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# ASSESSMENT OF NEUROPHYSIOLOGICAL PARAMETERS OF THE NERVOUS SYSTEM IN NON-FERROUS FOUNDRY WORKERS

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*A comprehensive assessment of the health status includes the functional exploration of the central and peripheral nervous systems. Results of the neurophysiological examination allow elaboration of effective personified therapeutic and preventive programs for the core personnel of non-ferrous metal industry.*

*Our objective was to study functional disorders of the central and peripheral nervous systems in smelter operators for further development of risk-based rehabilitation programs for workers engaged in production of non-ferrous metals.*

*Two cohorts of male workers were examined. The case cohort included 60 smelter operators of a large metallurgical plant situated in the Sverdlovsk Region and the control cohort consisted of 50 unexposed employees. The cohorts were matched by age and years of work experience. The mean age of smelter operators was 37.8 ± 7.9 years and their mean length of current employment was 4.1 ± 4.6 years, while the total length of work under hazardous occupational conditions was 7.1 ± 6.0 years. The case cohort included 39 operators of refinery boilers (mean age: 35.6 ± 7.2 years, mean length of employment: 4.2 ± 4.7 years) and 21 operators of the ore thermal furnace (mean age: 41.9 ± 7.6 years, mean length of current employment: 3.9 ± 4.4 years). All subjects underwent a neurocognitive examination (higher brain function testing), electroneuromyography, the somatosensory evoked response test, and electroencephalography.*

*The results of examining the higher brain function enabled us to form the neurocognitive profile of the workers. We revealed signs of mild cognitive impairment in 30 % and a decrease in the cognitive reserve in 35 % of the cases. The diagnosed peripheral nervous system disorders included distal sensory polyneuropathy of the upper and lower extremities, carpal and cubital tunnel syndromes, cervical and lumbar radiculopathy.*

*The comprehensive neurophysiological examination helps detect early changes in the central and peripheral nervous systems. The findings should be taken into account when developing personal medical rehabilitation programs.*

***Keywords:*** *neurophysiological examination, polyneuropathy, compression neuropathies, neurocognitive profile, cognitive reserve, somatosensory evoked potentials, prevention and treatment programs, combined toxicity.*

Preserving good health and increasing healthy working life expectancy are the priorities of the government policy in the Russian Federation[1] [1]. A comprehensive assessment of health status that includes testing for functional neurological disorders facilitates elaboration of effective personalized preventive and therapeutic programs implemented within the Concept of Predictive, Preventive and Personalized Medicine [1–4]. The



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[1] Zabolevaemost' naseleniya po osnovnym klassam boleznei [Morbidity of population by the main disease categories]. *Rosstat: Federal State Statistics Service*. Available at: https://rosstat.gov.ru/folder/13721 (June 11, 2023) (in Russian); Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing: official website. Available at: https://www.rospotrebnadzor.ru (June 11, 2023) (in Russian).

issue of a combined effect of occupational toxicants on workers maintains the relevance of searching for early diagnostic and effective preventive and therapeutic measures for exposed personnel [5–9]. Effects of certain toxic pollutants, particularly lead, on the nervous, hematopoietic, and digestive systems have been previously demonstrated; they are manifested by disturbances in epigenetic status; oxidative DNA damage; changes in reticulocyte count; oxidative stress; neurobehavioral changes; gene polymorphisms of glutathione peroxidase, paraoxonase, and metallothionein-4; and calcium metabolism with bone mineral density [10–21]. Dangerous variants of the combined toxicity of zinc oxide and copper oxide nanoparticles have been identified. In addition, it has been established that the exposure to nanoparticles of silver, gold, oxides of copper, iron, aluminum, zinc, lead, nickel, and silicon induces a statistical increase in nuclear DNA fragmentation [7–9].

Since 2019, the project for maintaining health of the core personnel in metallurgical industry has been implemented on the basis of the Yekaterinburg Medical Research Center for Prophylaxis and Health Protection in Industrial Workers [6]. Smelter operators of the refining department of the metallurgical (smelting) shop are at high risk of occupational and work-related diseases associated with exposure to a combination of adverse factors (work heaviness and toxicants, such as lead, copper, zinc, antimony, arsenic, and cadmium). Findings of a neurophysiological examination allow the development of effective personified preventive and therapeutic programs focused on the main targets for pathological processes (central and / or peripheral nervous systems) [6–9, 11].

Our **objective** was to study functional disorders of the central and peripheral nervous systems in smelter operators for further development of risk-based rehabilitation programs for workers engaged in production of non-ferrous metals.

**Materials and methods.** Two cohorts of male workers matched by age, seniority and level of education were examined at the clinic of the Yekaterinburg Medical Research Center. The control cohort consisted of 50 unexposed employees and the case cohort included 60 smelter operators aged 25 to 53 years (mean age: 37.8 ± 7.9 years) having the work history of 0 to 18 years (mean length of current employment: 4.1 ± 4.6 years). The total duration of work in hazardous conditions was 7.1 ± 6.0 years. The case cohort included 39 operators of refinery boilers aged 25 to 49 years (mean age: 35.6 ± 7.2 years, mean length of employment: 4.2 ± 4.7 years) and 21 operators of the ore thermal furnace aged 27 to 53 years (mean age: 41.9 ± 7.6 years, mean length of current employment: 3.9 ± 4.4 years), all with the work history ranging from 0 to 18 years.

According to the results of a special assessment of working conditions for all cases, the time-weighted average (TWA) concentration of lead was up to 1.94 times higher than its maximum permissible concentration (MPC), which is characteristic of Class 3.1 of working conditions. Concentrations of copper and zinc oxide were below the corresponding MPCs at all workplaces, with the exception of that of the ore thermal furnace operator where the TWA concentrations of both copper and zinc oxide were 1.02 times higher than their MPCs (up to 0.51 mg/m$^3$ with the average daily MPC of 0.5 mg/m$^3$). “Control” measurements of the levels of lead and its inorganic compounds in the workplace air of refinery boiler operators showed a 46.6, 30.4, and 48.4-fold excess of the TWA corresponding to Class 3.4 of working conditions in terms of lead compound concentrations and total chemical exposure.

The control cohort consisted of 50 men of similar age (*Me* = 51 (48; 55) years) never exposed to occupational risk factors in the

industrial setting. Workers with traumatic nerve injury, demyelinating diseases of the nervous system, hereditary diseases, diabetes mellitus, thyroid diseases, and a cardiac pacemaker were not eligible for inclusion in the study.

Electroneuromyography was performed using a Dantec® Keypoint® G4 workstation, Denmark, with analysis of indicators (latency of sensory and motor responses (ms), motor and sensory nerve conduction velocity (m/s), amplitude of the motor response (Am, mV) and sensory response (As, μV), F-wave).

When testing somatosensory evoked potentials (SSEPs) using a Neuro-MEP-4 auditory-visual stimulation unit, Neurosoft, Russia, peak potentials and interpeak intervals were measured at different stimulation frequencies of 3–5 Hz. The amplitude of components (potentials), peak and interpeak latencies were analyzed.

Electroencephalography (EEG) was also performed using the Neuro-MEP-4 unit according to a standard method.

A comprehensive neurological examination of the subjects was carried out with assessment of clinical indicators, a neuropsychological testing (Montreal Cognitive Assessment or the MoCA test, with a score of 26–30 points considered to be normal), tests of semantic associations and speech sound disorders with 15 or over words taken as the norm. These tests evaluated the global cognitive function and its components, such as concentration, executive functions, memory, attention, language, abstract reasoning, and visuoconstructional skills.

The study was conducted using non-invasive methods and it complies with the ethical standards of the Bioethical Committee of the Research Institute for Complex Problems of Hygiene and Occupational Diseases, developed in accordance with the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects as amended in 2013 and the "Rules of Clinical Practice in the Russian Federation" approved by Order no. 266 of the Russian Ministry of Health dated June 19, 2003.

**Results and discussion.** Higher brain function test results helped establish the neurocognitive profile of the examined workers. Findings of the MoCA test showed that 35 % of the cases scored 19–24 points, 35 % scored 26 points (the suggested cut-off score), and 30 % scored 27 points or over. At the same time, a score of 26 or over was registered in 90 % of the controls with no pronounced cognitive impairment detected in this cohort.

***Testing of semantic skills and phonological disorders.*** The findings showed specific features of the neurocognitive profile of the cases, including disorders of spatial orientation (20 %) and poor alternating trail making (15 %), constructional apraxia of the frontal type (the clock-drawing task) (15 %), impaired semantic speech activity (30 %), reduction in phonetically mediated associations (40 %) indicating the subcortical-frontal dysfunction, impaired memorization and reproduction processes (40 %) (frontal-subcortical disorders), impaired conceptual thinking (generalization) (20 %), decreased attention (30 %), and preserved executive functions (100 %). The evaluation of semantic and phonetic test results revealed a decrease in phonetically mediated associations compared to semantically mediated ones as a sign of subcortical-frontal dysfunction. We revealed signs of mild cognitive impairment in 30 % and a decrease in the cognitive reserve in 35 % of the cases. It is worth noting that neither cases nor controls had any complaints at the time of testing.

Electroneuromyography results showed statistically more significant changes in the case cohort ($p < 0.05$). We detected signs of entrapment neuropathies of the upper extremity in 20 % of the cases (increased latency in sensory and motor conduction ve-

locity along the median nerves at the level of the carpal tunnel and along the ulnar nerves at the level of the cubital tunnel, decreased As of the median nerve at the level of the carpal tunnel). In 35 % of the cases, we observed signs of a decreased amplitude of M-response and diagnosed conduction block related to motor axonal neuropathy in the peripheral nerves of lower limbs in 25 % and in the peripheral nerves of upper limbs – in 10 % of them. In 30 % of the cases, we registered sensory conduction abnormalities, such as prolongation of latency, a decrease in the amplitude and nerve conduction velocity; of these, along the sensory fibers of the upper and lower limbs – in 20 % and 10 %, respectively. In 15 % of the cases, ENMG parameters were normal.

The analysis of somatosensory evoked potentials in the control cohort showed that all indicators were normal. During the study, the parameters of peaks of the indicators in the case cohort were also within the normal range (Table 1).

Table 1

Upper extremity somatosensory evoked potentials in the case cohort

| Level | Potentials | Latency, ms |
|---|---|---|
| C3'-Fz (cortex) | N20 | 22.1 ± 1.6 |
| | P23 | |
| | N30 | |
| | P45 | |
| C7-Fz (cervix) | N11 | |
| | N13 | 13.2 ± 0.9 |
| | N14 | |
| | P18 | |
| (Erb's point) | N9 | 10.7 ± 0.88 |
| | P8 | |

We revealed signs of afferentation impairment at the subcortical-cortical level when analyzing interpeak intervals in the case cohort. In measurements of upper extremity somatosensory evoked potentials, N13 was assessed as the potential reflecting mainly the postsynaptic activation of the nuclei of the medulla oblongata and N20 – as that mainly reflecting the activity of generators in the thalamus or thalamocortical radiations. The conduction time from the lower parts of the brainstem to the cortex, determined by the time interval between components N13 and N20, was increased. The N13–N20 interval for C7-Fz–C3'-Fz was 8.9 ± 0.6, while the N30–P37 interpeak latency for C7-Fz–Cz-Fz1 was 2.2 ± 1.6. Prolongation of the conduction time from the lower brain stem to the cortex indicates conduction dysfunction at this level (Table 2).

Table 2

Interpeak intervals between upper extremity somatosensory evoked potentials in the case cohort

| Level | Interpeak interval | Latency, ms |
|---|---|---|
| Erb-Fz – C7-Fz | N9–N13 | 4.6 ± 0.8 |
| Erb-Fz – C3'-Fz | N9–N20 | 10.1 ± 0.77 |
| C7-Fz – C3' Fz | N13–N20 | **8.9 ± 0.6** |

When measuring lower extremity SSEPs, the activity of generators in subcortical structures (N30) and the potential primarily reflecting cortical activation of the somatosensory area of the corresponding projection of the leg (P37) were within normal limits (Table 3).

Table 3

Lower extremity somatosensory evoked potentials in the case cohort

| Level | Components | Latency, ms |
|---|---|---|
| L3-R (lumbar) | N22 | 25.2 ± 2.5 |
| C7-Fz (cervix) | N30 | 30.1 ± 3.0 |
| Cz-Fz (cortex) | P37 | 42.4 ± 3.3 |
| | N45 | 50.3 ± 3.2 |

When analyzing the interpeak activity, we registered a slight prolongation of the

N30–P37 interpeak latency indicating conduction dysfunction at the subcortical-cortical levels (Table 4).

Table 4

Interpeak intervals between upper and lower extremity somatosensory evoked potentials in the case cohort

| Level | Interpeak interval | Latency, ms |
|---|---|---|
| L3-R – Cz-Fz | N22–P37 | 19.1 ± 1.55 |
| L3-R – C7-Fz | N22–N30 | 7.5 ± 1.07 |
| C7-Fz – Cz-Fz | **N30–P37** | 12.2 ± 1.6 |

Thus, we registered a change (slowing down) of afferentation at the subcortical (stem)-cortical level in the cases when testing upper and lower extremity SSEPs.

When analyzing EEG data, no significant differences were found between the cohorts.

**Conclusion.** The results of analyzing the functional state of the central and peripheral nervous systems in the workers occupationally exposed to a number of toxicants showed the predominance of such distal disturbances of motor and sensory conduction as compression lesions of the nerves, as well as signs of axonal pathology, mainly at the lumbar level. The integrated approach enabled us to determine specific characteristics of the neurocognitive profile and to detect initial frontal-subcortical disorders and a decrease in cognitive reserve. When testing upper and lower extremity SSEPs in the cases, we registered a change (slowing down) of afferentation at the subcortical (stem)-cortical level. Our findings are consistent with those obtained in other studies [4, 5, 10, 13, 14]. The revealed changes have enabled us to elaborate personal medical rehabilitation programs including neuroprotective techniques aimed at the main pathogenetic targets.

We believe that a comprehensive neurophysiological examination should be part of the regular health checkup of workers exposed to toxicants at workplaces, including those engaged in non-ferrous industry, as it helps detect early neurological changes.

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**Conflict of interests.** The authors have no conflict of interests to declare.

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