Chronic low-level mercury exposure, BDNF polymorphism, and associations with cognitive and motor function.


Battelle Centers for Public Health Research and Evaluation, Seattle, WA 98109, USA. echeverr@battelle.org

Potential cognitive and motor effects from exposure to elemental mercury (Hg(0)) were examined in the presence and absence of a polymorphism (Val66Met) in brain-derived neurotrophic factor (BDNF). A group of 194 male dentists (DDs) and 233 female dental assistants (DAs) were occupationally exposed to mercury and had no history of kidney or nervous system disorders. Acute exposure was measured using spot urinary Hg (HgU) concentrations (average 3.32 and 1.98 microg/l, respectively) and indices of chronic occupational exposure (26.3 and 14.9 years, respectively, weighted for historical exposures). The BDNF status was 68% and 66% wild type, 26% and 30% single substitution, and 5% and 4% full mutation for DDs and DAs, respectively. DDs and DAs were evaluated separately. Regression analyses controlled for age, premorbid intelligence, alcohol consumption, and education. Statistically significant adverse associations with HgU (p<.05) were found for nine measures among DDs (Digit Span (Forward), Digit and Spatial Span (Backward), Visual Reproduction, Finger Tapping (Dominant, Alternate, and Alternate Partialed), Hand Steadiness, and Tracking), and eight measures among DAs (Digit Span (Forward), Visual Reproduction, Pattern Discrimination (Rate), Symbol Digit (Rate), Trailmaking B, Finger Tapping (Dominant and Alternate Partialed), and Hand Steadiness). The BDNF status was associated with four measures in DDs and three measures in DAs. Joint effects were found for Finger Tapping (Alternate and Alternate Partialed) in DDs and Hand Steadiness and Trailmaking B in DAs. Joint effects were additive in all cases. Performance on verbal intelligence and reaction time were not associated with either HgU or BDNF status. A test of threshold effect for the association of Hand Steadiness with HgU demonstrated no lower boundary in both DDs and DAs. No associations were observed with estimates of chronic mercury exposure. Our findings are applicable to exposure levels of the general population and identify a potentially vulnerable group with a BDNF polymorphism.

The association between a genetic polymorphism of coproporphyrinogen oxidase, dental mercury exposure and neurobehavioral response in humans.

Echeverria D, Woods JS, Heyer NJ, Rholman D, Farin FM, Li T, Garabedian CE.

Battelle Centers for Public Health Research and Evaluation, 1100 Dexter Avenue North, Suite 400, Seattle, WA 98109, United States; Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, WA, United States.

We previously described a polymorphism in exon 4 of the gene encoding the heme biosynthetic pathway enzyme, coproporphyrinogen oxidase (CPOX4), which significantly modifies the effect of mercury exposure on urinary porphyrin excretion in humans. Here, we examined potential consequences of this polymorphism ("CPOX4") on performance within neurobehavioral domains, symptoms, and mood that are known to be affected by elemental mercury (Hg degrees).
exposure in human subjects. A behavioral test battery was administered on the day of urine and
buccal cell collections for 194 male dentists (DDs) and 233 female dental assistants (DAs)
occupationally exposed to Hg degrees for an average of 19 and 10 years, respectively. Subjects
had no history of health disorders and were employed for a minimum of 5 years in the dental
profession. Respective mean urinary mercury (HgU) levels in DDs and DAs were 3.32 (4.87)
mug/l and 1.98 (2.29) mug/l. Corresponding indices of chronic occupational Hg degrees
exposure, weighted for historical exposure, were 27.1 (20.6) and 15.2 (12.3). The frequencies of
the homogygous common (A/A), heterozygous (A/C), and homozygous polymorphic (C/C)
genotypes were 75%, 23% and 2% for DDs and 73%, 25%, and 2% for DAs, respectively. DDs
and DAs were evaluated separately. Regression analyses controlled for age, premorbid
intelligence, alcohol consumption, and education. Statistically significant associations with HgU
(p<0.05) were found for nine measures among DDs (BEES Digit Span(Forward and Backward),
WMS-R Visual Reproduction(N Correct), BEES Symbol Digit(Rate), BEES Finger
Tapping(Dom/Non-dom), (and Alternate Partialed), Hand Steadiness(Factor1), and BEES
Tracking), and eight measures among DAs (BEES Digit Span(Forward), BEES Symbol Digit(Rate), BEES Pattern Discrimination (Rate), BEES Trailmaking B, BEES Finger
Tapping(Dom/Non-dom, and Alternate Partialed), Hand Steadiness(Factor1), and Vibration
Sensitivity(Hits)). CPOX4 status was associated with four measures in DDs (BEES Spatial
Span(Forward), BEES Pattern Memory(N Correct), BEES Symbol Digit(Rate), and BEES
Vigilance(Hit)) and five measures in DAs (BEES Digit Span(Forward), WMS-R Visual
Reproductions(N Correct), BEES Symbol Digit(Rate), BEES Simple and Choice Reaction
Time(Move). Both groups experienced an additive effect (no interaction term) for HgU and the
CPOX4 polymorphisms on the Digit(Rate) whereas DAs also had additive effects for BEES Digit
Span(Forward) and for Beck's Depression factor 'Worthlessness'. These exploratory findings
suggest that the CPOX4 polymorphism may affect susceptibility for specific neurobehavioral
functions associated with mercury exposure in human subjects.