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Exposure to hazardous air pollutants and the risk of amyotrophic lateral sclerosis

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ABSTRACT

Background: Amyotrophic lateral sclerosis (ALS) is a serious and rapidly fatal neurodegenerative disorder with an annual incidence of 1–2.6/100,000 persons. Few known risk factors exist although gene–environment interaction is suspected. We investigated the relationship between suspected neurotoxicant hazardous air pollutants (HAPs) exposure and ALS. **Methods**: A case–control study involving sporadic ALS cases ($n = 51$) and matched controls ($n = 51$) was conducted from 2008 to 2011. Geocoded residential addresses were linked to U.S. EPA NATA data (1999, 2002, and 2005) by census tract. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using conditional logistic regression. **Results**: Residential exposure to aromatic solvents significantly elevated the risk of ALS among cases compared to controls in 2002 (OR = 5.03, 95% CI: 1.29, 19.53) and 1999 (OR = 4.27, 95% CI: 1.09, 16.79) following adjustment for education, smoking, and other exposure groups. Metals, pesticides, and other HAPs were not associated with ALS. **Conclusions**: A potential relationship is suggested between residential ambient air aromatic solvent exposure and risk of ALS in this study.

1. Introduction

Amyotrophic lateral sclerosis (ALS) is a debilitating neurodegenerative disorder occurring among 1–2.6 per 100,000 persons worldwide each year (Govoni et al., 2012). The aetiology is unknown for 90%–95% of cases, termed sporadic, and few known risk factors exist that include older age, male sex, and certain genetic mutations (Nelson, 1995; Morahan and Pamphlett, 2006). The potential association of environmental exposures, such as metals, pesticides, and solvents, has been implicated in ALS, but results have been inconsistent and a gene–environment interaction is suspected (Mitchell, 2000; Schmidt et al., 2008). Recently, there has been significant interest recently in the use of air toxic exposure and risk driven toxicant models available for the entire country (Windham et al., 2006). Previous studies have examined the association between air pollution and development of neurologic disorders such as Alzheimer's disease, Parkinson's disease, and parkinsonism (Lucchini et al., 2003; Finkelstein and Jerrett, 2007; Weuve et al., 2009; Loane et al., 2013). However, exposure to hazardous air pollutants (HAPs) has not been investigated in relation to ALS.

It is appealing to explore the potential association of suspected neurotoxicants found in air pollution in the urban environments of

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Pittsburgh, Pennsylvania (Pa) and Philadelphia, Pa, that have nearby industries including chemical plants, oil refineries, metal fabricators, steel mills, coke ovens, coal mines, coal-fired power plants, paint/dye manufacturers, and Superfund and National Priorities List (NPL) sites. Additionally, the majority of W. Pa residents often remain in the area throughout their lifetime, providing an ideal research setting for studying the effects of environmental exposures and the risk of sporadic ALS. The specific aim of our study was to investigate the potential relationship of residential exposure to suspected neurotoxicant HAPs and development of sporadic ALS.

2. Methods

2.1. Study population

The study area consisted of six W. Pa counties surrounding Pittsburgh (Allegheny, Armstrong, Beaver, Butler, Washington, Westmoreland) and six counties surrounding Philadelphia (New Castle [Delaware]; Union, Somerset, and Sussex [New Jersey]; Montgomery and Philadelphia [Pa]). Inclusion criteria required residence in one of the above counties for ≥1 year as well as the ability to speak English. Cases and controls were excluded for any of the following criteria: 1) a blood relative with ALS (first, second, or third degree) due to investigation of sporadic ALS; 2) the following neurological disorders: dementia, Alzheimer's disease, Parkinson's disease, parkinsonism, or poliomyelitis/post-polio syndrome; and 3) previous travel to the Mariana group islands including Guam due to the previously increased incidence of ALS. Persons with dementia and Alzheimer's disease were excluded to ensure reliability of survey responses. Those with neurologic disorders with similar etiologies to ALS, such as Parkinson's disease and parkinsonism, were excluded although no such exclusions were made. Matching criteria for cases and controls involved: age at ALS onset (±5 years), race, and sex.

El Escorial World Federation of Neurology criteria were consulted, along with available clinical history and/or radiology results, for the diagnosis of ALS as definite, probable or possible by neurologists with board certification (Brooks, 1994). Recruitment of ALS cases took place over a 19-month period (December 2008–July 2010) from three neurology clinics with ALS centers, two in Pittsburgh and one in Philadelphia. Cases were diagnosed with ALS from November 1998–March 2010, with the majority (63.6%) of diagnoses occurring between January 2008 and March 2010. Details of the study methods have been previously reported (Malek et al., 2014). Of the 106 eligible cases, 78 participated in the overall study (73.6% response rate) and 66 cases (57 from W. Pa and 9 from Philadelphia) were included in the analysis as controls were not identified for twelve cases. Non-participation by eligible cases was attributed to initial disinterest, change of mind about participating, lost to follow-up, or passing away before completing the interview.

Controls were recruited from 2009 to 2011 from two sources due to the later addition of Philadelphia as a study site. In W. Pa, outpatient hospital controls were recruited from general neurological practice waiting rooms ($n = 57$), while population-based controls ($n = 9$) were identified using a random number generator from a mailing list ($n = 2000$) obtained through an online consumer marketing company for the greater Philadelphia area (Infogroup. InfoUS et al., 2010 November 15).

The study received approval from the Institutional Review Boards of the University of Pittsburgh, Allegheny General Hospital, and Drexel University College of Medicine, and written informed consent was obtained from all participants. Participants were compensated for their time and effort in participating in the study.

2.2. Exposure assessment

A detailed questionnaire, which obtained information on personal lifestyle factors, medical history, hobbies, as well as lifetime residential and occupational history, was administered in person by trained interviewers. The questionnaire was an adaptation of the ALS Risk Factor Questionnaire developed by the ALS Consortium of Epidemiologic Studies (ACES, 2005).

Residential addresses of cases and controls were geocoded via batch processing using ArcGIS StreetMap North America, version 10 (Redlands, CA, USA) or manually geocoded using the online program GeocodeDVD (East Brunswick, NJ, USA) and linked by census tract to U.S. Environmental Protection Agency (EPA) National-Scale Air Toxics Assessment (NATA) data for HAPs for the years 1999, 2002, and 2005 (ESRI, 2010; GeoLytics, 2011). Historical exposure at different time periods was constructed by assigning the current residential address at the time of each NATA assessment to that

Table 1
Selected characteristics of participants according to case status.[a]

Characteristic	Cases ($n = 66$) n (%)	Controls ($n = 66$) n (%)	p
Male	45 (68.2)	45 (68.2)	1.00
Caucasian	65 (98.5)	65 (98.5)	1.00
Western Pennsylvania region	57 (86.4)	57 (86.4)	1.00
Age (years)			
Mean ± SD[b]	57.1 ± 13.2	56.4 ± 13.5	0.07
18–44	12 (18.2)	13 (19.7)	0.87
45–54	13 (19.7)	17 (25.8)	
55–64	17 (25.8)	17 (25.8)	
65–74	18 (27.3)	15 (22.3)	
≥75	6 (9.1)	4 (6.1)	
Educational level			
Less than high school	4 (6.1)	2 (3.0)	0.82
High school graduate	20 (30.3)	22 (33.3)	
Vocational/technical training	6 (9.1)	3 (4.5)	
Some college	17 (25.8)	17 (25.7)	
College graduate (associate or bachelor's)	13 (19.7)	16 (24.2)	
Graduate degree	6 (9.1)	6 (9.1)	
Marital status			
Single	6 (9.1)	6 (9.1)	0.56
Married or cohabiting	54 (81.8)	50 (75.8)	
Divorced or widowed	6 (9.1)	10 (15.2)	
Smoking status			
Never	27 (40.9)	24 (36.4)	0.59
Ever (≥100 cigarettes)	39 (59.1)	42 (63.6)	
Years at residence (mean ± SD)[b]			
1999 NATA assessment ($n = 94$)	20.9 ± 14.4	17.1 ± 12.7	0.15
2002 NATA assessment ($n = 102$)	21.2 ± 16.0	18.2 ± 12.9	0.28
2005 NATA assessment ($n = 100$)	24.7 ± 16.0	20.2 ± 14.1	0.19
Occupation[c,d]			
Managerial and professional speciality	14 (21.2)	10 (15.6)	0.22
Technical, sales, and administrative support	15 (22.7)	24 (37.5)	
Service	9 (13.6)	5 (7.8)	
Precision production, craft, and repair	15 (22.7)	19 (29.7)	
Operators, fabricators, and labourers	10 (15.2)	6 (9.4)	
Farming, forestry, and fishing	1 (1.5)	0 (0)	
Full-time homemaker	2 (3.0)	0 (0)	

Abbreviations: SD, standard deviation; NATA, National-Scale Air Toxics Assessment.
[a] Data is provided for the original study cohort although the number of participants varied for the three comparison years as a result of the number of successfully geocoded residences.
[b] Paired t-tests were carried out for mean age and mean years living at residence for each NATA assessment.
[c] Occupation was classified according to 1980 U.S. Census Industrial and Occupational Classification Codes.
[d] The analysis excluded two controls who did not hold jobs as of the reference date.