Brain Stimulation Eases Parkinson's Symptoms

Patients on implants and medication regimen saw improvements in quality of life, motor function.

BY JOHN R. BELL
Associate Editor

Patients with Parkinson's disease who received continuous electrical stimulation to the subthalamic nucleus experienced significantly greater improvements in various measures of quality of life and motor function after 6 months than did patients who received medication alone, Dr. Günther Deuschl and colleagues reported.

Results of a new randomized controlled trial from the German Parkinson Study Group of a nonblinded, intention-to-treat population of 78 patient pairs (156 patients) were reported by Dr. Deuschl of Christian Albrechts University in Kiel, Germany, and his colleagues. Patients were recruited from centers in Germany and Austria. One patient in each pair continued to receive an individualized medication regimen alone, while the other received pulsed electrostimulation to the subthalamic nucleus via a surgically implanted device in addition to the medication regimen; stimulation was ongoing and adjusted for each patient (N. Engl. J. Med. 2006;355:896-908).

Primary outcomes were changes in quality of life, as reflected in scores on the Parkinson's Disease Questionnaire (PDQ-39) summary index, and changes in symptom severity after medication withdrawal, as measured by the Unified Parkinson's Disease Rating Scale, Part III (UPDRS-III), the investigators reported.

In 50 of the 78 pairs, the patient who had received neurostimulation showed greater improvements in PDQ-39 summary score than the patient treated with medication alone. The mean PDQ-39 summary score went from 41.8 at baseline in the neurostimulation group to 31.8 at 6 months—an improvement of 24%. In the medication-only group, the mean score was 39.6 at baseline and 40.2 after 6 months.

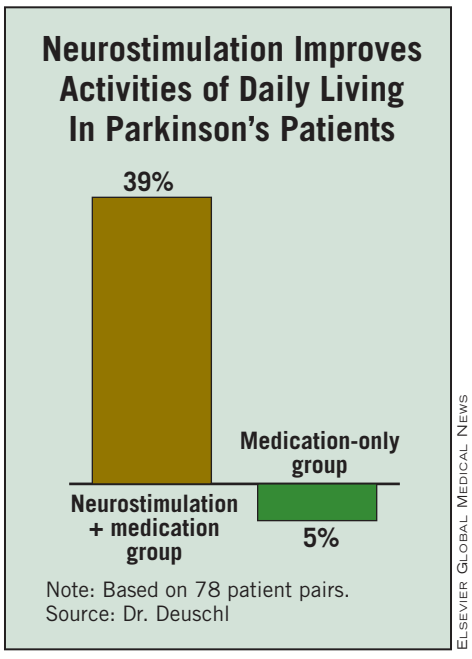
Motor function (level of symptom severity) in each patient was assessed via the UPDRS-III after a 12-hour withdrawal of antiparkinsonian medications at baseline and at 6 months. In 55 pairs, the patient treated with neurostimulation had a better UPDRS-III score than the nonstimulated patient without medication, reported Dr. Deuschl and colleagues. The neurostimulation group's mean score was 48.0 without medication at baseline, improving to 28.3 at 6 months. For the nonstimulation group, the mean score barely changed, going from 46.8 at baseline to 46.0 at 6 months.

A dyskinesia assessment was collected via patient diaries, and different medications and dosages were converted to equivalents for comparison. Also administered were the Schwab and England scale for activities of daily living, the Montgomery and Asberg Depression Rating Scale, the Brief Psychiatric Rating Scale, and the Medical Outcomes Study 36-item Short-Form Health Survey.

Most measures showed significant mean improvements for the neurostimulation group versus slight declines for the medication-only group; the exceptions were nonsignificant, except for medication dosage, which declined for both groups, but far more so in the neurostimulation group (49% vs. 10%, respectively). Notably, the neurostimulation patients saw a 39% improvement in activities of daily living, versus a 5% decline in the medication-only patients. Psychiatric measures did not differ significantly between the two treatment groups.

The investigators reported 13 adverse events—10 in the neurostimulation group and 3 in the medication-only group. Three patients in the neurostimulation group died, one as a result of a hematoma occurring during surgery, one from pneumonia, and one from suicide. A patient in the medication group died after driving during a psychotic episode.

The overall results demonstrate "superior efficacy" of neurostimulation, the investigators concluded, with "significant and clinically meaningful improvement in quality of life … [and] longer periods and better quality of mobility with less dyskinesia. These changes … led to improvement in measurements of activities of daily living, emotional well-being, stigma, and body discomfort." However, these benefits should "be weighed against the risk of complications related to surgery," Dr. Deuschl and colleagues cautioned. ■



Parkinson's More Benign in Women

BY KERRI WACHTER
Senior Writer

WASHINGTON — Women who develop Parkinson's disease do so at an older age than affected men, are more likely to present with a tremor-dominant form, and have higher levels of striatal dopamine transporter, according to data presented at the World Parkinson Congress.

"Several findings in our study indicated a more benign phenotype for women with Parkinson's disease," said Dr. Charlotte Haaxma of Raboud University in Nijmegen, the Netherlands.

Dr. Haaxma and her colleagues retrospectively studied 253 patients with Parkinson's disease (PD) seen at their clinic between 1988 and 2003 to assess gender differences. Men accounted for 62% of patients. Patients were excluded from the study if they were taking levodopa or another dopamine agonist, had the disease for longer than 10 years, had physical disabilities resulting from another disease, used non-PD drugs, or were demented.

The researchers assessed the age at onset, presenting symptoms, estrogen status, Unified Parkinson Disease Rating Scale (UPDRS) motor scores, and dopamine transporter levels measured by [I-123]FP-CIT single-proton emission computer tomography (SPECT) imaging. UPDRS motor scores were assessed every 3-6 months.

Women were slightly older at the age of onset (53 years) than men (51 years). Women were also more likely to present with tremor—67% vs. 48%. "This gender difference remained intact throughout all age categories," said Dr. Haaxma.

This finding prompted the researchers to look more closely at patients with tremor as the presenting symptom. Patients who presented with tremor were on average age 55 years at onset, compared with patients who presented with bradykinetic rigidity (age 50 years at onset).

"Women were older at symptom onset. They presented more often with tremor, and, if so, had an even higher age at onset," said Dr. Haaxma. In addition, "the more children that a woman had, the higher the age at onset—2.7 years later per child," said Dr. Haaxma. Women also had onset 0.5 year later for each fertile year. No correlations were found for age of menarche or estrogen therapy with age at onset.

Mean UPDRS motor scores were comparable for both genders at onset and the rate of degeneration did not differ between genders. However, tremor-dominant patients had a 38% slower rate of UPDRS motor score decline than bradykinetic-rigid subtype patients.

In terms of [I-123]FP-CIT SPECT imaging, women had a 16% higher mean binding than men, indicating higher striatal levels of dopamine transporter. However, the rate of dopamine transporter loss did not differ between genders. The tremor-dominant group tended to have a slower rate of deterioration, though this trend did not reach statistical significance.

The researchers proposed two hypothetical models to interpret the findings. In the first model, women have higher dopamine striatal levels and therefore take longer to reach the point of symptom onset. "Further, the estrogen effect of parity and other items associated with high cumulative estrogen levels might … delay the moment of symptom onset further," said Dr. Haaxma.

In the second model, women have a slower rate of progression, so they take longer to reach symptom onset. Estrogen effects would translate into an even slower rate of decline. However, once symptoms start, the estrogen effect decreases, and men and women deteriorate with similar speed. ■

Olfactory Deficits Seen in Early Parkinson's Disease

WASHINGTON — Researchers in Japan have used functional magnetic resonance imaging to identify brain activation deficits associated with olfactory dysfunction in patients with Parkinson's disease, according to data presented at the World Parkinson Congress.

In a study of 10 patients with Parkinson's disease (PD) compared with 10 healthy controls, the researchers found significant brain activation in the cerebral cortex in control patients exposed to strong odorants, while PD patients showed little brain activation. Olfactory dysfunction appears to be one of the earliest symptoms of the disease.

"In PD, brain activation by odorant stimulation was significantly decreased. Hyposmia in PD is not a simple reflection of impairment in sniffing," said Atsushi Takeda, Ph.D., of Tohoku University in Sendai, Japan.

The PD study participants had an average Hoehn and Yahr stage score of 2.2 and their mean L-dopa dosage was 243 mg. "So they were in the early stage of Parkinson's disease," Dr. Takeda noted.

However, current olfactory tests for early PD detection rely on subjective responses by the patient and can potentially be influenced by environmental factors, such as temperature and humidity. "Most importantly, possible impairment in sniffing, as one of the motor symptoms of Parkinson's disease, may influence olfactory perception," said Dr. Takeda.

The researchers used vanillin and toluene as olfactory stimulants. Patients were exposed to no odorants for 30 seconds, followed by odorant exposure for 30 seconds. This cycle was repeated six times.

To maintain constant odorant stimulation during the "on" periods, the researchers designed a special system with an evaporator and computer-controlled valves to allow exposure to the odorant and a high-pressure compressor to move the odorant to the subject wearing a face mask in the MRI tube. The researchers used a 1.5-T machine to obtain T2* images that were analyzed using statistical parametric mapping.

—Kerri Wachter