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Sequelae of fume exposure in confined space welding: A neurological and neuropsychological case series

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Abstract

Welding fume contains manganese (Mn) which is known to be bio-available to and neurotoxic for the central nervous system. Although an essential metal, Mn overexposure may cause manganism, a parkinsonian syndrome. The present welder study sought to improve the clinical portrait of manganism and to determine dose–effect relationships. The welders were employed in the construction of the new Bay Bridge (San Francisco) and welded in confined spaces for up to 2 years with minimal protection and poor ventilation. Neurological, neuropsychological, neurophysiological, and pulmonary examinations were given to 49 welders. Clinical cases were selected on the basis of *apriori* defined criteria pertaining to welding history and neurological/neuropsychological features. Among the 43 eligible welders, 11 cases of manganism were identified presenting with the following symptoms: sleep disturbance, mood changes, bradykinesia, headaches, sexual dysfunction, olfaction loss, muscular rigidity, tremors, hallucinations, slurred speech, postural instability, monotonous voice, and facial masking. Significant associations between outcome variables and cumulative exposure index (CEI) or blood Mn (MnB) were obtained with CEI for variables implicating attention and concentration, working and immediate memory, cognitive flexibility, and verbal learning; and with MnB for executive function, cognitive flexibility, visuo-spatial construction ability, and visual contrast sensitivity. This study strongly suggests that neuropsychological features contribute in a dose–effect related way to the portrait of manganism usually characterized by tremor, loss in balance, diminished cognitive performance, and signs and symptoms of parkinsonism.

Keywords: Manganese exposure; Neuropsychological; Neurological; Motor; Vision; Emotional status; Adults; Clinical cases; CATSYS

1. Introduction

Manganese intoxication was first described in 1837 by John Couper (UK) in pyrolusite ore grinding workers who were observed with signs and symptoms which presently would prompt diagnosis of manganism. Reports of health effects from manganese (Mn) in welding fume exposures have been relatively recent (Racette et al., 2005). Table 1 summarizes our review of the literature of health effects of Mn exposure in the domains of tremor, motor, neurocognitive, memory, vision, sleep, sexual function, and mood for the period of 1955–2006. Apart from the study by Mergler et al. (1999) on environmental Mn exposure, these occupational Mn exposure studies, other than the relatively few in welders (highlighted in bold), deal with exposures from mining and smelter activities, ferroalloy and dry battery production, and pesticide (Maneb) manipulation.

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Table 1
Literature review of neurological and neuropsychological signs and symptoms in studies on workers exposed to manganese

	Authors	Participants E = Mn-exposed C = non-exposed	Tremor	Motor	Neurocognitive	Memory	Vision	Sleep	Sexual	Mood
1	Penalver (1955)	Not known	(+)	(+)	(+)	ne	ne	(+)	(+)	(+)
2	Schuler et al. (1957)	$E = 83$	(+)	(+)	(+)	ne	ne	(+)	(+)	(+)
3	Abd El Naby and Hassanein (1965)	$E = 45$	(+)	(+)	(+)	ne	ne	(+)	(+)	(+)
4	Mena et al. (1967)	$E = 13$, $C = 114$	(+)	(+)	(+)	(+)	ne	(+)	(+)	(+)
5	Tanaka and Lieben (1969)	$E = 7$	(+)	(+)	(+)	ne	ne	(+)	(+)	(+)
6	Smyth et al. (1973)	$E = 71$, $C = 71$	(+)	(+)	(+)	ne	ne	ne	ne	ne
7	**Chandra et al. (1974)**	**$E = 12$ $C = 20$**	**(+)**	**(+)**	**ne**	**ne**	**ne**	**(+)**	**ne**	**(+)**
8	Cook et al. (1974)	$E = 6$	(+)	(+)	(+)	(+)	ne	(+)	(+)	ne
9	Barbeau et al. (1976)	$E = 10$	(+)	(+)	ne	ne	ne	(+)	(+)	ne
10	Chandra et al. (1981)	$E = 60$ $C = 20$	(+)	(+)	ne	ne	ne	(+)	ne	ne
11	Yamada et al. (1986)	Case study	(+)	(+)	ne	ne	ne	(+)	(+)	(+)
12	Roels et al. (1987)	$E = 141$ $C = 104$	(+)	(+)	ne	(+)	ne	(+)	ne	(+)
13	Ferraz et al. (1988)	$E = 50$ $C = 19$	(+)	(+)	(+)	(+)	ne	(+)	(+)	(+)
14	Huang et al. (1989)	$E = 6$	ne	(+)	(+)	ne	ne	(+)	ne	ne
15	**Wang et al. (1989)**	**$E = 132$**	**(+)**	**(+)**	**ne**	**ne**	**ne**	**(+)**	**ne**	**(+)**
16	Wolters et al. (1989)	$E = 4$	(+)	(+)	ne	ne	ne	ne	ne	ne
17	Iregren (1990)	$E = 30$ $C = 60$	ne	(+)	ne	(+)	ne	ne	ne	ne
18	Hua and Huang (1991)	$E = 29$ $C = 19$	ne	(+)	(+)	(−)	ne	ne	ne	ne
19	Wennberg et al. (1991)	$E = 30$ $C = 60$	ne	(+)	ne	(+)	ne	(+)	(+)	(−)
20	Roels et al. (1992)	$E = 92$ $C = 101$	(+)	(+)	ne	(−)	ne	ne	ne	ne
21	Wennberg et al. (1992)	$E = 30$ $C = 60$	ne	(+)	ne	ne	ne	ne	ne	ne
22	Reidy et al. (1992)	$E = 21$ $C = 11$	ne	(+)	(+)	(−)	(−)	(+)	ne	(+)
23	**Nelson et al. (1993)**	**Case study**	**ne**	**(+)**	**(+)**	**(+)**	**ne**	**ne**	**ne**	**ne**
24	Meco et al. (1994)	Case study	(+)	ne	(+)	ne	ne	ne	ne	ne
25	Mergler et al. (1994)	$E = 115$ $C = 115$	(+)	(+)	(+)	(−)	(−)	(+)	(+)	(+)
26	**Sjögren et al. (1996)**	**$E = 12$ $C = 39$**	**(−)**	**(+)**	**(+)**	**(+)**	**ne**	**(+)**	**ne**	**(−)**
27	Crump and Rousseau (1999)	$E = 123$	ne	(+)	ne	(−)	ne	ne	ne	ne
28	**Kim et al. (1999a,b)**	**Case study**	**(+)**	**(+)**	**(+)**	**ne**	**ne**	**ne**	**ne**	**ne**
29	**Kim et al. (1999a,b)**	**$E = 2$**	**(+)**	**ne**	**ne**	**ne**	**ne**	**ne**	**ne**	**ne**
30	Lucchini et al. (1999)	$E = 61$ $C = 87$	(+)	(+)	ne	(+)	(−)	(+)	ne	(+)
31	Mergler et al. (1999)[a]	$E = 273$	(+)	(+)	(+)	(+)	(−)	ne	ne	ne
32	**Jin et al. (1999)**	**$E = 98$ $C = 29$**	**ne**	**(+)**	**(+)**	**ne**	**ne**	**ne**	**ne**	**(+)**
33	**Discalzi et al. (2000)**	**Case study**	**(+)**	**(+)**	**ne**	**ne**	**ne**	**ne**	**ne**	**ne**
34	**Racette et al. (2001)**	**$E = 15$ $C = 100$ $C = 6$**	**(+)**	**(+)**	**(+)**	**ne**	**ne**	**ne**	**ne**	**(−)**
35	Sinczuk-Walczak et al. (2001)	$E = 75$ $C = 62$	ne	(+)	(+)	ne	(−)	(+)	ne	(+)
36	**Bowler et al. (2003a)**	**$E = 76$ $C = 42$**	**(+)**	**(+)**	**(+)**	**(+)**	**(+)**	**(+)**	**(+)**	**(+)**
37	Myers et al. (2003)	$E = 509$ $C = 67$	(−)	(+)	(+)	ne	ne	ne	(+)	(+)
38	**Sadek et al. (2003)**	**Case study**	**(+)**	**(+)**	**(+)**	**(+)**	**ne**	**ne**	**ne**	**ne**
39	Bast-Pettersen et al. (2004)	$E = 100$ $C = 100$	(+)	(+)	(−)	ne	(−)	ne	ne	(−)
40	**Beuter et al. (2004)**	**E (Mn) = 10 $C = 11$ PD = 10**	**(+)**	**ne**	**ne**	**ne**	**ne**	**ne**	**ne**	**ne**
41	Koller et al. (2004)	$E = 13$	(+)	(+)	(+)	ne	ne	(+)	ne	*ne*
42	Yuan et al. (2006)	$E = 68$ C = 42	ne	(−)	(+)	(+)	(+)	(+)	(+)	(+)
43	**Bowler et al. (2006a)**	**$E = 47$ $C = 42$**	**(+)**	**(+)**	**(+)**	**(+)**	**ne**	**ne**	**ne**	**(+)**
44	**Bowler et al. (2006b)**	**Case study**	**(+)**	**(+)**	**(+)**	**(+)**	**ne**	**(+)**	**(+)**	**(+)**

(+) positive findings; (−) findings not significant; ne, not examined or reported. Bolded type indicates welding studies.
[a] Environmental Mn exposure.

Manganese has been shown to cause a parkinsonian syndrome sometimes referred to as manganism which is often misdiagnosed as Parkinson's disease (PD). Similarities between symptoms of PD and manganism include tremor, masked facies, generalized bradykinesia (abnormal slowed movement associated with movement initiation difficulties) and cogwheel rigidity (Feldman, 1999). Differences may include more frequent dystonia (slow, involuntary, arrhythmic muscle contractions) in manganism and a tendency to fall backward in PD and falling forward in manganism. Magnetic resonance imaging (MRI) can be used to reveal Mn^{2+} deposition in the brain, exhibiting a T1-weighted signal hyperintensity, especially in the globus pallidus and striatum, in both animals (Shinotoh et al., 1995) and humans exposed to manganese (Nelson et al., 1993; Kim et al., 1994, 1998, 1999a,b; Lucchini et al., 2000; Dietz et al., 2001; Gasparotti et al., 2002). PD is associated with lesions in the *substantia nigra pars compacta* and does not produce similar MRI abnormality as manganism (Kim, 2006). Other differentiating features between manganism and PD are younger age of onset and little or no response to L-dopa among the manganism cases (Lu et al., 1994; Feldman, 1999; Koller et al., 2004). Case reports of neurological findings in career welders exposed to Mn have revealed dystonia bilaterally in the shoulders and distal four limbs, as well as other parkinsonian features (Sato et al., 2000; Koller et al., 2004; Bowler et al., 2006b).

In patients who have had manganese intoxication, the MRI can have diagnostic value provided the scans are done within less than 6 months of cessation of exposure (Lucchini et al., 2000), whereas blood, serum or urine Mn concentrations are not very useful for neurotoxic risk assessment. Nevertheless, increased manganese levels in blood were often found in groups of workers exposed to Mn dust and fumes (Roels et al., 1987, 1992; Wang et al., 1989; Lucchini et al., 1995, 1997, 1999; Sjögren et al., 1996; Deschamps et al., 2001; Chia et al., 1993; Mergler et al., 1994; Yim et al., 1998; Moon et al., 1999). Herrero et al. (2006) described findings of markedly elevated urinary manganese levels after administration of a chelating agent (CaEDTA) to seven patients, one of whom was a welder affected by Mn-induced parkinsonism, but urinary Mn is not frequently used as an exclusive biomarker for Mn exposure because the kidney is not a major excretion route.

Neuropsychological testing procedures developed over the past two decades have been shown to be successful tools to differentiate Mn-exposed welders from controls (Sjögren et al., 1996; Bowler et al., 2003a, 2006a,b). Recently, we conducted a study in a group of 49 welders working on the new San Francisco Bay Bridge using neurological and neuropsychological methods (Bowler et al., 2006c). A neurological risk assessment of this welder group estimated an excess lifetime risk for disabling or fatal health outcome (Park et al., 2006). The present investigation builds on this initial health study and its objectives are (1) to select clinical cases based on neurological and neuropsychological signs and symptoms; (2) to determine if in this group of cases dose–effect relationships exist between neurological, neuropsychological, and neurophysiological functions and Mn concentration in whole blood or the cumulative exposure index (CEI); and (3) to improve knowledge on a neurological/neuropsychological portrait of manganism.

2. Methods

2.1. Participants and exclusion criteria

The San Francisco/Oakland Bay Bridge was damaged during the 1989 earthquake and reconstruction of a vulnerable portion of the bridge began in 2003. During the first 1.5 years of welding on the support piers of the new bridge, a group of welders reported concerns over welding fume exposures. Most bridge welders reported that they wore no personal protective equipment and that ventilation was minimal. This is supported by an audit by a California State auditor who reported that CAL-OSHA was found to have failed to detect or investigate the bridge contractor's possible underreporting of alleged workplace injuries and illnesses and failed to follow up on behalf of the six complaints it received from 2002 through 2005 of injured bridge workers (California State Auditor, 2006). The majority of the welders employed on this project reported health complaints, which resulted in the workers' compensation evaluations. Additionally, we conducted a multi-disciplinary study of their neurological, neurophysiological, sensory and pulmonary function along with detailed work assessments.

A total of 49 welders (men $n = 45$, women $n = 4$) were evaluated for their neuropsychological function in relation to exposure to manganese and other metals in welding fumes. The welders were self-referred for clinical neuropsychological workers' compensation evaluations because they had symptoms of neurotoxicity which they feared may have been associated with welding fume exposures on the bridge. These workers were found, based on employer records, to constitute between 85% and 90% of the welders employed for several months or more on this project (Park et al., 2006). The 10–15% of welders who did not request an evaluation could not be queried as to their health condition due to unavailable contact information. After excluding the four women (too few to analyze as a group) and two male welders [scores on Test of Memory Malingering indicative of low effort (Tombaugh, 1996)], the results of 43 welders remained for further selection of cases.

2.2. Selection of clinical cases

The clinical cases selection criteria for the initial eligible group of 43 is illustrated in Fig. 1. These criteria were based on (1) work history: BB welding 6 months or more and prior welding 3 years or more; (2) at least three of self-reported symptoms which were previously associated with Mn exposure; and (3) results of neurological examination of at least one of the asymmetric features or a score of ≥ 2 on two different Unified Parkinson' Disease Rating Scale (UPDRS) motor areas. The neurological criteria were first developed by Racette et al. (2005) for their evaluations of welders. The final selected group fulfilling all three criteria consisted of 11 clinical cases.

2.3. Evaluation procedures and data collection (I–V)

The data collected in this study are, in part, drawn from workers' compensation evaluations stimulated by workers' health complaints during their work on the Bay Bridge. The participants signed informed consent forms approved by San Francisco State University's Institutional Review Board and agreed to the use of their data from their workers compensation evaluations, which included HIPAA consents, mandated by the Health Insurance Portability and Accountability Act of 1996. The workers compensation evaluations consisted of a comprehensive *neuropsychological examination* (*I*), administered by the author, neuropsychologist colleagues and trained staff. These evaluations included a clinical history and a neuropsychological test battery which were conducted within approximately 3–4 months of the study. In January 2005, the following examinations and tests were administered by a multi-disciplinary team of experts:

- a clinical neurological examination (II) carried out by a board-certified neurologist (WK) who also administered the motor and the activities of daily living scales of the Unified

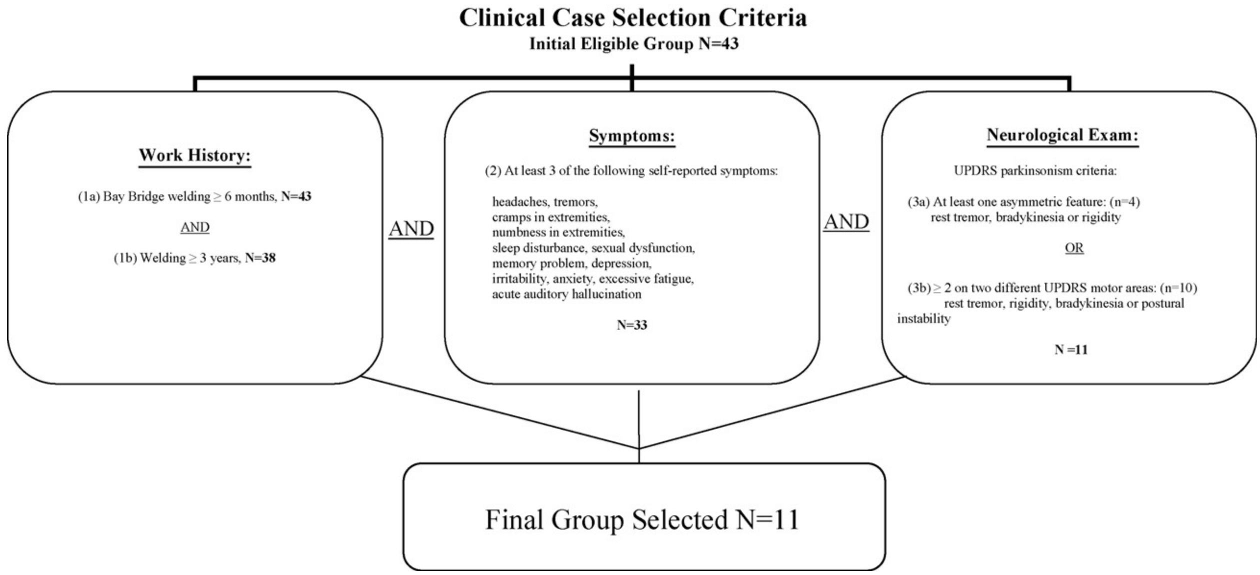

Fig. 1. Paradigm for selection of clinical cases among Bay Bridge welders.

Parkinson' Disease Rating Scale (Fahn and Elton, 1987; Goetz et al., 2003);

- a neurophysiological assessment (III) comprising (a) postural hand tremor and body sway tests (CATSYS-2000, Danish Product Development™, 1996) administered by a doctoral student (MB); (b) the University of Pennsylvania Smell Identification Test (UPSIT), a scratch and sniff smell test, explained by a trained staff; and (c) visual function tests, i.e. the Snellen test to ascertain adequate visual acuity, the Lanthony 15-hue test (Lanthony, 1978) for color vision, and the Vistech Contrast Sensitivity test for contrast sensitivity (Ginsburg, 1987);
- a spirometric test (IV) supervised by a licensed pulmonary technician;
- an assessment of exposure (V) to Mn and other neurotoxicants by eliciting details on work and exposure histories by an expert in industrial toxicology (HAR), by the measurement of Mn and lead (Pb) in blood, and by air samples taken when working on the Bay Bridge in confined spaces.

2.3.1. Neuropsychological examination

2.3.1.1. Neuropsychological test battery. The following tests for their workers compensation evaluation were administered: for neurocognitive function, Wechsler Adult Intelligence Scale (WAIS-III) and Wechsler Memory Scale (WMS-III) (Wechsler, 1997); for executive function and cognitive flexibility, Delis-Kaplan Executive Function System (D-KEFS) (Delis et al., 2001), Rey-Osterrieth complex figure (Lezak, 1995), Stroop Color Word Test (Golden, 1978); for verbal function, Boston Naming and Controlled Oral Word Association Test (COWAT) (Lezak, 1995); for divided attention Auditory Consonant Trigrams (ACT) (Mitrushina et al., 1999); for motor function, Fingertapping, Dynamometer (Lezak, 1995), and Santa Ana Pegboard (Amler et al., 1995); and for neuropsychiatric symptomatology, the Symptom Checklist 90-R (SCL-90-R) by Derogatis (1992). These tests are described in detail elsewhere (Bowler et al., 2003a,b, 2006a).

2.3.1.2. Clinical interpretation. The neuropsychological test performances were scored according to the respective manuals of the test publishers. The neuropsychological raw test results (WAIS-III, WMS-III, D-KEFS, Rey-Osterrieth, Stroop, Boston Naming, COWAT, Fingertapping, Dynamometer, and Santa Ana Pegboard) were scored according to the norms of the test publishers and then transformed into z-scores in order to derive impairment ratings. Scores between the 25th percentile ($z = -0.7$) and 75th percentile ($z = +0.7$) are clinically considered within the normal range, thus any score below $z = -0.7$ is suggestive of clinical impairment. However, prior literature has implicated differences on the neuropsychological test performance among whites and non-whites in the US (Kaufman et al., 1991). Thus, the definition of impairment was established with the relevant correction for non-whites, utilizing the following more conservative impairment ratings: <-1.0 S.D. (for whites) or <-1.25 S.D. (for non-whites) of scores lower than the mean of the reported test norms were categorized as borderline to mild impairment and <-1.5 S.D. or <-1.75 S.D. as moderate to severe, respectively (Anger et al., 1997; Bowler et al., 2001; Manly et al., 1998, 1999). For the SCL-90-R, T-scores based on gender-adjusted adult norms were employed to derive impairment ratings according to the manual (Derogatis, 1992). T-scores of 60–63 were classified as borderline to mild, and T-scores >65 as moderate-severe.

2.3.2. Clinical neurological examination

The neurologist used the UPDRS along with his standard neurological examination to assess symptoms of parkinsonism. The UPDRS examination (Movement Disorder Society Task Force for Rating Scales for Parkinson's Disease, 2003) assesses activities of daily living based on historical information, and motor function based on clinical examination. The motor scale also scored for bradykinesia by summing scores of fingertaps, hand movements, rapid alternating movements of hands, leg agility, arising from a chair, gait, and body bradykinesia/hypokinesia. A postural instability score was computed from the neurologist's ratings by summing scores for postural tremor of hands, posture, and postural stability (retropropulsion test).

2.3.3. Neurophysiological assessment

(a) Postural sway was tested in four experimental conditions and in the following sequence: the subject standing on the platform without foam underneath the feet, (1) eyes open and (2) eyes closed, and with foam underneath the feet, (3) eyes open, and (4) eyes closed. Several parameters are calculated. Mean sway is a simple mean of the distances from the mean force center position to all recorded force center positions during the test. Transversal sway and the sagittal sway is the simple mean of the recorded *x*- and *y*-values of the force center in a coordinate system, respectively. Sway area is the area of the smallest polygon which includes the total trajectory of the force center in the horizontal force plate plane. Sway velocity is defined as the average travel speed of the force center in the horizontal force plate plane calculated by dividing the total length of the force center trajectory (in millimeter) with the recording period length. Sway intensity is defined as the root mean square of accelerations, recorded in the 0.1–10.1 Hz band during the test period. For the sway test results, an unpublished normative database on men of similar age and socio-economic background (blue collar from Quebec, provided by one of the authors, MB) was used since the testing method slightly differed from that used by Deprés et al. (2000). Cutoffs of >-1.0 S.D. and >-1.5 S.D. were used to indicate borderline-mild and moderate-severe impairment, respectively.

(b) For the UPSIT test, clinical olfactory diagnosis was made according to age- and gender-adjusted percentile norms from the manual (Doty, 1995). Diagnosis of mild-microsmia was classified as borderline-mild impairment, whereas moderate microsmia, severe microsmia, and anosmia were categorized as moderate-severe.

(c) For the color vision and contrast sensitivity tests, the impairment ratings were derived according to the test manual (Lanthony, 1978; Ginsburg, 1987).

2.3.4. Spirometric test

Test results were evaluated according to the American Thoracic Society Standards and Guidelines (American Thoracic Society, 1986) and rated by a board-certified pulmonologist (RPB) as mild, moderate, or severe impairment.

2.3.5. Exposure assessment

(a) Blood samples of 4 mL were collected by venipuncture using Vacutainer tubes (BD #367734) and the concentrations of Mn and Pb in whole blood were determined by means of high-resolution ICP-MS.

(b) A cumulative exposure index based on duration and type of welding activity (Fig. 2) was constructed for each welder using employer-commissioned air sampling data collected at various locations on the bridge project for CAL-OSHA compliance purposes. Average levels of Mn and other metals in the air samples at the Bay Bridge construction site from January 2003 to June 2004 were computed within three time periods (January to June 2003, July to December 2003, and January to June 2004) by type of welding: automated welding (FCAW) and manual stick welding (SMAW). For the period July to December 2004, for which no air data were available, levels from the preceding period were used. The individual CEI was calculated using the self-reported percent of time each welder performed FCAW or SMAW during their employment on the bridge. The greater productivity of FCAW results in higher levels of welding fumes compared to SMAW. Welding fume Mn exposure involves, on the one hand, the parent base metal and, on the other hand, rods and filler wires for SMAW and

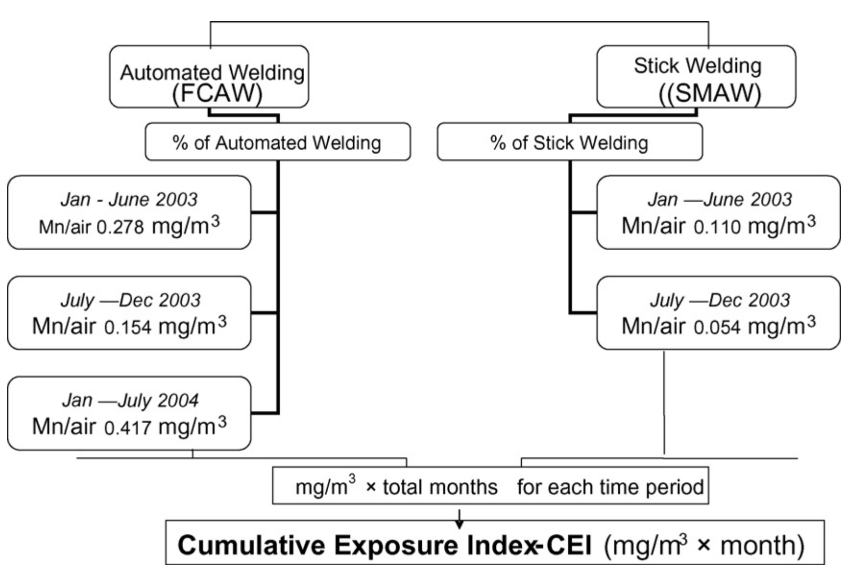

Fig. 2. Construction of the cumulative exposure index (CEI) based on type of welding, air Mn measurements, and months of welding on Bay Bridge.

FCAW, respectively (Harris, 2002). As can be seen in Fig. 2, FCAW generated higher levels of Mn in air than SMAW. This was taken into account based on percent of time used for each welding process. Percent of time was then multiplied by estimated average levels of Mn-air for the two welding types, multiplied by the number of months worked within the three time periods, and then summed.

2.4. Statistics

Descriptive statistics were used for the demographic characteristics and the neuropsychological test results. Multiple regression analyses were performed to examine association between neuropsychological or neurophysiological test scores and the concentration of Mn in blood (MnB) or the CEI. The regression analyses were controlled for ethnicity, years of education, age, and total years of welding prior to the Bay Bride when they were not adjusted previously in the test publisher norms. When applicable, the corresponding demographic variables were entered in the first step of the model. In the second step of the model, variance accounted for (R^2) represents the respective exposure variable, either CEI or MnB.

3. Results

Table 2 shows characteristics of demographics, work history, reported use of respirators, and exposure. Two welders reported smoking in the past and only one (9.1%) is currently smoking. Air manganese and CEI averaged 0.22 mg/m^3 and 2.73 mg/m^3 × month, respectively. Eight (73%) of the selected welder cases had elevations in their MnB levels (>10 μg/L), while all cases showed blood lead levels <5 μg/dL and none was iron deficient. Comparison between the group of 11 selected clinical cases and the group of 32 non-selected welders indicated no difference ($p > 0.05$) on MnB level [mean (S.D.): 9.93 μg/L (2.68) versus 9.50 μg/L (2.48)). The average length of time of confined space welding at the Bay Bridge was 17.6 months for the selected cases, which is also not different from the non-selected group. Appropriate ventilation was not in place during the first 1.5 years of operation and only rarely (3.2%) were respirators worn.

Table 2
Demographics, work history, and exposure for the selected Bay Bridge welders

	N	Mean or %	S.D.	Range
Demographics				
Age	11	43.9	9.4	29–15
Years of education	11	12.1	1.4	11–16
Ethnicity				
Non-white	6	54.5%		
White	5	45.5%		
Work history				
Years of welding prior to Bay Bridge	11	16.8	10.9	1.2–32
Months of welding at Bay Bridge	11	17.6	6.4	8.1–28
Type of welding at Bay Bridge (% of time)				
FCAW	11	69.6	27.9	0–95
SMAW	11	22.3	16.2	5–50
Cartridge respirator at Bay Bridge (% of time)				
Before April 2004	11	3.2	10.6	0–35.3
After April 2004	9	88.3	23.7	37.5–100
Welding at Bay Bridge ≤1 month prior to assessment	6	54.5%		
Exposure				
Mn in blood (μg/L)	11	9.93	2.68	5.85–14.6
Pb in blood (μg/dL)	11	2.45	0.72	1.24–3.89
Mn in air (mg/m^3)	11	0.22	0.08	0.006–0.312
Cumulative exposure index (mg/m^3 × month)	11	2.73	1.29	0.073–4.724

3.1. Prevalence of abnormalities

Table 3 shows the prevalence of impairment as revealed by the neuropsychological/neurophysiological (borderline to mild or moderate to severe) and neurological (UPDRS) exams. They are compared to the prevalence of signs and symptoms "self-reported" during the clinical history interview with the principal neuropsychologist (RMB). All 11 clinical cases were found to have graphomotor-tremor on the neuropsychological exam (parallel lines drawing test), whereas the CATSYS detected only 4 cases with tremor, among them the 2 cases identified by the UPDRS examination. Nine cases had bradykinesia on the UPDRS exam and among them eight (72.7%) had complained of symptoms of bradykinesia at the time of the clinical interview with the neuropsychologist. In the clinical interview, postural stability complaints were reported by six welders who were among the 10 cases detected by the UPDRS exam. Among the 10 welders for whom results for the CATSYS postural sway tests were obtained (1 welder wore cowboy boots which were too tight to remove), 7 showed postural instability among them 2 in the eyes-closed/standing-on-foam condition. Facial masking complaints were reported to the neuropsychologist by all 11 welders, whereas only 4 were diagnosed with facial masking by the neurologist. Seven of the 11 welder cases presenting with movement abnormalities (e.g. tremor) were referred for MRI. Two cases showed abnormality: one had a subtle increase of T1-signal intensity in the globus pallidus and the other showed scattered foci of T_2-prolongation within cerebral white matter bilaterally.

The neurologist's evaluation did not include sensory and autonomous nervous system functions, neither did it ascertain for cognitive and neuropsychiatric symptoms. Sexual and sleep complaints were highly prevalent (respectively, in 8 and 11 welders) at the time of the clinical interview, while the sensory complaints of 9 welders were surprisingly well corroborated by the UPSIT smell identification and vision tests. As to memory/cognitive deficits, all the welders had complaints of non-verbal memory loss, while the neuropsychological examination detected six welders with delayed non-verbal memory scores, four with delayed verbal memory scores and two were found to have impaired working memory. Neuropsychiatric symptom reports were high as well: 10 welders reported depression and

Table 3
Prevalence (%) of impairment in neuropsychological and neurological domains in the group of 11 selected welder cases as revealed by the respective expert evaluation

Neuropsychological/neurological domains	Neuropsychologist' s evaluation				Neurologist's evaluation	
	Clinical interview	Neuropsychological and neurophysiological exam			UPDRS exam	
	Self-reported signs and symptoms	Borderline to mild	Moderate to severe	Total	Motor score ≥ 1	ADL[a] assessment
Movement						
Tremor						
Self-reported	90.9	–	–	–	–	–
Intensity (UPDRS)	–	–	–	–	18.2	100
Intensity (CATSYS)	–	9.1	27.3	36.4	–	–
Parallel lines drawing test	–	72.7	27.3	100	–	–
Bradykinesia	72.7	–	–	–	81.8	–
Rigidity	72.7	–	–	–	0	–
Postural instability						
Self-reported	54.5	–	–	–	–	–
UPDRS	–	–	–	–	90.9	27.3
CATSYS sway test[b]	–	20.0	50.0	70.0	–	–
Facial masking/facial muscle tightening	100	–	–	–	36.4	–
Monotonous voice/soft voice	27.3	–	–	–	45.5	54.5
Slurred speech	63.6	–	–	–	–	–
Micrographia/changes in handwriting	63.6	–	–	–	–	72.7
Gait abnormalities	63.6	–	–	–	27.3	54.5
Muscle problem	90.9	–	–	–	–	–
General parkinsonism symptoms	81.8	–	–	–	–	81.8
Autonomous nervous system						
Sexual dysfunction	72.7	–	–	–	–	–
Sleep disturbance	100	–	–	–	–	–
Sensory decline						
Olfaction (UPSIT smell identification)	81.8	36.4	36.4	72.8	–	–
Vision (color and contrast sensitivity)	81.8	9.1	81.8	90.9	–	–
Memory/cognitive decline						
Delayed non-verbal memory[c]		27.3	27.3	54.6	–	–
Delayed verbal memory[d]	100[e]	10.0	30.0	40.0	–	–
Working memory[f]		0	18.2	18.2	–	–
Neuropsychiatric symptoms[g]						
Depression	90.9	18.2	63.6	81.8	–	–
Anxiety	90.9	9.1	72.7	81.8	–	–
Psychoticism	27.3	9.1	54.5	63.6	–	–

[a] ADL = activities of daily living.
[b] Mean sway and/or sway intensity recorded in four experimental conditions (for details see Section 2); $N = 10$.
[c] Rey-Osterrieth complex figure (delayed).
[d] WMS: auditory delayed index and word list-II recall; $N = 10$.
[e] General memory decline problem.
[f] WAIS: Working Memory Index.
[g] Symptom Checklist-90-R (Derogatis, 1992).

anxiety and 9 were found to score abnormally elevated on the Symptom Checklist-90-R, while only 3 admitted to having psychotic symptoms but 7 endorsed these on neuropsychiatric tests.

Spirometry findings were analyzed with partial regression analyses and smoking as a co-variable, because the group of 11 comprised 2 ex-smokers and 1 current smoker. Smoking appears to have some impact on the spirometric findings.

3.2. Neuropsychological test scores

The 11 selected welder cases were as a group clinically impaired on seven domains of neuropsychological function—they scored below the 25th percentile of their age peers on 16 tests of neuropsychological function (mean z-scores, S.D.s, and ranges are shown in Table 4 by domain; bolded mean z-scores indicate clinically impaired tests). As can be noted,

Table 4
Mean z-scores[a] of impaired neuropsychological test scores by domains

	N	Mean	S.D.	Range
Verbal function				
Verbal IQ	10	−0.75	0.81	−2.27–0.40
Verbal comprehension index	10	−0.75	0.98	−2.20–0.60
Vocabulary	10	−0.73	0.99	−2.00–0.67
Auditory perception				
Comprehension	11	−0.73	0.66	−2.33–0.00
Memory				
Logical memory I	10	**−1.30**	0.95	−2.33–0.00
Logical memory II	9	−0.96	1.02	−2.33–0.67
Verbal paired associates I	10	−0.83	0.45	−1.67–0.00
Verbal paired associates II	10	−0.80	0.74	−2.00–0.00
Auditory recognition	9	−0.74	0.72	−1.67–0.67
Auditory immediate memory index	10	**−1.22**	0.68	−2.33–−0.20
Auditory delayed memory index	9	−0.94	0.76	−2.40–0.33
Verbal learning				
Word list I first recall	10	−0.87	1.00	−2.33–1.33
Word list I total recall	10	−1.17	0.91	−2.67–0.67
Word list II recognition	10	−0.97	1.14	−3.00–0.67
Motor function				
Finger tapping dominant score	11	−0.70	1.22	−2.90–2.30
Dynamometer dominant hand	11	**−1.56**	0.79	−3.20–−0.40
Dynamometer non dominant hand	11	**−1.10**	0.74	−2.00–0.60
Santa Ana dominant hand	11	**−3.26**	0.80	−4.60–−2.18
Santa Ana non dominant hand	11	**−2.77**	0.69	−4.08–−1.68
Cognitive flexibility				
Stroop Color Test	11	**−1.14**	1.17	−3.00–0.70
Stroop Color Word Test	11	**−1.03**	1.41	−3.00–1.60
Digit symbol	11	−0.91	0.86	−2.33–0.33
Similarities	10	−0.83	1.11	−2.67–0.67
Processing speed				
Performance IQ	11	−0.75	0.75	−2.00–0.60
Processing speed index	11	−0.92	0.75	−2.47–0.20
Symbol search	11	−0.79	0.76	−2.67–0.00
Cancelation H test, seconds	11	**−1.15**	2.13	−5.55–0.65
Trail A test	11	**−1.30**	1.48	−3.30–1.80
Divided attention				
Auditory Consonant Trigrams 3 s	11	**−1.49**	1.54	−3.74–1.21
Auditory Consonant Trigrams 9 s	11	**−1.23**	1.26	−3.64–0.80
Auditory Consonant Trigrams 18 s	11	**−1.31**	0.90	−3.00–−0.16
Visuo-spatial memory				
Rey-Osterrieth immediate recall	11	**−1.66**	2.03	−7.00–0.50
Rey-Osterrieth delayed recall	11	**−1.50**	2.11	−7.00–1.10

[a] Mean bolded z-score ≤ -1 represents impairment.

the welder group was found to be impaired in the domains of: memory (two tests); verbal learning (one test); motor function (four tests); cognitive flexibility (two tests); processing speed (two tests); divided attention (three tests); visuo-spatial memory (two tests). There was no clinical impairment and no difference on long-term verbal functions involving reading skills, naming and word knowledge, suggesting these functions are 'hold' functions, resistant to deterioration from Mn exposure. This has also been reported in a group of workers overexposed to ethylene dichloride (Bowler et al., 2003b).

Table 5a
Multiple regression using blood Mn as predictor with controlling for ethnicity and total welding years prior to Bay Bridge

Domains	N	β	ΔR^2	p
Cognitive flexibility				
Stroop Color T-score (age adjusted)	11	−0.494	0.187	**0.025**
Stroop Color Word T-score (age adjusted)	11	−0.657	0.330	0.053
Visuo-spatial				
D-KEFS Design Fluency-Switching (age SS)	11	−0.591	0.267	0.066
D-KEFS Design Fluency-Total Correct (age SS)	11	−0.907	0.629	**0.008**
D-KEFS Design Fluency-Attempted Design (age SS)	10	−0.986	0.644	**0.007**

$p < 0.05$ are bolded.

3.3. Dose–effect relationships

The results of the dose–effect relationship study are summarized in Tables 5a–5c, and significant results have their p-value bolded. Tests that showed a trend for statistical

Table 5b
Multiple regressions using Mn cumulative exposure index as a predictor with controlling for ethnicity, years of education, total welding years prior to Bay Bridge, and/or age

Domains and Tests	N	β	ΔR^2	p
Attention, concentration and working memory				
WAIS digit span forward (raw)	11	−0.716	0.168	**0.047**
WAIS digit span backward (raw)	11	−1.243	0.505	**0.003**
Digit span (age SS)	11	−0.934	0.289	**0.005**
Working Memory Index score (WAIS)	10	−1.089	0.374	**0.015**
Working Memory Index score (WMS)	10	−0.753	0.179	0.052
Auditory recognition (age SS)	10	−1.103	0.383	0.079
Auditory Consonant Trigrams 3″ delay	11	−1.192	0.464	**0.013**
Auditory Consonant Trigrams 18″ delay	11	−1.150	0.432	**0.034**
Auditory Consonant Trigrams total score	11	−1.164	0.443	**0.049**
Arithmetic (age SS)	11	−1.029	0.351	0.058
Verbal learning and auditory perception				
WMS III word list1 1st recall total (age SS)	10	−0.602	0.114	0.078
WMS III word list1 contrast 1 (age SS)	10	1.283	0.519	**0.047**
Comprehension (age SS)	11	−1.142	0.432	**0.024**
Cognitive flexibility				
D-KEFS Sorting Correct sorts (age SS)	10	−1.172	0.433	0.098
Vision				
Single place errors left eye (color vision)	11	0.779	0.198	0.097

$p < 0.05$ are bolded.

Table 5c
Results of multiple regression ($N = 10$) on CATSYS postural sway by blood Mn controlling age in the first step

	Sway 1			Sway 2			Sway 3			Sway 4		
	β	ΔR^2	p	β	ΔR^2	p	β	ΔR^2	p	β	ΔR^2	p
Mean sway	0.34	0.11	–	0.76	0.56	**0.05**	0.71	0.49	**0.05**	0.72	0.50	**0.05**
Transversal sway	0.70	0.48	**0.05**	0.84	0.69	**0.01**	0.73	0.52	**0.05**	0.70	0.48	**0.05**
Sagittal sway	−0.07	0.00	–	0.61	0.37	–	0.61	0.37	–	0.68	0.46	**0.05**
Sway area	0.59	0.34	–	0.81	0.65	**0.01**	0.72	0.50	**0.05**	0.74	0.53	**0.05**
Sway velocity	0.72	0.50	**0.05**	0.94	0.86	**0.00**	0.86	0.72	**0.01**	0.84	0.69	**0.01**
Sway intensity	0.64	0.40	**0.05**	0.76	0.56	**0.01**	0.76	0.56	**0.05**	0.84	0.70	**0.01**

Sway 1: eyes open, Sway 2: eyes closed, Sway 3: eyes open and on the platform, Sway 4: eyes closed and on the platform.
$p < 0.05$ are bolded as significant values.

significance ($p < 0.10$) are also shown as 11 cases are considered to be a small a sample to derive null hypothesis testing. Analyses were adjusted for age, education, ethnicity, and total years welded prior to working on the Bay Bridge, unless the normative data used for the tests had already adjustments for age or education. In multiple regression analyses, the inverse dose–effect relationships between MnB and test results were significant ($p < 0.05$) for Stroop Color (cognitive flexibility) and D-KEFS Design Fluency-Total correct and Attempted designs (visuo-spatial function), and there were relevant trends ($0.05 \leq p \leq 0.10$) for Stroop Color Word and D-KEFS Design Fluency-Switching (Table 5a). Multiple regression between the CEI and test results (Table 5b) showed after co-variate adjustment seven significant and three relevant inverse relationships in the domain of attention, concentration and working memory, i.e. WAIS Digit Span forward, backward and total; Working Memory Index for WAIS and WMS; and the three conditions of the Auditory Consonant Trigram test, and Arithmetic. In the domain of Verbal Learning and Auditory Perception, significant or relevant associations were noted for Word List-1, first recall and contrast and comprehension; and in the domains of Cognitive Flexibility and Vision, D-KEFS Sorting Correct and color vision single place errors on the left eye showed relevant trends with CEI. Table 5c indicates the results of multiple regressions between MnB and the CATSYS postural sway conditions adjusted for ethnicity. Significant associations were noted for transversal sway, sway velocity and sway intensity in all four conditions, while mean sway and sway area showed dose–effect with MnB for the sway conditions 2, 3, and 4 only.

Partial regression plots (Fig. 3) illustrate the importance of the inverse slopes for the regression lines of the residuals for the age-adjusted Working Memory Index and Auditory Consonant Trigrams Total Score as a function of CEI, and Stroop Color Word, and D-KEFS Design Fluency-Total correct (adjusted for ethnicity, education, total years of prior welding) with MnB. Slopes of the partial regressions support the dose–effect relationships (Table 5) indicating that increased MnB and higher CEI result in lower performance.

These results indicate that increases in MnB and exposure to Mn in air during the welding on the bridge as estimated by the CEI are associated with diminished attention, concentration and working memory, lower verbal learning ability and auditory perception, reduced cognitive flexibility, and subtle vision impairment.

4. Discussion

This report deals with 11 clinical welder cases selected out of a group of 43 welders with documented exposure to manganese from confined space welding on the San Francisco/Oakland Bay Bridge. The main neurological feature for their selection was the presence of signs and symptoms as revealed by the neurologist with the UDPRS-examination, a validated tool for detection/evaluation of parkinsonism. The specific symptoms picked up by the UPDRS-exam were: tremor ($n = 11$), bradykinesia ($n = 9$), postural instability ($n = 10$), micrographia/changes in handwriting ($n = 8$), and other characteristic abnormalities involving face, voice, and gait ($n = 4$–6) (Table 3). As shown in Table 1, extrapyramidal impairment (tremor and motor) has been frequently reported over the last 50 years in different occupational settings with exposure to manganese, among them also welding. Since the 1980s, however, neuropsychological testing has undeniably enhanced the clinical neurological examination of Mn-exposed subjects in that it consistently (see Table 1) contributed to a more complete portrait definition of manganese neurotoxicity including in addition to movement/coordination other CNS functions as well. The neuropsychological signs and symptoms (Tables 3 and 4) detected in the 11 clinical welder cases are thus not epi-phenomena but an intricate part of the neurotoxic portrait of manganese. They included tremor, divided attention, loss in speeded visual scanning, tracking sequencing and visuo-spatial memory. The welders' scores on hold-tests (verbal naming and reading skills), resistant to deterioration, were comparable to the publishers' reference values. Psychomotor speed, with the exception of gross motor grip strength and tactile manipulative ability, also was unimpaired in comparison to norms of the general population. This latter finding may be due to a 'healthy worker effect': indeed, the welders studied here, more likely than not, had the ability to perform manually at a higher than average speed prior to their Mn exposure and were selected for those qualities in pre-employment screening. They did not show the same severity in neuropsychological impairment as some of the older welders who have previously been described in the literature. Moreover, their motor functions are not yet as slow as in reports of other Mn-exposed welder groups (Chandra et al., 1974; Wang et al., 1989; Sjögren et al., 1996; Racette et al., 2001; Bowler et al., 2003a, 2006a). Although the 11 cases welded on average about 17 years prior

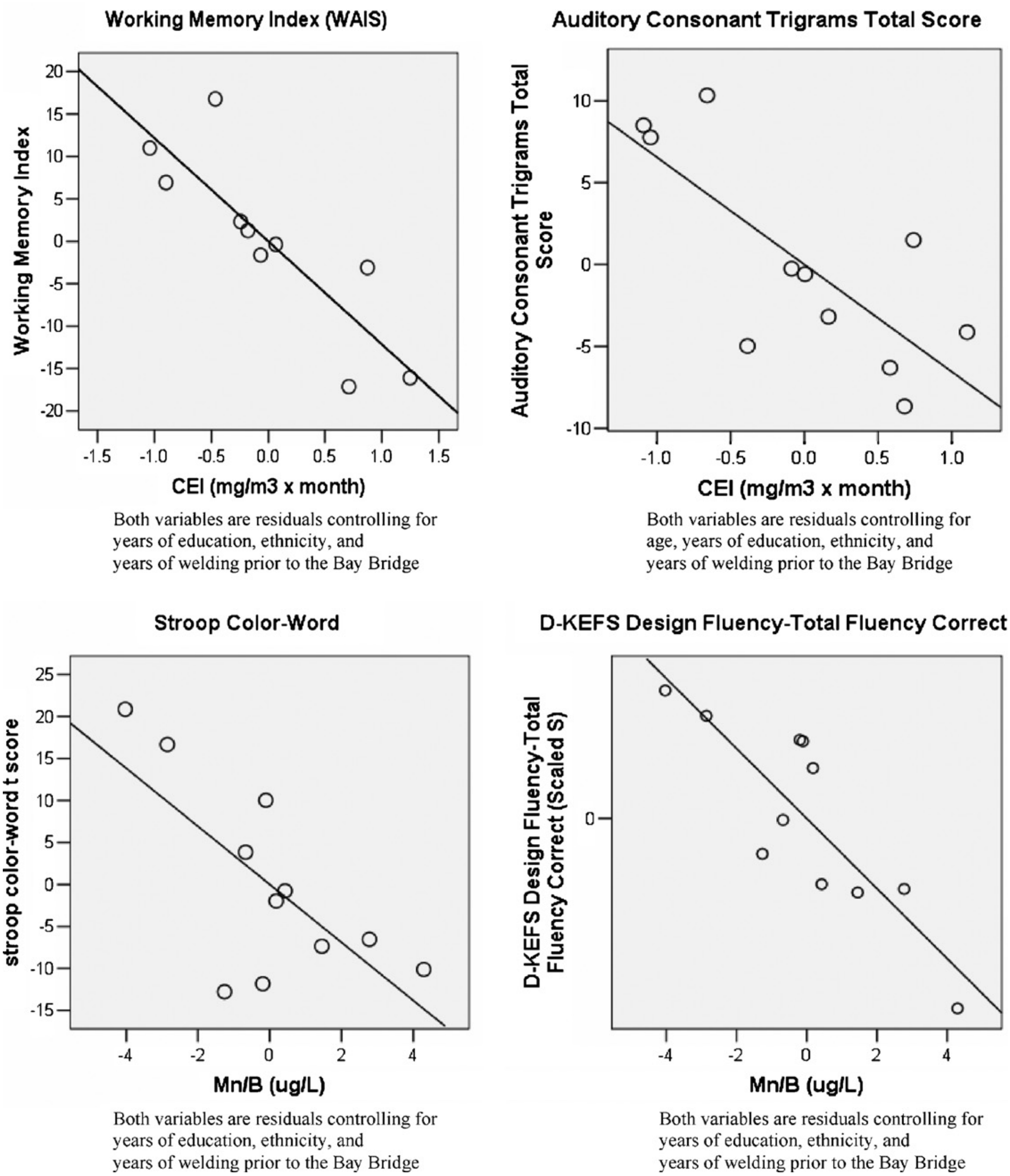

Fig. 3. Partial regression plots between CEI or MnB and neuropsychological test results adjusted for years of education, ethnicity (non-white or white), years of welding prior to the Bay Bridge, and/or age.

to the bridge, they reported to have had no unprotected, poorly ventilated confined space welding prior to their work on the bridge. However, the domains of neurocognitive and neurological impairment reported in these welder studies is consistent with those in the present 11 welder cases, although few studies utilized test batteries as comprehensive as used here. In addition to the outcome of the UPDRS-exam, neuropsychological testing also showed that the majority of the selected welders presented with neuropsychiatric symptoms ($n = 7$–9) and sensory decline, i.e. 8 with loss in olfaction (UPSIT smell identification) and 10 with loss in either color vision or contrast sensitivity (Table 3). This is not surprising as signs of sensory and neuropsychiatric impairment were found associated with inhalation exposure to manganese (Mergler et al., 1994; El-Zein et al., 2003; Bowler et al., 2003a).

Comparison between neurological, neuropsychological and neurophysiological examinations shown in Table 3 indicates that the bridge welders' self-reports to the neuropsychologist and during the neurologist examination identified the same general parkinsonism signs and symptoms in 9 out of 11 welders, while other signs and symptoms were self-reported more often by the welders to the neurologist than the neuropsychologist such as monotonous soft voice (5 versus 3) and facial masking (11 versus 4). Bradykinesia, however, was observed in nine by the neurologist while eight reported it to the neuropsychologist. Neuropsychological dysfunction was found in standardized neuropsychological testing as shown in Table 4. All 11 welders had valid test scores based on tests of effort. This implies that neuropsychological scores may be a strong predictor of neurological clinical caseness of manganism. The findings corroborate the previous description of neurological signs and symptoms (Feldman, 1999; Racette et al., 2001; Koller et al., 2004). Both neurological and neuropsychological methods are complementary in the diagnosis of manganism with neuropsychological testing contributing a more quantitative, standardized measurement.

Affect and mood testing indicated that the levels of clinical depression and anxiety for the 11 selected cases were more than two S.D.s above the mean indicating high levels of mood disturbance. The clinical cases had symptoms of dysphoric mood and affect, signs of withdrawal of life interests, lack of motivation and loss of vital energy in addition to having clinical signs such as nervousness, tension and trembling with possible panic attacks and feelings of terror. Psychoticism scores were also moderately elevated which support the welders' statements of having hallucinations while exposed to welding fumes in the confined spaces on the bridge. These findings also replicate those of other studies of Mn and mood effects as classified in the review of neuropsychiatric effects of Mn by Bowler et al. (1999).

Apriori efforts at case definition for occupational manganism were made by an international expert committee of the Quebec-Canada IRSST (the equivalent of the US Department of Occupational Health and Safety) (Ostiguy et al., 2005). The case definition did, however, not include specific neurological characteristics, e.g. scores on the UPDRS, which would facilitate replicating this approach proposed by this expert committee. The Canadian IRSST report does not describe neurological or neuropsychological test norms in the criteria for manganism, although the categories of the necessary criteria are similar to the present case definition, with the exception of requiring an L-dopa trial (with negative results), and MRIs (with positive results if imaging is done within 6 months of active welding). This present report indicates that even though a Mn-exposed welder may have a wide variety of clinical symptoms, elevated MnB levels, and have worked in areas with significantly elevated Mn in air, abnormalities on MRI may not necessarily be present in manganism. This points to a weakness in the Canadian criteria and should be taken into account when diagnosing workers exposed to Mn.

The mean MnB levels for the bridge welders was 9.93 μg/L and is in line with the whole blood mean Mn concentrations found in eight studies dealing with groups of Mn-exposed workers from different industrial settings where health effects were reported, i.e. 8.1–11.3 μg/L (Roels et al., 1987, 1992; Sjögren et al., 1996; Lucchini et al., 1995, 1997, 1999; Deschamps et al., 2001; Mergler et al., 1994; Moon et al., 1999). The extremely low mean MnB value of 2.9 μg/L (Li et al., 2004) and the rather high mean values, i.e. 23 μg/L (Yim et al., 1998), 25.3 μg/L (Chia et al., 1993); and 25.2 μg/L and 31.3–146 μg/L (Wang et al., 1989); are difficult to grasp in case the homeostatic mechanisms for manganese were intact. It is a very important finding that this group of 11 clinical welders cases had MnB concentrations from 5.85 μg/L to 14.6 μg/L with a concomitant dose-dependent deterioration of neuropsychological functions (see multiple regression results) which is paralleled by significant inverse associations between neuropsychological performances and the cumulative dose of air-Mn (CEI) over a relatively short exposure period (8.1–28 months).

Prior welding years was controlled in the multiple regression analyses in the group of 11 clinical cases as theoretically prior welding might have been a potential confounder.

The variable years of welding prior to the bridge was not significantly associated with MnB in the larger group of 43 ($r = 0.198$, $p = 0.24$) but months of welding on the bridge was significantly associated with elevated MnB ($r = 0.326$, $p < 0.05$), indicating that elevated MnB is associated with exposure on the bridge and reduced performance. The selected 11 cases show a clear and likely reproducible portrait of health effects indicative of manganism which is supported by strong dose–effect relationships with blood Mn and the CEI. Although the larger group of Bay Bridge welders, also showed significant dose–effect relationships with Mn in blood or CEI, the variances accounted by MnB or CEI in the 11 clinical cases were significantly higher, i.e. for MnB (14–68% versus 7–22%, 11 clinical cases versus larger group) and for CEI (11–52% versus 7–20%). This suggests that the criteria used for selecting the most affected welders from the larger group were successful in identifying welders with a consistent portrait of manganism. This expanded description of manganism includes the classical extrapyramidal signs and symptoms of parkinsonism (tremor, masked facies, bradykinesia) and the neuropsychological findings described here and in the studies of welders and others with occupational Mn exposures (see Table 1). It is important to note that the remaining 32 non-selected welders also experienced significant health effects and may have probable manganism. It should be pointed out, that the literature on Mn-exposed workers indicates primarily tremor, motor, and neurocognitive effects (Table 1), however, neurologists may not often include neurophysiological tests in test batteries for Mn-exposed subjects nor are sufficiently standardized tests of memory and mood. These tests are recommended for future studies of Mn effects as they provide more complete characterization of the range of effects.

In conclusion, the Mn effects in the Bay Bridge welders, who had not previously welded in confined spaces, demonstrated neurological, neurophysiological and neuropsychological signs, symptoms and clinical impairment. It is hoped that at least some of these adverse health effects will be reversible. A treatment protocol for memory enhancement with volunteers from the group of confined space welders is currently underway. It would also be highly informative to initiate a prospective investigation in these welders to determine reversibility of effects (all but one welder no longer works on the bridge). It is clear that personal and workplace protections as well as appropriate surveillance are needed to protect welders working in confined spaces. CAL-OSHA cited numerous violations on the bridge during the 2003 and 2004 work period. If appropriate ventilation had been in place at the beginning of the new Bay Bridge construction, the results we report here might have been prevented or minimized. Inhalation of respirable Mn particles may via the lung alveoli lead to a rather quick systemic absorption of manganese that bypasses the hepatic homeostasis and crosses the blood/brain barrier making Mn exposure from welding fumes a greater neurotoxic risk than Mn exposure from other types of occupational Mn exposure such as in mining, dry cell battery production and chemical manufacturing.

Further epidemiologic studies of neurological and neuropsychological functions of welders are needed to confirm the emerging portrait of adverse effects of welding without adequate protection and ventilation. Plans are underway to identify a larger welder population to help replicate these neurological and neuropsychological findings, and confirm this portrait of the health effects of Mn exposure.

Disclaimer of Conflict of Interest

The first author (RMB) was paid by the participants' employer to conduct neuropsychological evaluations of the employees as part of State and Federal Workers' Compensation administrative law proceedings. The welders workers compensation attorneys made a contribution for the medical assistants and their incidental supplies during the 2 days of the study in January 2005. These welder's participants, in turn, agreed to participate for free in the study. None of the authors has been retained by any of the participant-welders nor their attorneys to serve as expert witness or consultant. They have not received compensation from any of the participants, and have volunteered their time on this study in the interest of science.

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