Reprinted from

RESEARCH REVIEWS

MARCH 1953

Brain Surgery by Sound

William J. Fry

OFFICE OF NAVAL RESEARCH
DEPARTMENT OF THE NAVY WASHINGTON, D. C.
Brain Surgery by Sound

William J. Fry

...is Head of the Bioacoustic Laboratory at the University of Illinois, where he is investigating ultrasound as a tool for studying the structure and function of biological systems.

Brain and spinal operations are among the most delicate which the surgeon is called upon to perform, for death or paralysis can result when even a small volume of vital nerve tissue is destroyed. Moreover, with even the most expert of modern operating procedures, such injuries sometimes are unavoidable; cutting out a deep-buried growth, for example, may involve the laceration of surrounding healthy tissue. For this and other reasons, our work in applying ultrasonic waves to neurosurgery may open new possibilities for successful brain surgery.

Brain surgery, up to the present time, has involved either direct cutting of brain tissue or the coagulation of the tissue by the insertion of electrically excited probes into the region to be destroyed. A program at the University of Illinois partially supported by ONR, has shown that much finer and more delicate operations may be performed by subjecting the region of the brain requiring treatment to a focused beam of inaudible (ultrasonic) sound. Such "surgery" has already been accomplished on animals and its extension to humans awaits only the construction of an instrument suitable for hospital use.

When research was started, we did not actually envision any such immediate practical application, but were merely investigating the possible effects of inaudible sound on nerve tissue. Frogs were used in our first experiments, which subjected to high-intensity sound the region of the back immediately over the portion of the spinal cord containing the nerve cell bodies which control the muscles of the hind legs. The sound, transmitted to the frog through water, produced permanent paralysis of the legs after a brief exposure. The minimum time required to obtain this effect was dependent on the sound intensity—that is, as the intensity increased, the time required for paralysis decreased.

There was a minimum intensity, however—a threshold value—below which no paralysis occurred no matter how long the animal was subjected to the sound. This threshold intensity is very high compared to the intensity of audible sounds. If a frog is exposed to sound above the threshold value, but for a time insufficient to cause paralysis, the frog is more easily paralyzed by a second exposure which takes place minutes later. This increased susceptibility has been found up to 15 minutes after an exposure.

In subsequent investigations various portions of the brains of cats and monkeys have been irradiated by focusing the sound beam on the
selected region. In this way very small sections, of the order of a few millimeters in linear dimensions, can be affected without disturbing the neighboring tissue. In the studies on cats and monkeys, an opening is made in the skull through which the sound beam is passed. This procedure is necessary because high-frequency sound is greatly absorbed in bone. After the animal recovers from the anesthetic it is examined for changes in muscle control, coordination of movement, etc. Following this phase of the investigation, which may require a period of months, the animal is sacrificed and the changes in the brain produced by the sound are studied microscopically.

The determination of the underlying mechanism was an objective of the program. Why did the sound produce such effects on nerve tissue? It was at first thought that the temperature changes produced by the high-intensity sound might account for these effects. The amount of heating produced in the tissue was therefore determined by direct measurements made with imbedded thermocouples. However, these showed that the effects produced by the sound occur well below the region of damaging temperature levels. Temperature changes, then, are clearly not responsible for the changes in the brain tissue. Additional evidence of this is obtained from studies made with frogs subjected to multiple exposures of the sound. The time interval between exposures can be chosen so that the temperature of the tissue returns to normal between exposures. Permanent changes in the nervous system can nevertheless be produced.

The changes made by the sound may possibly stem from its direct action on large molecules or higher organizations in the individual cells of the tissue. This could, perhaps, account for the great differences in the susceptibility of various types of tissue to change by sound. It is possible, for example, to arrange the dosage to destroy nerve cell bodies in any desired region of the brain or spinal cord without deleterious effects on the blood vessels or nerve tracts in the same region. It is even possible to depopulate a region of large nerve cells and not change appreciably the population of the small nerve cells in the region. Such selective action furnishes an ideal technique for studies on brain structure and function.

A portion of this cat's anatomy has been subjected to a focused beam of sound, causing a permanent motor deficit. Note the abnormally raised hind leg (left) and the awkward position of the front legs (right).
The adult rat above, subjected to a sound dosage just after birth, was left with hind legs paralyzed. Note, above right, the small size of this rat as compared with a normal rat. Picture at right shows another with paralyzed tail as well as hind legs.

The great advantage of this method as compared with direct cutting away or coagulation of brain tissue is the range of susceptibility of the components of the brain to action by the sound. In cutting and coagulation, all tissue in a given region is destroyed: nerve cells, nerve fibers, and blood vessels. Thus there is obviously no possibility of differentiating between different types of nerve cells or of producing a partial depopulation of the nerve cells in a region. Even more serious, parts of the nervous system not directly connected with the region being operated on are affected because of the interruption of the blood supply and fiber tracts. Moreover, with these older methods, the production of a lesion of a special shape in the nervous system also presents difficulties. When a suitably controlled focused beam of inaudible sound is used to produce lesions, all of these difficulties are surmounted.

As a specific example of the work currently in progress on the structure of nervous systems and its relation to function, we can describe briefly the changes in behavior which occur in cats when the bulbo-occipital inhibitory formation is subjected to a focused beam of sound. All cats treated in this way showed a permanent motor deficit with a resting posture of extended fore limbs and slightly flexed hind limbs. Although the pattern of muscle movement and control (and the goose-step walk of the fore legs) are best illustrated by motion pictures, still shots are useful for some aspects. The first picture shows how the cat's hind legs are raised abnormally in walking, as if it were continually stepping over an obstacle. The awkward position of the fore limbs as the cat eats is shown in the second picture. The legs are displaced laterally and toward the rear of the animal, which appears indifferent to being placed in clumsy positions.
Some effects of irradiating regions of the spinal cord with sound are illustrated in the pictures of adult rats which had been subjected to the sound just after birth. The first picture shows the position of the paralyzed hind legs as the animal moves about. The tail, unaffected, is used normally. The marked longitudinal compression of the posterior region of the treated animal can be seen in the second picture. Note also the small size of this rat in comparison with the normal rat. The next picture shows an adult female rat which was subjected one day after birth to a sound dosage which paralyzed both hind limbs and tail.

Our work up to the present time has been accomplished with a single beam-focusing sound source, which produces lesions small in cross section but relatively long. To obtain lesions small in all three dimensions, a multiple-beam instrument, now under development at this laboratory, will be used. The conditions of the irradiation will be chosen so that only in the region where the beams intersect will the sound level be high enough to produce permanent changes in the nerve tissue. Thus it will be possible to reach any desired region of the brain and produce a change therein without damage to tissue through which the sound beam must pass to reach this region. It is visualized that this type of apparatus may be used in human neurosurgery.

It is expected that the use of inaudible sound in the treatment of disorders of the nervous system may bring within the scope of medical therapy a wide variety of pathological conditions which can not now be treated successfully. In addition it appears that, because of the nature of the changes produced by the sound, including the non-interruption of blood vessels, many conditions now handled by standard neurosurgical practice could probably be better treated by the use of focused inaudible sound.