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Vanadium exposure-induced neurobehavioral alterations among Chinese workers

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ABSTRACT

Vanadium-containing products are manufactured and widely used in the modern industry. Yet the neurobehavioral toxicity due to occupational exposure to vanadium remained elusive. This cross-sectional study was designed to examine the neurotoxic effects of occupational vanadium exposure. A total of 463 vanadium-exposed workers (exposed group) and 251 non-exposed workers (control group) were recruited from a Steel and Iron Group in Sichuan, China. A WHO-recommended neurobehavioral core test battery (NCTB) and event-related auditory evoked potentials test (P300) were used to assess the neurobehavioral functions of all study subjects. A general linear model was used to compare outcome scores between the two groups while controlling for possible confounders. The exposed group showed a statistically significant neurobehavioral alteration more than the control group in the NCTB tests. The exposed workers also exhibited an increased anger-hostility, depression-dejection and fatigue-inertia on the profile of mood states ($p < 0.05$). Performances in the simple reaction time, digit span, benton visual retention and pursuit aiming were also poorer among exposed workers as compared to unexposed control workers ($p < 0.05$). Some of these poor performances in tests were also significantly related to workers' exposure duration. P300 latencies were longer in the exposed group than in the control ($p < 0.05$). Longer mean reaction times and more counting errors were also found in the exposed workers ($p < 0.05$). Given the findings of our study and the limitations of neurobehavioral workplace testing, we found evidence of altered neurobehavioral outcomes by occupational exposure to vanadium.

1. Introduction

Vanadium is widely distributed in the earth's crust and is a major trace metal found in fossil fuels such as oil, coal and shale. Vanadium compounds are extensively used in the production of metal alloys and sulfuric acid (as a catalyst), in petroleum and chemical engineering, and in welding. More than 90% of industrial vanadium is used for making steel. The market demand for vanadium over the past three years has shown a continued increase worldwide demand, most notably in China, for its higher strength in vanadium steel (Bunting, 2006). Extensive industrial application has led to vanadium-related occupational exposure. In addition, the combustion of fossil fuels containing vanadium results in a significant environmental exposure to vanadium.

Earlier studies have shown that vanadium exposure may cause respiratory dysfunction (Woodin et al., 2000; Todaro, 1991; Musk and Tees, 1982), hematologic and biochemical alterations, renal toxicity (Al-Bayati et al., 1989; Zaporowska and Waailewski, 1992; Jandhyala and Horn, 1983), reproductive and developmental toxicity (Lahav et al., 1986), immunotoxicity, mutagenicity (Chakraborty et al., 2000), and neurotoxicity (Sanchez et al., 1998; Poggioli et al., 2001; Avila-Costa et al., 2004). The cases of death due to exposure to vanadium compounds have also been reported in literature (Sjoberg, 1950). Most of reported vanadium toxicological studies are conducted in animal models; only relatively small numbers of studies are done on occupational workers. While some studies have shown vanadium-induced neurotoxicity, the question as to whether vanadium exposure causes neurobehavioral alterations, was unanswered. Since the central nervous system (CNS) is sensitive to vanadium toxicity, an in-depth study on vanadium-induced neurobehavioral changes, especially under chronic, low-level occupational exposure, became necessary.

The neurobehavioral core test battery (NCTB) is widely used testing method established by the World Health Organization

Abbreviations: NCTB, neurobehavioral core test battery; P300, event-related auditory evoked potentials test; CNS, central nervous system.

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(WHO) for early detection of CNS impairment caused by neurotoxic agents present in the working environment. It provides a rapid, stable and effective test for cognitive and neurobehavioral toxicology (Johnson, 1990; Anger et al., 2000; Anger, 2003). Event-related auditory evoked potential test (P300) has been used in clinics and laboratories to test psychological alterations for its unique association with certain cognitive functions such as the decision making processes, etc. (Soltani and Knight, 2000; Braverman and Chen, 2006). The purpose of this study was to test the hypothesis that occupational exposure to vanadium in a low-dose, long-term exposure condition may lead to the early onset of neurobehavioral changes among vanadium-exposed workers. The NCTB and auditory event-related potentials (P300) were used in assessing the neurobehavioral outcomes.

2. Materials and methods

2.1. Study population

The participants were selected from a Steel and Iron Group in Panzhihua area, China. The manufacturer is located in the Sichuan Province, a mountainous region of south-western China. The factory has been in manufacture of vanadium-containing products since 1989 and currently has more than 4000 workers. Study subjects were recruited to the exposed and control groups based on their job classification. The exposed group comprised 463 workers who had worked in the vanadium-containing steel production workshop for at least 1 year, whereas the workers of the control group (251) were recruited from a workshop that belongs to the same Steel and Iron Corporation but produces the steel products without containing vanadium. The two factories were established around the same time; the vanadium products workshop has been in operation since 1989 and the cold rolling mill in the non-vanadium steel workshop was built in 1993. The workers in both workshops were trained by the same vocational training school. The cold rolling mill is located about 5 km (3.1 miles) away from the vanadium production workshop. The data by routine occupational safety monitoring of air vanadium level indicate that vanadium smoke time-weighted average concentration in the exposed group was 0.216 mg/m^3, while the value in the control group is 0.013 mg/m^3.

The workers in both workshops underwent the routine physical examination under the health surveillance for normal function of skin, mucous membranes, lung, heart, liver, kidneys and blood system. All study subjects in the current control and exposed groups have passed these exams and were considered the "healthy" workers. The definition, however, does not exclude the abnormality in the central nervous system, and/or the cardiovascular system, among others.

The mean ages were (39.5 ± 7.8) years (range: 20–60) and (37.1 ± 5.8) years (range: 20–60), respectively, for the vanadium-exposed group and controls. Both group workers had the similar socioeconomic status (salary, education, etc.) and background environmental factors (place of residence, etc.). Subjects in both groups at the time of interview had reported no exposure to other toxic substances, radiation therapy, or substance abuse. There were no statistically significant differences in smoking and alcohol consumption between the vanadium-exposed workers and the controls.

2.2. NCTB examination

Participating subjects were invited to the West China School of Public Health Sichuan University. A written consent form was obtained from each subject prior to the onset of the study. The study protocol received official approvals from the Office of Clinical Investigation at Sichuan University, which is responsible for ethical and subject protection issues in the university. Medical examinations were conducted to rule out conditions related to central or peripheral nervous system illnesses, musculoskeletal problems or psychiatric disorders, such as epilepsy, Parkinson's disease, Alzheimer's disease, hyperthyroidism, and color blindness. None of the workers were found to have any major health issues at the time of tests. The neurobehavioral tests were conducted in the morning (8:00–12:00). The tests were conducted in a group setting. The POMS test, Santa Ana dexterity, digit symbol, Benton visual retention and pursuit aiming test were conducted in a big room with the curtains that separate participants. Simple reaction time and digital span were tested with the subject alone in an enclosed quiet room.

The NCTB includes a profile of mood states (POMS) questionnaire and a set of neurobehavioral tests. The POMS questionnaire consists of six mood scales: anger-hostility, confusion-bewilderment, depression-dejection, fatigue-inertia, tension-anxiety and vigor-activity. The participants were asked to fill out the questionnaire, which cover the basic demographic information (e.g., age and educational status), the information on smoking, alcohol consumption, medications, recent medical history, subjective symptoms, and the job description including type of job, duration of work, and total duration of vanadium-related work.

2.3. Neurobehavioral tests

The neurobehavioral tests included: (1) simple reaction time, including two extreme values, fastest simple reaction time, slowest simple reaction time and mean simple reaction time; (2) digit symbol; (3) Santa Ana dexterity, including preferred hand and non-preferred hand; (4) digital span, including forward value and backward value; (5) Benton visual retention; and (6) pursuit aiming (PA), including total PA and correct PA. We used all of these tests to assess the participants' neurobehavioral reaction or status.

Simple reaction time. Simple reaction time was assessed using the standard reaction time tester (Model M40305, Midwest Group, Beijing, China). The reaction time test is a classic test used to assess psychomotor speed. The subject was asked to press a button in his/her preferred hand, as quickly as possible, in response to the presentation of a stimulus. The stimulus was randomly selected from among two colors, i.e., red or green.

Santa Ana dexterity test. A plastic base plate with 12 pegs fitted in 4 rows was used. Each peg was removed, turned 180° and replaced in its slot. The objective was to turn as many pegs as possible in 30 s. The test was repeated twice for each hand. The number of pegs successfully turned was recorded as the test score. Mean scores were calculated separately for the preferred and non-preferred hand.

Digit span. In the digit forward sequence the tester read groups of 3–8 numbers and the participant was requested to repeat each sequence exactly as they heard them. The digit backwards sequence ran from two to eight digits and the participant was requested to repeat them in the exact reversed order. The score was the total number of correct individual sequences relayed.

Digit symbol test. A worksheet contained a list of numbers that were associated with certain simple symbols and a list of random digits from one to nine with blank squares below each digit. The participant was required to fill the blank squares with the symbols paired to their corresponding digits, and to do so as quickly as possible within 90 s. The number of correct matches was recorded for each participant.

Benton visual retention test. A design was shown to the participant for 10 s and then removed from view. The participant was immediately asked to draw the design from recall using a sheet of paper of the same size as the design. The number of complete correctly recalled pictures was calculated.