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The relationship between pesticide exposure during critical neurodevelopment and autism spectrum disorder: A narrative review

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Highlights

- Exposure to low-dose pesticide is closely related to autism spectrum disorder (ASD).
- Gut microbiota dysbiosis induced by exposure to low-dose pesticide may be associated with ASD.
- Exposure to low-dose pesticide causes changes in neuronal morphology, synapse, and glial cells observed in ASD.

Abstract

Agricultural pesticides have been one of the most extensively used compounds throughout the world. The main sources of contamination for humans are dietary intake and occupational exposure. The impairments caused by agricultural pesticide exposure have been a significant global public health problem. Recent studies have shown that low-level agricultural pesticide exposure during the critical period of neurodevelopment (pregnancy and lactation) is closely related to autism spectrum disorder (ASD). Inhibition of acetylcholinesterase, gut microbiota, neural dendrite morphology, synaptic function, and glial cells are targets for the effects of pesticides during nervous system development. In the present review, we summarize the associations between several highly used and frequently studied pesticides (e.g., glyphosate, chlorpyrifos, pyrethroids, and avermectins) and ASD. We also discusse future epidemiological and toxicological research directions on the relationship between pesticides and ASD.

Introduction

Pesticides consist of various chemical substances used to control and repel pests and impede the growth of weeds. Humans are exposed to pesticides through occupations involving the production, transportation, delivery, and use of pesticides, living in areas with high pesticide residues, and enrichment in the food chain. Pesticides are toxic chemicals that inevitably result in human health risks (Mostafalou and Abdollahi, 2017). Chronic exposure to pesticides may be associated with diseases, such as cancer, hormone disorders, asthma, behavioral abnormalities, and cognitive deficits (Council On Environmental, 2012). The rapidly developing nervous system of fetuses and infants is particularly susceptible to disruptions caused by environmental chemicals (e.g., pesticides) because of the poorly developed blood-brain barrier and immune system (Mascarelli, 2013). Even low pesticide exposure can cause serious damage to the development of infants and children (Damalas and Eleftherohorinos, 2011). Pesticide exposure during pregnancy is associated with neurological disorders in the offspring, including autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), and cognitive deficits (Mostafalou and Abdollahi, 2017). ASD (i.e., autism) is a neurological disorder that appears in early childhood and is characterized by markedly persistent deficits in social interaction, communication skills, and repetitive stereotyped behaviors (Lord et al., 2018). It is widely believed that a combination of genetics and the environment contributes to the development of ASD. Moreover, genetic abnormalities seemingly contribute to the majority of the variations. However, recent studies have found a smaller role for genetics and a larger contribution by environmental factors than previously thought (Bolte et al., 2019). Exposure to pesticides in early life causes severe central nervous damage due to the rapidity of early neurogenesis. Consequently, the association between pesticide exposure during pregnancy and lactation and the development of ASD in children has become a hot topic of research.

Indeed, the association between pesticides and adverse neurodevelopment effects in children has been generalized in several substantial and well-rounded reviews (Colborn, 2006; Dorea, 2021; Eaton et al., 2008; Gonzalez-Alzaga et al., 2014; Munoz-Quezada et al., 2013; Saunders et al., 2012). Most of these reviews assessed the adverse effects of pesticides on cognitive competence, attention, and motor skills. Surprisingly, little is known about the association between pesticides and ASD. In this review, we searched the peer-reviewed articles through August 2021 to identify articles from PubMed database searches using the key words “pesticide AND autism” or “pesticide AND autism spectrum disorder” or “pesticide AND ASD”. The reference lists of relevant records were then searched to identify articles that might have been missed in the database search. Only articles published in English that studied ASD and ASD-like behaviors were included in the evaluation. The majority of the review discusses the available evidence linking exposure to pesticides with increased risk of ASD from human epidemiology studies, animal studies, and studies of molecular mechanisms. We also provide a brief discussion of future directions for research on the relationship between pesticide exposure and ASD.

Section snippets

Prevalence of autism spectrum disorder may exceed the predictions

In addition to exhibiting core symptoms (persistent deficits in social interaction and communication skills; repetitive, stereotyped behaviors), patients with ASD may suffer from a variety of psychiatric or neurological disorders, including hyperactivity and attention disorders (e.g., attention deficit hyperactivity disorder), anxiety, depression, and epilepsy, which are fairly prevalent (Lord et al., 2020). Males are more likely to develop ASD, epidemiological administrative and

The pathogenesis of autism

Although the etiology of ASD remains unclear, many studies have suggested a possible association between ASD and multiple environmental and genetic risk factors (Hu et al., 2020). Notably, individuals with susceptibility genes are more likely to develop ASD when exposed to environmental hazards. Over the past decade, there have been many studies using model systems or postmortem brain tissue to investigate the molecular pathophysiology of ASD (Lord et al., 2020; Parikshak et al., 2016; Wang et

The correlation between pesticides and ASD

Although early twin studies suggested a heritability rate of up to 80–90% for ASD with little contribution from environmental factors. However, recent studies have shown that environmental factors account for as high as 40–50% of the contribution ratio to ASD (Modabbernia et al., 2017). Many pesticides are designed to eliminate insects and rodents by affecting their nervous system. Although not designed as neurotoxicants, herbicides and fungicides are neurotoxic to exposed animals (Roberts et

Conclusions and future directions

In this review, we presented a consolidated understanding of pesticides closely related to the etiology of ASD, providing indirect evidence for the plausibility linking pesticides exposure during pregnancy and lactation (the critical developmental periods) to ASD. The possible associations and mechanisms leading to ASD were also discussed from epidemiological and toxicological evidences. Abnormalities in gut microbiota, neuronal dendritic morphology, axonal morphology and function,

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Author contributions

Conceptualization, Mingdan You, Xiu He, and Ying Tu; validation, Mingdan You, Guaghong Yang; writing—original draft preparation, Xiu He., Ying Tu; writing—review and editing, Mingdan You, Guaghong Yang, Yawen Song; supervision, Guaghong Yang; funding acquisition, Mingdan You, Xiu He; All authors have read and agreed to the published version of the manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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