Brain Damage and Memory Loss From ECT

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Peter Sterling, PH.D.
Associate Professor (Neurobiology)
Department of Anatomy
School of Medicine
University of Pennsylvania
Philadelphia, Pa. 19174

Introduction

My original training and research activities for the last sixteen years have been concerned with the fundamental structure and functioning of the brain. The investigations in my laboratory focus on the intimate "wiring" of nerve cells and on how this determines the responsiveness of neurons to sensory stimuli. As course director for Neurobiology at the University of Pennsylvania School of Medicine, it is my responsibility to organize the teaching of basic concepts of the brain to medical students. I also teach advanced courses on brain structure and function to graduate and postdoctoral students, including sometimes neurologists and neurosurgeons.

ECT became a concern to me about six years ago when I learned that it is still practiced on human beings. It seemed a procedure so violent that I could not imagine performing it on the delicate circuitry in the brains of my experimental animals. Still, the question of whether an apparently violent procedure actually causes damage must be answered with evidence. Accordingly, I have spent many hours over the last six years studying the scientific literature on the effects of ECT on the brain and on memory in order to answer this question for myself.

The literature is at first difficult to comprehend because the effects of ECT on brain structure and functioning are variable. Some investigators find damning evidence of brain damage while others do not and conclude that the procedure is benign. It seemed to me finally that, if the most carefully controlled studies, using the most sensitive methods, find positive evidence of damage, those are the studies one must attend to. It also helped me to consider the specific question of damage in the broad context of what is known by basic scientists about the brain. Therefore, the testimony to follow explains first

this broader context -- why the brain is so vulnerable to insult, the mechanisms that have evolved to protect the brain, and the ways in which these are breached by ECT. In this context one can appreciate the evidence also to be presented that structural damage and functional losses, particularly to long-term memory, accompany ECT.

Scope and Complexity of the Brain

The brain is the controlling organ of the body. It receives information from the outside world through the 5 senses. It also receives information from the inside of the body regarding all the body's internal functions: heart rate, blood pressure, amount of glucose (sugar), oxygen, carbon dioxide, hormones, etc., in the blood. It also contains information, coded originally in the genes, regarding the needs that all humans share: the drives for hunger, thirst, sex, and so on. As particular kinds of information is taken into the brain by the various sensors, it is stored. Old information, when needed, is retrieved for comparison with new information so that decisions can be made. These decisions include the obvious, conscious ones, such as whether we shall get out of bed in the morning, or what clothes we shall wear. They also include decisions of which we are not conscious that have consequences for every cell in the body, such as how high the blood pressure should be, how much of a particualr hormone should be secreted, how much blood should be distributed to one organ or another.

The Demands of Complexity

It is a general rule that the more complex a structure is, the more closely regulated its operation must be. In a complex structure, foundations must be firmer and the tolerances closer. The safeguards against disruption

must be numerous and of a "fail-safe" variety. A simple hut needs no foundation but there can be no mistakes in the planning or construction of a skyscraper. The simpler the structure, furthermore, the less vulnerable it is to disruption. A hut will most likely survive an earthquake and in any case can be repaired, but a skyscraper, even with all its safeguards, is subject to irreparable collapse. This rule applies to the body as well. Let us compare a relatively simple tissue, the skin, to the most complex organ, the brain.

The skin is exposed directly to the environment and is frequently damaged by mechanical trauma. Its cells have the capacity to divide; new cells easily replace worn or damaged ones. Skin cells must be supplied with nutrients and oxygen from the blood, but their requirements are quite flexible. They can metabolize a variety of substances: fatty acids, glucose, amino acids; they can operate for a while without oxygen and can tolerate wide variations in blood supply. The skin cells are not very sensitive to temperature -- that is why we can sit in the sun or plunge into ice water without damage.

The brain is entirely different. Its 10-100 billion neurons are all present at birth. Nerve cells do not divide to replace their losses. Therefore, any loss of cells is permanent. The death of a single neuron represents a loss of up to 100,000 inputs and 100,000 outputs for a total loss of 10 billion connections. Obviously, the brain must be protected from mechanical trauma.

The brain, unlike the skin, has virtually no metabolic flexibility. It can metabolize only glucose and not fatty acids or amino acids. This is one reason why the glucose levels in the blood must be maintained at all times. A sharp fall in blood glucose leads rapidly to failure of brain function and coma. Oxygen supply to the brain must also be maintained for there is hardly any reserve supply. If a pressure cuff is placed around the neck and inflated,

a human subject goes blind and loses consciousness in 6 seconds. If he breathes pure nitrogen, consciousness is lost in 17-20 seconds. After 3-4 minutes without oxygen at normal body temperature, there is generalized brain damage; after 4-5 minutes, the damage is irreversible.

Brain temperature must also be closely regulated. Everyone is familiar with their own experience with the deterioration of brain function that occurs in fever where temperature rises only a degree or so above normal. Aspirin, by restoring normal temperature, brings relief. Temperature rises that are only slightly greater than a common fever may cause convulsions and can do permanent damage. Clearly, brain function cannot withstand the extreme changes in blood glucose, oxygen supply, or temperature that bother the skin not at all.

Protective Mechanisms of the Brain

Mechanical protection. The first level of mechanical protection for the brain is the thick bone of the skull. There is an active protection too: because the skull has sensitive nerve endings on the outside, we learn early not to bang it into hard objects. Inside the skull, the brain is protected by 3 separate layers of casings. There is a tough, fibrous outer casing called the "dura" ("hard"). Beneath the dura there is a second, more delicate membrane called the "arachnoid". This encases the brain in a special fluid called "cerebrospinal fluid" ("CSF"). Thus, the brain is suspended in fluid in the same way the delicate embryo is suspended within the womb. Within limits, mechanical shocks to the head are absorbed by this fluid and are not transmitted to the brain. The third membrane layer is called the "pia". It is applied directly to the brain's surface, forming the last major protective

barrier. Blood vessels must penetrate the pia to reach neural tissue itself.

Protection of blood supply. Even though the brain is only about 2% of the body's weight, it uses 20% of the body's oxygen supply because of its high rate of metabolism. The brain controls its own blood flow and gives itself highest priority along with the heart. If there is not enough blood to go around, the blood supply is shut down to the gut, kidney, skin and muscle -- always to preserve flow to brain and heart. If blood pressure falls so low that the heart has difficulty pumping blood to the head, the brain shuts off messages to muscle, causing collapse (fainting). With the head at the same level as the heart as a result of fainting, the crucial blood supply can more easily be maintained. Thus, fainting is an important protective mechanism for the brain.

Blood flow through the brain itself is automatically regulated so that it doesn't depend on changes in blood pressure for the body as a whole. If the systemic pressure falls, valves in the brain's vessels open up a bit to maintain flow. Another role for these valves is to protect the delicate brain capillaries from excessively high pressures. This control of blood flow and pressure breaks down during convulsions, a point to which we shall return.

Protecting the brain's chemical composition: the blood-brain barrier. In most tissues the blood vessels are somewhat "leaky". Although red blood cells do not normally escape, some large molecules, such as proteins, and many smaller molecules do escape from vessels into the surrounding tissues. Were this to occur in the brain, it could be disastrous. First, the tiny channels between nerve cells could be plugged by larger molecules and barriers would be established to the normal flow of ions and nutrients. Second, if large mole-

cules leaked from vessels into the brain, water would follow them (to maintain osmotic neutrality). The tissue would then swell. Although most tissues can swell and shrink without causing any difficulty, swelling is a serious matter for the brain because it is encased in bone. If it were to swell, pressure inside the skull would build up. Delicate structures would be squashed against bone, and the blood supply would be cut off by the rise in intracranial pressure. Third, the composition of the blood varies somewhat, even though it is regulated by kidney, liver and other organs. The blood sometimes contains toxic substances that some tissues, such as liver, can handle, but which may damage the brain. In general, the brain's chemical composition must be regulated far more perfectly than that of any other organ.

Accordingly, there are several lines of defense against changes in the brain's chemical composition that would result from leaky blood vessels. These defenses are referred to collectively as the "blood-brain barrier". First, the vessels are sealed off from the brain by mechanical adhesions between the cells called "tight junctions". Second, a set of select substances that the brain needs are actively pumped into the brain from the blood. Third, undesirable substances, or those whose concentration must be actively controlled in the brain, are actively pumped out of the brain. You can get some feeling for these precesses in slide 1. The brain on the left is from a cat with an intact blood-brain barrier. Blue dye which was injected into the blood was prevented from entering the brain by the blood-brain barrier. All the other tissues, however, are blue. On the right, the blood-brain barrier has been destroyed by irradiation (Klatzo and Seitleberger, 1967). Here, the vessels have become leaky and dye has penetrated the brain. This slide, therefore, has two purposes: to illustrate the existence of the blood-brain

barrier and to indicate that it can break down under certain insults. This will be highly relevant when we consider the effects of electrical shock.

Protection of neural stability by inhibition. One additional protective mechanism must be described before the effects of electrical shocks can be assessed. Nerve cells can either "excite" (turn on) or "inhibit" (turn off) each other. The inhibitory mechanisms are important here for one particular reason. Inhibition serves to dampen the excitation, and without it the excitatory tendencies of nerve cells go out of control. All cells tend to be excited simultaneously and tend to reexcite each other until massive neural activity swamps out any sensible, coordinated pattern. Such generalized excitation leads to massive, sustained contraction of the musculature, called a "fit", a convulsion, or a "seizure". Thus, a fit or seizure is a state in which, for one reason or another, the excitatory processes in the brain temporarily overwhelm the damping, inhibitory processes. A seizure, therefore, is evidence that one of the brain's protective mechanisms has temporarily been overwhelmed.

To summarize: 1. The brain is an organ of extraordinary complexity and is more complex in man than in lower animals.

2. Its complexity makes it extremely vulnerable to the slightest environmental insults which other tissues of the body could withstand. Neurons once lost as the result of insult are not replaced.

3. To prevent insult, many protective mechanisms, including mechanical, physiological, and behavioral mechanisms have evolved.

Relation Between Observations on Humans and Non-Human Mammals

I have showed a slide from the brain of a cat and will continue to refer to studies on other mammals. It is appropriate to ask, therefore, whether these studies are pertinent to the human brain since there are many differences between human and animal brains. The major difference between humans and animals that is relevant in the present context is that the human brain is a greater and more complex edifice. To return to the earlier analogy, it is more like a skyscraper than a hut. It needs even more protection, not less. All the protections I have discussed so far exist in humans and are, if anything, exaggerated in humans. In the remainder of my testimony, I shall refer to animal studies only where we can be reasonably sure that the human tissue would react in the same general way.

Effects of ECT on the Brain

We are now in a position to appreciate some of the effects of electrical shocks to the brain. Let us begin by describing the nature of the shock itself (reviewed by Grahn, etal., 1977). Typically, the electrodes of the ECT instrument are placed on the temples. Such ECT instruments usually contain nothing but a simple transformer that steps up the voltage from the wall outlet from 110V to about 150V. The machine may or may not have an automatic timing device to limit the duration of the shock. The current that passes through the head (between the electrodes) is limited mainly by the electrical resistance of the head. The total power drawn is about 60 watts -- enough to light a conventional light bulb. The result is not very different from what would be accomplished by plugging 2 pieces of metal into a wall outlet and placing their other ends on the temples -- except that the voltage from the

wall outlet is a little lower. The duration of a typical ECT shock is 1/10-3/4 of a second.

Events triggered by electrical shock. The electricity passing through the brain causes massive, simultaneous excitation of vast numbers of neurons. The inhibitory mechanisms that normally hold neurons in check and shape the normal EEG rhythms are overwhelmed by the excitation. As the excitation builds and swamps the inhibitory mechanisms, it spreads throught the brain. When the excitation reaches the motoneurons of all the body's muscles, there is massive, convulsive muscular contraction. The muscles contract so powerfully that tendons may be torn from the bones, the bones themselves may be broken, teeth chipped and broken, and so on. The massive requirements for oxygen and the interruption of breathing caused by the convulsion often causes anoxia. Accompanying the convulsion, there is a tremendous rise in blood pressure: changes in arterial pressure from 80mm Hg to 220mm Hg, or almost 200%, have been recorded (Plum, etal, 1968). This overall response resembles the "grand mal" seizure that occurs in epilepsy.

In recent years some of these consequences of the electrical shock have been ameliorated. The muscle contractions can be prevented by administration of a drug that blocks transmission of impulses from nerve to muscle. The ensuing paralysis protects bone and muscle, and also permits oxygen to be administered by artificial respiration. Under these conditions, the brain is well protected from anoxia. On the other hand, this procedure (paralysis) is frightening. Patients are therefore usually pretreated with barbiturate anesthetics so that their consciousness of their treatment is dulled or lost entirely. The effect of barbiturate anesthetic is to decrease the excitability

of neurons in the brain. Larger shocks must, therefore, be employed to evoke a grand mal seizure than would be needed without the drugs. Thus, although the patient may gain from the paralysis and the administration of oxygen, he probably also loses by the higher voltage requirement. There is no evidence that these drug treatments substantially alter the electrical and chemical phenomena within the brain that I shall now describe.

Brain changes during ECT. The massive neural activity evoked by the electrical shock causes and requires major changes in the metabolism and blood supply of the brain.

1. The neurons, because they are so active, require much more oxygen and nutrients. Therefore, with the onset of the seizure, cerebral blood flow rises dramatically -- as much as 400%. Cerebral oxygen consumption also rises as much as 400%. In accomplishing such massive increases in blood flow, the automatic mechanisms that normally regulate cerebral blood flow are overwhelmed. For the duration of the seizure and for sometime following it, blood flow to the brain becomes like that of must other tissues in the body -- proportional to the arterial pressure forcing the blood through the vessels. These changes accompanying ECT are not modified by the administration of anesthetic, paralytic drugs or oxygen (Plum, etal., 1968; Posner, etal., 1969).

2. The extremely high cerebral blood pressure and the breakdown in autoregulation of cerebral blood flow during the seizure frequently ruptures small, and occasionally large, vessels in the brain. Madow (1956) reviewed 42 cases of autopsy assembled from 26 published reports on patients who had recently received ECT. Twenty-five (60%) had either petechial hemorrhages or large infarcts. About three-quarter of these patients were over forty, but the frequency of hemorrhage in the group under forty was the same as for

the older group. There seems every reason to suspect, therefore, that subarachnoid or intracerebral bleeding accompanies ECT about half the time. This is supported by numerous studies in animals autopsied after being subjected to ECT. For example, Alpers and Hughes (1942) found bleeding in 23/30 cats (77%); Heilbrunn(1943) found petechial or larger hemorrhages in all of the rats that convulsed in his experiments to ECT; Heilbrunn and Weil (1942) made similar findings in 17/21 (81%) rabbits. Wherever bleeding occurs in the brain, neurons lose their supply of oxygen and nutrients -- and die.

Some studies failed to find hemorrhages in animals following ECT, but most of these seem not comparable to the human cases. In two, the voltage applied was far below what is employed on humans (Masserman and Jacques, 1947; Winkleman and Moore, 1944). Others used only a single shock rather than, as is common for humans, a series of treatments (Windle, 1948; Alexander and Lowenbach, 1944). Another study with negative findings (Siekert, etal, 1950) used a small sample (5) of young monkeys (5-7 lbs., corresponding to an age of about one and a half years). Since damage is greater in older animals with less flexible vascular systems (Hartelius, 1952), this negative result on a small sample is not astonishing, nor does it contradict the many positive findings of damage. The positive findings cannot be attributed to poor preservation of the brains after death. While poor preservation makes difficult judging the condition of neurons or glia, it cannot cause bleeding within the brain. Nor can the bleeding be attributed to "old" methods of ECT (no paralysis or oxygen). One would expect under the old conditions the brain to be anoxic, with arrested circulation. This would lead to a lack of blood in the brain, the opposite of what is reported. Thus, the later modifications of ECT can relieve the threat of cerebral anoxia, but not the threat of high pressure, bleeding, loss of blood-brain barrier, or edema.

3. The electrical shock causes damage to the blood-brain barrier. (Aird, etal., 1956; Angel, etal., 1965; Lee and Olszewski, 1961). This has been shown experimentally in animals, and there is every reason to believe that it happens in humans as well. Whether this is caused by the huge rises in cerebral blood pressure is unknown. Whatever the cause, the loss of this protective barrier exposes the brain tissue to components of the blood from which it is normally protected. For example, if a patient has been taking drugs of any kind, the brain may be exposed to much higher levels of the drugs than normally cross the blood-brain barrier.

4. The combination of raised cerebral blood pressure and ruptured blood-brain barrier often causes another problem, cerebral edema. The high pressure forces proteins and other substances out of the now "leaky" vessels into the brain tissue. As noted earlier, fluid tends to follow these substances and the tissue begins to swell. This process once started can become disastrous because a "vicious circle" is started. As the pressure inside the skull rises from the swelling, capillaries are closed. Their linings are damaged by anoxia making them even more leaky. This leads to more edema and damage (Fishman, 1975; Klatzo and Seitleberger, 1967). Edema has been noted in the human retina, an easily visible part of the brain, as a consequence of shock (Winnik, etal., 1966). Patients cannot be protected from this process by drugs that lower blood pressure, because the extra pressure is needed to supply the brain's huge metabolic needs during the seizure. It has been noted in experimental animals and man that rises in blood pressure accelerate the spread of edema (Fishman, 1975;Shutta, etal., 1968; Klatzo and Seitleberger, 1967) and the leakage of trace materials from the blood-brain barrier (Lee and Olszewski, 1961; Klatzo and Seitleberger, 1967). It has also been noted that

individuals with high blood pressure "have a significant predisposition to cerebral edema" (Klatzo and Seitleberger, 1967, P.148). Where the swelling is great enough to block the blood supply to neurons -- or even to slow it below the extreme needs of the active tissue -- nerve cells will become anoxic and die.

5. Even where there is adequate oxygen, neurons may die because they use up the metabolites that they need to function. It has been demonstrated that during a seizure, the "respiratory quotient" of the brain shifts markedly. This shift indicates a change in cerebral metabolism away from the use of glucose as fuel. Here is what a prominent neurology group had to say about the changes in cerebral metabolism that they measured during ECT-induced seizures in man:

> If endogenous substances essential to normal cerebral metabolism are depleted during seizures, one might expect post-ictal brain dysfunction until repletion even without hypoxia. At some point during repeated seizures, depletion of cerebral substances might become irreversible and permanent brain damage ensue. Thus, post-ictal EEG flattening and coma need not imply cerebral hypoxia (Posner, etal., 1969, P.394).

Translated into English, this means that even if the brain receives enough oxygen during a seizure, the brain may exhaust its sources of nutrients and be irreversibly damaged. It means that the abolition of electrical activity and the coma that sometimes follows a seizure can occur even though adequate oxygen is supplied.

6. There are changes in a host of brain chemicals as the result of ECT (reviewed by Essman, 1973). Synthesis of protein and RNA are inhibited within five minutes of ECS, with the decrease persisting for a number of hours. The levels of neural transmitters (acetylcholine, norepinephrine, serotonin) and their related enzymes also change. For example, acetylcholine and the

enzyme that destroys it, acetylcholinesterase, fall after ECT but rise above normal levels within 2 hours. These changes are reflected in the choline levels in the cerebrospinal fluid, which in man and monkey are increased 24 hours following a single ECT and remain elevated for at least a week after multiple ECT. Changes in serotonin, an important neural transmitter, last up to 5 months. The time courses of these changes are very comlex, and their meaning is not yet understood. Nevertheless, each of the chemicals listed has been shown to play some role in memory, and I would anticipate that significant changes in any one of them might contribute to the changes in memory that have been demonstrated to follow ECT.

7. Following ECT, there is a marked rise in cerebral levels of arachidonic acid (Essman, 1973; Bazan, N.G., 1970, 1971). This compound has been shown to cause aggregation of blood platelets when injected into the cerebral blood supply, resulting in small "strokes" throughout the brain (Furlow, T.W., Jr. and Bass, N.H., 1975). Conceivably the rise in arachidonic acid associated with ECT could be a source of the brain damage to be described later.

Changes in the Electroencephalogram (E.E.G.)

The EEG changes markedly during and following ECT. Before describing these changes, it is necessary to explain what the EEG represents. The electrical activity of neurons can be studied in two ways -- either by recording the electrical activity of one neuron at a time to see how it responds to particular environmental events -- or by recording outside the skull from a large population of neurons and their supporting "glial" cells. It is something like pushing a microphone close to one member of an orchestra (single neuron) and listening to his theme or withdrawing the microphone in order to listen to the whole

(EEG). In the first case, one can make out the individual notes; in the second, one hears the overall rhythm, pitch, and loudness, but blended in such a way that the detailed contributions cannot be discerned. When the rhythms of millions of individual nerve cells are merged in the EEG, the resulting broader rhythms have fairly characteristic features in normal and pathological states. When something is wrong, one cannot identify precisely what it is -- especially since glial cells as well as nerve cells contribute to the EEG rhythm -- but one can be sure that something is wrong. In awake adults, a beta-rhythm is normally seen with a frequency of about 15-60/ sec. and an amplitude of 5-10uV (low voltage-fast activity). If the person closes his eyes, the rhythms, particularly over the visual area, may slow a little and increase in amplitude, changing to an alpha-rhythm of 8-10 sec., 50uV. In sleep the rhythm slows to a delta-rhythm, still slower (1-5/sec.) and higher in amplitude (20-200uV).

These slow delta rhythms are rarely recorded in normal, awake adults. They do appear, however, in various pathological states and are interpreted as evidence of pathology such as tumor, epilepsy, raised intracranial pressure, mental deficiency, depression of consciousness by toxic or other factors. For example, lack of oxygen and lack of glucose in the brain both cause the appearance of these large, slow delta waves. Again, we cannot say precisely what these rhythms mean or how they arise from the individual elements, but they do seem to convey the overall "mood" of the brain.

It is not at all surprising that the EEG is altered during the ECT seizures because the seizure itself is an interruption of the normal electrical rhythms. Furthermore, it is to be expected that the EEG would be abnormal for some time after a seizure because of the outpouring of potassium ions from neurons. It is significant, however, that in many patients the EEG remains

abnormal for many months. Here, I should like to cite several studies in some detail.

In 1944 Mosovich and Katzenelbogen studied the EEGs of 82 patients before and after ECT. Although the study is old, it is a model of good scientific work, particularly in that it studied patients before treatment and followed them for 10 months afterwards. The currents used were 300-600MA, within the range used today. The study showed that of 42 patients with normal EEGs before ECT, half (21) had abnormal EEGs following treatment. One-third of these abnormalities were severe "cerebral dysrhythmias". The EEG patterns resembled those commonly seen in epileptic patients in the periods between epileptic seizures. Of 40 patients with moderate EEG abnormalities before ECT, 13 showed cerebral dysrhythmia afterwards. To produce these changes a relatively few sessions sufficed, for they were found in 9/60 patients who had only 3-15 ECT. The frequency of damage increased with increasing number of shocks: after 16-42 shocks, half the patients (11/22) showed cerebral dysrhythmia. These changes were often extremely long lasting. Thus, 68/82 patients showed the dysrhythmia the day following ECS, and 20 patients still had the pattern 10 months later. For all anyone knows, the changes were permanent (Mosovich and Katzenelbogen, 1944).

These findings have been confirmed in modern studies using anesthesia, oxygen, and muscle paralysis. For example, Abrahms, etal. (1972) found significant slow delta waves when either bilateral or unilateral ECS was administered. When the shock was restricted to one side, the EEG changes were found on that side. Volavka, etal., (1972) showd that the amount of delta activity in the EEG was related to the number of shocks administered. These studies had the additional advantage that the EEG expert who read the records did not know how the patients had been treated, i.e., the readings were done "blind".

Abrahms,etal., 1972) cite four additional studies done between 1965-1970 with similar EEG findings.

Summary and Conclusions Regarding the Effects of ECT on the Brain

1. During a seizure induced by ECT, there is a tremendous rise in blood pressure and a breakdown of the blood-brain barrier. These two events separately or in combination often cause hemorrhage, edema, and possibly toxic effects because the brain is exposed to chemicals in the blood from which it is normally protected. All of these phenomena cause the irreversible death of neurons in the brain (reviewed by Blackwood and Corsellis, 1976).

2. ECT alters the metabolism of brain proteins, RNA, and neural transmitters whose production is normally regulated carefully. Although the gross metabolism of these substances may later return to normal, their temporary alteration may have permanent effects in the brain. In fact, the very reason that hundreds of scientists around the world are studying the relation between these substances and memory is because small changes in their production might be the way that memories are stored.

3. EEG studies spanning a 28 year period show that ECT alters brain physiology from normal to abnormal. These changes, principally a slowing of the EEG waves, are similar to those found in epilepsy, mental deficiency, and other neuropathologies. The EEG changes associated with ECT appear to be extremely long-lasting; very possibly they are permanent. They do not tell us whether a patient has lost his memory -- for that you have to ask the patient. They do tell us that ECT can cause profound alterations in brain function.

4. All of the changes that follow ECT vary from animal-to-animal and from person-to-person. Thus, blood pressure rises in one study were small

in one case, only 23%, but large in others (up to 400%). Cerebrovascular hemorrhages are found commonly, but not invariably (about 60% of the time); similarly, about half the patients show EEG abnormalities.

Loss of Memory for Past Events Following ECT

Losses of memory for past events commonly occur following insult to the brain, for example, following mechanical injury or from chronic toxic states such as alcoholism (Russell, 1971; Whitty and Zangwill, 1966). It should not be surprising that memory loss also accompanies the damage done to the brain by ECT. Such losses have been documented in numerous case reports dating back to the 1940s (Levy, etal., 1942). In some cases the loss is catastrophically complete: memory is erased for professional skills as well as orientation to places and friends (e.g., Roueché, 1974). More commonly, the loss is "patchy": some events are lost while others are remembered; recent events are more likely to be lost than those in the distant past, but amnesias can extend backward for several years and can include events of early childhood that date back 20 to 40 years; some memories return while others do not (Janis, 1948; A Practicing Psychiatrist, 1965; Brody, 1944; Valentine,etal, 1968; Medlicott, R.W., 1948; Squire, etal, 1975).

One's confidence that there must be substance to these case reports is strengthened by the hesitations of some physicians experienced in the use of ECT to employ it on patients engaged in intellectual work (e.g., Stromgren, 1973) and in the widespread adoption, especially in Europe, of unilateral ECT. In this method the electrodes are not placed on both temples, bot on one side of the head only, in the frontal and parietal regions. The passage of current is therefore largely restricted to one side of the brain. The electrodes are

usually placed on the so-called "non-dominant" side, the side concerned with spatial, rather than verbal tasks. With this treatment the EEG changes are limited to the non-dominant hemisphere, and patients report fewer and less severe losses of memory for past events. Clearly, in order for there to be less memory and loss and less brain damage (EEG changes) with unilateral ECT, there must be substantial amounts of it with bilateral ECT (Abrahms, etal., 1972; Stromgren, 1973; Valentine, 1968; Zinkin and Birtchnell, 1968; D'Elia, 1970; Heshe and Roeder, 1976; Lancaster, etal., 1958). Lest it be prematurely concluded that no damage is done by unilateral ECT to the "non-dominant" hemisphere, it is well to realize that the functions of this hemisphere are just beginning to be appreciated and that methods for assessing its function remain primitive (e.g., Ornstein, 1973).

Various objective tests have been used to determine whether memory loss occurs following ECT, including standard I.Q. tests, the Benton test, the Paired Associates test, and tests devised specifically for assessing memory following ECT (e.g., Bender, 1947; Brunschweig, etal., 1971; Dornbush, etal, 1971; Squire and Chace, 1975). Most of the tests require the patient to learn and remember new material of very simple kinds. For example, can a patient memorize a list of words, numbers or faces and recall them after an hour, a day or a few weeks? Others test recognition of remote events that are not intimately connected with the patients' lives, for example, recognition of the names of old television programs (Squire and Chace, 1975). One of these reports shows that patients have more difficulty recalling their own past than in learning new material and that amnesias recover more slowly than do the processes required for new learning (Brunschweig, etal., 1971). Until recently, such tests revealed very little impairment, and it was com-

mon to conclude that patient reports of memory loss are nothing more than complaints associated with their illness or merely an underestimation of their true memory abilities (Squire and Chace, 1975). No study, however, has tried to document this hypothesis, and several solid studies reporting substantial memory losses find no association between the degree of memory loss and the patient's emotional health. Teuber, etal., (1976) studied 34 patients who had been subjected to cingulotomy (brain surgery) for relief of their mental illness. Many of these patients had been subjected to ECT prior to their surgery. On a battery of nine standardized psychological tests, significant deficits were found correlated not with the surgery but rather with the patients' history of ECT.

> "We found that individuals whose prior treatments had included ECT were inferior to normal control subjects and to patients who had been spared ECT, and this inferiority was apparent on the following measures: verbal and nonverbal fluency, delayed alternation performance, tactual maze learning, continuous recognition of verbal and nonverbal material, delayed recall of a complex drawing, recognition of faces and houses, and identification of famous public figures. In some cases, the degree of deficit was related to the number of ECT received, patients who had been given more than 50 ECT being significantly worse than those who had sustained fewer than 50." (Teuber, etal., 1976, P. 76).

This study is one of the most thorough applications of objective tests to ECT patients; one would like to see it repeated on patients who had not also sustained surgical brain damage. Yet, it does not tell us what individual patients knew about themselves before and after their ECT. This question received a clear answer in the early 1950s.

The Janis Studies. One series of studies, those of Dr. Irving Janis of Yale University, stands out in the scientific literature on the effects of

ECT on memory for the past (Janis, 1950a; Janis, 1950b; Janis and Astrachan, 1951). Janis, unlike most investigators, studied patients before as well as after ECT and could, therefore, determine whether individual patients showed changes. He studied patients not merely for a few days or weeks following ECT but for up to 3½ months. Janis did not primarily use artificially devised tests but actually asked patients about the details of their lives, covering the following topics: 1) school history, 2) job history, 3) history of the mental disorder, 4) sexual and marital relationships, 5) family relationships, 6) childhood experiences, 7) miscellaneous, e.g., details of the layout and furnishing of the home, 8) outstanding life experiences; e.g., personal failures and troubles, best and worst experiences of one's life, etc. In these interviews he pressed patients for minute detail. For example, he asked the name, location, years of attendance for each school; reasons for transferring or leaving; names of teachers; subjects failed and reasons for failure; difficulties with school authorities; description of the graduation ceremony on the last day of school. In this way he built up a rich account of personal memories so that he could compare the amount of detail that was supplied following ECT.

The Janis studies were carefully controlled. For patients who were to receive ECT, there was another group who matched the shock patients in age, education, type and degree of illness, and form of psychotherapy. These control patients were interviewed in the same detailed way as the shock patients, both initially and at the same later intervals. In this way Janis could be certain that any losses in memory he might find would be due to the ECT and not to the course of the illness or some other unidentified factor. At the end of the study, Janis asked both the shock and the control patients to state

what they thought the purpose of the interviews was. Their replies indicated that none of them suspected that the purpose was to test their memory. They could not have been "faking" responses to determine the outcome of the study because they did not suspect that a study was underway.

The shock patients in this study received standard treatment (60 cycle, AC., 3 times/week). The number of shocks was relatively modest, between 8-27, with an average of 17. No differences were noted between patients who received different numbers of shocks.

The results of Dr. Janis' study are, in my opinion, conclusive proof that serious losses of personal memories are caused by ECT and that the losses persist. Here is an example of what he found. First, a 38 year old woman before ECT:

> Case E. -- A 38 year old female schizophrenic (borderline or mixed); 10 electroshocks.
>
> Before ECT. (Q. How did your illness begin?)....About four years ago, right after I lost my child ... I took thyroid then which caused palpitations. I didn't know , at the time, that that caused it. I felt terrified by them. It was a real panic, as if I were on railroad tracks with a train coming. I was trying to be very brave about the death of my baby, going to work in the hospital where it died, collecting legal papers on it, and so forth, trying to be the super-woman. Then I had the palpitations; a friend told me I should get psychiatric help. I saw my family doctor and he sent for a neurologist. I spent the night at my doctor's office and then I went to the H Sanatorium for a week. I was hopeful of getting all better. They didn't feel I was really ill. After that, I began analysis. (Janis, 1950a.)

Note that a single question elicits a long account that is rich in detail. Information flows without prompting by the interviewer. Here is the same woman 3 1/2 weeks after a series of 10 shocks:

Three and One-Half Weeks after ECT.

Q. Did you take some medication after the loss of your child?
A. I don't remember.
Q. Thyroid?
A. I think so.
Q. What reaction did you have to it?
A. I don't know.
Q. During that period did you have any special symptom which disturbed you?
A. I felt depressed.
Q. Anything else?
A. I don't recall.
Q. Did you have palpitations?
A. I vaguely remember having palpitations now that you mention it.
Q. How did you feel about them at the time?
A. I don't recall how I felt.
Q. How did you feel at the moment when you had the palpitations?
A. Probably not too well.
Q. Did you ever go to a sanatorium?
A. Yes, I remember going to one.
Q. What was the name of it?
A. I don't recall the name.
Q. What were the circumstances that led to your going there?
A. I don't remember why I went or what happened, I remember being there though.
Q. How long were you there?
A. I don't remember. I don't think it was for very long. I really can't reconstruct that whole period. (Janis, 1950a, pp. 369-370.

Note that the woman has many gaps in her recall and needs specific prompting by the interviewer. Sometimes she recalls facts when prompted ("now that you mention it ....."). Dr. Janis gives several additional detailed examples and summarizes as follows:

> ... the examples fail to convey the extensiveness and variety of personal experiences subject to amnesia in each individual case. Every one of the 19 patients included in the study showed at least several instances of amnesia and in many cases there were from ten to twenty life experiences which the patient could not recall . (Janis, 1950a; my italics.)

In contrast, the control patients were able to reproduce practically all the material they had given in the initial interview, and they recalled it

so readily that the examiner rarely needed to resort to raising questions giving specific cues so often required by the ECT patients. In fact, most of the control patients improved between the tests, as one would have expected because of the stimulation of "reliving" old events (Janis and Astrachan, 1951). Janis discovered amnesias in patients diverse in personality type and intellectual status, in patients with different types of mental disorders, in patients who improved psychologically, and in those who did not improve. These amnesias were in some instances for emotionally upsetting material, e.g., related to the illness, but in other instances were for emotionally "neutral" material as well. Furthermore, Janis notes, "many patients were distressed about their failure to recall past experiences and frequently made definite efforts to secure information about the events for which they were amnesic". He says, "The patients usually expressed little conviction about the occurrence of such experiences and were unable to reconstruct the details beyond what they had been told about it." (Janis, 1950a, P. 376). Janis notes that there was no tendency for patients to "protect" their amnesias since they sometimes actively sought for cues to help them remember. Therefore, even strong motivation to remember did not help.

A later study employing a somewhat different set of questions revealed "gross amnesic gaps" such as total failures to recall a particular job. Again, there were also more subtle amnesias such as failure to recall details of a specific event. Janis found, in addition to the gross gaps and subtle losses, a slowness and a great effort in recalling details. In some cases, details returned, but only with great effort and with the help of cues provided by the examiner (Janis and Astrachan, 1951). In his published papers, Janis reports following half of the shocked patients for $2\frac{1}{2}$-$3\frac{1}{2}$ months after

the end of ECT. He found that in each case most of the instances of amnesia persisted. Janis continued to follow six of these patients for a full year and found that the amnesias persisted (Janis, 1976).

The Janis studies employed the most sensitive method of any in the literature and the one that most directly addresses the concern of the patients, the loss of their own memories of their pasts. It would seem to me incumbent upon any researcher who fails to find memory loss using an artificially-devised test to explain the Janis results. The simplest explanation at present is that the artificial tests are not as sensitive. No author so far has mounted serious criticism of the Janis studies, nor has anyone repeated them. The Janis results fit well with the evidence cited earlier that ECT causes organic brain damage. Overall, the evidence convinces me that ECT is far from benign. If, for others, doubts remain as to whether ECT impairs human memory, the first step toward settling the issue should be a careful and thorough repetition of the Janis studies.

OVERALL CONCLUSIONS

1. Convulsions caused by electrical shocks to the brain are accompanied by alterations within the brain. Many of the brain's natural protections are broken down. Mentioned in particular are the massive rise in blood pressure, the breakdown of cerebral autoregulation of blood flow, and the breakdown of the blood-brain barrier.
2. Such changes can lead to alterations in brain chemistry and physiology. The change most easily measured in humans is the alteration of the EEG toward a form that is commonly recognized as pathological.

3. Such changes are also associated in many studies with gross pathology such as brain swelling (edema) and particularly brain hemorrhages which lead to the irreversible death of neurons.
4. Such changes are also associated with persisting, probably permanent amnesias for life events and experiences.
5. Such amnesias may only be detected when patients are questioned in detail about their life histories before and following the administration of shocks.
6. At all levels, from changes in blood pressure to losses in memory, there is extreme variability. Losses can, however, be catastrophic after only a few shocks. In general, the younger and healthier the animal or person, the less permanent damage may result.
7. Such losses of memory can and do occur without any necessary changes in overall intelligence as measured by a psychological test and without any other detectable neurological abnormalities. This finding is common not only with ECT but in brain damage accompanying other kinds of insult such as trauma or toxicity.

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