



REVIEW ARTICLE

DEEP BRAIN STIMULATION; HISTORY'S FRUITION OR A FUTURE'S FRUSTRATION?

*Hani Alharbi and Muhanad Alsarrani

Maastricht University, Netherlands

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ABSTRACT

Initially Deep Brain Stimulation was thought to act like the functional ablation, after many studies showed DBS acts by antidromic activation and that responses depend on both GABAergic and glutamatergic transmission. This understanding helps greatly on weighing the risk-benefits ratio of treatment, because the advances of psychosurgery technological benefits have dramatically increased while the risks have been reduced. In the course of time, we come to realize that different parts of the brain do different things. There are areas of the brain dedicate to control your movement, vision, memory and so on. When these work well, the nervous system works well and everything is function. However, once in the while, things do not go so well and there is trouble in the circuits, where some neurons misfire and causing trouble, or sometime they are underactive and they are not working, as they should. The manifestation of this depends on where in the brain these neurons are. So when these neurons in the motor circuit, motor dysfunction will result, such as Parkinson disease. When the malfunction in the circuit that regulate your mood you will get depression or mania, and when it is in the memory you will get Alzheimer disease. The main principle of DBS is to interfere with the circuit and turn them up or turn them down. What makes DBS superior to ablation? DBS can be adjusted based on the symptoms or the progress of disease and overall it is reversible, and less damaging than lesion surgeries.

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INTRODUCTION

Before we start our journey into the amazing world "the brain", I would like you to take a few seconds to imagine how your life would be if you could have amagic bottom where you can turn it "on" or "off" to adjust your mood, to become happy when are depressed, or even healthier. I know it is hard to believe but science has made the magic to become real. Our brain is a fantastic control cabinet; it organizes and makes the whole body function in the right way. However, when something goes wrong in the brain, dysfunction and handicapped may results. If we look back into the past, we can see that the treatment of psych-neurological problems has been there for long time. Surgeons knew that the brain was involved somehow in neurological and psychiatric diseases. At the beginning, the dominant thought was that if you have a psychiatric disease, you must be possessed by evil spirit, and the way to treat this disease is by making a hole in your skull and let the evil spirit escapes. Neurosurgery was common at that time 7000 years ago. Initially Deep Brain Stimulation (DBS) was thought to act like the functional ablation, after many studies showed DBS acts by antidromic activation and that responses depend on both GABAergic and glutamatergic transmission.

This understanding helps greatly on weighing the risk-benefits ratio of treatment, because the advances of psychosurgery technological benefits have dramatically increased while the risks have been reduced. In the course of time, we come to realize that different parts of the brain do different things. There are areas of the brain dedicate to control your movement, vision, memory and so on. When these work well, the nervous system works well and everything is function. However, once in the while, things do not go so well and there is trouble in the circuits, where some neurone misfire and causing trouble, or sometime they are underactive and they are not working, as they should. The manifestation of this depends on where in the brain these neurones are. So when these neurone in the motor circuit, motor dysfunction will result, such as Parkinson disease. When the malfunction in the circuit that regulate your mood you will get depression or mania, and when it is in the memory you will get Alzheimer disease. The main principle of DBS is to interfere with the circuit and turn them up or turn them down. What makes DBS superior to ablation? DBS can be adjusted based on the symptoms or the progress of disease and overall it is reversible, and less damaging than lesion surgeries. Stem cells located in the brain stop dividing; there is a reactivation of some sections of chromosomes beginning to form specific structures of neurons and connections. Since then, the cell can be considered a full-fledged neuron. One of them is our memory. Another area of the brain is responsible for movement. This explains the partial

*Corresponding author: Hani Alharbi,
Maastricht University, Netherlands.

and complete recovery of the relevant functions of the brain. Deep brain stimulation is an evolution of the two surgical procedures. It helps to control the symptoms of certain disorders, such as Parkinson's disease, idiopathic tremor and multiple sclerosis. Nowadays, the investigators study the use of deep brain stimulation for certain types of mental disorders, including obsessive-compulsive disorder, personality disorders and severe depression which are resistive to other forms of treatment. Deep brain stimulation may be a good treatment option for the treatment of difficult mental states. The thalamus works as a "relay station" for the signals, coming to and from other parts of the brain, including the amygdale. That is associated with fear and stress.

Our next stop of the journey is to see how DBS system works. DBS consists of three parts, they are: a thin, insulated wire, it is an electrode that is placed in the brain; neurostimulator, similar to a pacemaker, which is usually placed under the skin near the collarbone, but may be located in other parts of the body; the third one is also thin insulated wire, that does for the neurostimulator. DBS for adults usually consists of two distinct operations. 1st stage is usually carried out under local anesthesia, that means one do not sleep, but do not feel pain. If the procedure is carried out among children, they are given general anesthesia. To carry out the procedure the head must be placed in a special frame and fixed with the screws to hold it during the procedure. Numbing medicine also extends to the scalp, it is the place where the surgeon will drill a small hole in the skull and will place the electrode in a certain area of the brain. If both sides of the brain are being treated, the surgeon will open both sides of the skull, and the two wires will be inserted. There will be spent a great variety of neurological tests, just to be sure that the electrodes are rightly inserted. 2nd stage is performed under general anesthesia. The terms of this stage of operation depends on how and where the stimulator will be placed in the brain. The surgeon makes a small hole, usually just below the collar bone and implants the nerve stimulator. The expansion cable is also placed behind the ear. Expansion wire is connected to neurostimulator.

These tiny pulses interfere and block the electrical signals which cause the symptoms and tremors, movement disorders; they can be associated with Parkinson's disease, essential tremor, or obsessive-compulsive disorder. This operation can be an alternative one, especially for patients with severe symptoms of Parkinson's disease, which cannot be controlled just with the help of medications. Surgery does not cure Parkinson's disease, but may help in reducing the severity of symptoms, such as: tremors, rigidity and slow movements. Deep brain stimulation can also be used to treat the following conditions: tremor, dystonia, hand tremors associated with multiple sclerosis called Tourette's syndrome and obsessive-compulsive disorder. DBS is considered to be safe and effective. Risks are associated with deep brain stimulation may include: an allergic reaction; difficulties with concentration; dizziness; infection; leakage of cerebrospinal fluid, which can lead to headache or meningitis; loss of balance; slight loss of movement; problems with vision; temporary pain or swelling; temporary tingling on face, arms or feet. Usually, DBS is well conducted and does not damage the nerve cells as well as other surgical treatment of Parkinson's disease. Many patients notice a significant improvement of the symptoms after the treatment. However, most of them still need to take medications in smaller doses to improve their quality of life. This operation is risky for people over 70 years of age and for those who suffer

from chronic illness. DBS procedure can be canceled if it is necessary. Most of people, who had DBS, spent 3 days in the hospital. The doctor can prescribe some necessary antibiotics to prevent any possible infection. There most concerning issues of this procedure is the lack of strict selection criteria, psychiatric assessment and optimal imaging approaches. Despite the beneficial results of DBS in treating neuromotor dysfunction in patients who suffer from epilepsy or Parkinson disease, there are risk factors associated with DBS, even changes of personality could be a major risk. In one case of a Dutch patient with Parkinson's disease, DBS has led to increase the motor function; however, untreatable mania was induced, which left the patient incompetent. Mania subsided only when the stimulator was turned off, but then motor impairment reappeared. The patient reported "Now I feel like a machine, I've lost my passion, I don't recognize myself anymore!" Some identify changes of personality and personal identity authenticity and estrangement respectively are the main ethical problem in evaluating DBS.

However, Synofzik and Schlaepfer point out that personality and identity are not valid ethical criteria, because alteration of personality or personal identity is sometimes intended. Affecting personality is the main intended outcome in psychiatric DBS: 'if mood and cognitive behavior - would not change, for example, in DBS in a patient with obsessive-compulsive disorder or with major depression, it could not be considered an effective treatment'. Even in Parkinson's disease, where the main intended outcome is ameliorating motor function, change of personality or identity cannot be an ethical criterion, as Parkinson's disease itself alters a patient's personality. A change of personality in patients severely affected by Parkinson's disease might well be welcomed. Surely, not all personality changes are unproblematic. The investigators of Oxford and Virginia Universities are developing the new technology, it is associated with implantation of artificial memories, so that's the way they are trying to control the operation of the brain. At the moment, the scientists are working on one method, calling "record in memory". With the help of insects, they try to carry out the procedure. However, the most probable thing, that soon, the experts will be able to provide the technology for more complex organisms.

Following the procedure, it is possible to reprogram the whole body of insect. For example, to make them insensible to certain smells. It is quite difficult to apply such an operation for a person, so this perspective remains to be purely theoretical aspect. The scientists proved that "Microchip of increasing short-term memory of man" finally exists. Our memory often lets us down. It is sufficient to compare the ability of human memory and the memory of an ordinary computer. The child will take weeks to memorize the multiplication table, and what about the computer, it is sufficient to complete the necessary task. It is possible for the people to do the same. The New York Times types "The main difference is the main unit of our memory. Computers distribute the information logically, and the person has no idea what and where to keep the information. We do not remember where we save the information, and whereto receive the correct answer, we use definite signals". The group of scientists from Toronto provided a technique known as deep brain stimulation, which can make a small, but significant difference in the memory. Mankind has been experimenting for a long time, with various ways of modifying the brain, to get the

features which are unavailable, in natural everyday condition. As a rule, these methods are limited to be used only from natural or synthetic substances, because they influence directly on the whole brain. The scientists have one definite instrument which is able to affect some areas, selectively and locally. This instrument is an electric or magnetic field, and its use sometimes leads to surprising results. According to the pharmacological researches in the area of synaptic contacts under the influence of the electric power, NMDA-receptor production increases. This increases the flexibility of the nerve tissue, giving it temporary condition in which neurons tend to rebuild their connections in response to an external stimulus, such as a new learning behavior. For example, in 2009, Leonardo Cohen from the National Institute of Neurological Disorders (Maryland, USA), showed that tDCS improved the ability for learning simple exercises on coordination, and this improvement was maintained three months after the experiment.

Learning processes of the brain stimulation have an impact on a number of other properties of the mind. In particular, this technique is seriously considered as an advanced way for the treatment of depression, post-traumatic stress, delays in speech and mental development and other nervous disorders. It turned out, that the effect of the constant current, affects the area located above the temple, and it is called a dorsolateral prefrontal area. The person becomes afraid of everything, especially when one has to take any risky decision. In addition to reviving memories, deep stimulation can sometimes bring into real action the human mind. It is worth noting the successful experiment of the whole team of doctors and neurologists, who have managed to recover the brain functions of a man, who passed six and a half years out of consciousness. He got an extensive head injuries and lost the ability to communicate. Tomography studies proved that, some important parts of the cortex left untouched, but they were not able to function. The scientists proved that deep brain stimulation eliminates overeating. The number of people all over the world suffers from obesity, and it keeps on rising. Recent studies showed that the consumption of foodstuffs, high in calories, activates some areas of the brain which are associated with reward.

As a result, the researchers are interested in information, how changes in the brain, may be responsible for the human desire to consume more calories than one need. There is a lot of different information in our everyday life about DBS. Some scientist proved that it is possible to eliminate overeating, others, that the doctors may prevent anorexia. Scientists from Canada, first of all, studied the problem, in order to understand whether the procedure is safe for people with severe cases of malnutrition and anorexia nervosa. It was the first case when scientists have used electrodes for the brains of people suffering from severe forms of anorexia. They treated 6 women aged 24 to 57 years, to which previous therapy has not helped. The investigators worked on those areas of the brain that affect mood and anxiety, during the whole 9 months. Anorexia nervosa has many levels, and it is necessary to treat its root. For many people, this condition is associated with the difficulties of their mood regulation. After 9 months of the study, 3 women felt much better quality of life, and started gaining weight. However, they were able to maintain their weight at the level they had already reached. That is, they couldn't do since the beginning of disease. The procedure occurred with some difficulties and serious consequences. One

patient, two weeks after the beginning of treatment, had a heart attack, and another a panic attack during the procedure. One patient was lucky, the mood, anxiety and weight did not change in the end of the investigation. Electrical brain stimulation improves the memory. Deep brain stimulation improves its cognitive functions. During the whole life, in the hippocampus are forming the new cells (part of the brain responsible for learning and perception of new information). After the whole procedure, in six weeks, the researchers estimated how the new cells affect the memory. An experiment with animals showed that deep brain stimulation improves spatial learning and memory. The scientists showed that stimulation of certain areas of the brain, may lead to the formation of new functional cells. Stimulation of the brain stops the tick. Scientists call this "Tourette's syndrome". The first signs of Tourette's syndrome are already visible from the childhood. A child suddenly starts winking, making faces, shaking or jerking his shoulders and head. The majority of people suffer from depression and anxiety. Despite the small number of people suffering from syndrome, the results are encouraging. More frequently they are caused by lesions of the striatum. Movements are the same in its manifestations (sharp, quick, jerky); sometimes people cause themselves really serious injuries, because they cannot control the sudden movements. Sometimes, the Tourette's syndrome makes the children showing indecent abusive words and rude gestures. Those patients are well aware of the unacceptability and the inadequacy of their behavior. They want to, but cannot control their behavior. Further studies will prove that, deep brain stimulation is a safe and effective treatment for Tourette's syndrome. The duration of treatment is 2 months or more. Among the side effects of treatment, there are some symptoms like: excessive fatigue, weight gain, dysphoria, parkinsonism, intelligent anti-aliasing, memory problems, personality changes, school and social phobias, sexual dysfunction, torsion dystonia, expressed autonomic disorders - constipation, dry mouth, mist, agranulocytosis, jaundice. Monotherapy, is often insufficient for a full correction of disorders in Tourette syndrome. Therefore, some clinicians prefer to conduct the complex therapy. Implementation of combined therapy in practice is always complicated, and it is particularly difficult to carry it out, when the basic medications are psychiatric.

The scientists go on studying the type of treatment and the risks of side effects, such as cerebral hemorrhage, or undesirable changes of motor function. At the moment, DBS is an experimental treatment and is not considered for children's treatment. Symptoms appear in a different order and with different intensity, they are significantly impairing for the quality of life of all the patients. Things like gait disturbance, handwriting, facial expressions and speech, etc. brings to disability. Drug treatment helps the people just a little and for a short period of time. Furthermore, drugs have side effects, which sometimes, worse the symptoms in general. There are strong indications and contraindications about DBS, they are: idiopathic Parkinson's disease for more than 5 years; one should be not older than 70-75 years; there is a positive response to the medicine levodopa; serious chronic disease (cardiovascular, cancer, etc.); no frequent falls during the loss of balance; no memory disorders; the patient has no mental illness. About the mainstay of Parkinson's treatment, there are various medications that increase the levels of dopamine in certain areas of the brain or prevent its rapid destruction. These drugs do not cure the disease, but it helps in reducing the unpleasant symptoms, and allows remaining active. Modern

medications for Parkinson's disease are very efficient and allow keeping on working for a long time. The problem is that this disease is usually very progressive. During the first years of disease, the doctor will have to prescribe the drugs in small doses, it gradually becomes necessary to add additional drugs to increase the dose. One requires help in performing daily activity type, such as dressing, bathing, eating, and walking. Unfortunately, the surgery is not the solution to all problems. If this affects both hemispheres, and a place of destruction of subcortical structures has been chosen is not entirely accurate, there is a possibility of serious complications, such as impaired speech and cognitive functions. The pulse generator can be easily programmed by the computer that sends the commands via radio signals. Only in two or four weeks later, the first pulse generator is turned on and adjusted. The configuration process may take several weeks; while the modes of stimulation and drugs will be finally selected to suppress the symptoms of Parkinson's disease.

If one takes the decision about the surgery, should be careful because, this operation may prevent the future use of new treatments for Parkinson's disease, such as transplantation of brain cells. That will not happen if deep brain stimulation is simply disabled. Ethical discussion with respect to informed consent for DBS interventions especially focuses on the impact of patients' expectations and their possible desperation "Bell *et al.* report that healthcare providers from five Canadian DBS centers identified extremely high expectations as a key challenge, which could undermine patients' understanding of risks and benefits. Consequently, these patients are prone to a higher risk of being disappointed with the real outcome of the intervention. In part, due to overestimated media reports on 'miracle cures' through DBS, it was hard for healthcare providers to ensure patients appreciate that DBS is no cure for Parkinson's disease and that the favorable outcome of the most fortunate patients could not be guaranteed. Thus, accurate reporting is recommended not only for the media but also for the DBS centers, as showing only the most favorable outcomes, for example, in a public presentation, might trigger patients' unrealistic expectations too. Realistic expectations are equally recommended for more experimental interventions such as DBS in psychiatry, including the appreciation that the intervention is not an approved treatment but research.

Brain-hardware interfaces in the case of DBS provide significant therapeutic options for Parkinson's disease and might be beneficial for other disorders as well. Ethical consideration will help to improve this intervention and realize its full beneficial potential. Outcome measurements need to be improved with respect to patients' subjective reports, and guidelines are needed for thoroughly and carefully testing further DBS applications. Parkinson's disease may be treated with dancing. A new method for Parkinson's disease was offered by the Israelis. We are talking about a certain varieties of dance therapy. In the later stages of Parkinson's disease, this dance therapy, or, as it is called, a gyro-kinetic therapy, probably will not help. It can bring tangible benefits, if one starts using it at the beginning of the disease. The creator of the new method is Alex Kert, an Israeli physician. This method unites only selected music, and movements which can help the people with affected nervous system. Kert says that, this method is able to help one learning to live with the disease and gain some control over it. Experimental studies show that treatment with dances slows down the progress of the disease, allowing one to avoid the increasing of the dosage, necessary

for Parkinson's drugs. Being treated with dances is something astonishing. A lot of people had never heard about it. But it is extremely beautiful. Dance and rhythmic music inhibit consciousness, especially the concentration on their mind on their own, caused by the disease. If one is full of splash, then there is an active immersion of humanity in one's desires, materialism, sensuality, sexuality and enjoyment of life. To sum up, we have seen that DBS is a nonsurgical treatment of reducing tremor and blocking stationary movements in patients with motion disorders. Small electric shocks are delivered to the *thalamus* especially in the treatment of multiple sclerosis, or the *globus pallidus* which is associated with the treatment of Parkinson's disease, rendering these parts of the brain inactive without surgically destroying them. Such diseases like Parkinson's, Tourette's syndrome, as it was found, can be easily treated. There are some risks of the treatment, but one should risk once, to be happy for the rest of life. There are some ways of treatment, which are safe. Being attentive to one's health is the most important mission considering those syndromes. The procedure of treatment can help the adults and children, as well. Children can be cured but not with the help of surgery. There are other methods.

Old people should be careful; the surgical treatment can be rather dangerous for people older than 70 years old. The surgery, does not cure the disease entirely, but helps a patient to be more active. There is a possibility to reduce some symptoms, such as tremors and slow movements. Deep brain stimulation is always well conducted. The doctors do their best not to damage the cells of the brain. There is a risk to feel not good after the surgery. Some people may have painful symptoms, like headache, vision problems, fever, irritation etc. We should always remember that, life is not long enough to live it badly. Some people are not lucky enough, and they suffer from such diseases. One should never give up. There is no need thinking that the like is coming up to the end. Maybe it has just started.

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