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PON1 Genotype and Enzyme Activity, Organophosphate Pesticide Exposure, and Attention and Cognition in Children

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Background: Organophosphate pesticides (OPs) are associated with compromised attention and cognition in children. Our research has suggested that PON1 genotype is directly associated with neurodevelopment in toddlerhood, and may also modify associations between OP exposure and neurodevelopment.

Objective: To investigate the independent and interactive relationships of PON1 genotype and enzyme activity and in utero OP exposure with neurobehavioral outcomes at ages 5 and 7.

Methods: In a longitudinal cohort, we measured OP metabolites in maternal pregnancy urine, analyzed PON1192 and PON1-108 genotypes for mothers and children, measured PON1 enzyme activity in maternal prenatal, neonatal (cord), and child age 5 blood samples, and examined associations with attention and cognition at ages 5 and 7.

Results: Child PON1 enzyme activity showed independent and interactive associations with attention at age 5. Children with highest (>75th%) arylesterase (ARY) and chlorpyrifos-oxonase (CPO) levels measured in cord blood or at age 5 demonstrated significantly better performance on an attention task. Among children with the lowest enzyme activity levels at age 5, concurrent OP metabolite levels were inversely associated with performance. Maternal and child enzyme activity and genotype showed independent associations with cognition, though no effect modification. Most notably, ARY levels at age 5 were associated with better processing speed at age 7, and children with PON1-108 TT genotype showed consistent, though not statistically significant, verbal deficits.

Conclusion: Findings suggest that PON1 genotype/enzyme may directly influence children's neurobehavioral profile at early school age, but provide limited evidence that PON1 modifies effects of OPs on neurobehavioral outcomes.

Keywords: PON1, genotype, organophosphate pesticides, attention, cognition, children