Reward-Based Behavior Common in Parkinson's

BY BETSY BATES
Los Angeles Bureau

SAN DIEGO — Obsessive or impulsive reward-based behavior was reported by nearly 6 in 10 patients with Parkinson's disease answering an anonymous survey, adding to the suspicion that dopaminergic medications may influence impulse control.

Patients who had suffered from Parkinson's disease for more than 5 years, as well as those taking certain combinations of medications, were most likely to report such behaviors as obsessive or recurrent thoughts, the need to repeatedly check or organize, or impulsive eating, shopping, or gambling.

Dr. Jennifer S. Hui and her associates at the movement disorders center of the University of Southern California, Los Angeles, distributed anonymous questionnaires to 161 patients with Parkinson's disease. Among the 97 patients who returned surveys, 57 acknowledged engaging in at least one reward-based behavior, 34 respondents reported two such behaviors, and 20 acknowledged three or more.

The most commonly reported behaviors were obsessive or recurrent thoughts (25 patients); the urge to repeatedly check or organize (21 patients); the urge to go shopping (15); feeling the need to eat or starve (13); the urge to gamble (12); and an increased interest in sex (10).

In smaller numbers, patients endorsed a wide range of behaviors—including an increased interest in pornography, a change in usual sexual practices, the desire to increase the dose of medications for enhanced mood, and the need to "live on the edge"—and even reported compulsive bridge playing.

Nearly half of patients felt these behaviors represented a "distinct change in their personalities," Dr. Hui reported in a poster presented at the annual meeting of the American Neurological Association.

Patients reporting reward-based behaviors were more likely than were others to be taking combinations of medications, especially Sinemet (carbidopa/levodopa) and Mirapex (pramipexole dihydrochloride). In the survey, 16 of 19 patients taking that combination of drugs acknowledged obsessive or impulsive behavior. Nine of 14 patients taking Sinemet (carbidopa/levodopa) and Requip (ropinirole) also reported such behaviors.

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Some have theorized that dopamine agonists may contribute to reward-based behaviors because of their effect on the dopaminergic mesolimbic reward circuit. Other factors, such as personality, genetic susceptibility, and brain changes associated with the disease itself, may be involved as well, Dr. Hui said in an interview.

Although the science is far from clear, class action suits were filed in the United States and Canada last year alleging that Mirapex, manufactured by Boehringer Ingelheim, was responsible for their gambling addiction.

Dr. Hui said several prospective studies are underway to further clarify the issue, including one that will follow patients from the time they begin taking dopamine agonists, to examine the effect of personality, medication, and comorbid depression on the expression of reward-based behaviors.

"We have just started to enroll, but already two patients have described a distinct change in their behavior (hypersexuality and rearranging/shopping) within weeks of starting the agonist," she noted.

On the other hand, 6 of 15 patients in the study presented at the meeting were not taking any of the three listed dopamine agonist medications, and yet they said they, too, suffered from impulse-control behaviors.

The likely explanation, then, is that combinations of factors probably contribute to the behaviors, although drugs theoretically could certainly play a key role.

"The dopaminergic mesolimbic mesocortical system is the core circuit underlying subjective pleasure produced by food, sex, and pathological addictions. Recent positron emission tomography (PET) studies have indicated the dopaminergic reward circuitry is deficient in Parkinson's disease," Dr. Hui and her coinvestigators concluded.

"The effect of exogenous dopamine on this altered reward system may explain behavioral abnormalities in Parkinson's disease patients." ■

Occipital Region Hardest Hit by Cerebral Amyloid Angiopathy

BY KERRI WACHTER
Senior Writer

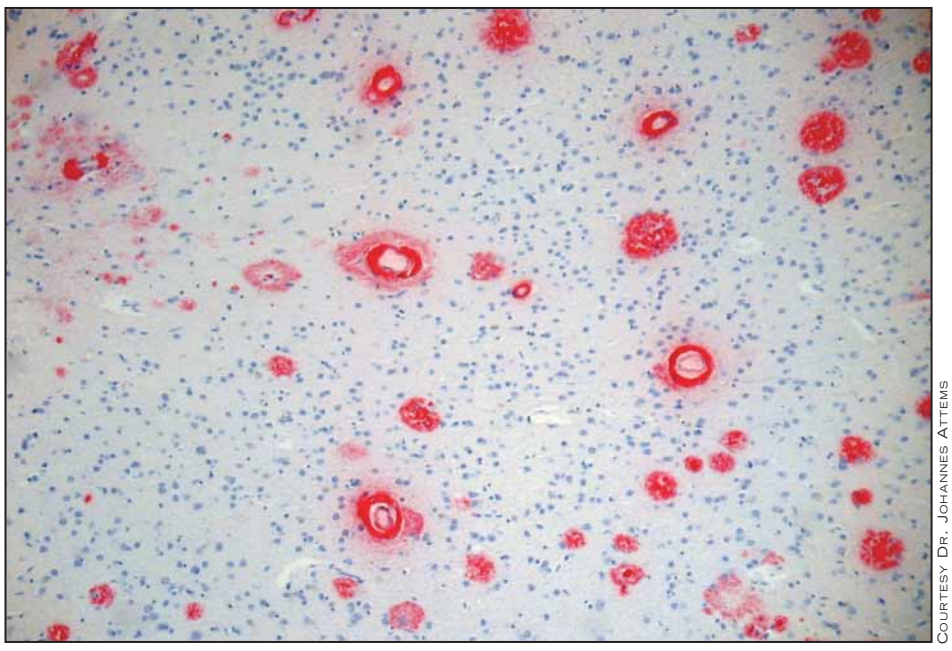
PORTO, PORTUGAL — Cerebral amyloid angiopathy appears to disproportionately affect the occipital region, according to findings presented at the Fourth International Congress on Vascular Dementia.

In a study involving the postmortem neuropathologic evaluation of brains from 113 subjects (61% women), the incidence and severity of cerebral amyloid angiopathy (CAA) was highest in the occipital region, followed by the frontal, hippocampal, and frontobasal areas. The occipital region was significantly more frequently and more severely affected than the other regions, said Dr. Johannes Attems, of the Otto Wagner Hospital in Vienna.

Cerebral amyloid angiopathy (CAA) is defined by the deposition of amyloid-β peptide in cerebral vessels and has been associated with Alzheimer's disease (AD). Despite the association with AD, CAA has been shown to be an independent risk factor for cognitive decline.

Dr. Attems and his colleagues looked at the topographical distribution of CAA in the vessels of the brain, as well as the relationship between CAA and AD. In all, 63 patients had a clinical diagnosis of dementia and 50 were nondemented. Dementia was assessed retrospectively from hospital charts based on ICD-10 criteria of a Mini-Mental State Examination score less than 20. Subjects ranged in age from 54 to 102 years at the time of death.

Neuropathologic assessment of AD was performed using Consortium to Establish a Registry for Alzheimer's Disease (CERAD) criteria, Braak stages, and National Institute on Aging/Reagan Institute (NIA-Reagan) criteria. In this cohort, 43 subjects had high-grade AD pathology, 16 had medium-grade AD pathology, 37 had low-grade AD pathology, and had no AD pathology.



COURTESY DR. JOHANNES ATTEMS

Immunostaining of tissue with cerebral amyloid angiopathy using modified Bielschowsky silver stain shows severe thickening of the cortical vessel walls.

Sections were immunostained with modified Bielschowsky silver stain and a commercially available monoclonal human amyloid-β antibody for the detection of amyloid-β in cerebral vessels. The severity of amyloid-β deposition in vessels—and CAA—was semiquantitatively assessed in the frontal, frontobasal, hippocampal, and occipital regions. The researchers used a 5-point scoring system. A grade of 0 signified no amyloid-β was present, while grade 4 signified severe amyloid-β deposition.

Within a region, scores were totaled separately for meningeal and cortical vessels. These values were totaled for a regional score. A mean overall score was then calculated using the regional values. In order to better estimate the relative contribution of the separate regional scores, the overall score was subtracted from each regional score to yield relative scores.

CAA was present in 77 cases. In these subjects, "Independent of the region, meningeal vessels were always affected more frequently and more severely than cortical vessels," said Dr. Attems. However the differences between meningeal and cortical vessels were only statistically significant in the occipital region.

"CAA prevalence was significantly higher in cases with high-grade AD pathology, compared with cases with no to medium pathology," said Dr. Attems. Overall CAA severity increased with increasing AD pathology. This was true in all of the regions, though only the relative contribution of CAA in the occipital region increases significantly with increasing AD pathology.

"This means that—at least statistically—increasing AD pathology shifts the topographic distribution of CAA even more towards the occipital cortex," he said.

Interestingly, of the brains with no AD pathology, 24% had evidence of CAA. Conversely, 24% of brains with AD pathology showed no evidence of CAA. "We have cases with severe CAA but without any AD pathology and on the other hand, case with high AD pathology completely lacking CAA," said Dr. Attems. This suggests that neuritic AD pathology and CAA might represent different entities.

Demented subjects more frequently showed signs of CAA and CAA total scores were greater than in nondemented patients. This finding suggests a significant association between CAA and dementia, said Dr. Attems. However, after controlling for clinical criteria the association was no longer statistically significant.

"The combination of AD pathology and CAA might synergistically contribute to the development of clinical dementia," said Dr. Attems.

Interestingly, among patients with a CAA total score greater than 0, there was no difference in the prevalence of CAA between cases with high versus low AD pathology. Also the CAA total score did not increase with increasing AD pathology in this subgroup. ■