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1. Learning Outcomes

After studying this module, you shall be able to

- Learn the importance of electroencephalography in the study of brain
- Learn the procedure and evaluation of the electrical stimulation of the brain
- Understand the procedure and evaluation of stimulating the brain in its depth called the deep brain stimulation
- Learn the procedures to evaluate other techniques like cranial electrotherapy stimulation, trans-cranial magnetic stimulation electro convulsive technique, and vagus nerve stimulation method.

2. Introduction

Brain Imaging is progressively becoming the most important tool of investigation. A_variety of such techniques now provide sensitive details of the brain structure and functions. Many imaging techniques are non-invasive and can monitor data along the continuum of their duration.

Brain imaging provides data to identify structures and functions of brain areas in normal as well as abnormal functions. Several diseases of the brain can, thus, be identified, and potential therapies may be delineated. The effects of such therapies on brain can also be studied through the imaging techniques.

Imaging techniques may be used to study the cellular networks, genetic compositions, and functions. Such techniques have unique value in the study of the nervous system, though they are used to image other parts of the body as well. The potential target areas of the brain under research in this procedure are the cortex, thalamus, hypothalamus, basal ganglia, amygdala, hippocampus, and the limbic system, among others.

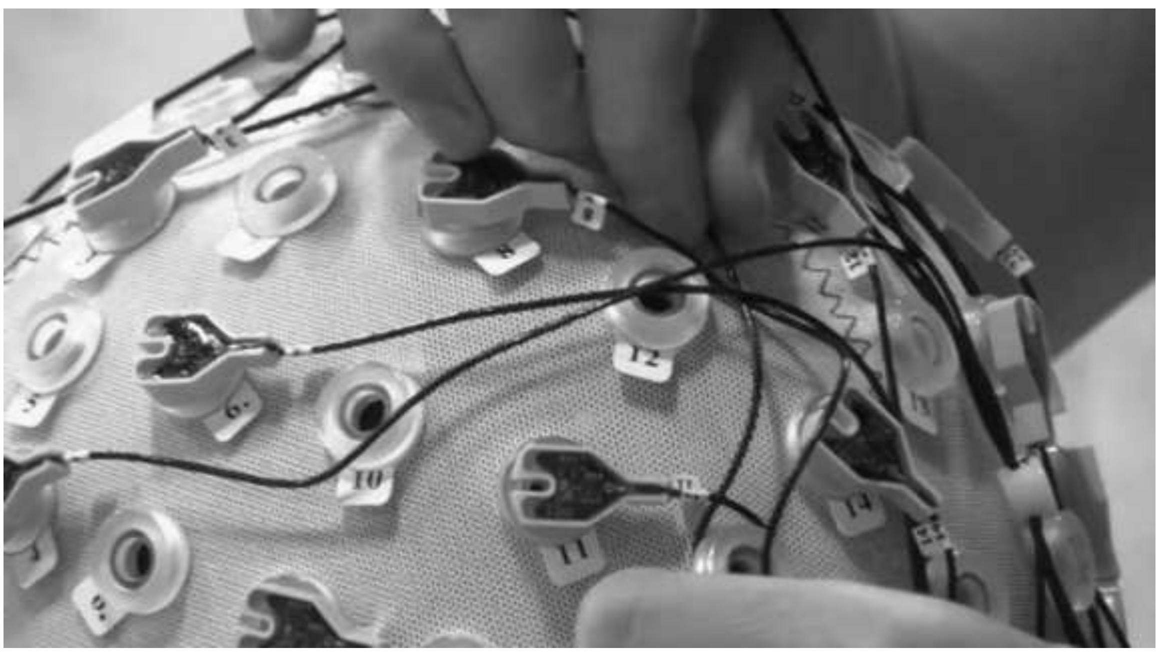
There are two aspects of the use of electrophysiological research in the field of neuropsychology. Firstly, it is a tool to record the structure and functions of the brain in times of health and disease. Secondly, it is a tool to stimulate the brain to effect certain treatments or cure for several pathological conditions. The electroencephalography is used primarily to understand the functions of the brain whereas the other techniques mentioned below are primarily of the therapeutic use

3. Electroencephalography (EEG)

Millions of neurons in the brain remain in an electrically charged condition. The electrical charge is produced by a chemical process involving the movement of several ions across the membranes of the cell. The movement of ions changes the resting level of neurons into action potentials, which indicates an electrical change in the cells. The movement of ions is caused by certain proteins in the brain cells. The changes in the electrical potentials of neurons can be picked up by the metal electrodes since electricity can be conducted through the metal. When these metal electrodes are inserted into the brain tissue, they pick up electrical changes which are measured by a voltmeter. Such recordings are called the electroencephalographs (EEG).

The electrical impulses are too small to be detected by the observation with an unaided eye. Microscopes are needed for the purpose. The size of such changes, also known as the nerve impulses is generally recoded from a group of neurons which are showing similar electrical changes on stimulation. Activity of a single neuron is too minute and too isolated to be understood and analyzed. The electrodes can better pick up electrical activity from the surface of the brain rather than from its deep structures. The EEG patterns are important indicators of several conditions related to brain, such as; various stages of sleep and pathological conditions like epilepsy, among others.

Electroencephalography is a non-invasive technique that senses electrical impulses in the brain due to neuronal activity using electrodes placed on the patient's scalp. The recording of conventional EEG represents changes in electrical activity in the order of tens of milliseconds, and is used to monitor responsiveness, coma and brain death; locate areas of damage following head injury; and investigate epilepsy. The spatial resolution of the EEG techniques is limited due to the layers of cerebrospinal fluid, skull, and scalp between the electrodes and the current source in the brain. Consequently, the electrical potential distribution on the scalp is blurred and it is difficult to determine the location of regions of activity. The following figure shows electrodes planted for recording EEG from the scalp of the organism;



High Resolution EEG provides a numerical estimate of the electrical potentials near the cortex surface, and it has been used as a tool in the study of cortical activation during external stimulation and the study of cognitive under specific patterns of brain stimulation. .

In EEG, electrodes collect nerve impulses from the brain, and display them on the computer, which may be printed on the electroencephalograph paper. Such recordings are known as electroencephalograms. The EEG patterns may be recorded for specifically produced sensory input, such as; high intensity lights or loud music etc.This is the study of the electrical activity of the brain.
The EEG can detect change over milliseconds. Several other methods of imaging the neuronal activity in the brain, such as; scanning the emission of positrons through PET (Positron Emission Tomography), and studying the magnetic resonance of cells through the f MRI (functional magnetic resonance) have been used. The measurement of blood flow in the brain, an indirect study of its function, has been done using the techniques, such as; SPECT, and fMRI. The study of the metabolic activity of the brain is done using methods like PET and NIRS. Several methods can be used in combination to see all such functions simultaneously. The oscilloscopes have been devised to compute the changes in their inbuilt computers to study the brain for different functions as differentiated from each other. The spatial as well the temporal resolution of the neural tissue can be taken up simultaneously.

Process of EEG

The standard EEG is a painless procedure of about one hour. The patient lies down on a padded bed. Electrodes are fixed onto the scalp. The electrical impulses generated by the brain are picked up by the electrodes.

The sleep EEG is a record of brain activity during sleep, and is generally carried on for two to three hours. It is important to conduct it in a quiet room where the patient can fully relax.

A portable cassette recorder is required to be attached to the electrodes fixed on the patient's scalp for taking up the ambulatory EEG. It is record of brain activity when the patient is in motion, i.e., he is moving from one place to another. The patient can do normal activities as the electrodes are on. It may take about twenty four hours to complete the procedure.

The more relaxed a person is the greater the amplitude and the lower the frequency of the waves. The lower the amplitude and the greater the frequency, the more likely it is that the person is in an excited state.

Eye and jaw movements can cause fluctuating electrical fields across the scalp thus subjects are requested to remain still and to minimize eye blinks/movements

Potential risks with EEG

The Spatial resolution is poor in comparison to other imaging techniques. The patient may be asked not to take certain seizure or antidepressant medications 1 to 2 days before having an EEG. This may make the person more prone to having a seizure, which is exactly what the doctor would like to measure. During an EEG, the doctor may encourage things that stimulate seizures, such as deep breathing or flashing lights, so that he or she can see what happens in the brain during the seizures.

4. Electrical Stimulation of the Brain (ESB)

This method involves insertion of electrodes into the brain of a living animal and sending of a weak electric current into the brain to mimic a nerve impulse (i.e. a false nerve impulse will make the brain react as if real impulse from sensory receptor has been received).

After the exciting discovery that the nerves and the muscles could be electrically stimulated, the method of electrical stimulation of the brain became one of the most important method to study the localization of various functions in the cerebral cortex. Localization of motor activity in the frontal cortex was the first established research in this context. The study of the functions of hypothalamus is another area of research with this method of electrical stimulation of the brain (ESB), also known as the method of stimulation in animals as well as human beings.

The research into the study of brain body relationship took an impetus with the invention of the stereotaxic apparatus, and the development of techniques to gather EEG records of live normally behaving animals in a chronic fashion. Stereotaxic apparatus with stereotaxic atlas is a devise to precisely locate areas of the brain. The chronic implants are done through inserting micro-electrodes in brain tissue in an anaesthetized animal, and then bringing it back to consciousness without removing the micro-electrodes. So, that particular area remains in a constant state of stimulation. This approach has been used to discover pleasure centre in the brain, and other functions of hypothalamus and frontal cortices, in particular. This method, in fact, has helped researchers to map the whole body parts and functions on the total territory of the cerebral cortex.

The following picture of the monkey shows that the diameter of the pupil can be electrically controlled as if it were the diaphragm of a photographic camera lens

http://www.cerebromente.org.br/n18/history/stimulation_i.htm)

Using the electrical stimulation method, Olds and Milner (1954) observed that some animals seem to behave in a manner that increased the amount of intracranial stimulation that they received. Further investigation demonstrated that rats will press a lever as rapidly as 2000 times each hour to obtain electrical brain stimulation, and they will continue responding at this rate for twenty-four hours or longer. They will ignore other rewards, such as water or food, to continue working for electrical stimulation.

One of the problems of micro-electrode research is that when they are inserted into the brain tissue, they activate the nearby neurons even if they are four millimeters away. It happens with neurons whether they are near the tip of the microelectrode or slightly above in the vicinity of the insulated microelectrode. As the current gets increased, the number of neurons thus activated also increases, and the current spreads to slightly farther off areas. Such findings have been revealed through the two-photon excitation microscopy. It makes it a bit difficult to establish the brain behavior relationship. The neuron in the areas near the microelectrode gets depolarized even without the chemical process of synaptic transmission.

Electrical stimulation of the brain is one of the best methods to study the functions of the brain. However, stimulation also is a method to destroy or lesion out areas of the brain. If not handled properly, it will lead to unwanted damage of the brain areas. Lesion, however, has been found useful for the treatment of certain pathological conditions of the brain like tumors, Parkinson's disease, psychosurgery and focal epilepsy. It also throws light on the abnormal ly functioning areas of the brain.

The electrical stimulation of the brain (ESB) provides insight into functioning of the brain but the problem in interpretation is that no single area of the brain is the only source of a behavior/emotion. Besides, the ESB provoked behavior is compulsive and stereotypical. It does not perfectly mimic natural behavior. The ESB effects may depend on a multitude of factors depending on individual reactivity. The ESB does not induce a beneficial permanent change. Instead, it may produce only a transient emotional tranquility.

. Variants of Electrical Stimulation of the Brain

A large number of techniques to electrically stimulate the brain have been developed. Most of them have been developed for therapeutic purposes. A few examples are described below;

- Cranial Electrotherapy Stimulation (CES)
- Deep Brain Stimulation (DBS)
- Tran cranial Magnetic Stimulation (TMS)
- Electro-convulsive Technique (ECT)
- Vagus Nerve Stimulation (VNS)

A brief description of each one of them is given below;

5. Cranial Electrotherapy Stimulation (CES)

In order to treat minor psychiatric problems, such as; depression, generalized anxiety, sleeplessness, and overwhelming stress reaction, Cranial Electrotherapy Stimulation (CES) may be used. It involves applying small currents across the patient's head which mildly stimulates the brain.

It stands verified that cranial electrical stimulation reduces the stress levels of an individual. The mode of action of this procedure is not very clear. One of the hypotheses is that it reduces the disequilibrium caused by multiple systems of arousal that accompany stress. However, this procedure is not habit forming or addictive.

The investigations have revealed that the nerve impulses initiated by the procedure of cranial electrical stimulation lead to the release of certain neurotransmitters, such as; nor-epinephrine, dopamine, serotonin, DHEA, and endorphins etc. It is also linked with decrease in the level of cortisol. After a CES treatment, patients are in an alert, yet relaxed state, characterized by increased alpha and decreased delta brain waves as seen through the electroencephalograph. The production of such neurotransmitters takes place in a balanced manner. It, thus, stabilizes the neuro-hormonal system of the organism.

The procedure of cranial electrical stimulation involves a current given to the hypothalamus. The nature of nerve impulses can be interpreted through the analysis carried out by the computer. The foci of nerve impulse generation can be in the deeper layers of the brain as much as on the cortical surface. A comparison of the cortical and sub cortical magnitude of stimulation can be interpreted for the study of arousal patterns under states of emotions.

6. Deep Brain Stimulation (DBS)

Sometimes, pathologies are related to the irregular electrical activity in deep circuits of the brain. The procedure of deep brain stimulation (DBS) involves surgically implanting electrodes, or wires, in the brain that deliver electrical impulses to the brain tissue and consequently change this activity.

This system of electrical impulses has three parts,. They all are under the skin:

- The wires, leads, or electrodes implanted in the brain
- A battery pack , or a generator, or IPG, that generates electrical impulses
- Wires that connect the electrodes and the generator

The generator is carefully programmed for each patient to deliver electrical impulses to the carefully demarcated sites in the brain. The process is specifically monitored for every patient's unique brain anatomy, individual symptoms and specific disease so that everyone achieves some relief.

Electrodes are implanted in selected areas of the brain, and then electrically stimulated to see their effects on the brain.

Deep brain stimulation is done when the patients is awake. Light sedatives may be given. It has generally been done under two conditions;:

- **Stage 1**: The neurosurgeon makes a very precise roadmap of the brain with images obtained through an MRI or CT scan. Once the target areas are located, the surgeon implants the wires, or electrodes, in the brain. Patients usually stay in the hospital for 1-2 days after this surgery.

- **Stage 2**: The neurosurgeon implants the battery pack and connecting wires in the chest 10 to 14 days after Stage 1. Patients are usually awake and can go home the same day. The generator that controls the electrical impulses in the brain is turned on two weeks after the implantation.

. The surgery relieves symptoms, but it is not a total cure. It can also take up to six months of adjustments after surgery for some patients to achieve optimal results.. Significant relief has been reported by patients of Parkinson's disease, dystonia, tremor, Tourrette's disorder, depression, obsessive compulsive disorder, among others. However, the procedure may be risky for older patients, those having hypertension, and those suffering from seizures. Infection due to implanted devices may be another complication.

In a specialized research, the neuronal activity during the cognitive functioning of an organism is the focus of analysis.

Potential Risks of DBS

The risks associated with the implant procedure for Medtronic DBS Therapy may include serious complications such as coma, intracranial hemorrhage, seizures, paralysis, cerebral spinal fluid leakage and weakness. Some of these may be fatal. Medtronic DBS Therapy may cause worsening of some symptoms associated with Obsessive-Compulsive Disorder, and may cause changes in mood. Stimulation parameters may be adjusted to minimize side effects and attain maximum symptom control.

7. Trans cranial magnetic stimulation (TMS)

Trans cranial magnetic stimulation (TMS) is a method in which invasion of the brain is not required. It causes depolarization or hyper polarization in brain cells. It is carried out by using a rapidly changing magnetic field; which can cause activity in specific or general parts of the brain with little discomfort. It, thus, allows for study of the brain's functioning and interconnections. Another variation of TMS, repetitive Trans cranial magnetic stimulation (rTMS) has also been developed.

Tran's cranial stimulation method involves the use of a magnet to stimulate the brain. In this procedure, short electromagnetic pulses are transmitted to the brain through a coil. The coil is held against the forehead of the individual. The stimulation of the brain tissue happens when the pulses pass through the skull. It is targeted at a specific region of the brain. The targeted areas have to be carefully localized since the pulse reaches only around two inches into the tissue of the brain. The strength of the magnetic fields is to be kept as much as is normally needed in the procedure of magnetic resonance imaging. The method of Trans cranial magnetic stimulation has been successfully used to treat disorders like dystonia, i.e. loss of muscular tone, depression, tinnitus, Parkinson's disease, migraine, and even stroke. For general studies involving the relationship between brain and behavior also, this technique has been found to be very beneficial.

The shape of the skull is not a smooth surface. Therefore, conduction of electricity or magnetism cannot be uniformly distributed across its surface. Even the pathway of the flow of this current is difficult to follow and chart out, Deep Trans cranial magnetic stimulation, which is a variant of the above mentioned procedure, reaches up to about six centimeters deep into the layers of the brain. The deeper layers which control movements of the limbs, thus, can be monitored through this technique.

The Trans magnetic stimulation produces neural activity below the cortical surface. The activity in muscles, called the motor evoked potentials can, thus, be generated by stimulating the primary motor areas in the frontal cortex. The muscle activity can be recorded in the form of electromyography. Similarly, stimulation of the visual cortex of the brain produces flashes of light which may be seen by the individual. In other regions of the cerebral cortex, the participant does not consciously experience any effect, but his or her behavior may be slightly altered (e.g., slower reaction time on a cognitive task), or changes in brain activity may be detected while performing certain sensory motor tasks

TMS can be used to study damage from stroke, multiple sclerosis, amyotrophic lateral sclerosis, movement disorders, motor neuron disease and injuries and other disorders affecting the facial and other cranial nerves and the spinal cord. TMS has been suggested as a means of assessing short-interval intra-cortical inhibition (SICI)

Repetitive TMS (rTMS) may be used for therapeutic purposes also. It may be utilized to restore balance in motor areas of the two hemispheres in stroke patients. The evaluation of its effectiveness is simultaneously provided

The effects of rTMS are longer lasting. If the intensity of stimulation is larger, it increases the excitability of the cortico spinal tract. It produces effects similar to the long term potentiation or the long term depression depending on the higher or the lower intensity of stimulation.

8. Electroconvulsive Techniques(ECT)

It is a procedure to administer electric shock to produce seizures in the brain for a fraction of a second to cure chronic conditions. The procedure has been substantially modified to minimize the intensity and extent of seizures produced in the brain. Electroconvulsive techniques are of immense value in the case of patients who do not respond to chemotherapy. Depression, bipolar disorder, suicidal ideation, and catatonia are the conditions where it has been most frequently tried.

Tranquilizers and general anesthesia with muscle relaxants are needed to be administered before starting the procedure. The muscle relaxants can prevent dangerously strong muscular contractions and movements. An electric current is passed through the brain via the electrodes placed on the predetermined sites on the brain. It results in the convulsions for about one minute. It is assumed to cause bio-chemical changes in the brain. It directly affects the functioning of the brain.

The patient's body shows no signs of seizure, nor does he or she feel any pain because he is under anesthesia. He may feel extremely tired after he awakens after about five minutes. He may be able to resume normal activities after about one hour.

The side effects of ECT are numerous. They involve stomach problems, severe headaches and even severe memory problems. The memory problems may last longer than others after the course of ECT treatments is over. About 10-12 such procedures may be needed for a severely depressed patient. The side effects are more pronounced in the bilateral ECT where electrodes are implanted on both sides of the brain compared to the newer method of unilateral ECT which requires electrodes to be fixed only on one side, i.e., the right side of the scalp.

9. Vagus nerve stimulation (VNS)

Vagus, the tenth cranial nerve, serves certain important areas of the brain and the body. In order to stimulate these areas, the vagus nerve itself may be stimulated. A device is implanted under the skin which stimulates the left vagus nerve. It sends excitation to brain areas such as; hypothalamus and other areas which control mood, sleep, and other functions. Stimulation of vagus nerve also affects functions of the lungs, intestines, and heart.

Vagus nerve stimulation was first used for controlling seizures in epilepsy. Its effectiveness in depression was later recognized. The electrical impulse that appeared to alter certain neurotransmitters associated with mood were serotonin, norepinephrine, GABA and glutamate.In 2005, the U.S. Food and Drug Administration (FDA) approved VNS for use in treating major depression in certain specified circumstances.

The procedure of vagus nerve stimulation is a complicated one. In this, a pulse generator has to be implanted in the patient’s chest on the upper left side. It is connected to the left vagus nerve in the neck region via a wire which travels below the skin only. Pulses to the vagus nerve are sent through the generator. The electrical pulses lasting about thirty seconds each are sent after every five minutes. It can be neatly programmed into the generator. The vagus nerve, then, stimulates the related brain and body areas to produce the desired effects. It may cause slight coughing and hoarsening of voice, but the procedure is painless

The magnet placed on the chest is the procedure to deactivate or to reactivate. Deactivating is generally required when the side effects become rather too uncomfortable for the patient. It may also be needed when the patient gets physically tired since it may obstruct breathing.

Vagus nerve originates at the level of medulla and carries both sensory and motor fibers. The affererent fibers of the vagus nerve connect to the nucleus of the solitary tract .The solitary tract projects to other locations in the central nervous system. Little is understood about exactly how vagal nerve stimulation modulates mood and seizure control .It has been hypothesized that alteration of nor-epinephrine release caused by projections of solitary tract to the locus coeruleus, elevated levels of inhibitory GABA , and inhibition of aberrant cortical activity by reticular system activation may be the basis of the beneficial effects.

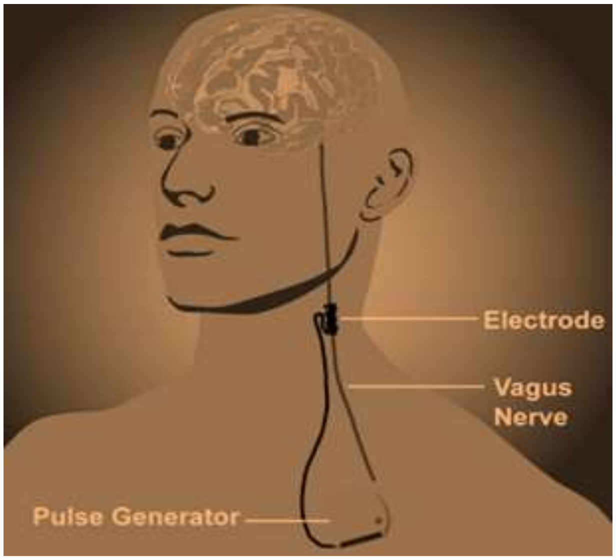
Direct vagus nerve stimulation requires the surgical implantation of a stimulator device. On the other hand, the cyberonics VNS devices consist of a titanium-encased generator about the size of a pocket watch with a lithium battery to fuel the generator, a lead wire system with electrodes, and an anchor tether to secure leads to the vagus nerve.

An incision is made in the upper left chest and the generator is implanted into a little pouch on the left chest under the clavicle. A second incision is made in the neck, so that the surgeon can access the vagus nerve. The surgeon then wraps the leads around the left branch of the vagus nerve, and connects the electrodes to the generator. Once successfully implanted, the generator sends electric impulses to the vagus nerve at regular intervals. In order to avoid negative side effects on the heart, the left vagus nerve is stimulated.

Other wearable devices are being tested and developed by that involve trans-cutaneous stimulation and do not require surgery. These devices are similar to TENS (Trans-cutaneous electrical nerve stimulation) devices that are often used for pain management.

The method of Trans-cutaneous vagus nerve stimulation (t-VNS) allows for the stimulation of the vagus nerve without surgical procedure. Electrical impulses are targeted at the auricle (ear), at points where branches of the vagus nerve have coetaneous representation. The method has been found to be useful in the treatment of epilepsy as well as for the management of pain.

(Source: http://pages.uoregon.edu/cfc/projects-bbl.htm)



Some of the major negative side effects of vagus nerve stimulation method are infections, hoarseness of voice, throat and neck pain, difficulty in swallowing and breathing, and the infections arising out of the surgical procedures. Additional surgeries may have to be carried out to correct such complications.

10. Summary

- Electro physiological recordings are important measures of the structural investigations of the brain.
- Electroencephalogram is indicative of normal and pathological conditions of the brain.
- In Cranial Electrotherapy Stimulation, a weak electric current is applied across the patients head which has beneficial effects in anxiety, depression , insomnia etc.
- In Deep Brain Stimulation, the electrodes are implanted in the brain which deliver electrical impulses and change its activity
- In Transcranial Magnetic Stimulation, electromagnetic induction is used to induce electric currents in the neurons.
- Through Electro Convulsive Technique, seizures are produced in the brain which affect chronic conditions of depression and others.
- In Vagus Nerve Stimulation, surgically implanted pulse generator in the chest produces impulses in brain.