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Effects of Parkinsonism on Health Status in Welding Exposed Workers

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Abstract

Background—Previous studies suggest that welders frequently display parkinsonian signs, such as bradykinesia and tremor. Demonstrating that these parkinsonian findings are associated with reductions in quality of life (QoL) or health status could have important repercussions for worker safety and performance.

Methods—Subjects included 394 active workers exposed to welding fumes and evaluated for parkinsonism by movement disorders experts in a worksite-based epidemiology study. Subjects were diagnosed with parkinsonism if the Unified Parkinson Disease Rating Scale motor subsection part 3 (UPDRS3) score was >15. All subjects completed a Parkinson's disease (PD) symptom questionnaire and the PDQ39, a widely used QoL and health status measure for PD.

Results—Total PDQ39 score and all subscores were greater in welders with parkinsonism than welders without parkinsonism, with the most significant differences observed for mobility, emotional well-being, and activities of daily living (ADL's). The PDQ39 scores for welding exposed workers with parkinsonism were similar to scores seen in a group of early PD patients.

Conclusion—Parkinsonism in active, welding exposed workers is associated with reductions in health status and QoL affecting a broad range of categories and within the range seen in early PD.

Keywords

Parkinson disease; parkinsonism; quality of life; welding; health status

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INTRODUCTION

The cause of PD is unknown in most cases, although monogenetic factors account for approximately 17% of young onset PD.[1] The impact of risk factor genes[2] are likely mediated through complex interactions with previously implicated environmental exposures, such as pesticides[3] and heavy metals.[4] Epidemiologic evidence for elevated risk of parkinsonism or PD is mixed in metal exposed workers, although variability in case definition and diagnostic accuracy among cohort studies of welders complicates data interpretation.[5;6] An estimated 598,000 people living in the United States have occupational exposure to welding fume. [7] Although welding fume is a complex mixture of particulate fume and gases, most welding health effects research has focused on manganese (Mn), an established neurotoxicant.[8] Blood levels of Mn can be elevated in welders[9] and many reports indicate that clinical and subclinical neurologic impairments occur in these workers.[6] The degree to which these neurologic impairments are associated with symptoms or are associated with changes in health status is unclear. Demonstrating that parkinsonism in welders is associated with reductions in health status and quality of life (QoL) specific to PD may provide further insight into the pathophysiology of these clinical signs.

There are various methods for determining disease impact in subjects with PD, including quantification of the effect of disease on health status or on QoL. Health status specifically refers to the influence of disease on functional level, whereas QoL addresses more complex issues such as personal satisfaction related to function.[10] Health status and QoL measures are commonly employed to measure the influence of disease or treatment intervention on a patient's function and "social and material world".[11] The PDQ39 is a widely used health status questionnaire with good internal consistency, test-retest reliability, construct validity, and sensitivity to changes in health status. [12] [13;14] The PDQ39 takes approximately fifteen minutes to complete and contains 39 questions assessing eight dimensions of health: mobility, ADL, emotional well-being, stigma, social support, cognition, communication, and body discomfort. The PDQ39 is scored on a 0–100 scale with lower scores corresponding to better health status with higher scores correlating with advancing stage of disease.[13] These properties make the PDQ39 a useful tool to determine the impact of parkinsonism on perceived health status in Mn-exposed workers.

MATERIALS AND METHODS

Informed Consent

This study was approved by Human Subjects committees at Washington University and the University of Washington. Written informed consent was obtained from each subject before participation in the study.

Subjects and Design

Subjects for this study were participants in a worksite-based epidemiological study of the relationship between welding fume exposure and parkinsonism. This report presents findings from a group of workers who completed the PDQ39 as part of a sub-study which was begun after the start of the larger study. Active worker subjects were recruited from two Midwestern shipyards and one indoor fabrication shop from active union membership lists provided to our research team by local trade unions. To be included in this study, workers needed to be employed at one of these worksites. No workers were excluded from participation. All subjects were engaged in shipbuilding or repair or heavy equipment fabrication. A research coordinator attempted to contact union members to elicit their participation. Recruitment for the larger epidemiology study is ongoing. The a priori

hypothesis was that parkinsonism in welders would be associated with similar deficits in QoL and health status as newly diagnosed idiopathic PD patients.

Assessments

Welding Exposure Questionnaire- All subjects completed a validated welding exposure assessment questionnaire at the time of the examination.[15] In addition to detailed questions about welding exposures, the questionnaire includes a validated tobacco questionnaire to assess exposure to tobacco, since tobacco use consistently demonstrates a strong inverse relationship with PD in epidemiologic studies.[16] The questionnaire also includes questions about exposures to pesticides, caffeine, and alcohol, drawn from a previous epidemiology survey of PD,[17] since these exposures may serve as confounders for the relationship between welding and parkinsonism. Self-reported job duties and titles were summarized for descriptive purposes.

Clinical Assessment- Each subject was examined by a board certified neurologist, with fellowship training in movement disorders, using the (UPDRS3).[18] Examiners were blinded to exposure history, medical history, and PDQ39 score.

For the purpose of this study, we used a case definition of “parkinsonism” of UPDRS3 score ≥ 15 because most idiopathic PD patients become symptomatic and present for medical attention when motor scores on the UPDRS3 are >15 .[19] As a result, we predicted that this threshold would reflect motor dysfunction that would likely be associated with functional impairment in parkinsonian welders. Normal welders were defined as those workers with UPDRS3 scores less than 6. Subjects were excluded from analyses if they were on a dopamine receptor blocking medication or if co-morbid neurologic disease affected the UPDRS3 rating. Workers with UPDRS3 scores falling between these case definitions (UPDRS3 6 to <15) were combined for analysis as an intermediate group. A group of early PD subjects (disease duration less than five years) treated in the Movement Disorders Center at Washington University School of Medicine and with available PDQ39 data were evaluated to investigate differences in health status between PD and parkinsonism in welding exposed workers.

PD symptom Questionnaire- To determine if parkinsonian signs were associated with typical PD symptoms, we administered a standardized PD symptom questionnaire to all subjects. This nine item questionnaire has excellent sensitivity and specificity for detecting PD.[20]

QoL and Health Status- To assess QoL and health status among welding exposed workers, we administered the PDQ39 which assesses health status and health related QoL and has been extensively validated in PD subjects.[13]

Statistical Analysis

All statistical analyses were calculated using SAS v9.2. Descriptive data calculations in the form of medians and ranges were performed for the total study sample as well as stratified by the welders with UPDRS3 ≥ 15 , UPDRS3 6 - <15 and UPDRS3 <6 groups. We conducted logistic regression modeling to evaluate UPDRS3 score as a predictor of QoL as measured using the PDQ39. Six of the eight health dimensions of QoL were dichotomized as having a score greater than 10 and a score of 0, based upon the observation that patients with early PD have scores in the mid-teens.[21] Exceptions to this were systematically adjusted based on the general distribution of the health dimensions scores. Specifically, Social Support was dichotomized as having a score of greater than 20 and 0, and Emotional Well-Being, Body Discomfort, and Cognition were dichotomized as having a score of greater than 25 and less than 10. Participants with scores that did not meet these categorical definitions were excluded from the respective health dimension models to minimize misclassification.

Logistic regression modeling was also used to evaluate the risk of being diagnosed with parkinsonism and the risk of having a UPDRS3 score greater than or equal to 15 as predicted by symptoms evaluated using the PD symptoms questionnaire. The symptoms were categorized as yes or no. We analyzed by individual symptoms as well as by having “one or greater” and “two or greater symptoms” compared to “no symptoms”.

Welder subjects with a UPDRS3 score of less than 6 were used as the reference population in all models including the evaluation of subjects with a clinical categorization of parkinsonism. All models were adjusted for smoking (ever/never) and age at exam.

RESULTS

Of 1010 active workers recruited for the larger epidemiology study, 562 workers agreed to participate. This health status/ QoL study began after the larger epidemiology study; as a result, 394 active workers were enrolled. None of the workers declined to complete questionnaire. The overwhelming majority of workers were male (93%), white (98%), and the mean age was 50.0. (The workforce in this community is predominantly white.) Subjects were excluded from analysis for the following reasons: female gender (n=29), neurologic comorbidity (n=6), non-white or Hispanic (n=8). Female and non-white subjects were excluded from this analysis due to small numbers. After exclusions, 351 subjects were included in the data analysis. We found that 41 subjects (11.6%) had UPDRS3 $\geq$ 15. There was no significant difference between the frequency of a positive family history among the three categories of workers (Pearson Chi-Square p>0.05).

The clinical phenotype in the workers meeting our case definition of parkinsonism was primarily symmetric bradykinesia with associated axial signs. Lower extremity rigidity was more common than upper extremity rigidity. Postural/action tremor was more common than rest tremor. (Table 1) None of the subjects in this study had a “cock” gait, characteristic of severe Mn poisoning.[8] None of the subjects in this study were taking parkinsonian medications.

The means of the total PDQ39 score and all subscores were greater in welders with UPDRS3 $\geq$ 15 and with UPDRS3 6 - <15 as compared to welders with UPDRS3<6. (Table 2) The most notable differences between welders with UPDRS3 $\geq$ 15 and welders with UPDRS3<6 were in total scaled score, mobility, ADL's, stigma, and communication. Welder subjects with an intermediate degree of parkinsonism (UPDRS3 6 - <15) had PDQ39 total and subscores that were between our subjects with UPDRS3 $\geq$ 15 and welders with UPDRS3<6. Welders with UPDRS3 $\geq$ 15 also had higher scores than early PD patients on several PDQ39 subscales. (Table 2)

Overall, welders with UPDRS3 $\geq$ 15 had increased odds for worsening QoL and health status across all domains when compared to welders with UPDRS3<6. The odds of having higher total scaled PDQ39, ADL, emotional well being, and communication scores were significantly increased when subjects had UPDRS3 $\geq$ 15 as compared to welders with UPDRS3<6. (Table 3) Workers with scores falling into the intermediate category, UPDRS3 6 - <15, had modest elevated odds of having higher total PDQ39 scaled score, ADL's, and stigma as compared to welders with UPDRS3<6. A sensitivity analysis using workers with UPDRS3 scores less than three instead of UPDRS3<6 did not significantly change the magnitude or direction of these differences.

To determine if parkinsonian workers had typical symptoms of PD, we also administered a short, self-report PD symptoms questionnaire[20;22] to all subjects. In subjects with UPDRS3 $\geq$ 15, 44% had at least one PD symptom and 17% had two or more PD symptoms. In contrast, welders with UPDRS3<6, 76% reported having no PD symptoms and 8%

reported having two or greater symptoms. Workers with UPDRS3 $\geq$ 15 had greater odds of having one of the PD symptoms on the questionnaire than welders with UPDRS3 <6 although most of these differences were not statistically significant, suggesting that the clinical signs were more related to the health status abnormalities than the symptoms. The highest odds ratios were for small handwriting, hypophonia, and shuffling gait. (Table 4) Workers with UPDRS3 6 - <15 had a similar frequency of PD symptoms to welders with UPDRS3<6.

DISCUSSION

There are several important findings of this study. First, the prevalence of parkinsonism we found in these welding-exposed active workers was quite high considering that the frequency of workers with UPDRS3 $\geq$ 15 approached the frequency of parkinsonian signs found in the elderly.[23] These subjects had not been diagnosed with any neurologic condition but the neurologic findings do appear to be associated with functional impairments. For this study, we used more conservative criteria than in a previous study and still found a prevalence of parkinsonism of 12%, as compared to 6%–12.8% in welders in Alabama.[6] Of course, with only half of eligible workers examined, thus far, the prevalence may be somewhat lower if the majority of the remaining workers had normal examinations. Nevertheless, the prevalence of parkinsonism in active workers is still quite high. These findings are not surprising given substantial evidence of clinical and subclinical motor abnormalities associated with occupational Mn exposure. A study of workers in a Mn oxide and salt producing plant found that those exposed to low levels of Mn (approximately 1mg/m³) had slower simple reaction times on a standardized reaction time test, and more hand tremor, as measured by a standardized hand steadiness assessment.[24] Similarly, foundry workers in Sweden exposed to even lower Mn levels demonstrated slower reaction time, reduced finger-tapping speed, reduced tapping endurance, and diadochokinesis.[25] Manganese exposed workers in a Mn alloy facility had slower computerized finger tapping scores and less hand steadiness in another study.[26] None of these studies investigated the impact of parkinsonian findings on worker health status. It is important to note that our study does not specifically address the cause-effect relationship between welding fume and these parkinsonian findings. Detailed cumulative lifetime dose reconstruction is ongoing and will be used to determine the relationship between welding dose exposure and parkinsonism.

A second important finding of this study is that welding-exposed workers with parkinsonian findings have substantial reductions in health status affecting a broad range of categories. The QoL impairments manifested in this population extend far beyond what would be expected in a healthy population of workers and may have important occupational and social implications for this working population. Several studies have shown that workers with depressive symptoms, such as poor emotional well-being, are at increased risk of injury in the workplace.[27] There is also an increased risk of injury in workers with at least one disease/illness as compared to healthy workers.[28] While the relationship between parkinsonism and perceived health status/QoL and job performance in welders needs further study, it is possible that these workers may experience decreased productivity and/or may be at risk for additional occupational injuries and associated work absenteeism.

The elevations in PDQ39 total and subscores in parkinsonian welders in our study were within the range of typical PDQ39 scores for early PD patients.[29] [21] Previous studies in patients with Hoehn & Yahr stages I and II PD, and the data from patients in our movement disorders center, demonstrate that PD patients present with PDQ39 scores in the teens to twenties. In our welders, the most significant elevations in PDQ39 subscores were in ADL's, communication, and stigma. While the communication and ADL's abnormalities probably reflect the well described motor impairments associated with Mn exposure, the emotional

well being abnormalities may be consistent with the cognitive behavioral effects seen in Mn exposed workers.[30] Emotional well being, communication, and cognition subscores of the PDQ39 were higher in our welders with parkinsonism than our early PD patients. More detailed study of the neuropsychological impacts of chronic welding fume exposure in healthy workers is clearly warranted, but was beyond the scope of this study which focused on the impact of parkinsonism in welding exposed workers on health status.

Although our study demonstrates a relationship between abnormalities in health status and parkinsonism in welding exposed workers, the number of symptoms subjects experienced was quite modest. This may reflect the relatively lower sensitivity of traditional PD symptoms for detecting parkinsonism in this population compared to the more detailed QoL health status questions contained in the PDQ39. Of the individual symptoms, micrographia was most predictive of having parkinsonism, but the modest number of subjects with parkinsonism reduced the precision of these estimates. Frequency of positive answers on the symptom questionnaire was not particularly predictive of parkinsonism. However, if cognitive impairments are the first evidence of neurotoxicity in welding exposed workers, symptom questionnaires focused on motor symptoms may not be sufficient to identify cases reliably. Ideally, a combination of PD symptoms and health status questionnaires could be used to identify workers who may have developed parkinsonism and could be used to screen workers as part of routine occupational health examination. This would be far more practical than expert physical examinations in all workers and will be an important long term goal of this study.

There are several potential limitations to this study. Although this is a reasonably large, worksite-based sample of welding exposed workers, assessing a larger population may alter the relationship between parkinsonism and the measures of perceived health status found in this study if there is a volunteer bias among symptomatic welders. In addition, the PDQ39 may not be as specific for PD as suggested in the literature. None of the PD specific QoL or health status questionnaires have been adequately validated for their specificity to PD, although they do have face validity for the known health effects of PD. However, this population of active workers was quite healthy, based upon medical history, so we believe that co-morbid disease does not likely explain these findings. We were careful to exclude subjects with any co-morbid neurologic disease that would affect the motor ratings. Similarly, the UPDRS was designed to monitor PD subject progression in clinical trials so it is possible that nonspecific motor findings may explain some of the neurologic findings. Accordingly, to improve diagnostic validity, we established a threshold for the diagnosis of parkinsonism, UPDRS>15, which should minimize the likelihood that cases would consist of subjects with nonspecific motor findings. This study was therefore an attempt to test the assertion that health status impairments found in parkinsonian subjects among welders were similar to those typically seen in idiopathic PD. Nevertheless, we cannot exclude the possibility that nonspecific motor signs may contribute, in part, to the health status impairments. Finally, as previously noted, determining the dose-response relationship between welding fumes and parkinsonism was beyond the scope of this report, but with the development of validated metrics for cumulative welding exposure, we expect to investigate the relationship between lifetime welding exposure and perceived health status as well as clinical disease definitions.

In summary, workers exposed to welding fumes have previously undiagnosed motor abnormalities that are associated with measurable impairments in health status and QoL, within the range seen in early idiopathic PD. This study adds to previous literature, suggesting that welding exposed workers frequently demonstrate clinical signs of PD, by investigating the health status and QoL impact of these findings. The impact of these abnormalities on work performance and safety will be an important focus of future research.

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Table 1 Clinical Characteristics of Parkinsonian Welders^a

Clinical Feature	Mean UPDRS3 Score (SD)		
	Total	More affected	Less affected
Upper Limb Bradykinesia	7.7 (2.6)	4.0 (1.5)	3.7 (1.4)
Upper Limb Rigidity	2.2 (1.4)	1.2 (0.7)	1.0 (0.8)
Lower Limb Bradykinesia	2.1 (1.1)	1.2 (0.7)	0.9 (0.7)
Lower Limb Rigidity	2.4 (1.4)	1.2 (0.8)	1.2 (0.7)
Rest tremor	0.2 (0.6)	0.1 (0.4)	0.1 (0.3)
Action/postural tremor	1.1 (1.2)	0.6 (0.7)	0.5 (0.6)
Axial Signs ^b	3.7 (1.7)	N/A	N/A

^aWelders with a UPDRS3 score ≥ 15 ; n = 41^bIncludes neck rigidity, facial masking, arising from chair, posture, gait, postural instability, body bradykinesia

Table 2

PDQ39 Total and Health Dimension Scores by Diagnostic Category

	Total scaled score	Mobility	ADL ^b	Emotional well-being	Stigma	Social support	Cognition	Communication	Body discomfort
Parkinson disease patients	13.0 (11.6)	12.1 (15.3)	13.0 (20.1)	11.5 (13.6)	16.9 (19.9)	7.8 (14.4)	13.4 (14.4)	9.6 (11.6)	24.3 (18.0)
Parkinsonism among welders	UPDRS3 ^a ≥15	10.5 (15.5)	10.9 (19.1)	20.5 [†] (20.3)	4.4 [†] (8.3)	16.1 (24.3)	17.3 (15.8)	14.8 (19.0)	28.7 (23.4)
	UPDRS3 6 - <15	5.3 [†] (10.4)	3.3 [†] (8.7)	14.0 (16.9)	2.6 [†] (7.2)	7.8 (16.2)	12.4 (15.2)	5.1 [†] (11.0)	20.0 (21.3)
Normal	7.4 [†] (8.0)	4.8 [†] (10.6)	2.1 [†] (5.7)	13.7 (16.2)	1.5 [†] (4.2)	6.7 (13.4)	12.8 (15.1)	5.8 (10.8)	19.3 (18.5)

All data reported as mean value (standard deviation);

^aUPDRS3 = Unified Parkinson Disease Rating Scale Motor subsection part 3;

^b Activities of Daily Living;

[†] a 2-tailed t-test determined that mean values were significantly different than the PD patients (p<0.05)

UPDRS3^a Score and Clinical Category as Predictors of PDQ39 Total and Subscore Dimensions

Table 3

	Total scaled score	Mobility	ADL ^b	Emotional well-being	Stigma	Social support	Cognition	Communication	Body discomfort
Parkinsonism: UPDRS3 ^a 15+ vs Normal: UPDRS3 <6	2.8 (1.1–7.0)	2.3 (0.8–6.1)	4.7 (1.6–13.7)	4.0 (1.4–11.8)	3.3 (1.1–10.4)	2.5 (1.1–6.0)	1.8 (0.7–5.0)	3.2 (1.4–7.3)	2.8 (1.1–7.2)
Parkinsonism: UPDRS3 ^a 6 - <15 vs Normal: UPDRS3 ^a <6	1.1 (0.6–1.9)	0.9 (0.4–1.8)	1.4 (0.6–3.5)	1.1 (0.6–2.3)	1.6 (0.7–3.8)	1.1 (0.6–2.0)	0.8 (0.4–1.7)	0.8 (0.4–1.4)	1.0 (0.6–1.9)

^aUPDRS3= Unified Parkinson Disease Rating Scale Motor subsection 3;

^b Activities of Daily Living: Results presented as odds ratios (95% Confidence Interval), adjusted for age at examination and smoking (ever/never)

Table 4

Risk of Parkinsonism as Predicted by Specific Symptom

Symptoms	UPDRS3 ^a 15+	UPDRS3 ^a 6 – <15	UPDRS3 ^a <6	Odds Ratio ^b (95% CI) UPDRS3 ^a ≥15 vs UPDRS3 ^a <6	Odds Ratio ^b (95% CI) UPDRS3 ^a 6 – <15 vs UPDRS3 ^a <6
Arise From Chair	6	14	17	1.0 (0.4–2.8)	0.5 (0.2–1.1)
Handwriting smaller	5	11	6	2.9 (0.8–10.7)	1.8 (0.7–4.7)
Voice Softer	3	5	5	2.0 (0.4–9.4)	0.6 (0.2–2.1)
Poor balance when walking	6	14	11	1.9 (0.6–5.9)	1.0 (0.4–2.2)
Feet freeze	1	1	0	NA	NA
Face less expressive	2	4	3	1.8 (0.3–12.9)	0.9 (0.2–4.2)
Arms and legs shake	5	16	8	2.3 (0.7–8.1)	1.8 (0.7–4.5)
Trouble buttoning buttons	3	7	4	1.7 (0.3–8.0)	1.1 (0.3–3.8)
Shuffle Feet tiny steps	1	3	1	2.0 (0.1–35.1)	3.3 (0.3–34.7)
Having 2 or greater symptoms vs. no symptoms	7	23	11	3.0 (1.0–8.9)	1.0 (0.6–1.7)
Having 1 or greater symptoms vs. no symptoms	18	40	31	2.6 (1.2–5.8)	1.5 (0.7–3.4)

^aUPDRS3= Unified Parkinson Disease Rating Scale motor subsection 3;

^b Adjusted for Age at examination and cigarettes (ever/never)