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RAMAZZINI DAYS 2007 JUBILEE CELEBRATION

25th Anniversary of the Collegium Ramazzini

25-28 OCTOBER 2007
CARPI, ITALY

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distribution of genetic polymorphism on health risk assessments for alcohol is presented as a case study

Session B

Manganese exposure as a determinant of Parkinsonian damage

Roberto Lucchini

Department of Applied and Experimental Medicine – Section of Occupational Health, University of Brescia, Italy

medlav@med.unibs.it

Background: Manganese is an essential element for humans and animals. Nevertheless, prolonged exposure to low doses can determine a manganese overload in the central nervous system and this may favour the onset of Parkinsonian disturbances. Ferroalloy plants operated in Valcamonica, a valley in the Italian pre-Alps, for about a century, causing environmental exposure to manganese and other metals in the surroundings and downwind. A high prevalence of Parkinsonian disturbances (crude 296/100,000; 95% CI: 284.80-307.20; standardized 407/100,000; 95% CI: 393.87-420.12) was observed in this area. The Standardized Morbidity Ratios (SMRs) for Parkinsonism had resulted also associated with the concentrations of manganese measured in settled dust.

Methods: A cross sectional study was planned to compare parkinsonian patients residents in Valcamonica and in other non-exposed areas of the same province. Age- and sex-matched healthy individuals from the corresponding areas were also recruited as controls. Patients were examined with questionnaires assessing clinical, occupational, residential history and life habits. An extended battery of neurological and neuropsychological tests was administered, including also computerized tremor measurement, and MRI brain scan of the basal ganglia and globus pallidus, which is the elective location of manganese deposition. Genetic polymorphism of genes involved in Dopamine metabolism and the biomarkers of exposure to neurotoxic metals were also assessed. A two-ways analysis of variance was performed considering a factor related to the case/control classification and a factor related to the residential area.

Results: A group of 65 patients and 52 healthy controls residents in Valcamonica, and 28 patients and 14 healthy controls non residents in Valcamonica agreed to participate. Age and sex were not balanced between the groups, and therefore were used as covariates in the subsequent analyses. The age at onset of the disease was lower in women compared to men, independently from the residential area. Patients from the Valcamonica area showed a less frequent familiarity for parkinsonism, a more severe clinical severity as expressed by the UPDRS scale, a stronger impairment of cognitive and motor functions as measured with MMS, Token e Trial Making tests. The tremorimetric measurement showed higher tremor intensity, and lower frequency in the patients compared to the controls, independently from the residential area. MRI parameters did not differ between cases and controls, nor between the different residential areas. The genetic variables showed a different allelic distribution of DRD4 gene between cases and controls, non resident in Valcamonica. Cases showed higher blood iron and lower haemoglobin levels compared to controls, independently from the residential areas. Blood lead and urinary manganese resulted significantly higher among the cases and controls residents in Valcamonica compared to cases and controls non resident in Valcamonica.

Conclusions: Prolonged exposure to neurotoxic metals may have caused an increased frequency of parkinsonian disturbances in the examined population. Patients with environmental exposure showed a more severe phenotype of the diseases, whereas genetic factors were more significant among non exposed patients.