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Motor function in adults of an Ohio community with environmental manganese exposure

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ABSTRACT

Objectives: The objective of the present study was to evaluate motor function in order to assess the effects of long-term, low-level environmental manganese (Mn) exposure in residents of an Ohio community where a large ferro- and silico-Mn smelter has been active for more than 50 years.
Methods: One hundred residents from the Mn-exposed Ohio community were evaluated using the Unified Parkinson's Disease Rating Scale (UPDRS), a postural sway test, and a comprehensive questionnaire exploring demographics and general health. The results were compared to those of 90 residents from a demographically similar comparison town in Ohio. Mn exposure was assessed using modeled airborne Mn and blood Mn (Mn-B). The UPDRS was employed to evaluate parkinsonian motor features. Postural sway was measured using a CATSYS 2000 (Danish Product Development).
Results: No significant difference between the exposed and comparison groups was evident as to Mn-B, demographics or major health outcomes. The risk of abnormal UPDRS performance using "Motor and Bradykinesia" criteria was increased in the Mn-exposed group after adjustment for potential confounders such as the presence of other neurotoxic metals, factors affecting susceptibility to Mn, potential factors influencing motor performance, and other possible demographic confounders. No participant was diagnosed with clinical manganism by neurological examination. After adjustment for various potential confounders, the Mn-exposed group showed significantly higher postural sway scores under eyes-open conditions than the comparison group.
Conclusions: Subclinical findings on the UPDRS and postural sway in the Mn-exposed group may possibly reflect early subtle effects of chronic low-level Mn exposure. However, the cross-sectional study design, the small to medium effect sizes, and the little biological plausibility are limiting the possibility of a causal relationship between the environmental Mn-air exposure and the early subclinical neurotoxic effects observed.

1. Introduction

Exposure to high levels of manganese (Mn) in occupational environments may affect health, causing symptoms similar to those of Parkinson's disease (PD) with neurological and neuropsychological sequelae. The syndrome has been termed "manganism" and can occur following long-term airborne Mn (Mn-air) exposure that is usually higher than 2 mg/m^3, but susceptible individuals may develop clinical features after exposure to levels as low as 1 mg/m^3 (WHO, 1981). At lower exposure levels, less severe, preclinical neurobehavioral effects have been widely reported in various occupational settings (Bast-Pettersen et al., 2004; Bowler et al., 2007b; Iregren, 1999; Lucchini et al., 1999; Mergler et al., 1994; Roels et al., 1987, 1992, 1999). The main adverse manifestations are dose-related impairment of motor function, a negative effect on mood, cognitive deficits, and reduced coordination (Iregren, 1999; Levy and Nassetta, 2003; Zoni et al., 2007).

Little is known, however, about the possible neurobehavioral effects of environmental exposure to Mn-air. A community study conducted in Mexican villages close to Mn extraction and refining plants showed average Mn-air concentrations of 0.10 μg/m^3 in the mining village and 0.03 μg/m^3 in a reference

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village. In a Mn-exposed group, neurobehavioral testing revealed dose-dependent alterations in motor and cognitive functions (Rodriguez-Agudelo et al., 2006). In a Canadian community study, Mergler et al. (1999) found an association between decreased neurobehavioral function and higher Mn concentration in blood (Mn-B), although Mn-air levels were low (Baldwin et al., 1999). Two ecological population studies addressed the potential influence of environmental Mn exposure on the prevalence of parkinsonian disorders (Lucchini et al., 2007) or PD (Finkelstein and Jerrett, 2007), respectively in the Brescia province (Italy) and Ontario (Canada). Recently, two reports have appeared on residents exposed to environmental Mn in an Ohio community (USA) (Haynes et al., 2010; Standridge et al., 2008). The latter authors reported an effect of chronic low-level Mn exposure on postural balance. Haynes et al. (2010) reported a relationship between hair Mn level in residents and modeled ambient Mn-air concentration.

The Unified Parkinson's Disease Rating Scale (UPDRS) was originally developed in the 1980s (Fahn et al., 1987) and has become the most widely used clinical modality for assessing parkinsonian motor impairment and disability (Movement Disorder Society Task Force, 2003; Ramaker et al., 2002). The scale which was used in the present work is officially termed UPDRS Version 3.0 (Fahn et al., 1987). The scale has four components: Part I, "Mentation, Behavior and Mood"; part II, "Activities of Daily Living (ADL)"; part III, "Motor"; and part IV, "Complications". One of the core advantages of the UPDRS is that it was developed as a compound scale to capture multiple aspects of PD. The scale assesses both motor disability (part II: UPDRS ADL) and motor impairment (part III: UPDRS Motor). In addition, part I addresses mental dysfunction and mood, whereas part IV explores treatment-related motor and non-motor complications (Ramaker et al., 2002). Although specifically developed to assess PD, the UPDRS has also been used to rate parkinsonian features of other conditions, including those of normal aging, progressive supranuclear palsy, Lewy body dementia, and manganism (Ballard et al., 1997; Bennett et al., 1997; Beuter et al., 1999; Cubo et al., 2000; Koller et al., 2004; Lazeyras et al., 2002; Sikk et al., 2007).

Postural balance testing has proven to be useful in identifying subclinical neuromotor abnormalities occurring secondary to exposure to various neurotoxicants (Bhattacharya, 1999; Bhattacharya et al., 1990, 2006; Kuo et al., 1996; Sack et al., 1993; Smith et al., 1997). Several occupational studies have utilized postural balance testing in the context of Mn exposure (Bowler et al., 2007a,b; Chang et al., 2009; Chia et al., 1993, 1995; Kaji et al., 1993; Kim et al., 2007; Young et al., 2005). Only two previous reports have evaluated the influence of chronic non-occupational Mn exposure on postural balance (Hudnell, 1999; Standridge et al., 2008).

In Marietta, OH, community groups have expressed health concerns over continued industrial Mn pollution caused by a facility operated by Eramet Marietta Inc. (EMI). EMI has produced ferro- and silico-Mn for the steel industry commencing in the early 1950s, and historically high levels of Mn-air emissions were recorded in the first decades of operation (US-EPA, 1984). The present cross-sectional study sought to assess subclinical health effects, potentially associated with Mn-air emissions, in the Marietta community. Mount Vernon, OH, was selected as a comparison town because of demographic similarity to Marietta (U.S. Census Bureau, 2001a,b) as well as the lack of any major industry (US-EPA, 2010b).

The objective of the present study was to assess whether long-term low-level environmental Mn-air exposure in residents of an Ohio community is associated with impairment of motor function evaluated using the UPDRS Motor and ADL subscales and a postural sway test.

2. Methods

2.1. Participants

Subjects who had lived for at least 10 years in the Mn-exposed town (Marietta, Washington County, OH) or the comparison town (Mount Vernon, Knox County, OH), and who were 30–75 years of age, were recruited. A random selection design was chosen to enhance generalizability of results. A maximum of two eligible members were recruited from each selected household. Exclusion criteria included a work history at EMI; a history of having lived in Marietta for Mount Vernon participants; the presence of a neurodegenerative disease (multiple sclerosis, Alzheimer's dementia, Huntington's chorea, or PD); a history of a brain ailment (meningitis, encephalitis, stroke requiring hospitalization for more than 1 day, a condition requiring brain surgery, any prior head injury, or epilepsy); a history of a serious psychiatric condition (schizophrenia, any major psychiatric diagnosis, or bipolar disorder); current treatment with anticonvulsive drugs; alcohol/drug dependence; a history of a hepatic condition; pregnancy; current nursing status; being medically unfit to participate in the study; or a history of exposure to hazardous chemicals (pesticides, fungicides, herbicides, carbon monoxide, and/or neurotoxic metals).

In Marietta, a total of 1732 invitation letters were mailed to randomly selected households of whom 264 individuals expressed interest and 122 were eligible for testing. In Mount Vernon, 2297 invitation letters were sent, 245 individuals expressed interest, and 117 were eligible. In all, 270 respondents to the random mailings were excluded on the basis of our exclusion criteria, or were unable to participate. Of the 239 subjects who were both interested and eligible, 191 participants (exposed: $n = 100$, comparison: $n = 91$) from 150 households (exposed: $n = 76$, comparison: $n = 74$) were tested. One participant from the comparison town was excluded after testing because of inadequate residency duration. Thus, data from 100 Mn-exposed and 90 comparison participants were available for analysis.

The Ohio Department of Health (ODH), the US and Ohio Environmental Protection Agencies (EPAs), and the Agency for Toxic Substances and Disease Registry (ATSDR) provided technical assistance, input into the study design, and review of the San Francisco State University (SFSU) protocol. The institutional review boards of SFSU and the ODH each granted research approval. Written informed consent was obtained from each participant prior to testing. Data collection occurred during August 2009.

2.2. Exposure assessment in Marietta, OH

High-temperature industrial processes such as smelting and steel production are significant sources of fine particles that are enriched with toxic metals (Schroeder et al., 1987) and which have the potential of causing contamination of the environment with airborne fine particulate. This has been recognized for the Marietta site in health consultation reports (ATSDR, 2009) which show levels of ambient air Mn that exceed the RfC of 0.050 $\mu g/m^3$ (US-EPA, 1993) derived for respirable particulate. Using 2001 Mn-air emission data, the US-EPA performed Mn-air dispersion modeling for the Marietta area as a part of the present study. Deposition was not included in the model. The AERMOD modeling system (US-EPA, 2009b) also included terrain information, and 1994–1998 surface and upper air meteorological data from the records of weather service stations located at the Parkersburg (WV) airport and in Dayton (OH), respectively (NOAA, 2010; USGS, 2010; WebMET, 2010). A geographic information system grid overlay was created to map Mn-air exposure (respirable particulate only) within the study area. An annual average Mn-air concentration, in $\mu g/m^3$, was