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Low Dose Effect of Chronic Lead Exposure on Neuromotor Response Impairment in Children is Moderated by Genetic Polymorphisms

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ABSTRACT Previous research on children of the Cincinnati Lead Program Project (CCLP) showed a strong correlation of blood lead level with postural balance impairment. Here we investigated whether this association is dependent on genetic polymorphisms that are implicated with lead metabolism and/or neuromotor disorders, suggesting the role of gene-environment interaction in neurotoxicity of lead exposure in early life of children. Genotyping was done for 10 polymorphic sites on 83 children from the CLPP cohort, on whom postural balance measurements and average blood lead levels (PbB05) were available. Analysis of variance and regression analysis were performed to examine genotype-dependency on lead and postural balance. Heterogeneity tests of lead-postural balance regression coefficients were done to examine genotype dependency of lead-balance association. Two loci, Vitamin D Receptor (VDR) and Dopamine Receptor D3 (DRD3), showed suggestive evidence of genotype dependency of toxicokinetics of lead. Regression coefficients of PbB05 on postural sway area (s_A) under all test conditions were significantly heterogeneous for at least one or more of these genes. The three-way link between PbB05, postural sway, and genotypes suggested that at least three genes, Dopamine Receptor D2 (DRD2-A), Vitamin D Receptor (VDR), and N-Acetyltransferase 2 (NAT2), may be involved in moderating the detrimental effect of lead exposure on postural balance response. These observations provide preliminary evidence that toxicokentic effect of lead on neuromotor response may be moderated by genotypes at several genes.