Letters

COMMENT & RESPONSE

In Reply We thank Fuller-Thomson and Munro for their thoughtful comments on our recent study,[1] which identified robust associations between several outdoor air pollutants and adolescent psychotic experiences using data from the Environmental Risk (E-Risk) Longitudinal Twin Study. A 2-pollutant model, including fine particulate matter with aerodynamic diameters of less than 2.5 and nitrogen oxides (NO_x), showed that associations were driven by nitrogen species. Road vehicle emissions (particularly from diesel engines) are the primary source of nitrogen species such as NO_x and nitrogen dioxide (NO_2) in cities. Our findings provide initial evidence that air pollution levels could contribute to the well-established association between urban living and psychosis.

Fuller-Thomson and Munro raise the question of whether our measures of NO_x and NO_2 could be a proxy for prenatal and early-life exposure to tetraethyl lead. We welcome this interesting hypothesis but believe it is unlikely to entirely explain our findings.

In the United Kingdom, where the E-Risk Study is based, lead, a known neurotoxin, was not banned from gasoline until 2000. Children in the E-Risk Study were born in 1994 and 1995 and were exposed to lead from motor vehicle emissions until around age 6 years. It is indeed likely that adolescents with high NO_x/NO_2 exposure also had high lead exposure in infancy.

Fuller-Thomson and Munro describe converging evidence linking lead exposure to psychotic disorders,[2] including higher blood lead levels in individuals with first-episode psychosis. We agree that early-life lead exposure could plausibly increase the risk of psychosis. Indeed, members of our team recently conducted the world's longest mental health follow-up of lead-tested children born in the era of leaded gasoline,[3] to their knowledge, and found that blood lead levels at age 11 years were associated with increased thought disorder symptoms (including psychotic experiences) across adulthood.

Unfortunately, with our study design, we cannot separate the influence of NO_x and NO_2 from other nonmeasured vehicle-emitted pollutants, such as heavy metals, likely to be found in airways enriched with nitrogen species. Furthermore, as we discuss in our study,[1] our findings could more generally implicate factors correlated with road traffic. Noise pollution, which could increase risk for psychotic experiences by disrupting sleep and increasing stress, warrants consideration.

However, the evidence suggests that the associations we found were unlikely to be due solely to confounding by lead exposure. First, lead exposure from gasoline would have occurred early in life and, presumably, its influence manifest before age 18 years (that was the conclusion of our recent mental health follow-up[3]). However, associations between adolescent NO_x/NO_2 exposure and adolescent psychotic experiences were unchanged by adjustment for earlier childhood psychotic symptoms. Second, nitrogen species are potent oxidants and are suspected to injure nervous system tissue along known biological pathways[4] that could contribute to the etiology of psychotic experiences. More generally, rodent studies have shown that diesel exhaust emissions lead to neuroinflammation and dopaminergic neurotoxicity even without the presence of lead.[5]

Recent improvements in the availability and resolution of air pollution models will provide new opportunities to examine associations between air pollutants and mental health while considering lead and other traffic-related exposures.

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Published Online: July 17, 2019. doi:10.1001/jamapsychiatry.2019.1699

Conflict of Interest Disclosures: Dr Newbury reports salary support from the UK Economic and Social Research Council. Dr Reuben reports salary support from the National Institute of Environmental Health Sciences. Dr Fisher reports salary support from the British Academy.

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