can be applied to combat the violence-triggering mechanisms in the brains of the nondiseased." Clearly, a biological solution to the problem of violence is sought.

Mark and Ervin suggested that abnormal brain foci in the amygdala are responsible for a significant amount of violent crimes. They believe that these abnormal foci often respond to internal and external stimuli by triggering violent behavior. Mark and Ervin have implanted stimulating electrodes in patients that display a history of episodic violence and claim to be able to locate the "brain triggers" by determining the area from which violent behavior can be evoked. The treatment consists of destroying the area believed to be responsible for the abnormal behavior.

The relevance of temporal lobe structures for aggressive behavior can be traced back to the seminal studies of Klüver and Bucy (1939), although there were several earlier reports that contained similar observations (for example, Brown and Shäfer, 1888; Goltz, 1892). Most investigators now believe that the temporal lobes and particularly the amygdala nuclei play an important, although complex, role in the expression of aggression, but Klüver and Bucy and all subsequent investigators have emphasized the very many different behavioral changes that follow destruction of this brain region in animals (see Valenstein, 1973, pp. 131-143).

In addition to a "taming" of monkeys (and other animals) after temporal lobe ablation, hypersexuality, increased orality, and a so-called psychic blindness<sup>1</sup> have also been observed. Others have emphasized the emotional "flatness" of the amygdalectomized animal (e.g., Schwartzbaum, 1960). The behavior changes may take very different forms, even diametrically opposite expression, under different circumstances. Amygdalectomized monkeys may become less aggressive toward man, but as Rosvold, Mirsky, and Pribram (1954) reported, the changes in dominance patterns between animals may be more dependent on the history of their social interactions than on the particular brain area destroyed.

Arthur Kling and his colleagues have recently reported even more striking evidence of the fallacy of describing complex change in response tendencies by such shorthand expressions as "increased tameness" (Kling, Lancaster, and Benitone, 1970; Kling, 1972). Kling captured and amygdalectomized wild monkeys in Africa and on Caijo Santiago near Puerto Rico. Control monkeys that were captured and released rejoined their

<sup>&</sup>lt;sup>1</sup> "Psychic blindness" refers to a loss of higher integrative visual functions rather than to a loss in visual acuity.

troupe although some initial fighting was necessary. Before they were released, the amygdalectomized monkeys seemed tamer when approached by the experimenters, but when released into their own troupe they were completely unable to cope with the complexities of monkey social life. The behavior of the amygdalectomized monkeys was often inappropriate. Sometimes they displayed aggression toward dominant animals. a trait never exhibited before. In not too long a period, all the amygdalectomized monkeys either were driven from or retreated out of the troupe and eventually either died of starvation or were killed by predators. These observations demonstrate the multiplicity of behavioral changes that usually occur following brain lesions and the dependency of these on environmental conditions. In this context, it is interesting that the compulsive sexual mounting commonly observed in amygdalectomized monkeys housed in the laboratory was not seen under natural conditions.

The results of amygdalectomy in humans have been less systematically studied. These operations have been performed on patients exhibiting aggressive, hyperkinetic, and destructive behavior, usually (but not always) accompanied by temporal lobe epilepsy. While hypersexuality and orality have been observed to occur postoperatively in humans, most neurosurgeons claim these symptoms are rare and when they occur they subside after several months (see Valenstein, 1973, pp. 209-233, for a review of the clinical literature). Although "psychic blindness" has not been reported, there exist only a few serious studies of intellectual changes following amygdalectomy in humans. In one study, Ruth Andersen (1972) tested 15 patients after amygdalectomy, and even though 13 of them had undergone only unilateral operations, she reported evidence of a loss of ability to shift attention and respond emotionally. Anderson (1972, p. 182) concluded, "Typically the patient tends to become more inert, and shows less zest and intensity of emotions. His spontaneous activity tends to be reduced and he becomes less capable of creative productivity.

"With these changes in initiative and control of behavior, our

patients resemble those with frontal lesions. It must be pointed out, however, that the changes are very discrete and there is no evidence of serious disturbance in the establishment and execution of their major plans of action.

"Presumably he will [function best] in well-structured situations of a somewhat monotonous and simple character."

Typically, amygdalectomy in humans involves destruction of an appreciable proportion of this structure. For example, Heimburger, Whitlock, and Kalsbeck (1966) and Balasubramaniam, Kanaka, and Ramamurthi (1970) estimated that they had destroyed more than 50 percent of the amygdala on each side. In view of the animal literature and Ruth Andersen's observations, one might suspect that had adequate postoperative testing been generally used, intellectual and emotional deficits would have been detected more often. Mark and Ervin (1970, p. 70) implied that their lesions need not be large because of the use of stimulating electrodes to locate the discrete focus that is triggering the violence. They argued that postoperative deficits would be minimized by the smaller, more selective stereotaxic lesions their technique makes possible. For example: "tiny electrodes are implanted in the brain and used to destroy a very small number of cells in a precisely determined area. As a surgical technique, it has three great advantages over lobectomy: it requires much less of an opening in the surfaces of the brain than lobectomy does; it destroys less than one-tenth as much brain tissue: and once the electrodes have been inserted in the brain, they can be left without harm to the patient until the surgeon is sure which brain cells are firing abnormally and causing the symptoms of seizures and violence."

It is important, therefore, to examine critically the validity of the claim that electrical stimulation is a reliable means of locating a "brain trigger of violence."

A few years ago, while studying the elicitation of behavior by hypothalamic electrodes, we noticed an interesting trend (Cox and Valenstein, 1969). In each of the rats we had implanted two electrodes, one on each side of the midline, but usually not symmetrically placed. We observed that in a number of animals the same response was evoked from very different placements, whereas in other animals either different or no specific behavior was elicited from electrodes that often seemed to be in the same locations (fig. 7). We concluded that within certain anatomical limits, a "prepotent response" tendency of the animal (Valenstein, 1969) appeared to be a more important determinant of the behavior evoked than the exact location of the electrode in the brain.

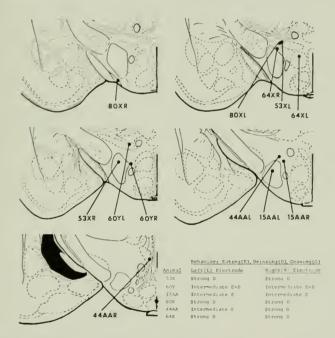


FIG. 7. Illustration of different anatomical locations for two electrodes that evoked the same behavior in a given animal. (Data from Valenstein, Cox, and Kakolewski, 1970. Brain diagrams from König and Klippel, 1963.)

Many were skeptical of our conclusion and cited examples from the literature or from their own laboratory experiences that demonstrated that two electrodes could evoke different behaviors in the same animal. We had never denied this, but had argued that many electrodes evoke states that are sufficiently

similar, yet not specifically identifiable, so that the stimulated animal's behavioral characteristics become a major determinant of the effects produced by stimulation. Additional information has been accumulating supporting our impression. In a recent study using monkeys, it was noted that drinking was elicited initially in some by only a few electrodes, but over time an increasing number of electrodes situated at different brain sites gained the capacity to evoke drinking. Stimulation at an equally varied distribution of sites in other monkeys did not evoke drinking. Some monkeys seem to respond to brain stimulation at many different sites by drinking, whereas others do not (Bowden, Galkin, Rosvold, In press). A similar conclusion may be drawn from an earlier study by Wise (1971) in which rats were implanted with electrodes capable of being moved up and down within the brain (fig. 8). It was found that in some rats eating and drinking were continuously evoked as the electrode was advanced over a large dorsoventral portion of the hypothalamus, but in other rats, these behaviors were not observed in response to stimulation at any site (fig. 9).

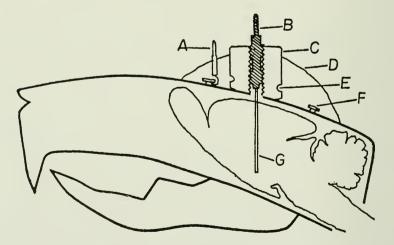


FIG. 8. Sketch of an electrode assembly that can be raised and lowered in the animal's brain. (See Wise, 1971, for details.)

Panksepp (1971, p. 327) has also provided information that supports our "prepotency hypothesis." He has studied the elicitation of mouse-killing responses in rats and has concluded that

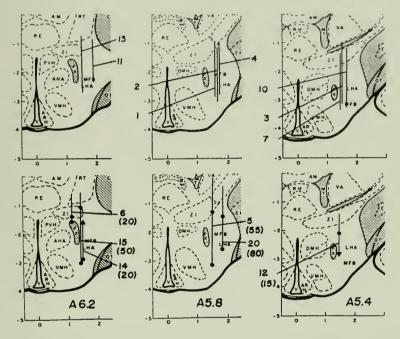


FIG. 9. Path of electrodes used to explore brain for regions evoking eating and drinking. Electrodes were advanced in 0.5 mm. steps descending along the path of the tract. Upper sections show paths of electrode penetrations that did not evoke eating or drinking. In lower sections, both eating and drinking were evoked from all positions between upper and lower circles. Each electrode was placed in a different animal. (See Wise, 1971, for more details.)

the ability to elicit mouse-killing by stimulating the brain of a rat "... interacted with the behavioral typology of individual animals, animals normally inclined to kill mice were more likely to kill during hypothalamic stimulation than nonkillers. Thus, the electrically elicited response was probably not determined by specific functions of the tissue under the electrode but by the personality of the rat." In regard to humans, Kim and Umbach (1973) reported the effects of stimulating the amygdala of aggressive and nonaggressive patients. They concluded that during amygdala stimulation of aggressive patients "aggressiveness increased, whereas no aggressive reaction was observed in non-violent cases. Thus the amygdaloid complex seems not to be specific for anxiety alone or for aggression alone, and shows no specificity of the subnuclei for these emotional states."

There is little reason, therefore, to believe that brain stimulation is a reliable technique for locating discrete foci that trigger violence even if such foci exist. In the violence-prone patients sent to Mark and Ervin, violence can be triggered by a great number of brain stimulation sites and probably also by a pinch on the skin. The ability of stimulation techniques to ferret out a "critical focus" is far from what it has been touted to be. Indeed, the fact that Mark and Ervin found it necessary to make bilateral lesions to produce any significant effect strongly suggests that no "critical focus" was found. Also supporting this interpretation is the fact that the bilateral lesions are usually made progressively larger until the desired behavior change is believed to have been achieved. Although Mark and Ervin have presented their approach very seductively by implying that they can locate and eliminate small and discrete "brain triggers of violence," in actual practice they seem to be performing "standard" bilateral amygdalectomies.

There is little doubt that there are well-documented cases where the onset of assaultive behavior can be traced to temporal lobe damage. There is also little doubt that there are cases where, by all reasonable standards, surgery has led to considerable improvement in behavior (Gloor, 1967). There has, however, been a gross exaggeration of the amount of violence that can be attributed to brain pathology. The evidence presented by Mark and Ervin is extremely weak. It consists mainly of a recitation of parallel statistics on the numbers of murders, rapes, assaultive acts, automobile accidents, and assassinations, on one hand, and the number of cases of epilepsy, cerebral palsy, mental retardation, and other indications of brain damage, on the other. Not only are no causal connections established, but the statistical evidence does not support the conclusion that the correlation of brain damage and violence is high.<sup>1</sup> Mark and Ervin have also bolstered their general argument by implying that brain pathology was the cause in such dramatic and violent incidents as the Charles Whitman shooting from the University of Texas tower.<sup>2</sup>

Totally neglected in their description was Whitman's personal history, which could readily have provided an explanation for his violence without any brain pathology. Nor was there any mention that Whitman's carefully laid plans did not conform to the pattern of sudden, unprovoked, episodic violence that Mark and Ervin have described as characteristic of those with abnormal brain foci. It may be relevant to point out that according to the newspapers, Whitman's brother was shot to death in a barroom dispute not too long ago. Is it likely that a temporal lobe tumor was the cause here, too?

There is a danger that the frustration produced by the inability to effectively reverse the accelerating rate of violence will cause those whose minds run toward simplified behaviorcontrol schemes to accept the delusion that biological solutions are available for what are primarily social problems. The varying amount of violence prevalent at different times and in different societies makes it clear that violence is primarily a social

<sup>1</sup> The older neurological and psychiatric literature often contained statements that epileptics, particularly temporal lobe epileptics, are prone to violence. Most neurologists today refute the earlier figures. Current estimates of the incidence of violence among epileptics ranges between 1 and 4 percent and if corrections are made for age (onset of temporal lobe epilepsy is later than for other epilepsies) the relationship is no higher for the temporal lobe subgroup. Rodin (1973) induced seizure in 150 epileptic patients using the EEG activating drug, bemigride. He reported that there was no incident of aggressive behavior during or after the psychomotor automatisms that occurred in 57 of the patients. He argued that the often-reported relationship between aggression and psychomotor epilepsy has been exaggerated.

<sup>2</sup> It had been frequently stated that a cancerous tumor (glioblastoma multiforme) was situated in the amygdala. Actually, because of the mishandling of the brain at the time of autopsy, the location of the tumor was never clearly established (Frank Ervin, personal commun.).

phenomenon. If drug-related crimes are excluded, most of the present upsurge in violence can be related to the rejection of previously accepted social roles, the large numbers of people who do not believe they have a vested interest in the stability of our society, and the increasing belief that our institutions cannot or will not initiate the changes that are needed. These are not easy problems to remedy, but we will surely be in serious trouble if a number of influential people become convinced that violence is mainly a product of a diseased brain rather than of a diseased society.

# PSYCHOSURGERY

The current controversy over what has been called the "resurgence of psychosurgery" places a responsibility on those of us studying the brain and behavior-whether or not we welcome the opportunity-to offer some light in the midst of all this heat. Anyone who has participated in a public discussion of this issue realizes that psychosurgery is one of those topics on which most people prefer to have one soul-satisfying emotional outburst rather than attempt to draw conclusions from very complex and often conflicting data. While I have nothing against emotional catharsis, there is an obligation to examine the logic of the arguments and the relevant evidence as impartially as possible, if we are to make a contribution to something besides our own psychological well-being. Some of the political and social arguments that have been introduced have aroused such passion that people are forced to take sides on these issues and in the process forget that there may be a patient in desperate need of help. It is possible to make only a few remarks and I offer these in an effort to set the stage for some constructive dialogue by placing the problem in perspective. The serious ethical and legal questions concerning informed consent, adequate review of experimental medical procedures, and operations on children or those committed to psychiatric and penal institutions cannot be discussed here (see Shapiro, 1974, and Valenstein, 1973).

No discussion on this topic would be complete without at least one person arguing against psychosurgery by reminding us that the brain is the seat of our personality, humanity, creativity, capacity to learn, to experience emotion, and even of our soul.<sup>1</sup> It is certainly true that if we remove the brain all of these capacities will be lost, with the possible exception of the soul. I do not want to appear facetious or to denigrate these human qualities, but I want to emphasize that we must talk about particular parts of the brain and the functions that are regulated by these parts. It is well known that many people have had localized brain tumors removed with little, if any, detectable loss in these human capacities.

It is often argued that psychosurgery is unique in that healthy tissue is destroyed for a presumed therapeutic purpose. In truth, however, psychosurgery is really not that unique in this regard. There are several medical procedures that involve the destruction of healthy tissue in order to accomplish some therapeutic advantage. For example, removal of a normal endocrine gland to arrest some pathological process is not uncommon. Unquestionably, there are important differences between removing an endocrine gland, where replacement hormonal therapy is possible, and destroying part of the brain, but there also exist procedures other than psychosurgery that involve destruction of normal brain tissue. It is instructive to consider a few such examples.

Dr. Irving Cooper of St. Barnabas Hospital in New York has done more than 10,000 brain operations on patients suffering from such movement disorders as Parkinsonian tremors, various types of spasticity, and choreoathetosis. While not everyone concurs, Cooper (1969) reported a high percentage of success.

<sup>1</sup>For example, the preamble to a bill controlling psychosurgery passed in June, 1973, by the Oregon State legislature (Senate Bill 298) reads: "Whereas it is acknowledged that the human brain is the organ which gives man his unique qualities of thought and reason, personality and behavior, emotion and communication. And, indeed, is that unique structure importing to man his soul and ethical being; and

"Whereas these things being so, the free and full use of brain is the absolute and inalienable right of each individual, a prerequisite for making choices, possessing insight and judgement, and in health providing for the exercise of citizenship..."

In all likelihood, Cooper destroyed healthy brain tissue (in the ventral thalamus or basal ganglia) as he freely admits in his writings. It is important to appreciate that in many instances there is some loss of function unrelated to the regulation of movement that is incurred. For example, in one review Cooper and his colleagues (Cooper et al., 1968) pointed out that following surgery 58 percent of the patients suffer "mild," and 28 percent "moderate," deficits in speech articulation, phonation, and even the selection of appropriate words. The danger of such undesirable side effects does not necessarily rule out a therapeutic procedure. The risks must be weighed against the possible benefits.

To cite a different example. Many cases of temporal lobe epilepsy are classified as idiopathic—that is, of unknown origin. Indeed, Dr. Wilder Penfield of the Montreal Neurological Institute wrote that he believed that in a number of instances the basic disorder may actually exist in some subcortical region and be projected to the temporal lobe. Nevertheless, there are many people with excellent credentials and extensive experience who would agree that the removal of a restricted part of the temporal lobe has helped patients with otherwise intractable episodes of seizures, although here too undesirable side effects in some cases serious—are not unknown.

In other cases of intractable epilepsy the cutting of the corpus callosum, the most extensive fiber connections between the two sides of the brain, has significantly decreased the incidence of seizures according to Drs. Bogen and Vogel of the California College of Medicine. No one believes that the corpus callosum in these patients was not perfectly normal before surgery. Here too there were deficits produced by the surgery. Sperry and his colleagues, for example, have demonstrated striking deficits in these "split-brain" people, but it takes special testing to reveal them (see Gazzaniga, 1970). Postoperatively, the patients function quite well in normal life situations, certainly much better than when they were plagued by a number of grand mal seizures every day.

Admittedly these surgical procedures are controversial and

drugs have decreased the need for them. It should be noted, however, that many would argue that these surgical techniques are still very helpful for the elimination of some intractable symptoms and that a loss-benefit analysis would justify their use. Therefore, with respect to the issue of destroying healthy tissue, psychosurgery should not be thought of as a unique therapeutic practice. It is more realistic to view it as one end of a continuum differing mostly on the clarity of the diagnosis rather than the treatment.

It is true that as of now there is virtually no reliable evidence linking psychiatric disorders to brain pathology.<sup>1</sup> It is important to note, however, that there are few brain scientists prepared to rule out the possibility that significant relationships between psychiatric condition and brain abnormalities may be found in the future. One of the difficulties thus far encountered in the search for a relationship is that evidence of pathology in the nervous system is much more subtle than it is in other organs. It certainly is possible that functional abnormalities in the brain of psychotic patients can never be detected by the relatively low magnification of the light microscope. It has been reported that the electron microscope has revealed significant defects in the fine aborizations of neurons in the brains of some mental defectives. It is possible that the greater degree of magnification afforded by the electron microscope may reveal structural abnormalities in selective regions of the brains of some psychiatric patients.

Unless one argues for the independence of mind and body, the possibility of structural or biochemical abnormalities cannot be ruled out. It should be noted that even if regional brain abnormalities are found, it is not necessary to assume that these were the initial cause of the psychiatric disorder. Abnormal

<sup>1</sup>Dr. Fred Plum's recent observation that "schizophrenia has been the graveyard of many neuropathologists" refers to the fact that a large number of early pathologists wasted much of their professional lives pursuing false leads. These leads could not be substantiated by others or were shown to be brain artifacts resulting from the deteriorated physical condition of long term institutionalized patients (see Kety and Matthysse, 1972).

brain functioning could be a by-product of abnormal behavior produced by environmental contingencies. Nevertheless, once produced, such brain functioning could play a major role in maintaining abnormal behavior, emotionality, and thought processes. We certainly do not object to this type of reasoning when applied to disorders that we label psychosomatic. When a substantial number of neuroscientists believe that brain abnormalities, perhaps of a biochemical nature, will eventually be linked to some psychiatric disorders, measures that close the door to future investigation of this possibility should be discouraged.<sup>1</sup>

Still another argument raised is that the rationale for psychosurgery, that is, the physiological evidence that justifies the procedure, is very primitive. This is true enough and I have discussed the problem in detail elsewhere (Valenstein, 1973). We should observe, however, that a number of medical treatments is based on the empirical evidence that they work despite the fact that understanding of the physiological mechanisms responsible for their action are not available. If we demanded a good rationale for all medical treatment we would not even use aspirin, not to mention psychopharmacological drugs and electroconvulsive shock treatment. (Incidentally, despite considerable criticism of the possible overuse of electroconvulsive treatment and its poorly understood mechanisms for inducing change, the majority of psychiatrists maintain that it is still the most effective way of arresting some cases of very severe depression.)

Judging from accounts in the popular news media, the issue that has caused the most concern is the charge that psychosur-

<sup>1</sup>Of interest here is a recent poll of the Society for Neuroscience, an organization that includes among its members most of the leading brain scientists in this country. Of the 873 respondents, 74% (16% disagreed and 10% had no opinion) expressed the belief that psychosurgery should be available to patients suffering from incapacitating mental disorders provided adequate safeguards are taken. A great majority (76%) of the members felt, however, that a commission should be established "to promulgate guidelines for selecting and evaluating patients, for certifying that there is a recognized functional disorder, for determining that psychosurgery is an appropriate last resort, for obtaining informed consent and for follow-up and record keeping."

gery may be used as a political instrument to control people, particularly so-called militant blacks. These charges have been accepted as true and repeated by many people who have made no effort to check the facts. My own view, after carefully surveying the literature and doing some direct checking, is that the charges cannot be substantiated and that they were really demagogic attempts to add emotional fire to the issue and to secure political allies.<sup>1</sup> It is clear that we have to be vigilant and monitor carefully the practices in state and private institutions where there may be disproportionate representations based on race, social class, or sex. As real and as serious as that problem may be, however, it is quite different from some of the charges we have been hearing. It should be noted that a substantial proportion of the 500 to 600 psychosurgical patients operated on in the United States each year are not institutionalized, but are private patients referred by psychiatrists.

In the minds of many, psychosurgery is thought of as a behavior-control technique of potentially wide applicability rather than as an experimental therapeutic procedure for intractable psychiatric disorders. This belief has had a very significant influence on legislation presently being considered. For example, in the proposed federal legislation (H.R. 6852)

<sup>1</sup>To the best of my knowledge, the person most responsible for this belief is the psychiatrist Peter Breggin. Breggin has charged that "these brain studies are not oriented toward liberation of the patient. They are oriented toward law and order and control-toward protecting society against the so-called radical individual." In his statement attacking psychosurgery, which was read into the Congressional Record (February 24, 1972, vol. 18, no. 26), Breggin implied that Dr. O. J. Andy, a Mississippi neurosurgeon, concealed that he was operating mainly on blacks. This and similar charges have been repeated by many people as well as in such magazines as Ebony (Mason, 1973) apparently without troubling to check the facts. However, in answer to my inquiry, Dr. Andy wrote that of the approximately 40 psychosurgical operations he has performed, only 5% (i.e., 2 cases) were black. At a symposium on psychosurgery at the 1973 American Psychological Association Meeting in Montreal, Dr. William Scoville, the outgoing president of the International Psychosurgical Association, stated that he has never performed psychosurgery on a black person. The speculation by Mark, Sweet, and Ervin (1967) that the more violent participants in a riot may have some brain pathology has undoubtedly caused much anxiety about future applications. Nevertheless, their psychosurgical patient population does not reflect any racial bias.

outlawing psychosurgery these procedures are defined as brain surgery for the purpose of:

"(A) modification or control of thoughts, feelings, actions, or behavior rather than the treatment of a known and diagnosed physical disease of the brain;

"(B) modification of normal brain function or normal brain tissue in order to control thoughts, feelings, action, or behavior"

Similar wording can be found in other proposed legislation or legislation that has already been passed. Clearly the concern that these techniques will be used to control people has provided a good part of the motivational impetus behind such legislation. It is understandable that black congressmen and women are among the leading supporters of the above legislation. Apparently, they have been convinced that psychosurgery is a technique for controlling behavior that has been or is likely to be selectively used against one segment of the population. It is most important that precedent-setting legislation aimed at curtailing experimental medical procedures be considered carefully and not hastily framed in response to a distorted representation of the problem.

This critique of many of the common arguments against psychosurgery should not be construed as my support for these surgical procedures. My reasons for presenting this point of view are twofold. On the one hand, I believe that if psychosurgery is criticized on the wrong grounds the legislative remedies may take a form that would establish a dangerous precedent. Also, a criticism of irrelevant arguments or unsubstantiated charges can help to focus our attention on what should be the main issue, namely, Can destruction of a part of the brain be justified on therapeutic grounds? This question is easier to ask than to answer. Even if all the data on the consequences of a particular psychosurgical procedure were in agreement and their meaning unambiguous, it would still be possible to reach opposite conclusions because of personal weights assigned to gains and losses in different capacities. Is a flattening of emotional responsiveness, for example, balanced by freedom from a crippling anxiety?

It is not possible for me to present any firm conclusions, let alone to substantiate them, on the approximately one-dozen different brain operations that could be called psychosurgery. Raising some of the main problems that will have to be faced in evaluating any psychosurgical procedure may serve some useful purpose. To begin, we have to face the likelihood that the results of any brain operation probably will always contain an element of unpredictability that will not be completely eliminated by any increased technical precision. This is true in part because the ramifications of destroying any part of the brain must depend upon the total personality of the patient, or if you prefer, on the total neuronal context that must mediate the impact of destruction of any one part of the brain. Moreover, there is usually some compensation for loss in function following brain damage, but the amount of compensation varies with individuals for a great number of reasons we cannot go into at this time.

Another problem in evaluating psychosurgery is that the available evidence leaves much to be desired. In the first place, most of the testing of patients following psychosurgery was done at a time when the patient population and the surgical procedures were different from those that exist today. The older prefrontal lobotomy procedures destroyed much larger brain areas than do the current so-called fractional operations. Although most of the older operations involved rotating surgical knives inside the brain in order to disconnect large areas of the prefrontal cortex, present-day techniques may limit destruction to an area 3 to 5 mm. in diameter. There is also little doubt that the more modern methods of stereotaxic surgery make it possible to reach specific brain targets with much more precision than was previously possible.

No purpose is served by reviewing in detail the results of the older prefrontal lobotomy procedures. The results were extremely variable and one can without difficulty find evidence on both sides of the controversy. There is evidence in the literature demonstrating a blunting of emotional responsiveness, lowering of performance on at least some parts of IQ tests, an

inability to maintain goal-directed behavior, the triggering of epileptic seizures, and other neurological problems following prefrontal lobotomy. There are also a number of studies that reported significant psychiatric improvement following the operations, no IQ loss, and an increased ability to hold a job. Some of the studies that reached this positive conclusion involved relatively long-term follow-ups and some, such as those conducted by the Connecticut Lobotomy Committee or the British Board of Control Study, included substantial samples of patients (Moore et al., 1948). The Columbia-Greystone study, which involved more than 50 participating investigators and a battery of 35 psychological tests (selected from a list of more than 100 that were considered), concluded that there was no evidence that topectomy (one type of prefrontal operation) produced any permanent loss in learning ability, memory, creativity, imagination, intellectual achievement, social or ethical attitudes, or even sense of humor (see Mettler, 1949, 1952; Landis, Zubin, and Mettler, 1950). These studies can all be criticized on various methodological grounds; the test instruments were probably insensitive to important changes in behavioral capacities, and the estimates of improvement often gave exaggerated weighting to the elimination of behavior troublesome to the hospital staff or society in general while placing considerably less emphasis on the qualitative aspects of the postoperative adjustment level.

While we can learn much from examining the older prefrontal lobotomy literature-particularly in respect to methodological points in the way such studies should or should not be conducted-it is not possible to apply specific conclusions to the brain operations performed today. Very different brain areas are often involved, even where the surgery is still directed at prefrontal areas. There are fewer studies reporting results following selective damage to limbic and hypothalamic structures. It is probably safe to conclude that the added precision of the newer operations has resulted in many fewer instances of gross behavioral deterioration, or neurological side-effects such as epilepsy. However, our information about the emotional and intellectual changes produced by the newer psychosurgical procedures is very inadequate.

Neurosurgeons have neither the training nor the time to conduct the type of studies needed to evaluate adequately the changes produced by their brain operations. Postoperative changes are usually reported in gross terms listing percentages of patients exhibiting different degrees of improvement in poorly defined categories ranging from "completely cured" to "no change." There are few examples where postoperative evaluative tests were designed to measure changes in those capacities that animal studies have emphasized as likely to be altered. Indeed, many neurologists and neurosurgeons have displayed an amazing "tunnel vision" toward animal studies. They have been quick to see clinical applications in animal studies, but often quite blind to the results that should have cautioned them against the operation and influenced their evaluative procedures. A few examples are offered to illustrate this point.

There is some familiarity with the circumstances that encouraged Egas Moniz, the Portuguese neurologist and Nobel laureate, to initiate prefrontal lobotomy. It will be recalled that at the International Neurology Congress in London in 1935 Carlyle Jacobsen presented his results on the behavior changes in chimpanzees following destruction of their frontal lobes. Prior to the operation, one of the chimpanzees-the nowfamous Becky-had a temper tantrum every time she made a mistake in the testing situation. After frontal lobe surgery, however, she showed no evidence of emotional disturbance under similar circumstances. Moniz was sitting in the audience. and according to John Fulton, the session chairman: "Dr. Moniz arose and asked if frontal lobe removal prevents the development of experimental neurosis in animals and eliminates frustrational behavior, why would it not be feasible to relieve anxiety states in man by surgical means." The main thrust of Jacobsen's presentation, namely, that the operated animals were no longer able to perform certain problem-solving tasks (particularly those involving delayed responses) was *ignored*. Within three months, Moniz had persuaded his neurosurgical colleague, Almeida Lima, to operate on their first patient.

Anterior cingulotomy is another psychosurgical procedure used by several surgeons today. Here, too, a careful reconstruction of the history reveals a striking "tunnel vision." John Fulton's description of the animal experiments by Wilbur Smith (1945) and Arthur Ward (1948) in a number of influential speeches had a direct influence on the adoption of cingulotomy procedures by a number of people in England, France, and in the United States. Fulton reported that following cingulotomy monkeys became tamer. A closer examination of Ward's description of the postoperative behavior of the monkeys reveals the inadequacy of the term "tameness" to summarize all the changes that occurred. For example, Ward said:

there is an obvious change in personality. The monkey loses its preoperative shyness and is less fearful of man. It appears more inquisitive than the normal monkey of the same age. In a large cage with other monkeys of the same size, such an animal shows no grooming behavior or acts of affection towards its companions. In fact, it treats them as it treats inanimate objects and will walk on them, bump into them if they happen to be in the way, and will even sit on them. It will openly eat food in the hand of a companion without being prepared to do battle and appears surprised when it is rebuffed. Such an animal never shows actual hostility to its fellows. It neither fights nor tries to escape when removed from a cage. It acts under all circumstances as though it had lost its "social conscience." This is probably what Smith saw and called "tameness." It is thus evident that following removal of the anterior limbic area, such monkeys lose some of the social fear and anxiety which normally governs their activity and thus lose the ability to accurately forecast the social repercussions of their own actions.

Perhaps the most striking example of "tunnel vision" comes from a psychosurgical procedure that involves destruction of the ventromedial hypothalamus in persons diagnosed as pedophilic homosexuals, that is, men who seek out sexual opportunities with young boys. Dr. F. Roeder and his colleagues at the University of Göttingen in Germany received their inspiration while watching a film at another International Neurology Congress, held in Brussels in 1957 (Roeder et al., 1971, 1972).

Roeder described his response to this film which depicted the hypersexual behavior of cats amygdalectomized by Leon Schreiner and Arthur Kling, "the behavior of male cats with lesions of the amygdalar region in some respects closely approached that of human perversion. The films convinced us that there was a basis for a therapeutic stereotaxic approach to this problem in man." Roeder was referring to work on cats by Arthur Kling which demonstrated that ventromedial hypothalamic lesions eliminated the hypersexuality previously produced by amygdala lesions. Roeder and his colleagues proceeded to make stereotaxic lesions in the ventromedial hypothalamic nucleus in man. Based on experience with a relatively small patient population studied in a cursory way, Roeder and his associates reached the disquieting if not shocking, conclusion about their surgical procedure that "there is no doubt that experimental behavioral research has afforded us a basic method to eliminate or to control pedophilic homosexuality by means of an effective psychosurgical operation in the area of the sex behavior center." Those of us who study the brain and behavior in animals know of the voluminous literature implicating the ventromedial hypothalamic nucleus in endocrine regulation, appetite, and many other functions. There is also good evidence that irritability and aggressiveness can be produced by lesions in this area. However, once the focus was directed at sexual behavior, the other important behaviors regulated by this brain area were ignored.

Similar comments could be made in reference to a recent report on producing stereotaxic lateral hypothalamic lesions to combat obesity in humans (Quaade, 1974). As Marshall (1974) pointed out in a comment on Quaade's report, the lateral hypothalamus is not specifically involved in "monitoring the energy needs of the organism and transforming such information into an urge to eat." In animals, lateral hypothalamic damage also produces sensory changes leading to inattentiveness to external stimuli and impairment in sexual activation, learning ability, and memory.

A point that apparently has to be made over and over again is

that there are very few parts of the brain that control only one behavior. People studying a given area of the brain may emphasize either control of appetite, aggression, endocrine balance, or sexual behavior, and so forth, depending on their own interests. I have stressed this "tunnel vision" problem because it illustrates the danger of superficial contacts between experimentalists and clinicians. There are many consequences of this lack of communication. Obviously, in some instances, operations should never have been performed. In a great many instances, behaviors and capacities that should have been assessed were completely neglected in the postoperative evaluation of patients. What is needed is not some hastily conceived legislation that may set a precedent hindering all investigations in experimental medicine. We clearly need better controls to protect patients, but it must be recognized that this cannot be accomplished unless more meaningful interactions between research scientists and clinicians are established.

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