

# Pesticide Exposure May Add to Parkinson's Risk

BY JEFF EVANS

**T**he risk for developing Parkinson's disease that is associated with pesticide exposure appears to be especially high in people who are professionally exposed to the chemicals and those who carry certain polymorphisms for glutathione S-transferase genes, according to findings from two new case-control studies.

The studies strengthen the already well-documented association between pesticide exposure and Parkinson's disease (PD) by including a more detailed assessment of exposure to the chemicals for analyzing dose-effect relationships, especially for different classes of insecticides, fungicides, and herbicides, as well as examining the role of genetic traits in determining individual susceptibility to PD.

Dr. Alexis Elbaz of the Institut National de la Santé et de la Recherche Médicale, Paris, and his colleagues conducted extensive in-person interviews about professional exposure to pesticides with 247 patients with PD and 676 matching control patients. All of the participants came from the same French health insurance organization for workers in agriculture and related occupations. The patients with PD had been diagnosed a median of 1.5 years before the study (*Ann. Neurol.* 2009 [doi:10.1002/ana.21717]).

Dr. Elbaz and his associates found that for men, the odds of developing PD increased with the number of years of professional use of pesticides. This relationship was stronger for men with PD onset after age 65 years than it was for men with younger onset. Women with pesticide exposure also were significantly more likely to develop PD

than were those without exposure, the investigators reported.

Of the three broad categories of pesticides that the investigators analyzed— insecticides, fungicides, and herbicides— only insecticide exposure in men was associated with a significantly increased odds of developing PD (odds ratio 2.2). This association followed a dose-effect relationship, which was strongest for older-onset PD patients. In women, only fungicide exposure was associated with significantly increased odds of developing PD (odds ratio 3.5).

In multivariate analyses of men overall and of men with older-onset PD, only organochlorine insecticides remained associated with PD after adjusting for other pesticide families that the men had been exposed to.

During 1941-1990, patients with older-onset PD had used organochlorines in each 10-year period more often than their matched controls had, whereas there was no difference in use during the same periods between patients with younger-onset PD and their matched controls. Each of the control groups used organochlorines, as well as insecticides and pesticides overall, at similar frequencies.

The finding that the association between PD and professional pesticide use was stronger for older males is "consistent with the view that genetic susceptibility plays a stronger role in younger-onset cases, while environmental factors play a stronger role for older-onset cases," the investigators wrote.

This was supported in the study by a similar number of years of pesticide exposure between both older-onset cases (13 years) and in younger-onset cases (12 years) and a higher cumulative lifetime hours of exposure for younger-onset cas-



The odds of developing Parkinson's disease increased with the number of years of professional use of pesticides.

es (88 hours), compared with older-onset cases (52 hours).

In a separate study, Dr. Ruey-Meei Wu, of the department of neurology at National Taiwan University Hospital, Taipei, and her coinvestigators genotyped 125 patients (69 women) with sporadic idiopathic PD and 162 age- and gender-matched control patients (90 women) from a rural area of southern Taiwan for four glutathione S-transferase (GST) genes (GSTM1, GSTP1, GSTT1, and GSTZ1).

Overall, 69 PD patients and 70 control patients were exposed to pesticides (herbicides, insecticides, and fungicides) used in professional farming or gardening. These patients had been exposed to pesticides for a range of 1 to 50 years, Dr. Wu and her colleagues reported at a poster session of the International Congress of Parkinson's Disease and Movement Disorders in Paris.

GST polymorphisms have been reported to reduce the efficiency of the substrate selectivity or stability of the

enzymes. In brain tissue, GSTs function as scavengers that eliminate the formation of intracellular free radicals that are generated from the metabolism of drugs, toxins such as pesticides, or xenobiotics. GSTs have the potential to modify a person's susceptibility to developing PD after pesti-

cide exposure by increasing oxidative stress in the brain, leading to the degeneration of dopaminergic neurons, Dr. Wu said in an interview.

Pesticide exposure was an independent risk factor for PD. Only the GSTP1 Val 105 polymorphism, which occurred in about 20% of the patients, significantly increased the risk for the development of PD. This polymorphism raised the odds of developing PD by a factor of 2.2. The risk for PD was greatest among patients who had been exposed to pesticides for more than 35 years.

Those who carried the GSTP1 Val 105 polymorphism and were exposed to pesticides had even higher risk of developing PD. There was a trend for increasing PD risk that became stronger and more significant in pesticide-exposed patients who carried an additional putative high-risk GST genotype.

None of the investigators in either study had any conflicts of interest to declare. ■

## MRI Has Limited Diagnostic Value in Early Parkinsonism

BY SUSAN LONDON

SEATTLE — Magnetic resonance imaging performed in the first year or two of parkinsonism seldom yields information useful for establishing the diagnosis.

The final diagnosis in patients with parkinsonism may remain uncertain for years and has historically relied on clinical evaluation and follow-up, lead author Dr. Marie-Josée Langlois said at a poster presentation at the annual meeting of the American Academy of Neurology.

Current guidelines do not specify a clear role for MRI in this setting.

Dr. Langlois and her coinvestigator, Dr. Michel Panisset, both of the University of Montreal, reviewed the charts of consecutive patients with parkinsonism who were evaluated at their institution between

1992 and 2003 and had at least 5 years of follow-up.

Of the 114 patients studied, 25 (22%) had an MRI in the year before or after the initial consultation for parkinsonism. The imaging took place a mean of 1.7 years after the parkinsonism diagnosis.

"Atypical clinical findings and a younger age were the main reasons for doing an MRI," Dr. Langlois reported. All but two of the imaged patients had findings such as an early onset of falls or a

poor response to levodopa, or were aged 50 years or younger.

"We did not find many specific MRI changes," she said. Of the 25 patients who underwent this imaging, 19 (76%) had normal results, and 6 (24%) had basal ganglia abnormalities.

In the latter group, the abnormalities had a vascular etiology in four patients. Two patients had the same final diagnosis after a mean 6-year follow-up as their initial diagnosis (Parkinson's disease and



'Atypical clinical findings and a younger age were the main reasons for doing an MRI.'

DR. LANGLOIS

progressive supranuclear palsy), while two had a change in diagnosis (from focal signs to Parkinson's disease, and from Wilson's disease to Parkinson's disease).

The other two patients with basal ganglia abnormalities on

MRI had changes consistent with multiple system atrophy, which was already suspected clinically. In both cases, this initial diagnosis remained unchanged with follow-up.

Overall, in the MRI group, Parkinson's disease (versus atypical or secondary parkinsonism) was the initial diagnosis in 24% of patients and the final diagnosis in 56%. This pattern differed significantly from that in the no-MRI group, which had a mean follow-up of 7 years: Parkinson's disease was the initial diagnosis in 63% of those patients, and the final diagnosis in 76%.

"MRI was not that useful in establishing the initial diagnosis or in changing the diagnosis" in this population with parkinsonism, Dr. Langlois commented.

MRI appears to serve mainly as confirmation of a clinically

suspected diagnosis of Parkinson's disease when the results are normal, she noted. "But it may in some cases confirm a clinical diagnosis of atypical parkinsonism, for example, or, if there is a clinical suspicion of a vascular cause, confirm it."

Other studies that have found higher rates of abnormalities on MRI were conducted in patients who had had parkinsonism for 3.5-5 years, she noted, "so it was not that surprising that with a delay of about 1 year, there is not much change in the MRI."

However, she added, high-field MRI with fine slices through the basal ganglia and brainstem might reveal changes at such early time points, a possibility that should be explored in a prospective trial.

Dr. Langlois reported that she had no conflicts of interest in relation to the study. ■