Neurosciences News Letter

Jaslok Hospital and Research Centre

Message From Dr. Paresh K. Doshi

Dear Colleague

It gives me a great pleasure to bring out this update on the Functional neurosurgery program under my guidance. New therapies have emerged during past couple of years. Long term follow up of established treatments are available to let us make informed decisions. I would like to share with you some original research work that has been initiated and contributed through our program through this newsletter. I take this opportunity to wish you Happy Diwali and a joyous new year.

Regards,

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Update on subthalamic nucleus (STN) stimulation for Parkinson's disease (PD).

The first STN deep brain stimulation surgery (DBS) was reported by Prof. Benabid in 1993. Seventeen years have passed and around **75000** DBS surgeries have been performed worldwide with approximately 600 surgeries performed in India (Medtronic database). We have performed around **200** surgeries since 1998-2010. This is the single largest experience in India with the second largest centre having performed not more than 100 surgeries.

Outcome of STN DBS :

In multicentre long term (5-6 yrs.) follow up study it was found that STN DBS improved off phase motor UPDRS scores by 50.5%; dyskinesias and ADL were significantly improved. There was significant reduction in anti PD medications.[1] Another meta-analysis of outcome, which evaluated 22 studies, found improvements of 30% in off phase motor UPDRS, 56% reduction of levodopa equivalent dose (LEDD) and 69% reduction in dyskinesias. Off periods were reduced by 68%. The most common serious adverse event reported was intracranial hemorrhage in 3.9% of patients.[2] These results are similar to our results showing improvement of 54% in motor UPDRS and 38% reduction in LEDD in 26 patients followed up for 4 years[3] (Fig. 1).

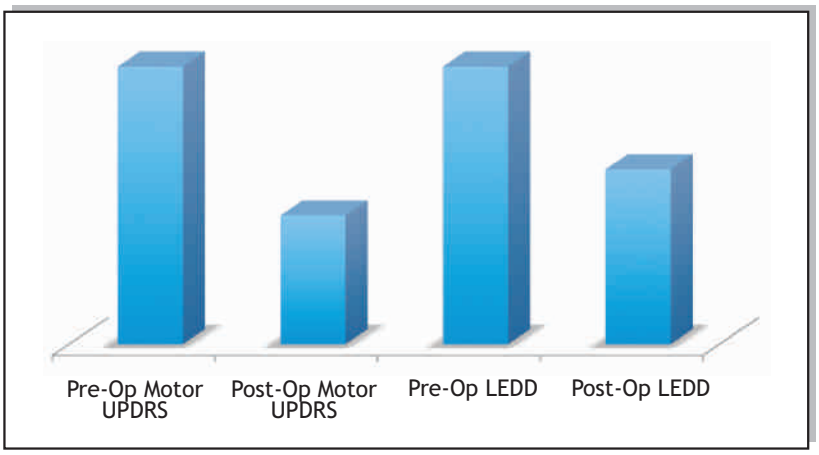

Fig. 1. Four year follow up of STN DBS
(Doshi et al, Mov. Disord 2006)

DBS now being advocated for early motor fluctuations:

The average duration of PD in patients under going DBS from 1993-2000 was 12-14 years. However, during the past decade the average disease duration has come down significantly. There is now growing evidence that DBS performed already with beginning motor fluctuations and an average disease duration of 7 years, may lead to earlier improvement of motor deficits and quality of life, thus preventing disease-related psycho-social decline, and extending the period of beneficial effects of STN-DBS.[4] Agid and his group performed a randomized controlled trial between early surgery and best medical treatment in patients with average disease duration of 6.7 years. After 18 months, they found that surgery improved Quality of life by 24% (0% medical management, p< .05), the severity of parkinsonian motor signs "off" medication, levodopa-induced motor complications, and daily levodopa dose were **reduced** by 69%, 83%, and 57% in operated patients and **increased** by 29%, 15%, and 12% in the group with medical treatment only (p < 0.001). Adverse events were mild or transient, and overall psychiatric morbidity and anxiety improved in the surgical group. They concluded that STN DBS should be considered a therapeutic option early in the course of Parkinson disease.[5] There is a multicentre trial known as EARLY-STIM underway in Europe to confirm these results.

DBS in elderly patients:

Few literature reviews (<10) have been published about the role of DBS in elderly patients. The consensus of these reviews is that while it is efficacious in improving motor complications of Parkinson's disease, it does not improve the axial UPDRS scores or quality of life and results in higher morbidity. We evaluated 37 patients above 65 years undergoing STN DBS between 1998-2008. The average age was 70 years and the mean follow up was 33.52 months. To evaluate the correct impact of surgery on these patients we included the analysis of Zarit Caregiver Burden Inventory (ZCBI) to understand its influence on caregiver. The improvement in total UPDRS and motor UPDRS were not significantly different as compared to the similarly matched (preoperative) UPDRS cohort of our younger patients (Fig. 2). However, the reduction of Levodopa dosage was less as compared to that in younger patients. ZCBI improved from a mean of 36.9 to 26.9. Caretakers of all patients' felt that STN DBS had positively affected there and the patients' QOL. The most common complication included intraoperative and post operative confusion. We did not find any difference in the rate of other complications. To minimize complications we have adopted special preoperative, intra operative and postoperative protocols, which include personalized nursing care, shortened operative time, minimal number of microelectrode recording trajectory, different intraoperative stimulation protocol and neurophysiological assessment etc. We conclude that STN DBS continues to provide effective control of some of the cardinal disabling motor symptoms resulting in improved patient care and reducing the caretaker burden.

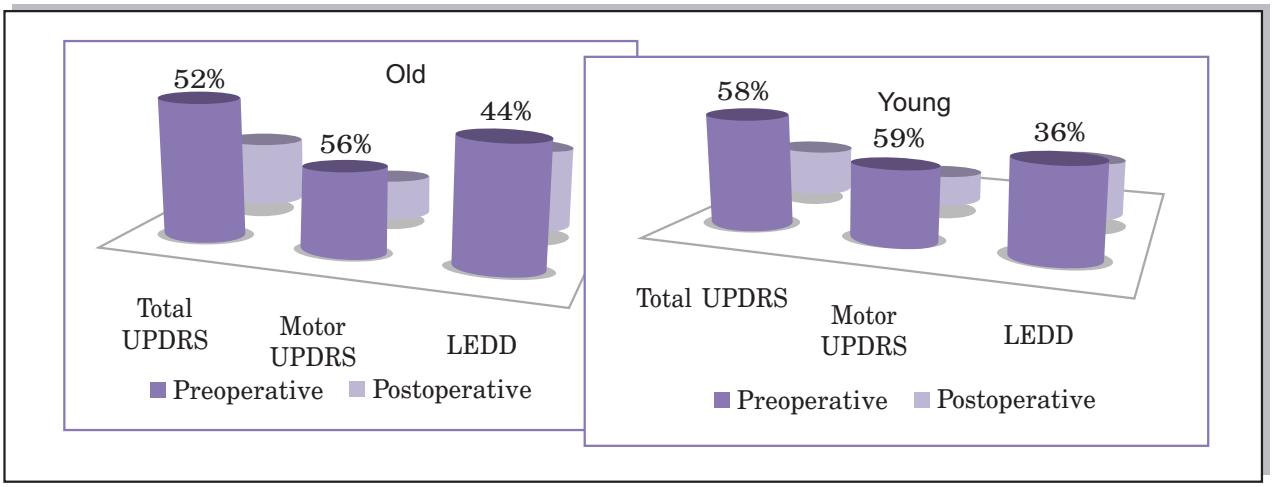

Fig. 2. Comparative outcome measures in young and old patients with STN DBS

DBS for Hallervorden-spatz disease:

As we know this is a progressive neurodegerative disease characterized by extrapyramidal dysfunction and dementia. The pathophysiology involves abnormal iron accumulation in the brain due to alteration in metabolism. The MRI picture is quite diagnostic with hypointensities the region of globus pallidi, known as "eye of tiger" sign. Patients have severe dystonia, which relentlessly progress over time. We had a 13 years old girl, who was completely bed ridden due to HVS with a BFMDRS of 120 (Max. score 120) (Fig. 3). She was in this clinical state for more than 3 years. She had become cachectic due to swallowing difficulty and constant dystonia. Following proper counseling, we planned to perform bilateral GPi DBS last year. We also performed gastrostomy to improve her nutrition. We used a rechargeable pacemaker to ensure longer battery life. At the last follow up (one year) she was able to stand with some support, take a few steps with the physiotherapist (Fig. 4) and her BFMDRS score had dropped to 56 i.e. more than 50% reduction. She has started accepting oral feeds and we are planning to remove her gastric tube.

Fig. 3.
Nbia- Pre operative-bed bound

Fig. 4.
Nbia postoperative walking

Epilepsy Surgery Program:

We started our epilepsy surgical program way back in 2002. Dedicated epileptologist, pediatric neurologist and neurophysiologist support surgical program. We have all the essentials for epilepsy surgical program in place, which include facilities for extended video EEG, PET scanning, neuropsychological assessment and advanced imaging facilities with 3T-MRI for functional mapping. We have performed all types of epilepsy surgeries including temporal lobectomy, corpus callosotomy, hemispherotomy and lesion excisions. **There are special cost effective packages available for non-affording patients.**

Anterior temporal lobectomy for refractory epilepsy arising from mesial temporal lobe sclerosis has now become a standard of care therapy for this condition. At the Jaslok Hospital and Research Centre, the Epilepsy Clinic screens patients for this condition and then patients undergo a comprehensive evaluation prior to selection for this surgery.

About 55-70% of patients undergoing temporal lobe resection become completely seizure free. **Of the 78 surgeries performed at our institution**, data analysis was performed on the first 30 patients with a minimum 3 year post-operative follow-up. In our series of patients Engel's class 1 outcome post surgery was observed in twenty-four patients, Class 2 in five and Class 3 in 1 patient. This means that effective seizure control was achieved in more than 90% of patients. Six of them are off medications (20%) and anti-epileptic drugs (AEDs) are being tapered in five patients. Two patients have remained seizure free for two years after AED discontinuation, and thereby are "cured" (Ozkara2008). Surgical outcome in our series is better than that reported in the literature due to careful patient selection. This has been accomplished without any permanent surgical morbidity or mortality.

Surgery for Psychiatric disorders:

Surgery for intractable neuropsychiatric illness has generated considerable controversy related to the widespread and indiscriminate use of psychosurgery in the 1940s and 1950s when no effective psychotropic agents were available. Today, despite the vast array of new, selective psychotropic medications available, many neuropsychiatric illnesses remain refractory and, consequently, some patients remain severely disabled. These patients might be considered appropriate candidates for surgery if the overall result and level of functioning could be improved.

Last year 25 psychiatrists from across India met in Mumbai, to evaluate the evidence of Psychiatric disorders surgery (PDS) and formulate guidelines for offering the same. (www.neurologicalsurgery.in). Treatment resistant OCD with a YBOCS score of >25 was considered as a main indication.

Recently we had a 61-year-old gentleman who suffered from OCD for more than 20 years. His YBOCS score was 38-40/40. He had been confined to house for last several years and had not been able to collect his pension due to his inability to sign. After considering all the options, we performed anterior capsulotomy for him. (Fig. 5). Intraoperatively he reported improvement in his anxiety and mood. One week postoperatively, though he has become little lethargic his OCD symptoms have significantly reduced (YBOCS=9), depression improved to 6 and he has no anxiety.

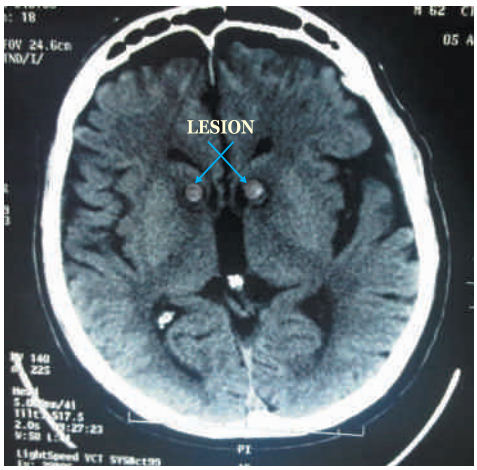

Fig. 5. Postoperative axial CT Scan showing bilateral anterior capsulotomy

Occipital Nerve Stimulation for Intractable Migraine:

Patients with intractable migraine can benefit from stimulation of the occipital nerves. Migraine headaches can be modulated via trigemino-cervical complex connecting the trigeminal and occipital nerves through brain stem with projections on to thalamus. Matharu and Godsby showed this in 2003. Till date approximately 40 cases have been performed and there are two ongoing trials to look at the efficacy of this therapy. We performed one such case last year. The patient was on more than 20 tablets a day, virtually for 25 days a month. He had a good response to stimulation. He could switch on the stimulator at the onset of attack and abort it.

[1] Moro E, Lozano AM, Pollak P, Agid Y. Long-term results of a multicenter study on subthalamic and pallidal stimulation in Parkinson's disease. Mov Disord. 2010 Apr 15; 25(5): 578-86

[2] Kleiner-Fisman G, Herzog J, Fisman DN, Mov Subthalamic nucleus deep brain stimulation: summary and meta-analysis of outcomes. Mov Disord 2006 Jun; 21 Suppl 14:S290-304

[3] Doshi PK, Chhaya N, Aggrawal A, et al. Chronic bilateral STN DBS in advanced Parkinson's disease-4 yrs. Follow up. Mov Disord vol 21, suppl. 15 pS682, 2006.

[4] Schnitzler A, Fuchs G, Baas H, Dillmann U, et al. Early deep brain stimulation for Parkinson's disease. Fortschr Neurol Psychiatr. 2010 Mar; 78 Suppl 1:S37-40. Epub 2010 Mar 1

[5] Schüpbach WM, Maltête D, and Houeto JL, et al. Neurosurgery at an earlier stage of Parkinson disease: a randomized, controlled trial Neurology. 2007 Jan 23; 68(4): 267-71. Epub 2006 Dec 6.

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