

as a transporter of brain Fe and Mn and, another goal of the study was to measure brain regional changes in transporter levels using Western blot analysis. As expected, there was a significant effect of Fe deficiency ( $P < 0.05$ ) on decreasing Fe concentrations and increasing Mn concentrations throughout the brain. Transporter protein in all regions increased due to ID compared to control levels ( $P < 0.05$ ). Keywords: Manganese, Transport, Iron. (Supported by NIEHS 10563.)

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# **CHARACTERIZATION OF WELDING FUMES AND THEIR POTENTIAL NEUROTOXIC EFFECTS.**

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Serious questions have been raised regarding a possible causal association between neurological effects in welders and the presence of manganese in welding consumables. The objectives of the study are to: (1) construct an automated, computer-controlled welding fume generation system to simulate real workplace conditions and (2) examine the potential neurotoxic effect of manganese in rats after pulmonary exposure to different welding fumes. The system is comprised of a programmable six-axis robotic welding arm and a water-cooled arc welding torch. A flexible trunk has been attached to the robotic arm of the welder and is used to collect and transport fume from the vicinity of the arc to the animal exposure chamber. Of the metals measured, manganese comprised ~10–15% of the stainless and mild steel fume generated as determined by inductively coupled plasma atomic emission spectroscopy. Size distribution analysis indicated the mass median aerodynamic diameter of the generated particles to be approximately 0.24  $\mu\text{m}$ . As determined by scanning electron microscopy, the generated aerosols were mostly arranged as chain-like agglomerates of primary particles. These fume characterization studies have indicated that particle morphology, size, and chemical composition are comparable to welding fume generated in the workplace. Initial animal inhalation studies are underway. Sprague–Dawley rats are being exposed to 15 or 40  $\text{mg}/\text{m}^3$  of welding fume for 3 h/day for 10 or 30 days. After exposure, manganese concentrations will be determined in a number of discrete brain regions. Neurotoxicity will be detected and quantified by measuring the increased expression of glial fibrillary acidic protein and using silver degeneration staining technology. Because dopaminergic systems have been implicated as targets of manganese exposure, levels of dopamine and tyrosine hydroxylase, biomarkers of dopaminergic neuronal damage, also will be measured. With the development of this novel system, it will be possible to establish an animal model using controlled welding exposures to investigate the possible mechanisms by which welding fumes may affect the central nervous system. Keywords: Welding fume, Manganese, Neurotoxicology

*Disclaimer: The finding and conclusions of this abstract have not been formally disseminated by NIOSH and should not be construed to represent any agency determination or policy.*

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# **DISCOVERY OF BIOMARKERS OF MANGANESE EXPOSURE IN HUMANS.**

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The lack of a reliable biomarker for manganese (Mn)-induced Parkinsonism has hampered the diagnosis and therapeutic intervention of Mn neurotoxicity. We have determined airborne levels of Mn during welding practice and serum concentrations of possible biomarkers, aiming to establish the relationship between long-term, low-level exposure to Mn and altered serum levels of Mn, Fe, Cu, Zn, and Pb as well as proteins associated with Fe metabolism in career welders. Mn-exposed group consisted of welders who have engaged in electric arc weld in a vehicle manufacturer, while the control subjects were employees in the same factory but not in the welding profession. Average serum levels of Mn and Fe among welders were significantly higher than those of controls ( $p < 0.01$ ). Among the welders, serum concentrations of both metals were highest in the youngest age group ( $\leq 30$  years), an evidence of relationship to recent, active exposure. While serum Cu concentrations in welders were unchanged, blood Pb concentrations and serum Zn levels in welders were significantly increased and decreased, respectively, compared to controls. Concentrations of serum ferritin and transferrin were increased among welders; however, serum transferrin receptor levels were significantly decreased in comparison to controls. Linear regression revealed a positive association between serum Fe and ferritin levels and welder's employment years; yet serum transferrin receptor levels were inversely associated with serum Mn concentrations. Biochemical assays showed that the activity of erythrocytic superoxide dismutase (SOD) in welders was reduced by 24% compared to controls ( $p < 0.05$ ), while the levels of serum malondialdehyde (MDA) were increased by 78% ( $p < 0.05$ ). These findings suggest that occupational exposure to the welding fume among career welders disturbs the homeostasis of trace elements in the systemic circulation and induces oxidative stress. Although the feasibility of using proteins associated with Fe metabolism as the biomarker for Mn exposure remains to be further explored, serum Mn may serve well as a reasonable biomarker for assessment of recent exposure to airborne Mn. Keywords: Biomarker, Iron, Ferritin. (Supported by NIH/NIEHS Grant ES-08146.)

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# **NEUROCHEMICAL CHANGES IN THE LIVING NON-HUMAN PRIMATE BRAIN FOLLOWING MANGANESE EXPOSURE.**

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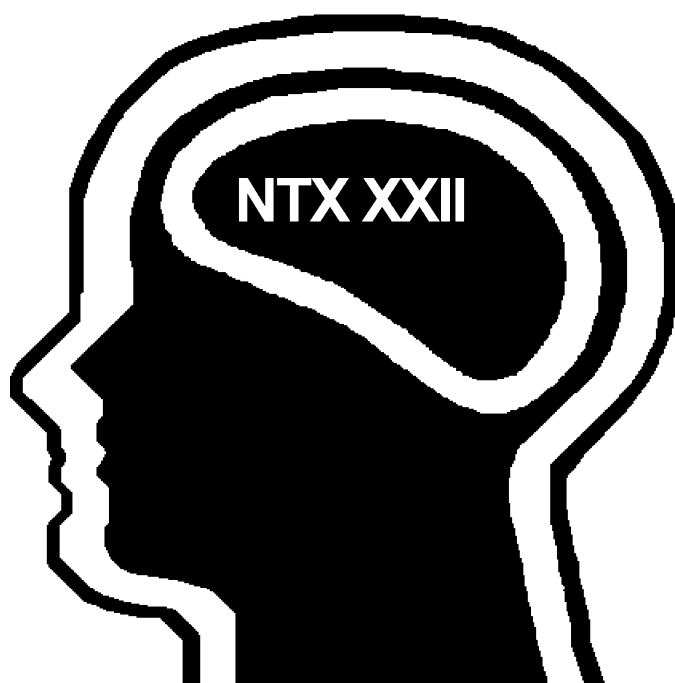
Occupational exposures to manganese (Mn) are known to cause a Parkinsonian-like syndrome in humans and non-human primates. The precise molecular mechanism(s) by which Mn



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