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Environmental Toxicity and Poor Cognitive Outcomes in Children and Adults

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Abstract

Extensive literature has already documented the deleterious effects of heavy metal toxins on the human brain and nervous system. These toxins, however, represent only a fraction of the environmental hazards that may pose harm to cognitive ability in humans. Lead and mercury exposure, air pollution, and organic compounds all have the potential to damage brain functioning yet remain understudied. In order to provide comprehensive and effective public health and health care initiatives for prevention and treatment, we must first fully understand the potential risks, mechanisms of action, and outcomes surrounding exposure to these elements in the context of neurocognitive ability. This article provides a review of the negative effects on cognitive ability of these lesser-studied environmental toxins, with an emphasis on delineating effects observed in child versus adult populations. Possible differential effects across sociodemographic populations (e.g., urban versus rural residents; ethnic minorities) are discussed as important contributors to risk assessment and the development of prevention measures. The public health and clinical implications are significant and offer ample opportunities for clinicians and researchers to help combat this growing problem.

Introduction

The effect of environmental toxins on the brain and nervous system has been studied and documented extensively. A majority of the existing research has focused on the detrimental effects of heavy metals, however, while it appears that exposure to heavy metals represents only a portion of the total environmental health risks. For example, the damaging effects of air pollution on the brain, and particularly on intelligence, are being increasingly viewed as a significant concern. Another important concern is exposure to organic chemical compounds (such as polychlorinated biphenyls and dioxins) with toxic effects. What is particularly troubling about these compounds is that they can accumulate in animals and therefore can be delivered to humans via food products (Tuomisto, Vartianen, & Tuomisto, 2011).

Pollution is a complex issue affecting under-developed as well as developed countries. Socioeconomic issues are also relevant; people living in urban or impoverished areas may face greater exposure. Combatting pollution is a unique challenge, as it can require

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significant participation and economic support across all levels of government, from local municipalities all the way up to national authorities. All of these factors make pollution a broad research subject. As a result, this article will focus on some of the more recent developments and concerns regarding a few noteworthy pollutants. First, some of the major findings of the effects of the heavy metals lead and mercury on cognitive function will be reviewed. Although lead and mercury have been studied previously and extensively as mentioned earlier, they were included in this article due to recent developments regarding exposure. For example, the acceptable blood lead levels (BLLs) in children have decreased steadily over time. Mercury has reemerged as a threat due to its persistence in the food supply, particularly seafood.

Second, this article will also explore the potential effects of air pollutants and organic chemical pollutants on cognition. Special attention is given to the effects of pollution on specific population groups as well as more universal effects throughout each section of the article. The discussion on air pollution was included in this article because it is being increasingly viewed as a potential problem and its mechanisms of action are still not completely understood. Discussion on the effects of organic compounds was also included in this article due to growing concerns about exposure through the food supply. Finally, public health and clinical implications for health care providers are discussed.

Lead and Mercury

Children

The potential health effects of high exposure to lead have been studied comprehensively. Over the past few decades a debate has persisted, however, about how much exposure is necessary to produce negative health effects, especially in children. Indeed, the Centers for Disease Control and Prevention (CDC) have steadily lowered the threshold for BLLs in children considered dangerous by 88%, from 60 μg/dL to 10 μg/dL over the last 40 years (CDC, 2006).

More recently, increasing data have also indicated that even children with blood lead concentrations <10 μg/dL are at significant risk for reduced cognitive development and functioning, including IQ deficits and poor academic performance (Bellinger, 2008; Jusko, 2008; Lanphear et al., 2005; Liu, Li, Wang, Yan, & Liu, 2013). In fact, no threshold has been determined for this effect. Accordingly, the CDC recently eliminated the terminology “level of concern.” Rather, children with elevated blood lead concentrations will be identified using a reference value based on the 97.5th percentile of the National Health and Nutrition Examination Survey–generated blood lead concentration distribution in children aged 1–5 years old; currently, this value is 5 μg/dL (CDC, 2012). Prenatal exposure to lead via vertical transmission from mother to child, including at levels below 10 μg/dL, is also a concern and can have detrimental effects on cognitive function and IQ in infants and children (Jedrychowski et al., 2009).

Mercury is another heavy metal that poses a significant health threat to children. It is of significant concern that mercury (in the form of methylmercury) is found in fish and shell-fish, which are readily available for consumption as part of a child’s diet. In fact, the Food

and Drug Administration (FDA) currently advises that young children, pregnant women, and nursing women avoid the four fish (shark, swordfish, king mackerel, and tilefish) that contain high levels of mercury (FDA, 2004). FDA also advises that these individuals consume no more than 12 ounces of fish and shellfish lower in mercury per week (FDA, 2004). These cautionary guidelines are due to growing evidence from the scientific community about the potential negative health effects of accumulating mercury via diet.

In a study of preschool children in Spain, elevated hair mercury levels were associated with a higher frequency of oily fish consumption as well as a delay in cognitive development (Freire et al., 2010). In a study on adolescents, however, higher hair mercury levels were associated with improved visual-spatial capabilities, which the authors posit may be due to general benefits of fish consumption (e.g., increased protein, increased omega-3 fatty acids) outweighing the risks of mercury accumulation (Torrente, Colomina, & Domingo, 2005). It is possible that mercury's impact is more pronounced when children are younger, when their developing neurocognitive systems are more vulnerable to harm. Some prenatal studies have distinguished between the effect of higher mercury levels and the effect of higher maternal fish consumption. In a study that examined mercury levels due to atmospheric exposure instead of exposure due to diet, higher mercury levels in young children were associated with decreased IQ (Trasande, Schecter, Haynes, & Landrigan, 2006). Despite the consensus that higher mercury levels are associated with negative effects on cognition (Oken et al., 2008), higher maternal fish consumption has been associated with a beneficial impact on cognition, even though increased fish consumption would suggest elevated mercury levels (Oken et al., 2008). This may be due to the variety of fish consumed, as different species of fish contain differing amounts of mercury, as discussed previously (FDA, 2004).

Adults

Lead also has negative effects on adults. Several studies have found an association between higher lead levels and declines in cognitive performance (Shih, Hu, Weisskopf, & Schwartz, 2007; Weuve et al., 2009), which may or may not be reversible (Winker, Ponocny-Seliger, Rudiger, & Barth, 2006). A concern also exists that low-level accumulation of lead over a long period of time, such as in the elderly, may also be harmful to cognitive performance (Stewart & Schwartz, 2007). Stewart and Schwartz even posit that the manifestation of "normal" cognitive decline due to age may be in fact due to an accumulation of neurotoxins, such as lead, over time. A concern is also that exposure to lead may later lead to the emergence of dementia disorders, particularly Alzheimer's disease (AD) (Basha & Reddy, 2010). Other researchers, however, have found no link between elevated lead levels and decreased cognition in adults (Nordberg, Winblad, Fratiglioni, & Basun, 2000).

Although evidence suggests an accumulation of low amounts of mercury appears to have a negative impact on children's cognition, less evidence exists to support a similar relationship in adults. A study of individuals occupationally exposed to mercury found that effects were small and difficult to detect on a case-by-case basis (Rohling & Demakis, 2006). Another study examined individuals who received mercury alloy amalgam-based dental implants and found no relation with cognition (Sundstrom, Bergdahl, Nyberg, Bergdahl, & Nilsson, 2010). Similarly, the link between elevated mercury and cognition in older adults is

unconvincing (Weil et al., 2005). The same is true for the connection between mercury exposure and AD; associations between the two exist but they have not been found to be significant (Mutter, Naumann, Schneider, & Walach, 2007). It is possible that individuals with higher mercury levels may be benefitting from higher fish consumption, which could mitigate mercury's harmful effects. Indeed, the potential interaction between mercury and selenium has been under investigation, where the increased levels of selenium found in fish may mitigate the effects of mercury (Mozaffarian & Rimm, 2006).

Potential Mechanisms of Action

The mechanism for the toxic health effects seen from lead and mercury exposure is thought to primarily involve the brain. Lead is believed to raise oxidative stress, stimulate apoptosis of neurons, and affect neurotransmitter release (Shih et al., 2007). Lead can circulate in the blood or accumulate in bones, where it can escape into the blood during periods of bone turnover (Shih et al., 2007). When in the blood, lead is capable of substituting for calcium, allowing it to cross the blood-brain barrier and disrupt other calcium-based properties (Shih et al., 2007). It may be through these mechanisms that lead can directly affect cognitive performance. Regarding the potential link between lead and AD, research has focused on the possible epigenetic effects of lead. In studies of primates, early exposure to lead resulted in increased expression of genes associated with AD (Wu et al., 2008). Separate brain imaging studies in rodents and monkeys have found increases in amyloid plaques in the frontal lobe as well as changes in structural plasticity in the hippocampus (White et al., 2007; Wu et al., 2008).

Mercury is also believed to target the brain. According to the Agency for Toxic Substances and Disease Registry (ATSDR), inorganic, or elemental, mercury is converted into a divalent mercury ion, which can bind to thiol or sulfhydryl groups in proteins, resulting in disruption of protein structure and function (ATSDR, 1999). This may induce oxidative stress, lipid peroxidation, and mitochondrial dysfunction (ATSDR, 1999), which may promote the decline in cognitive performance. Methylmercury obtained via diet can accumulate in both the adult and fetal brain and is slowly transformed into inorganic mercury, which can act via the aforementioned mechanisms (National Academies of Science, 2000). A brain imaging study found that the areas of the brain most vulnerable to the toxic effects of mercury are the calcarine region, pre- and postcentral gyri, and the temporal transverse gyrus (Taber & Hurley, 2008). Granule cells in the cerebellum are also susceptible to harm (Taber & Hurley, 2008).

Air Pollution

Children

One major focus of research on the effects of air pollution is its potential impact on children. Due to the fact that children are continuously undergoing neurological and physical changes, they may be more susceptible to the harmful effects of toxins (Pinkerton & Joad, 2000). This is in contrast to adults, whose nervous systems are more mature and developed, and therefore more resistant to injury. Much of the research on children is centered on the effects of nitrogen dioxide (NO_2) and its influence on the respiratory system (U.S. Environmental

Protection Agency [U.S. EPA], 2010). NO_2 principally acts as an irritant on the mucosa of the eye, nose, and throat as well as the rest of the respiratory tract and can decrease lung function in those with pulmonary disease (U.S. EPA, 2010).

Researchers are become increasingly worried, however, about the neurological effects of NO_2. In a study of schoolchildren in China, researchers found a significant association between air pollution, particularly levels of NO_2, and poorer results on neurobehavioral tests designed to measure the children's sensory, motor, and psychomotor functions (Wang et al., 2009). A separate study examined the effects of indoor NO_2 exposure from gas appliances in children and found a dose-response effect between NO_2 levels and cognitive outcomes such as overall cognitive function, verbal abilities, and executive functioning (Morales et al., 2009). Children with greater exposure to NO_2 also had an increased risk of developing attention-deficit hyperactivity disorder (Morales et al., 2009).

Other studies have not focused solely on the harmful effects of nitrogen dioxide but on air pollution's effects as a whole. Using black carbon as a marker for air pollution in an urban birth cohort study, Suglia and coauthors (2008) found that increased amounts of black carbon were predictive of decreased cognitive function based on assessments with the Kaufman Brief Intelligence Test as well as on the Wide Range Assessment of Memory and Learning. In addition, a separate study of air pollution comparing children living in Mexico City to those living in less polluted areas of Mexico found significant deficits in the areas of fluid cognition, memory, and executive functions among the Mexico City children (Calderón-Garcidueñas et al., 2008).

Adults

Air pollution may be equally detrimental to the developed and mature nervous systems in adults. In a study using national data on pollution levels and neurobehavioral test results from the Third National Health and Nutrition Examination Survey, Chen and Schwartz (2009) found a significant association between ozone levels and decreased test results after adjusting for sociodemographic factors. These findings are limited, however, by the authors' use of older data, indicating the need for further examination in a longitudinal study (Chen & Schwartz, 2009). The elderly may be particularly at risk for the potential health effects of air pollution. In a study conducted on elderly residents of urban China, increases in air pollution were associated with difficulties in cognitive functioning as well as performing activities of daily living (Sun & Gu, 2008). Among elderly women in Germany, an association as well as a dose-response relationship was found between long-term exposure to traffic-related air pollution and mild cognitive impairment (Ranft, Schikowski, Sugiri, Krutmann, & Kramer, 2009). Increased levels of ambient traffic-related air pollution (as marked by black carbon) was also associated with decreased cognitive function in a separate study of older men in the U.S. (Power, Weisskopf, Coull, Spiro, & Schwartz, 2011). Some researchers have expressed concern that these declines in cognition due to air pollution could be precursors to neurodegenerative diseases such as dementia and AD (Block & Calderón-Garcidueñas, 2009).

Potential Mechanisms of Action

Regarding the causal mechanism between air pollution and its potential negative health effects, human studies have suggested the brain as a potential target for injury, but the cross-sectional design often utilized in these studies makes it difficult to determine whether exposure to polluted air occurs before or after the negative cognitive effects are present. One of the first studies focused on findings in feral dogs exposed to polluted urban environments (Block & Calderón-Garcidueñas, 2009), and found damage to parts of the brain linked to the nasal pathway, such as the olfactory bulb, implicating the nasal pathway as a potential entry way for pollutants (Calderón-Garcidueñas et al., 2010). In the future, imaging studies in the brain and nervous system may provide clues as to which areas are most vulnerable. A study in mice exposed to air pollution identified the dorsal vagal complex as a potential target (Villarreal-Calderon et al., 2010). In addition, examination by brain MRI of children and dogs in Mexico City exposed to air pollution showed the prefrontal cortex as a potential target as white matter hyperintense lesions were found there (Calderón-Garcidueñas et al., 2008).

A study using animal as well as human models identified multiple potential pathways for damage to the brain and central nervous system (Block & Calderón-Garcidueñas, 2009), including neuroinflammation, altered immune system responses, aggregation of proteins, and the direct toxic effects of the pollutants themselves (Block & Calderón-Garcidueñas, 2009). Air pollutants are thought to increase proinflammatory signals in the body as a whole, eventually leading to inflammation in the brain and thereby also affecting the immune system (Block & Calderón-Garcidueñas, 2009). Inflammation and changes in immune system cells, such as microglia, can result in direct damage to brain tissue or damage to the blood-brain barrier, potentially making it easier for pollutants to enter and accumulate in the brain (Block & Calderón-Garcidueñas, 2009). In addition, these pollutants can have direct toxic effects on brain tissue. For example, ozone is a reactive oxygen species that can damage the brain by inducing oxidative stress (Block & Calderón-Garcidueñas, 2009). The presence of multiple mechanisms makes it difficult to determine which effect is most responsible for the damaging effects and underscores the need for further research in this area.

Organic Compounds

Children

Concern about the class of organic chemical compounds known as polychlorinated biphenyls (PCBs) is not new. Although PCBs are commonly used as dielectrics in electrical equipment, fears about their toxicity and persistence in the environment led to a ban by the U.S. Congress in 1979 and by the Stockholm Convention on Persistent Organic Pollutants in 2001 (Porta & Zumeta, 2002). Due to their strong chemical and biological stability, however, concerns about the effects of PCBs still linger. PCBs can accumulate in food chains and are found in animal tissues (Ribas-Fitó, Sala, Kogevinas, & Sunyer, 2001). Currently, the greatest source of PCB exposure in humans is food, particularly fish and animal fats (Ribas-Fitó et al., 2001).

A literature review conducted approximately a decade ago reported an association between PCB exposure and adverse cognitive effects (Ribas-Fitó et al., 2001). A more recent study also found the same relationship (Korrick & Sagiv, 2008). Prenatal exposure to PCBs also appears to have deleterious effects (Jacobson & Jacobson, 2002; Park et al., 2010). One of these studies, however, also found that in children prenatally exposed to PCBs who were also breast-fed, no negative effects were evident, suggesting a possible role of the beneficial nutrients in breast milk offsetting the effects of PCBs (Jacobson & Jacobson, 2002).

Dioxins are another set of organic chemical pollutants that have growing health concerns. Also known as polychlorinated dibenzo-*p*-dioxins (PCDDs), dioxins are persistent environmental contaminants produced as byproducts of industrial processes, such as incineration, smelting, and refining (Tuomisto et al., 2011). Like PCBs, dioxins are highly stable and can accumulate in animals, particularly in their fat stores (Tuomisto et al., 2011), where exposure to humans can occur via diet in addition to industrial exposure.

A few studies have linked dioxins to cognitive or neurobehavioral deficits. Perinatal dioxin exposure was associated with decreases in cognitive and motor abilities (Schellart & Reits, 2008). Prenatal dioxin exposure has also been implicated as a potential risk factor (Vreugdenhil, Lanting, Mulder, Boersma, & Weisglas-Kuperus, 2002). A study conducted in Japan warned about the potential neurobehavioral effects of dioxins to the offspring of heavy fish consumers or residents living near a solid waste incinerator (Yoshida, Ikeda, & Nakanishi, 2000). A separate study, however, found no decreases in the cognitive test performance of children potentially exposed to dioxins by breast-feeding (Patandin et al., 1999), again raising the possibility that breast-feeding confers specific protective benefits to counteract the effects of the dioxins.

Adults

In addition to the potential effects on children, PCBs and dioxins may also have harmful effects on adults. Fewer studies, however, have explored these links. Concern is growing about the links between PCB exposure and impairments in cognitive functions in adults and older adults, with potential links to dementia (Lin, Huang, Yeh, Kuo, & Ke, 2010). It has been suggested that neurocognitive deficits occur only in women with PCB exposure, not exposed men (Lin, Huang, Yeh, Kuo, & Ke, 2008). Dioxin exposure in adults is also a concern. Air Force veterans exposed to high dioxin levels while serving in the Vietnam War have demonstrated decreases in several measures of memory functioning (Barrett, Morris, Akhtar, & Michalek, 2001). The amount of literature on this topic is limited, however, due to the focus on children. Clearly, further research is needed to evaluate the significance of these associations.

Potential Mechanisms of Action

The potential mechanism by which PCBs or dioxins exert their effects is unclear. A comprehensive review by Kodavanti (2005) examined three possible mechanisms: decreased release of neurotransmitters, disruption of intracellular signaling, and hormonal imbalances. A study by Lein and co-authors (2007) investigated the effect of PCB exposure on neuronal connectivity in rats and found PCBs altered connectivity in critical regions in the brain such

as the hippocampus, cerebellum, and cortex, but similar evidence in humans is lacking. Hormonal imbalance is another concern. In a study of rats, PCBs interfered with the neuroendocrine system, resulting in impaired sexual differentiation of the female hypothalamus (Dickerson, Cunningham, Patisaul, Woller, & Gore, 2011). PCBs may also alter the brain capillary endothelium, as a study in mice found (Seelbach et al., 2010).

The biological mode of action for dioxin's effects is also unknown. One possibility is dioxin's interaction with the aryl hydrocarbon hydroxylase (Ah) receptor (Charnley & Kimbrough, 2006). Binding to the Ah receptor up-regulates enzymes such as the P450 cytochromes, which are responsible for both activating and deactivating toxins (Charnley & Kimbrough, 2006). It is currently unclear how exactly the deficits in neurocognition may result, however. A summary of the sources and potential mechanisms of toxicity for the pollutants mentioned can be found in Table 1.

Sociodemographic Issues

An important consideration of the negative impact of pollution on humans is whether it may affect certain socioeconomic groups more than others. For example, in terms of lead exposure, blood levels higher than the CDC's previous threshold of 10 μg/dL are much more common among minority children, children in low-income families, and children living in older homes (Bellinger, 2008). Similar patterns are seen for mercury (Friere et al., 2010). Although air pollution is generally thought to affect individuals more equally, this may not be the case. In a study of more than 150,000 public schoolchildren in Orange County, Florida, it was found that Hispanic and African-American children had greater exposure to air pollution than Caucasian children, and African-American children had greater exposure than Hispanic children (Chakraborty & Zandbergen, 2007). PCB exposure follows similar trends. Korrick and Sagiv (2008) concluded that a sociodemographic disadvantage may enhance PCB toxicity while a sociodemographic advantage may mitigate PCB toxicity.

Sociodemographic findings are important for identifying individuals with potentially greater risk of exposure and subsequent negative outcomes. For example, living in urban areas, where exposure is greater and where minority groups make up a larger percentage of residents, may be responsible for these findings (Chen & Schwartz, 2009). Living in rural areas presents its own unique risks due to greater exposure to agricultural pesticides such as organophosphates (Lizardi, O'Rourke, & Morris, 2008). Questions about unequal exposure to pollutants are important areas for further study and may provide significant insight into developing strategies to mitigate the risks of exposure.

Discussion

An important consideration discussed by Winneke (2011) is that when studying pollutants, IQ is generally used to quantify the effects on neurological function. Although this is useful in determining regulatory cutoffs, it is not as helpful in clinical settings (Winneke, 2011). Instead, assessment tools that focus on particular areas such as executive function measures or outcome measures can be used to assess specific effects rather than global effects. For example, use of specific screening instruments for mild cognitive impairment, a precursor stage that often leads to dementia, can be used to investigate the role of lead and mercury in

the development of neurodegenerative disorders. Overall, these tools were created on a neuropsychological basis and relate to specific neurologic disorders and are therefore better equipped to identify problem areas and lead to the development of appropriate interventions (Winneke, 2011).

The findings from the above studies suggest how exposure to these toxic pollutants can result in neurological defects. One major issue with these studies, however, is that it is often difficult to determine if exposure to the pollutants is the true cause of these defects. For example, exposure to the pollutants may have occurred after neurological effects were present. Or perhaps a known or unknown confounding variable may be responsible for the effects. For example, socioeconomic or genetic risk factors may play a role. Another issue is that the people in the study may have differing levels of exposure, making it difficult to quantify a potential dose-response relationship.

In vitro studies may only be able to fill in some of the gaps left by population studies. Using cell cultures, researchers may be able to deduce the mechanisms of action of toxins and pollutants on a cellular and biochemical level. As pointed out by Cannon and Greenamyre (2011), however, these studies cannot reproduce the complexity of the human nervous system, and therefore are not able to model the pathogenesis of these neurological defects. Animal studies may potentially serve as the best way to study pollution's effects until more superior research methods are developed. In animal models, exposure can be quantified and assessed methodically. This is especially important for air pollution, which is particularly difficult to quantify exposure in human studies. Animal models may also serve as a way to model the mechanisms of action of pollutants on the nervous system as a whole, rather than just on a cellular level.

One potential future area of study is the difference in impact on neurologic function between prenatal exposure and postnatal exposure. As discussed earlier, prenatal exposure to lead, mercury, PCBs, and dioxins has been linked to neurological effects. One critical difference between these exposure periods is the route of exposure. During the prenatal period, the developing fetus is exposed to pollutants via the bloodstream through the placenta and umbilical cord. Postnatal exposure may occur through different routes such as inhalation, ingestion, absorption, etc. In particular, it would be interesting to study if air pollution exposure (which occurs through an inhalation route after birth) has neurodevelopmental effects in fetuses exposed via the bloodstream through umbilical cords. Although many have studied the effects of smoking during the prenatal period, the effects of air pollution as a whole during this same time period are unknown.

Conclusion

Pollution is a significant and complex problem that affects infants, children, adults, and seniors. Airborne and organic chemical pollutants have received less attention in the literature than heavy metals but are a growing cause for concern. Even though the deleterious effects of heavy metals such as lead and mercury have been well studied, there is a growing debate over newly proposed methods of exposure as well as what amount of exposure is unsafe. In addition, significant concern exists that air pollution can significantly

affect the developing nervous systems of children as well as the mature nervous systems of adults. Researchers have thus far been unable to pinpoint the exact mechanisms of injury. Air pollution may act via multiple pathways, imparting wide-reaching effects on the brain and central nervous system. Organic chemical pollutants such as PCBs and dioxins also are increasingly viewed as emerging threats due to their prolonged persistence in the environment and ability to accumulate in food chains. Future studies must explore the effects of PCBs and dioxins on adult populations. Evidence from the study of sociodemographic factors provides important and compelling data to prompt further consideration of pollution exposure and effects across different populations. Careful study of exposure levels for different socioeconomic groups is an important study for future research in order to identify at-risk groups.

A popular technique in assessing the neurological effects of pollutants is the use of global measures such as IQ, which is useful for determining cutoffs and acceptable levels of exposure. The use of specific scales and outcome measures in future studies may be more useful clinically. Another potential area of study in the future is comparing the effects of pollutants in prenatal versus postnatal time periods. Differing routes of exposures as well as different developmental stages may lead to different effects.

The difficulty with studying the effects of pollutants on the nervous system via human studies is that exposure is hard to quantify. In vitro cell culture studies may elicit the mechanisms of action of pollutants on a cellular level but cannot reproduce the complexity of the nervous system. Animal studies allow exposure to be quantified in a more complex model, but results may not be comparable to human studies. Improvements in brain imaging studies may provide more helpful clues in the future. Treatment and prevention become a reality only when the underlying mechanisms are fully understood.

Combatting these effects of pollution requires an interdisciplinary approach that encompasses multiple professions and fields of study. For example, public health officials can use public outreach programs to educate vulnerable populations on how to reduce exposure. Multidisciplinary research in the fields of biology, chemistry, ecology, neurology, and more can address gaps in the science and better identify the mechanisms and potential effects of different pollutants on the brain while potentially shaping public health policy, contributing to legislation and regulation, and stimulating research and development of environmental technologies.

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TABLE 1

Summary of Sources and Potential Mechanisms of Action for Pollutants

Pollutant	Source of Exposure	Potential Mechanisms of Toxicity
Lead	Paint from old buildings Soil near heavily used streets and roads or factories	Increased oxidative stress Stimulation of apoptosis Impairment of neurotransmitter release
Mercury	Consumption of fish and shellfish (particularly shark, swordfish, king mackerel, and tilefish)	Disruption of protein structure and function Increased oxidative stress, lipid peroxidation, and mitochondrial dysfunction
Air pollution	Factories, automobiles, and other machinery	Neuroinflammation Altered immune system response Aggregation of proteins Direct toxic effects
Polychlorinated biphenyls	Consumption of fish and animal fats	Impairment of neurotransmitter release Disruption of intracellular signaling Hormonal imbalance Altered neuronal connectivity
Dioxins	Consumption of animal fats	Interaction with aryl hydrocarbon hydroxylase receptor