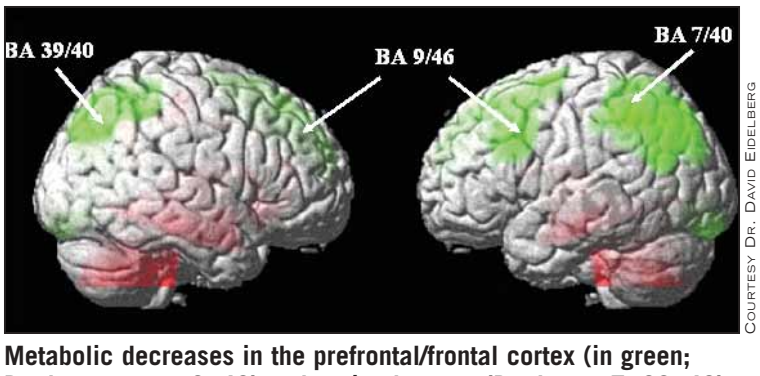
Serial PET Predicted PD-Induced Cognitive Loss

BY KERRI WACHTER
Senior Writer

WASHINGTON — Cognitive changes in Parkinson's disease can be seen on positron emission tomography imaging and correlate well with psychological tests, according to data reported in a poster at the World Parkinson Congress.

Dr. David Eidelberg, director of the Center for Neurosciences, and his colleagues at The Feinstein Institute for Medical Research at the North Shore-Long Island Jewish Health System in Manhasset, New York, studied 47 Parkinson's disease (PD) patients (31 men and 16 women) using ^{18}fluorodeoxyglucose PET imaging to identify metabolic patterns associated with cognitive function in PD. In addition to affect, four domains—memory/verbal learning, attention/executive function, visuospatial function, and general cognitive function—were assessed with neuropsychological testing. "We looked for patterns in the brain that correlated with their psychologic performance," Dr. Eidelberg said.



COURTESY DR. DAVID EIDELBERG

Metabolic decreases in the prefrontal/frontal cortex (in green; Brodmann areas 9, 46) and parietal cortex (Brodmann 7, 39, 40) typify PDCP for mild/moderate cognitive impairment.

The patients were an average age of 58 years and had PD for an average of 12 years. General cognitive function was assessed using the Mini-Mental State Examination. PET scans were analyzed using network analysis that isolates different aspects of neural circuits that correlate with a person's cognitive function. Analysis revealed a significant pattern of covarying metabolic reductions in the parietal cortex, anterior cingulate area, and medial frontal lobe (see illustration in which the left and right panels represent the right and left hemispheres, respectively). This pattern correlated negatively with performance on the California Verbal Learning test, Stroop test, digit symbol test, and Hooper Visual Organization test, and positively with the Trail Making test, but not with affect. The researchers also validated this PD cognitive-related pattern (PDCP) in 21 patients with PD, who were scanned twice over a 2-month period. Comparison of the test-retest results showed that PDCP was highly reliable as a predictor of psychological performance. "What makes this appealing is that there is a way to measure cognitive function indirectly," Dr. Eidelberg said.

The researchers also investigated two clinical applications for the technique. First, they computed the PD-related pattern (motor function) and PDCP in 15 early-stage patients, who were scanned at baseline and at 2 and 4 years. PDCP expression was significantly elevated at the third time point with respect to both baseline and the second time point. "The motor pattern is higher typically and progresses like a straight line. The PDCP starts slower and may not be a straight line in terms of its evolution," he said.

In PD the motor and cognitive changes have different time courses. Cognitive changes have a later evolution in the course of the disease. "Treating the motor component of Parkinson's disease, which is what we all do, does not appear to really do much for cognition and at times makes it worse," Dr. Eidelberg said.

The researchers also prospectively computed PDCP expression for PD patients on and off treatment during consecutive days. "While the levodopa and deep brain stimulation were very helpful in the elevated PD-related pattern network, the same interventions in the same people had no real effect on PDCP," he said. This finding implies that new therapies are needed to treat cognitive changes.

The data validate PDCP as a stable and reproducible imaging marker of cognitive function in PD. Unlike the PD motor-related pattern, the nonmotor pattern evolves slowly over time and its expression is not altered by therapeutic interventions targeting the motor manifestation of PD. ■

Higher Suicide Rates Reported in Parkinson's Patients After DBS

BY DOUG BRUNK
San Diego Bureau

SAN DIEGO — Parkinson's disease patients who have undergone subthalamic nucleus deep brain stimulation have higher rates of completed and attempted suicide than do others with the disease, Dr. Valerie Voon reported at the annual meeting of the American Academy of Neurology.

The rate of completed suicides following deep brain stimulation (DBS) for Parkinson's disease (PD) was found to be 0.4% and the rate of attempted suicides 0.9% in the largest multicenter study of its kind, said Dr. Voon, a psychiatrist with the National Institute of Neurological Disorders and Stroke, Bethesda, Md.

The researchers noted that the suicide rate among PD patients within the first year after undergoing subthalamic DBS was 11- 37 times higher than the suicide rate in the general population, based on World Health Organization data. The rate was 4-13 times higher in postoperative year 2 and dropped to baseline in postoperative years 3 and 4.

The rate of suicide is 10 times lower in PD patients who have not undergone DBS, when compared with the World Health Organization's general population data, she added.

Dr. Voon and her associates surveyed 75 movement disorders centers in North America and Europe to locate PD patients who underwent subthalamic nucleus DBS and subsequently attempted or completed suicide. Participating centers had published medical literature on DBS and had operated on more than 100 DBS patients.

Of the 75 centers, 55 responded and provided data on 5,255 PD patients who underwent subthalamic nucleus DBS. Following DBS, 22 of the patients completed suicide (0.4%) between 1 month and 4 years.

The researchers also found that 47 patients attempted suicide (0.9%). The attempted suicides took place between approximately 1 week and 8 years following DBS.

Preoperatively, three completed and three attempted suicides were reported. These patients were on DBS wait lists.

"The highest risk period is in the first 10 months to 1.5 years" after DBS, she said. "At 10 months time, 50% of the events had already occurred. At 17 months, 75% of the events had occurred."

Logistic regression analysis based on a study of 70 controls revealed that the following factors were independently associated with an increased risk of suicide: past history of impulse control disorder or substance abuse, being single, or having postoperative depression.

Suicide "has significant implications and it's potentially quite preventable," said Dr. Voon, "so patients and families should be aware of this risk." ■

Dopamine Agonist/Levodopa Combo Linked to Compulsions

BY AMY ROTHMAN SCHONFELD
Contributing Writer

SAN DIEGO — The specific drug combination of a dopamine agonist and levodopa may trigger the onset of pathological behaviors, including compulsive gambling, hypersexuality, and compulsive shopping in a subset of patients with Parkinson's disease, according to the results of two independent investigations on a total of 485 patients presented at the annual meeting of the American Academy of Neurology.

"Although since 2000 there have been case reports [of pathologic behaviors], these are the first systematic detailed evaluations of these patients," said Dr. Oksana Suchowersky of the University of Calgary, Alberta, Canada. In her study, 188 patients with Parkinson's disease (PD) were surveyed for difficulties with gambling. Twelve patients met DSM IV criteria for pathological gambling, equivalent to a lifetime prevalence rate of 6%, compared with 1.5% in the general population.

All patients who developed pathological gambling had been recreational gamblers before starting PD medications, and all had been treated with levodopa plus a dopamine agonist, rather than with levodopa (0 of 93 patients) or bromocriptine (0 of 14 patients) monotherapy. The risk of developing pathological gambling appeared to be a class effect of the dopamine agonists, with no significant differences among those treated with pramipexole (10%), pergolide (17%), or ropinirole (17%).

Dr. Valerie Voon, a psychiatrist who conducted research at the Toronto Western Hospital Movement Disorders Centre, investigated pathological gambling, hypersexuality, and compulsive shopping in 297 patients with PD. She found that overall lifetime prevalence (which includes both past and current behaviors) for the group was 6%, which increased to 16% in patients taking levodopa and dopamine agonist in combination. The lifetime prevalence was 3.4% for pathologic gambling, 2.4% for hypersexuality, and 0.7% for compulsive shopping; 10%-20% of patients exhibited more than one disorder.

One hypothesis is that these obsessive behaviors reflect excessive stimulation of the limbic reward system in susceptible individuals. Risk factors that may increase susceptibility to compulsive behaviors include younger age of PD onset, novelty-seeking personality traits, and history of alcohol abuse. Stage of disease was ruled out as a risk factor.

These findings suggest that clinicians should regularly query patients with PD and family members about excessive behaviors, which may take the form of hobbies, collections, sexual behavior, or shopping. Early identification can help physicians make adjustments that may rectify the problematic behaviors, including switching dopaminergic agonists, discontinuing therapy if possible, or even substituting deep brain stimulation for long-term dopaminergic therapy. The latter option should be used with caution, since Suchowersky found that 5% of 39 deep brain stimulation patients actually developed pathologic gambling after surgery.

Left unchecked, serious psychosocial consequences may result from these behaviors, including isolation, shame, depression, marital discord, and suicidal thoughts. Among Dr. Voon's patients, pathologic gambling led to a mean loss of $125,000, while some of Dr. Suchowersky's patients "literally lost the farm." ■

Pages 16a—16b