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[Environ Health Perspect. 2010 Jan;118\(1\):144-9.](#)

Childhood brain tumors, residential insecticide exposure, and pesticide metabolism genes.

Nielsen SS, McKean-Cowdin R, Farin FM, Holly EA, Preston-Martin S, Mueller BA.

Public Health Sciences Division, Fred Hutchinson Cancer Research Center, Seattle, Washington, USA.

Background: Insecticides that target the nervous system may play a role in the development of childhood brain tumors (CBTs). Constitutive genetic variation affects metabolism of these chemicals. **Methods:** We analyzed population-based case-control data to examine whether CBT is associated with the functional genetic polymorphisms PON1C-108T, PON1Q192R, PON1L55M, BCHEA539T, FMO1C-9536A, FMO3E158K, ALDH3A1S134A, and GSTT1 (null). DNA was obtained from newborn screening archives for 201 cases and 285 controls, \leq 10 years of age, and born in California or Washington State between 1978 and 1990. Conception-to-diagnosis home insecticide treatment history was ascertained by interview. **Results:** We observed no biologically plausible main effects for any of the metabolic polymorphisms with CBT risk. However, we observed strong interactions between genotype and insecticide exposure during childhood. Among exposed children, CBT risk increased per PON1-108T allele [odds ratio (OR) = 1.8; 95% confidence interval (CI), 1.1-3.0] and FMO1-9536A (*6) allele (OR = 2.7; 95% CI, 1.2-5.9), whereas among children never exposed, CBT risk was not increased (PON1: OR = 0.7; 95% CI, 0.5-1.0, interaction $p = 0.005$; FMO1: OR = 1.0; 95% CI, 0.6-1.6, interaction $p = 0.009$). We observed a similar but statistically nonsignificant interaction between childhood exposure and BCHEA539T (interaction $p = 0.08$). These interactions were present among both Hispanic and non-Hispanic white children. **Conclusion:** Based on known effects of these variants, these results suggest that exposure in childhood to organophosphorus and perhaps to carbamate insecticides in combination with a reduced ability to detoxify them may be associated with CBT. Confirmation in other studies is required. **Editor's Summary** Established risk factors for childhood brain tumors (CBTs) are limited to ionizing radiation and rare heritable syndromes, but studies have reported some evidence of associations with insecticide exposures. Searles Nielsen et al. hypothesized that susceptibility might be increased in children with gene polymorphisms relevant to insecticide metabolism, including PON1C-108T, PON1Q192R, PON1L55M, BCHEA539T, FMO1C-9536A, FMO3E158K, ALDH3A1S134A, and GSTT1 (null). DNA was extracted from archival screening samples for 201 cases and 285 population-based controls \leq 10 years of age and born in California or Washington State between 1978 and 1990. Insecticide exposures during pregnancy and childhood were classified based on interviews with participants' mothers. The authors report that numbers of variant alleles (0, 1, or 2) or the presence (versus absence) of the GSTT1 null genotype were not associated with CBT based on adjusted odds ratios, but they observed multiplicative interactions between insecticide exposure during childhood (any versus none) and variant alleles of PON1-108T, FMO1C-9536A, and BCHEA539T. Results need to be confirmed in other study populations, but the authors conclude that findings are consistent with increased risks of CBT among children with a reduced capacity to detoxify insecticides.

PMID: 20056567 [PubMed - in process]

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