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# **The Impact of Air Pollution on Neurocognitive Development: Adverse Effects and Health Disparities**

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### **Abstract**

Air pollution is recognized as a major public health concern. The number of deaths related to ambient air pollution has increased in recent years and is projected to continue rising. Additionally, both short- and long-term air pollution exposure has been linked with deleterious effects on neurocognitive function and development. While air pollution poses as a threat to everyone, people of color and individuals of lower socioeconomic status are often exposed to elevated levels of air pollution as a function of systemic racism and classism. Further, given additional disparities in access to healthcare and other compounding stressors, adverse effects of air pollution on neurocognitive health are exacerbated among individuals who hold marginalized identities – making effects both less likely to be detected and treated. This review examines evidence of the effects of air pollution on neurocognitive development across the lifespan and incorporates an environmental justice perspective to highlight disparities in air pollution exposure across race and socioeconomic status. Lastly, upon the reviewed evidence, limitations of past research and recommendations for policy are discussed.

#### **Keywords**

air pollution; neurocognitive development; health disparities; environmental justice

## **Introduction**

Addressing and mitigating poor air quality has been a long-standing environmental and public health issue. In the United States, the Clean Air Act (CAA), the first federal air quality law intended to limit air pollution, was enacted in 1963 (CAA, 1963). Over the past half-century, the CAA and other environment protection laws have helped to drastically reduce air pollution nationally. However, after decades of reduced emissions, the United States experienced a 5.7% increase in fine particulate matter (PM<sub>2.5</sub>) from 2016 to 2018 (Clay, Muller & Wang, 2021). Increases of natural gas emissions, nitrate production from motor vehicles, and wildfires in recent years have negatively impacted ambient air quality

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and contributed to these national increases of  $PM_{2.5}$  and other harmful air pollutants. Air pollution has been fully recognized as a significant public health problem (Kelly & Fussell, 2015), with increased levels of  $PM<sub>2.5</sub>$  contributing to an estimated 9,700 premature deaths and \$89 billion in damages in the U.S. alone (Clay, Muller & Wang, 2021). Exposure to fine particulate matter has also been associated with adverse effects on cognitive and brain development, with implications for physical and mental health outcomes (Bakolis et al., 2021; Genc et al., 2012; Zhang, Chen & Zhang, 2018). Further, there are widespread inequities present in exposure to air pollution and its resultant effects (Pratt et al., 2015; Zou et al., 2014). The present review outlines the effects of air pollution on neurocognition over development, the disproportionate impact of air pollution on historically marginalized groups, and recommendations for policy.

Air pollution represents a combination of diverse components, including particulate matter (PM), gases, organic compounds, and toxic metals (Costa et al., 2014; Genc et al., 2012) that can be found in both outdoor and indoor air. Although there are many types of air pollutants inside the Earth's atmosphere (e.g., elevated levels of ozone, lead, sulfur dioxide, nitrogen dioxide, carbon monoxide), this review's primary focus is the impact of  $PM_{2.5}$  and ultrafine particulate matter (UFPM), given these compounds' ability to enter the circulatory system and penetrate organs, including the brain (Costa et al., 2014; Miller et al., 2021). Particulate matter is characterized by its size and aerodynamic features that affect biological properties (Genc et al., 2012; Oudin, 2020). Fine particulate matter is classified as  $< 2.5$  µm and UFPM as < 0.1 μm (Genc et al., 2012) and is believed to be the most widespread and threatening air pollutant (Costa et al., 2014; Suades-González et al., 2015).

Across different research studies, multiple methods have been used to estimate exposure to air pollution and its constituent compounds. Many of the research studies in the present review rely on participants' reported zip code or reported residential address, then use pollutant measurements from nearby municipal monitoring sites to provide an estimate of annual exposure. Over time, the models used to estimate pollution exposure from such measurements have evolved, incorporating algorithms such as land-use regression that draw on geographical characteristics of the terrain, climate patterns, and human land use to improve their predictive ability (Hoek et al., 2008). However, it has also been noted that these approaches have limitations in their ability to provide exact measures of personal air pollution exposure, including missing data, missing geographic areas (dependent on the location of monitoring sites), and failing to capture variations in pollutant exposure as a function of where people live versus work/study (Gray, Edwards, & Miranda, 2013). A more limited number of research studies in the present review have incorporated direct personal monitoring of air quality (i.e., at participants' residential or school sites, or using devices carried by participants), used participant residential addresses to compare between individuals living relatively close versus far from major roadways to examine relative pollutant exposure, or used biomarkers of benzene collected from participant urine samples as a more direct marker of traffic-related pollution exposure (i.e., Kicinski et al., 2015). However, these approaches also have practical limitations, especially in large-scale population studies.

Along with long-documented effects on respiratory and cardiac function (Brunekreef & Holgate, 2002), recognition that air pollution adversely affects the brain and nervous system has been growing in the past two decades (Genc et al., 2012). Converging observations across animal, in vitro, and human studies suggest that the biological mechanisms by which air pollution may harm neurocognitive development include increases in oxidative stress and neuroinflammation (reviewed in Costa et al., 2014; Costa et al., 2020). Early studies of postmortem brain tissue from canines from the Mexico City area (characterized by high levels of air pollution) relative to control samples from a less-polluted region suggested that higher air pollution exposure might be linked to elevated neuroinflammation, DNA damage, and evidence of neurodegeneration in cortical and glial cells (Calderón-Garcidueñas et al. 2002, 2003). In vitro studies confirm cytotoxic effects of particulate matter exposure, resulting in elevated oxidative stress and inflammation (Block et al., 2004; Xu et al., 2020). Consistent with these findings in animal and *in vitro* models, studies in humans have reported higher levels of proinflammatory markers in cerebrospinal fluid of the brain as a function of air pollution exposure (Calderón-Garcidueñas et al., 2008).

Such changes at the cellular level may serve as mechanisms underlying observed adverse effects of air pollution on human health. Short-term exposure to harmful air is associated with increased risk of asthma-related emergency room visits (Dominici et al., 2006; Yang et al., 2019; Zheng et al., 2015), increased inflammation (Dauchet et al., 2018; Tsai et al., 2019), and short-term cognitive decline (Shehab & Pope, 2019). Chronic exposure to air pollution is associated with higher incidences of cardiovascular diseases (Brook et al., 2010; Chi et al., 2016; Rajagopalan, Al-Kindi, & Brook, 2018; Tonne et al., 2007), respiratory diseases (Katanoda et al., 2011; Kravitz-Wirtz et al., 2018; Raju et al., 2019), neurodegenerative disorders (Costa et al., 2017; Oudin, 2020; Power et al., 2016), and neurodevelopmental delays (Block et al., 2012; Clifford et al., 2016; Costa et al., 2017). Prolonged exposure to ambient air pollution has been linked to increased rates of depression (Gładka, Rymaszewska, & Zato ski, 2018; Kim et al., 2016), aggressive behavior (Burkhardt et al., 2020), and other mental health challenges (Miller et al., 2019; Tzivian et al., 2015).

While detrimental effects of air pollution on human health are well-established, its impact has been inequitably distributed, with some communities affected more than others. Global evidence (including studies from North American, South American, European, Asian, and African locations) indicate a link between socioeconomic status (SES) and exposure to air pollution: specifically, individuals that experience economic hardship are more likely to reside in areas with elevated levels of air pollution (Evans & Kantrowitz, 2002; Martins et al., 2004; Hajat, Hsia & O'Neill, 2015; Yang & Liu, 2018; Ofoezie et al., 2022). In the United States, Americans of color are disproportionately exposed to and negatively impacted by air pollutants relative to White Americans (Hadeed et al., 2021; Wooduff et al., 2003).

Taken together, this manuscript reviews recent evidence of the impact of air pollution (with a particular focus on  $PM_{2.5}$  and UFPM) on neurocognitive function and development and related health disparities. We largely focus on evidence from studies based in the United States, but also draw on findings from studies conducted globally. We note that the evidence reviewed generally indicates consistent findings regarding the adverse

impact of air pollution across geographic regions, but that the present review does not systematically compare for differences in outcomes as a function of location. Additionally, given variability in the neurocognitive outcomes examined relative to air pollution exposure across studies in current literature, we review evidence from studies utilizing a broad range of cognitive, behavioral, and neural outcomes, including measures of cognitive performance from multiple domains (such as attention, memory, visual, verbal, and motor function) as well as related measures such as IQ and academic performance, sleep and behavioral outcomes (such as hyperactivity), and measures of brain structure, function, and connectivity. We use a lifespan perspective, examining adverse effects of air pollution at ages ranging from gestation to older adulthood, as well as intersecting influences of poverty and racism associated with disparities in the adverse effects of air pollution on cognition and neurodevelopment. Finally, on the basis of the reviewed evidence, we will present policy recommendations to address both the impact of air pollution generally as well as in terms of racial, ethnic, and socio-economic disparities. These policy recommendations are primarily framed within the United States context, given that the reviewed evidence is largely United States-based, as are the manuscript authors.

#### **Impact of Air Pollution on Cognition and Behavior Over the Lifespan**

A growing literature provides evidence that air pollution exposure adversely effects cognitive and behavioral outcomes across a broad range of domains and over the course of the lifespan. In the present section, we highlight key findings from this literature, organized chronologically from the prenatal and infant stage through adolescence to older adulthood.

The early years of life are critical for the development of cognitive processes, including attention, memory, language and motor functions, essential to adaptive behavior and daily activities (Johnson & Munakata, 2005; Kundakovic & Champagne, 2015). An ever-growing body of research has implicated air pollution as a harmful agent that disrupts cognitive functioning and development. There is mounting evidence that adverse cognitive outcomes are associated with exposure to fine particulate matter beginning in the prenatal period. Utilizing data from 1,109 mother-child dyads in Massachusetts, Harris and colleagues (2015) found that prenatal residential proximity to major roadways (i.e., higher exposure to traffic-related air pollutants) measured during the third trimester predicted lower verbal and nonverbal skills as well as poorer visuomotor abilities in middle childhood (at ~8 years of age), controlling for demographic and parental factors, neighborhood income, and predictors of indoor pollution. Furthermore, a systemic review of 126 recent epidemiological studies examining air pollution exposure and neuropsychological development during infancy and early childhood identified a significant association between air pollution during gestation and infant cognitive development (Suades-González et al., 2015). Specifically, exposure to high levels of  $PM<sub>2</sub>$ , during the prenatal period was linked to delayed global, verbal, and psychomotor development during infancy.

There is also evidence that prenatal exposure to air pollutants can adversely affect sleep and behavioral outcomes during early childhood. Bose and colleagues (2019) examined gestational  $PM<sub>2</sub>$ <sub>5</sub> exposure, estimated from reported residential addresses, and sleep outcomes subsequently in childhood in a sample of parents and children from Mexico City,

a geographic region characterized by high levels of air pollution (Calderón-Garcidueñas et al., 2016; Mahady et al., 2020). Bose et al. identified a sensitive period at 31-35 weeks of gestation (i.e., during the third trimester), during which  $PM<sub>2.5</sub>$  exposure was significantly associated with decreased total hours of sleep later during the preschool years. The American Association of Sleep Medicine (AASM) recommends that children between the ages of three and five years old get 10-13 hours of sleep every day (Paruthi et al., 2016). However, the sample of children examined in Bose et al. (2019) averaged 7.8 hours of sleep a day, well below this recommendation, even when controlling for SES, mother's body mass index, season, and maternal age. Bose et al. (2019) also found that prenatal PM<sub>2.5</sub> exposure at 1-8 weeks (i.e., during the first trimester) was associated with lower sleep efficiency (defined as the percentage of time spent in bed asleep vs awake) during the children's preschool years. The authors linked these poor sleep outcomes to heightened regional pollution exposure during pregnancy. Importantly, reduced sleep hours and poor sleep quality during this developmental stage can lead to challenges in cognitive function, weight problems, and behavioral maladjustment (Spruyt, 2019).

Exposure to high levels of air pollution during infancy are also associated with elevated rates of neurodevelopmental disorders such as attention deficit/hyperactivity disorder (ADHD) (Aghaei et al., 2019; Costa et al., 2020; Siddique et al., 2011; Thygesen et al., 2020). A 2016 meta-analysis of the relationship between early life exposure to air pollution and Autism Spectrum Disorder (ASD) risk provided limited evidence of toxicity for this association, with the strongest observed relationship between air pollution and ASD diagnosis for  $PM_{2.5}$ (Lam et al., 2016). Notably, this meta-analysis included both studies of prenatal as well as postnatal exposure, but did not systematically test for differences in the association between pollution and ASD diagnosis as a function of exposure period. Relatedly, longitudinal data from the Cincinnati Childhood Allergy and Air Pollution Study, which recruited Cincinnatiarea children from families living near (< 400 metres) or far (> 1500 metres) from a major highway or bus route, indicates that exposure to higher levels of traffic-related air pollution during the first year of life predicts subsequent rates of hyperactivity, a key behavioral characteristic of ADHD, at ~7 years of age (Newman et al., 2013).

These studies together provide important evidence that exposure to air pollution during the prenatal period and early life is associated with adverse effects on cognitive and behavioral outcomes. However, given limited research literature investigating this relationship as well as heterogeneity in analysis approaches, observed results, and studied periods of exposure over the course of pregnancy, it is currently an open question whether specific critical periods during pregnancy exist whereby air pollution exposure presents a greater or lesser threat to cognitive development (Suades-González et al., 2015). Some studies of brain development have suggested that air pollution exposure during pregnancy might be most impactful on neural outcomes during the third trimester, as discussed in more detail below (see in The Impact of Air Pollution on Brain Health Over the Lifespan).

Along with evidence that poor air quality during early development is associated with adverse cognitive and behavioral outcomes, studies suggest that improving air quality might improve such outcomes as well as related metrics such as academic performance. Stafford (2015) conducted a natural quasi-experiment that included virtually every elementary

school within a Texas school district and reported that students' standardized test pass rates improved with mold removal  $(\sim 3-4\%$  increase), renovations to air ventilation  $(\sim 2-3\%$ increase), and roofing replacement  $(\sim 3\%$  increase) in the schools. These results remained significant even after controlling for confounding variables such as student attendance, school finances, and sociodemographic characteristics. On the basis of these observations, Stafford (2015) posited that renovations to improve schools' indoor air quality may be a cost-effective way to improve students' test scores, relative to other strategies such as reducing classroom sizes. While PM2.5 concentrations were not directly characterized in this study, Stafford's results suggest a relationship between air quality and cognitive/ academic performance to be explored further in future work. These findings also highlight one possible strategy for mitigating the impacts of poor air quality, an issue we return to later in the paper.

Adolescence is also a critical period for cognitive and behavioral development (Steinberg, 2005) but the impact of air pollution exposure on cognitive performance in adolescence has been understudied relative to its impact earlier in childhood. Kicinski et al. (2015) conducted an initial study investigating the association between traffic-related air pollution (characterized using biomarkers of benzene from urine samples as well as self-reported exposure to traffic) and performance on a series of neurobehavioral tasks (assessing sustained attention, short-term memory, and manual motor speed) in an adolescent sample (N=606) based in the Netherlands. They reported that increased traffic-related pollution exposure was associated with decreased sustained attention – specifically, for every one standard deviation (SD) increase in composite traffic-related air pollution exposure, they observed a 0.26 SD decrease in sustained attention performance (approximately one-third of the effect size of maternal education on attentional performance in this sample). On the other hand, Kusters et al. (2022) examined associations between prenatal and childhood air pollution exposure (using estimates based on residential address) and cognitive and behavioral outcomes (including processing speed, working memory, fluid reasoning, and IQ measures) in adolescents 13-16 years old (N=4683) from the Generation R longitudinal study conducted in the Netherlands. For the most part, these relationships were insignificant (or even positive, as observed between exposure to a small number of pollutant compounds and fluid reasoning as well as verbal IQ; these positive results were interpreted as reflecting negative residual confounds, selection bias, or chance). While further research needs to be done to characterize these relationships further, taken together, current findings indicate that air pollution is associated with adverse cognitive and behavioral outcomes during infancy and childhood in terms of lower verbal and nonverbal skills, visuomotor abilities, delayed psychomotor development, sleep, and academic performance, as well as poorer attentional performance in adolescence.

In addition to evidence indicating that ambient air pollution adversely impacts cognitive functioning in early life, numerous studies demonstrate that air pollution has negative effects on cognitive performance in adulthood as well. In a sample of 1,764 American adults ages 20-59 years in the Third National Health and Nutrition Examination Survey (NHANES-III), Chen and Schwartz (2009) observed cross-sectional associations between greater long-term exposure to air pollution (assessed using participants' residential location at the time of study enrollment and measurements of annual  $PM_{10}$  levels to approximate long-term

exposure to ambient air pollution; note that  $PM_{2.5}$  levels were not measured in this study) and reduced cognitive performance (measures of reaction time, visuomotor speed, sustained attention, perceptual functioning, and short-term memory). La Nauze and Severnini (2021) provided further cross-sectional evidence for the relation between air pollution and cognitive functioning: by examining performance on popular brain-training games as a function of users' geographic location (measured by zip code) within the United States, they were able to characterize the relationship between  $PM_{2.5}$  exposure (estimated by zip code using monitoring data) and adult cognitive functioning across seven domains (verbal, attention, flexibility, memory, math, speed, and problem solving). Their results suggested that increasing levels of  $PM_{2.5}$  were associated with poorer cognitive performance, with the strongest deleterious effects observed on memory performance. Additionally, the inverse relationship between  $PM<sub>2.5</sub>$  exposure and cognitive performance was strongest in low-performing individuals, suggesting that PM<sub>2.5</sub> exposure might compound with other influences to exacerbate inequalities in cognitive performance. Finally, in this sample, the strongest negative relationship between air pollution exposure and cognitive performance was observed in young to middle-aged adults (under 50 years). Given that adults in this age range comprise a large portion of the workforce (Bureau of Labor Statistics, 2022), this finding implies that air pollution might impact group-level work performance, with major economic implications.

Adverse effects of air pollution on cognitive performance have also been observed in older adulthood. A recent systematic review identified multiple studies, both longitudinal and cross-sectional, demonstrating that elevated exposure to  $PM<sub>2.5</sub>$  was negatively associated with verbal learning and working memory abilities in older adults globally (Clifford et al., 2016). Additionally, by reviewing global epidemiological and experimental data, Oudin (2020) identified that long-term air pollution exposure was associated with elevated risk of Alzheimer's disease (AD), vascular dementia, and mild cognitive impairment in older adults. Delgado-Saborit et al. (2021) highlight further evidence, both longitudinal and cross-sectional, that chronic exposure to high levels of air pollution was associated with declining global cognition and visuo-spatial abilities in older adults at an accelerated rate beyond normative aging; this decline was also associated with increased risk of developing dementia. Given exponential growth of older adults as a proportion of the United States population (Vespa, 2018), the link between air pollution exposure and accelerated agerelated cognitive decline is particularly important from a public health standpoint.

Taken together, this reviewed evidence demonstrates the negative impact of air pollution on cognitive functioning. These adverse effects can be observed in a wide range of cognitive domains across the lifespan, with widespread implications for daily behavior, academic and behavioral outcomes, as well as rates of cognitive decline and dementia later in life.

#### **The Impact of Air Pollution on Brain Health Over the Lifespan**

Along with adverse effects on cognition and behavior, air pollution exposure has been associated with alterations in the development of brain structure, function, and connectivity across the lifespan. Organized similarly to our review of cognitive and behavioral outcomes

above, the present section reviews evidence regarding the impact of air pollution on brain health, spanning from the prenatal stage to older adulthood.

Exposure to PM $_2$ <sub>5</sub> during pregnancy, estimated using measurements of pollutant compound concentrations and traffic exposure by birth county, has been linked to low birthweight (Bell et al., 2010) which increases risk of neurological disorders, intellectual impairment, and other developmental challenges (Martinussen et al., 2005). Bell et al. (2010) further suggested that the relationship between  $PM<sub>2</sub>$  exposure and low birth weight may be more robust for exposure during the third trimester. Additionally, Nawrot et al. (2018) reported that  $PM<sub>2.5</sub>$  exposure during the third trimester, estimated from monitoring site data using residential address, influenced methylation of circadian pathway genes in both parent and fetus. Given the critical role of circadian rhythms (internal processes that regulate the sleep-wake cycle) in biological, psychological, and social development (Foster, 2020), such disruption can have serious health implications, including elevated risk of premature birth (Kajeepeta et al., 2014, Reschke et al., 2018), adverse experiences at birth (van den Berg et al., 2017), and neurological disorders (Nawrot et al., 2018). Ambient PM<sub>2.5</sub> exposure is also associated with alterations in brain structure and function during development (Bell et al., 2005; Block et al., 2012; Calderón-Garcidueñas et al., 2016; Costa et al., 2017). A recent systematic review (de Prado Bert et al., 2018) of effects of air pollution exposure on the brain over the course of development suggested that children with greater exposure to  $PM_{2.5}$  displayed reduced white matter structure throughout the brain, including in the frontal, parietal, and temporal lobes, which in turn were associated with deficits in attention, short-term memory, and learning abilities, as well as deleterious effects on behavioral and psychomotor development in children. While not directly measuring for differences in the relative impact of air pollution on the brain as a function of prenatal period exposure, de Prado Bert et al. (2018) also suggest that the third trimester of pregnancy might be particularly critical given that neuron myelination starts during this period and follows specific spatiotemporal ordering (Baumann & Pham-Dinh, 2001) that may be disrupted by exposure to toxins (Maiuolo et al., 2019). However, as when considering cognitive and behavioral outcomes, additional research is needed to pinpoint critical periods during pregnancy where brain development and neural outcomes may be most vulnerable to the impact of air pollution exposure.

While early life is a critical period for brain development, large-scale functional networks of the brain continue to mature through childhood and adolescence; evidence suggests that the impact of air pollution on neurodevelopment also continues through this period. Pujol et al. (2016) used functional magnetic resonance imaging (fMRI) to examine effects of traffic pollution exposure on functional brain connectivity during a sensory task in a Barcelona-based sample of children ages 8-12 years. Increased exposure to traffic-related air pollution, measured directly at children's school sites during class time for two 1-week periods separated by 6 months, was associated with reduced integration and segregation in brain networks supporting both internally- and externally-guided cognition (the default mode network and task-related networks; Fox et al., 2005), as well as poorer attention and motor task performance. Herting and colleagues (2019) conducted a systematic review of structural and function MRI studies to evaluate how early-life exposure to ambient air pollution affects neurodevelopment, and identified that higher levels of outdoor air pollution

were associated with abnormalities (both decreases and increases) in white matter, cortical and subcortical gray matter, and brain volume within pre-adolescent children (under 13 years old). Finally, Miller and colleagues (2021) examined longitudinal effects of PM<sub>2.5</sub> and early life stress (ELS), as well as their interaction, on adolescent brain development in a sample of 115 San Francisco and San Jose Bay Area adolescents.  $PM_2$ , exposure was estimated for each participant using satellite-derived estimates of  $PM_{2.5}$  concentrations relative to reported residential address. Miller et al. identified changes in brain volume associated with both independent and interactive effects of ELS severity and  $PM_{2.5}$  levels; further, adverse effects of  $PM_{2.5}$  were attenuated in adolescents with histories of more severe ELS. Together, the results of these studies demonstrate the negative impact of air pollution on brain development and associated cognitive function during childhood and adolescence.

In contrast to literature examining effects of air pollution on neurodevelopment in childhood and adolescence, relatively few studies have examined effects of air pollution on brain health in older adulthood. In one such study, Hedges and colleagues (2019) evaluated the crosssectional relation between estimated exposure to atmospheric toxins, based on reported residential address, and hippocampal volume in a United Kingdom-based sample of adults between 40-69 years. The study observed reduced left hippocampal volume with increasing exposure to  $PM_{2.5}$ ; these effects were significant even when controlling for age, sex, bodymass index, overall health, alcohol use, smoking, education attainment, and socioeconomic status. These findings are particularly alarming given the vital role of the hippocampus in learning and memory, and observations of reduced cognitive function in association with hippocampal volume reductions in cognitive aging, dementia, and neuropsychiatric diseases (Hedges et al., 2019). Relatedly, Chen and colleagues (2015) longitudinally examined the adverse effects of ambient  $PM_{2.5}$  (estimated using residential history and monitoring data) on brain matter in a sample of 1,403 older women (age range: 71-89 years) in the United States-based Women's Health Initiative Memory Study (WHIMS). Chen et al. observed that in this sample, greater long-term exposure to  $PM_{2.5}$  predicted significant reductions in frontal lobe, temporal lobe, and corpus callosum white matter volume, independent of demographic factors, SES, lifestyle factors, and geographical region (although notably, in contrast to Hedges et al. (2019), Chen et al. (2015) did not observe a significant relationship between  $PM<sub>2.5</sub>$  exposure and hippocampal volume). Finally, exposure to particulate matter and environmental nanoparticles has been identified as a risk factor for the development of neuroinflammation and neurodegeneration in older adulthood (Calderón-Garcidueñas et al., 2016; Costa et al., 2017). In recent years, there has been increasing evidence linking air pollution to diseases of the central nervous system (CNS), including stroke, Alzheimer's disease, Parkinson's disease, and neurodevelopmental disorders (Block et al., 2012; Genc et al., 2012). Taken together, these findings indicate that air pollution has deleterious effects on brain health and development at all stages of the lifespan, with widespread health, economic, and human costs.

#### **Disparities in Exposure to and Impact of Air Pollution**

While there is mounting evidence that environmental contaminants pose a threat to all of us, exposure to low air quality does not affect everyone to the same extent. In particular, growing evidence indicates that exposure to air pollution might vary as a function of race

and socioeconomic status as a result of systemic racism and classism. These differences in air pollution exposure compound with other group disparities in health, education systems, and other factors to amplify disparities in related health outcomes, including those in the neurocognitive domain. These compounding disparities and the need to address them has been recognized as a fundamental issue of environmental justice by the Environmental Protection Agency (EPA) and other federal agencies in the United States [\(https://www.epa.gov/ej-research](https://www.epa.gov/ej-research)). Below, we review evidence of racial/ethnic and SESrelated disparities in air pollution exposure and impact, and advocate for evidence-based policy changes to reduce both air pollution exposure as well as disparities in its impact. Given that our policy recommendations below are targeted towards the United States, we primarily focus on evidence of United States-based disparities, although note that studies have suggested that similar racial/ethnic- and socioeconomic status-related disparities in air pollution exposure exist globally, including in France (Havard et al., 2009), Ghana (Rooney et al., 2012), India (Kopas et al., 2020), and China (Yang et al., 2022) and that calls have been made for more comprehensive studies of pollution-related health disparities outside the United States as well as comparatively (Jerrett, 2009).

Decades of research has demonstrated that exposure to air pollutants varies as a function of socioeconomic status (SES): specifically, lower-SES communities have often been the target of policies resulting in greater concentrations of air pollution (Ferguson et al., 2020) such as higher exposure to traffic and industrial emissions (Havard et al., 2009). A study conducted in North Carolina revealed that neighborhood-level concentration of fine particulate matter, estimated using air quality monitoring data and numerical output, was significantly associated with three SES-related factors: median household income, percentage of people living below the poverty line, and percentage of people with less than a high school education within the population (Gray, Edwards & Miranda, 2013). Further, Hajat et al. (2013) reported that in the Multi-Ethnic Study of Atherosclerosis (MESA), a large population-based study conducted in several regions of the United States, increased SES at both the neighborhood- and individual-level was significantly inversely correlated with air pollutant concentration levels (estimated for each participant's home address using a combination of air quality monitoring data, personal sampling, measures of housing quality, and geographic covariates), even after adjusting for demographic variables and metropolitan area. This relationship was larger for neighborhood-level SES, although relationships between pollutant levels and both SES measures were significant. The significant inverse relationship between neighborhood-level SES and air pollutant levels may be understood as the product of policy decisions leading to elevated traffic and industrial emissions exposure in lower-SES neighborhoods; the similar relationship observed for individual-level SES may also reflect such community-level influences as well as related factors at the individual level (i.e., housing quality and direct proximity to roadways; but Hajat et al. also note that the extent to which individual- and neighborhood-level SES variables in the MESA dataset capture shared variance remains unclear given differences in their data collection).

In addition to the disparities in exposure and adverse effects of air pollution across socioeconomic status, people of color are also disproportionately impacted by air pollution. Nationally, this can be understood as a legacy of the United States' longstanding history of racist segregation policies, corresponding disparities in neighborhood development, and

broader structural violence towards racial and ethnic minorities (Namin et al., 2020; Smith & Stovall, 2008; Woo et al., 2019). Using census block group data from American urban areas, Ash and Fetter (2004) reported that Black and African American populations are higher in cities with higher levels of air pollution; and within those cities, Black populations are higher in heavily polluted neighborhoods, as are Latino populations. Using urban census tract data from across the United States, Zou and colleagues (2014) provided further evidence that on average, African Americans, Native Americans and Indigenous people, along with Asian Americans and Pacific Islanders (AAPI), are exposed to greater levels of air pollutants than White Americans.

While there is mounting evidence that socioeconomic status and systemic race/ethnicitybased discrimination each predict ambient air pollution exposure independently, effects of economic and racial-ethnic disparities can also compound. Grineski, Bolin, and Boone (2007) uncovered that in the Phoenix metropolitan area, neighborhood-level SES was negatively associated with estimated carbon monoxide (CO) levels, indicating that neighborhoods with lower SES had higher levels of CO. Grineski et al. also reported that racial/ethnic neighborhood composition was a significant and positive predictor of exposure to CO pollution: specifically, neighborhoods with higher proportions of Native Americans and Latino immigrants had higher levels of CO, independent of SES. Housing tenure was also a significant predictor of CO exposure: areas with higher proportion of renters (relative to homeowners) had higher levels of CO. These results are especially concerning given that the Phoenix Metropolitan area is the fifth largest metropolitan area in the U.S., one of the fastest growing areas in the country, and has failed to meet EPA standards for atmospheric pollutants for decades (Grineski, Bolin, & Boone, 2007). These findings indicate that while poor air quality poses a health threat to everyone in a given region, historically marginalized communities might be particularly exposed to the harmful effects of air pollution.

In addition to increased exposure to air pollution at the neighborhood level, low-income and historically marginalized communities may also be exposed to elevated air pollution within the household. Poverty is strongly related to increased exposure to household air pollutants including greater use of high-emission fuel sources, such as biomass and coal, for cooking, heating and lighting (Hadeed et al., 2021). Additionally, individuals from low-SES and historically marginalized communities might spend more time indoors, given reduced access to recreational spaces and opportunities as well as perceived neighborhood concerns, placing them at greater vulnerability to indoor pollutants, such as cigarette smoke and household chemicals (Ferguson et al., 2020; Woo et al., 2019). Housing in such communities might also be more poorly ventilated and in poorer condition, contributing to greater risk of indoor air pollution exposure (Tieskens et al., 2021).

This increased exposure to air pollution compounds with other health disparities to amplify adverse pollution-related health outcomes for vulnerable communities. People from lower SES groups tend to have worse overall health than individuals of high-SES, which could make them more susceptible to the damaging effects of air pollution (Bell et al., 2005). Additionally, people of color and lower-SES individuals experience elevated levels of psychosocial stress related to discrimination; this stress exposure has been shown to predict poorer health outcomes including heightened vulnerability to air pollution's adverse effects

(Block et al., 2012, Nardone et al., 2018). Multi-directional relationships between increased susceptibility, heightened exposure to polluted air, financial hardship, and discriminationbased stress may have cumulative effects on people's overall physical and socioemotional well-being. Furthermore, poor people tend to have less access to health care – and lower quality care – than people of higher socioeconomic status, which might make addressing the physical effects of exposure to air pollution even more difficult (Kravitz-Wirtz et al., 2018).

Differences in air pollution exposure may also have contributed to disparities in wideranging outcomes related to the Coronavirus disease 19 (COVID-19) pandemic (Brandt et al., 2020). While the evolving nature of the pandemic, confounding socioeconomic variables, geographic differences, and underestimation of case and mortality data present challenges to quantification of the relationship between air pollution exposure and COVID-19 outcomes, a recent review indicated a significant positive association between air pollution and averse COVID-19 health outcomes globally in 91% of papers included (Bhaskar et al., 2023). A growing literature indicates broader racial disparities in COVID-19-related outcomes; in the United States, this has included disparities in case rates (Credit, 2020; Ramprasad et al., 2022), hospitalization (Ogedegbe et al., 2020; Romano et al., 2021), mortality (Alcendor, 2020; Parpia et al., 2021), and "long COVID", characterized by symptoms persisting for three months or more after COVID-19 infection (Jacobs et al., 2023). The detrimental effects of air pollution on health and disparities in these effects may have contributed to disparities in COVID-19 outcomes. It is likewise possible that disparities in COVID-19 outcomes and related ongoing adverse health outcomes (including long COVID and elevated risk of other subsequent adverse health events including stroke and cardiac disease post-infection; Ahmed et al., 2022; Xie et al., 2022) may position marginalized communities to be further negatively affected by ongoing air pollution exposure, but to our knowledge this bidirectional relationship has not been explored in the literature and remains an important question for future research. Thus, compounding effects of COVID-19, air pollution, and systemic racism and classism on brain health and cognitive function have yet to be fully characterized.

The U.S. Environmental Protection Agency (EPA) has recognized that race-, ethnicity-, and income-based discrimination plays a role in the inequitable distribution of environmental health burden: addressing such disparities has been identified by the EPA as a major goal and an issue of environmental justice (USEPA, 2022). Uneven urban development and residential segregation have pushed people of color into communities with fewer public goods (Grineski, Bolin & Boone, 2007), including green spaces (Nardone et al., 2021), opportunities for outdoor recreation (Winter et al., 2020), and pharmacies (Qato et al., 2014), as well as increased industrial and freeway exposure (Woghiren-Akinnifesi , 2013; Houston et al., 2004). This is in spite of the fact that people of color have been identified as consuming fewer goods and services and having a smaller "carbon footprint" on average, relative to white people (Tessum et al., 2019). This body of research illustrates the disparities in benefit and burden existing in the consumption of goods and exposure to air pollutants across race/ethnicity and SES (Zou et al., 2014), as well as interactions between race/ ethnicity and SES in predicting exposure to harmful air pollutants (Ash & Fetter, 2004; Brochu et al., 2011).

Although environmental justice and equity issues have garnered the interest of researchers, policy holders, advocacy groups, and the general public, very few studies have assessed the cumulative risks of holding historically marginalized identities (i.e., racial-ethnic minorities in the U.S. and/or being of low-SES) in addition to heightened exposure to ambient air pollutants on human health (Smith & Laribi, 2022). One recent study (Schulz et al., 2020) examined the joint effects of race-based residential segregation, neighborhood socioeconomic factors, and environmental pollutant exposure (estimated using air quality monitoring and modeling data) in the Detroit Metropolitan Area and reported that racebased residential segregation was associated with increased rates of all-cause mortality (all deaths that occurred within a population, regardless of the cause). This effect was mediated by education attainment level, income inequality across the area, and exposure to  $PM<sub>2.5</sub>$ . Additionally, there were significant associations between each individual pathway and the all-cause mortality rate, indicating that each factor can partially explain regionallevel all-cause mortality rates. Despite these indicators that historic marginalization, SES, and pollution exposure interact with one another to predict all-cause mortality, their cumulative risk on other specific health consequences, such as neurocognitive outcomes, remains to be fully examined. A recent pilot study (Medrano et al., 2022) provides an important step in this direction by investigating cognitive performance as a function of realtime measured personal exposure to  $PM_{2.5}$  (measured using personal monitoring devices carried by participants for a three-day period) and zip code-aggregated Social Vulnerability indices, and reported initial evidence that higher real-time  $PM<sub>2.5</sub>$  exposure was negatively associated with cognitive performance as well as with socioeconomic metrics (higher parental education and income). Medrano et al.'s study was limited by use of a relatively small convenience sample (N=30 families with a child between the ages of 7 and 11 years old) and a constrained timeline; additional studies with larger, more diverse samples measured over longer periods of time will be beneficial in disentangling the cumulative impacts of air pollution and social vulnerability on neurocognitive outcomes.

#### **Recommendations for Policy**

The evidence reviewed here indicates that air pollution has major and adverse effects on neurocognitive development. Further, there are disparities in these effects, with some communities impacted more than others. A number of potential actions will help to address these issues. First, as noted by Clay, Muller & Wang (2021), ambient air pollution has increased since 2016 and this might be largely due to increased vehicle emissions. One strategy to address this increase might be to expand electric vehicle rebate programs, encouraging purchase and use of lower-emission vehicles. Additionally, increased investment into public transit infrastructure might increase its usage, thus decreasing air pollution by lowering vehicle emissions output. Investment in sustainable energy sources more broadly will also reduce air pollution by promoting transition away from use of high-emission fossil fuels.

In addition to these strategies to reduce emissions output generally, recommendations have also been put forward to specifically address the problem of inequity in pollution exposure and related health outcomes. While many previous environmental interventions have disproportionately benefited high-income communities, The Union of Concerned

Scientists, a nonprofit advocacy organization, has recommended prioritizing investments in electric transit and school buses serving communities of color and lower income to decrease emissions exposure in these communities, decreasing racial and income disparities in pollution impact (Pinto de Moura, 2019). Additionally, while electric vehicle rebate programs could encourage purchase of lower-emission vehicles generally, such programs could prioritize low- to moderate-income individuals in particular, helping to mitigate disparities in pollution impact as well.

Furthermore, given that green space is lacking in marginalized communities and improves air quality (Jennings et al., 2015; Wen et al., 2013), prioritizing the development of green spaces in such communities could also help reduce disparities in pollution exposure and related health outcomes. Increases in green space also offer many other health benefits for communities: along with reducing air pollution, green space also decreases noise and heat pollution (Andersson et al., 2015; Douglas et al., 2017), promotes stress recovery and positive mental health outcomes (Bratman et al., 2019; Nutsford & Pearson, 2013), and is negatively associated with neighborhood-level crime (Bogar et al., 2016; McCabe, 2014). In addition to these recommendations to reduce disparities in exposure to and the impact of air pollution specifically, these considerations can be considered part of the larger need to address structural disparities disadvantaging marginalized communities (Rigolon et al., 2021).

In addition to strategies improving outdoor air quality, steps to improve indoor air quality are important as well. As demonstrated by Stafford (2015), ventilation systems renovations improving indoor air quality in schools have been associated with significant improvements in students' cognitive, behavioral, and academic outcomes. Removal of harmful indoor contaminants (e.g., mold, asbestos), renovating air ventilation systems, and updating roofing and wall panels are all proven cost-efficient ways to reduce indoor air pollution and improve air quality. In addition to support for such improvements in older buildings, regulatory standards for indoor air quality should be developed and enforced. Current air quality regulations generally do not go beyond addressing outdoor air conditions, despite indoor air pollution posing a serious threat to public health (Roselund, 2020).

Finally, government agencies should both aim to better enforce current regulations and develop future environmental policies. Many large sources of air pollutants, such as factories and coal mines, are not properly regulated and penalized for failing to meet federal air quality standards (Payne-Sturges et al., 2019). Additionally, state governments and individual organizations need to be held accountable for failing to provide and regulate safe air for their residents (Melnick, 2010; Jacob & Winner, 2009). The 2022 Supreme Court decision curtailing EPA authority to reduce greenhouse gas emissions from power plants (Huang, 2022) is a concerning step in the wrong direction regarding such regulatory authority.

#### **Conclusion**

Air pollution has been fully recognized as a public health concern. Scientists have established a clear link between air pollution and negative health outcomes. As reviewed

in the present manuscript, prenatal exposure to fine particulate matter can impact fetal programming and early development, while air pollution exposure during infancy and childhood is associated with poorer outcomes in a wide range of neurocognitive measures. Air pollution also adversely affects health outcomes in adulthood, including elevated rates of Alzheimer's disease, dementia, and cognitive impairment in older adults.

Further, environmental justice advocates and environmental inequity researchers have brought to light the disproportionate exposure and harmful effects of air pollution amongst people of color and low socioeconomic status. Despite historically contributing the least to environmental pollutants, people of color and low-income individuals are experiencing the most damaging and lasting effects of air pollution and climate change more broadly. We all deserve the right to clean air and we should all be invested in climate change policy. Given the economic and human costs of air contaminants, it is imperative that local and federal legislators prioritize recommendations such as those we have outlined here to ensure that every person has access to clean and safe air.

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#### **References**

- Ahmad SJ, Feigen CM, Vazquez JP, Kobets AJ, & Altschul DJ (2022). Neurological sequelae of COVID-19. Journal of Integrative Neuroscience, 21(3), 77. [PubMed: 35633158]
- Alcendor DJ (2020). Racial disparities-associated COVID-19 mortality among minority populations in the US. Journal of clinical medicine, 9(8), 2442. [PubMed: 32751633]
- Alzheimer's Association. (2019). 2019 Alzheimer's disease facts and figures. Alzheimer's & Dementia, 15(3), 321–387.
- Aghaei M, Janjani H, Yousefian F, Jamal A, & Yunesian M (2019). Association between ambient gaseous and particulate air pollutants and attention deficit hyperactivity disorder (ADHD) in children; a systematic review. Environmental Research, 173, 135–156. [PubMed: 30909100]
- Andersson E, McPhearson T, Kremer P, Gomez-Baggethun E, Haase D, Tuvendal M, & Wurster D (2015). Scale and context dependence of ecosystem service providing units. Ecosystem Services, 12, 157–164.
- Ash M, & Fetter TR (2004). Who lives on the wrong side of the environmental tracks? Evidence from the EPA's risk-screening environmental indicators model. Social Science Quarterly, 85(2), 441–462.
- Bakolis I, Hammoud R, Stewart R, Beevers S, Dajnak D, MacCrimmon S, … & Mudway S (2021). Mental health consequences of urban air pollution: prospective population-based longitudinal survey. Social Psychiatry and Psychiatric Epidemiology, 56(9), 1587–1599. [PubMed: 33097984]
- Baumann N, & Pham-Dinh D (2001). Biology of oligodendrocyte and myelin in the mammalian central nervous system. Physiological reviews, 81(2), 871–927. [PubMed: 11274346]
- Bekkar B, Pacheco S, Basu R, & DeNicola N (2020). Association of air pollution and heat exposure with preterm birth, low birth weight, and stillbirth in the US: A systematic review. JAMA Network Open, 3(6), e208243–e208243. [PubMed: 32556259]
- Bell ML, O'Neill MS, Cifuentes LA, Braga AL, Green C, Nweke A, … & Sibold K (2005). Challenges and recommendations for the study of socioeconomic factors and air pollution health effects. Environmental Science & Policy, 8(5), 525–533.
- Bell ML, Belanger K, Ebisu K, Gent JF, Lee HJ, Koutrakis P, & Leaderer BP (2010). Prenatal exposure to fine particulate matter and birth weight: variations by particulate constituents and sources. Epidemiology (Cambridge, Mass.), 21(6), 884. [PubMed: 20811286]

- Block ML, Wu X, Pei Z, Li G, Wang T, Qin L, … & Veronesi B (2004). Nanometer size diesel exhaust particles are selectively toxic to dopaminergic neurons: the role of microglia, phagocytosis, and NADPH oxidase. The FASEB journal, 18(13), 1618–1620. [PubMed: 15319363]
- 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. [PubMed: 22981845]
- Bogar S, & Beyer KM (2016). Green space, violence, and crime: A systematic review. Trauma, Violence, & Abuse, 17(2), 160–171.
- Borgschulte M, Molitor D, & Zou E (2022). Air pollution and the labor market: Evidence from wildfire smoke (No. w29952). National Bureau of Economic Research.
- Bose S, Ross KR, Rosa MJ, Chiu YHM, Just A, Kloog I, … & Wright RJ (2019). Prenatal particulate air pollution exposure and sleep disruption in preschoolers: Windows of susceptibility. Environment International, 124, 329–335. [PubMed: 30660846]
- Bratman GN, Anderson CB, Berman MG, Cochran B, De Vries S, Flanders J, … & Daily GC (2019). Nature and mental health: An ecosystem service perspective. Science Advances, 5(7), eaax0903. [PubMed: 31355340]
- Brochu PJ, Yanosky JD, Paciorek CJ, Schwartz J, Chen JT, Herrick RF, & Suh HH (2011). Particulate air pollution and socioeconomic position in rural and urban areas of the Northeastern United States. American Journal of Public Health, 101(S1), S224–S230. [PubMed: 21836114]
- Brook RD, Rajagopalan S, Pope CA III, Brook JR, Bhatnagar A, Diez-Roux AV, … & Kaufman JD (2010). Particulate matter air pollution and cardiovascular disease: an update to the scientific statement from the American Heart Association. Circulation, 121(21), 2331–2378. [PubMed: 20458016]

Brunekreef B, & Holgate ST (2002). Air pollution and health. The Lancet, 360(9341), 1233–1242.

- Bureau of Labor Statistics. (2022, July). Household Data Annual Averages: Employment Status of the Civilian Noninstitution Population by Age, Sex, and Race [Table 3]. 2021 Annual Report of Labor Force Statistics from the Current Population Survey. U.S. Department of Labor. [https://](https://www.bls.gov/cps/demographics.htm) [www.bls.gov/cps/demographics.htm](https://www.bls.gov/cps/demographics.htm)
- Burkhardt J, Bayham J, Wilson A, Berman JD, O'Dell K, Ford B, … & Pierce JR (2020). The relationship between monthly air pollution and violent crime across the United States. Journal of Environmental Economics and Policy, 9(2), 188–205.
- Calderón-Garcidueñas L, Azzarelli B, Acuna H, Garcia R, Gambling TM, Osnaya N, … & Rewcastle B (2002). Air pollution and brain damage. Toxicologic pathology, 30(3), 373–389. [PubMed: 12051555]
- Calderón-Garcidueñas L, Kulesza RJ, Doty RL, D'Angiulli A, & Torres-Jardón R (2015). Megacities air pollution problems: Mexico City Metropolitan Area critical issues on the central nervous system pediatric impact. Environmental Research, 137, 157–169. [PubMed: 25543546]
- Calderón-Garcidueñas L, Leray E, Heydarpour P Toress-Jardón R, & Reis J (2016). Air pollution, a rising environmental risk factor for cognition, neuroinflammation and neurodegeneration: The clinical impact on children and beyond. Neuroepidemiology, 2016, 69–80.
- Calderón-Garcidueñas L, Mora-Tiscareño A, Ontiveros E, Gómez-Garza G, Barragán-Mejía G, Broadway J, ... & Engle RW (2008). Air pollution, cognitive deficits and brain abnormalities: a pilot study with children and dogs. Brain and cognition, 68(2), 117–127. [PubMed: 18550243]
- Calderón-Garcidueñas L, Maronpot RR, Torres-Jardon R, Henriquez-Roldan C, Schoonhoven R, Acuna-Ayala H, … & Swenberg JA (2003). DNA damage in nasal and brain tissues of canines exposed to air pollutants is associated with evidence of chronic brain inflammation and neurodegeneration. Toxicologic pathology, 31(5), 524–538. [PubMed: 14692621]
- Chen JC, & Schwartz J (2009). Neurobehavioral effects of ambient air pollution on cognitive performance in US adults. Neurotoxicology, 30(2), 231–239. [PubMed: 19150462]
- Chen JC, Wang X, Wellenius GA, Serre ML, Driscoll I, Casanova R, … & Espeland MA (2015). Ambient air pollution and neurotoxicity on brain structure: evidence from women's health initiative memory study. Annals of Neurology, 78(3), 466–476. [PubMed: 26075655]
- Chi GC, Hajat A, Bird CE, Cullen MR, Griffin BA, Miller KA, … & Kaufman JD (2016). Individual and neighborhood socioeconomic status and the association between air pollution

and cardiovascular disease. Environmental Health Perspectives, 124(12), 1840–1847. [PubMed: 27138533]

- Clay K, Muller NZ, & Wang X (2021). Recent increases in air pollution: evidence and implications for mortality. Review of Environmental Economics and Policy, 15(1), 154–162.
- Clean Air Act: 42 U.S.C. §§7401 et seq. (1963).
- 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. Environmental Research, 147, 383–398. [PubMed: 26945620]
- Costa LG, Cole TB, Coburn J, Chang YC, Dao K, & Roque P (2014). Neurotoxicants are in the air: convergence of human, animal, and in vitro studies on the effects of air pollution on the brain. BioMed Research International, 2014.
- Costa LG, Cole TB, Coburn J, Chang YC, Dao K, Roque PJ, (2017). Neurotoxicity of traffic-related air pollution. Neurotoxicology, 59, 133–139. [PubMed: 26610921]
- Costa LG, Cole TB, Dao K, Chang YC, Coburn J, & Garrick JM (2020). Effects of air pollution on the nervous system and its possible role in neurodevelopmental and neurodegenerative disorders. Pharmacology & Therapeutics, 210, 107523. [PubMed: 32165138]
- Credit K. (2020). Neighbourhood inequity: Exploring the factors underlying racial and ethnic disparities in COVID-19 testing and infection rates using ZIP code data in Chicago and New York. Regional Science Policy & Practice, 12(6), 1249–1271.
- Dauchet L, Hulo S, Cherot-Kornobis N, Matran R, Amouyel P, Edmé JL, & Giovannelli J (2018). Short-term exposure to air pollution: associations with lung function and inflammatory markers in non-smoking, healthy adults. Environment International, 121, 610–619. [PubMed: 30312964]
- de Prado Bert P, Mercader EMH, Pujol J, Sunyer J, & Mortamais M (2018). The effects of air pollution on the brain: a review of studies interfacing environmental epidemiology and neuroimaging. Current Environmental Health Reports, 5(3), 351–364. [PubMed: 30008171]
- Delgado-Saborit JM, Guercio V, Gowers AM, Shaddick G, Fox NC, & Love S (2021). A critical review of the epidemiological evidence of effects of air pollution on dementia, cognitive function and cognitive decline in adult population. Science of the Total Environment, 757, 143734. [PubMed: 33340865]
- Dominici F, Peng RD, Bell ML, Pham L, McDermott A, Zeger SL, & Samet JM (2006). Fine particulate air pollution and hospital admission for cardiovascular and respiratory diseases. The Journal of the American Medical Association, 295(10), 1127–1134. [PubMed: 16522832]
- Douglas O, Lennon M, & Scott M (2017). Green space benefits for health and well-being: A lifecourse approach for urban planning, design and management. Cities, 66, 53–62.
- Evans GW, & Kantrowitz E (2002). Socioeconomic status and health: the potential role of environmental risk exposure. Annual Review of Public Health, 23(1), 303–331.
- Ferguson L, Taylor J, Davies M, Shrubsole C, Symonds P, & Dimitroulopoulou S (2020). Exposure to indoor air pollution across socio-economic groups in high-income countries: A scoping review of the literature and a modelling methodology. Environment International, 143, 105748. [PubMed: 32629198]
- Flores-Pajot MC, Ofner M, Do MT, Lavigne E, & Villeneuve PJ (2016). Childhood autism spectrum disorders and exposure to nitrogen dioxide, and particulate matter air pollution: a review and meta-analysis. Environmental Research, 151, 763–776. [PubMed: 27609410]
- Foster RG (2020). Sleep, circadian rhythms and health. Interface Focus, 10(3), 20190098. [PubMed: 32382406]
- Genc S, Zadeoglulari Z, Fuss SH, & Genc K (2012). The adverse effects of air pollution on the nervous system. Journal of Toxicology, 2012.
- Gładka A, Rymaszewska J, & Zato ski T (2018). Impact of air pollution on depression and suicide. International Journal of Occupational Medicine and Environmental Health, 31(6), 711–721. [PubMed: 30281038]
- Gray SC, Edwards SE, & Miranda ML (2013). Race, socioeconomic status, and air pollution exposure in North Carolina. Environmental Research, 126, 152–158. [PubMed: 23850144]

- Grineski S, Bolin B, & Boone C (2007). Criteria air pollution and marginalized populations: environmental inequity in metropolitan Phoenix, Arizona. Social Science Quarterly, 88(2), 535– 554.
- Hadeed SJ, O'Rourke MK, Canales RA, Joshweseoma L, Sehongva G, Paukgana M, … & Harris RB (2021). Household and behavioral determinants of indoor PM2. 5 in a rural solid fuel burning Native American community. Indoor Air, 31(6), 2008–2019. [PubMed: 34235761]
- Hajat A, Diez-Roux AV, Adar SD, Auchincloss AH, Lovasi GS, O'Neill MS, … & Kaufman JD (2013). Air pollution and individual and neighborhood socioeconomic status: evidence from the Multi-Ethnic Study of Atherosclerosis (MESA). Environmental Health Perspectives, 121(11-12), 1325–1333. [PubMed: 24076625]
- Hajat A, Hsia C, & O'Neill MS (2015). Socioeconomic disparities and air pollution exposure: a global review. Current Environmental Health Reports, 2(4), 440–450. [PubMed: 26381684]
- Harris MH, Gold DR, Rifas-Shiman SL, Melly SJ, Zanobetti A, Coull BA, … & Oken E (2015). Prenatal and childhood traffic-related pollution exposure and childhood cognition in the project viva cohort (Massachusetts, USA). Environmental Health Perspectives, 123(10), 1072–1078. [PubMed: 25839914]
- Havard S, Deguen S, Zmirou-Navier D, Schillinger C, & Bard D (2009). Traffic-related air pollution and socioeconomic status: a spatial autocorrelation study to assess environmental equity on a small-area scale. Epidemiology, 223–230. [PubMed: 19142163]
- Hedges DW, Erickson LD, Kunzelman J, Brown BL, & Gale SD (2019). Association between exposure to air pollution and hippocampal volume in adults in the UK Biobank. Neurotoxicology, 74, 108–120. [PubMed: 31220475]
- Herting MM, Younan D, Campbell CE, & Chen JC (2019). Outdoor air pollution and brain structure and function from across childhood to young adulthood: A methodological review of brain MRI studies. Frontiers in Public Health, 7, 332. [PubMed: 31867298]
- Hoek G, Beelen R, De Hoogh K, Vienneau D, Gulliver J, Fischer P, & Briggs D (2008). A review of land-use regression models to assess spatial variation of outdoor air pollution. Atmospheric environment, 42(33), 7561–7578.
- Houston D, Wu J, Ong P, & Winer A (2004). Structural disparities of urban traffic in Southern California: implications for vehicle-related air pollution exposure in minority and high-poverty neighborhoods. Journal of Urban Affairs, 26(5), 565–592.
- Huang D. (2022, July 9). The Supreme Court dealt a terrible blow to children's health. New York Times. [https://www.nytimes.com/2022/07/09/opinion/environment/climate-change-supreme-court](https://www.nytimes.com/2022/07/09/opinion/environment/climate-change-supreme-court-epa-children-health.html)[epa-children-health.html](https://www.nytimes.com/2022/07/09/opinion/environment/climate-change-supreme-court-epa-children-health.html)
- Jacob DJ, & Winner DA (2009). Effect of climate change on air quality. Atmospheric Environment, 43(1), 51–63.
- Jacobs MM, Evans E, & Ellis C (2023). Racial, ethnic, and sex disparities in the incidence and cognitive symptomology of long COVID-19. Journal of the National Medical Association, 115(2), 233–243. [PubMed: 36792456]
- Jennings V, & Johnson Gaither C (2015). Approaching environmental health disparities and green spaces: an ecosystem services perspective. International Journal of Environmental Research and Public Health, 12(2), 1952–1968. [PubMed: 25674782]
- Jerrett M. (2009). Global geographies of injustice in traffic-related air pollution exposure. Epidemiology, 20(2), 231–233. [PubMed: 19234414]
- Johnson MH, & Munakata Y (2005). Processes of change in brain and cognitive development. Trends in Cognitive Sciences, 9(3), 152–158. [PubMed: 15737824]
- Kajeepeta S, Sanchez SE, Gelaye B, Qiu C, Barrios YV, Enquobahrie DA, & Williams MA (2014). Sleep duration, vital exhaustion, and odds of spontaneous preterm birth: a case–control study. BMC Pregnancy and Childbirth, 14(1), 1–10. [PubMed: 24383788]
- Katanoda K, Sobue T, Satoh H, Tajima K, Suzuki T, Nakatsuka H, … & Tominaga S (2011). An association between long-term exposure to ambient air pollution and mortality from lung cancer and respiratory diseases in Japan. Journal of Epidemiology, 1102090211–1102090211.

- Kelly FJ, & Fussell JC (2015). Air pollution and public health: emerging hazards and improved understanding of risk. Environmental Geochemistry and Health, 37(4), 631–649. [PubMed: 26040976]
- Kim KN, Lim YH, Bae HJ, Kim M, Jung K, & Hong YC (2016). Long-term fine particulate matter exposure and major depressive disorder in a community-based urban cohort. Environmental Health Perspectives, 124(10), 1547–1553. [PubMed: 27129131]
- Kloog I, Melly SJ, Ridgway WL, Coull BA, & Schwartz J (2012). Using new satellite based exposure methods to study the association between pregnancy PM 2.5 exposure, premature birth and birth weight in Massachusetts. Environmental Health, 11(1), 1–8. [PubMed: 22236490]
- Kopas J, York E, Jin X, Harish SP, Kennedy R, Shen SV, & Urpelainen J (2020). Environmental justice in India: incidence of air pollution from coal-fired power plants. Ecological Economics, 176, 106711.
- Kravitz-Wirtz N, Teixeira S, Hajat A, Woo B, Crowder K, & Takeuchi D (2018). Early-life air pollution exposure, neighborhood poverty, and childhood asthma in the United States, 1990– 2014. International Journal of Environmental Research and Public Health, 15(6), 1114. [PubMed: 29848979]
- Kundakovic M, & Champagne FA (2015). Early-life experience, epigenetics, and the developing brain. Neuropsychopharmacology, 40(1), 141–153. [PubMed: 24917200]
- La Nauze A, & Severnini ER (2021). Air pollution and adult cognition: Evidence from brain training (No. w28785). National Bureau of Economic Research.
- Mahady JA, Octaviano C, Araiza Bolanños OS, Loópez ER, Kammen DM, & Castellanos S (2020). Mapping opportunities for transportation electrification to address social marginalization and air pollution challenges in Greater Mexico City. Environmental Science & Technology, 54(4), 2103– 2111. [PubMed: 31909600]
- Maiuolo J, Macrì R, Bava I, Gliozzi M, Musolino V, Nucera S, … & Mollace V (2019). Myelin disturbances produced by sub-toxic concentration of heavy metals: The role of oligodendrocyte dysfunction. International journal of molecular sciences, 20(18), 4554. [PubMed: 31540019]
- Martinussen M, Fischl B, Larsson HB, Skranes J, Kulseng S, Vangberg TR, … & Dale AM (2005). Cerebral cortex thickness in 15-year-old adolescents with low birth weight measured by an automated MRI-based method. Brain, 128(11), 2588–2596. [PubMed: 16123146]
- McCabe A. (2014). Community gardens to fight urban youth crime and stabilize neighborhoods. International Journal of Child Health and Human Development, 7(3).
- Medrano J, Crnosija N, Prather RW, Payne-Sturges D (2022). Bridging the environment and neurodevelopment for children's health: Associations between real-time air pollutant exposures and cognitive outcomes. Frontiers in Psychology, 13:933327, 10.3389/fpsyg.2022.933327 [PubMed: 36329746]
- Melnick RS (2010). Regulation and the courts: The case of the Clean Air Act. Brookings Institution Press.
- Miller JG, Dennis EL, Heft-Neal S, Jo B, & Gotlib IH (2021). Fine particulate air pollution, early life stress, and their interactive effects on adolescent structural brain development: A longitudinal tensor-based morphometry study. Cerebral Cortex, bhab346
- Miller JG, Gillette JS, Manczak EM, Kircanski K, & Gotlib IH (2019). Fine particle air pollution and physiological reactivity to social stress in adolescence: the moderating role of anxiety and depression. Psychosomatic Medicine, 81(7), 641. [PubMed: 31460967]
- Namin S, Xu W, Zhou Y, & Beyer K (2020). The legacy of the Home Owners' Loan Corporation and the political ecology of urban trees and air pollution in the United States. Social Science & Medicine, 246, 112758. [PubMed: 31884239]
- Nardone A, Rudolph KE, Morello-Frosch R, & Casey JA (2021). Redlines and greenspace: The relationship between historical redlining and 2010 greenspace across the United States. Environmental Health Perspectives, 129(1), 017006. [PubMed: 33502254]
- Nawrot TS, Saenen ND, Schenk J, Janssen BG, Motta V, Tarantini L, … & Bollati V (2018). Placental circadian pathway methylation and in utero exposure to fine particle air pollution. Environment International, 114, 231–241. [PubMed: 29524919]

- Newman NC, Ryan P, LeMasters G, Levin L, Bernstein D, Hershey GKK, … & Dietrich KN (2013). Traffic-related air pollution exposure in the first year of life and behavioral scores at 7 years of age. Environmental Health Perspectives, 121(6), 731–736. [PubMed: 23694812]
- Nutsford D, Pearson AL, & Kingham S (2013). An ecological study investigating the association between access to urban green space and mental health. Public Health, 127(11), 1005–1011. [PubMed: 24262442]
- Oudin A (2020). Short review: Air pollution, noise and lack of greenness as risk factors for Alzheimer's disease-epidemiologic and experimental evidence. Neurochemistry International, 134, 104646. [PubMed: 31866324]
- Parpia AS, Martinez I, El-Sayed AM, Wells CR, Myers L, Duncan J, … & Pandey A (2021). Racial disparities in COVID-19 mortality across Michigan, United States. EClinicalMedicine, 33.
- Paruthi S, Brooks LJ, D'Ambrosio C, Hall WA, Kotagal S, Lloyd RM, … & Wise MS (2016). Recommended amount of sleep for pediatric populations: a consensus statement of the American Academy of Sleep Medicine. Journal of Clinical Sleep Medicine, 12(6), 785–786. [PubMed: 27250809]
- Payne-Sturges DC, Marty MA, Perera F, Miller MD, Swanson M, Ellickson K, … & Hertz-Picciotto I (2019). Healthy air, healthy brains: advancing air pollution policy to protect children's health. American Journal of Public Health, 109(4), 550–554. [PubMed: 30789769]
- Pinto de Moura M,C (2019, July 16). Who Breathes the Dirtiest Air from Vehicles in Colorado? The Equation. <https://blog.ucsusa.org/cecilia-moura/colorado-air-pollution/>
- Power MC, Adar SD, Yanosky JD, & Weuve J (2016). Exposure to air pollution as a potential contributor to cognitive function, cognitive decline, brain imaging, and dementia: a systematic review of epidemiologic research. Neurotoxicology, 56, 235–253. [PubMed: 27328897]
- Pratt GC, Vadali ML, Kvale DL, & Ellickson KM (2015). Traffic, air pollution, minority and socio-economic status: addressing inequities in exposure and risk. International Journal of Environmental Research and Public Health, 12(5), 5355–5372. [PubMed: 25996888]
- Pujol J, Martínez-Vilavella G, Macià D, Fenoll R, Alvarez-Pedrerol M, Rivas I, … & Sunyer J (2016). Traffic pollution exposure is associated with altered brain connectivity in school children. Neuroimage, 129, 175–184. [PubMed: 26825441]
- Qato DM, Daviglus ML, Wilder J, Lee T, Qato D, & Lambert B (2014). 'Pharmacy deserts' are prevalent in Chicago's predominantly minority communities, raising medication access concerns. Health Affairs, 33(11), 1958–1965. [PubMed: 25367990]
- Ogedegbe G, Ravenell J, Adhikari S, Butler M, Cook T, Francois F, … & Horwitz LI (2020). Assessment of racial/ethnic disparities in hospitalization and mortality in patients with COVID-19 in New York City. JAMA network open, 3(12), e2026881–e2026881. [PubMed: 33275153]
- Rajagopalan S, Al-Kindi SG, & Brook RD (2018). Air pollution and cardiovascular disease: JACC state-of-the-art review. Journal of the American College of Cardiology, 72(17), 2054–2070. [PubMed: 30336830]
- Raju S, Keet CA, Paulin LM, Matsui EC, Peng RD, Hansel NN, & McCormack MC (2019). Rural residence and poverty are independent risk factors for chronic obstructive pulmonary disease in the United States. American Journal of Respiratory and Critical Care Medicine, 199(8), 961–969. [PubMed: 30384774]
- Ramprasad A, Qureshi F, Lee BR, & Jones BL (2022). The relationship between structural racism and COVID-19 related health disparities across 10 metropolitan cities in the United States. Journal of the National Medical Association, 114(3), 265–273. [PubMed: 35221074]
- Reschke L, McCarthy R, Herzog ED, Fay JC, Jungheim ES, & England SK (2018). Chronodisruption: An untimely cause of preterm birth?. Best Practice & Research Clinical Obstetrics & Gynaecology, 52, 60–67. [PubMed: 30228028]
- Rigolon A, Browning MH, McAnirlin O, & Yoon H (2021). Green space and health equity: a systematic review on the potential of green space to reduce health disparities. International Journal of Environmental Research and Public Health, 18(5), 2563. [PubMed: 33806546]
- Rogalsky DK, Mendola P, Metts TA, & Martin WJ (2014). Estimating the number of low-income Americans exposed to household air pollution from burning solid fuels. Environmental Health Perspectives, 122(8), 806–810. [PubMed: 24833615]

- Romano SD, Blackstock AJ, Taylor EV, Felix SEB, Adjei S, Singleton CM, … & Boehmer TK (2021). Trends in racial and ethnic disparities in COVID-19 hospitalizations, by region—United States, March–December 2020. Morbidity and Mortality Weekly Report, 70(15), 560. [PubMed: 33857068]
- Rooney MS, Arku RE, Dionisio KL, Paciorek C, Friedman AB, Carmichael H, … & Ezzati M (2012). Spatial and temporal patterns of particulate matter sources and pollution in four communities in Accra, Ghana. Science of the Total Environment, 435, 107–114. [PubMed: 22846770]
- Roselund C. (2020, May 13). Why is indoor air pollution largely unregulated? Rocky Mountain Institute.<https://rmi.org/why-is-indoor-air-pollution-largely-unregulated/>
- Schulz AJ, Omari A, Ward M, Mentz GB, Demajo R, Sampson N, … & Wilkins D (2020). Independent and joint contributions of economic, social and physical environmental characteristics to mortality in the Detroit Metropolitan Area: A study of cumulative effects and pathways. Health & Place, 65, 102391. [PubMed: 32738606]
- Shehab MA, & Pope FD (2019). Effects of short-term exposure to particulate matter air pollution on cognitive performance. Scientific Reports, 9(1), 1–10. [PubMed: 30626917]
- Siddique S, Banerjee M, Ray MR, & Lahiri T (2011). Attention-deficit hyperactivity disorder in children chronically exposed to high level of vehicular pollution. European Journal of Pediatrics, 170(7), 923–929. [PubMed: 21191614]
- Smith A, & Laribi O (2022). Environmental justice in the American public health context: trends in the scientific literature at the intersection between health, environment, and social status. Journal of Racial and Ethnic Health Disparities, 1–10.
- Smith JJ, & Stovall D (2008). 'Coming home' to new homes and new schools: critical race theory and the new politics of containment. Journal of Education Policy, 23(2), 135–152.
- Spruyt K. (2019). A review of developmental consequences of poor sleep in childhood. Sleep Medicine, 60, 3–12. [PubMed: 30660750]
- Stafford TM (2015). Indoor air quality and academic performance. Journal of Environmental Economics and Management, 70, 34–50.
- Steinberg L. (2005). Cognitive and affective development in adolescence. Trends in cognitive sciences, 9(2), 69–74. [PubMed: 15668099]
- 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. [PubMed: 26241071]
- Tessum CW, Apte JS, Goodkind AL, Muller NZ, Mullins KA, Paolella DA, … & Hill JD (2019). Inequity in consumption of goods and services adds to racial–ethnic disparities in air pollution exposure. Proceedings of the National Academy of Sciences, 116(13), 6001–6006.
- Thygesen M, Holst GJ, Hansen B, Geels C, Kalkbrenner A, Schendel D, … & Dalsgaard S (2020). Exposure to air pollution in early childhood and the association with Attention-Deficit Hyperactivity Disorder. Environmental Research, 183, 108930. [PubMed: 31810593]
- Tieskens KF, Milando CW, Underhill LJ, Vermeer K, Levy JI, & Fabian MP (2021). The impact of energy retrofits on pediatric asthma exacerbation in a Boston multi-family housing complex: a systems science approach. Environmental Health, 20(1), 1–9. [PubMed: 33407552]
- Tonne C, Melly S, Mittleman M, Coull B, Goldberg R, & Schwartz J (2007). A case–control analysis of exposure to traffic and acute myocardial infarction. Environmental Health Perspectives, 115(1), 53–57. [PubMed: 17366819]
- Tsai DH, Riediker M, Berchet A, Paccaud F, Waeber G, Vollenweider P, & Bochud M (2019). Effects of short-and long-term exposures to particulate matter on inflammatory marker levels in the general population. Environmental Science and Pollution Research, 26(19), 19697–19704. [PubMed: 31079306]
- Tzivian L, Winkler A, Dlugaj M, Schikowski T, Vossoughi M, Fuks K, … & Hoffmann B (2015). Effect of long-term outdoor air pollution and noise on cognitive and psychological functions in adults. International Journal of Hygiene and Environmental Health, 218(1), 1–11. [PubMed: 25242804]
- United States Environmental Protection Agency. (2022). Environmental Justice. Retrieved from [https://](https://www.epa.gov/environmentaljustice) [www.epa.gov/environmentaljustice](https://www.epa.gov/environmentaljustice)

- van den Berg CB, Chaves I, Herzog EM, Willemsen SP, van der Horst GTJ, & Steegers-Theunissen RPM (2017). Early-and late-onset preeclampsia and the DNA methylation of circadian clock and clock-controlled genes in placental and newborn tissues. Chronobiology International, 34(7), 921–932. [PubMed: 28613964]
- Vespa J. (2018, March 13). The graying of America: More adults than kids in 2035. United States Census Bureau. <https://www.census.gov/library/stories/2018/03/graying-america.html>
- Wen M, Zhang X, Harris CD, Holt JB, & Croft JB (2013). Spatial disparities in the distribution of parks and green spaces in the USA. Annals of Behavioral Medicine, 45(suppl\_1), S18–S27. [PubMed: 23334758]
- Winter PL, Crano WD, Basáñez T, & Lamb CS (2020). Equity in access to outdoor recreation— Informing a sustainable future. Sustainability, 12(1), 124.
- Woghiren-Akinnifesi EL (2013). Residential proximity to major highways—United States, 2010. CDC Health Disparities and Inequalities Report—United States, 2013, 62(3), 46.
- Woo B, Kravitz-Wirtz N, Sass V, Crowder K, Teixeira S, & Takeuchi DT (2019). Residential segregation and racial/ethnic disparities in ambient air pollution. Race and Social Problems, 11(1), 60–67. [PubMed: 31440306]
- Woodruff TJ, Parker JD, Kyle AD, & Schoendorf KC (2003). Disparities in exposure to air pollution during pregnancy. Environmental Health Perspectives, 111(7), 942–946. [PubMed: 12782496]
- Woodruff TJ, Parker JD, & Schoendorf KC (2006). Fine particulate matter (PM2. 5) air pollution and selected causes of postneonatal infant mortality in California. Environmental Health Perspectives, 114(5), 786–790. [PubMed: 16675438]
- Xie Y, Xu E, Bowe B, & Al-Aly Z (2022). Long-term cardiovascular outcomes of COVID-19. Nature medicine, 28(3), 583–590.
- Xu F, Shi X, Qiu X, Jiang X, Fang Y, Wang J, … & Zhu T (2020). Investigation of the chemical components of ambient fine particulate matter (PM2. 5) associated with in vitro cellular responses to oxidative stress and inflammation. Environment international, 136, 105475. [PubMed: 32007923]
- Yang S, Liang X, Dou Q, La Y, Cai J, Yang J, … & Zhao X (2022). Ethnic disparities in the association between ambient air pollution and risk for cardiometabolic abnormalities in China. Science of The Total Environment, 838, 155940. [PubMed: 35580681]
- Yang Y, Ruan Z, Wang X, Yang Y, Mason TG, Lin H, & Tian L (2019). Short-term and long-term exposures to fine particulate matter constituents and health: A systematic review and metaanalysis. Environmental Pollution, 247, 874–882. [PubMed: 30731313]
- Zhang X, Chen X,  $\&$  Zhang X (2018). The impact of exposure to air pollution on cognitive performance. Proceedings of the National Academy of Sciences, 115(37), 9193–9197.
- Zheng XY, Ding H, Jiang LN, Chen SW, Zheng JP, Qiu M, … & Guan WJ (2015). Association between air pollutants and asthma emergency room visits and hospital admissions in time series studies: a systematic review and meta-analysis. PloS One, 10(9), e0138146. [PubMed: 26382947]
- Zou B, Peng F, Wan N, Mamady K, & Wilson GJ (2014). Spatial cluster detection of air pollution exposure inequities across the United States. PLoS One, 9(3), e91917. [PubMed: 24647354]