## Lead and cognitive function in *ALAD* genotypes in NHANES III

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**Background and objectives:** Lead is a neurotoxic metal whose pharmacokinetics varies in persons with different aminolevulinic acid dehydratase (*ALAD*) genotypes. These genotypes may modify the effect of lead on cognitive function by altering the amount of lead in nervous tissue or by altering biochemical pathways that produce other neurotoxic substances. The objective of this work was to determine if genetic variants in *ALAD* affect the relationships between blood lead levels and cognitive function in children and adults participating in the third National Health and Nutrition Examination Survey (NHANES III).

**Methods**: With data from the second phase of NHANES III, regression models were used to estimate the slopes between measurements of cognitive function and blood lead concentration in persons with different *ALAD rs1800435* genotypes, and to test for differences in the slopes between genotypes.

**Results**: As blood lead levels increased in 12 to 16 year old children (n = 840), their performance on the WRAT arithmetic and reading tests, and the WISC-R block design and digit span tests decreased. In adults 20 to 59 years old (n = 2090), simple reaction time decreased as blood lead level increased in the *ALAD CC+GC* group. In adults 60 years and older (n = 1796), the number of correct answers on a test of memory did not vary by blood lead level.

**Discussion/Conclusion:** Cognitive performance in 12 to 16 year old children decreased as blood lead level increased. Blood lead may decrease reaction times in adults by altering the concentration of δ-aminolevulinic acid, which can bind to the receptors of γ-aminobutyric acid, an inhibitory neurotransmitter in the central nervous system [3]. The lack of relationship between blood lead and test performance in adults may be due to the low blood lead levels, the insensitivity of the tests used, or statistical power that was not large enough.