

Paresthesias Among Community Members Exposed To The World Trade Center Disaster

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Objective: Paresthesias can result from metabolic disorders, nerve entrapment following repetitive motions, hyperventilation pursuant to anxiety, or exposure to neurotoxins. We analyzed data from community members exposed to the World Trade Center (WTC) disaster of September 11, 2001, to evaluate whether exposure to the disaster was associated with paresthesias. **Methods:** Analysis of data from 3141 patients of the WTC Environmental Health Center. **Results:** Fifty-six percent of patients reported paresthesias at enrollment 7 to 15 years following the WTC disaster. After controlling for potential confounders, paresthesias were associated with severity of exposure to the WTC dust cloud and working in a job requiring cleaning of WTC dust. **Conclusions:** This study suggests that paresthesias were commonly associated with WTC-related exposures or post-WTC cleaning work. Further studies should objectively characterize these paresthesias and seek to identify relevant neurotoxins or paresthesia-inducing activities.

The World Trade Center (WTC) Environmental Health Center (EHC) is a treatment program for community members (local workers, residents, clean-up workers) who developed physical and mental health symptoms after exposure to dust and fumes from the destruction of the WTC towers on September 11, 2001 (referred to herein as “9/11”). Most patients presented to the program because of upper or lower respiratory symptoms, frequently accompanied by symptoms consistent with gastroesophageal reflux.^{1,2}

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Within several years of the WTC disaster, we noted that some patients were complaining of neurologic symptoms consistent with peripheral paresthesias, prominent symptoms among patients with peripheral neuropathy. One of the most common types of neuropathy is a symmetric length-dependent polyneuropathy that may be seen in diabetes, autoimmune disorders, heavy metal exposure, and alcohol exposure. Because of the length-dependence, symptoms are often first noted in the leg, but they also can appear in the upper extremities. Formal questions eliciting the presence of both upper and lower extremity paresthesias therefore were added to the standarized questionnaire administered at enrollment.

Known neurotoxins including lead, aluminum, cadmium, manganese, tin, and complex hydrocarbons were present in WTC dust,^{3–10} and clean-up activities could have exposed workers to organic solvents. Some of these could have caused peripheral neuropathies and paresthesias. One symptom of lead poisoning, for example, is paresthesia, including weakness of the fingers and wrist.¹¹ Early symptoms of exposure to n-hexanes can also include paresthesias of the feet and fingers.¹² A study of workers exposed to organic solvents found an increased prevalence of paresthesias of both upper and lower extremities.¹³

Community members had potential for acute exposure to WTC contaminants, including possible neurotoxins, from the debris created and dispersed in dust clouds originating from the collapsing buildings. In addition, chronic exposures from resuspended dust were potentially experienced by workers and residents who returned to the neighborhood after the disaster.¹⁴ Neurotoxins also may have been in fumes from fires that burned for months after 9/11, fueled by building materials and the contents of the destroyed buildings. Many individuals helped clean buildings near the WTC towers (clean-up workers), and others were involved in cleaning of interior workplaces or places of residence. Clean-up activities might have exposed individuals to additional neurotoxins present in cleaning fluids, solvents or paints, including n-hexanes, trichloroethylene, and methyl-n-butyl ketone.¹⁵ Repetitive motions of both the upper and lower extremities might also result in paresthesias due to nerve entrapment or carpal tunnel syndrome.¹⁶

The variety of toxic exposures during and after 9/11 provides biological plausibility for a WTC-induced pathogenesis of neurological conditions. We report on the prevalence and risk factors for paresthesias among patients of the WTC EHC. Our hypothesis was that WTC exposures and severity of exposure were associated with the occurrence of paresthesias of both the lower and upper extremities.

METHODS

Patient Population

At initial presentation, all WTC EHC patients were asked to provide informed consent to allow their clinical and questionnaire data to be used for research. The NYU School of Medicine Institutional Review Board and the Office of Research of Bellevue Hospital Center and New York City Health and Hospitals Corporation approved the consent forms. All patients whose data are included in the present report signed informed consents.

The WTC EHC focuses on the health care needs of community members, including local workers, residents, students, or passers-by exposed to dust and fumes on and after 9/11.^{1,2} In 2008, the WTC EHC became part of a network of federally funded centers that evaluated and treated individuals for WTC exposure and related disease conditions; these programs were mandated in 2010 under the James Zadroga 9/11 Health and Compensation Act. As part of this mandate, we enrolled and maintained patients in the program if an initial evaluation documented exposure to the WTC disaster and presence of certifiable WTC-related health conditions, that is upper or lower respiratory symptoms, symptoms consistent with gastroesophageal reflux, cancer, or mental health symptoms consistent with post-traumatic stress disorder (PTSD), depression, or anxiety.

Clinical Evaluation

Patients responded to face-to-face-administered questionnaires that inquired into presence and severity of respiratory symptoms and mental health status, demographic characteristics, and various factors related to possible WTC exposure.¹ At enrollment, patients underwent venipuncture for complete blood counts and blood chemistries. We added questions (Table 1) on paresthesias (ie, sensations of tingling, prickling, or numbness) to the WTC EHC intake questionnaire in 2008. For the present analyses, we created a dichotomous (never vs sometimes through “almost continuously”) dependent variable reflecting paresthesias of either the upper or lower extremities in the year before interview.

We performed screening spirometry at the initial visit, using methods previously described.^{17,18} Forced expiratory volume in 1 second (FEV₁) was calculated as a percentage of predicted values from the National Health and Nutrition Examination Survey (NHANES).¹⁹ We discarded spirometric data if standard quality control criteria were not met. Subjects were then categorized as having abnormal FEV₁ if measured FEV₁ was less than 80% of the NHANES-predicted value.

Mental Health

We assessed mental health status via standardized questionnaires administered in English or Spanish. We used the PTSD Checklist Stressor-Version (PCL) for symptoms of PTSD.²⁰ A score more than 44 was used to define probable PTSD.²¹ The Hopkins Symptoms Checklist-25 was used to assess symptoms of depression and general anxiety.²² Mean scores at least 1.75 on the 15 items associated with depression (each item of which was scored from 1, “not at all,” to 4, “extremely”) was used as a cut-point for positivity for depression. Mean score at least 1.75 on the 10 items associated with anxiety was used as a cut-point for anxiety. The CAGE Questionnaire was used as a screen for alcohol dependence, with a score at least 2 used to categorize persons with alcohol abuse.²³

TABLE 1. Questions on Peripheral Neuropathy Included in the World Trade Center Environmental Health Center

1. In the past year, did you experience a prickling or tingling feeling, with or without an asleep feeling, in your feet or legs?
2. In the past year, did you experience a prickling or tingling feeling, with or without an asleep feeling, in your arms or hands?
3. I experience this sensation
 - a. Never
 - b. Occasional
 - c. Often
 - d. almost continuous
4. How many years ago did you notice persistent prickling or tingling in your hands or feet?
5. Did you notice persistent prickling or tingling in your hands or feet before 9/11/01?
6. Did you notice persistent prickling or tingling in your hands or feet after 9/11/01?
7. How many months or years after 9/11/01 did you experience persistent prickling or tingling in your hands or feet?
8. Did you experience this before 9/11?

WTC Dust and Fume Exposure Evaluation

We estimated the severity of exposure to the dust clouds according to responses to a question asking about the amount of dust on a person’s body, clothes, and hair. We grouped responses into three categories: (a) not in dust cloud, or no dust on person; (b) little, able to brush off; or covered but could brush some off before getting home (c) covered, could not brush most off before getting home; or entirely covered and could not brush it off.

Statistical Methods

All statistical analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC). We used odds ratios (ORs) and 95% confidence intervals (CIs) to explore associations between prevalent paresthesia symptoms at enrollment and various risk factors. We used the nonparametric Wilcoxon test to evaluate differences in quantitative variables between those with and without paresthesias, and unconditional multiple logistic regression analysis (as implemented in SAS PROC LOGISTIC) to analyze risk factors for paresthesia with a stepwise fitting strategy with *P* value less than 0.05 required for a variable to remain in the model. We used multinomial logistic regression analysis (via SAS PROC LOGISTIC) to investigate how ORs varied by frequency of paresthesia (never vs occasional, often, or almost continuous), and also by location of paresthesias (none vs isolated paresthesia of the upper extremities, isolated paresthesias of the lower extremities, and contemporaneous paresthesias of both the upper and lower extremities).

RESULTS

Participants

From January 1, 2008, through October 30, 2015, we enrolled and consented 3193 subjects into the Bellevue Hospital WTC EHC. Fifty-two (1.6% of the consented population) did not respond to the question on the frequency of prickling or tingling in the year preceding interview and were dropped from the analysis leaving a sample of 3141 participants. As summarized in Table 2, the population was diverse, with 50% of the population women; a wide range of ages, with 98% being less than 64 years old at enrollment; 25% self-reporting as Hispanic; nearly 11% reporting a diagnosis of diabetes; and 13% reporting having had cancer. Only 10% reported current tobacco use.

Frequency of Report of upper and Lower Extremity Paresthesias

Many patients reported experiencing paresthesias in the year before enrolling in the WTC EHC. Similar percentages of the population reported paresthesias of the upper (46%, 1446) or lower (44%, 1383) extremity. Most of those reporting paresthesias had paresthesias of both extremities (1033, or 33% of all subjects), with

TABLE 2. Prevalences and Odds Ratios of Demographic and Health Variables for Paresthesias of the Upper or Lower Extremities in the Year Before Interview ($n=3,141$)

Variable Value	N	N (%) With Paresthesia	OR 95% CI	P
Gender				0.006
Male	1,537	839 (55)	1.0	
Female	1,604	954 (59)	1.22 (1.06–1.41)	
Age on 9/11/2001				0.01
<25	308	118 (38)	0.43 (0.33–0.55)	
25–34	467	288 (62)	1.10 (0.88–1.38)	
35–44	990	587 (59)	1.0	
45–54	954	560 (59)	0.98 (0.81 1.17)	
55–64	356	202 (57)	0.90 (0.70–1.15)	
≥65	66	38 (58)	0.93 (0.56–1.54)	
Year of enrollment				<0.0001
2008–2010	1,595	873 (55)	1.0	
2011–2013	939	527 (56)	1.06 (0.90–1.24)	
2014–2015	607	393 (65)	1.52 (1.25–1.84)	
Race				0.0006
Caucasian	1,659	910 (55)	1.0	
African–American	706	441 (62)	1.37 (1.14–1.64)	
Asian and other	330	172 (52)	0.89 (0.71–1.14)	
Refused to answer	446	270 (61)	1.26 (1.02–1.56)	
Ethnicity*				<0.0001
Not Hispanic	2,347	1,272 (54)	1.0	
Hispanic	793	520 (66)	1.61 (1.36–1.90)	
Diabetes				<0.0001
No	2,787	1,527 (55)	1.0	
Yes	340	258 (76)	2.60 (2.00–3.37)	
Cancer				0.23
No	2,712	1,537 (57)	1.0	
Yes	415	248 (60)	1.13 (0.92–1.40)	
Smoked tobacco (ever)				
No	1,860	1,030 (55)	1.0	
Yes	1,271	759 (60)	1.19 (1.03–1.38)	
Smoked tobacco in the past 4 weeks				
No	2,799	1,576 (56)	1.0	
Yes	332	213 (64)	1.39 (1.10–1.76)	
Body mass index				
<25	906	468 (52)	1.0	
25–30	1,248	723 (58)	1.29 (1.09–1.53)	
≥31	882	561 (64)	1.64 (1.35–1.98)	
Paresthesia before 9/11/01				<0.0001
No	3,010	1,670 (55)	1.0	
Yes	109	106 (97)	28.4 (9.0–89.5)	

CI, confidence interval; OR, odds ratio.

*One person refused to self-classify by ethnicity.

11% (346) of patients reporting isolated paresthesias of the lower extremities and 13% (407) reporting isolated paresthesias of the upper extremities. Hereafter, we focus on risk factors for paresthesia of either the upper or lower extremities, without regard in our primary analyses for either the location of the paresthesias or their reported frequency.

Odds Ratios for Paresthesias

Clinical Characteristics

Table 2 summarizes associations of paresthesias with demographic characteristics and comorbid conditions. The strongest associations were with histories of paresthesias before September 11, 2001, and diabetes mellitus. In addition, there were significant associations with female sex, African–American race, and Hispanic ethnicity.

WTC Exposures

Multiple exposure variables were significantly associated with paresthesias (Table 3). Acute exposure to the WTC dust cloud

on 9/11 was associated with a significantly elevated OR for paresthesias, as was the severity of exposure to WTC dust, as indicated by the extent of being covered with dust on 9/11. Cleaning of WTC dust at work was associated with an increased OR for paresthesias; this category included those who self-classified as “clean-up workers” as well as others who did not, but nonetheless reported cleaning their workplaces as part of their jobs upon returning to work after 9/11. The associations of paresthesias with the various demographic and WTC exposure variables remained statistically significant and did not change substantially when data from individuals with diabetes or paresthesia before September 11, 2001, were deleted from the analytic data set (data not shown).

Medical and Mental Health Symptoms

There were significantly elevated ORs for paresthesias associated with respiratory symptoms and reduced lung function as measured by FEV₁ (Table 4). Elevated anxiety, depression and PTSD scores also were significantly associated with paresthesias (Table 5), but there was no association between elevated

TABLE 3. Prevalences and Odds Ratios of WTC Exposure Variables for Paresthesias of the Upper or Lower Extremities in the Year Before Interview ($n=3,141$)

Variable	N	N (%) With Paresthesia	OR 95% CI	P
Exposure group				<0.0001
Local workers	1,855	1,094 (59)	1.0	
Residents	728	367 (50)	0.71 (0.60–0.84)	
Rescue/Recovery	59	31 (53)	0.77 (0.46–1.29)	
Clean-up worker	153	111 (73)	1.83 (1.27–2.65)	
Other and missing	346	190 (55)	0.84 (0.67–1.07)	
Caught in WTC dust cloud				0.0002
No	1,357	724 (53)	1.0	
Yes	1,782	1,068 (60)	1.31 (1.13–1.51)	
Severity of WTC dust on person on 9/11/2001				<0.0001
0 (not covered or n/a)	1336	715 (54)	1.0	
1 (lightly covered)	500	257 (51)	0.92 (0.75–1.12)	
2 (heavily covered)	1,273	801 (63)	1.47 (1.26–1.72)	
Cleaned workplace after 9/11/2001				<0.0001
No	2,628	1,446 (55)	1.0	
Yes	470	322 (69)	1.78 (1.44–2.19)	
Cleaned own apartment after 9/11				0.4
No	2,485	1,411 (57)	1.0	
Yes	605	355 (59)	1.08 (0.90–1.29)	

CI, confidence interval; OR, odds ratio; WTC, World Trade Center.

CAGE scores and paresthesias. The number of alcoholic drinks consumed per day also did not differ substantially between those with paresthesia [median = 1 drink per day, interquartile range (IQR) = 0 to 2 drinks per day] and those without paresthesia (median = 1 drink per day, IQR = 0 to 2 drinks per day; Wilcoxon $P=0.8$).

Multiple Logistic Regression

As summarized in Table 6, most factors that were statistically significant in bivariable analyses continued to be significant in a multivariable logistic regression model that included the potential confounding variables of sex, race, ethnicity, tobacco use, diabetes, and cancer. As expected, paresthesias were strongly associated with preexisting paresthesias before 9/11. Environmental exposures to the WTC dust and fumes, including exposure to the WTC dust cloud, having been heavily covered in dust from the collapse of the towers, and cleaning one's workplace remained significantly associated with the presence of paresthesias. The OR for later years of intake, that is, 2014 to 2015 compared with 2008 to 2010 was also significantly elevated. Inclusion of variables for depression, anxiety,

and PTSD in the model reduced the ORs for the most severe coverage of one's person with dust on 9/11 to 1.30 (95% CI = 1.08 to 1.56) from 1.50 (95% CI = 1.35 to 2.15) but did not affect the OR for cleaning WTC dust at the workplace (adjusted OR = 1.69, 95% CI = 1.32 to 2.18). Adjustment of the logistic regression models for blood glucose levels, or alcohol use, another potential cause of peripheral neuropathy,²⁴ did not alter substantially the magnitudes of the ORs for paresthesias associated with WTC exposure variables (data not shown).

Table 7 summarizes a multinomial logistic regression analysis in which individuals reporting different frequencies of paresthesias are treated as having distinct conditions, or separate values of this ordinal dependent variable. The ORs for paresthesias of all three frequencies were elevated in later years (2014 to 2015) compared with the reference years of 2008 to 2010. Within each model, the ORs for paresthesias increased with increasing severity of the coverage of one's body and clothes with dust on 9/11. Across all three models, there were significantly increased ORs for paresthesias associated with female sex, Hispanic ethnicity, and histories of smoking, diabetes, and cancer.

TABLE 4. Prevalence and Odds Ratios for Paresthesias by New-Onset-Post-9/11/2001 Respiratory Symptoms, Abnormal Forced Expiratory Volume in 1 second (FEV1), Abnormal R5 on Oscillometry

Symptom With Onset post-9/11/2001		N Responding	N (%) With Paresthesia	OR (95% CI)
Cough	No	1,099	527 (48)	1.0
	Yes	2,033	1,261 (62)	1.77 (1.53–2.06)
Daytime wheezing	No	1,519	745 (49)	1.0
	Yes	1,612	1,042 (65)	1.89 (1.65–2.19)
Dyspnea with exercise	No	708	270 (38)	1.0
	Yes	2,406	1,501 (62)	2.69 (2.26–3.20)
Dyspnea at rest	No	2,009	993 (49)	1.0
	Yes	1,122	793 (71)	2.46 (2.11–2.88)
Nasal drip or sinus congestion	No	1,149	553 (48)	1.0
	Yes	986	1,236 (62)	1.78 (1.53–2.06)
FEV1 <80% of NHANES predicted	No	2,164	1,189 (55)	1.0
	Yes	976	604 (62)	1.33 (1.14–1.55)

CI, confidence interval; OR, odds ratio.

TABLE 5. Prevalence and Odds Ratios for Paresthesias by Dichotomized Psychological Scores and the CAGE Questionnaire for Alcoholism

Symptom With Onset Post-9/11/2001		N Responding	N (%) With Paresthesia	OR (95% CI)
Depression score*	<1.75	1,310	625 (48)	1.0
	≥1.75	1,409	942 (67)	2.21 (1.89–2.58)
Anxiety score*	<1.75	1,519	745 (49)	1.0
	≥1.75	1,612	1,042 (65)	1.89 (1.65–2.19)
PCL [†] score for probable PTSD*	≤44	2,087	1,058 (51)	1.0
	>44	1,003	706 (70)	2.31 (1.97–2.71)
CAGE score [‡]	<2	2,464	1,420 (58)	1.0
	≥2	246	141 (57)	0.99 (0.76–1.29)

CI, confidence interval; OR, odds ratio.

*422 subjects were missing scores on psychological measures.

†PTSD Checklist Stressor-Version score.

‡431 subjects were missing scores on the CAGE questionnaire.

The findings from multinomial logistic regression analysis treating paresthesias in different bodily locations as different conditions are summarized in (Table 8). The OR for being heavily covered with WTC dust on 9/11 was significantly elevated among persons with paresthesias of the upper extremities only, paresthesias of the lower extremities only, and paresthesias of both the upper and lower extremities when compared with the group with no paresthesias. The ORs for having a job that included cleaning WTC dust

was elevated among those with isolated paresthesias of the lower extremities and those with paresthesias of both the upper and lower extremities, while the OR for the upper extremities failed to achieve statistical significance ($P=0.16$).

DISCUSSION

We found a high prevalence of peripheral paresthesias among community members enrolled in the WTC EHC. These symptoms

TABLE 6. Logistic Regression Analysis of Risk Factors for Paresthesia Without Psychological Variables (model 1, $n=2,992$) and Including Psychological Variables (model 2, $n=2,565$)

Variable	OR for Paresthesia (Model 1)	OR for Paresthesia (Model 2)
	OR (95% CI)	OR (95% CI)
Year of enrollment (2011–2013 vs 2008–2010) (2014–15 vs 2008–2010)	1.11 (0.92–1.32) 1.54 (1.24–1.90)	1.06 (0.88–1.29) 1.47 (1.14–1.90)
Gender (Female vs male)	1.25 (1.06–1.46)	1.19 (1.00–1.42)
Race (African–American vs Caucasian) (Asian and Others vs Caucasian) (No answer vs White)	1.35 (1.11–1.65) 0.92 (0.70–1.19) 0.72 (0.54–0.97)	1.44 (1.16–1.80) 0.91 (0.69–1.21) 0.66 (0.48–0.91)
Ethnicity (Hispanic vs not Hispanic)	1.93 (1.50–2.48)	1.77 (1.35–2.32)
Body mass index (25 to <30 vs ≤25) (≥30 vs ≤ 25)	1.18 (0.98–1.43) 1.30 (1.06–1.61)	1.25 (1.02–1.53) 1.38 (1.10–1.74)
Paresthesia before 9/11 (Yes vs No)	29.6 (9.3–94.1)	29.9 (9.38–95.4)
Diabetes (Yes vs No)	2.31 (1.75–3.05)	2.11 (1.55–2.87)
Smoked in the last 4 weeks (Yes vs No)	1.47 (1.14–1.90)	-
Covered in dust (lightly covered vs no dust on person) (heavily covered vs no dust on person)	1.04 (0.83–1.29) 1.50 (1.27–1.78)	0.96 (0.75–1.22) 1.30 (1.08–1.57)
Cleaning job (Yes vs No)	1.70 (1.35–2.15)	1.69 (1.32–2.18)
Depression score (<1.75 vs ≥1.75)		1.31 (1.04–1.65)
Anxiety score (<1.75 vs ≥1.75)		1.64 (1.29–2.08)
PCL score for probably PTSD (≤44 vs >44)		1.36 (1.06–1.75)

CI, confidence interval; OR, odds ratio.

TABLE 7. Multinomial Logistic Regression Analysis of Risk Factors for Paresthesia by Frequency of Reported Paresthesia in the Year Before Intake Compared With the Reference Group of 1,300 Subjects Without Paresthesias in the Year Before Enrollment

Frequency of Paresthesia: Variable	Odds Ratios for Paresthesia Occasional (n = 1,042)	Odds Ratios for Paresthesia Often (n = 367)	Odds Ratios for Paresthesia Almost Always (n = 304)
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Gender: (Female vs male)	1.21 (1.02–1.44)	1.37 (1.07–1.75)	1.27 (0.97–1.67)
Year of enrollment: (2011–2013 vs 2008–2010)	1.12 (0.92–1.36)	1.05 (0.79–1.39)	1.15 (0.84–1.59)
(2013–2015 vs 2008)	1.31 (1.03–1.67)	1.48 (1.07–2.05)	2.32 (1.66–3.25)
Race			
(African–American vs Caucasian)	1.36 (1.09–1.69)	1.35 (0.99–1.84)	1.35 (0.97–1.89)
(Asian and Others vs Caucasian)	0.86 (0.64–1.15)	1.13 (0.76–1.68)	0.94 (0.59–1.48)
(No answer vs Caucasian)	0.85 (0.62–1.16)	0.84 (0.55–1.29)	0.44 (0.27–0.72)
Ethnicity:			
(Hispanic vs not Hispanic)	1.76 (1.34–2.30)	1.86 (1.30–2.67)	2.24 (1.53–3.28)
Paresthesia before 9/11:			
(Yes vs No)	30.15 (9.40–96.7)	34.15 (10.1–114)	28.18 (8.05–98.6)
Diabetes:			
(Yes vs No)	2.05 (1.51–2.77)	1.83 (1.23–2.72)	3.51 (2.41–5.11)
Covered in dust			
(Lightly covered vs no dust on person)	1.15 (0.90–1.47)	0.96 (0.67–1.37)	0.84 (0.56–1.27)
(Heavily covered vs no dust on person)	1.59 (1.32–1.91)	1.44 (1.11–1.87)	1.44 (1.08–1.90)
Cleaning job:			
(Yes vs No)	1.61 (1.25–2.08)	1.62 (1.14–2.28)	2.74 (1.93–3.88)
Cancer			
(Yes vs No)	0.90 (0.69–1.18)	1.03 (0.71–1.49)	1.93 (1.37–2.71)
Body mass index			
(25 to <30 vs ≤25)	1.20 (0.98–1.47)	1.42 (1.05–1.93)	1.22 (0.87–1.70)
(≥30 vs ≤ 25)	1.16 (0.92–1.46)	1.92 (1.38–2.65)	1.65 (1.16–2.35)

CI, confidence interval; OR, odds ratio.

were associated with severity of exposure to WTC dust on 9/11 and cleaning of workplaces. The association with WTC exposure and cleaning exposure remained significant after adjusting for known risks for paresthesias, including anxiety, preexisting paresthesias, and diagnoses of diabetes or cancer. Although we cannot determine causality from our data, the possibility of a causal relationship between WTC dust exposure and paresthesias is strengthened by (a) the high frequency of paresthesias; (b) the continued association between paresthesia and WTC exposure variables after controlling for potential confounders; and (c) the association of paresthesia with decreased lung function and respiratory symptoms, which themselves may be measures of WTC exposure. Arguing in favor of a psychosomatic origin for at least some of the paresthesias was the reduction in the OR, from 1.50 to 1.30, associated with heavy

coverage with dust on 9/11 following entry of psychological variables into the model. Psychological variables, including depression, anxiety, and PTSD, may themselves reflect WTC exposure, however, and could have reduced the ORs associated with these variables without themselves being causally associated with the observed paresthesias.

Paresthesias may occur as the result of neuropathy or, in the setting of lesions of central sensory pathways, can be due to hyperventilation and other metabolic derangements. Our data demonstrated an association of paresthesia with metabolic derangement of diabetes. However, there is also biologic plausibility for the paresthesias in our patient population being manifestations of peripheral neuropathy following WTC exposure. The dust and fumes contained known neurotoxins, including lead, aluminum,

TABLE 8. Multinomial Logistic Regression Analysis of Risk Factors for Paresthesia by Location of Paresthesia Compared With 1,296 Subjects Without Paresthesias in the Year Before Enrollment

Variable	Odds Ratios for Paresthesia of Upper Extremities (n = 335)	Odds Ratios for Paresthesia of Lower Extremities (n = 367)	Odds Ratios for Paresthesia of Both Upper and Lower Extremities (n = 989)
	OR* (95% CI)	OR* (95% CI)	OR* (95% CI)
Covered in dust Lightly covered vs no dust on person	1.07 (0.75–1.52)	1.25 (0.90–1.74)	0.96 (0.74–1.24)
Heavily covered vs no dust on person)	1.45 (1.11–1.90)	1.51 (1.17–1.95)	1.58 (1.31–1.91)
Cleaning job: Yes vs No	1.30 (0.90–1.89)	1.42 (1.00–2.02)	2.16 (1.68–2.79)

CI, confidence interval; OR, odds ratio.

*Adjusted for gender, year of enrollment, race, ethnicity, paresthesia before 9/11, diabetes, cancer, and body mass index.

and n-hexanes.^{7–14} Our findings are also buttressed by recent publications showing neurologic abnormalities among individuals involved in WTC rescue and recovery work^{25,26} and slowed nerve conduction velocities an in vitro rat sciatic nerve model.²⁷

Many participants in our study reported paresthesias of both the upper and lower extremities. There are potentially several explanations for this finding beyond our primary hypothesis of exposure to neurotoxins in WTC dust and fumes. Carpal tunnel syndrome can produce paresthesias in the upper extremities and may have been the result of repetitive motions associated with 9/11-related cleaning. Alternatively, exposures to solvents and other toxic materials during cleaning tasks could have resulted in paresthesias. However, the finding of upper and lower extremity symptoms also raises the possibility that there may be a severe underlying neuropathy or an uncommon etiology.^{28–30} Given these issues and the highly subjective nature of paresthesias, objective testing with electrodiagnostic techniques and histologic studies will be critical in clarifying the etiology and extent of neuropathic damage in the WTC (9/11) group.

Entry into the WTC EHC occurred years after the WTC disaster. The findings of stronger and significant ORs among individuals enrolled in 2013 to 2015 compared with those enrolled in earlier years is consistent with a slow deterioration in neurological health in the years following 9/11. Longitudinal analyses of WTC EHC patients who have yet to report paresthesias could help clarify whether such a model has merit. A small study of n-hexane-induced neuropathy suggested a continued deterioration in peripheral-neuropathy associated measures months after exposure ceased.¹⁴ Symptoms also worsened in the months after exposure among individuals with neuropathies due to glue sniffing.³¹ Our finding of an increasing prevalence in reported symptoms with an increasing year of enrollment in the WTC EHC is consistent with a slowly evolving process.

Our study sample of community members was multiracial and multiethnic with multiple comorbid conditions. Our finding of increased ORs among African–Americans and Hispanics may reflect the more common involvement of members of these minority groups in maintenance and cleaning operations compared to members of other racial/ethnic groups. Alternatively, these findings could reflect cultural differences in somatization of symptoms.^{32,33}

Of importance, we identified the expected associations of paresthesias with diabetes, a well-known cause of peripheral nerve damage, and cancer, for which paraneoplastic syndromes and chemotherapeutic treatments can commonly cause neuropathies and paresthesias. Despite the presence of these potential confounders, the association of post-9/11 paresthesias with WTC dust exposures remained significant after controlling for diabetes and cancer. We also identified an association between paresthesias and mental health symptoms, including anxiety. Anxiety, particularly when associated with hyperventilation, can be associated with paresthesias. However, the association of paresthesias with WTC exposures remained significant even after accounting for psychological conditions.

There are several limitations to our study. The population that we analyzed consisted of individuals who were self-referred as a result of exposure to the events of September 11, 2001, and symptoms (primarily respiratory) believed to be due to that exposure. As such, our sample does not include an unexposed subgroup. However, neurologic symptoms have not been in the rubric of “certifiable” conditions required for entry into the WTC Health Program.² Thus, associations of neuropathy with exposure variables may be less susceptible to self-referral biases than would be other conditions, such as respiratory symptoms or illnesses.

The common occurrence of paresthesias in the sample means that ORs reported here cannot be interpreted as estimates of the relative risk, as that interpretation depends on the rare disease

assumption. The ORs we report are nonetheless valid measures of association between exposure variables and paresthesia.

We cannot suggest mechanisms for the paresthesias associated with WTC exposures. However, the high prevalence of these symptoms in such a large sample warrants further investigation including studies that would go beyond self-reported symptoms to objective measures, such as electromyographic studies and skin biopsies to evaluate nerve fiber densities. Exposure of animal models to WTC dust and component chemicals from the WTC dust might clarify biological mechanisms of the WTC-associated neurological symptoms. The implications of neurological disease acquired from 9/11 exposure are significant clinically for future treatment protocols and patient care, and scientifically, for the understanding of toxin-mediated neuronal injury.

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