

What's Hot in Parkinson's Disease?

More Evidence and More Choices for DBS Therapy: The Time Has Come to Tailor Surgical Therapies

Two new important deep brain stimulation (DBS) trials highlight the importance of tailoring therapy for individual Parkinson's disease patients. The PD SURG trial results (conducted by a multicenter team of collaborative investigators from all over Britain) include a one year follow-up of Parkinson's disease deep brain stimulation (DBS) patients. The trial was randomized, and it compared DBS to best medical therapy. The primary outcome variable was quality of life, and interestingly, patients in the best medical therapy arm had access to apomorphine pumps. Though sites were allowed to use the subthalamic nucleus target (STN), the globus pallidus interna target (GPI), and even lesion therapy (e.g. pallidotomy), 174/178 (98%) of patients in the surgery group were implanted with subthalamic nucleus DBS. There was a five point improvement noted in quality of life scores in the surgical compared to medical group. Although compared to other studies the quality of life improvement was less robust, this may have reflected a longer study duration, or potentially even disease progression. There were unmistakable improvements in dyskinesias, and on time in the surgical group, although diaries were not utilized.

Though not a perfect trial, its large size and use of a medical control group along with access to apomorphine pumps made it unique among recent DBS studies. The results underscored the powerful influence that DBS can have on motor fluctuations. Additionally, these SURG investigators plan in the future a long term (9 year) follow-up, and this will surely enlighten the field as to disease progression, and other issues potentially important to DBS cohorts.

One hidden aspect of this trial was the report of the "reasons why patients sought DBS surgery." Severe off periods, dyskinesia and tremor were far and away the most common indications cited for DBS therapy. As DBS moves into a tailoring phase, (the right target and approach for a particular symptom or symptom cluster) this type of information will be very useful to clinicians.

It is fascinating to see that 98% of implants were placed in the subthalamic nucleus in this study, despite the

option for surgeons to use a different target. Though the subthalamic target has many strengths, it also has relative weaknesses. Emerging data is now strongly suggestive that the motor outcomes in pallidum and subthalamic nucleus are actually similar, and that targets in the future should be tailored for individual patients and individual symptoms.

The results of the long-awaited Department of Veterans Affairs "Subthalamic Nucleus (STN) Versus Globus Pallidus (GPi) Trial" were announced shortly after the PD SURG trial. Two hundred and ninety-nine patients were randomized and patients were followed carefully for two years post-implantation. The results of this study, like the NIH COMPARE trial published in 2009, confirmed that motor outcomes were equivalent whether implanted in STN or in GPi. There were however, subtle differences between brain targets, and as more data emerges we will hopefully be able to start matching patient profiles to specific brain targets.

Can we say the PD-SURG trial and the Veterans Affairs DBS trial were a surge forward for the PD community? The answer is certainly yes, as the publication of more carefully controlled DBS trials will be important in guiding the therapy. There is now solid evidence supporting the efficacy of DBS in select patient populations, and emerging data that may help us in selecting the right target for the right patient to create "a truly tailored approach."

Read Dr. Okun's monthly column, "What's Hot in PD?" online at www.parkinson.org.

AUTHOR: MICHAEL S. OKUN, MD, NPF National Medical Director

References: Follett KA, Weaver FM et al. "Subthalamic versus Pallidal Deep Brain Stimulation for Parkinson's Disease." *New England Journal of Medicine*, June 3, 2010, Vol. 362 (22), pp. 2077-2091.

Williams A, et al. "Deep brain stimulation plus best medical therapy versus best medical therapy alone for advanced Parkinson's disease (PD SURG trial): a randomized, open-label trial." *The Lancet Neurology*, June 2010, Vol. 9, Issue 6, pp. 581-591.

