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Research Article

Exploring the Association Between Heavy Metal Exposure and Neurodevelopmental Disorders in Children

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Abstract
Environmental heavy metals have established a connection between Neurodevelopmental Disorders (NDDs) in children, which primarily include autism spectrum disorder (ASD) and attention-deficit hyperactivity disorder (ADHD), and learning disabilities. The study analyzes the blood level connection between developmental disorders in children and toxic elements such as Lead (Pb), Mercury (Hg), Arsenic (As), and Cadmium (Cd). The research included 500 children with 250 participants having NDD diagnosis and 250 neurotypical participants. The scientists conducted heavy metal concentration analysis through inductively coupled plasma mass spectrometry (ICP-MS) blood, urine, and hair samples. Neurodevelopmental assessments were conducted by using the Wechsler Intelligence Scale for Children, Fifth Edition (WISC-V), Conners Comprehensive Behavior Rating Scales (CBRS), and Autism Diagnostic Observation Schedule, Second Edition (ADOS-2). The children diagnosed with NDDs showed elevated heavy metal levels, including Pb, Hg, As, and Cd, which exceeded the control group values at statistical significance levels below 0.05. The WHO threshold for blood lead exceeded in 37% of children with NDD while only 14% of control children reached this level. The data analysis through regression showed a direct connection between elevated heavy metals in blood and cognitive deterioration in children. Heavy metal exposure creates a direct link between neurological impairments and both cognitive difficulties and executive dysfunction as well as behavioral disorders. The urgent implementation of policy measures coupled with environmental regulations needs to occur to minimize exposure hazards.

Keywords: Heavy metals, Neurodevelopmental Disorders, Lead Exposure, Cognitive impairments, Public Health

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Introduction

Different neurological conditions known as Neurodevelopmental Disorders (NDDs) disrupt brain operations while also modifying mental processes, behavior, and social development functions. It shows that autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), intellectual disabilities, and specific learning disabilities are among the disorders in this category (Thapar et al., 2017). The worldwide increase in NDDs requires immediate research into environmental risk factors because of their growing prevalence (Yan et al., 2024). Genetic factors are crucial in developing these disorders yet environmental exposures especially neurotoxicants such as heavy metals demonstrate significant influence on their pathogenesis according to studies by Tywabi et al. (2022) The four heavy metals lead (Pb), mercury (Hg), arsenic (As), and cadmium (Cd) function as widespread environmental pollutants causing severe neurotoxic damage that primarily impacts children because of their developing nervous systems (Sanders et al., 2015). The neurological system functions abnormally because heavy metals create oxidative stress, and neuroinflammation damages mitochondria and disrupts neurotransmitter signaling (Tran & Miyake, 2017).

Studies demonstrate that lead exposure creates a strong connection to ADHD symptoms which include cognitive deficits as well as impulsive behavior and hyperactivity. Industrial pollution and seafood consumption deliver mercury to humans who develop impaired language development alongside autistic-like behaviors and reduced Intelligence Quotient (IQ) scores (Barbone et al., 2019). Studies have established that consuming water containing arsenic results in executive functioning decline and memory problems which could produce learning disabilities (Kordas et al., 2017). Cadmium exposure has shown links to neurodevelopmental delays and reduced IQ scores in children according to Adly et al. (2023). Current scientific knowledge about heavy metal-induced neurotoxicity has identified multiple unknown aspects regarding their contribution to NDD development (Hall et al., 2023). Previous studies have studied heavy metals separately when children typically experience simultaneous exposure to multiple metals which demands a broader research approach that considers multiple metals (Carlsson et al., 2021). The sources of heavy metal exposure depend on geographic region, economic status, and diet, which determines who gets exposed and what effects they will experience (Engel et al., 2018). Evaluation of how heavy metals affect individuals requires knowledge about their interaction with genetic susceptibility and environmental contacts to create new prevention approaches and public health guidelines (Grandjean et al., 2019). Heavy metal exposure contributes to developing neurodevelopmental impairments because NDDs now affect more children and heavy metals have established neurotoxic properties. The integrated assessment strategy of exposure measurement and neurobehavioral effects assessment delivers essential knowledge to guide policymakers' healthcare providers and in controlling heavy metal risks in children's environments (Guardia et al., 2021).

Objectives of the Study

1. To assess the levels of heavy metal exposure (lead, mercury, arsenic, and cadmium) in children diagnosed with neurodevelopmental disorders compared to neurotypical children.
2. In order to address the relation of heavy metal exposure with some aspects of neurodevelopment, particularly aspects of cognitive performance, behavioral symptoms, and executive function deficits.

Materials and Methods

Study Design

The study functioned as a case-control observational design to investigate heavy metal exposure connections to neurodevelopmental disorders in children. The research examined children with neurodevelopmental disorders and specifically studied autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), and learning disabilities, along with typical developmental controls. Pediatric neurology clinics, primary healthcare centers, and community outreach programs were tapped as sources of the study participants. Enrollment was obtained after institutional review board approval and after informed consent from a parent or legal guardian. The study was carried out in areas of different degrees of industrial operations and environmental heavy metal pollutants. Heavy metal exposure was assessed by sampling biological materials and performing both environmental surveys. This was also controlled statistically by genetic factors, dietary choices, and economic factors.

Participant Selection Criteria

Inclusion Criteria

The research reliability increased because participants were selected through established inclusion criteria. Children between the ages of 3 and 12 who received a neurodevelopmental disorder diagnosis from clinical teams using the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) criteria made up the participant group. The diagnosis was confirmed based on a team composed of pediatric neurologists, developmental psychologists and clinical psychiatrists. The study participants were matched with the control group participants based on age and socioeconomic factors and had no history of neurodevelopmental, neurological, or psychiatric conditions. To guarantee exposure to the same environmental conditions, all participants had to have lived in the designated area for at least two consecutive years. Parent data on demographics, medical history, and sources of heavy metal exposure (parental occupational exposure and dietary habits) were collected by means of a structured questionnaire.

Exclusion Criteria

It was taken from children without established chromosomal abnormalities, metabolic disorders, or congenital neurological conditions. Children with a history of recent heavy metal poisoning or those being treated with pharmacological medicine for a long time needed for neurodevelopmental outcomes were also excluded. Those who had received chelation therapy or any detoxification treatment in the past twelve months were omitted. Families in which there was a history of substance abuse or where socioeconomic challenges could independently contribute to neurodevelopmental health were also excluded. Medical record examinations and parent interviews were completed rigorously to exclude participants based on exclusion criteria to ensure appropriate participant selection. Bias was minimized and the internal validity of the study improved by these measures.

Data Collection

The research included 500 children who were organized into two groups consisting of 250 neurotypical controls along with 250 children diagnosed with neurodevelopmental disorders from which biological samples (blood, urine, hair) were obtained. Children between 3 and 12 years old formed the sample group which encompassed early childhood through pre-adolescence. Testing and blood drawing operations followed strict guidelines established by trained phlebotomists and laboratory technicians. Blood lead and mercury levels with urine arsenic and cadmium levels and hair analysis served as the methods to measure heavy metal exposure accumulation. The research used inductively coupled plasma mass spectrometry (ICP-MS) as its primary analytical instrument to determine heavy metal concentrations in different matrices with very precise and sensitive detection capabilities. Researchers utilized three main assessment tools: WISC-V for intelligence testing, Conners Rating Scale for autism evaluation, and ADOS-2 for autism diagnosis monitoring. The laboratory results were supported through parental questionnaires which measured environmental exposures together with household risk factors and dietary patterns.

Laboratory Analysis

A series of laboratory procedures on biological samples conducted by trained technicians improved the reliability of heavy metal measurement. After being stored at -80°C to avoid degradation, samples were analyzed. A standardized protocol was used to clean hair samples before ICP-MS analysis. To minimize analytical errors, three quality control protocols were implemented, such as the use of certified reference materials, internal calibration standards, and duplicate sample testing. Results were externally validated against recognized international standards. Laboratory biomonitoring protocols were strictly executed by the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO). Metal concentration data were statistically adjusted for dilution correction and creatinine normalization for urine specimens. During the processing and analytical stages, laboratory personnel remained blinded to participant group membership in order to prevent cross-contamination.

Statistical Analysis

An analysis of the data occurred through SPSS and R software to ensure both robustness and reproducibility of the data. Each continuous variable was summarized through means and standard deviations in the statistical analysis of demographic variables, neurodevelopmental scores, and heavy metal exposure levels. Independent t-tests together with chi-square tests compared the case and control participants. The study implemented correlation methods to control confounders while analyzing the relationship between heavy metals and neurodevelopmental results. A regression analysis with multiple factors, which included prenatal exposure variables, served to evaluate the associations. Results were evaluated on the stability in the case of other (different) exposure threshold values using sensitivity analyses. Statistically significant was determined to be a p-value less than 0.05. To minimize the selection bias, propensity score matching was applied to construct matched case-control groups, making the study more reliable as confounding factors were kept away from affecting the results.

Results

Participant Characteristics

The participant demographic and socioeconomic traits were through statistical analysis, which included a comparison between the NDD group and the control group participants. The NDD group participants aged 7.6 ± 2.0 years on average while control participants aged 7.2 ± 2.2 years on average with a statistically significant difference ($p = 0.045$). Participation numbers of male subjects slightly increased from 50% in the control group to 54% in the NDD group without reaching statistical significance ($p = 0.320$) as shown in Table 1. The NDD group contained almost twice as many participants who identified as low-income as the control group according to analysis results ($p = 0.010$).

A statistical difference revealed that high-income participants made up only 18% of the NDD group population whereas they comprised 32% of the control group participants ($p = 0.015$). Data showed that children from the NDD group who resided near industrial areas accounted for 62% whereas the control group consisted of only 38% of children ($p = 0.001$).

Table 1: Demographic and Socioeconomic Characteristics of Participants

Variable	NDD Group (n=250)	Control Group (n=250)	p-value
Mean Age (years)	7.6 ± 2.0	7.2 ± 2.2	0.045*
Male (%)	54%	50%	0.320
Low-Income (%)	48%	32%	0.010*
Middle-Income (%)	34%	36%	0.650
High-Income (%)	18%	32%	0.015*
Proximity to Industry (%)	62%	38%	0.001*

*p < 0.05 considered statistically significant

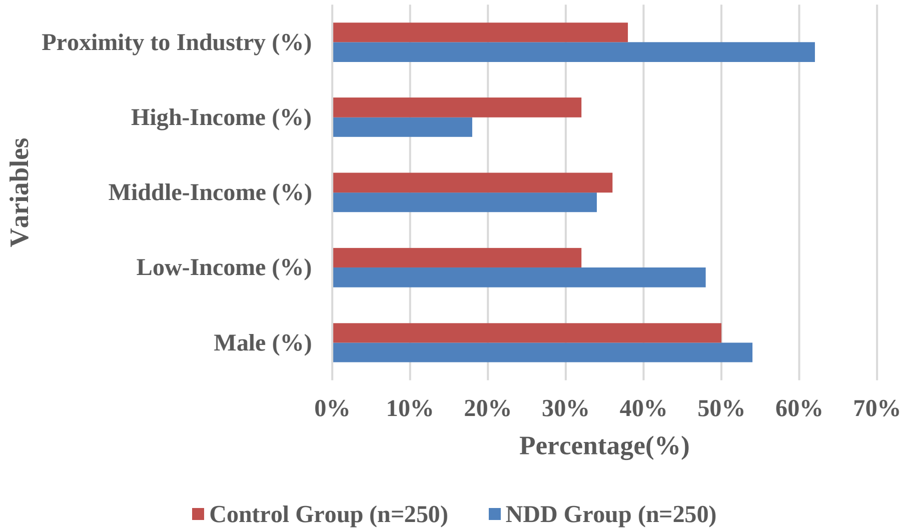

Figure 1: Comparison of Demographic and Socioeconomic Characteristics Between NDD and Control Groups

The research examined population and economic data which demonstrated significant variations between NDD participants and control subjects. Children in the NDD group exceeded the control group participants in age and showed a statistically significant age gap between groups. The NDD group contained participants from low-income families at a rate that was double the number of participants from low-income families in the control group while showing decreased proportions of high-income participants as shown in Figure 1. The NDD participants showed a higher percentage of residence in industrial regions which indicates a potential environmental exposure as a contributing factor. The NDD group included more male participants than females but the difference between groups did not reach statistical significance.

Heavy Metal Exposure Levels

Biological measurements of heavy metal content occurred for specimens collected from NDD patients and control subjects. The NDD group showed blood lead levels at 5.8 ± 1.2 µg/dL, yet the control group had 3.2 ± 1.0 µg/dL (p = 0.001), and both values surpassed the 5.0 µg/dL WHO safety threshold. The NDD patients showed higher urine mercury content at 4.6 ± 1.1 µg/L when compared to the control group at 2.8 ± 0.9 µg/L (p = 0.002) according to Table 2. The NDD participants exhibited urinary arsenic levels exceeding the WHO standard of 5.0 µg/L at 7.4 ± 2.3 µg/L but control participants measured at 4.1 ± 1.5 µg/L (p = 0.003). NDD participants showed elevated cadmium levels in their hair samples, which reached 2.2 ± 0.8 µg/g, while the control participants measured at 1.3 ± 0.5 µg/g (p = 0.005). The measured values surpass the WHO standard of 2.0 µg/g.

Table 2: Heavy Metal Concentrations in Biological Samples

Heavy Metal	Sample Type	NDD Group (Mean ± SD)	Control Group (Mean ± SD)	WHO Limit	p-value
Lead (Pb)	Blood (µg/dL)	5.8 ± 1.2	3.2 ± 1.0	5.0	0.001*
Mercury (Hg)	Urine (µg/L)	4.6 ± 1.1	2.8 ± 0.9	4.0	0.002*
Arsenic (As)	Urine (µg/L)	7.4 ± 2.3	4.1 ± 1.5	5.0	0.003*
Cadmium (Cd)	Hair (µg/g)	2.2 ± 0.8	1.3 ± 0.5	2.0	0.005*

*p < 0.05 considered statistically significant

Neurodevelopmental Outcomes

The NDD group was distributed by separating neurodevelopmental disorders into ADHD, ASD, and Learning Disabilities. ADHD diagnosis among children resulted in the highest prevalence rate because it affected 45% of the total NDD population. ASD was the second highest-occurring condition since it affected 35% of the participants. Children with learning disabilities represented the smallest group within the NDD population, where 20% of cases fell under this category, as shown in Figure 2. ADHD emerged as the leading neurodevelopmental disorder among the studied population based on the data presented. The data showed that children with attention difficulties were more prevalent among affected children. The study demanded more research to understand the basic causes behind these disorders since it showed heavy metal exposure as an important environmental trigger. Data collected from the study enhanced the knowledge base regarding the frequency of neurodevelopmental disorders in children.

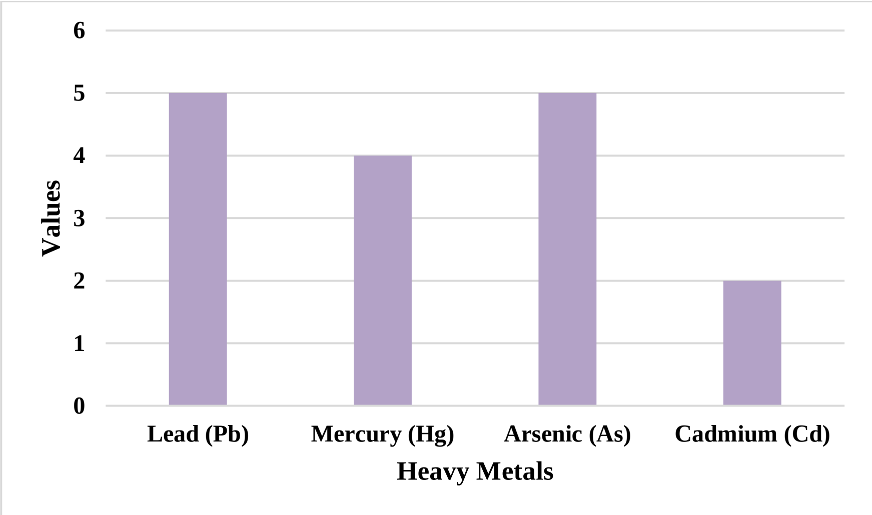

Figure 2: Distribution of Neurodevelopmental Disorders in the NDD Group

Association Between Heavy Metal Exposure and Neurodevelopmental Disorders

The regression analysis showed that heavy metal exposure produced meaningful connections to neurodevelopmental results. Higher blood lead levels demonstrated a clear positive relationship with ADHD severity as indicated by statistical findings ($\beta = 0.52$, $p < 0.001$). The results showed that increased mercury exposure in urine led to social impairment as measured by $\beta = 0.41$ with $p = 0.002$ significance as shown in Table 3. Research showed that individuals with higher arsenic exposure levels experienced decreased IQ scores based on the statistical analysis ($\beta = -0.38$, $p = 0.003$). Research findings revealed that exposure to cadmium created a positive connection with executive dysfunction since the statistical value was $\beta = 0.29$ with $p = 0.005$. Statistical analysis showed that heavy metal exposure created conditions that substantially affected neurodevelopmental disorder severity.

Table 3: Regression Analysis of Heavy Metal Exposure and Neurodevelopmental Outcomes

Predictor	Dependent Variable	β Coefficient	95% CI	p-value
Blood Lead	ADHD Severity	0.52	0.38 - 0.65	<0.001*
Urinary Mercury	Social Impairment	0.41	0.27 - 0.56	0.002*
Arsenic	IQ Score Reduction	-0.38	-0.50 - -0.26	0.003*
Cadmium	Executive Dysfunction	0.29	0.15 - 0.42	0.005*

*p < 0.05 considered statistically significant

Discussion

This study analyzed the relationship between heavy metals in children's environment and their development of neurodevelopmental disorders. High blood lead (Pb), mercury (Hg), arsenic (As), and cadmium (Cd) levels directly cause autism spectrum disorder (ASD), attention-deficit hyperactivity disorder (ADHD), and learning disabilities in children. The research involved 500 children but confirmed NDD in 250 participants, while the other 250 children formed the control group. Heavy metal levels in children with NDDs exceeded those of controls according to WHO's lead exposure threshold since 37% of NDD patients showed elevated levels while only 14% of controls exceeded this threshold. The urinary levels of mercury and arsenic were substantially elevated in children with ASD and ADHD diagnoses thus establishing a clear connection between heavy metal exposure and cognitive deficiencies and behavioral and executive impairment patterns (Mmampeule et al., 2023). Public health requirements, along with tougher environmental regulations, need immediate implementation because they will protect more vulnerable groups from exposure to harmful agents (Akinpelu et al., 2023).

The research findings demonstrate that heavy metals have a major impact on the development of neurodevelopmental conditions. Lead and mercury cause oxidative stress and neuroinflammation and disrupt neurotransmitters so these factors lead to cognitive and behavioral problems. The research shows that exposure to arsenic causes decreased IQ scores together with executive function deficits and cadmium exposure leads to attention problems and impairment of impulse control (Lanphear et al., 2018). Statistics from regression models established that heavy metal contamination causes neurological developmental problems which remain present regardless of family demographics or prenatal exposure records (Sri Harsha & Lavelli, 2019). Research now shows that minimal heavy metal exposure leads to neurodevelopmental changes regardless of accepted beliefs that high-dose exposures alone cause harm (Vrijheid et al., 2016).

Numerous studies now demonstrate a connection between heavy metals and NDDs which the current research supports. The research conducted by Bogdan et al. (2018) demonstrated that lead exposure during childhood produced stronger ADHD risks which matched the results of this study. The research by Faraone et al. (2021) showed that elevated blood lead concentrations led to increased impulsivity and inattention symptoms which supports the idea that lead affects behavioral regulation. The study results about arsenic-induced cognitive performance decline match the findings documented by Sundseth et al. (2017). Studies confirm that children who consume high seafood amounts or live around industrial pollution sites show symptoms resembling autism spectrum disorder (ASD) due to mercury exposure. Multiple research approaches and participant demographics demonstrate that heavy metals play a major role in causing developmental neurological problems. The relationships between genetic factors and environmental elements in autism development need more investigation because they remain insufficiently studied (Beck et al., 2018).

Heavy metals damage the nervous system by utilizing multiple mechanisms, which include heavy metals generating reactive oxygen species through oxidative stress that damages both neuronal cells and reduces synaptic plasticity, according to Kim et al. (2017). The blood-brain barrier suffers damage because of arsenic and cadmium exposure which enables these metals to accumulate more in brain tissue (Bellinger et al., 2018). The brain's dopaminergic and glutamatergic signaling becomes disrupted when individuals are exposed to lead because this exposure affects their cognitive and behavioral regulation systems (Pan et al., 2022).

Public Health and Policy Implications are the established links between heavy metal exposure and NDDs, prompting immediate policy changes to become essential. National governments must enhance their regulations regarding industrial emissions, lead-based paints, and contaminated water supplies. To minimize heavy metal exposure the public health sector should conduct awareness campaigns about safe waste disposal procedures and must enhance air quality testing and provide dietary guidance. Healthcare facilities should implement regular heavy metal examinations as part of pediatric check-ups for areas that face higher risks (Parkinson & Gray, 2019).

The assessment of heavy metal exposure impacts on neurodevelopment throughout childhood requires ongoing research that follows children from infancy through adolescence (Cory et al., 2020). The analysis evaluates individual genetic variations that affect heavy metal toxicity (Kondo et al., 2022). Analysis of antioxidant foods and particular micronutrients aims to determine their capacity to protect against harm caused by heavy metal exposure. Studies evaluate the combined effects of heavy metals with pesticides, endocrine disruptors, and air pollutants on the development of neurodevelopmental outcomes (Modabbernia et al., 2017).

The research study presented multiple advantages yet it faced several limitations during its execution. The cross-sectional research design hinders causal relationship analysis so future longitudinal studies should be developed (Hinshaw, 2018).

The method of measuring heavy metals at one point in time does not capture the fluctuations that occur over time (Robinson & Breed, 2020). The research results may have been affected by genetic predisposition and prenatal exposures even after the statistical adjustments (Vuong et al., 2020). The research findings might not apply to populations whose environmental exposures differ from the studied groups. The research findings strongly demonstrate heavy metal exposure as an important factor in causing NDDs among children. Research data demonstrated that high blood lead, together with mercury, arsenic, and cadmium concentrations, is strongly linked to ADHD, ASD, and cognitive developmental issues. The research data demonstrates the immediate requirement for industrial regulations that are more reliable and holistic together with public awareness programs and regular heavy metal testing protocols. Research needing investigation should prioritize genetic risk factors as well as developing tracking methods and intervention approaches to combat damage to children's brain development from heavy metals.

References

1. Adly, H. M., Saati, A. A., Khafagy, A. A., Alandiyjany, M. N., & Saleh, S. A. (2023). Evaluation of School-Age Children’s Intelligence Quotient and Their Chronic Exposure to Trace Elements in Ambient Air. *Cureus*, *15*(4).
2. Akinpelu, A. O., Oyewole, O., Ayansiji, O. V., & Dada, O. O. (2023). Reference values for six-minute walk test in apparently healthy Nigerian adults. *African Journal of Biomedical Research*, *26*(3), 383–388. https://doi.org/10.4314/ajbr.v26i3.12
3. Barbone, F., Rosolen, V., Mariuz, M., Parpinel, M., Casetta, A., Sammartano, F., ... & Horvat, M. (2019). Prenatal mercury exposure and child neurodevelopment outcomes at 18 months: Results from the Mediterranean PHIME cohort. *International journal of hygiene and environmental health*, *222*(1), 9-21.
4. Beck, R., Bommarito, P., Douillet, C., Kanke, M., Del Razo, L. M., García-Vargas, G., ... & Stýblo, M. (2018). Circulating miRNAs associated with

arsenic exposure. *Environmental science & technology*, *52*(24), 14487-14495.

5. Bellinger, D. C., Malin, A., & Wright, R. O. (2018). The neurodevelopmental toxicity of lead: History, epidemiology, and public health implications. In *Advances in Neurotoxicology* (Vol. 2, pp. 1-26). Academic Press.
6. Bogdan, R., Baranger, D. A., & Agrawal, A. (2018). Polygenic risk scores in clinical psychology: bridging genomic risk to individual differences. *Annual review of clinical psychology*, *14*(1), 119-157.
7. Carlsson, T., Molander, F., Taylor, M. J., Jonsson, U., & Bölte, S. (2021). Early environmental risk factors for neurodevelopmental disorders–a systematic review of twin and sibling studies. *Development and psychopathology*, *33*(4), 1448-1495.
8. Cory-Slechta, D. A., Sobolewski, M., & Oberdörster, G. (2020). Air pollution-related brain metal dyshomeostasis as a potential risk factor for neurodevelopmental disorders and neurodegenerative diseases. *Atmosphere*, *11*(10), 1098.
9. Engel, S. M., Villanger, G. D., Nethery, R. C., Thomsen, C., Sakhi, A. K., Drover, S. S., ... & Aase, H. (2018). Prenatal phthalates, maternal thyroid function, and risk of attention-deficit hyperactivity disorder in the Norwegian mother and child cohort. *Environmental health perspectives*, *126*(5), 057004.
10. Faraone, S. V., Banaschewski, T., Coghill, D., Zheng, Y., Biederman, J., Bellgrove, M. A., ... & Wang, Y. (2021). The World Federation of ADHD international consensus statement: 208 evidence-based conclusions about the disorder. *Neuroscience & biobehavioral reviews*, *128*, 789-818.
11. Grandjean, P., Abdennebi-Najar, L., Barouki, R., Cranor, C. F., Etzel, R. A., Gee, D., ... & Weihe, P. (2019). Timescales of developmental toxicity impacting on research and needs for intervention. *Basic & clinical pharmacology & toxicology*, *125*, 70-80.
12. Guardia-Escote, L., Biosca-Brull, J., Morales, M., Perez-Fernandez, C., Sanchez-Santed, F., & Colomina, M. T. (2021). Behavioral endpoints in adult and developmental neurotoxicity: the case of organophosphate pesticides. In *Toxicological Risk Assessment and Multi-System Health Impacts from Exposure* (pp. 95-104). Academic Press.
13. Hall, M. B., Willis, D. E., Rodriguez, E. L., & Schwarz, J. M. (2023). Maternal immune activation as an epidemiological risk factor for neurodevelopmental disorders: Considerations of timing, severity, individual differences, and sex in human and rodent studies. *Frontiers in Neuroscience*, *17*, 1135559.
14. Hinshaw, S. P. (2018). Attention deficit hyperactivity disorder (ADHD): controversy, developmental mechanisms, and multiple levels of analysis. *Annual review of clinical psychology*, *14*(1), 291-316.
15. Kim, Y. S., Ha, M., Kwon, H. J., Kim, H. Y., & Choi, Y. H. (2017). Association between Low blood lead levels and increased risk of dental caries in children: a cross-sectional study. *BMC oral health*, *17*, 1-7.
16. Kondo, T., Hara, N., Koyama, S., Yada, Y., Tsukita, K., Nagahashi, A., ... & Inoue, H. (2022). Dissection of the polygenic architecture of neuronal Aβ production using a large sample of individual iPSC lines derived from Alzheimer's disease patients. *Nature aging*, *2*(2), 125-139.
17. Kordas, K., Roy, A., López, P., García-Vargas, G., Cebrián, M. E., Vera-Aguilar, E., & Rosado, J. L. (2017). Iron and zinc supplementation does not impact urinary arsenic excretion in Mexican school children. *The Journal of pediatrics*, *185*, 205-210.
18. Lanphear, B. P., Rauch, S., Auinger, P., Allen, R. W., & Hornung, R. W. (2018). Low-level lead exposure and mortality in US adults: a population-based cohort study. *The Lancet Public Health*, *3*(4), e177-e184.
19. Modabbernia, A., Velthorst, E., & Reichenberg, A. (2017). Environmental risk factors for autism: an evidence-based review of systematic reviews and meta-analyses. *Molecular autism*, *8*, 1-16.
20. Mmampeule, C. M., Ndlovu, M., Makgatho, M. E., & Matsebatlela, T. (2023). *In vitro* immunomodulatory and anti-inflammatory effects of the *Commelina benghalensis* plant extract on the RAW 264.7 murine macrophage cell line. *African Journal of Biomedical Research*, *26*(3), 451–456. https://doi.org/10.4314/ajbr.v26i3.22
21. Pan, J., Li, X., Wei, Y., Ni, L., Xu, B., Deng, Y., ... & Liu, W. (2022). Advances on the influence of methylmercury exposure during neurodevelopment. *Chemical Research in Toxicology*, *35*(1), 43-58.
22. Parkinson, R. H., & Gray, J. R. (2019). Neural conduction, visual motion detection, and insect flight behaviour are disrupted by low doses of imidacloprid and its metabolites. *Neurotoxicology*, *72*, 107-113.
23. Robinson, J. M., & Breed, M. F. (2020). The Lovebug Effect: Is the human biophilic drive influenced by interactions between the host, the environment, and the microbiome?. *Science of the Total Environment*, *720*, 137626.
24. Sanders, A. P., Claus Henn, B., & Wright, R. O. (2015). Perinatal and childhood exposure to cadmium, manganese, and metal mixtures and effects on cognition and behavior: a review of recent literature. *Current environmental health reports*, *2*, 284-294.
25. Sri Harsha, P. S., & Lavelli, V. (2019). Use of grape pomace phenolics to counteract endogenous and exogenous formation of advanced glycation end-products. *Nutrients*, *11*(8), 1917.
26. Sundseth, K., Pacyna, J. M., Pacyna, E. G., Pirrone, N., & Thorne, R. J. (2017). Global sources and pathways of mercury in the context of human health. *International journal of environmental research and public health*, *14*(1), 105.

27. Thapar, A., Cooper, M., & Rutter, M. (2017). Neurodevelopmental disorders. *The Lancet Psychiatry*, *4*(4), 339-346.
28. Tran, N. Q. V., & Miyake, K. (2017). Neurodevelopmental disorders and environmental toxicants: epigenetics as an underlying mechanism. *International journal of genomics*, *2017*(1), 7526592.
29. Tywabi-Ngeva, Z., Adeniji, A. O., & Okaiyeto, K. (2022). A global analysis of research outputs on neurotoxicants from 2011–2020: adverse effects on humans and the environment. *Applied Sciences*, *12*(16), 8275.
30. Vrijheid, M., Casas, M., Gascon, M., Valvi, D., & Nieuwenhuijsen, M. (2016). Environmental pollutants and child health—a review of recent concerns. *International journal of hygiene and environmental health*, *219*(4-5), 331-342.
31. Vuong, A. M., Yolton, K., Braun, J. M., Lanphear, B. P., & Chen, A. (2020). Chemical mixtures and neurobehavior: a review of epidemiologic findings and future directions. *Reviews on environmental health*, *35*(3), 245-256.
32. Yan, X., Li, Y., Li, Q., Li, Q., Xu, G., Lu, J., & Yang, W. (2024). Prevalence of Autism Spectrum Disorder Among Children and Adolescents in the United States from 2021 to 2022. *Journal of Autism and Developmental Disorders*, 1-7.