

# Decreases in short-term memory, IQ, altered brain metabolic ratios in urban APOE4 children

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A new study by researchers at the Universities of Montana, Carleton, and North Carolina, and the Centro de Ciencias de la Atmósfera, Universidad Nacional Autónoma de México, heightens concerns over the detrimental impact of the apolipoprotein E (APOE)  $\epsilon$ 4 allele—the most prevalent genetic risk for Alzheimer's disease—upon cognition, olfaction, and metabolic brain indices in healthy urban children and teens. These findings are published in the *Journal of Alzheimer's Disease*.

These children have lifetime exposures to concentrations of [air pollutants](#) above the current USA standards, including [fine particulate matter](#) (PM 2.5). Metropolitan Mexico City is an example of extreme urban growth and serious environmental pollution and 8 million children are involuntarily exposed to harmful concentrations of PM 2.5 every day since conception.

The study focused on children's and teens' cognitive and olfaction responses using the Wechsler Intelligence Scale for Children (WISC-R) and the University of Pennsylvania Smell Identification Test. Researchers measured three major brain metabolites in hippocampus, pons and the white matter of the frontal and parietal lobes using proton magnetic resonance spectroscopy. Carriers of the APOE  $\epsilon$ 4 versus  $\epsilon$ 3 children had a key metabolite NAA/Cr ratio reduced in the right frontal white matter and showed significant decrements on attention, and short-term memory.

A worrisome finding in this study was the below-average scores in Verbal and Full Scale IQ (>10 points) in the Mexico City carriers of the gene associated with the risk for Alzheimer. APOE4 children had problems with odor detection and failed to identify the smell of soap more often than  $\epsilon$ 3 carriers. Interestingly, this finding strongly

correlated with the left hippocampus ml/Cr ratio, a ratio of key importance in Alzheimer's patients.

"APOE  $\epsilon$ 4 is likely playing a role in Mexico City children's response to their cumulative air pollution exposures. Of importance for health and educational issues, since Mexico City children mostly attend underprovided public schools that do not help in the development of executive function skills and do not build cognitive reserves, the >10 point IQ difference will likely have a negative impact on academic and social issues, including bullying and teen delinquency," said investigators Lilian Calderon-Garcidueñas, MD, PhD, The Center for Structural and Functional Neurosciences, University of Montana, and Amedeo D'Angiulli, PhD, Department of Neuroscience, Carleton University.

"The results add to growing data suggesting APOE  $\epsilon$ 4 carriers could have a higher risk of developing early AD if they reside in a polluted urban environment," added Dr. Calderon-Garcidueñas.

The authors argue that sustained exposures to urban air pollution result in cognitive underperformance and metabolic brain changes that reflect glial and neuronal alterations. The combined effects of residency in a highly polluted city and APOE  $\epsilon$ 4 could lead to an acceleration of neurodegenerative changes. Air pollution is a serious public health issue and exposures to concentrations of air pollutants at or above the current standards have been linked to neuroinflammation and neuropathology. In the US alone, 200 million people live in areas where pollutants such as ozone and fine particulate matter exceed the standards. There are significant associations between exposures to particulate matter and increased mortality due to stroke, cardiovascular, and respiratory events. The

problem in children living in megacities like Mexico City is much worse.

There is an urgent need to have a broader focus on APOE  $\epsilon$ 4 and air pollution interactions impacting children's brains and their responses could provide new avenues towards the unprecedented opportunity for Alzheimer's disease prevention. The authors concluded: "We have a 50-year window of opportunity between the time urban children experience the detrimental effects we are describing here, and when they will present with mild cognitive impairment and dementia. APOE  $\epsilon$ 4, the most prevalent genetic risk factor for AD, has been understudied in children and teens. We need support for studying the current pediatric clinical and imaging evidence in highly exposed urban [children](#). Our efforts should be aimed to identify and mitigate environmental factors influencing Alzheimer's disease."

**More information:** "Decreases in Short Term Memory, IQ, and Altered Brain Metabolic Ratios in Urban Apolipoprotein  $\epsilon$  4 Children Exposed to Air Pollution," by Lilian Calderon-Garcidue<sup>as</sup>, Antonieta Mora-Tiscare<sup>o</sup>, Maricela Franco-Lira, Hongtu Zhu, Zhaohua Lu, Edelmira Solorio, Ricardo Torres-Jardón and Amedeo D'Angiulli, [DOI: 10.3233/JAD-142685](https://doi.org/10.3233/JAD-142685), published online in advance of the Journal of Alzheimer's Disease, Volume 45, Issue 3 (March 2015).

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