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Alteration of saliva and serum concentrations of manganese, copper, zinc, cadmium and lead among career welders

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Abstract

Human saliva offers a unique noninvasive approach for populational study. Purposes of this study were to investigate the feasibility of using saliva manganese (Mn) concentration as a biomarker of Mn exposure among career welders and to study the variations of Mn, copper (Cu), zinc (Zn), cadmium (Cd), and lead (Pb) in saliva as affected by the welding profession. Forty-nine male welders, of whom 28 were in the low exposed group and 21 in the high exposed group, were recruited. Control subjects were 33 military soldiers without metal exposure. Ambient Mn levels in breathing zones were 0.01, 0.24 and 2.21 mg/m³ for control, low, and high exposed groups, respectively. Saliva samples were collected to quantify metals by inductive coupled plasma mass spectrometer (ICP-MS). Saliva concentrations of Mn and Cu were significantly higher in welders than in controls ($p < 0.01$); the variation in saliva levels appeared likely to be associated with airborne Mn levels among study populations. Saliva levels of Zn were significantly lower in welders than in controls ($p < 0.05$), while Cd and Pb levels in saliva were unchanged. Significant associations were observed between saliva and serum for Mn ($r = 0.575$, $p < 0.05$) and Cu ($r = 0.50$, $p < 0.05$). Moreover, saliva Mn concentrations were higher among welders with 5–10 years of employment than those with less than 5 years of employment. Linear regression analysis revealed a significant correlation between saliva Mn and Cu and between saliva Mn and Zn. Taken together, these data suggest that Mn concentrations in saliva appear reflective of welders' exposure to airborne Mn and their years of welding experience, respectively. Elevated Mn levels among welders may alter the homeostasis of Cu and Zn.

Keywords

Saliva; Welders; Manganese; Copper; Zinc; Cadmium

1. Introduction

The relationship between manganese (Mn) exposure and Parkinsonism has long been established (Mena et al., 1967; Barbeau et al., 1976; Tanner, 1989; Wang et al., 1989). In severe cases, the patients exhibit extrapyramidal disorders, such as imbalance in walking or on arising and tremor (Inoue and Makita, 1996; Jiang et al., 2006). Noticeably, the symptoms of Mn intoxication, once established, usually become progressive and irreversible, reflecting to some extent the permanent damage of neurologic structures. Thus,

the early diagnosis is crucial for prevention of Mn intoxication in occupational and environmental settings.

Previous studies from this laboratory has determined trace metal concentrations, such as Mn, iron (Fe), zinc (Zn), copper (Cu) and lead (Pb), in serum or the whole blood samples of welders (Li et al., 2004). Serum levels of Mn and Fe are significantly higher among welders than control subjects; however, the increase in serum levels of Mn is not associated with welder's employment age. A later study from this group further suggests that serum concentrations of ferritin and transferrin among welders are increased in comparison to controls (Lu et al., 2005). A more recent study from this group has attempted to compare Mn levels in red blood cells (MnRBC) to Mn levels in plasma (MnP) or the whole blood (MnB) among Mn-exposed smelting workers (Jiang et al., 2007). The MnRBC of both exposed workers and controls are significantly higher than the values of MnB or MnP. Interestingly, the pallidal index values (PI) of magnetic resonance imaging (MRI) signals among Mn-exposed workers are significantly associated with MnRBC. While these studies provide the useful information on Mn exposure-related changes of biological parameters, the levels of Mn in saliva as well as the factors that may affect saliva Mn concentrations have never been explored.

Human saliva is produced by salivary glands including parotid, submandibular, and sublingual glands. The daily secretion of saliva ranges between 800mL and 1500 mL, which contains mainly water (98%), electrolytes, mucus, antibacterial constituents, and various enzymes (Guyton and Hall, 1996; Reznick et al., 2006). In general, the composition of saliva reflects those of typical extracellular fluids; yet the active transport and secretion mechanisms in salivary production processes render the saliva distinctive in its ionic composition. For example, saliva contains much higher quantities of potassium and bicarbonate ions and much less sodium and chloride ions than plasma. Thus, saliva does not simply a replica of serum, but rather it has its own chemical and biochemical properties allowing it for potential uses in clinical diagnosis.

Because of the ready access and noninvasive sampling nature, the saliva serves as an ideal biological matrix alternative to blood samples for large-scale risk assessment in general population. However, the quantitative analysis of metal concentrations in saliva, including Mn, among Mn-exposed welders has not been performed.

This study was designed to test the hypothesis that the concentrations of metal ions in saliva may change as the function of Mn exposure among welders. Specifically, this study was aimed at determining (1) the study sites where Mn exposure could be analyzed in a dose-related fashion, (2) changes in saliva metal concentrations, i.e., Mn, copper (Cu), zinc (Zn), cadmium (Cd), and lead (Pb), in Mn-exposed welders in comparison to nonexposed control subjects, (3) the correlation between the prevalence of the altered saliva metal concentrations and the external Mn exposure indices, and (4) the variations of saliva metal concentrations as the function of metals in serum.

2. Subjects and methods

2.1. Factory and production processes

Two factories were chosen for this study for their intensive, day-to-day indoor welding application. Factory A is located in the northeast of Beijing metropolitan region and manufactures the steel frames for building constructions. The welding workshop has the area 120m × 60 m, with the height of 12 m. There are windows and fans located near the roof. Factory B is located in Taian, Shandong Province, and mainly constructs oil transportation cylinder tanks. The tank has the diameter of 3 m with the length of 5.5 m. There are two

openings on the top of the tank with the diameter of 1 m. The openings were open when the welding was in progress. During the production process, the welders in Factory B work both inside and outside of the cylinder tanks, while welders in Factory A primarily work indoor in the workshop but not inside of a confined space. The electric arc weld has been a primary technique in the welding practice in both factories. The J506, J4303 and J502 are the major welding rods employed and the daily consumption is 5–10 kg/person/day. Both factories are not adjacent to any other metal industries.

2.2. Study population

A total of forty-nine welders (28 from Factory A and 21 from Factory B) who have been regularly engaged in the daily weld with a potentially high level of exposure were selected for this study. They were all males with an average age of 30.6 years. The welders worked 7–8 h per day with the average employment history of 8.1 years (range: 5 months–35 years). The control subjects consisted of 33 soldiers, who were recruited from a military unit stationed nearby Factory A; they had no history of occupational exposure to Mn and other metals. They were all males with an average age of 29.1 years. The demographic data of study populations are summarized in Table 1.

Study subjects in both welder and control groups at the time of interview had no reported exposure to other toxic substances, radiation therapy, or substance abuse. There were no statistically significant differences in smoking and alcohol consumption between welders and controls (Table 1).

2.3. Collection of personal data and biological samples

The standardized interviews and sample collection took place in clinic offices within the factories and military unit. The written informed consent forms were obtained from all subjects prior to interview. A scheduled interview with a questionnaire lasting approximately 60 min was conducted by trained interviewers to obtain detailed information on occupational history, job description, socioeconomic status, lifestyle, and family and personal medical history.

The participants were asked to fast overnight prior to the study. Blood samples were collected in the morning of the day of examination, followed by neurological examination on the same day. Five milliliters of venous blood was drawn from a cubical vein, let stand at room temperature for 15 min, and centrifuged at 12,000 rpm for 10 min to separate serum. The subjects were then asked to gargle with deionized, ultrapure water for three times, followed by chewing the cottonend of saliva collector (Malvern Medical Developments Ltd., Worcester, U.K.) for 5 min. The saliva collection devices were centrifuged at 3000 rpm for 10 min to remove the foam and precipitates. The supernatant (about 3 mL of saliva) was then separated and stored in another sets of clean tubes. All samples were stored at –20°C until analyses. All test tubes used in the study were free of metal contamination, as pre-tested by atomic absorption spectrophotometry (AAS).

2.4. Air sample collection and analysis

Three different locations in the workshop of either factory were identified as the monitor sites according to the positions where welders usually worked. In Factory B, air samplers were also placed inside of the oil cylinder tank. Air samples were collected by a Model BFC-35 pump equipped with a filter that has a diameter of 40 mm with particulate matter below a cut size of 0.8 µm. Air flow was pumped at a flow rate of 5 L/min for 4 min at one hour after the welding started. At each monitoring site, the samples were collected in duplicates every other hour for two more times on the same day (total 4 h). The mean values of all three duplicated samples were presented in this report.

The filters were digested with 5 mL of HClO₄–HNO₃ mixture (1:9 vol/vol) at 200°C. The dry residues were dissolved in 10 mL of 1% HCl. The solutions were diluted by 20–50-fold prior to AAS. Air Mn concentrations were measured by a model HITACHI Z-5000 flame AAS according to a China National Standard Operation Protocol (GB/T16018-1995) for occupational safety surveillance.

2.5. Determination of Mn, Cu, Zn, Cd and Pb in serum and saliva by ICP-MS

Concentrations of all metal ions in serum and saliva were determined by an inductive coupled plasma mass spectrometry (ICP-MS, Thermo Elemental, USA) according to the method described by Hardcastle et al. (2002) and Muniz et al. (2001). Aliquots (1 mL) of serum or saliva samples were diluted with 9 mL of 1% nitric acid (v/v, >18 Ω cm²) immediately before the assay. The samples were then quantified by ICP-MS using freshly made metal standards on the day of analysis. The detection limit of the current method was 0.07, 0.18, 0.64, 0.05 and 0.14 ng/mL of assay solution for Mn, Cu, Zn, Cd, and Pb, respectively. The batch-to-batch precision for serum samples was 2.04%, 1.95%, 1.50%, 1.34% and 2.46% for Mn, Cu, Zn, Cd and Pb, respectively, and for saliva samples was 2.86%, 2.90%, 3.34%, 1.60% and 3.06% for Mn, Cu, Zn, Cd, and Pb, respectively. The recoveries of this method, as determined by adding known metal quantities to the serum or saliva samples, were between 94 and 110%.

2.6. Statistical analyses

Records of interviews and other reports were reviewed and abstracted for demographic data. All data are expressed as the mean ± S.D. unless otherwise stated. Associations between serum and saliva concentrations of Mn and Cu as the function of welder professional years were analyzed by a linear regression. The differences between two means were analyzed by one-way analysis of variance (ANOVA).

2.7. Materials

AAS and ICP-MS standards of Mn, Cu, Zn, Cd and Pb were purchased from Alfa Products, Danvers, MA.

3. Results

3.1. Airborne Mn levels

Airborne Mn level in the control group (0.01 mg/m³) was less than the maximum allowable concentration (MAC) of Mn (0.2 mg/m³) according to the national standard set out by the Chinese Ministry of Public Health (TJ36-79). The mean value of airborne Mn in welders' breath zone in Factory A was 0.24 mg/m³, which is slightly higher than the MAC value. When the air samples inside of the oil tank in Factory B were monitored during the welding practice, the Mn level (2.2 mg/m³) was nearly 10-fold greater than the MAC (Table 1). Airborne Mn concentrations outside the oil tank during the welding (0.1 mg/m³) were below the MAC values. Noticeably, the welders in Factory B usually work alternately in and out of the oil tanks.

3.2. Concentrations of metals in saliva and serum

Saliva concentrations of Mn, Cu, Zn, Cd and Pb in welders and controls were summarized in Table 2. In comparison to control subjects, the data that combined welders from two factories showed statistically significant increases in saliva concentrations of Mn (46%, $p < 0.01$) and Cu (45%, $p < 0.01$). The changes of saliva Mn concentration appeared to be exposure-dose-related (Fig. 1). Saliva concentrations of Zn were significantly lower than

that of control group (-27% , $p < 0.05$). Although, the concentrations of Pb and Cd in saliva were lower than that of controls, the differences did not reach the statistical significance.

Serum concentrations of five metals in welders and controls are summarized in Table 3. Analyses by combining welders of two factories revealed that there were 72% increase in serum concentration of Mn ($p < 0.01$), 18% increase in Cu ($p < 0.01$), and 11% decrease in Zn ($p < 0.01$) among Mn-exposed welders in comparison to those in controls. Similar to saliva Mn, the changes of serum Mn concentration appeared also to be exposure-dose-related (Fig. 1). The variations in Pb and Cd concentrations in serum between low and high exposed groups were too large to yield any conclusive judgment.

Compared to the average concentration of saliva Mn in control subjects, about 71% and 81% welders from the Factory A and B, respectively, had saliva Mn level higher than that of controls (Fig. 2). With regard to serum Mn concentration, 86% welders from Factory A and all of the welders (100%) in Factory B had serum Mn levels higher than that of control subjects (Fig. 2).

3.3. Years of employment and concentrations of metals in saliva

A linear regression analysis was used to explore whether saliva concentrations of Mn changed as the function of welder's length of exposure. When the data were analyzed individually within each welder group, no significant correlation between saliva Mn and years of employment was found; neither was there a correlation when the data from two groups were merged for combined analysis. The years of welder's employment from two factories were further stratified into <5 year, between 5 years and 10 years, and >10 years. Saliva and serum Mn concentrations were significantly higher in the group with 5–10 years of employment than those in the group with <5 years of employment ($p < 0.05$) (Table 4). There was no statistically significant difference between the groups of <5 years of employment and >10 years of employment or between groups of 5–10 years of employment and >10 years of employment.

3.4. Correlations between levels of Mn and other metals in saliva or serum

When saliva concentrations of Mn, Cu, Zn, Cd and Pb were plotted against serum concentrations of the same metal, significant correlations were observed for Mn ($r = 0.545$, $p < 0.05$) and Cu ($r = 0.504$, $p < 0.05$), but not for Zn, Cd and Pb (Fig. 3).

Changes of metal concentrations (Cu, Zn, Cd and Pb) in saliva and serum were further analyzed as the function of Mn in the same biological fluid (Table 5). There were significant positive associations between Mn and Cu in saliva as well as in serum. Zn concentrations in saliva or serum, however, were inversely associated with those of Mn in the same body fluids. There were no significant correlations between Mn and Cd, or between Mn and Pb in either saliva or serum (Table 5).

4. Discussion

Mn is an important ingredient in welding rod and steels. Cutting and welding metal pieces in modern industry increase chances for welders to be exposed to Mn emitted in welding fumes. The average airborne concentrations of Mn in two studied plants were 0.24–2.21 mg/m³. The highest Mn level inside the oil cylinder tank during exposure assessment in the Factory B reached 11.1 mg/m³, about 55-fold higher than the maximum allowable concentration (0.2 mg/m³). While this study was not specifically designed to examine clinical syndromes of Mn intoxication, signs of hand tremors were indeed seen among welders in both factories, along with complaints of insomnia and dizziness. Four welders in

the Factory B were recommended for further clinical evaluation by occupational physicians for possible manganism. In another study we reported earlier, of 142 factories in Beijing area, about 20–50% of workshops had airborne Mn levels surrounding welders' breathing zones that exceeded the MAC. Moreover, there were 39 cases of Mn poisoning identified from 3200 welders (Wang et al., 2001; Crossgrove and Zheng, 2004). The results from the current study are in agreement with our previous observations and support a definite occupational risk among welders to expose to airborne Mn.

For a large-scale risk assessment, measurement of Mn and other metal concentrations in saliva samples provides several advantages. First, saliva is secreted by salivary glands, containing ingredients of body extracellular fluids. Interestingly, essential metal ions are not merely passively diffused from glands to saliva, but rather actively transported into it. Thus, in theory, the chemistry of saliva differs from that of serum, which provides an additional means for biochemical assessment of toxic exposure in humans. Second, the sample of saliva can be readily obtained; the operation is simple and the procedure proven to be readily acceptable to our study subjects. Collection of saliva is noninvasive and can be done in any location even on the work site. Finally, saliva samples are convenient for storage and transport and stable for metal analysis. The limitation in using saliva samples pertains to interfering factors including mainly the dental diseases such as dental ulcer, unities and oral candidiasis. In clinic, saliva samples have been used to substitute blood samples or as additional tool in diagnosis of certain diseases, such as oral tumour, hepatitis and AIDS, in monitoring of drug concentrations in the body, such as corticosteroid, and in assessing serum erythropoietin according to saliva erythropoietin levels (Fliss et al., 2000; King et al., 2000; Warnakulasuriya et al., 2000; Zhevachevsky et al., 2000). Our own experience from the current research demonstrated that the saliva may be a useful matrix for metal toxicity studies.

The current study suggested that long-term, chronic exposure to Mn in welding fume had a significant impact on saliva concentration of Mn. The increases in saliva Mn levels appeared to be exposure-dose-related. When welder's years of employment were stratified into three employment groups, saliva Mn concentrations in the group with 5–10 years of employment were higher than those with less than five employment years, suggesting a work-length related increase in saliva Mn. Exposure to Mn in welding fume also had significant effects on saliva concentration of Cu and Zn, i.e., an increase in saliva Cu and a decrease in saliva Zn. Similar to saliva Mn, the changes in these two metals in saliva seemed likely to be associated with airborne Mn levels in the work sites. Thus, it appeared evident that metal concentrations, particularly Mn, Cu and Zn, are altered as the function of occupational exposure to welding fume in the operating environment.

Are the saliva metal concentrations better biomarkers than blood metal concentrations for assessment of Mn exposure, then? Saliva concentrations of Mn, Cu and Zn were, in fact, either increased or decreased in patterns very similar to serum concentrations of same metal ions. Linear regression analyses, revealed significant correlations between serum and saliva for Mn ($r = 0.57, p < 0.05$) and Cu ($r = 0.50, p < 0.05$). There were no relationships between serum and saliva Zn, Cd or Pb. Thus, variations in saliva metal levels may mirror, only partly, the changes of the concentrations of these metals in serum. With regard to the degree to which metal concentrations changed in saliva and serum as the function of exposure, the percentage of changes in serum Mn (72% increase vs. controls) was larger than that in saliva Mn (46%). The changes of serum Cu (18%) and Zn (–11%), however, were smaller than those in saliva Cu (45%) and Zn (–27%). The data distribution, on the other hand, appeared to be much tighter in serum samples than in saliva (Fig. 2), possibly due to a lesser variation or interference in drawing serum samples than in collecting saliva samples.

Blood Mn concentrations are known to be a poor indicator to assess Mn internal dose (Li et al., 2004; Lu et al., 2005). From the current study, no statistically significant associations were found between employment years and saliva or serum Mn when all welder's data were combined for analysis. While saliva and serum Mn concentrations were higher in the group with 5–10 years of employment than the <5 year group, saliva and serum Mn concentrations in welders of <10 years of employment did not differ significantly from other groups. This discrepancy was due to the fact that the welders in 5–10 year group were relatively young and engaged more frequently in spot welding, whereas those with >10 years of employment were more often as the senior in directing younger welders. Thus, similar to blood Mn, the variation in saliva Mn concentrations were only partly associated with welder's employment years.

Taken together, we believe that saliva samples provide an additional means for assessment of metal concentrations in body extracellular fluids; however, it is difficult to conclude that saliva samples offer definite advantages over the traditional blood samples.

Noticeably, saliva Mn concentrations were significantly association with saliva Cu as well as saliva Zn; the same was true for serum Mn and serum Cu or Zn. Scheuhammer and Cherian (1981) report that following chronic administration of Mn as MnCl₂ to rats, the Zn content decreases in nucleus amygdalate and hypothalamus and the Cu content increases in striatum, cerebral ganglion and cerebellum. Li et al. (2004) report that with serum Mn increasing, serum Cu and Fe among welders increase, but serum Zn decreases. Change of Cu and Zn by elevated Mn corresponds with the lipid peroxidative damage (Lu et al., 2005). Since both Cu and Zn are actively participating in cellular redox reactions, alterations in the homeostasis of both metals may potentiate the cellular damage resulting from reactive oxygen species. This may ultimately contribute to Mn-induced neurotoxicity.

In conclusion, exposure to Mn in welding fume resulted in altered levels of Mn, Cu, and Zn in saliva and serum of welders. The changes in saliva Mn concentrations appeared to be likely associated with airborne Mn concentrations in work sites and mirrored partly the change in serum Mn concentration. Thus, the saliva samples may be used as an additional tool for determination of Mn levels in the body. However, its utility as a reliable biomarker for estimating Mn body burden or used for assessment of internal exposure remains uncertain.

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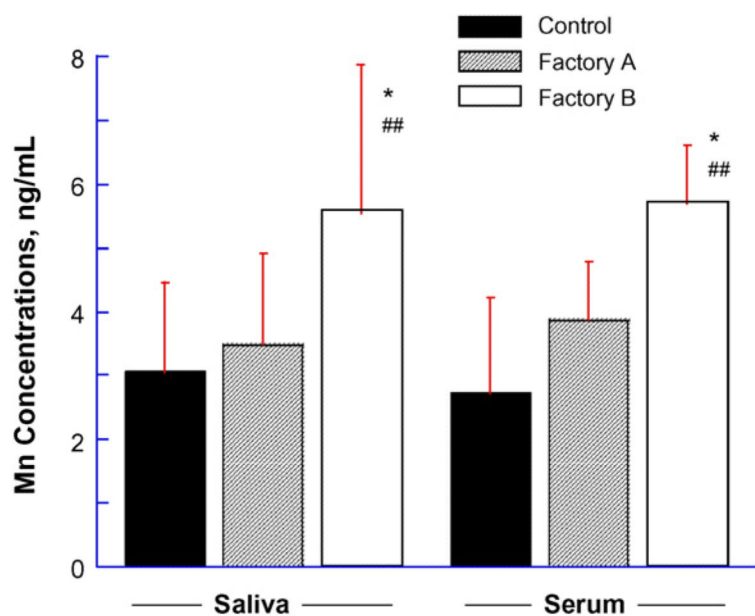


Fig. 1.

Mn concentrations in saliva and serum of welders and control subjects. Mn levels in body fluids were determined by ICP-MS. There were 28 and 21 welders from Factory A and B, respectively. The control group consisted of 33 military soldiers. Data represent mean \pm S.D. * $p < 0.05$ compared to controls; $p < 0.01$ compared to values in Factor

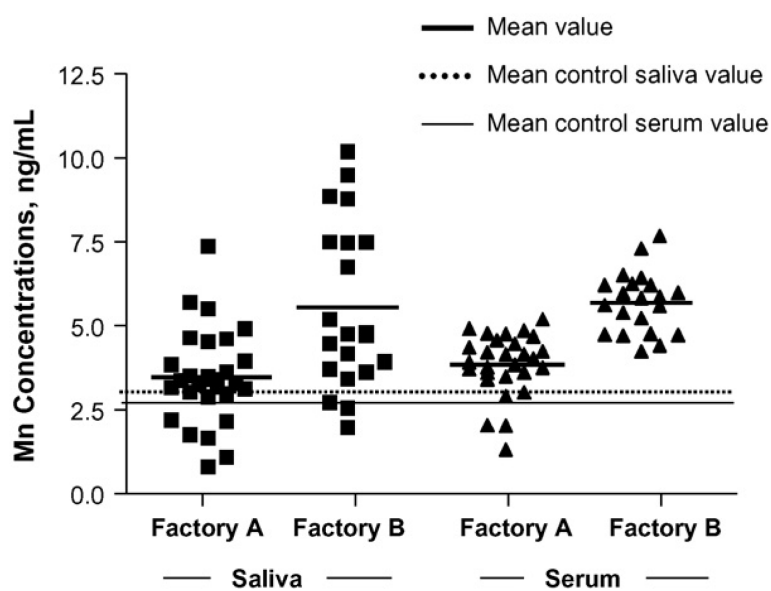


Fig. 2. Distribution of Mn concentrations in saliva and serum of welders and control subjects. There were 28 and 21 welders from Factory A and B, respectively. The mean values for control subjects were expressed in horizontal lines.

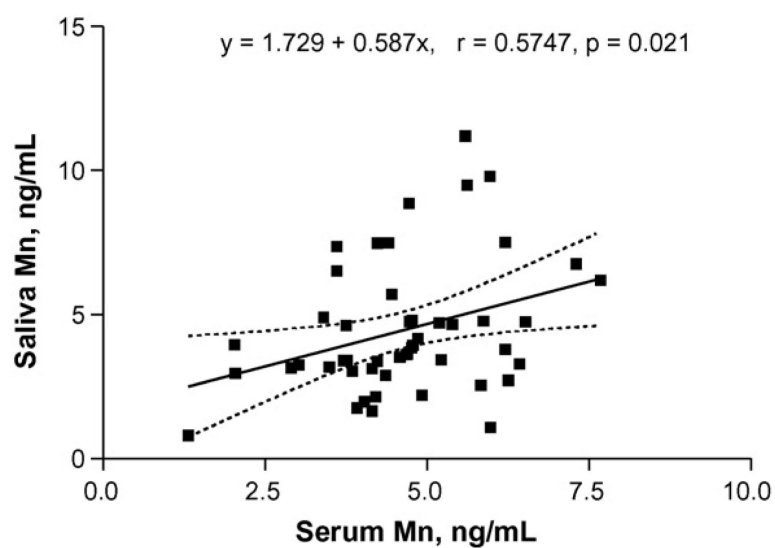


Fig. 3. Correlation between saliva Mn and serum Mn among 49 welders. Data were analyzed by linear correlation with 95% confidence interval, with a correlation coefficient (r) = 0.5747 and $p < 0.05$.

Table 1

Summary of demographic data among welders and control subjects

	Control	Welders		
		Factory A	Factory B	Combine
Number of cases	33	28	21	49
Mean age (yr) (95% CI)	29.1±6.8 (18–34)	29.0±9.1 (18–53)	31.7±9.1 (26–45)	30.6±9.8
Years in welding employment (95% CI)	0	4.7±2.4 (0.4–19)	10.3±4.4 (5.8–17)	8.1±3.6*
Initial working age (yr) (95% CI)	21.0±2.9 (18.9–23.2)	21.4±2.5 (18.3–24.5)	22.2±3.9 (19.9–24.6)	22.0±3.5
Smoking (%)	45.5	40.0	46.2	44.4
Alcohol (%)	36.4	40.0	30.1	33.3
Airborne MnO ₂ (mg/m ³) (95% CI)	0.01 (0–0.03)	0.24±0.07* (0.01–1.0)	2.21±1.17**,# (0.02–11.1)	0.60**

Data represent mean±S.D.:

*
 $p < 0.05$,**
 $p < 0.01$ compared with the control workers;#
 $p < 0.01$ compared with workers in Factory A.

Table 2

Concentrations of five metals in saliva of welders and control subjects

Parameters	Control	<u>Mn exposed</u>		
		Factory A	Factory B	Combine
Case number	33	28	21	49
Mn (μg/L)	3.04±1.40	3.47±1.42	5.55±2.31 ^{*,##}	4.45±2.17 ^{**}
Cu (μg/L)	19.6±13.6	23.1±9.06	35.7±16.0 ^{**}	28.5±13.9 ^{**}
Zn (μg/L)	260±132	220±74.3	152±132 ^{*,#}	191±107 [*]
Cd (μg/L)	0.43±0.43	0.42±0.27	0.28±0.15 ^{*,##}	0.36±0.24
Pb (μg/L)	25.5±14.4	28.8±12.1	19.6±9.32 [*]	24.9±11.8

Data represent mean±S.D.:

*
 $p < 0.05$,**
 $p < 0.01$ compared with controls;#
 $p < 0.05$,##
 $p < 0.01$ compared with welders in Factory A.

Table 3

Concentrations of five metals in serum of welders and control subjects

Parameters	Control	<u>Mn exposed</u>		
		Factory A	Factory B	Combine
Case number	33	28	21	49
Mn (μg/L)	2.70±1.50	3.85±0.90	5.68±0.91 ^{*##}	4.64±1.30 ^{**}
Cu (μg/L)	822±159	792±154	1207±303.4 ^{**}	970±308 ^{**}
Zn (mg/L)	1.18±0.214	1.09±0.16	0.99±0.10 ^{*#}	1.05±0.15 ^{**}
Cd (μ/L)	0.60±0.42	0.63±0.57	0.19±0.10 ^{**}	0.40±0.46 [*]
Pb (μg/L)	28.3±15.6	29.9±12.7	7.19±6.80 ^{*##}	19.5±14.4

Data represent mean±S.D.:

^{*}
 $p < 0.05$,^{**}
 $p < 0.01$ compared with controls;[#]
 $p < 0.05$,^{##}
 $p < 0.01$ compared with welders in Factory A.

Table 4

Serum and saliva Mn concentrations among welders with different length of service

Group	<i>n</i>	SaUva Mn (μg/L)	Serum Mn (μg/L)
<5 years	19	3.69 ± 1.53	3.73 ± 0.90
5–10 years	15	4.38 ± 1.94*	5.31 ± 1.30*
>10 years	15	5.20 ± 2.83	5.11 ± 1.10

Data represent mean ± S.D.:

* $p < 0.05$ compared with welders of <5 years.

Table 5

Correlation coefficients between Mn and other metals in serum and saliva of Mn-exposed welders

	Cu-Mn	Zn-Mn	Cd-Mn	Pb-Mn
Saliva	$r = 0.678$ ($p < 0.05$)	$r = -0.540$ ($p < 0.05$)	$r = -0.109$	$r = -0.098$
Serum	$r = 0.894$ ($p < 0.05$)	$r = -0.585$ ($p < 0.05$)	$r = -0.239$	$r = -0.409$ ($p > 0.05$)

Data from welders in both factories were combined and analyzed by linear regression.