

Air Pollution and Risk of Neurobehavioral Problems: Is *APOE* ϵ 4 Status a Factor?

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Traffic-related air pollution (TRAP) has been associated with adverse respiratory, cardiovascular, and neurological outcomes,^{1,2,3} associations that may be moderated by an individual's genetic background.² A recent report in *Environmental Health Perspectives* suggests that school-age children who are carriers of a genetic allele called *APOE* ϵ 4 may be more susceptible to adverse neurobehavioral outcomes in association with TRAP exposures.⁴

In the past 10–15 years, studies have examined the relationship between TRAP and not only age-related neurodegenerative diseases^{5,6} but also adverse neurodevelopmental outcomes in children. The latter have included slower growth in cognitive function over time,⁷ higher attention and behavior problem scores,⁸ and a smaller volume of the caudate nucleus, a structure within the basal ganglia.⁹

The *APOE* gene encodes apolipoprotein E, a lipid-transporting protein in the brain. Carrying the ϵ 4 allele of *APOE*, as opposed to alternative alleles ϵ 2 and/or ϵ 3, is a risk factor for Alzheimer's disease.¹⁰ In both the young and the elderly, *APOE* may moderate the risks associated with environmental exposures, with TRAP as a case in point. For example, a study of children living in highly polluted Mexico City reported that brain magnetic spectroscopy imaging results differed between 22 children who were *APOE* ϵ 4 carriers and 28 who were not.¹¹

In the present study,⁴ researchers hypothesized that children's *APOE* ϵ 4 status could strengthen the relationship between TRAP exposure and negative neurodevelopmental outcomes. They used

data from the Brain Development and Air Pollution Ultrafine Particles in School Children (BREATHE) project. This cohort study examines TRAP-associated effects on cognitive function, behavior, and brain morphology among 2,897 Barcelona children 7–11 years of age.⁸

The current analysis involved 1,667 children with genotype data. The children completed cognitive tests up to four times in a year, and about 10% had undergone magnetic resonance imaging of the brain. Their parents completed questionnaires on behavior problems, while their teachers assessed them on symptoms associated with attention deficit/hyperactivity disorder.

TRAP exposure was estimated based on concentrations of polycyclic aromatic hydrocarbons, NO₂, and elemental carbon measured at the children's schools. Among the 23% of the children who were *APOE* ϵ 4 carriers, TRAP was more strongly associated with higher behavioral problem scores, less improvement on some cognitive function scores over time, and smaller caudate volumes, compared with noncarriers.

The differences in children's ability to improve their attentiveness scores may have long-lasting consequences, says study author Silvia Alemany, a postdoctoral fellow at the Barcelona Institute for Global Health. "For instance," she says, "this may not only affect their school performance but also the development of higher cognitive functions that rely on the consolidation of attention."

Caution is needed in interpreting the study findings due to the lack of a replication sample, nonsynchronous assessment of TRAP



A new study adds to the evidence that children who carry the *APOE* ϵ 4 allele may be more susceptible to adverse neurological effects of traffic-related air pollution exposures. Image: © lisegagneiStockphoto.

levels and outcomes, and inconsistencies between parent and teacher assessments. Nevertheless, the in-depth and sensitive assessments of several neurodevelopmental outcomes were particular strengths.

“When we think about some of the kinds of behavioral and neuropathological changes that are getting picked up in these studies, they don’t relate to a single neurodevelopmental disorder—a lot of these features are shared by multiple neurodevelopmental disorders,” says Deborah Cory-Slechta, a professor of environmental medicine, pediatrics, and public health sciences at the University of Rochester Medical Center, who was not associated with the study. “They share so many of these features that we have to start thinking about the risk much more broadly. I think this particular study reinforces that.”

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