Proceedings of the 2nd International Conference on Environmental Geoscience and Earth Ecology
DOI: 10.54254/2753-8818/37/20240168

Linking $PM_{2.5}$ to autism spectrum disorder

Anni Zhao

San Marino High School, CA, USA

azhao3@student.smusd.us

Abstract. This paper elaborates the potential link between $PM_{2.5}$ air pollution and Autism Spectrum Disorder (ASD), exploring mechanisms such as placental transmission, oxidative stress, signal transduction, and endocrine disruption. Referencing studies from Southwestern Pennsylvania, Shanghai, and animal experiments, together they reveal a consistent association between $PM_{2.5}$ exposure during prenatal development and an increased risk of ASD. Mechanistically, $PM_{2.5}$ is found to affect placental function, induce oxidative stress, and disrupt endocrine pathways, providing insights into potential pathways for neurodevelopmental disorders. The analysis emphasizes the impact on communities of lower socioeconomic status, where $PM_{2.5}$ exposure is higher, emphasizing the need for environmental protection. Hence, global research efforts are encouraged when considering the current lack of understanding on ASD prevalence in diverse populations. In the broad scope, this work contributes to the growing amount of evidence that links environmental factors, particularly air pollution, to neuropsychiatric development, urging further exploration into the impacts of pollution on human health.

Keywords: autism spectrum disorder, $PM_{2.5}$, neuropsychiatric development

1. Introduction

Coined as the "world's largest environmental threat" by UNECE [1], air pollution is defined as the contamination of air by particles such as carbon monoxide and lead, and it has already been found to significantly increase risks in diseases such as cardiovascular diseases and many forms of cancer [2]. In particular, $PM_{2.5}$ pollution, defined as pollution particles less than 2.5 microns, has breathable fine particles that cause major health concerns to the public. When an individual breathes in $PM_{2.5}$ pollution, the particles attack the immune system by causing inflammation in the bronchial, making $PM_{2.5}$ a high-risk factor for various respiratory illnesses [3]. In addition to lung damage, recent research has found a correlation between prenatal $PM_{2.5}$ inhalation and neuroinflammation, which can cause many types of neuropsychiatric disorders such as autism spectrum disorder (ASD).

Autism Spectrum Disorder, a neurodevelopmental disorder that impedes the social skills of an individual, is currently suggested to be caused mostly by genetics. Several genetic risk factors include having a sibling with ASD, having a low birth weight, and having Down Syndrome or Fragile X Syndrome. Autism can be diagnosed at any age, but symptoms are typically present in an individual at around the age of two [4]. For children, a diagnosis typically involves the assessment of the child's language and cognitive abilities, and an observation of the child's behavior by professionals.

When diagnosed early enough, modern treatments may prove remarkably effective in

© 2024 The Authors. This is an open access article distributed under the terms of the Creative Commons Attribution License 4.0 (https://creativecommons.org/licenses/by/4.0/).

DOI: 10.54254/2753-8818/37/20240168

regulating behavioral symptoms, allowing one to experience a close-to-normal social life. In most cases, autism is a lifelong disorder. ASD treatment must be personalized for everyone as Autism is a spectrum disorder, meaning each person's symptoms can vary in category and intensity [5]. However, common treatments often include medication and psychotherapy, both of which pose heavy financial and psychological burdens on the family. According to a study conducted in 2014, the median cost of ASD treatment was estimated to be USD $31,483 per year for a family regardless of the age of diagnosis [6].

2. Case Studies

With the increases in ASD diagnosis and $PM_{2.5}$ air pollution, more studies are trying to prove $PM_{2.5}$ as a potential cause of Autism. In a case-control study conducted in Southwestern Pennsylvania, $PM_{2.5}$ exposure and Autism diagnosis were analyzed from three months before maternal pregnancy until year two of the newborn. The levels of exposure were measured from both the residence and workplace, leading to the conclusion that $PM_{2.5}$ exposure increases the risk of youth Autism by about 50% [7].

In another study with data from Shanghai, 124 ASD cases and 1240 controls during two to three years after birth were studied regarding individual exposure to PM_1, $PM_{2.5}$, and PM_{10}. According to the authors, this is the first study in China that was conducted to analyze the relationship between children's long-term exposure to air pollution and Autism development. It was discovered that there are stronger associations between PM and ASD during 2nd and 3rd years after birth, which is the critical period during child development [8].

Animal studies have also explored the relationship between air pollutants and ASD. One such study conducted behavioral tests on rodents that were exposed to particulate matter and other gaseous exposure (PGE), gaseous exposure alone (GE), and Autism-like model rats (ALM). When presented with novel and familiar rats, ALM and PGE rats alike exhibited their inability to distinguish social novelty, a trait commonly associated with Autism. Using the Y-maze test decreases in alternation behaviors and memory defects in PGE, GE, and ALM rats were found. Furthermore, PGE rats buried more marbles than other groups (GE and control), which is a sign of increased repetitive behavior, another common symptom of Autism. In addition to the behavioral assessments, the oxytocin receptor (OXTR) protein, catalase activity (CAT), and Glutathione (GSH) levels were also measured to be lower in PGE, GE, and ALM rats than those of the control rats. The reduction in OXTR, CAT, and GSH suggests the presence of multiple mechanisms, precisely signal transduction and oxidative stress, that enable $PM_{2.5}$ to penetrate the nervous system and lead to Autism-like symptoms [9].

3. Mechanisms

As more research studies have found a correlation between $PM_{2.5}$ and the prenatal development of autism, various mechanisms can be proposed given the ambiguity of Autism causes. The possible pathways can be categorized into placental transmission, oxidative stress, signal transduction, and endocrine disruption.

An organ developed during pregnancy that transfers oxygen and nutrients to the fetus [10], recent studies have found it capable of being affected by $PM_{2.5}$. When Familari et al. exposed placental cells to PM, cell growth was significantly inhibited compared to the control group with no exposure to the particles, suggesting that not only can PM2.5 reach the placenta, but it can also cause placental defects [11]. Placental dysfunction can subsequently lead to higher risks of fetal ASD development [12, 13]. Exposure to $PM_{2.5}$ also led to increased IL-4 cytokine levels in mice according to Melo et al. When the secretion of inflammatory cytokines is triggered, the cytokines travel from the peripheral system to the central nervous system through the damaged intestinal barrier, ultimately causing neuroinflammation, a phenomenon commonly associated with psychiatric disorders such as ASD.

Oxidative stress occurs when the production and accumulation of reactive oxygen species (ROS) is imbalanced [14], and several elements connected to oxidative stress have been found to be affected in Autism patients. A disruption in the equilibrium of ROS was discovered when Bos et al.

DOI: 10.54254/2753-8818/37/20240168

exposed mice to $PM_{2.5}$ for five days [15]. This overproduction of ROS can ultimately disrupt cell signaling pathways, leading to apoptosis and many diseases. In patients with ASD, a reduction in the Glutathione (GSH) oxidative marker has been observed. GSH is mainly responsible for the removal of ROS, so a low level of GSH suggests that $PM_{2.5}$ -induced oxidative stress can possibly be a partial cause of ASD [16]. In the $PM_{2.5}$ exposed rats from Emam et al.'s research, a decrease in catalase activity was also seen. Catalase breaks down hydroxide, forming water and oxygen to protect the cell from oxidative damage, so a reduction in catalase activity suggests some degree of oxidative damage and its connection to ASD during children's developmental years [17].

The oxytocin receptor (OXTR) handles the binding of the oxytocin ligand to start a signal transduction pathway that affects maternal prosocial behavior [18, 19]. However, the OXTR also affects the development of the fetal nervous system, which can potentially lead to Autism development when the OXTR protein is reduced in the PGE rats from Emam et al.'s research.

According to Zhou et al's study conducted in Hangzhou, $PM_{2.5}$ from industry sites showed higher endocrine disruption potential [20]. As a defective endocrine can affect a mother's homeostasis, it can be hypothesized that fetal development would likewise be affected, potentially resulting in an offspring with ASD.

4. Discussion

This analysis has provided recent evidence that possibly links $PM_{2.5}$ as a cause of Autism through the possible pathways of placental transmission, oxidative stress, endocrine disruption, and inflammation. As communities of lower socioeconomic status (SES) experience more $PM_{2.5}$ air pollution, neurodevelopmental disorders such as ASD could have a detrimental impact on these kinds of societies as they also lack resources for diagnosis, treatment, and public awareness. Hence, by identifying prenatal $PM_{2.5}$ inhalation as a possible cause of ASD, environmental protection could prove its significance even in the neuropsychiatry of the future generation.

As mentioned above, families of lower SES are still missing assets for diagnosis, and the current data on ASD cases are still unable to accurately reflect the demography of children with Autism in the United States alone. In addition, the lack of Autism case studies conducted in Middle Eastern and Asian countries illustrates the inability to assume the relationship between $PM_{2.5}$ and Autism on a global scale.

With increasing evidence that suggests the damaging effects of air pollution and $PM_{2.5}$, the physical and mental health problems $PM_{2.5}$ can cause on humans become clearer. These results shed light on the possibility for all types of pollution (i.e., water pollution, soil pollution) to have a negative impact on human neurology and open a new gateway for future research to further link the environment to our neuropsychiatric development.

5. Conclusion

This paper has explored the burgeoning evidence linking PM2.5 air pollution with the risk of Autism Spectrum Disorder (ASD), elucidating potential biological pathways such as placental transmission, oxidative stress, signal transduction, and endocrine disruption. The synthesis of case studies and experimental research underscores a discernible connection between prenatal exposure to PM2.5 and an elevated risk of ASD, with mechanistic insights suggesting interference in crucial neurodevelopmental processes. Notably, the impact of PM2.5 exposure is disproportionately borne by communities of lower socioeconomic status, amplifying both the environmental justice and public health dimensions of this issue.

Our investigation reaffirms that environmental factors, specifically airborne particulates smaller than 2.5 microns, may play a significant role in the etiology of neuropsychiatric conditions, including ASD. The findings advocate for a heightened emphasis on environmental protection policies, especially those targeting air quality improvements, to mitigate the neurodevelopmental risks to future generations. Moreover, the paper highlights a pressing need for global research collaborations to build a more

DOI: 10.54254/2753-8818/37/20240168

comprehensive understanding of ASD prevalence and its environmental determinants across diverse populations.

As we move forward, it is imperative that public health strategies incorporate the findings of such research, fostering preventive approaches and interventions aimed at reducing PM2.5 exposure, particularly among vulnerable pregnant populations. The synthesis of our research contributes to the imperative dialogue on the nexus between environmental health and neuropsychiatric development, urging ongoing investigation into the multifaceted impacts of pollution on human health.

References

[1] United States Environmental Protection Agency. "Air Pollution and Health." UNECE, nece.org/air-pollution-and-health.

[2] World Health Organization. "Types of Pollutants." World Health Organization, 2021, www.who.int/teams/environment-climate-change-and-health/air-quality-andhealth/health-impacts/types-of-pollutants.

[3] "Particulate Matter (PM) Basics." USEPA, United States Environmental Protection Agency, 2018, www.epa.gov/pm-pollution/particulate-matter-pm-basics.

[4] National Institution of Mental Health. "Autism Spectrum Disorder." National Institute of Mental Health, www.nimh.nih.gov/health/topics/autism-spectrum-disorders-asd.

[5] Centers for Disease Control and Prevention. "Treatment and Intervention Services for Autism Spectrum Disorder." Centers for Disease Control and Prevention, 2019, www.cdc.gov/ncbddd/autism/treatment.html.

[6] Horlin C, Falkmer M, Parsons R, Albrecht MA, Falkmer T. (2014). "The Cost of Autism Spectrum Disorders." PLoS ONE, edited by Jennifer Gladys Mulle, 9(9), p. e106552. https://doi.org/10.1371/journal.pone.0106552.

[7] Talbott EO, Arena VC, Rager JR., Michanowicz DR, Sharma RK, Stacy SL. (2015). "Fine Particulate Matter and the Risk of Autism Spectrum Disorder." *Environmental Research*, 140, pp. 414–20, https://doi.org/10.1016/j.envres.2015.04.021.

[8] Chen G, Jin Z, Li S, Jin X, Tong S, Liu S, Yang Y, Huang H, Guo Y. (2018). "Early Life Exposure to Particulate Matter Air Pollution (PM1, PM2.5 and PM10) and Autism in Shanghai, China: A Case-Control Study." *Environment International*, 121, pp. 1121–27, https://doi.org/10.1016/j.envint.2018.10.026.

[9] Emam B, Shahsavani A, Khodagholi F, Zarandi SM, Hopke PK, Hadei M, Behbahani H, Yarahmadi M. (2020). "Effects of PM2.5 and Gases Exposure during Prenatal and Early-Life on Autism–like Phenotypes in Male Rat Offspring." *Particle and Fibre Toxicology*, 17(8), https://doi.org/10.1186/s12989-020-0336-y.

[10] Mayo Clinic. "Placenta: How It Works, What's Normal." Mayo Clinic, 3 Dec. 2022, www.mayoclinic.org/healthy-lifestyle/pregnancy-week-by-week/in-depth/placenta/art-

[11] Familari M, Näav Å, Erlandsson L, de Longh RU, Isaxon C, Strandberg B, Lundh T, Hansson SR, Malmqvist E. (2019). "Exposure of Trophoblast Cells to Fine Particulate Matter Air Pollution Leads to Growth Inhibition, Inflammation and ER Stress." *PLoS One*, edited by Hai-Yan Lin, 14(7), p. e0218799, https://doi.org/10.1371/journal.pone.0218799.

[12] Villamor E, Susser ES, Cnattingius S. (2022). "Defective Placentation Syndromes and Autism Spectrum Disorder in the Offspring: Population-Based Cohort and Sibling-Controlled Studies." *European Journal of Epidemiology*, 37(8), pp. 827–36, https://doi.org/10.1007/s10654-022-00884-3.

[13] de Melo JO, Soto S, Katayama IA, McCarthy CG, Pires AC, Veras MM, Shinohara N, de Castro I, Heimann JC, Saldiva PHN. (2015). "Inhalation of Fine Particulate Matter during Pregnancy Increased IL-4 Cytokine Levels in the Fetal Portion of the Placenta." *Toxicology Letters*, 232(2), Elsevier BV, pp. 475–80, https://doi.org/10.1016/j.toxlet.2014.12.001.

[14] Pizzino G, Irrera N, Cucinotta M, Pallio G, Mannino F, Arcoraci,V, Squadrito F, Altavilla D, Bitto A. (2017). "Oxidative Stress: Harms and Benefits for Human Health." *Oxidative*

DOI: 10.54254/2753-8818/37/20240168

Medicine and Cellular Longevity, 2017(8416763), pp. 1–13, https://doi.org/10.1155/2017/8416763.

[15] Bos I, De Boever P, Emmerechts J, Buekers J, Vanoirbeek J, Meeusen R, Van Poppel M, Nemery B, Nawrot T, Panis LI. (2012). "Changed Gene Expression in Brains of Mice Exposed to Traffic in a Highway Tunnel." *Inhalation Toxicology*, 24(10), pp. 676–86, https://doi.org/10.3109/08958378.2012.714004.

[16] Kwon D, et al. (2919). "Protective Effect of Glutathione against Oxidative Stress-Induced Cytotoxicity in RAW 264.7 Macrophages through Activating the Nuclear Factor Erythroid 2-Related Factor-2/Heme Oxygenase-1 Pathway." *Antioxidants (Basel, Switzerland)*, 8(4), p. 82, https://doi.org/10.3390/antiox8040082.

[17] ScienceDirect. "Catalase." Science Direct, www.sciencedirect.com/topics/earth-and-planetary-sciences/catalase.

[18] Pierzynowska K, Gaffke L, Żabińska M, Cyske Z, Rintz E, Wiśniewska K, Podlacha M, Węgrzyn G. (2023). "Roles of the Oxytocin Receptor (OXTR) in Human Diseases." *International Journal of Molecular Sciences*, 24(4), p. 3887, https://doi.org/10.3390/ijms24043887.

[19] Chatterjee O, Patil K, Sahu A, Gopalakrishnan L, Mol P, Advani J, Mukherjee S, Christopher R, Prasad, TSK. (2016). "An Overview of the Oxytocin-Oxytocin Receptor Signaling Network." *Journal of Cell Communication and Signaling*, 10(4), pp. 355–60, https://doi.org/10.1007/s12079-016-0353-7.

[20] Zhou Q, Chen J, Zhang J, Zhou F, Zhao J, Wei X, Zheng K, Wu J, Li B, Pan B. (2021). "Toxicity and Endocrine-Disrupting Potential of PM2.5: Association with Particulate Polycyclic Aromatic Hydrocarbons, Phthalate Esters, and Heavy Metals." *Environmental Pollution*, **292**, p. 118349, https://doi.org/10.1016/j.envpol.2021.118349