

## A B S T R A C T

**Background:** An apparent excess of teachers and healthcare workers among the Parkinson's disease patients of a large tertiary care movement disorders clinic suggested the hypothesis that high exposure to viral (or other) respiratory infections in these occupations might be a risk factor for Parkinson's disease.

**Methods:** A case-control study of the association between occupation and Parkinson's disease was conducted. Cases (414) were all Parkinson's disease patients seen at the University of British Columbia Hospital Movement Disorders Clinic between 1986 and 1993, residing in Greater Vancouver, and under 65 in 1991. Controls (6,659) were randomly selected from the 1991 Canadian Census.

**Findings:** Parkinson's disease was associated with teaching (OR 2.50, 95% CI 1.67-3.74) and occupation in healthcare services (OR 2.07, 95% CI 1.34-3.20), but there were several other substantial associations, both positive and negative.

**Interpretation:** While referral bias cannot be ruled out, the authors find the consistency of the overall pattern of associations with the respiratory infection hypothesis striking.

## A B R É G É

**Contexte :** un nombre démesuré d'enseignants et de travailleurs des soins de santé, parmi les personnes atteintes de la maladie de Parkinson soignées dans une grande clinique de soins tertiaires spécialisée dans les troubles moteurs, a amené à formuler l'hypothèse voulant qu'une forte exposition aux infections respiratoires d'origine virale ou autre dans ces professions pouvait constituer un facteur de risque de contraction de la maladie de Parkinson.

**Méthode :** Une étude cas-témoins de la corrélation existant entre la profession et la maladie de Parkinson a été effectuée. Tous les cas (414) étaient des malades atteints de la maladie de Parkinson soignés à la clinique spécialisée dans les troubles moteurs de l'hôpital de l'université de la Colombie-Britannique entre 1986 et 1993, résidant dans l'agglomération de Vancouver, et âgés de moins de 65 ans en 1991. Les témoins (6 659) avaient été choisis de façon aléatoire à partir du Recensement de la population canadienne de 1991.

**Résultats :** la maladie de Parkinson a été corrélée à l'enseignement (RO 2,50, 95 % IC 1,67 – 3,74) et aux professions du secteur de la santé (RO 2,07, 95 % IC 1,34 – 3,20), mais on a constaté plusieurs autres corrélations importantes, tant positives que négatives.

**Interprétation :** bien que toute subjectivité ne puisse être écartée, les auteurs ont été frappés par la corrélation générale avec l'infection respiratoire.

# Occupational Risk Factors in Parkinson's Disease

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Parkinson's Disease (PD) is an important public health problem with a high estimated prevalence, 341/100,000 in a door-to-door survey conducted in the United States.<sup>1</sup> An important component of the pathogenesis is loss of dopamine-producing neurons from the substantia nigra.<sup>2</sup> The cause of this loss is a matter of intense investigation, and important genetic links have been identified.<sup>3-16</sup> However, genetic factors alone do not appear to account for the observed distribution of the disease.<sup>10,17-22</sup> The disorder is likely to have several specific genetic and environmental causes,<sup>23-25</sup> contributing in varying proportions in individual cases.<sup>26</sup> Environmental damage to dopaminergic neurons may result from toxic chemical exposures (such as 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine, known as MPTP), and from certain viral infections.<sup>27-33</sup> The currently established environmental causes of nigral neuron injury do not seem to account for the observed number of Parkinson's disease cases, however.

Occupational studies provide a useful approach to investigation of environmental exposures as these may be concentrated with particular intensity in certain occupations. The purpose of this study was to examine the association between Parkinson's disease and occupation based on data from the records of the Movement Disorders Clinic (MDC) at the University

of British Columbia Hospital, Vancouver, British Columbia. The clinicians of the Movement Disorders Clinic had made the informal observation of an apparent excess of school teachers and those in healthcare occupations among their patients, and had proposed that this might reflect higher exposure to viral respiratory tract infections circulating in schools and healthcare facilities.

## METHODS

We obtained information from an existing computer database on all 891 patients with Parkinson's disease from the Greater Vancouver area (as defined by telephone exchanges) seen at the Movement Disorders Clinic from 1986 to 1993 inclusive. All patients were originally referred by primary care physicians or neurologists. Diagnosis of PD was made and/or confirmed by neurologists specializing in the field of movement disorders, based on accepted criteria (two of the following on examination: parkinsonian tremor, rigidity, bradykinesia, masked facies, micrographia, or postural imbalance; and absence of specific signs of other diseases that may produce these signs). This database did not contain systematic information on occupation. One of us (YW) extracted additional information on occupation at the time of diagnosis of PD from records and contacted patients or their family members where there was no clear information in the clinical record. Occupations were coded according to the 1980 version of the Standard Occupational Classification.

The distribution of occupations in this patient group was compared to that in the 1991 Canadian Census by using the

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Canadian Census Analyzer individual microdata files (Computing in the Humanities and Social Sciences, University of Toronto, website). We obtained information on place of residence, age, gender and occupation in 1991 for a random sample of 20,000 individuals from British Columbia, and selected those who were from the Greater Vancouver Census Metropolitan Area.

Controls were restricted to being at least 15 years of age. (There were no MDC cases under 15.) Because the Census database records only current occupation, the previous occupation of retired people could not be ascertained. We therefore restricted both cases and controls to those under age 65 in 1991. A further difficulty occurred with the occupational category "not applicable". In the MDC database this category referred, almost exclusively, to women not employed outside the home. In the Census, it included this same group but also students, unemployed persons, and retired persons, and these could not be distinguished. Since we excluded persons over 65, we assumed that the remaining Census individuals in this category were primarily women doing unpaid work at home. However, to avoid having all the results depend on this assumption, once the odds ratio for "not applicable" was calculated, all cases and controls with this categorization were excluded from all further calculations.

Odds ratios, adjusted for age and sex, were calculated by Mantel-Haenszel methods. Cornfield 95% confidence intervals were computed. Calculations were performed using the statistical package STATA (Stata Corporation, College Station, Texas).

## RESULTS

Of 891 PD patients, 447 were under 65, and of these we were unable to ascertain an occupation for 33, leaving 414 eligible cases. There were 6,659 correspondingly eligible controls. The distribution of age and gender in our cohort is shown in Table I, and additional information on the number and age of cases is shown in Table II. All cases and controls were entered into the calculation of the odds ratio for occu-

		Occupation Identified		Occupation "Not Applicable"	
		Controls	Cases	Controls	Cases
Female	Number	2632	125	709	21
	Mean age (SD)	35.7 (12.0)	53.4 (8.9)	42.1 (15.9)	56.5 (8.3)
Male	Number	3029	300	289	1
	Mean age (SD)	36.8 (12.4)	53.9 (9.0)	38.0 (18.3)	
Total	Number	5661	425	998	22
	Mean age (SD)	36.3 (12.2)	53.7 (8.9)	40.9 (16.7)	56.6 (8.1)

Census Code	Occupational Group	Cases	Age of Cases: Mean (SD)	Female Cases (%)	Mantel-Haenszel Odds Ratio† [95% CI]
1	Management, Administration	28	48.3 (9.9)	21.4	0.48 [0.32-0.72]***
2	Sciences, Engineering	25	55.6 (8.3)	4.0	1.39 [0.85-2.27]
3	Social sciences, Law, Library	13	52.6 (9.0)	23.1	2.49 [1.27-4.88]**
4	Teaching	40	53.2 (8.7)	57.5	2.50 [1.67-3.74]***
5	Medicine, Health	34	55.5 (7.9)	52.9	2.07 [1.34-3.20]***
6	Art, Literature, Recreation, Religion	9	53.9 (11.1)	55.6	1.00 [0.48-2.11]
7	Clerical	36	52.9 (9.6)	52.8	0.58 [0.40-0.85]**
8	Sales, Commodities services	52	54.7 (8.5)	13.5	1.08 [0.77-1.51]
9	Service – food, lodging	43	54.0 (8.6)	32.6	1.11 [0.77-1.59]
10	Farming/ Horticulture	9	54.6 (7.6)	0	0.68 [0.32-1.41]
11	Other primary: forestry, logging, mining, oil/gas field	15	54.3 (11.5)	0	3.79 [1.72-8.37]***
12	Processing – ore, metal, glass, stone, rubber, wood, etc.	17	57.2 (5.7)	17.6	1.22 [0.68-2.20]
13	Machine related	23	51.5 (8.6)	13.0	0.75 [0.48-1.19]
14	Construction	9	54.4 (7.0)	0	0.31 [0.15-0.63]***
15	Transport equipment operating	16	54.6 (8.0)	6.3	0.89 [0.50-1.59]
16	Material handling, Printing/utilities, Equipment operating	23	54.7 (9.0)	26.1	1.32 [0.80-2.16]
99	Not applicable	22	56.6 (8.1)	95.5	0.16 [0.10-0.26]***

† excluding category 99 except for the odds ratio for category 99.  
\* p < 0.05  
\*\* p < 0.01  
\*\*\* p < 0.001

pation "not applicable", which represents primarily but not exclusively women not employed outside the home. This group was excluded from further analyses leaving 392 cases and 5,661 controls.

Odds ratios adjusted for age and sex are summarized in Table II. Several of the odds ratios are substantially elevated. In particular, those for teachers (OR=2.50, 95% CI 1.67-3.75) and medical workers (OR=2.07, 95% CI 1.34-3.20) confirm the previous informal observation of an elevated risk in these groups. The greatest elevation, however, was for the category "other primary occupations" which includes forestry, logging, mining, and oil/gas field exploration with an odds ratio of 3.8 (95% CI 1.7-8.4), and there was also a substantial elevation for social service workers (OR=2.49, 95% CI 1.27-4.88).

On the other hand certain groups had substantially reduced estimated risks: occupation "not applicable" which is primarily women not employed outside the home (OR=0.16, 95% CI 0.10-0.26), and construction work (OR=0.31, 95% CI 0.15-0.63). There were also reductions for administration and clerical work.

## DISCUSSION

The large odds ratios among teachers and those in medicine and health services occupations are consistent with, but do not prove, our hypothesis of an infectious disease etiology for some cases of PD. Women doing unpaid work at home and construction workers appear to carry a substantially reduced risk of developing PD. Although these associations were not

hypothesized *a priori*, they also seem consistent with an etiologic role for respiratory infections. Similar arguments can be made for social workers (elevated risk) and managerial and clerical workers (reduced risk), although the effects are less marked in these occupational groups.

The strongest positive association was for "other primary occupations" which includes forestry and mining workers. A possible explanation for this is that these occupations may involve living in crowded sleeping conditions in remote camps, conditions which would be conducive to the spread of respiratory infections. This explanation is speculative in that we do not have actual data on the living conditions of persons in these occupations in British Columbia.

A high risk of PD has been reported to be associated with farming and horticultural industries,<sup>6,23,34,35</sup> but our data did not show any significant increase in odds ratio (0.68, 95% CI 0.32-1.41). This negative finding is difficult to interpret, however, since our study was limited to an urban/suburban area, and the meaning of "farming" in such a context is not clear.

Because of the exceptionally strong negative association of "not applicable" with PD, including this group as part of the reference group in calculating odds ratios for the other occupations would tend to make them spuriously elevated. We avoided this problem by excluding this category from the other analyses. An additional reason for exclusion is that this category may not be equivalent between cases and controls. Concrete evidence for this concern is found in Table I: the female predominance in this category is much stronger in the MDC patients (21/22) than in the Census (709/998).

The diagnosis of PD requires expert assessment of physical signs and exclusion of other diagnoses. Although the cases for this study came from a clinic specializing in movement disorders, some may not have been followed long enough to exclude other variants of Parkinson's syndrome.<sup>36-38</sup> However, this would tend to weaken any associations between PD and exposures, not create spurious ones.

Referral bias might be an explanation for the associations that we found. It is

possible, for example, that teachers and healthcare workers with Parkinsonian symptoms were more likely to make a specific request for referral to a specialty clinic than were housewives, construction workers, and clerical workers. Furthermore, occupational information gathering for controls was quite different from that for cases. For controls we had occupation at the time of the Census, whereas for cases we had occupation at the time of the diagnosis. We attempted to reduce this discrepancy by using the 1991 Census, midway through the study period, but this is an imperfect remedy. Other sources of inaccuracy, such as recall bias, may also have operated differently for cases and controls. Because of these issues, our results are not conclusive and a more detailed study including more direct measures of exposure to respiratory tract illnesses is planned. Nevertheless, we find the observed pattern of associations consistent overall with the respiratory tract infection hypothesis.

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