A Section 508–conformant HTML version of this article
is available at https://doi.org/10.1289/EHP11224.

Invited Perspective: HEPA Filters—An Effective Way to Prevent Adverse Air Pollution Effects on Neurodevelopment?

Ulrike Gehring[1] *and Mireia Gascon*[2,3,4]

[1]Institute for Risk Assessment Sciences, Utrecht University, Utrecht, Netherlands
[2]Barcelona Institute for Global Health, Barcelona, Spain
[3]Universitat Pompeu Fabra, Barcelona, Spain
[4]CIBER Epidemiología y Salud Pública, Madrid, Spain

https://doi.org/10.1289/EHP11224

Refers to https://doi.org/10.1289/EHP10302

Air pollution is a major risk to public health globally that affects nearly every organ system,[1] and growing evidence indicates adverse effects of exposure to air pollution on the central nervous system.[2,3] The mechanisms underlying the neurological effects are not yet fully understood, but oxidative stress, chronic neuroinflammation, disruption of the blood–brain barrier, microglia activation, and white matter abnormalities are likely involved.[4] To the best of our knowledge, previous studies on effects on neurodevelopment were all observational; randomized controlled trials (RCTs), which are considered the gold standard in health research, are generally rare in environmental epidemiology because they are often considered unfeasible or unethical.[5] Therefore, the intervention study by Ulziikhuu et al. published in this issue of *Environmental Health Perspectives*[6] is a welcome addition to these observational studies. Fetal life is a period of particular interest for brain development and increased vulnerability to environmental stressors, given that this is a period of rapid growth, cell differentiation, and brain network development,[7,8] and early brain development can have long-lasting consequences for functioning.[9–11] Several studies reported that prenatal exposures to air pollutants—especially polycyclic aromatic hydrocarbons (PAHs), particulate matter with an aerodynamic diameter of ≤ 2.5 μm ($PM_{2.5}$), and nitrogen oxides—is associated with lower cognitive or psychomotor function and higher risks of behavioral problems, such as autism spectrum disorder in childhood.[12,13] Effects of prentatal exposure to air pollution during pregnancy have been suggested to be either direct, by air pollution crossing the placental barrier,[14] or indirect, by air pollution impairing placental functioning and decreasing transplacental nutrient and oxygen transport through systemic inflammation and oxidative stress.[15–17] However, gestation is likely not the only window of susceptibility given that there are also studies reporting associations with postnatal exposure.[12]

Ulziikhuu et al. conducted a single-blinded, parallel-group RCT among 540 nonsmoking pregnant women in Ulaanbaatar, Mongolia, where air pollution levels are high.[6] Participants were randomly assigned to an intervention group with high-efficiency particulate air (HEPA) filter air cleaners or to a control group with no air cleaners. HEPA filters have been shown to be effective in reducing exposures to indoor air pollutants.[18] Full-scale intelligence quotient (IQ) was assessed with the *Wechsler Preschool and Primary Scale of Intelligence, Fourth Edition*,[19] when the children were 4 years of age. In the intervention group, IQ scores were on average 2.8 points [95% confidence interval (CI): –0.1, 5.7] higher in an intention-to-treat analysis and 3.2 points (95% CI: 0.3, 6.0) higher in a complete case analysis, compared with the control group.

The use of an RCT is a strength of the study by Ulziikhuu et al.[6] Compliance with the intervention was relatively high, with HEPA filters being used during most of the pregnancy period by the intervention group participants [median (interquartile range): 70% (60–80%) of the time]. Still, the study has some limitations. As previously reported by Barn et al.[20] $PM_{2.5}$ levels measured in the participants' homes during pregnancy were lower in the intervention group than in the control group [40% (95% CI: 31%, 48%) lower at median 11 wk of gestation and 15% (95% CI: 0, 27%) lower at median 30 wk of gestation]. However, because no preintervention $PM_{2.5}$ measurements were performed, it remains unclear how much of the difference in $PM_{2.5}$ levels between the two study groups can be attributed to the intervention with the HEPA filters. Moreover, maternal blood cadmium levels were significantly lower (14%) in the intervention group than in the control group. Blood cadmium is a marker of secondhand smoke exposure that could have also been reduced by the HEPA filters, but food is another important source.[21] Without preintervention measurements also for blood cadmium, it remains unclear to what extent the difference between the two groups is attributable to the intervention. Therefore, it remains unclear whether differences in cognitive performance between the two study groups result from differences in $PM_{2.5}$ levels or differences in cadmium levels. This would be of interest to ascertain, given that there is some evidence for an association between cadmium exposure and cognitive development in children.[22–24] An analysis of the mutually adjusted associations of cognitive performance with $PM_{2.5}$ and cadmium levels might shed some light on this, but power could be an issue, given that measurements of $PM_{2.5}$ and cadmium were not available for all participants.[20]

Despite these limitations, the findings of this RCT by Ulziikhuu et al.[6] are of interest. Future studies with preintervention exposure measurements are needed to answer the questions on the extent to which specific exposures are reduced by the use of HEPA filters and which pollutant(s) are responsible for the observed association with lower IQ points. It is also important to stress here that, although there might be some potential in using HEPA filters for preventing adverse health effects of air pollution exposure, these health effects can be most effectively tackled by reducing emissions in the first place.

Address correspondence to Ulrike Gehring, Institute for Risk Assessment Sciences, Utrecht University, P.O. Box 80178, 3508 TD Utrecht, The Netherlands. Telephone: 31 (0)30 253 9486. Email: u.gehring@uu.nl

The authors declare they have no actual or potential competing financial interests.

M.G. acknowledges support from the Spanish Ministry of Science and Innovation and State Research Agency through the Centro de Excelencia Severo Ochoa 2019–2023 Program (CEX2018-000806-S), and support from the Generalitat de Catalunya through the Centres de Recerca de Catalunya Program.

Received 9 March 2022; Revised 13 April 2022; Accepted 2 June 2022; Published 24 June 2022.

References

1. Thurston GD, Kipen H, Annesi-Maesano I, Balmes J, Brook RD, Cromar K, et al. 2017. A joint ERS/ATS policy statement: what constitutes an adverse health effect of air pollution? An analytical framework. Eur Respir J 49(1):1600419, PMID: 28077473, https://doi.org/10.1183/13993003.00419-2016.
2. Volk HE, Perera F, Braun JM, Kingsley SL, Gray K, Buckley J, et al. 2021. Prenatal air pollution exposure and neurodevelopment: a review and blueprint for a harmonized approach within ECHO. Environ Res 196:110320, PMID: 33098817, https://doi.org/10.1016/j.envres.2020.110320.
3. Clifford A, Lang L, Chen R, Anstey KJ, Seaton A. 2016. Exposure to air pollution and cognitive functioning across the life course—a systematic literature review. Environ Res 147:383–398, PMID: 26945620, https://doi.org/10.1016/j.envres.2016.01.018.
4. Block ML, Elder A, Auten RL, Bilbo SD, Chen H, Chen JC, et al. 2012. The outdoor air pollution and brain health workshop. Neurotoxicology 33(5):972–984, PMID: 22981845, https://doi.org/10.1016/j.neuro.2012.08.014.
5. Allen RW, Barn PK, Lanphear BP. 2015. Randomized controlled trials in environmental health research: unethical or underutilized? PLoS Med 12(1):e1001775, PMID: 25562846, https://doi.org/10.1371/journal.pmed.1001775.
6. Ulziikhuu B, Gombojav E, Banzrai C, Batsukh S, Enkhtuya E, Boldbaatar B, et al. 2022. Portable HEPA filter air cleaner use during pregnancy and children's cognitive performance at four years of age: the UGAAR randomized controlled trial. Environ Health Perspect 130(6):067006, https://doi.org/10.1289/EHP10302.
7. Stiles J, Jernigan TL. 2010. The basics of brain development. Neuropsychol Rev 20(4):327–348, PMID: 21042938, https://doi.org/10.1007/s11065-010-9148-4.
8. Rice D, Barone S Jr. 2000. Critical periods of vulnerability for the developing nervous system: evidence from humans and animal models. Environ Health Perspect 108(suppl 3):511–533, PMID: 10852851, https://doi.org/10.1289/ehp.00108s3511.
9. Henrichs J, Schenk JJ, Barendregt CS, Schmidt HG, Steegers EA, Hofman A, et al. 2010. Fetal growth from mid- to late pregnancy is associated with infant development: the Generation R Study. Dev Med Child Neurol 52(7):644–651, PMID: 19832882, https://doi.org/10.1111/j.1469-8749.2009.03513.x.
10. Norris T, Johnson W, Petherick E, Cameron N, Oddie S, Johnson S, et al. 2018. Investigating the relationship between fetal growth and academic attainment: secondary analysis of the Born in Bradford (BiB) cohort. Int J Epidemiol 47(5):1475–1484, PMID: 30060064, https://doi.org/10.1093/ije/dyy157.
11. Davies C, Segre G, Estradé A, Radua J, De Micheli A, Provenzani U, et al. 2020. Prenatal and perinatal risk and protective factors for psychosis: a systematic review and meta-analysis. Lancet Psychiatry 7(5):399–410, PMID: 32220288, https://doi.org/10.1016/S2215-036 6(20)30057-2.
12. Suades-González E, Gascon M, Guxens M, Sunyer J. 2015. Air pollution and neuropsychological development: a review of the latest evidence. Endocrinology 156(10):3473–3482, PMID: 26241071, https://doi.org/10.1210/en.2015-1403.
13. Sunyer J, Dadvand P. 2019. Pre-natal brain development as a target for urban air pollution. Basic Clin Pharmacol Toxicol 125(suppl 3):81–88, PMID: 30884144, https://doi.org/10.1111/bcpt.13226.
14. Peterson BS, Rauh VA, Bansal R, Hao X, Toth Z, Nati G, et al. 2015. Effects of prenatal exposure to air pollutants (polycyclic aromatic hydrocarbons) on the development of brain white matter, cognition, and behavior in later childhood. JAMA Psychiatry 72(6):531–540, PMID: 25807066, https://doi.org/10.1001/jamapsychiatry.2015.57.
15. Carvalho MA, Bernardes LS, Hettfleisch K, Pastro LDM, Vieira SE, Saldiva SRDM, et al. 2016. Associations of maternal personal exposure to air pollution on fetal weight and fetoplacental Doppler: a prospective cohort study. Reprod Toxicol 62:9–17, PMID: 27103540, https://doi.org/10.1016/j.reprotox.2016.04.013.
16. van den Hooven EH, Pierik FH, de Kluizenaar Y, Hofman A, van Ratingen SW, Zandveld PYJ, et al. 2012. Air pollution exposure and markers of placental growth and function: the Generation R Study. Environ Health Perspect 120(12):1753–1759, PMID: 22922820, https://doi.org/10.1289/ehp.1204918.
17. Grevendonk L, Janssen BG, Vanpoucke C, Lefebvre W, Hoxha M, Bollati V, et al. 2016. Mitochondrial oxidative DNA damage and exposure to particulate air pollution in mother-newborn pairs. Environ Health 15:10, PMID: 26792633, https://doi.org/10.1186/s12940-016-0095-2.
18. Kelly FJ, Fussell JC. 2019. Improving indoor air quality, health and performance within environments where people live, travel, learn and work. Atmos Environ 200:90–109, https://doi.org/10.1016/j.atmosenv.2018.11.058.
19. Wechsler D. 2012. *WPPSI-IV: Wechsler Preschool and Primary Scale of Intelligence—Fourth Edition*. Bloomington, MN: Psychological Corporation.
20. Barn P, Gombojav E, Ochir C, Laagan B, Beejin B, Naidan G, et al. 2018. The effect of portable HEPA filter air cleaners on indoor $PM_{2.5}$ concentrations and second hand tobacco smoke exposure among pregnant women in Ulaanbaatar, Mongolia: the UGAAR randomized controlled trial. Sci Total Environ 615:1379–1389, PMID: 29751442, https://doi.org/10.1016/j.scitotenv.2017.09.291.
21. Schaefer HR, Dennis S, Fitzpatrick S. 2020. Cadmium: mitigation strategies to reduce dietary exposure. J Food Sci 85(2):260–267, PMID: 31957884, https://doi.org/10.1111/1750-3841.14997.
22. Gustin K, Tofail F, Vahter M, Kippler M. 2018. Cadmium exposure and cognitive abilities and behavior at 10 years of age: a prospective cohort study. Environ Int 113:259–268, PMID: 29459184, https://doi.org/10.1016/j.envint.2018.02.020.
23. Kippler M, Bottai M, Georgiou V, Koutra K, Chalkiadaki G, Kampouri M, et al. 2016. Impact of prenatal exposure to cadmium on cognitive development at preschool age and the importance of selenium and iodine. Eur J Epidemiol 31(11):1123–1134, PMID: 27147065, https://doi.org/10.1007/s10654-016-0151-9.
24. Wang Y, Chen L, Gao Y, Zhang Y, Wang C, Zhou Y, et al. 2016. Effects of prenatal exposure to cadmium on neurodevelopment of infants in Shandong, China. Environ Pollut 211:67–73, PMID: 26736057, https://doi.org/10.1016/j.envpol.2015.12.038.