

PROGRAM

EPICOH 2008 June 9-11

20th International
Conference on
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XX Congreso
Internacional en
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NEUREOH 2008 June 11-13

10th International Symposium
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X Simposio Internacional sobre
Métodos y Efectos
Neuroconductuales en la Salud
Ocupacional y Ambiental

Multiple Exposures, Multiple Effects

Heredia, Costa Rica



We-O-14 OCCUPATIONAL EXPOSURE TO MANGANESE AND ITS IMPACT ON PERFORMANCE: A POOLED ANALYSIS OF ORIGINAL SUBJECT DATA

* Meyer-Baron M, Albini E, Bast-Pettersen R, Ellingsen DG, He S, Iregren A, Lucchini R, Niu Q, Schaper M, Sjögren B, Thomassen Y, van Thriel C, Wang X, Yuan H, Yang Y, M. Schaper M, van Thriel C.

Background and aims: Reviews on the neurobehavioral impact of occupational exposure to manganese (Mn) repeatedly emphasized impairments of motor performance. Our meta-analysis of published data showed slight deficits in exposed workers with respect to both cognitive and motor performance. However, associations between performance variables and indicators of exposure sometimes contradicted hypotheses. Better performance associated with higher levels of Mn in blood seems to require further investigation. We try to enlighten effects and exposure-effect relationships by the use of the original data of the included epidemiological studies and will compare them to the before obtained results of the meta-analysis.

Methods: Hitherto five original data sets are available. They comprise the data of 333 exposed and 309 control subjects. Mean Mn in blood is $19.78 \pm 21.91 \mu\text{g/L}$. Group comparisons and regressions will be used for the analysis. In order to assure that differently measured confounders are adequately considered, the performance data will be regressed to the confounders considered in the individual study and the residuals of the regressions will be used for further calculations.

Results: A first preliminary computation showed a significant negative association between 2 variables of memory performance and Mn in blood ($N=127$, digit span forward $r=-0.20$, $p=0.02$; digit span backward $r=-0.21$, $p=0.02$).

Discussion and conclusions: The preliminary results suggest a relationship between performance and exposure. The fact that performance was negatively related to the biomarker in this analysis may point at differences owing to the different types of analyses. Final conclusions are not possible at this time as the sample was not identical with the one in the previous meta-analysis. The computations are ongoing and further studies will be included.

We-O-16 ENVIRONMENTAL MANGANESE EXPOSURE AND POSTURAL BALANCE IN ADULTS LIVING NEAR A MANGANESE REFINERY

*Haynes EN, Standridge JS.

Background and aims: Industrial and environmental exposures to Mn have been associated with neurobehavioral dysfunction including deficits in motor function. Marietta, Ohio is home to the only Mn refinery in North America which has been emitting Mn into the Marietta airshed for over 50 years. The goal of this study was to determine the effect of non-occupational exposure to manganese on postural balance.

Methods: In this cross-sectional study, we collected hair and blood for metal analysis. Postural balance was assessed using a validated force platform system. The system tests the visual, proprioceptive and vestibular systems. All participants underwent a trial of four test conditions: eyes open on the platform (EO), eyes closed on the platform (EO), eyes open on a 4 inch thick foam pad placed on the platform (FO), and eyes closed on a 4 inch thick foam pad placed on the platform (FC). Study participants resided within a 10 mile radius of the refinery for at least 3 consecutive years. The relationship between hair Mn and postural balance was analyzed with logistic regression. Postural balance of participants and controls were adjusted for significant covariates and compared by analysis of covariance.

Results: Twenty-nine subjects participated in the study; 22 participants and 22 controls were included in the statistical analysis. Participant age ranged from 19 - 68 years (mean 50 yrs). Mean residence distance from the refinery was 0.3 to 9.7 miles (mean 5.8 miles). Blood Mn ranged from $4.2 \mu\text{g/L}$ - $21.7 \mu\text{g/L}$ (mean $9.4 \mu\text{g/L}$). Hair Mn ranged from 1.2 - $12.4 \mu\text{g/g}$ (mean $4.4 \mu\text{g/g}$). We found a significantly positive association between postural balance and hair Mn (EO, $p=0.05$; EC, $p=0.03$). Measures of postural balance in subjects were significantly larger when compared to controls in sway length (EO & FO, $p<0.05$) and sway area (EO, FO, & FC, $p<0.05$).

Discussion and conclusions: Preliminary findings indicate subclinical abnormalities in postural balance among residents living within 10 miles of a ferromanganese refinery for at least 3 years. Manganese may interfere with the integration and processing of sensory inputs within areas of the brain that maintain balance. Further research on the effects of chronic exposure to manganese is needed.

We-O-15 EPIDEMIOLOGICAL STUDY ON EXPOSURE TO MANGANESE THROUGH TAP WATER AND FOOD AND NEUROBEHAVIORAL FUNCTIONS AMONG PRIMARY SCHOOL CHILDREN IN QUÉBEC (CANADA)

*Bouchard M, Mergler D.

Background and aims: Exposure to manganese (Mn) is known to be associated with risks of neurotoxic effects, primarily in workplaces where airborne particulates are readily available to the nervous system through inhalation. Manganese is also an essential nutrient, and most of the total intake comes from the diet, with a small contribution from water ingestion (typically 1%, but up to 20% depending on the concentration in water). Limited data suggest that high concentrations in drinking water may also be associated with neurological impairment. Several regions in Quebec (Canada) have naturally occurring high concentration of manganese in groundwater. We conducted a pilot study on 46 children (age 6-14 years) living in houses serviced by wells with two contrasting manganese concentrations ($160 \mu\text{g/L}$ and $600 \mu\text{g/L}$). Significant relations were observed between i) manganese in water and in hair, and ii) manganese in hair and increased teachers' reported hyperactive and oppositional behaviors. Treatment reduced manganese to $<25 \mu\text{g/L}$ in the 2 wells. Follow-up of 33 children 4 months later showed that mean hair manganese had decreased from $5.0 \mu\text{g/g}$ (SD 4.3) to $0.7 \mu\text{g/g}$ (SD 0.6). We undertook a larger investigation of exposure to manganese through tap water and children's neurobehavioral functioning.

Methods: Children are recruited through primary schools, in communities chosen to represent a large gradient of water manganese concentration. Manganese in children's hair and tap water are assessed. A dietary study is being conducted to determine manganese intake through food. The battery includes tests for IQ, cognitive flexibility, concentration, impulsivity, verbal memory, learning, dexterity, and motor speed. Hyperactive behaviors are assessed by teachers and mothers. Numerous covariates are assessed in order to control for stimulation from the home environment, socio-economical status, mothers' IQ, and depressive feelings.

Results: To date, 180 children (age 6-12 years) have been recruited from 3 communities; 114 have been tested. The mean concentration of manganese in water was 110, 240 and $800 \mu\text{g/L}$. Preliminary results on hair and water manganese, as well as their relationship to neurobehavioral performances will be presented.

Discussion and conclusions: This study should provide information to derive safe exposure levels for manganese in drinking water, using the benchmark-dose approach.

PESTICIDES EXPOSURES, SYMPTOMS AND NEUROBEHAVIORAL OUTCOMES IN WORKERS

We-O-17 ACUTE SYMPTOMS FOLLOWING EXPOSURE TO PESTICIDES IN SHEEP-DIPPING

*Cherry NM, Povey A.

Background and aims: Sheep-dippers commonly complain of an acute flu-like syndrome within hours of dipping sheep. It is unknown whether this is a cholinergic effect from the sheep-dip or due to some other exposure, perhaps endotoxins. It was hypothesized that if flu were caused by pesticides it would be more common in those with susceptibility polymorphisms and/or handling concentrates; if it were due to other exposures it would be related only to the total number of sheep dipped.

Methods: Cases, sheep dippers with chronic neuropsychological symptoms, and referents, sheep dippers without, were recruited for a study of genetic susceptibility to organophosphates (previously reported). Subjects also recorded whether or not they had experienced acute symptoms after dipping (flu). Polymorphisms at positions 192 and 55 on the PON1 gene were determined from venous blood. Flu ever/never was examined in relation to genetic susceptibility and dipping exposures. A case-crossover analysis was designed to identify variable features of the dipping process within subject, with exposures compared in the first year flu was reported and in the previous, flu-free, year.

Results: Among cases 156/175 (64.2%) reported flu, compared with 87/234 (35.8%) referents (OR=13.87; 95%CI 8.04-23.93). The report of flu was not significantly related to either of the polymorphisms previously shown to be related to chronic neuropsychological illness, although for position 192 the odds ratio for an R allele was raised slightly (cases; OR=1.44; 95%CI 0.55-3.75; referents OR=1.36; 95%CI 0.79-2.33). In cases flu was related to having worked as a plunger (OR=5.09 95%CI 1.43-18.17) but not to handling concentrates (OR=1.01 95%CI 0.27-3.70). In referents, flu was related to a life-time total of dipping more than 50,000 sheep (OR= 1.94 95%CI 1.10-3.43) but again not significantly to handling concentrates (OR=1.36 95%CI=0.64-2.91). In the case-crossover study the number of sheep dipped/day was greater in the flu year (mean flu 575; no flu 536; $p=0.006$), however the proportion handling concentrates was also higher in those with flu (86.3% v 82.0%).

Discussion and conclusions: The weak relation to susceptibility genes and concentrates together with the greater number of sheep handled suggests that factors other than pesticides may account for at least some flu-like symptoms.