Dystonia and Deep Brain Stimulation

What is Dystonia?

Dystonia is a term that both describes a neurological symptom and a group of disorders in which dystonia is the main symptom. Dystonia is characterized by involuntary, repetitive muscle contractions leading to twisting movements or a jerky tremor, and often also abnormal postures. The involuntary movements can affect muscles in only a single part of the body (focal dystonia), like around the eyes (blepharospasm), in the neck (cervical dystonia), an arm or a leg, or a larger region of the body such as in both the neck and arm (segmental dystonia), both an arm and a leg on the same side (hemi dystonia), or both upper and lower body, including the trunk or a leg (generalised dystonia).

The causes of abnormal dystonic movements are not fully known. But research indicates that the brain networks which control normal movements are disrupted through various underlying disorders. The disorders spans from genetic disturbances alone to focus or diffuse lesions from stroke, trauma or metabolic or degenerative disorders and can affect people in all ages. Some medications and toxic substances can also cause dystonia.

Deep Brain Stimulation (DBS) has been used as an effective treatment for dystonia for the last 15 – 25 years as well as for other movement disorders such as Parkinsons Disease and tremors. Deep Brain Stimulation is only given to patients that do not get sufficient symptom relief through medication including botulinum toxin injections.

What is Deep Brain Stimulation

Brain cells (neurons) communicate with each other with the help of electrical impulses and chemical signals, and these electrical signals are sent through the brain´s "power cords" which are called axons. Deep Brain Stimulation is a treatment in which the electrical impulses of brain cells and axons are affected by an electrical current. This current is sent chronically in short pulses to the brain tissue through electrodes which are implanted permanently in a specific area deep in the brain, hence the term *Deep* Brain Stimulation. The brain electrodes are connected to a combined impulse generator and battery by wires leaving the scull through small holes. The wires are inserted under the skin of the head and neck and further down to the impulse generator/battery which is normally placed under the skin in the upper chest area (or abdomen). The impulse generator is programmed by a neurologist to deliver a constant current of electrical impulses to the targeted areas of the brain to improve the patient's symptoms.

The most used target area for Deep Brain Stimulation in patients with dystonia is called Globus Pallidus internus (GPi). This is the target area that has been used on patients included in the best and most recognized studies of Deep Brain Stimulation in dystonia and that are referred to here. The GPi is located about 6-7 centimetres from the brain's surface and about 2 centimetres from the midline of the head.

How does Deep Brain Stimulation work?

It is not entirely clear how Deep Brain Stimulation works. However, by stimulating the brain cells with a high frequency current, the abnormal signals that are sent between brain cells through the axons are altered in a positive way. For patients with dystonia, the signals sent between the nodes that control voluntary movements are becoming more normal. One could say that the effect of Deep Brain Stimulation for dystonia is to reduce faulty signals to those brain areas that ultimately decide how our voluntary movements are performed . Although some of this effect may come early after the treatment has been intiated, more effect will develop over time because it takes time for the brain to adapt to the altered signals caused by the Deep Brain Stimulation. This is one of the reasons why it takes time (months to 1-2 years) to achieve the full effect of Deep Brain Stimulation for dystonia.

Since around 2015-2017 a new and improved generation of a Deep Brain Stimulation electrodes and impulse generators/batteries became available from the manufacturers of DBS systems. While the first generation of Deep Brain Stimulation electrodes had four ring contacts (from which the current reaches the brain), modern electrodes have a higher number of contacts which all have their own current supply from the impulse generator. This makes it possible to control the amount and direction of the current in a more specific way with the aim to improve the clinical improvement and limitate side effects related to stimulation.

Which Dystonia patients may be evaluated for Deep Brain Stimulation, and how beneficial is the effect?

Deep Brain Stimulation is not suitable for all dystonia patients. Accurate selection of patients is one of the most important factors to ensure that the treatment will work in a positive way. On a world scale, we now have about 20 years of experience with this treatment. The recommendation process for selecting suitable dystonia patients for DBS is based on research studies on patients who have received this treatment. These studies have shown that the best results are seen in patients with isolated dystonia disorder, thus in those who have dystonia (including dystonic tremor) as the only symptom and with no underlying neurological disorder that alters the brain structure. The effects in these cases are good (50-95 % improvement of dystonia symptoms) in up to 75% of patients. The best and most extensive documentation is related to generalised and segmental dystonia that affect more regions of the body. However, good effect from Deep Brain Stimulation has also been shown in patients with cervical/neck dystonia who no longer have adequate relief or good quality of life from botulinum toxin treatment. It is important to recognize that results will vary from patient to patient and that it may take longer for some patients to get the full effect of the stimulation. Today's data suggests that the full effect may take up to 1.5 years from the start of stimulation and some patients may achieve even further improvement with time beyond that.

Effect of DBS has also been observed in patients who have conditions where dystonia is combined with other movement disorders or have symptoms of another underlying illness or damage to the nervous system. The magnitude of improvement in these patients is however often more limited than in isolated dystonia patients and the treatment cannot improve neurological symptoms other than those caused by dystonia.

Physiotherapy and individually customised exercises are supplementary treatments that may help DBS treated patients to attain more normal movement patterns. This may require a lot of effort on the part of the patient, but results can provide further motivation. It is important that

the patients (or their family/carer) cooperate well with their therapist and are dedicated in following the exercise plan/ treatment.

DBS can generally not be offered to patients that require strong blood thinning medication (anticoagulants) or that have other conditions that increase the risk for complications such as bleeding, thrombosis or infection under surgery/treatment. But this must be individually evaluated at the DBS center. The patient must be able to undergo an MRI (see next section).

Which examinations should be made before Deep Brain Stimulation Treatment?

All patients are first evaluated and receive medical treatment at the neurological department of the patient's local hospital. Referrals for evaluation of DBS treatment are sent to the neurology department at the DBS center to which the patient belongs and is normally located at a university hospital. Further medical evaluations may be carried out there to ensure that a correct diagnosis and medical treatments including botulinum toxin injections have been thoroughly tested. A neurologist will examine the patient thoroughly regarding degree and severity of dystonia. Other neurological finds must also be examined. Normally the referring neurologist have already investigated the patient with an MRI of head/brain (and spine/spinal cord). However, MRI will often be repeated at the DBS center during the neurological evaluation or later in connection with the DBS surgery. In some cases a new MRI may add information about the etiology of the dystonia. It may also be necessary to carry out blood and urine tests. The DBS evaluation may also include a psychiatric and/or a neuropsychological investigation. Information from these assessments may provide arguments in favour of a good outcome following DBS, such as in several genetic dystonias and in tardive dystonia (:dystonia as side effect of antipsychotic medications).

Spinal fluid may also be tested on rare occasions. The final decision regarding whether DBS treatment is a suitable and possible treatment for a patient, is normally made at a joint meeting with several neurologists and neurosurgeons that together have an extensive knowledge and experience with this type of treatment.

Much of the above also applies to dystonia disorders occurring in children. In children dystonia most often is part of a more complex disorder, but DBS may still be a good treatment and it may be important to evaluate this possibility early rather than late in the disease course. In very rare cases, deep brain stimulation may be indicated as a life saving procedure, in the severe condition called Status Dystonicus which occurs the most frequently in children.

How does the surgery work?

The patient is admitted a few days prior to surgery to be prepared for the operation. At the start of the operation, the patient's hair will be shaved (partially) to reduce risk of infection. The operation is carried out under full anesthesia. The neurosurgeon places a metal frame on the patient's head followed by a CT scan. The CT images will then be compiled and compared in a data program to the MRI images taken the day before surgery (or taken up to a few weeks prior to surgery). The neurologist and neurosurgeon plan the target area in the brain from the MRI images. The neurosurgeon will then calculate where the target points are placed in relation to the metal frame placed on the patient's head. This way the specific location and placement of electrodes can be calculated. To place the electrodes, a small hole must be drilled into each side of the skull and an opening made to the meninges (membranes) that surround the brain.

The neurosurgeon can then insert a thin probe down to the target in a controlled way. While many centres earlier used microelectrode recordings during the procedure to aid the placing of the electrodes in the correct target, today most centres control the electrode placement by imaging.

Electrodes are fastened to the skull in a safe manner. (After the operation, these areas in the skull may become visible as small bulges.) The electrodes are then connected to extension cables that are placed under the skin of the head and neck and down to the subcutaneous tissue of the chest. Here the cables are connected to a combined impulse generator and battery. The impulse generator can be programmed from the outside by the neurologist and eventually by the patient with the help of a patient controller. After the operation patients are observed in a neurological monitoring section. Normally a transfer to a regular ward at the neurology department can occur the next day. Here all the regular follow-up and stimulator adjustments are done. The stimulation may be started during the hospital stay or at the time of the first follow-up visit. Most patients are fully functional the day after surgery and can be released from the hospital within 8-10 days after the operation.

Which side effects can occur with Deep Brain Stimulation ?

The most common side effect observed in dystonia patients treated with GPi-stimulation is some slurring of words or indistinct speech, but this is often just temporary. Other side effects that can be experienced are numbness of the hand or mouth/chin or a reduction in fine motor skills. With modern electrodes using directional DBS, however, side-effects like this, that are related to current spread outside the target, can to a large extent be avoided. But in some cases, a certain reduction in speech clarity must be accepted to maintain the positive effect on the dystonia.

Complications during surgery or post-surgery are rare, but may occur. Bleeding or blood clots can cause stroke-like symptoms, such as half-sided paresis and possible loss of language ability, but may also occur without causing neurological deficits. Bleeding or blood clots are the most serious complications and occur in approximately 0.5 % (to 2%) of patients. Infection at the stimulator-implant site may also occur (even late, months or year after DBS system implant). A stimulator-site infection may make it necessary to remove the affected part of the implanted system, and re-implant it again after prolonged treatment with anti-biotics. Deep brain stimulation system components may also brake. Removal due to infection or breakage of the system will interrupt the stimulation until re-implantation has successfully been performed.

Deep Brain Stimulation should be evaluated for all patients with persistent and troublesome dystonia and reduced quality of life despite medical treatment. For patients with primary/isolated, generalised, segmental or pronounced focal cervical dystonia, the effects are quite often good. If stimulation-related side effects occur they are normally mild and in most cases only temporary.
Very pronounced secondary dystonia can also be treated with effect, but the outcome is less predictable and the risk for complications somewhat higher. Improvement of dystonia will come gradually after stimulation has started. The degree of improvement will vary. The average improvement of dystonia symptom scores reported in controlled studies is 30 to 50% improvement at six months after surgery and 50 to 70% after three to five years. The treatment effect has been shown to last with chronic stimulation. If the treatment is interrupted due to error or damage to the electrodes, a flat battery, or if the impulse generator/battery must be removed due to infection, the dystonia symptoms will return within minutes to days.

Follow-up after surgery.

The stitches of the wounds must be removed 10-12 days after being released from the hospital. This is normally done by the patient's GP. The first follow-up will normally take place at the hospital four to six weeks after being discharged. In the meantime, the patient will get a sick leave and continue to recuperate at home. Some patients will require a longer period of sick leave. Follow-up checks at the hospital will require 1-3 days admission (rarely longer) to observe well the effects and any side effects by adjustment of the stimulator's electrical current. During the first year, patient´s normally come to follow-up checks at the hospital every three months, and subsequently every six months. With stable, good effect of the treatment, follow-up can be carried out once a year or less often.

Deep brain stimulation usually provides a significant reduction of pain associated with the dystonia, which is particularly common in cervical dystonia. Many patients will be able to reduce the intake of pain medication and after some time stop it completely. Other medications that some patients use for dystonia can also often be gradually reduced during the first 1/2 – 1 year of DBS treatment.

There are two types of batteries for stimulators; one that can be recharged and one that cannot be recharged. A rechargeable battery can last for more than ten years (and up to thirty years), while the non-rechargeable batteries need to be replaced after 2-5 years (depending on how much current is needed to yield the effect). Replacing the stimulator battery involves a small operation with local or generalized anesthesia and usually takes place completely without complications, but may, in line with the primary operation, involve a risk of infection.

Important points and practical advices for DBS-treated patients :

- The goal of DBS-treatment is to be able to live the best life possible and as one wishes.
- Patients should always inform their healthcare provider that they have an implanted DBS-system before undergoing a medical procedure. This is because an interaction may occur between the DBS-system and other medical technical equipment used during the procedure, even when both are functioning correctly.
- Most routine diagnostic procedures, such as X-ray, CT-scans and diagnostic ultrasound are not expected to affect the operation of the system.
- The stimulator should also be turned off when the patient undergoes investigations such as EEG, ECG, and neurography/EMG, otherwise the stimulator will disturb and yield artifacts to these investigations. However, turning off the stimulator may give involuntary movements that may yield artifacts too.
- During surgery and MRI examinations, however, it is recommended from the manufacturers of DBS-systems that the stimulator should be turned off due to safety. The doctor who orders the MRI or surgery should contact the neurology center that is responsible for the follow-up of the patient to clarify whether it is appropriate for the DBS-system to be turned off without sedation, and to check the integrity of the DBS system. As severe dystonia may return quickly after stimulation is turned off, care must be taken that this is not done if it may cause a lot of discomfort or even danger for the patient. Sedation or general anesthesia during MRI or surgery are often the best options to avoid this.

- For some DBS systems it is possible to do MRI examinations of the whole body. The treating neurologist and radiologist will always investigate whether this is the case and check the integrity of the DBS system.
- Patients who have implanted DBS systems cannot receive therapeutic ultrasound treatment from a physiotherapist/other therapists (but regular diagnostic ultrasound is no problem).
- During operations, to stop bleeding, unipolar diathermy is most often used, but in patients with implanted DBS-systems bipolar diathermy should always be used. If you have any questions about this, your treating physician can contact the implantation centre.
- DBS-systems should not be affected by the normal use of electrical appliances, such as household appliances, electrical tools, microwave ovens, systems with RF transmitters or microwave transmitters. A powerful magnetic field (electromagnet or permanent magnet) can change nerve stimulation from on to off, or from off to on, but does not change the programmed parameters.
- One should avoid or be careful when getting close to the following: theft detectors, security portals, large speakers with magnets, power lines, electrical substations, and power generators.
- If one suspects that an electrical device or magnet is interfering with the stimulator, move away or switch off the appliance.
- Diving deeper than 10 metres (33 feet) is not recommended. For other types of diving or pressure chamber patients should consult their r doctor about the effects of high pressure before diving or staying in a pressure chamber.
- Great heights do not affect the stimulator.
- It is possible to perform most types of sports, but DBS systems components may brake with sudden, forceful movements of the head or neck, such as when heading a football, or other similar situations.

Notes

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