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Short communication

Parkinson's disease and history of outdoor occupation

Elena Kwon [a], Lisa G. Gallagher [b], Susan Searles Nielsen [b], Gary M. Franklin [b], Christopher T. Littell [a], W.T. Longstreth Jr. [c,d], Phillip D. Swanson [c], Harvey Checkoway [b,d,*]

[a] United States Army, Madigan Army Medical Center, Department of Preventive Medicine, United States
[b] University of Washington, Department of Environmental and Occupational Health Sciences, Seattle, WA, United States
[c] University of Washington, Department of Neurology, Seattle, WA, United States
[d] University of Washington, Department of Epidemiology, Seattle, WA, United States

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ABSTRACT

Background: Human and animal studies, albeit not fully consistent, suggest that vitamin D may reduce risk of Parkinson's disease (PD). Ultraviolet radiation converts vitamin D precursor to the active form. This study examined the hypothesis that working outdoors is associated with a decreased risk of PD.
Methods: PD cases were enrolled from Group Health Cooperative, a health maintenance organization in the Puget Sound region in western Washington State, and the University of Washington Neurology Clinic in Seattle. Participants included 447 non-Hispanic Caucasian newly diagnosed PD cases diagnosed between 1992 and 2008 and 578 unrelated neurologically normal controls enrolled in Group Health Cooperative, frequency matched by race/ethnicity, age and gender. Subjects' amount of outdoor work was estimated from self-reported occupational histories. Jobs were categorized by degree of time spent working outdoors. A ten-year lag interval was included to account for disease latency. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated by logistic regression, with adjustment for age, gender, and smoking.
Results: Outdoor work was inversely associated with risk of PD (outdoor only compared to indoor only): OR = 0.74, 95% CI 0.44–1.25. However, there was no trend in relation to portion of the workday spent laboring outdoors and PD risk.
Conclusion: Occupational sunlight exposure and other correlates of outdoor work is not likely to have a substantial role in the etiology of PD.

1. Introduction

The etiology of Parkinson's disease (PD) remains poorly understood. Genetic factors alone account for only a small fraction of PD cases, indicating that environmental factors may have a prominent etiologic role [1]. The most well-established association with an environmental factor is cigarette smoking, with ever smokers having approximately half the risk of PD as never smokers [1]. Increased risk of fractures and osteoporosis in PD patients has been hypothesized to be due to vitamin D deficiency [2]. Subsequently, low vitamin D levels in prospectively obtained serum have been associated with an increased risk of Parkinson's disease in a Finnish cohort [3]. More recently, a case-control study of men in Denmark indicated that an increased extent of outdoor work was associated with a reduced risk of PD [4]. These findings are biologically plausible, given that ninety percent of vitamin D in adults is produced *in vivo* when ultraviolet radiation type-B (UV-B) rays strike the skin [5] and epidemiologic and experimental studies [2,6] suggest that vitamin D may protect against PD. Hence, we examined the relation between PD and outdoor work among men and women in a population-based case-control study in western Washington State.

2. Methods

2.1. Subjects

Newly diagnosed PD cases ($N = 490$) were identified at Group Health Cooperative, a health maintenance organization in the Puget Sound region, and the University of Washington Neurology Clinic, between 1992 and 2008. PD cases that were not diagnosed by a neurologist had their abstracted medical records reviewed by a panel of three independent board certified neurologists (W.T.L., P.D.S. & G.M.F.) as detailed previously [7]. A diagnosis required at least two of the four cardinal signs of PD (bradykinesia, cogwheel rigidity, postural reflex impairment and resting tremor). Cases with parkinsonism secondary to stroke or another disease or medication (e.g., Haloperidol, Metoclopramide, and Phenothiazines) were excluded. The majority

* Corresponding author. University of Washington, Department of Environmental and Occupational Health Sciences, Box 357234, Seattle, WA 98195, United States. Tel.: +1 206 543 2052; fax: +1 206 685 3990.
E-mail address: checko@u.washington.edu (H. Checkoway).

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of cases were interviewed within one year of diagnosis, and all cases were interviewed within four years.

Control subjects ($N = 644$) were randomly selected from enrollees of Group Health Cooperative with no history of PD or other neurodegenerative disorders and were frequency matched to cases by age, sex, race/ethnicity, clinic location and length of enrollment in Group Health Cooperative.

Cases and controls with a Mini-Mental State Exam score <24 were excluded. Due to variable UV-B absorption by skin tone [8] and racial and ethnic heterogeneity with respect to PD risk [1], the analysis was restricted to non-Hispanic Caucasians and included 456 cases (93%) and 595 controls (92%). Human Subjects Committees at the University of Washington, Group Health Cooperative, and Madigan Army Medical Center reviewed and approved the study. All subjects provided written informed consent.

2.2. Exposure assessment

During a structured interview, participants provided information on their entire occupational history [9]. The questionnaire included 62 specific job titles, and participants indicated whether they had ever worked at each of these jobs for longer than six months. Participants were asked to indicate the starting and ending year of employment. Participants could also report up to five additional job titles, and were asked to include part-time employment and multiple jobs held during a single time period. To account for the time period during which participants may have experienced PD symptoms, which could have limited their physical capacity and therefore restricted their occupational choices, we excluded the portions of occupational histories within 10 years of diagnosis (cases) or reference (controls). When imposing this 10-year lag time, sufficiently complete occupational data for the present analysis were available for 447 cases and 578 controls.

We estimated the amount of daily occupational outdoor exposure according to the reported job titles and duration of employment in each job. First, following the method of Kenborg and colleagues [4], each job was assigned to one of five exposure categories: exclusive indoor work, moderate outdoor work (<50% outdoor work), frequent outdoor work (50–75% outdoor work), maximal outdoor work (>75% outdoor work) and unclassifiable. After assigning categories, exposures were summarized using several measures for analysis: 1) all types of jobs in occupational history, 2) greatest degree of outdoor work in occupational history (as used in Kenborg et al., 2011 [4]), 3) degree of outdoor work in the longest duration job in the occupational history, and 4) total duration of years in an occupation with any outdoor work. For each of these summary measures, we categorized the subjects' exposure as "unclassified" if >25% of the subject's work years were spent in jobs for which the degree of outdoor exposure was "unclassifiable."

2.3. Data analysis

Relative risks were estimated by calculating odds ratios (ORs) using unconditional logistic regression models. We adjusted for sex, age (continuous) and cigarette smoking (ever vs. never and pack-years). The reference category for all analyses of occupational outdoor exposure was individuals who worked exclusively indoors. Following the example of Kenborg and colleagues [4], we included "unclassified" subjects in all models, to ensure that their exclusion would not bias the results. Statistical significance was set at a two-sided alpha of 0.05. Statistical analysis was conducted using Stata 11.1 (StataCorp, College Station, Texas).

3. Results

Characteristics of cases and controls are presented in Table 1. The number of jobs held (median 3 jobs) and the number of years worked (median 35–36 years) up to 10 years from diagnosis/reference were similar between cases and controls. Associations for the various measures of outdoor work and the risk of PD are presented in Table 2. Outdoor work appeared to confer a modest protective effect on risk of PD, but the possible inverse association was not statistically significant for any of the exposure indicators we considered. The greatest risk reduction was observed when the entire job history was considered and subjects with only outdoor work were compared to subjects with only indoor work (OR = 0.74, 95% CI 0.44–1.25). The OR for the intermediate exposure category (indoor and outdoor work) was intermediate in magnitude (p for trend = 0.26). Similar trends were observed when classifying study participants according to the job held with greatest degree of outdoor exposure throughout their occupational history, the job held for the longest duration and by the number of years they had spent working outdoors, although a dose–response relation was less apparent for these indicators of exposure. Results were not materially altered when we repeated analyses without applying exposure lagging (data not shown). The results were generally similar for men and women, although the potential inverse association between outdoor work and PD was somewhat stronger in men. The geographic location of each occupation was unknown, but when the analysis was restricted to the approximately 30% of participants who were born in Washington State (where our study was conducted), our results were not materially altered (data not shown).

4. Discussion

Results from this population-based case-control study show an inverse association between various measures of increased exposure to working outdoors and risk of developing PD, which is consistent with findings from a recent study conducted in Denmark [4] that classified exposure in a similar fashion. Both studies are similar in that both geographical regions, where much of the work presumably occurred, have limited UV-B exposure during the winter months [10]. Studies addressing the same association in lower latitude regions would indicate whether findings from our study and the study in Denmark may have under-estimated associations. Biological mechanisms that might protect outdoor workers from developing PD have been proposed and may involve vitamin D [2]. Ninety percent of vitamin D is produced *in vivo* when UV-B radiation strikes the skin [5]. Thus, higher levels of sunlight exposure would lead to higher levels of vitamin D.

Strengths of the study include its being population-based, inclusion of recently diagnosed cases, using case adjudication by neurologists, inclusion of both men and women, and controlling for some potential confounders, notably cigarette smoking. The prior study in Denmark examining the association between outdoor work and PD only included men and was unable to account for tobacco smoking [4]. Our study also has some limitations. Occupational exposure categories were based on self-reported job title. A worker's job duties

Table 1
Characteristics of non-Hispanic Caucasian Parkinson's disease (PD) cases and controls, Group Health Cooperative and University of Washington, 1992–2008.

Characteristics[a]	Cases $N = 456$ n (%)	Controls $N = 595$ n (%)
Age at diagnosis/reference years		
<60 yrs	116 (25)	106 (18)
≥60 yrs	340 (75)	489 (82)
Mean (std. dev.)	66 (10)	68 (8)
Median (range)	67 (28–88)	70 (43–86)
Gender		
Female	165 (36)	218 (37)
Male	291 (64)	377 (63)
Cigarette smoking		
Never	254 (56)	259 (44)
Ever	202 (44)	336 (56)
Pack-years (mean (std. dev.))[b]	25 (24)	28 (26)
Education		
<High school	16 (4)	35 (6)
High school	42 (9)	79 (13)
Some college	177 (39)	251 (42)
≥College degree	221 (48)	230 (39)
First-degree relative with PD[c]		
Yes	40 (9)	23 (4)
No	321 (70)	436 (73)
Birth year (median (range))	1932 (1908–1976)	1930 (1911–1957)
Number of jobs (median (range))[d]	3 (1–18)	3 (1–15)
Years worked (median (range))[d]	35 (2–56)	36 (2–58)

[a] Excludes 34 cases and 49 controls with other race/ethnicity.
[b] Among ever cigarette smokers.
[c] Percents exclude 95 cases and 136 controls with incomplete data on PD family history.
[d] Calculated with 10-year lag and excludes 9 cases and 17 controls without sufficient occupational history data.

Table 2
Risk of Parkinson's disease (PD) and outdoor work, Group Health Cooperative and University of Washington, 1992–2008.

Occupational classification[a]	All subjects			Men			Women		
	Cases	Controls	OR (95% CI)[b]	Cases	Controls	OR (95% CI)[b]	Cases	Controls	OR (95% CI)[b]
	$N = 447$	$N = 578$		$N = 285$	$N = 368$		$N = 162$	$N = 210$	
	n (%)	*n* (%)		*n* (%)	*n* (%)		*n* (%)	*n* (%)	
Type(s) of jobs									
Indoor only	188 (42)	228 (39)	1.00 (reference)	80 (28)	83 (23)	1.00 (reference)	108 (67)	145 (69)	1.00 (reference)
Indoor and outdoor[c]	159 (36)	218 (38)	0.87 (0.64–1.18)	119 (42)	177 (48)	0.73 (0.49–1.08)	40 (25)	41 (20)	1.23 (0.74–2.05)
Outdoor only	29 (6)	47 (8)	0.74 (0.44–1.25)	25 (9)	40 (11)	0.72 (0.40–1.30)	4 (2)	7 (3)	0.60 (0.16–2.21)
Unclassified[d]	71 (16)	85 (15)	1.00 (0.67–1.49)	61 (21)	68 (18)	0.96 (0.60–1.54)	10 (6)	17 (8)	0.83 (0.36–1.92)
p for trend[e]			0.25			0.15			0.82
Greatest % workday outdoors ever									
Indoor only	188 (42)	228 (39)	1.00 (reference)	80 (28)	83 (23)	1.00 (reference)	108 (67)	145 (69)	1.00 (reference)
<50%	44 (10)	61 (11)	0.85 (0.54–1.32)	30 (11)	39 (11)	0.85 (0.48–1.50)	14 (9)	22 (10)	0.75 (0.36–1.56)
50–75%	54 (12)	76 (13)	0.83 (0.54–1.29)	51 (18)	71 (18)	0.77 (0.48–1.25)	3 (2)	5 (2)	0.84 (0.19–3.70)
>75%	90 (20)	128 (22)	0.85 (0.60–1.22)	63 (22)	107 (29)	0.65 (0.42–1.02)	27 (17)	21 (10)	1.62 (0.86–3.04)
Unclassified[d]	71 (16)	85 (15)	1.00 (0.67–1.49)	61 (21)	68 (18)	0.96 (0.60–1.54)	10 (6)	17 (8)	0.83 (0.36–1.93)
p for trend[e]			0.40			0.06			0.20
Longest job, % workday outdoors									
Indoor only	300 (67)	378 (65)	1.00 (reference)	157 (55)	199 (54)	1.00 (reference)	143 (88)	179 (85)	1.00 (reference)
<50%	30 (7)	44 (8)	0.88 (0.53–1.45)	25 (9)	34 (9)	1.06 (0.60–1.88)	5 (3)	10 (6)	0.46 (0.15–1.40)
50–75%	33 (7)	55 (9)	0.75 (0.47–1.21)	31 (11)	52 (14)	0.77 (0.47–1.27)	2 (1)	3 (1)	0.94 (0.15–6.09)
>75%	13 (3)	16 (3)	0.97 (0.45–2.10)	11 (4)	15 (4)	0.92 (0.40–2.09)	2 (1)	1 (0.5)	2.09 (0.17–25.0)
Unclassified[d]	71 (16)	85 (15)	1.05 (0.73–1.52)	61 (21)	68 (18)	1.15 (0.76–1.74)	10 (6)	17 (8)	0.78 (0.34–1.80)
p for trend[e]			0.41			0.43			0.82
Years of outdoor work									
Indoor only	188 (42)	228 (39)	1.00 (reference)	80 (28)	83 (23)	1.00 (reference)	108 (67)	145 (69)	1.00 (reference)
<10	95 (21)	110 (19)	0.99 (0.69–1.41)	65 (23)	81 (22)	0.84 (0.53–1.32)	30 (19)	29 (14)	1.30 (0.73–2.31)
10–<20	30 (7)	53 (9)	0.64 (0.38–1.06)	19 (7)	42 (11)	0.45 (0.24–0.86)	11 (7)	11 (5)	1.25 (0.51–3.03)
≥20	63 (14)	102 (18)	0.79 (0.52–1.18)	60 (21)	94 (26)	0.76 (0.48–1.21)	3 (2)	8 (4)	0.44 (0.11–1.71)
Unclassified[d]	71 (16)	85 (15)	0.99 (0.67–1.48)	61 (21)	68 (18)	0.96 (0.60–1.54)	10 (6)	17 (8)	0.83 (0.36–1.93)
p for trend[e]			0.14			0.17			0.68

[a] Calculated up to 10 years prior to diagnosis (cases) or reference (controls) and excludes 9 cases and 17 controls without sufficient occupational history data.
[b] Adjusted for age (continuous), sex and smoking (ever/never and pack-years); restricted to non-Hispanic Caucasians.
[c] Work history contains both indoor job(s) and job(s) with outdoor work.
[d] >25% of work years could not be classified in terms of percentage of workday spent outdoors.
[e] Trend excludes unclassified category.

may be different than suggested by their job title, and job descriptions for workers with the same job title may vary considerably. Exposure categories were assigned without regard to case status, and thus any misclassification of exposure likely would be non-differential and may have generally weakened results. In addition, we did not have direct information on UV-B exposure or protection such as hats and sunscreen or time spent outdoors for recreation, nor were we able to fully take into account the geographical location of each occupation. Also we were not able to account for occupational pesticide use (which is largely outdoors). Adjustment for this exposure is not possible because none of the occupations that may have entailed pesticide exposure were exclusively indoors. This may have weakened results insofar as occupational pesticide exposure increases PD risk, but evidence for this is limited in our study [9]. There is also the possibility that pre-clinical symptoms of PD may have altered cases' work selection, although lagging exposures by 10 years should have minimized such potential bias.

5. Conclusions

This study adds some support to the hypothesis that vitamin D or other correlates of UV-B exposure resulting from outdoor work may reduce risk of PD. However, these exposures are not likely to have a substantial role in the etiology of PD.

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