

**SURGICAL TREATMENT FOR PARKINSON'S DISEASE****Abstract**

Parkinson's disease (PD) is second most common neurodegenerative disease after Alzheimer's disease. It is characterised by with motor symptoms and nonmotor features including cognitive and neuropsychiatric symptoms. Here we review various treatment modalities for Parkinson's disease with special emphasis on bilateral subthalamic nucleus (STN) deep brain stimulation (DBS). We review the indications, advantages, disadvantages of STN DBS and future of the same in the treatment of PD.

**INTRODUCTION**

Parkinson's disease is a movement disorder characterized by tremor, rigidity and bradykinesia. The first line therapy for the same is medical. But with advancement of this degenerative disease motor fluctuations, dyskinesia and other drug related side effects disable the patient's life. In this situation DBS can improve the motor symptoms, reduce the drug requirements and improve the quality of life.<sup>1</sup> The patient selection, methodology, complications and outcome of the same is discussed here.

**PARKINSONIAN DISORDERS**

In 1817, James Parkinson described in his essay on the Shaking Palsy the symptoms of Parkinsonian disorder.<sup>2</sup> Subsequently other features of this disorder were identified. He described four cardinal features of this disorder i.e. rest tremor, bradykinesia, rigidity, and postural instability. His description included Parkinson's disease and Parkinson plus syndrome.

**PARKINSON'S DISEASE**

PD usually affects the patients in fifth decade.<sup>3</sup> However, disease onset before fourth decade is not uncommon, and such patients are designated as Young onset PD. PD symptoms before the age of 20 years is even rarer and these patients are known as Juvenile PD patients. Both these conditions are rare affecting 5% of PD patients.<sup>4,5</sup> In our personal operated series, 25% of patients are young onset PD and only 1% patients of Juvenile PD.

**Tremor**

Rest tremor is the first symptom in 70% of PD patients. It has frequency of approximately 5 Hz and variable amplitude. It is typically more distal than proximal. It may be intermittent and is almost always asymmetric. Like most tremors, it is worsened by distraction and strong emotion.<sup>6</sup>

**Rigidity**

Parkinsonian rigidity is due to enhanced static or postural reflexes. The rigidity may be of either a "lead pipe" or "cogwheel" quality and is typically asymmetric.<sup>7</sup> The appendicular rigidity is more marked than the axial rigidity.

**Bradykinesia**

Of the cardinal features of PD, bradykinesia has the best correlation with disease severity.<sup>8</sup>

**Postural and gait instability**

The parkinsonian gait is characterized by shuffling of the feet, decreased arm swing and flexion of the neck and spine. Patients are unable to turn in a single step and break their turns into multiple small increments. But the body remains aligned with the feet during this process ("en bloc turns"). Both festination and retropulsion may be seen. Festination arises from an inability to return to an erect posture once leaning forward. Patients appear to chase their center of gravity. Retropulsion occurs as a result of patients' inability to recover from a backward-leaning posture.<sup>2</sup>

**PATHOPHYSIOLOGY OF PARKINSON'S DISEASE**

PD is manifested only after approximately 80% of striatal dopamine and 50% of nigral neurons are lost. It can occur because of both genetic predisposition and environmental exposure.<sup>8</sup>

Bradykinesia and rigidity can be explained by current models. According to the Alexander, DeLong, and Strick model, bradykinesia arises from excessive inhibition of the thalamus by the globus pallidus (pars) interna (GPi), either direct pathway of GPi overactivity or indirect pathway of overactivation of the GPi by an overactive subthalamic nucleus.<sup>9</sup>

**DIAGNOSIS**

PD has to be differentiated from Parkinson's Plus syndrome. These include, Dementia with Lewy Bodies, Progressive Supranuclear Palsy, Corticobasal Degeneration and Multiple System Atrophy. Some of indicators of Parkinson's Plus syndrome include, Symmetrical signs and symptoms; rapid progression of the disease; poor response to medications, including levodopa; repeated falls; vertical gaze restriction; early memory loss and cognitive decline; presence of cerebellar deficits, corticospinal tract signs; early autonomic dysfunction or postural instability; and dysphasia and pseudobulbar palsy. It is important to know these

symptoms as the treatment options and prognosis for the Parkinson's Plus syndrome is poor.<sup>10</sup>

### MEDICAL THERAPY

The initial choice of medical treatment for the Parkinson's disease is individualised. Young patients, patients with early PD; mild symptoms are offered centrally-acting anticholinergic medications, selective irreversible MAO-B inhibitors and amantidine. As the disease advances dopamine agonists and levodopa are introduced. In elderly patients, above 65 years, one can start levodopa from the beginning.

- a. Centrally-acting anticholinergic drugs (e.g. trihexyphenidyl and benztropine) can be effective at reducing tremor and dystonia but less effect on other symptoms. They should not be given to patients older than 65. The common side effects include dryness of mouth and urinary hesitancy.
- b. Selective irreversible MAO-B inhibitors (selegiline and rasagiline) inhibit degradation of dopamine. They have mild therapeutic effects as a monotherapy and augment L-DOPA given exogenously. Multiple additional neuroprotective mechanisms of action are proposed.<sup>11</sup>
- c. Amantidine –This antiviral reduces all symptoms of PD though modestly.<sup>12</sup> It also reduces L-DOPA-induced dyskinesia in advanced PD.<sup>13</sup>
- d. D2/3 dopamine agonists (ropinerole, pramipexole) bind post-synaptic striatal dopamine receptors and exert effect. Though the effect is inferior to L-DOPA, they are preferred for initial treatment as they have less dyskinesia or motor fluctuations.<sup>14</sup>
- e. L-DOPA- It is the gold-standard of medical therapy. This dopamine precursor is converted to dopamine in CNS by enzyme aromatic amino acid decarboxylase (AAAD).<sup>15</sup> The AAAD inhibitors (carbidopa or benserazide) reduce peripheral dopamine production and increase dopamine concentration. Adjunctive treatment with COMT enzyme inhibitors (entacapone and tolcapone) can improve the CNS delivery of L-DOPA through inhibition of degradation to 3-O-methyldopa (3-OMD).<sup>16</sup>

### ADVANCED PARKINSON'S DISEASE

Few years into the treatment patients of PD develop motor fluctuations. These are in the form ON-OFF phenomenon, sudden OFF periods, dyskinesias and hallucinations. It is believed that the pulsatile nature of the dopamine replacement therapies is the cause for this motor fluctuations. Patient progressively require higher doses, however, every incremental dose brings in its share of side effects, limiting its value.<sup>1</sup> This can now be addressed by surgical treatment.

### SURGICAL THERAPY

The breakthrough in the treatment came when Benabid and colleagues found high frequency (above 100Hz)

stimulation of thalamic nuclei produce lesion like effect and suppress tremors. During thalamic lesioning procedures stimulation below 100 Hz was found to augment and above 100 Hz was found to suppress tremor.<sup>17</sup> This was successfully applied to treat PD through both the targets, i.e. the subthalamic nucleus and internal pallidum (nuclei with known increased firing rates in PD).<sup>18</sup>

### Selection criteria

Proper patient selection is critical to the success of deep brain stimulation surgery (DBS). The selection of the patients for DBS is based on:

1. Diagnosis: The patient should have confirmed diagnosis of idiopathic Parkinson's disease. The criteria for the same is presence of bradykinesia with at least one of the other three symptoms namely: rigidity, resting tremor and postural instability. The patient with atypical PD (Parkinson's plus) should not be offered this therapy.<sup>19</sup>
2. Age: The age is debatable predictor factor but increased age will cause cognitive decline, associated co-morbidities and overall increase in surgical risk.<sup>20</sup> We carefully evaluate patients above 70 years and if we find them fit to undergo treatment, do not hesitate to offer them surgery. The oldest patient that has undergone DBS at our centre was 82 years old.
3. Disease duration- In order to avoid misdiagnosis of PD we offer surgery after 5 years of disease. The only exception being patients with severe tremors not controlled with levodopa or other medications, and in such cases we have offered surgery before five years.<sup>21</sup>
4. Disease severity- The motor fluctuations in response to dopaminergic drugs in the form of wearing off effect and dyskinesias are the most common indication for the DBS. Disabling tremor in the absence of above despite drug treatment is also an indication for DBS.<sup>22</sup>
5. L-DOPA responsiveness- It is the single most important predictive factor for positive outcome of DBS. A 30% improvement in the Unified Parkinson Disease Rating Scale III score has been used as one useful marker of positive outcome. The severe tremor resistance to L-DOPA is an exception to this.<sup>23</sup>
6. Cognitive impairment- Dementia is the most important and common exclusion criterion for DBS surgery.<sup>24</sup>
7. Psychiatric illness- Untreated psychiatric illness should be treated before the procedure. Treated depression will not exclude surgical option but adds to the caution.<sup>25</sup>

### TARGET FOR DBS

The globus pallidus internus (GPi) and the subthalamic nucleus (STN) are the two most commonly used targets.

**400** Initially, the GPi was preferred. But subsequently STN was found to be the superior target and STN DBS is considered to be gold standard surgical therapy.<sup>24,25</sup>

<sup>26</sup> Both targets have equal effect in reducing off-time motor symptoms and tremors. STN is superior to Gpi in reducing rigidity and bradykinesia, it has lesser battery usage and medication reduction is achievable to the extent of 40-100%. However, GPi is superior in dyskinesia suppression and gait stability. It has lesser impact on cognitive function.<sup>27</sup> Drug reduction is not achievable with GPi stimulation. We prefer to offer GPi stimulation to those elderly patients, who are significantly disabled by PD and have borderline cognitive deficits.

## **SURGERY**

DBS surgery is best performed by an experienced surgeon with expertise in stereotactic and functional neurosurgery who is a part of team that includes a movement disorder neurologist, neuropsychologist, psychiatrist, and neurophysiologist. We will go on to describe the protocols followed at our centre.

### **Presurgical Assessment**

Patient is admitted two days prior to surgery. The Unified Parkinson's disease Rating Scale (UPDRS) is carried out with best on and 12 hours off medication. The Video recordings using standard protocols are performed during on and off medical condition. Mini-Mental examination is performed to know the cognitive status. The fitness for surgery is done during this phase.

### **Preoperative anatomical target localisation**

STN is localized using a 3T magnetic resonance imaging. First an inversion recovery, sagittal sequence is performed anterior commissure (AC) and posterior commissure (PC) identified. Mid-commissural point identified. The STN is typically identified on a slice 2 mm posterior to the mid-commissural point. At this point STN is 11-12 mm lateral and 4 mm inferior to the intercommissural plane. The preoperative planning to reach the STN through precoronal trajectory is done and co-ordinates obtained.

### **Surgery**

Frame fixation-The surgery is performed using CRW (Cosman-Robert Wales) stereotactic system. The computed topography is performed with frame in situ. Axial computerized tomography (CT) scan is fused with the preoperative MRI using Framelink software. The trajectory is planned through precoronal burr hole avoiding vessels, ventricle and other eloquent structures. The co-ordinates obtained and verified with preoperative ones to rule out major discrepancy. Once this is done, the stimulating microelectrode is inserted through a precoronal burr hole through the predetermined trajectories. Usually three to four trajectories, separated radially around a central trajectory, are used for exploring the STN region. Microelectrode recording (MER) obtained. The position of STN is calculated depending on best MER recording. This is then followed by stimulation of STN at 130 Hz to look for clinical improvement in the PD symptoms. This is done by the neurologist in

the theatre. Similarly, the side effects are noted in each trajectory. The final position is confirmed at optimal improvement in rigidity and bradykinesia without any motor side effects. Once the confirmation of the STN target is obtained, the stimulating electrode is replaced with DBS electrode. Both the electrodes are implanted on the same day. Postoperative CT scan is performed to confirm the position of the electrodes. We implant the IPG (Implantable Pulse Generator) on the next day, under general anesthesia.

## **PROGRAMMING**

We keep the patient off medication overnight and do the programming the next day. First the monopolar programming is performed where single chosen contact point negative and IPG is on the positive side. The width of 60 msec and frequency of 130 Hz is kept. Each and every contact is assessed for improvement and side effects. The best contact with low threshold for improvement and high threshold for side effects is selected for final continuous stimulation. Drug reduction is commenced on day 3 or 4 postoperatively.<sup>1</sup>

## **RESULTS**

Meta-analysis of studies of patients undergoing DBS between 1993-2004 was performed by Kleiner-Fishman et al. They identified 37 cohorts with 921 patients. The mean improvement in the off phase UPDRS III symptoms was 52%, UPDRS II was 50% and the levodopa reduction was around 56%. The average reduction in dyskinesias was 69%. The quality of life (PDQ-39) scores also improved. The scores that significantly improved were stigma (54.4%), activities of daily living (51.6%), mobility (38.5%), bodily discomfort (35.8%), and emotional well-being (32.1%). Dimensions with modest benefit included social support (17.0%), cognition (16.5%) and communication (13.0%).<sup>28</sup> In our series the UPDRS II and III scores improved by 62% and 61% respectively at one year follow up. The levodopa reduction was 54%.<sup>1</sup>

## **Complications**

The complications rate reported in the literature varies between various series. The rates of surgical complications are quite variable in the literature and include intracranial hemorrhage (0%-10%), stroke (0%-2%), infection (0%-15%), lead erosion without infection (1%-2.5%), lead fracture (0%-15%), lead migration (0%-19%), and death (0%-4.4%).<sup>29,30-32</sup> The consensus statement on DBS in PD states that "There was consensus that the incidence of symptomatic intracranial hemorrhage is likely less than 2% for most centers and that lead fracture and migration are likely much lower in recent times owing to improved technology".<sup>33</sup> In our personal series the vascular and hardware complication rates were 0.6% and 4% respectively.<sup>34</sup>

## **SUBTHALAMOTOMY**

Although thalamotomy and pallidotomy are not used for treatment of PD, there is still a role of STN lesioning. Here a permanent lesion is created along the dorsolateral region of STN where kinesthetic neurons are located. The results

of subthalamotomy are similar to STN DBS in the short and long term.<sup>35</sup> The improvement however is variable and not as consistent as DBS. The added advantage of titrability and adjustability of the stimulation parameters offered by DBS makes it a more superior treatment. We offer subthalamotomy to patients who either cannot travel for follow up and programming or who cannot afford the surgery.

### STN DBS IN EARLY MOTOR COMPLICATIONS (NEJM TRIAL)

Recently a randomized multicentric study was conducted across Europe. 251 patients with less than 3 years of motor fluctuations and more than or equal to 4 years of disease duration were randomized between medical and surgical treatment. The study found that neurostimulation was superior to medical therapy with respect to motor disability ( $P < 0.001$ ), activities of daily living ( $P < 0.001$ ), levodopa-induced motor complications ( $P < 0.001$ ), and time with good mobility and no dyskinesia ( $P = 0.01$ ).<sup>36</sup>

### CONCLUSION

Patient with idiopathic Parkinson's disease with motor fluctuations should be referred to centers with an experienced team of experts in DBS surgery for surgical evaluation. In an appropriate candidate STN DBS is treatment of choice which effectively treats motor symptoms, reduce drug requirements and improve the quality of life. The benefits of DBS are sustained for several years. There is still role of STN lesioning for the treatment of Parkinson's disease.

### SURGICAL TREATMENT FOR EPILEPSY

#### Abstract

Epilepsy is a common neurological disorder. Patients who are refractory to 2 anticonvulsants for more than 2 years are to be evaluated further for the feasibility of surgery. The assessment battery includes detailed clinical history, 3T magnetic resonance imaging (MRI), Video EEG, neuropsychological assessment and functional MRI if needed. The surgical options include resective surgeries (anterior temporal lobectomy, Selective amygdalohippocampectomy, lesional surgery), disconnection surgeries (Subpial transaction, callosotomy) and resective plus disconnection surgery (Hemispherectomy). The indications, technique and effectiveness of each is discussed here.

### INTRODUCTION

Epilepsy is the second most commonly reported neurologic condition worldwide and affects people of both sexes and of all ages and socioeconomic statuses.<sup>37</sup> About 40% of newly diagnosed epilepsies are drug refractory and may be considered potential candidates for epilepsy surgery.<sup>38</sup> Despite development in neuroimaging, microneurosurgical techniques and proven effectiveness of epilepsy surgery, it is very much underutilized. Spectrum of surgical procedures from curative to palliative is discussed herewith.

### INDICATIONS OF SURGERY

The main criteria for epilepsy surgery have been formulated by Walker in 1974.

According to his suggestions, the following criteria have to be met to qualify for curative epilepsy surgery: (1) focal or regional seizure onset, (2) drug intractability with 2 anticonvulsants (3) seizures represent a severe handicap, (4) seizures exist for at least 2 years without tendency for remission and despite adequate medical treatment, (5) sufficient general and mental health state of the patient who is sufficiently motivated and compliant in order to collaborate preoperatively, intraoperatively (if necessary) and postoperatively.<sup>39</sup>

According to evidence-based guidelines the first indication for epilepsy surgery in all age groups is resistance to antiepileptic drugs.<sup>40,41</sup> Some modifications of Walker's criteria are (1) the demand for early surgery (at least in certain epilepsy syndromes such as mesial temporal lobe epilepsy, MTLE), (2) indications for "palliative" surgery, and (3) a more liberal indication in children.<sup>40,42</sup>

### CONTRAINDICATIONS

There are no evidence-based contraindications to epilepsy surgery, although the existence of a severe active psychiatric condition (e.g., active psychosis) or medical comorbidities precluding surgery are generally accepted as contraindications. However, surgery should be considered in such individuals with drug-resistant epilepsy if these conditions resolve. Failure to identify an epileptic focus after a complete surgical evaluation by an epilepsy specialist is usually a contraindication to surgery, except for patients with drop attacks. Here, corpus callosotomy may be beneficial in reducing the frequency of drop attacks.<sup>40</sup>

### PHILOSOPHY OF EPILEPSY SURGERY

The knowledge of various zones where the seizure originates and spreads remains essential for the success of epilepsy surgery

- The lesional zone: The area where the lesion is situated in case of lesional epilepsy is lesional zone.

It is generally accepted that the epileptogenic zone lies within or in close spatial neighbourhood of the macroscopic lesion (if present) in the majority of patients. But in few cases it may be away from the lesion.<sup>43</sup>

- The symptomatogenic zone – seizure semiology: It is the area of cortex that, when activated, produces the initial ictal symptoms or signs. It might include cortical areas at distance to the actual seizure onset zone that become activated (in the case of "positive" symptoms) or deactivated (in the case of "negative" symptoms) due to seizure spread.<sup>44,45</sup>
- The irritative zone: The irritative zone has been defined as the area of cortex that generates interictal spikes. It can be measured by non-invasive or invasive EEG, MEG and fMRI. The irritative zone

is usually more extended than the seizure onset zone.<sup>44</sup>

- Seizure onset zone: It is the cortical area that initiates clinical seizures. It can be of two types according to Lüders distinguished between the actual seizure onset zone and the potential seizure onset zone (Figure 1). Lüders suggested that incomplete resection of both the actual or the potential seizure onset zone may result in incomplete seizure control.<sup>46</sup>

## PREOPERATIVE EVALUATION

It includes:

- Detailed clinical history with emphasis on semiology of the seizure.
- Interictal 3T MRI to study abnormalities in the brain structure constitutes the primary investigation.
- Video EEG monitoring to record typical seizures,
- Neuropsychological assessment of baseline cognitive function
- Novel investigations novel functional imaging (e.g., functional MRI, PET, SPECT, functional connectivity) and neurophysiological diagnostic modalities (e.g., detection of high-frequency oscillations or assessment of neuronal connectivity using intracranial EEG recording, magnetoencephalography) have greatly enhanced presurgical planning by increasing the likelihood of identifying lesions not seen on MRI of the patient's brain.<sup>40</sup>

## RESECTIVE SURGERY

Surgical resection of the epileptogenic focus is the preferred surgical approach when possible. The extent of resection may range from simple lesionectomy to single or multiple lobectomies and is tailored based on the individual patient's seizure semiology, imaging findings, and ictal and functional mapping.

## ANTERIOR TEMPORAL LOBECTOMY (ATL)

### Indications

Whereas mesial temporal sclerosis is the most common pathologic basis of focal epilepsy in adults,<sup>47</sup> children demonstrate this finding less commonly and are more likely to have neoplastic lesions,<sup>48</sup> or congenital brain anomalies, such as cortical dysplasia, as the underlying substrate of refractory seizures.<sup>49</sup>

### Technique

Our technique is based on the technique described by Spencer et al. in 1984.<sup>50</sup> We perform 6 cm resection of temporal lobe (based on the anatomy of the vein of Labe) on the non-dominant side and 5 cm resection of middle and inferior temporal gyrus on the dominant side of the temporal lobe. We spare the superior temporal gyrus on the dominant side. There are several variations to this techniques based on individual centres experience and expertise.<sup>51</sup> Mortality after the ATL procedure is very

low, with reported rates ranging from 0 to 0.5% in large series.<sup>52,53</sup> Morbidity rates in a recent review ranged from 0 to 9.3% ,with the most common complications being visual field disturbance, infection, and neuropsychological changes, most notably declines in verbal memory when the dominant hemisphere was resected.<sup>52</sup>

## SELECTIVE AMYGDALOHIPPOCAMPECTOMY (SAH)

### Indications

One school of thoughts believe that sparing the neocortex, by performing SAH, reduces the cognitive morbidity and improved neuropsychological outcome. However, this theory has not been confirmed and various studies have shown equivocal results in postoperative neuropsychological function when comparing these SAH with standard ATL.<sup>54-56</sup> In centres not having adequate expertise in patient selection, the seizure control has been inferior with SAH than with ATL with amygdalohippocampectomy.

### Technique

SAH can be performed through several techniques including transsylvian , transcortical , and subtemporal approaches, with the selection dependent on the patient and the surgeon.

Two large meta-analyses of studies comparing the two procedures head to head found higher rates of seizure freedom after ATL than after SAH.<sup>57,58</sup> One study found no significant difference in intelligence quotient scores between patients receiving the two procedures, and one was unable to make significant conclusions regarding differences in neuropsychiatric outcomes between the two groups. The fact that seizure freedom after SAH may be lower in children than in adults.<sup>59</sup>

### Effectiveness of resective surgeries

Cohort studies and RCTs consistently show that, in focal drug-resistant epilepsy, resective brain surgery results in seizure freedom for about 57% of patients who undergo neocortical resections and for 70% of those who undergo anteromesial temporal resections, compared with 5%–8% of patients receiving optimum medical therapy.<sup>60-63</sup> In a recent RCT comparing medical therapy to early surgery in patients with temporal lobe epilepsy, 73% of patients in the surgical group became seizure free during the second year of follow-up, compared with 0% in the medical group.<sup>61</sup> A meta-analysis of one RCT and 19 observational studies comparing surgery with medical therapy found an absolute risk reduction of 42% (95% CI 32%–51%) for any seizure recurrence in patients who underwent surgery.<sup>64</sup> Similar surgical outcomes have been reported in cohort studies involving older patients.<sup>65</sup>

### Hemispherectomy

The use of cerebral hemispherectomy for control of seizures implies that the pathological processes of the epileptogenic brain, the seizure foci, are lateralized to one hemisphere, and that the other hemisphere has preserved its anatomical and physiological integrity.

The causes can be congenital or acquired.

Congenital etiologies regroup conditions such as infantile hemiplegia from prenatal vascular insult, hemimegalencephaly, diffuse non-hypertrophic dysplasia and Sturge-Weber disease, while acquired conditions such as cerebrovascular accident (hemorrhagic or embolic), head injury, cerebral infection, or chronic encephalitis of Rasmussen occur after early normal development.<sup>66</sup>

- a. Anatomical hemispherectomy: It consists in the anatomic removal of one cerebral hemisphere with or without the basal ganglia.<sup>66</sup>
- b. Hemidecortication: It consists in the removal of the whole cerebral cortex with sparing of the white matter, thus avoiding opening of the lateral ventricle.<sup>67</sup>
- c. Modified hemispherectomy: It is developed by Adams consisting of anatomical hemispherectomy followed by occlusion of the ipsilateral foramen of Monro with muscle to prevent communication between ventricular CSF and the hemispherectomy cavity, adding the reduction of the volume of the hemispherectomy cavity by tacking the convexity dura to the falx, the basal dura, and the tentorium, thus creating a large extradural space.<sup>68</sup>
- d. Functional hemispherectomy: It consists of an anatomical subtotal but physiologically complete hemispherectomy is based on principles of disconnection rather than excision.<sup>69</sup>
- e. Hemispherotomy: It consists in disconnecting the hemisphere with minimal brain tissue removal.

Two approaches have been described.

Delalande and colleagues proposed a vertical approach where the hemisphere is disconnected through a posterior frontal transcortical approach to the lateral ventricle.<sup>70-72</sup>

The lateral approach (Peri-insular hemispherotomy) is part of a continuum with the highest disconnection-versus-excision ratio in the technical variations of functional hemispherectomy.<sup>73,74</sup>

Long-term improvement in seizure control following hemispherectomy is anticipated in 90–95% of patients. This benefit can be further divided into two categories: those patients who become and remain seizure-free (70–85%) and those who continue to have some seizures but benefit from at least an 80% reduction in seizure frequency (10–20%). These figures reflect the experience of different surgeons, using different techniques, for different pathologies and are useful for discussion with patients and their families.<sup>75</sup>

## SUBPIAL TRANSACTION

### Indications

1. Focal seizures arising in eloquent cortex (with or without resective surgery of the adjoining area when the epileptogenic zone extends away from the eloquent cortex).<sup>76</sup>
2. Landau-Kleffner Syndrome. Landau-Kleffner

Syndrome (LKS) has been traditionally one of the main indications for MST in children. LKS is defined as an acute or progressive, acquired epileptic aphasia (AEA) or verbal auditory agnosia in previously normal children associated with the presence of epileptiform discharges over the central and superior temporal regions that become more frequent during sleep.<sup>77</sup>

3. Malignant Rolandic-Sylvian Epilepsy Syndrome. Malignant Rolandic-Sylvian Epilepsy (MRSE) syndrome was described by Otsubo et al. in children presenting with intractable sensorimotor partial seizures that progress to secondary generalization.<sup>78</sup>

### Rationale and technique

Rationale of MST consists of linear and parallel cuts 5 mm apart across the region defined as the epileptogenic zone. The principle is based on the selective destruction of the short horizontal fiber connections with preservation of vertically oriented neuronal elements.<sup>76</sup>

## CALLOSOTOMY

### Rationale

Corpus callosum is the largest white matter bundle connecting two cerebral hemispheres. In multifocal epilepsies seizure originate from various areas of brain and spread through corpus callosum to cause secondary generalization. Sectioning of corpus callosum can therefore reduce the generalization or bilateral synchronization.<sup>79</sup>

### Indication

The categories of patients considered for corpus callosotomy include those with multifocal or unresectable focal generalized epilepsy, progressive epileptic hemiplegic encephalitis (Rasmussen's syndrome), Forme-Fruste infantile hemiplegia with a functional hand, and the Lennox-Gastaut syndrome and Sturge-Weber syndrome.<sup>80,81</sup>

### Technique

The callosotomy can be partial (anterior 2/3<sup>rd</sup> resected) or complete (entire corpus callosum resected).<sup>79</sup> We advocate partial callosotomy to avoid complications of major disconnection syndrome.

### Seizure control

Spencer et al. reported that total corpus callosotomy prevented secondarily generalized seizures in at least 75% of patients, which is consistent with other series.<sup>82</sup> They found that total callosotomy was more than twice as effective as partial section. Fuiks et al. found that 70% of their 80 patients undergoing anterior callosotomy had significant improvement in their seizures, and 12.8% were cured.<sup>83</sup>

### Neuromodulation

It includes vagal nerve stimulation, direct cortical electrical stimulation (DCS), transcranial magnetic stimulation (TMS) which have shown promising results. Deep brain stimulation (hippocampal, anterior thalamic and STN)

404 and RNS are newer modalities under evaluation. Out of these VNS is only approved treatment modality and discussed here.

## VAGAL NERVE STIMULATION (VNS)

### Indications

VNS is one of the first neuromodulation techniques used for intractable epilepsy. It is an adjunctive therapy aimed at reduction in the frequency of seizures, especially in patients suffering from partial seizures (with or without secondary generalization); or generalized seizures, which are refractory to antiepileptic medications.<sup>84</sup>

### Technical aspects

Left Vagus nerve is selected for stimulation. It is approached through a carotid or transverse neck incision at the mid-neck level. The main vagal trunk is identified and exposed for 3-4 cm in the carotid sheath. Electrode coils are passed around the nerve without putting undue tension on the nerve or the coil. The electrodes are tunneled subcutaneously and connected to a pacemaker (after trial stimulation) implanted in the infraclavicular region.<sup>85</sup>

### Effectiveness

Randomized controlled trials have shown that vagal nerve stimulation can reduce seizures by 25% on average (95% CI 14%–34%),<sup>86</sup> and RCTs have also shown a net improvement (active minus control) in seizure frequency of 15% (Interquartile range 2%–24%) with hippocampal stimulation,<sup>87</sup> 20% ( $p = 0.01$ ) with recursive cortical stimulation,<sup>88</sup> and 26% ( $p = 0.001$ ) with stimulation of the anterior thalamus.<sup>89</sup>

## CONCLUSION

Surgery for epilepsy ranges from resection, disconnection to neuromodulation. It is very effective but underutilised modality of treatment. So it is necessary to spread the awareness regarding the same for the wellbeing patients suffering from this common disorder.

## CONFLICT OF INTEREST

None

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