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DIFFERENT OUTCOMES OF STEREOTACTIC ABLATION OF DIFFERENT TARGETS IN PATIENTS WITH MOVEMENT DISORDER

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ABSTRACT

*Background:*Parkinson's Disease (PD), Essential Tremors (ET), and Dystonia are movement disorder diseases managed surgically. Deep brain nuclei include the globus pallidus internus (GPI), ventral intermediate nucleus (VIM), and subthalamic nucleus (STN). Proper choice of the target is based on the appropriate diagnosis, patient's symptoms, and possible adverse effects following the ablative surgery.

*Methods:*We had 40 patients diagnosed with movement disorders. A complete neurological assessment was done on the patients. 3D MRI was done on the patients for diagnosis and preoperative target planning.

*Results:*We had 30 males and ten females. Twenty-four had PD, 14 had ET, and two had dystonia. We did pallidotomy in four cases, thalamotomy in 22 cases, subthalamotomy on eight patients, and combined pallidotomy and VIM thalamotomy on six patients. The thalamotomy group had a remarkable improvement in tremors. The subthalamotomy or combined pallidotomy and thalamotomy groups improved all three cardinal PD symptoms, the ON/OFF fluctuations, and a reduction in L-Dopa Induced dyskinesia. Patients who had a pallidotomy had an improvement in bradykinesia, and rigidity, improvement in the ON/OFF fluctuations, and a reduction in L-Dopa-induced dyskinesia.

Two patients suffered from hematoma, four ataxia, one contralateral hypothesia, and one hypophonia. One hemiballismus, two contralateral weaknesses, and one urine incontinence.

*Conclusions:*Proper planning and choice of target is an essential cornerstone to reaching the best results. When choosing the target for stereotactic ablation, all functional neurosurgeons dealing with movement disorders must know all anticipated outcomes and possible complications.

Keywords: Essential Tremors; Parkinson's Disease; Thalamotomy; Pallidotomy; Subthalamotomy; Movement Disorders

INTRODUCTION

Movement disorders are a group of common diseases affecting young, middle, and old-aged males and females. They cause significant disability and impair the quality of life of the affected individuals. Movement disorders are managed mainly by medical treatment. Medically refractory cases are candidates for surgical intervention. Parkinson's Disease (PD), Essential Tremors (ET), and Dystonia are movement disorder diseases that are FDA approved for surgical intervention. Deep brain nuclei, which are possible targets for stereotactic ablation for movement disorders, include the globus pallidus internus (GPI), ventral intermediate nucleus (VIM), and subthalamic nucleus (STN). Proper choice of the target is based on the appropriate diagnosis, patient's symptoms, and possible adverse effects following the ablative surgery. Here we present a series of 40 movement disorder patients who have undergone ablative surgery and the algorithm we follow in choosing the target.

METHODS

Our series included 40 patients diagnosed with movement disorder disease. Our inclusion criteria for the PD group included patients with advanced PD, showing decreased response to Levodopa/Carbidopa after at least three years of good response, patients with dyskinesia, and patients with ON/OFF fluctuations. Exclusion criteria included patients with secondary PD, decreased mental state, or psychiatric disorders. For the ET group, we had all patients with essential tremors not responding to medical treatment and

showing a decreased quality of life. Written informed consent was obtained from all participants; the research ethics committee approved the study at the Faculty of Medicine, Zagazig University. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for human studies.

Preoperative preparation and assessment: A complete neurological assessment was done on the patients, including preoperative medications, any associated neurological disability, a mini-mental state examination (MMSE), and psychiatric consultation. Pre- and postoperative Unified Parkinson's Disease Rating Scale (UPDRS) and ON duration are assessed for PD patients. For ET patients, pre and postoperative, The Research Group Essential Tremor Rating Assessment Scale (TETRAS) is assessed. 3D MRI was done on the patients for diagnosis and preoperative target planning. For the planning MRI, we do a 3D T1 MPRAGE, 3D T2 Space, 3D T2 Dark Fluid, 2D proton density (for visualization of the internal capsule), 2D T2 axial and coronal views, and 3D TOF for visualization of blood vessels. We use the cranial suite software (Neurotarget LLC, Nashville, Tennessee) for the planning. The preoperative lab included CBC, KFT, LFT, PT, PTT, INR, Bleeding time, Clotting Time, HBV, HCV, HIV, RBS, and urine analysis. One week before surgery, the patient would stop antiplatelet or blood thinners. Five days before surgery, the patient would go on a regimen of tranexamic acid 500 mg tab twice daily and Etamsylate 500 mg tab twice daily. All anti-PD medications were stopped 24 hours before the surgery. One hour before surgery, the patient is given a single dose of prophylactic antibiotic (1.5 gm of cefoperazone and sulbactam) and a shot of 10 mg of Vit K.

Target choice: we choose the target according to the predominant symptoms. For tremor dominant PD, we do a thalamotomy. For rigidity dominant, we do a pallidotomy or a subthalamotomy. We do a subthalamotomy or a combined pallidotomy and thalamotomy for rigidity and tremors. For ET, we would do a VIM thalamotomy.

Preoperative planning: after registration of the patient's MRI and identification of the anterior commissure, posterior commissure, and midline, we identify our targets indirectly using the Schaltenbrand and Wahren atlas, and then minor adjustments are made according to the radiology.

If the plan is to do a combined lesion, we adjust our planning so that the entry point of both targets is the same so that we can benefit from a single drill hole. Entry point through the brain should go through a gyrus, avoiding sulci to decrease the risk of bleeding. Birds eye or trajectory view is very important in the planning stage to avoid vital structures and ensure the electrode's axis is along the long axis of the nuclei, ***Fig 1***.

Surgery: We use an Elekta Leksell G-frame. Patients were awake with scalp block and local anesthetic (20 cc bupivacaine, 20 ccs of 10 % lidocaine, and two ccs of dexamethasone) at the site of entry of the brain electrode and points of fixation of the Leksell frame. BLPR is monitored by invasive arterial blood pressure monitoring.

After fixing the Leksell frame and applying the N-shaped indicator, we do a CT scan; after the image fusion using our software, we get our target's X, Y, and Z coordinates. We use a 4 mm twist drill for the entry point to avoid large openings and minimize CSF leak and pneumocephalus, which may cause brain shift and alter the coordinates. Following inserting the 2 mm bipolar electrode into the target, we apply a set of actions to confirm the target of choice.

We use an LG2 Radiofrequency generator (INNOMED) and a bipolar electrode with a 2mm X 2mm active tip. First, we do a low-frequency motor macrostimulation at 2 Hz to detect proximity to motor fibers. Then we do a high-frequency sensory stimulation at 100 Hz to detect proximity to sensory fibers. A therapeutic high-frequency macrostimulation at 200 Hz is then done to test for the sweet spot for the desired effect. The three stimulations are done starting at 0.5 volts and increasing gradually with increments of 0.25 volts. For the first two stimulations, the higher the voltage, the more distance from vital structures and the better. For the therapeutic stimulation, the lower the voltage, the more proximal to the sweet spot, the better. Adjustments are made to the final position of the electrode according to the produced effect of the macrostimulation.

After confirming the location of the electrode, a test lesion at 45^{o} C for ten seconds is done, and we wait for ten minutes to ensure there are no unwanted adverse effects. We do our lesion for 90 seconds at 80^{o} C. We do two lesions at the zero point, two at depth minus two, to ensure a satisfactory lesion with the persistence of the therapeutically desired effect for a long time. Before each lesion, we do macrostimulation and test for motor power, coordination, rigidity, and tremors during the stimulation, during, and after the lesion. Before moving the electrode, we ensure it cooled down to body temperature to avoid injuring any vital target or blood vessel.

Postoperative assessment: Immediate brain CT checks for unwanted intracerebral hematoma.

Collected data were presented in tables and suitable graphs and analyzed by computer software package (SPSS statistics) using appropriate statistical methods, with the p-value adjusted at 0.05.

RESULTS

Our study included 40 patients, 30 males, and ten females. The mean age (± SD) range was 50.6 years (± 14.4), 21 – 76 years. We had 24 patients who had PD, 14 patients who were diagnosed by ET, and two dystonia patients. Of the 24 patients who had PD, 18 patients had tremors, and 14 had rigidity and bradykinesia, ***Table 1***.

We did pallidotomy in four cases, VIM thalamotomy in 22 cases, subthalamotomy on eight patients, and combined pallidotomy and VIM thalamotomy on six patients; our targets were chosen according to the algorithm in ***Table 2***. Patients who had a thalamotomy had a remarkable improvement in tremors. Patients who had a subthalamotomy or a combined pallidotomy and thalamotomy had an improvement in all three cardinal PD symptoms, improvement in the ON/OFF fluctuations, and a reduction in L-Dopa Induced dyskinesia. Patients who had a pallidotomy had an improvement in bradykinesia, and rigidity, improvement in the ON/OFF fluctuations, and a reduction in L-Dopa Induced dyskinesia.

Of the patients who had thalamotomy, two suffered from hematomas managed conservatively and self-limited, and one had a small thalamic hematoma. The other had a small subdural rim. Two patients had ataxia, one had contralateral hypothesia, and one had hypophonia. All these complications were transient and resolved completely within two to three months.

Of the patients with subthalamotomy, one had hemiballismus, and two had ataxia. Of the patients with pallidotomy, one had a contralateral weakness, and one had urine incontinence. Of the patients with combined pallidotomy and thalamotomy, only one had a contralateral weakness. Improvement was better in patients who had a subthalamotomy, $p < 0.05$. The complication rate showed no statistical significance in any of the targets, $p > 0.05$.

Table 1 Patients' Demographics and Diagnosis

Age (Years)		Number of Male Cases	Number of Female Cases	Number of Parkinson's Disease Cases	Number of Essential Tremors Cases	Number of Dystonia Cases	
Mean	50.6	30	10	24		14	2
SD	14.4			Patients with Tremors	18		
Range	21 - 76			Patients with Rigidity and Bradykinesia	14		

Table 2: Target Lesions and complications; GP: Globus Pallidus Internus; VIM: Ventral Intermediate Nucleus; STN: Subthalamic nucleus

Target Nucleus	Number of Cases	Complications	Number of Cases
GPI	4	Contralateral weakness	1
		Urine incontinence	1
VIM	22	Hematoma	1
		Ataxia	2
		Hypothesia	2
		Hypophonia	1
STN	8	Hemiballismus	1
		Ataxia	2
Combined GPI and VIM	6	Contralateral Weakness	1

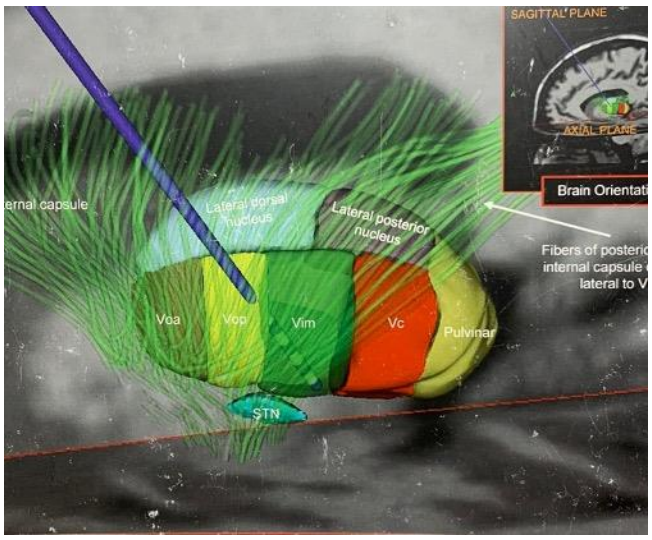

Figure 1: VIM and Related Structures (Copied from Medtronic manual for DBS Lead placement)

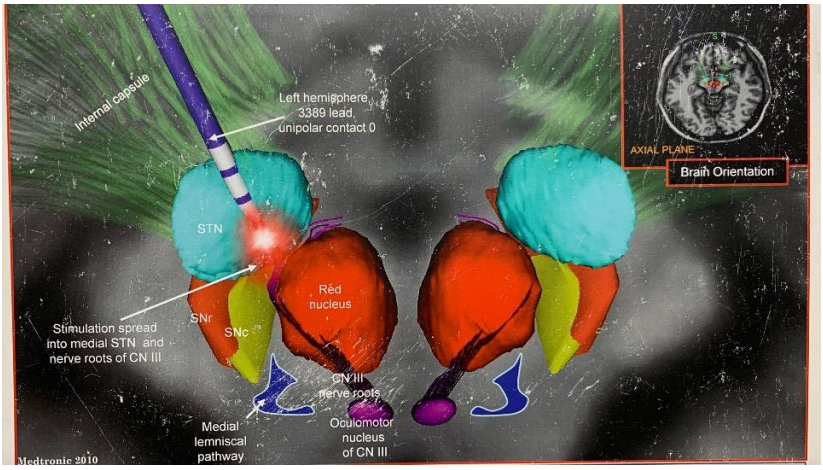

Figure 2: Subthalamic Nucleus anatomy and related Structures (Copied from Medtronic manual for DBS Lead placement)

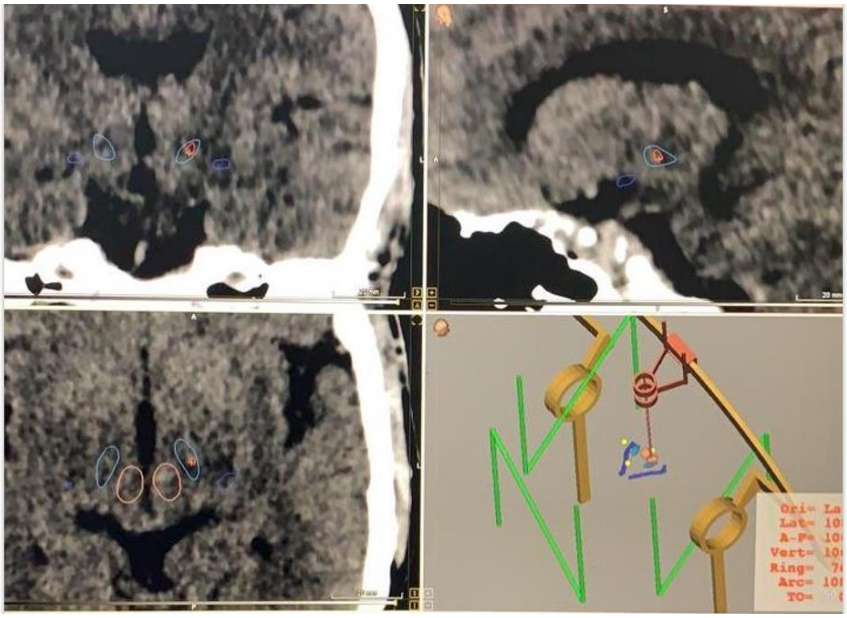

Figure 3: Postop CT showing Subthalamic Lesion

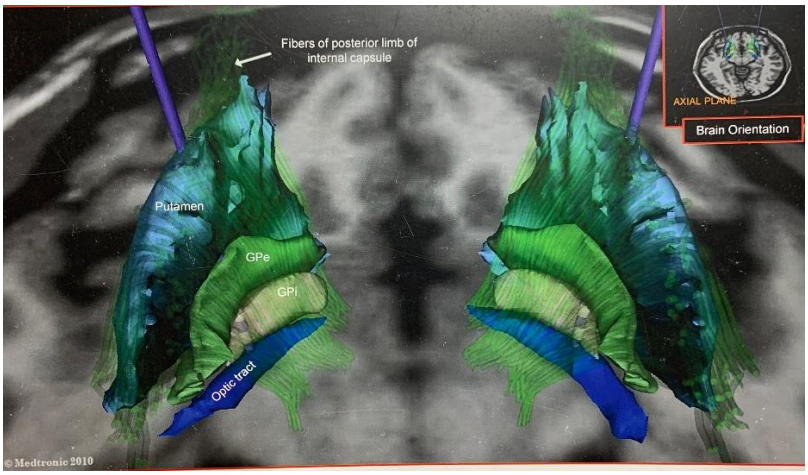

Figure 4: Globus Pallidus Internus and Related Structures (Copied from Medtronic manual for DBS Lead placement)

DISCUSSION

Movement disorders are a group of debilitating and disabling diseases affecting the patient's quality of life. Patients who fail to achieve reasonable symptomatic control with medications are candidates for surgical intervention. Movement disorders are common in young, middle, and old ages, both males and females, and more common in males than females. The most commonly treated movement disorders are ET, PD, and dystonia [1]. While ET is the most common movement disorder disease, PD is the most common brain degenerative disease after Alzheimer's. The number of PD patients seeking surgical treatment is far greater than PD patients because PD is more progressive over time, and ET is much better controlled by medication [2].

Our study had 40 movement disorders patients 30 of them were males, and ten were females. The mean age (± SD) range was 50.6 years (± 14.4), 21 to 76 years. Twenty-four patients had PD, 14 had ET, and two had dystonia. Of the PD patients, 18 were tremor dominant, and 14 were rigidity and bradykinesia prevalent.

For ET, we targeted the VIM; for PD, we targeted the VIM, STN, and GPI; or we did a combined GPI and VIM lesion. For dystonia, we targeted the GPI [3].

Patient candidates for surgery must undergo a full neurological assessment, including MMSE and psychiatric evaluation. Many authors discussed that advanced PD patients suffer from deterioration of mental and cognitive functions and are, therefore, not candidates for surgical intervention. Also, patients need detailed psychiatric evaluation because targeting the subthalamic nucleus may lead to any pre-existing psychiatric illness deterioration [4].

VIM:

VIM is the target for stereotactic lesions in ET and tremor dominant PD [5, 6]. Functional neurosurgeons must be aware of the anatomy of the thalamus and nearby structures, ***Fig 1***. An accurately placed lesion in the VIM produces reasonable control of static, postural, and kinetic tremors. Medially placed lesions may lead to hypophonia, and laterally placed lesions may lead to weakness due to internal capsule affection. Posterior or more ventral lesions may lead to paresthesias due to the affection of the ventralis caudalis nucleus of the thalamus or the medial lemniscus. A more ventral lesion may also lead to ataxia due to the affection of the brachium conjunctivum [7-9].

Hematomas following thalamotomy has been previously reported [10]. One of our cases had a small thalamic hematoma which was managed conservatively. One patient had a small subdural rim which resolved spontaneously over two weeks. Ataxia following thalamotomy has also been discussed by many authors [11]. Two patients showed ataxia with deviation to the contralateral side, two showed ipsilateral hypothesia, and one showed hypophonia. All these complications were transient and resolved with medical treatment in three to six months.

Many authors Field [12-14] discussed the benefits of thalamotomy. We targeted the VIM alone in 22 cases: 14 ET and eight tremors dominant PD. It was also targeted in combination with the GPI in six PD patients with all three cardinal PD symptoms. All the cases got a reduction in tremors as denoted by the decrease in

the UPDRS or the TETRAS. The tremors were better controlled in the upper limb than the lower limb.

STN:

The subthalamic nucleus was targeted in PD patients with all three cardinal PD symptoms, along with motor fluctuations and L-dopa-induced dyskinesia. Many functional neurosurgeons have used the subthalamic nucleus as a target, precisely the dorsolateral aspect of the subthalamic nucleus [15], ***Fig 2***. A well-placed lesion in the STN will improve all PD symptoms, including an improvement in motor fluctuations and L-dopa-induced dyskinesia. These last two improvements are due to a better response to medication, a prolonged-ON duration, and a reduction in the required daily dose of L-Dopa [16].

An inferiorly placed lesion may lead to diplopia due to a lesion in the nerve roots of the oculomotor nerve. A medially placed lesion will affect the red nucleus with consequent paraesthesia, discomfort, and warm sensation. The limbic system is located ventromedially to the STN; that's why a psychiatric evaluation is done before surgery. STN should be avoided in patients with depression or psychiatric illness. The internal capsule is lateral and anterior to the STN, which should be avoided to protect against contralateral weakness. The substantia nigra reticulata (Snr) is located ventral to the STN; a lesion in the SNr will lead to mood changes and akinesia [17-19].

We targeted the STN in eight PD patients with tremors, rigidity, bradykinesia, and L-dopa-induced dyskinesia, ***Fig 3***. One patient got contralateral hemiballismus which resolved after six weeks of medical treatment. Some authors have reported Hemiballismus following the subthalamotomy [20-22]. They suggest that hemiballismus may be due to a lesion confined to the dorsolateral sensorimotor STN, while a lesion that extends beyond the STN to involve the Zona increta carries less risk than a confined one. Another relation may be preoperative dyskinesia which has a higher risk of hemiballismus [22, 23]. Hemiballismus resolves in most cases but may persist in 8-10% and may require a pallidotomy to alter the neuronal firing rate of the GPI. Two patients got ataxia and improved after two weeks. Ataxia was reported in six out of ten cases in Raul Martínez-Fernández's study [24]. It was transient in all cases and resolved spontaneously.

GPI:

The posteroventral aspect of the GPI is a target in PD patients who has only rigidity and bradykinesia and is the only target for the dystonia [25, 26]. The internal capsule is medial to the GPI, and the optic tract is ventral to it, ***Fig 4***. Functional neurosurgeons must take great care of these vital structures during the planning to avoid weakness or visual deterioration [27, 28].

We targeted the GPI alone in two PD cases and two dystonia cases. And in combination with the VIM in six PD cases. For the PD, we improved the UPDRS in the ON period but didn't get a prolongation in the ON duration or a reduction in the drug doses. In the dystonia cases, the peripheral symptoms improved, but the axial symptoms required a bilateral lesion which couldn't be done in the same setting for fear of complications. One PD had a contralateral weakness, and one had transient urine incontinence.

CONCLUSIONS

Movement disorders are a group of debilitating diseases that impair the quality of life and cause severe disability to the patient. They consequently apply a significant burden on the patient and his family. Stereotactic ablation is an excellent surgical option for patients who fail to achieve reasonable symptomatic control with medications. Proper planning and choice of target is an essential cornerstone to reaching the best results. When choosing the target for stereotactic ablation, all functional neurosurgeons dealing with movement disorders must know all anticipated outcomes and possible complications. Further studies are required for fine-tuning the targets to the optimum site to get the best result with the least likely adverse effects.

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