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Modifying welding process parameters can reduce the neurotoxic potential of manganese-containing welding fumes

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ABSTRACT

Welding fumes (WF) are a complex mixture of toxic metals and gases, inhalation of which can lead to adverse health effects among welders. The presence of manganese (Mn) in welding electrodes is cause for concern about the potential development of Parkinson's disease (PD)-like neurological disorder. Consequently, from an occupational safety perspective, there is a critical need to prevent adverse exposures to WF. As the fume generation rate and physicochemical characteristics of welding aerosols are influenced by welding process parameters like voltage, current or shielding gas, we sought to determine if changing such parameters can alter the fume profile and consequently its neurotoxic potential. Specifically, we evaluated the influence of voltage on fume composition and neurotoxic outcome. Rats were exposed by whole-body inhalation (40 mg/m^3; 3 h/day × 5 d/week × 2 weeks) to fumes generated by gas–metal arc welding using stainless steel electrodes (GMA-SS) at standard/regular voltage (25 V; RVSS) or high voltage (30 V; HVSS). Fumes generated under these conditions exhibited similar particulate morphology, appearing as chain-like aggregates; however, HVSS fumes comprised of a larger fraction of ultrafine particulates that are generally considered to be more toxic than their fine counterparts. Paradoxically, exposure to HVSS fumes did not elicit dopaminergic neurotoxicity, as monitored by the expression of dopaminergic and PD-related markers. We show that the lack of neurotoxicity is due to reduced solubility of Mn in HVSS fumes. Our findings show promise for process control procedures in developing prevention strategies for Mn-related neurotoxicity during welding; however, it warrants additional investigations to determine if such modifications can be suitably adapted at the workplace to avert or reduce adverse neurological risks.

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1. Background

According to the Occupational Outlook Handbook 2014–2015, published by U.S. Department of Labor, Bureau of Labor Statistics, an estimated 500,000 workers are employed full-time in welding operations in the United States (Bureau of Labor Statistics, U.S. Department of Labor, 2014–2015). Globally, this figure exceeds 2,000,000 workers. Welders are a heterogeneous working

Abbreviations: ANOVA, analysis of variance; Ccl2, chemokine (C–C motif) ligand 2; cDNA, complementary deoxyribonucleic acid; Cu, copper; Dmt1, divalent metal transporter 1; Fe, iron; FESEM, field emission scanning electron microscopy; Gfap, glial fibrillary acidic protein; GMA-SS, gas metal arc stainless steel welding; HVSS, high voltage stainless steel fume particulates; ICP-AES, inductively-coupled plasma atomic emission spectroscopy; MMAD (GSD), mass median aerodynamic diameter (geometric standard deviation); Mn, manganese; MB, midbrain; MOUDI, micro-orifice uniform deposit impactor; MRI, magnetic resonance imaging; mRNA, messenger ribonucleic acid; Ni, nickel; Nos2, nitric oxide synthase 2 (inducible nitric oxide synthase or iNos); OB, olfactory bulb; Park5, Parkinson disease (autosomal dominant) 5 (also known as Uchl1, ubiquitin C-terminal hydrolase L1); Park7, Parkinson disease (autosomal recessive, early onset) 7 (also known as Dj1); Ppia, Peptidylprolyl isomerase A (also known as cyclophilin A); PCR, polymerase chain reaction; PD, Parkinson's disease; RNA, ribonucleic acid; RVSS, regular voltage stainless steel fume particulates; STR, striatum; Th, tyrosine hydroxylase; T-PER, tissue protein extraction reagent; TLV-TWA, threshold limit value-time weighted average; Tnfa, tumor necrosis factor alpha; Tuba, alpha tubulin; WF, welding fume; Zn, zinc.

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population, employed in a number of occupational settings that include open, well-ventilated spaces (*e.g.*, outdoors on a construction site) or confined, poorly-ventilated spaces (*e.g.*, ship hull, building crawl space and pipeline). One of the most common types of welding processes used in industry is gas–metal arc welding (GMAW). In this process, shielding gases (usually a combination of argon, helium, or carbon dioxide) are continually blown through the welding nozzle and over the arc to protect the weld from weakening due to oxidation. GMAW welding process utilizes mild, low alloy or stainless steel electrodes. Mild and low alloy steel electrodes are comprised mostly of iron (Fe) with varying amounts of manganese (Mn), while stainless steel electrodes contain chromium (Cr) and nickel (Ni), in addition to Fe and Mn (Beckett, 1996).

Welding generates a complex mixture of fine and ultrafine aerosols and gaseous by-products. The welding fume (WF) comprises an array of potentially toxic metals (*e.g.*, Fe, Mn, Cr, Ni), volatilized from the welding electrode or the flux material incorporated within the electrode. Gaseous by-products (*e.g.*, ozone, carbon monoxide) generated during welding operations originate from chemical reactions, ultraviolet irradiation of atmospheric elements or the use of shielding gases. The aerodynamic diameter of WF aerosols in the welder's breathing zone ranges from 100 nm to 1 μm (Zimmer and Biswas, 2001; Jenkins et al., 2005), which are easily respirable. The unique physicochemical characteristics of these fine and ultrafine aerosol fractions can influence their deposition within the olfactory or respiratory tracts. Physical characteristics such as, size, number, concentration, morphology and surface area can influence particle translocation and toxicity. Similarly, chemical characteristics such as solubility, elemental phase, surface composition and electronic/valence state, can influence elemental speciation, translocation and toxicological profile. Therefore, exposure to airborne WF particulates is of immense occupational concern.

An emergent concern is that exposure to WF may be associated with development of neurological dysfunction similar to Parkinson's disease (PD). Much of this apprehension has been attributed to the presence of Mn in WF consumables. Magnetic resonance imaging (MRI) of welders suspected of having neurological deficits revealed hyperintense T_1 signals in basal ganglia, including globus pallidus, striatum and midbrain (Nelson et al., 1993; Kim et al., 1999; Kim, 2004; Josephs et al., 2005). These observations are indicative of Mn accumulation in the brain. Further, there is a proposition of early-onset Parkinsonism among welders (Racette et al., 2001, 2005; Josephs et al., 2005; Bowler et al., 2006, 2007a,b). PD is characterized by progressive neurodegeneration of nigrostriatal dopaminergic neurons. While most forms of PD are sporadic, about 10% are linked to genetic defects. Identification of single gene mutations in familial forms of PD suggests that deletions and loss-of-function mutations of specific PD susceptibility genes (*PARK* genes) are associated with early-onset Parkinsonism (Kitada et al., 1998; Abbas et al., 1999; Lucking et al., 2000; Bonifati et al., 2003; Periquet et al., 2003; Rizzu et al., 2004; Neumann et al., 2004). Indeed, our recent findings link such PD susceptibility genes to occupational risk factors like welding and suggest that interaction of PD-related genes may modulate the neurotoxic outcome of exposure to WF (Sriram et al., 2010b).

As a consequence of the neurological health risks associated with welding, an immense need is felt to reduce adverse workplace exposures to WF. Therefore, controlling fume generation using appropriate ventilation and personal protective equipment to avert adverse exposures are standard safety recommendations. Unfortunately, several welding operations are performed in confined, poorly-ventilated spaces (*e.g.*, ship hull, building crawl space and pipeline), where local exhaust ventilation is impractical or sometimes ineffective. High fume concentrations in such confined workplace conditions may increase the risk for exposure. Thus, methodologies by which WF generation rate and/or welding practices can be modified to reduce toxic workplace exposures are sought after. Here, we show that by modulating a specific welding process variable, voltage, one can significantly alter fume composition and neurotoxicological outcome.

2. Methods

2.1. Welding fume generation system

Detailed characterization of the robotic welding system available at the National Institute for Occupational Safety and Health (NIOSH, Morgantown, WV) has been published previously (Antonini et al., 2006). In brief, the WF generation system consisted of a welding power source (Power Wave 455, Lincoln Electric, Cleveland, OH), an automated, programmable six-axis robotic arm (Model 100 Bi, Lincoln Electric, Cleveland, OH), and a water-cooled arc welding torch (WC 650 amp, Lincoln Electric, Cleveland, OH). Gas metal arc welding using a stainless-steel (SS) electrode (Blue Max E308LSi wire, Lincoln Electric, Cleveland, OH) was performed on A36 carbon steel base plates. Welding was performed at two different voltage settings, standard/regular voltage (25 V; RVSS) or high voltage (30 V; HVSS), keeping current and shielding gas constant (Table 1). The shielding gas was continually delivered to the welding nozzle at an air flow rate of 20 l/min. Both welding conditions produced very good weld bead quality, indicating that the welding process conditions have potential for adaptation in the industry (Fig. 1).

A flexible trunk was positioned approximately 18 inches from the arc to collect the generated fume and transport it to the animal exposure chamber (Hazleton H-1000; Lab Products, Maywood, NJ). The generated WF was mixed with humidified HEPA-filtered air to achieve the target concentration. Chamber fume concentration, temperature, and humidity were monitored. Mass concentration in the chamber was monitored in real-time with an aerosol monitor (DataRAM, Thermo Electron Co., DR-4000, Franklin, MA). Chamber concentrations of ozone (Ozone Analyzer, Model #450, Advanced Pollution Instrumentation, Inc., San Diego, CA) and carbon monoxide (1312 Photo-acoustic Multi-Gas Monitor, Innova Air Tech Instruments, Ballerup, Denmark) were monitored to prevent adverse exposures to test animals. Ozone and carbon monoxide

Table 1
Parameters for gas metal arc welding at regular and high voltage conditions.

	Regular voltage (RVSS)	High voltage (HVSS)
Weld process	Gas–metal arc welding (GMAW)	Gas–metal arc welding (GMAW)
Wire/electrode	Blue Max E308LSi (stainless steel)	Blue Max E308LSi (stainless steel)
Weld base plate	A36 Carbon steel plate	A36 Carbon steel plate
Wire feed rate	300 in/min	300 in/min
Voltage	**25 V**	**30 V**
Current	200 A	200 A
Shielding gas	Ar/CO_2 (95:5)	Ar/CO_2 (95:5)
Gas flow rate	20 l/min	20 l/min