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# Autism spectrum disorder and environmental pesticide exposure: insights from an integrative review

Transtorno do espectro autista e exposição ambiental aos agrotóxicos: evidências de uma revisão integrativa

Trastorno del espectro autista y exposición ambiental a pesticidas: perspectivas desde una revisión integradora

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**ABSTRACT**

**Objective:** To investigate whether there is a relationship between exposure to pesticides and autism spectrum disorder. **Methodos:** This study was followed by an integrative literature review, exploring articles published between 2020 and 2024 in the CAPES Periodicals databases, using descriptors such as “pesticides” and “autism spectrum disorder,” and included 10 of the 102 initially selected studies, all in English and with open access. **Results:** The research suggests a link between exposure to pesticides and an increased risk of ASD, mainly due to the neurotoxic effects of certain classes of pesticides. However, other factors, including genetic susceptibility and nutritional conditions, may also influence this relationship. **Final considerations:** Although the results are still inconclusive, prenatal exposure to pesticides tends to increase vulnerability to ASD, highlighting the need for further epidemiological research to support more effective and preventive public health policies.

**Keywords:** Autism, Human contamination, Pesticides.

**RESUMO**

**Objetivo:** Investigar se há relação entre a exposição aos agrotóxicos e o transtorno do espectro autista. **Métodos:** A partir deste estudo realizou-se uma revisão integrativa da literatura, explorando artigos publicados entre 2020 e 2024 na base de dados do Portal de Periodicos da CAPES, utilizando descritores como “pesticidas” e “transtorno do espectro do autismo”, e incluiu 10 dos 102 estudos inicialmente selecionados, todos em inglês e de acesso aberto. **Resultados:** A pesquisa sugere uma ligação entre a exposição a pesticidas e o aumento do risco de TEA, principalmente devido aos efeitos neurotóxicos de algumas classes de pesticidas. Contudo, outros fatores, incluindo a suscetibilidade genética e as condições nutricionais, também podem alterar essa relação. **Considerações finais:** Apesar dos resultados ainda serem inconclusivos, a exposição pré-natal a pesticidas tende a aumentar a vulnerabilidade ao TEA, sublinhando a necessidade de mais pesquisas epidemiológicas para fundamentar políticas públicas mais eficazes e preventivas na saúde coletiva.

**Palavras-chave:** Autismo, Contaminação humana, Pesticidas.

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**RESUMEN**

**Objetivo:** Investigar si existe una relación entre la exposición a pesticidas y el trastorno del espectro autista. **Metodos:** Este estudio realizó una revisión integradora de la literatura, explorando artículos publicados entre 2020 y 2024 en bases de datos del Portal de Publicaciones Periódicas de CAPES, utilizando descriptores como “pesticidas” y “trastorno del espectro autista”, e incluyó 10 de los 102 estudios inicialmente seleccionados, todos en inglés y de acceso abierto. **Resultados:** La investigación sugiere una relación entre la exposición a pesticidas y un mayor riesgo de TEA, principalmente debido a los efectos neurotóxicos de algunas clases de pesticidas. Sin embargo, otros factores, incluyendo la susceptibilidad genética y las condiciones nutricionales, también pueden influir en esta relación. **Consideraciones finales:** Aunque los resultados aún son inconclusos, la exposición prenatal a pesticidas tiende a aumentar la vulnerabilidad al TEA, destacando la necesidad de más investigaciones epidemiológicas para respaldar políticas públicas más efectivas y preventivas en salud pública.

**Palabras clave:** Autismo, Contaminación humana, Pesticidas.

## INTRODUCTION

Autism Spectrum Disorder (ASD) is a neurodevelopmental condition characterized by difficulties in learning, communication, behavior, and social interaction, often linked to sensory deficits that may result in hypersensitivity or hyposensitivity (BACH MA, et al*.,* 2020; DESALEGN AA, et al*.,* 2023).

The global prevalence of ASD has been steadily increasing. In the United States, recent statistics indicate that 1 in 36 children are diagnosed with ASD (INSTITUTO STEINKOPF, 2023). In Brazil, it is estimated that around 2 million individuals are on the spectrum. Initiatives such as the "Autism Map Brazil," launched in 2023, have been instrumental in gathering comprehensive sociodemographic data, offering valuable insights into the national autism landscape (INSTITUTO STEINKOPF, 2023).

There have been suggestions that genetics and environmental factors can influence the rise of ASD diagnoses (SCHMIDT S, 2021). Specific genetic mutations and gene variations can play a crucial role in developing ASD (BHANDARI R, et al., 2020).

Mutations in genes such as *MECP2*, *SHANK3*, and *PTEN*, along with duplications of chromosome 15q11-q13, have been strongly implicated in the development of ASD. These genetic anomalies are believed to disrupt critical neurological processes, contributing to the structural and functional abnormalities characteristic of ASD (CAMASIO A, et al., 2022).

Environmental factors play a critical role in modulating the risk of autism spectrum disorder (ASD), with exposure to environmental pollutants such as heavy metals (e.g., mercury and lead), chemical agents, and endocrine-disrupting compounds being particularly implicated. These exposures are especially detrimental during sensitive periods of neurodevelopment, such as the prenatal stage and early childhood, when the brain undergoes rapid growth and differentiation. Studies have identified associations between these exposures and an increased risk of ASD, highlighting the significance of pollutants found in pesticides and other environmental sources as contributors to developmental disruptions (SCHMIDT S, 2021). These substances have been linked to increased risks of neurodevelopmental disorders, highlighting the importance of minimizing environmental exposure during these vulnerable stages.

Pesticides, widely used in agriculture, are notably harmful to the nervous system (LUCERO B e MUÑOZ-QUEZADA MT, 2021). Pesticides are defined as products for pest control, primarily in agriculture, forestry, and aquaculture (BRASIL, 2023). The National Health Surveillance Agency (Anvisa) evaluates pesticide toxicity based on acute, chronic, carcinogenic, and mutagenic effects, ensuring safe usage (BRASIL, 2024). In 2023, Brazil sold approximately 720,000 tons of active pesticide ingredients, marking a 5% increase from the previous year. The most sold active ingredients include glyphosate, atrazine, 2,4-D, and mancozeb (BRASIL, 2023).

These chemicals are known to induce oxidative stress and disrupt the nervous system, mechanisms that are linked to neurodegenerative conditions and behaviors resembling ASD (SULE R, et al., 2022). Direct and indirect exposure to pesticide residues has been associated with various health issues, including cancer, allergies, chronic diseases, and depression in individuals directly exposed (FARIAS PRADO JA, et al., 2021). Furthermore, exposure to these compounds during pregnancy and early childhood can impair neurological development, potentially contributing to conditions like diabetes, obesity, and respiratory complications (GUZMAN-TORRES H, et al., 2023).

The aim of this integrative review is to investigate the link between pesticide exposure and the development of ASD, seeking to deepen our understanding of how these environmental factors may contribute to the disorder's onset and progression.

## METHODS

A integrative review of scientific articles was conducted to examine the relationship between pesticide exposure and ASD. This type of review aims to identify, select, evaluate, and synthesize the relevant evidence available on a specific topic. The integrative review follows a pre-established protocol, ensuring transparency and reproducibility of the methods used (HIGGINS JPT, et al., 2024). The methodological procedures included: formulation of the research question and review objectives; categorization of the studies; data analysis with interpretation of results; and synthesis of the review findings.

The PICO acronym was used as a strategy for formulating the research question, where the acronym stands for: "P" – Patient, defining the population or research problem; "I" – Intervention, specifying the intervention performed; "C" – Comparison, identifying the control group to be compared with the intervention group; and "O" – Outcome, defining the outcome to be evaluated (HOSSEINI MS, et al., 2024).

The PICO is a protocol used in integrative reviews to assist in the formulation of the research question. However, not all of its elements need to be necessarily completed, as the construction of the question depends on the specific characteristics of the review. Based on this acronym, the research question was formulated as follows: What is the relationship between pesticide exposure and the onset of Autism Spectrum Disorder?

**Table 1 -** Formulation of the Research Question Based on the PICO Acronym.

| P | I | C | O |
|---|---|---|---|
| Humans (children, adults) | Pesticide Exposure | - | Autism Spectrum Disorder |

**Origin:** Frederes JPMB, et al., 2026.

The article search was conducted by three independent reviewers between May and August 2024 using the CAPES Periodicals database. The descriptors in Health Sciences (DeCS) used for the search were: "pesticides" (as a synonym for agrochemicals, the term described in current Brazilian legislation) and "autism spectrum disorder," exclusively in English. The Boolean operator AND was applied between the descriptors. Articles were selected based on the presence of these descriptors in the title, abstract, and/or keywords of the articles retrieved.

Subsequently, the articles were imported into the Rayyan platform, where the selection process was conducted. The review included articles published in scientific journals between 2020 and 2024 that addressed the investigated topic, were open access, available in full-text format, and involved research conducted exclusively on humans.

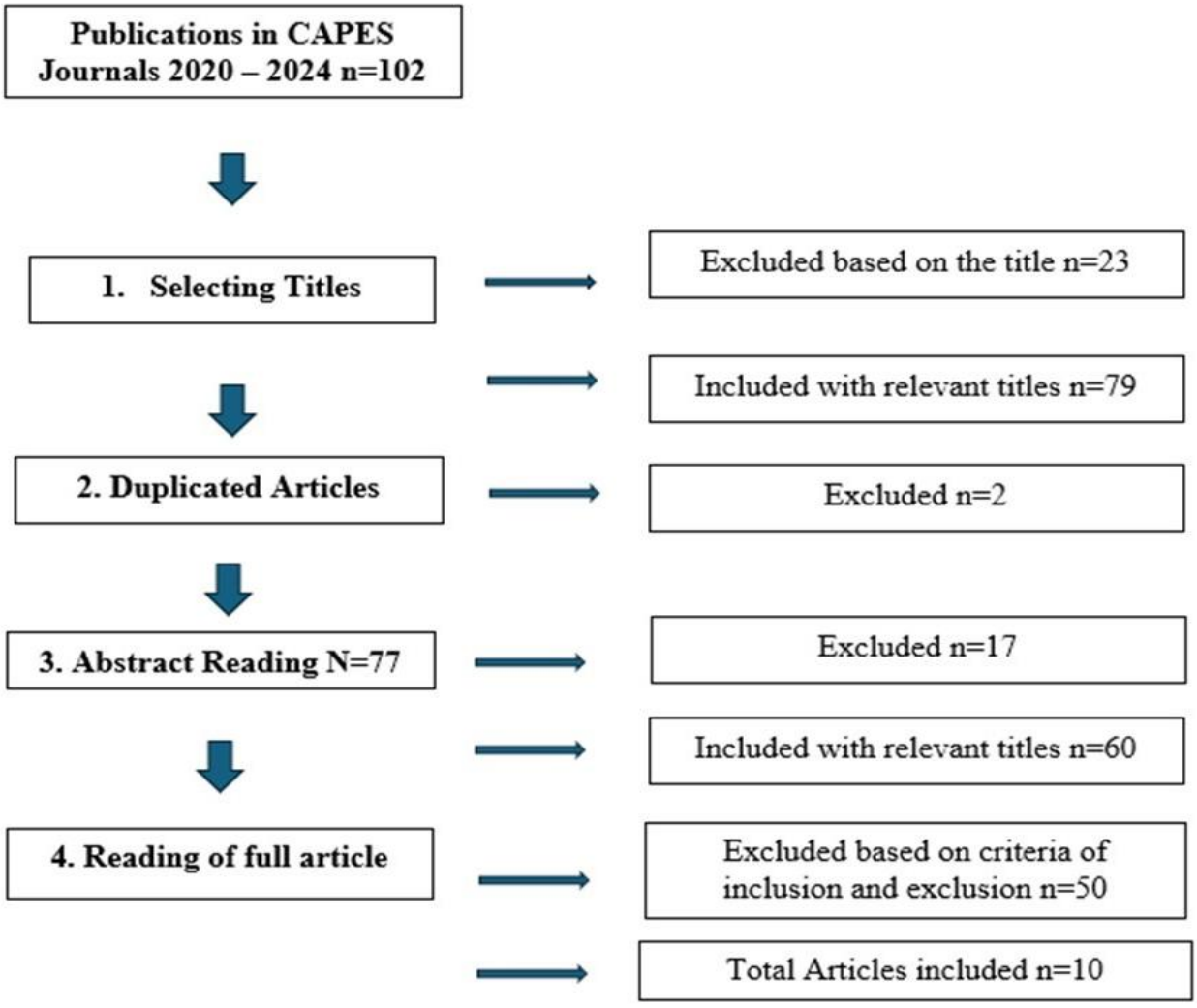
Exclusion criteria included reviews, systematic reviews, duplicate articles, theses, non-indexed articles, case reports, commentaries, studies involving animals, and publications that did not align with the review's objectives. The article selection process followed a step-by-step approach: first, the titles were reviewed, followed by the abstracts, and finally, the full texts. Inclusion and exclusion criteria were consistently applied at each stage.

All selected articles were compiled into a review table containing the following information: authors, year of publication, study design/type, primary objective, type of pesticide, research sample, country of origin, main results, and conclusions. The data analysis was performed descriptively.

## RESULTS AND DISCUSSION

The procedures adopted and the number of articles selected throughout the systematic review process are presented in **Figure 1**.

**Figure 1 -** Selection process and preliminary analysis of relevant scientific articles for the research.




**Source:** Frederes JPMB, et al., 2026.

From the analysis of the 10 selected scientific articles, information was characterized regarding the authors, year of publication, study design/type, primary objective, type of pesticide, research h sample, country of origin, main results, and conclusions. These details are summarized in **Table 2**.

**Table 2 -** Review table with key information extracted from the selected articles.

| N | Authors (Year) | Objective | Type of Study | Pesticide | Sample | Country | Results | Conclusion |
|---|---|---|---|---|---|---|---|---|
| 1 | Desalegn *et al.*, (2023). | Examined associations between persistent chemicals in breast milk and ASD risk, complemented by *in vivo* zebrafish experiments. | Epidemiological and experimental study. | PCBs, OCPs; PBDEs, ÿ-HCH | 1,199 mothers (humans) and zebrafish. | Norway. | Perinatal 0exposure to ɣ-HCH doubled ASD risk; zebrafish confirmed its neurotoxicity. | ɣ-HCH exposure increases ASD risk; further studies should assess its effects even at low levels. |
| 2 | Ongono *et al.*, (2022). | Analyzed the impact of residential proximity to agricultural crops and pesticide exposure on adaptive behaviors in children with ASD. | Observational study. | General agricultural exposure. | 224 children. | France | Proximity to crops (≤1000 m) was linked to poor communication skills in ASD children without intellectual disability. | Early exposure to agricultural pesticides may impair communication development in ASD children. |
| 3 | Lizé *et al.*, (2022). | Investigated prenatal exposure to organophosphate pesticides and ASD-related traits in children. | Observational study. | Organophosphates | 185 mother–child pairs. | France | Maternal exposure to CPF increased autistic traits, especially in boys. | Prenatal organophosphate exposure may elevate ASD-related traits. |
| 4 | Hai; Leng. (2022). | Assessed whether pesticide exposure contributes to gender differences in ASD incidence. | Epidemiological study | General use data. | General use data. | China | ASD prevalence and DALYs were four times higher in boys; rural pesticide exposure nearly doubled compared to urban areas. | Pesticide use may partly explain higher ASD rates in boys, especially in rural populations. |
| 5 | Joyce *et al.*, (2022). | Evaluated whether dietary pesticide residues are associated with ASD-related traits. | Observational study. | Organophosphates, piritramide, neonicotinoids. | 154 pregnant women. | United States. | No positive association found; nutrients in fruits/vegetables may mitigate pesticide effects. | Diet quality may buffer pesticide exposure impacts on ASD risk. |
| 6 | Bennett *et al.*, (2022). | Examined early-life exposure to pesticides, phthalates, and trace elements and their link to ASD, DD, and ADHD. | Epidemiological study. | Organophosphates, pyrethroids, carbamates, organochlorines. | 237 participants. | United States. | Multiple chemicals correlated with higher ASD risk, though significance decreased after adjustments. | Mixed pesticide exposure may contribute to ASD and other developmental disorders. |
| 7 | Román *et al.*, (2024). | Investigated ASD prevalence in regions with intensive agricultural pesticide use. | Population-based case–control study. | Organophosphates, pyrethroids, carbamates, organochlorines. | 52,393 residents (2,821 ASD cases). | Spain | Higher ASD prevalence in areas with greater pesticide use. | Living near high-use agricultural areas increases ASD risk, especially in males. |
| 8 | Bach *et al.*, (2020). | Explored associations between PCBs/OC pesticides and ASD, and gene interactions with GST variants. | Population-based case–control study. | PCBs e OC | 338 children. | Jamaica | No significant association found; possible dietary influence noted. | No direct link between PCB/OC levels and ASD, but further research warranted. |
| 9 | Schmidt, (2021). | Investigated gene–environment interactions in ASD using brain organoids. | Experimental study. | Chlorpyrifos. | Stem-cell-derived brain organoids. | United States. | CHD8 mutation combined with CPF exposure caused marked neurodevelopmental abnormalities | Gene–environment interactions amplify pesticide neurotoxicity in ASD. |
| 10 | Barkoski *et al.*, (2021). | Analyzed prenatal exposure to pyrethroids and ASD/neurodevelopmental outcomes in children. | Observational longitudinal study. | (3-PBA) | 203 mother–child pairs. | United States. | Higher urinary 3-PBA linked to slightly elevated ASD risk. | Prenatal pyrethroid exposure may modestly increase ASD risk. |

**Caption:** Autism Spectrum Disorder (ASD), Polychlorinated Biphenyls (PCBs), Organochlorine Pesticides (OCPs), Polybrominated Diphenyl Ethers (PBDEs), ɣ-Hexachlorocyclohexane (ÿ-HCH), Intellectual Disability (ID), Vineland Adaptive Behavior Scales (VABS-II), Disability-Adjusted Life Years (DALYs), Developmental Delay (DD), Other Early Concerns (OEC), Typical Development (TD), 3-Phenoxybenzoic Acid (3-PBA), Chlorpyrifos (CPF), Organochlorine Pesticides (OCs), Induced Pluripotent Stem Cells (iPSCs), Relative Risk Ratios (RRR), Voxel-Based Morphometry (VBM).
**Source:** Frederes JPMB, et al., 2026.

After examining the articles included in the table, it was found that there is a diversity in the types of studies predominant in the literature concerning the relationship between pesticides and ASD. Four main groups of studies were identified, with similar proportions: about one-third of the studies (4) are observational in nature; another third (3) are epidemiological studies; and the remaining third (3) includes experimental and control studies. Despite the diversity, there is still a lack of research on the topic, highlighting the need for further studies in this area.

Observational and epidemiological studies predominate in the literature and allow for the identification of associations between pesticide exposure and ASD risk in large populations. However, these designs do not establish cause-and-effect relationships, as they rely on retrospective data and are subject to confounding factors such as diet, socioeconomic conditions, and other environmental exposures. Ecological studies, in turn, contribute by revealing population-level patterns and generating initial hypotheses but present limitations regarding individual data accuracy due to the risk of ecological fallacy.

Regarding exposure assessment, there are significant differences among the methods employed. Studies based on indirect estimates, such as proximity to agricultural areas, are more accessible but less precise. In contrast, research using biological biomarkers, such as blood, urine, or breast milk, provides more objective and reliable measures, being considered the gold standard for assessing actual exposure. Therefore, the level of confidence in the evidence varies according to the study design and the methodology applied.

Regarding the geographical origin of the studies, four were conducted in the United States, two in France, and the remaining studies were conducted in China, Jamaica, Norway, and Spain. Most of the research was conducted in North America, followed by Europe, with a few studies conducted in Asia and Caribbean.

Countries like the United States have a higher rate of ASD diagnosis, with estimated prevalences around 1%, possibly related to improvements in diagnostic methods and greater social sensitivity to recognizing the disorder. This can trigger a cycle where more cases are diagnosed, leading to more research (FOMBONNE E, et al., 2021). In contrast, countries with less healthcare infrastructure, such as many in Caribbean and/or Latin America, may experience underreporting due to cultural, economic, and social barriers, as well as a lack of resources to perform proper diagnoses (SALARI N, et al., 2022).

In Brazil, awareness of ASD has been increasing, driven by initiatives such as public campaigns, supportive legislation, and the efforts of NGOs and social movements (BRASIL, 2022). According to the World Health Organization (WHO), the global prevalence of ASD ranges from 1% to 2% of the population, suggesting that approximately two million people in Brazil may have the diagnosis (WHO, 2020). In 2020, the Ministry of Health launched the Autism Identification Card (CIA) to facilitate access to rights and services, and April 2 was designated as World Autism Awareness Day. In this country, the entire month of April has also become known as Blue April, featuring nationwide awareness and advocacy activities (BRASIL, 2024). It is important to note that none of the studies included in this review were conducted in Brazil, which limits the applicability of the findings to the Brazilian population. The absence of local research hinders the evaluation of specific contextual factors, such as public policies, dietary habits, and environmental exposures, that may influence the prevalence and risk of ASD associated with pesticide exposure. This gap underscores the need for nationally based studies to better elucidate the relationship between pesticide exposure and ASD development within the Brazilian context (INSTITUTO STEINKOPF, 2023; SALARI N, et al., 2022).

Regarding the characteristics of the samples, most studies include children and mothers of children with ASD. Mothers, as central participants in studies on the relationship between pesticides and ASD, highlight the importance of maternal exposure during pregnancy and its impact on fetal development. Desalegn, et al. (2023) emphasize this relationship, suggesting that maternal exposure to pesticides may double the risk of autism in children.

Including mothers in research also facilitates the tracking of important environmental and dietary data, such as proximity to agricultural areas and the consumption of food with pesticide residues, and its effect on the development of ASD. In this regard, Ongono JS, et al. (2022) observed that children born to pregnant women living in agricultural areas and exposed to pesticides during pregnancy had poorer outcomes in communication

skills, while Joyce, et al. (2022) investigated the effect of pesticides in the mothers' diet and their correlations with ASD characteristics, suggesting that nutrients in food may mitigate the impact of pesticide toxicity on the maternal body.

Regarding the main chemical groups of pesticides related to ASD in the analyzed studies, there is a predominance of organophosphates, followed by pyrethroids. There are also mentions of carbamates, organochlorines, and polychlorinated biphenyls, among others. Thus, there is a notable prevalence of the relationship between the class of insecticides and ASD. It is important to highlight that the mode of action of insecticides primarily affects the central nervous system, interfering with its proper functioning. This explains the stronger association of these pesticides with ASD, a disorder linked to neurodevelopment. In this context, the predominance of organophosphates (OPs) in studies on ASD can be explained by various factors related to their neurotoxicity and the widespread agricultural use of these chemicals around the world (JOKANOVIC M, 2018). OPs act by inhibiting the enzyme acetylcholinesterase, which is responsible for breaking down acetylcholine, a neurotransmitter essential for neuromuscular function and signaling in the central nervous system. Thus, inhibition of this enzyme leads to an accumulation of acetylcholine, resulting in overstimulation of cholinergic receptors, which can cause neuronal damage, as well as other adverse effects on neurological development (BAI Y e WANG L, 2022).

The study by Lizé M, et al. (2022) shows that maternal prenatal exposure to organophosphates, such as chlorpyrifos and diazinon, has been associated with characteristics related to ASD, primarily among boys. Furthermore, another experimental study reveals that the combination of genetic mutations and exposure to organophosphates amplifies neurotoxic effects, indicating a possible gene-environment interaction in the development of ASD (SCHMIDT S, 2021).

The higher prevalence of ASD in boys has been investigated, pointing to a combination of genetic and hormonal factors. One of the main factors identified is prenatal exposure to testosterone, which influences brain development. In this regard, boys have larger brains and a more developed amygdala than girls, making this brain region more exposed in boys and accentuating these differences among children with ASD (WANG Z, et al., 2024).

Research on the X chromosome suggests that boys, having only one copy of this chromosome, are more vulnerable to genetic mutations associated with autism, such as the NLGN4 gene, which regulates communication between neurons. Additionally, a study published in 2022 identified differences in gene expression between boys and girls with ASD, suggesting that certain genes related to autism behave differently depending on sex, which could contribute to the higher predisposition in boys (WANG Z, et al., 2024).

Another important factor is the influence of sex hormones on brain development. The "extreme male brain" theory, proposed by Simon Baron-Cohen, suggests that elevated levels of fetal testosterone can influence brain development in a way that increases the risk of behaviors characteristic of autism (BARON-COHEN S, et al., 2011).

Hai Y e Leng G (2022), conducted a study in China highlighting gender differences in the incidence of ASD, suggesting that boys are four times more likely to develop the disorder compared to girls. Although gender disparity in autism is widely documented, this study suggests that pesticide exposure, particularly in rural areas, may contribute to this gap. One possible hypothesis to explain the increased vulnerability of male children to developing ASD when exposed to pesticides is that, generally, neurotoxic insecticides, such as organophosphates, may be metabolized differently between males and females. For instance, studies have shown that females of some mosquito species, such as *Aedes aegypti*, have a greater capacity for insecticide detoxification, making them less vulnerable than males (NAKAZATO BM, 2018). Given the similar mode of action of insecticides in human and animal species, this could explain the higher propensity of males to develop ASD.

Among the studies demonstrating a direct association between pesticide exposure and ASD risk, the work of Desalegn AA, et al. (2023) is particularly noteworthy. This study found a significant association between exposure to γ-hexachlorocyclohexane (γ-HCH) and an increased risk of ASD. Children exposed to higher

levels of this pesticide were twice as likely to be diagnosed with autism, suggesting a strong relationship between pesticide exposure and ASD development. Furthermore, experimental studies in zebrafish confirmed the neurotoxic effects of γ-HCH, highlighting its potential for neurological damage even at low doses.

Moreover, the use of the experimental model with zebrafish enhanced the understanding of the neurotoxic effects of this pesticide, showing that exposure can significantly impair neurological development in both humans and animals. This experimental model confirmed that even at low concentrations, γ-hexachlorocyclohexane can affect neurological development, suggesting that in vivo studies are essential to corroborate epidemiological findings (DESALEGN AA, et al., 2023).

Another important study, conducted by Román P, et al. (2024), investigated the prevalence of ASD in regions with high pesticide exposure in Spain. The results indicated that areas with intensive pesticide use had significantly higher rates of ASD. Geolocation as an exposure factor highlights the importance of public policies regulating pesticide use in areas near vulnerable populations. The association between residential environment and autism risk was also confirmed by Ongono JS, et al. (2022), who found a correlation between proximity to agricultural areas and decreased communication skills in children with ASD.

The study by Pignati WA, et al. (2022) highlights that residents of agricultural regions exposed to pesticides often report health issues, including respiratory and neurological symptoms, due to chronic pesticide exposure. These data suggest that, in addition to immediate effects, continuous exposure to chemicals may have long-term impacts on neurological development in children, possibly exacerbating conditions such as ASD.

Another study by the same author reinforces this concern by mapping the concentration of pesticide use in the country, revealing that areas with higher pesticide use coincide with regions of high prevalence of health problems related to chemical exposure. Proximity to agricultural cultivation areas in these regions not only increases the risk of ASD but is also associated with greater difficulties in the development of cognitive and communication skills in children already diagnosed (PIGNATI WA, et al., 2017).

Regarding prenatal maternal exposure to pesticides, several studies have addressed this aspect. Lizé M, et al. (2022) found an association between maternal exposure to chlorpyrifos and an increase in autistic traits in 11-year-old children, particularly among boys. This indicates that exposure during pregnancy can have lasting effects on children's neurodevelopment. This finding supports Barkoski JM, et al. (2021), who observed that exposure to the pyrethroid 3-phenoxybenzoic acid (3-PBA) in the second trimester of pregnancy was associated with an increased relative risk of ASD.

The gestational phase is particularly vulnerable to pesticide exposure due to the rapid development of the fetal brain, where pesticides can cross the placental barrier and affect the central nervous system. Organophosphates, such as chlorpyrifos, inhibit acetylcholinesterase, causing synaptic dysfunction, while oxidative stress caused by these chemicals impairs brain development, especially because the fetus has less efficient antioxidant mechanisms (SLOTKIN TA, 2011).

On the other hand, the study by Joyce EE, et al. (2022) presents an intriguing perspective by not confirming the hypothesis that consuming foods with pesticide residues during pregnancy increases the risk of ASD in children. The lack of a clear association between the ingestion of food with pesticide residues and the increased risk of ASD, as observed by Joyce EE, et al. (2022), can be explained by factors such as variability in the absorption and metabolism of pesticides, as well as the presence of protective nutrients in food. The antioxidant and anti-inflammatory compounds present in fruits and vegetables may mitigate the negative effects of pesticides. For example, phytochemicals found in vegetables can neutralize oxidative stress and reduce neurotoxicity, furthermore, a diet rich in organic foods may reduce exposure to pesticides, suggesting that food quality, rather than the mere presence of residues, may play a protective role against adverse outcomes, including ASD (NICASTRO HL, et al., 2015).

Although several studies have found an association between pesticides and ASD, some, like Bach MA, et al. (2020), did not find a significant relationship. This study offers a perspective that challenges the direct association between pesticides and ASD, as it did not find a significant relationship between exposure to PCBs and OCs and the risk of autism in Jamaican children. However, the authors' hypothesis about the influence of

dietary factors demonstrates the complexity of interactions between environmental exposures, diet, and health. This discrepancy compared to other studies underscores the importance of considering variables such as genetics and diet when investigating the effects of pesticides on neuropsychological development, highlighting the need for more comprehensive and controlled research.

Studies exploring gene-environment interactions provide a crucial perspective on the development of ASD. Modafferi S, et al. (2021) investigated how genetic mutations, such as those in the CHD8 gene, interact with environmental exposures like the pesticide chlorpyrifos. These studies showed that the combination of genetic predisposition and pesticide exposure can exacerbate effects on neurological development.

Artik A, et al. (2023) demonstrates that mutations related to autism, when combined with exposure to pesticides such as organophosphates, amplify behavioral and cognitive deficits. This suggests that genetic vulnerability may increase sensitivity to the neurotoxic effects of pesticides. Similarly, Shelton JF, et al. (2014) indicates that exposure to pesticides during pregnancy in mothers with a genetic predisposition to neurological disorders significantly increases the risk of ASD. These studies emphasize that individuals with genetic predisposition may be particularly at risk when exposed to toxic substances, such as pesticides, during critical periods of neurological development.

In addition to human studies, the validation of results using animal models also played an important role. For example, Desalegn AA, et al. (2023) used zebrafish to validate the neurotoxicity of ÿ-HCH. This experimental model confirmed that, even at low concentrations, this pesticide can affect neurological development, suggesting that in vivo studies are essential to corroborate epidemiological findings.

Despite numerous observational studies, such as Bennett BH, et al. (2022), suggesting a potential link between pesticide mixtures and ASD, these studies are hindered by several methodological limitations. A major challenge is isolating the impact of a single pesticide due to concurrent exposure to multiple chemicals. Furthermore, many findings lost their significance after adjustments for confounders and corrections for false discovery rates, underscoring the need for greater methodological rigor in future research. The importance of more precise and direct exposure measurements was emphasized by Ongono JS, et al. (2022), who proposed that incorporating biomarkers, such as blood or urine samples, could enhance analytical accuracy and yield more reliable results.

In this context, Zoccalli C, et al. (2024) emphasizes the value of using biomarkers, such as blood samples, to assess pesticide exposure, demonstrating that these direct methods can reveal significant associations between exposure and neurodevelopmental disorders. Longitudinal studies, like the one conducted by Barkoski JM, et al. (2021), are particularly crucial as they track the effects of exposure over time, from pregnancy to childhood. Ongoing assessments help identify the critical windows during which pesticides exert the most influence on neurodevelopment, distinguishing temporary effects from lasting changes (BARKOSKI JM, et al., 2021). Furthermore, Gonzalez-Casanova I, et al. (2018) highlights the importance of longitudinal approaches, showing that pesticide exposure during critical developmental periods, such as pregnancy, can have cumulative effects throughout childhood. These findings underscore the necessity for rigorous and direct methodologies to clarify the interactions between pesticides and child development, enhancing our understanding of the risks associated with exposure.

Overall, the results found in this review have important implications for public health, especially regarding the control of pesticide use in agricultural areas near residences. The stricter regulation of pesticide uses and monitoring of maternal exposure during pregnancy could be preventive factors for ASD, as shown in studies by Román P, et al. (2024) and Desalegn AA, et al. (2023). These findings reinforce the need for preventive strategies to protect vulnerable populations, such as pregnant women and children.

Based on the limitations and inconsistent results, many authors suggest the need for further studies exploring gene-environment interactions. Schmidt S (2021), for example, emphasizes the importance of expanding the use of brain organoids to simulate complex genetic and environmental conditions that occur in ASD.

Although there is evidence that exposure to pesticides may increase the risk of ASD, the studies are still insufficient to provide definitive conclusions. Therefore, it is suggested that more research be developed to seek increasingly conclusive evidence of this relationship.

## CONCLUSION

Maternal exposure to pesticides during pregnancy is considered a critical risk factor for the onset of ASD, as this period represents a window of vulnerability in fetal development. The pesticides appear to be a risk factor for ASD due to their high toxicity levels and their effects on the human body. However, it is important to consider that not all studies point to a direct relationship between pesticides and ASD. Some research has not found a significant association, indicating the presence of additional variables, such as diet and genetic factors, which may influence the results. This discrepancy between the findings of scientific research regarding pesticides as a factor in the predisposition to ASD onset suggests the need for further studies investigating this association. In this sense, this review emphasizes the importance of additional studies exploring the interaction between pesticides and ASD development. Such investigations are essential for advancing prevention strategies for this disorder and for seeking alternatives to mitigate the use of these chemicals, with a focus on public health protection.

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