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Prospective study on neurotoxic effects in manganese-exposed bridge construction welders

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ABSTRACT

Background: In a group of 43 confined space welders dose–effect relationships had been identified for adverse neurological/neuropsychological functional effects in relation to manganese (Mn) in blood or air (cumulative exposure index). The welders' exposure to Mn was unprotected and with poor ventilation, lasting on average 16.5 months. A follow-up examination 3.5 years later, after cessation of confined space welding, was carried out to re-assess the status of mood, movement/neuromotor and cognitive functions, and olfaction.

Methods: In 2008, 26 welders (70% response rate) were retested using a similar methodology as at baseline (Bowler et al., 2007). A general linear model was used to estimate individual-specific endpoint differences over time. Mean age was 47 years, mean years of education 12.4, and mean total years of welding 16.9 years. Thirteen participants no longer welded.

Results: At follow-up, mean blood Mn concentration had decreased from 10.0 to 8.4 μg/L ($p = 0.002$). Those still welding had higher blood Mn than those no longer welding (9.9 μg/L vs. 6.8 μg/L, $p = 0.002$). Several domains of cognitive functioning improved substantially as shown by large effect sizes. Emotional disturbance improved only slightly clinically, but complaints of depression and anxiety persisted. Motor dexterity/tactile function and graphomotor tremor improved significantly, while psychomotor speed remained unchanged. The findings of the neurological examination (UPDRS) did not change compared to baseline, whereas rigidity, dominant postural hand tremor and body sway worsened. Olfactory test scores remained depressed.

Conclusion: After 3.5 years of cessation of confined space welding, only cognitive function improved significantly, while olfactory, extrapyramidal, and mood disturbances remained constant or were exacerbated. This suggests differential intrinsic vulnerabilities of the brain loci involved with Mn exposure. As the Mn exposure of the Bay Bridge welders frequently exceeded the Cal-OSHA TLV of 0.2 mg Mn/m^3 at baseline, a more stringent preventive measure is recommended for confined space welding.

1. Introduction

Manganese (Mn) is of vital importance for humans in small amounts, but neurotoxicity occurs at higher doses. The first clinical description of a neurological syndrome – postural instability, frequent hallucinations, emotional lability – associated with inhalation exposure to Mn dust was made by Couper (1837) in a series of five pyrolusite ore (MnO_2) crushers. In the occupational setting, the syndrome became known as manganism and has been reported in miners, chemical industry and dry-cell battery workers, steel production and Mn alloy workers, and welders (Feldman, 1999; World Health Organization – International Programme on Chemical Safety, 1981). This neurotoxic condition, often described as Mn-induced parkinsonism, presents features similar to idiopathic Parkinson's Disease (IPD). However, it differs

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from IPD by younger age of onset, a normal [^{18}F]L-DOPA PET scan, lack of response to L-DOPA treatment, postural tremor, and Mn deposits (MRI scan) in the corpus striatum and globus pallidus during the chronic exposure phase (Feldman, 1999).

At present, the incidence of clinical cases of manganism is rather low; however, numerous articles report on mild neurotoxic effects associated with workplace inhalation exposure to Mn. Some of these effects have been termed "subclinical", implying that they can occur in otherwise asymptomatic individuals and may represent early indicators of manganism. The nature of these effects, the Mn exposure levels at which they occur and their potential for progression or reversibility are therefore of particular clinical and regulatory interest (MRC-IEH/IOM: Institute for Environment and Health/Institute of Occupational Medicine, 2004). Subclinical neurotoxic effects include basal ganglia-related perturbations (motor inefficiency), cognitive deficits (e.g. working and delayed memory problems), and mood disturbances.

Health compensation claims or law suits involving welders are not uncommon in the USA and concern is growing about the potential neurologic effects associated with Mn exposure from welding fumes (NIOSH, 2009). In particular, welders working in confined spaces (e.g. pipefitters, boiler makers, shipyard and construction workers) may experience elevated Mn exposures (Harris et al., 2005; Meeker et al., 2007). In the welding setting, there is a risk of being overexposed to readily bio-available Mn of respirable particulate through fumes from using Mn-containing rods, wires, fluxes and base metal (steel and alloys), especially when welding occurs without appropriate ventilation and/or personal protection equipment. Significant inverse dose–effect relationships were found for ambient air-Mn (cumulative exposure) and/or blood-Mn with performance on motor and/or cognitive tests in confined space bridge welders (Bowler et al., 2007) or shipyard and heavy machinery welders (Ellingsen et al., 2008). The former study also showed dose–effect with mood changes using the Symptom Checklist-90-Revised (SCL-90-R), whereas the latter did not when using the Q-16 symptom questionnaire – a less discriminative measure developed for solvent exposure.

In January 2005, we examined a cohort of confined space welders engaged in the construction of a new span of the San Francisco-Oakland Bay Bridge. Some time before this study, the welders had suffered from subacute Mn exposure episodes (with signs of *locura manganica*) during the active phase of the bridge reconstruction, as documented by industrial hygiene surveys from January 2003 to June 2004 conducted for Cal-OSHA compliance (Park et al., 2006, 2009). This baseline study revealed neurological, neuropsychological, and neurophysiological (sensory/autonomic) adverse effects significantly associated with the Mn concentration in whole blood and/or a cumulative Mn exposure index (CEI) (Bowler et al., 2007). This paper describes a follow-up health survey in this cohort of welders we conducted in August 2008. They were re-tested and neurological, neuropsychological, and olfactory functions were evaluated. The goal of this follow-up was to determine the potential reversibility of Mn-related health findings in the Bay Bridge cohort after 3.5 years reduction or cessation of Mn exposure through welding. We hypothesized that welders who had short-term subacute Mn exposure, once removed from over-exposure to Mn, will exhibit improved health outcomes.

2. Methods

2.1. Study population

At the 2005-baseline study, the initial welders' cohort of 43 males was on average 43.8 years old, had 12.6 years of education, welded on average 16.5 months on the bridge, and was exposed to Mn-containing welding fumes with little or no personal protection. Mean time-weighted average (TWA) of Mn-air ranged from 0.11 to 0.46 mg/m^3 [frequency above Cal-OSHA TLV of 0.20 mg/m^3 was 55% (88 samples out of 159 total non-short-term samples)] (Bowler et al., 2007). Of the 43 participants in the 2005-baseline examination, 26 were recruited for the 2008-follow-up study, of whom 13 were still occupied in welding operations. A minimum language proficiency was required to work on the Bay Bridge construction project, and therefore it was considered valid to use data from welders for whom English is a second language.

The majority of the Bay Bridge welder cohort had previously been involved in workers' compensation proceedings (all of the proceedings were completed prior to the follow-up study). In the consent form, participants were asked to take part in the study, in order to update information regarding their mental and physical health, as well as their work history since their earlier visit. The data collected in the present study were not used for purposes other than scientific research and were not provided or used in the welders' previously concluded workers' compensation proceedings. The researchers were not compensated by the workers' compensation legal team.

2.2. Procedures and study design

Approval for the follow-up study was obtained from the Institutional Review Boards (IRB) at San Francisco State University and the U.S. Department of Defense. From the original group of 43 welders, 6 had relocated out of the state of California, leaving 37 eligible for recruitment and testing. Among them, 6 were unreachable or did not return telephone calls and one person declined. For the remaining total of 30, follow-up appointments were scheduled for August 2008. Four did not appear for their appointments, resulting in a response rate of 26/37 (70.3%).

The study employed a prospective longitudinal design. The methodology used at follow-up was similar to baseline. Participants were introduced to the intent and methodology of the study with recruitment letters and telephone calls. On the testing day, each participant first signed the IRB consent forms outlining confidentiality procedures and was then assigned to a neuropsychological tester who was, whenever possible, the same person as at baseline. In the consent form, participants were asked to take part in the study in order to update information regarding their mental and physical health, as well as their work history since their earlier visit.

The neuropsychological tests were administered in the same order to all participants. Trained graduate students administered the motor, olfactory, and CATSYS (Danish Product Development, 1996) tests. A board-certified neurologist (JW), skilled and experienced in movement disorder assessments, re-administered the Unified Parkinson's Disease Rating Scale (UPDRS) (Fahn and Elton, 1987). Work and health histories related to the period after the baseline study were collected. The participants were briefly interviewed by the P.I. (RMB), followed by the neuropsychological testing and a neurological examination. Self-report measures of health symptoms and standardized mood scales (SCL-90-R), and BRFSS (Behavioral Risk Factor Surveillance System) were completed by the participants and reviewed for completeness. Blood samples were collected by a certified phlebotomist and analyzed for trace levels of Mn and Pb by the same Microbiology and Environmental Toxicology Laboratory at the University of California at Santa Cruz (Smith et al., 2007). Appropriate quality assurance procedures were followed throughout the course of the study. All test protocols were scored and double-scored using the respective test manuals and any differences in scoring were reviewed and resolved by the P.I. Double data-entry procedures were utilized. The data were entered into an SPSS 16 file and converted to a SAS v9.1 dataset.