

### Abstract

Autism spectrum disorder (ASD) is a neurological and developmental disorder that begins early in childhood and lasts throughout a person's life. ASD is characterized by impairment in interaction and social communication, in addition to pro-inflammatory cytokine imbalances with chronic neuroinflammation. Environmental exposures may increase the risk of ASD. There are evidences that as the residue crosses the blood-brain barrier and placenta the fetuses can be exposed to pesticides. The purpose of this study is to summarize and discuss the relationship between autism spectrum disorder and chlorpyrifos, an organophosphate insecticide. The narrative review was performed using MEDLINE, LILACS, Web of Science, Scopus and Science Direct as databases and pesticides, agrochemicals, insecticides, herbicides, *Autism disorder* as descriptors. Gestational contact with chlorpyrifos interferes early neuromotor development and causes deficits in social behaviour that can lead to long-term deficits in behavior and repetitive behavior, as a routine preference. Studies have shown that the contact of Chlorpyrifos with already autistic rats increased the characteristics of this disorder in the animals. In addition, contact with chlorpyrifos causes redox imbalance, oxidative stress, mitochondrial dysfunction associated with glutathione deficiency. Studies have also shown that there is a high probability of developing imbalances in the intestinal flora. Autistic individuals may as well exhibit proinflammatory cytokine imbalances and may suffer from hyperactive or dysfunctional immune systems, with chronic neuroinflammation, including neuroglial activation in the brain, and the presence of autoantibodies to brain proteins. Thus, we can conclude that exposures to agricultural pesticides such as Chlorpyrifos, through the uterine pathway are related to autism and that there is strong evidence that contact with pesticides may influence the development of autism spectrum disorder.

### Introduction

Autism spectrum disorder (ASD) is a neurological and developmental disorder that begins early in childhood and lasts throughout a person's life. ASD is characterized by impairment in interaction, social communication, restricted and stereotyped patterns of interests and behavior, intellectual disability or developmental delay, in addition to pro-inflammatory cytokine imbalances with chronic neuroinflammation. Environmental exposures may increase the risk of ASD. There are evidences that as the residue crosses the blood-brain barrier and placenta the fetuses can be exposed to pesticides. The purpose of this study is to summarize and discuss the relationship between autism spectrum disorder and chlorpyrifos, an organophosphate insecticide.

### Methods and Materials

Search for articles published between the years 2000 to 2018 in the Medline, Lilacs, Web of Science, Scopus and Science Direct databases. The descriptors used, in combination, were: pesticides, agrochemicals, insecticides, herbicides, autism disorder. Were included articles describing the occurrence of autism disorder in mothers in contact with organophosphate insecticide chlorpyrifos published in English, Portuguese and Spanish. We selected a total of 235 articles and exclusion criteria, such as articles published prior to the year 2000, review articles and articles in languages other than English, Portuguese and Spanish. We lastly reviewed and selected 15 articles for use in developing the review.

### Results

Gestational contact with chlorpyrifos interferes early neuromotor development and causes deficits in social behaviour that can lead to long-term deficits in behaviour and repetitive behaviour, as a routine preference. Studies have shown that the contact of chlorpyrifos with already autistic rats increased the characteristics of this disorder in the animals. In addition, contact with chlorpyrifos causes redox imbalance, oxidative stress, mitochondrial dysfunction associated with glutathione deficiency. Studies have also shown that there is a high probability of developing imbalances in the intestinal flora. Autistic individuals may as well exhibit proinflammatory cytokine imbalances and may suffer from hyperactive or dysfunctional immune systems, with chronic neuroinflammation, including neuroglial activation in the brain, and the presence of autoantibodies to brain proteins.

**Table 1.** Database and number of articles analyzed.

DATABASE	Nº de Artigos
LILACS	3
Medline	4
Science direct	4
Web of Science	1
Scopus	3
Total	15

**Figure 1.** Chemical structure Chlorpyrifos.



<http://portal.anvisa.gov.br/documents/111215/117782/C20%2B%2BChlorpirif%25C3%25B3s.pdf/f8ddca3d-4e17-4cea-a3d2-d8c5babe36ae>

### Discussion

Studies show complex early exposure to environmental stressors impact the correct neurodevelopment and brain processes. Organophosphate insecticides, among which chlorpyrifos (CPF), are widely diffused environmental toxicants associated with neurobehavioral deficits and increased risk of ASD occurrence in children. The mechanism of the long-term effects of gestational CPF remain undetermined. CPF administration during development alters the levels of monoamine systems and was found to modify the expression of numerous genes, many of which are involved in neuronal and glial development. and other regulated processes unrelated to the AChE inhibition.

### Conclusions

Thus, we conclude that exposures to agricultural pesticides such as chlorpyrifos, through the uterine pathway are related to autism and that there is strong evidence that contact with pesticides may influence the development of autism spectrum disorder. In addition, individuals with autism can develop gastrointestinal problems.

### Future Directions

Based on what was found in the studies analyzed, there is a need for further studies explaining and confirming the effects of Chlorpyrifos in pregnant women and the development of autism.

### Contact Information

Gislei Frota Aragão  
 State University of Ceará  
[frotaaragao@hotmail.com](mailto:frotaaragao@hotmail.com)  
[www.genit.com.br](http://www.genit.com.br)

### References

- LAN, A. et al. Prenatal chlorpyrifos leads to autism-like deficits in C57Bl6/J mice. *Environmental Health*, [s.l.], v. 16, n. 1, p.1-10, 2017. Springer Nature. <http://dx.doi.org/10.1186/s12940-017-0251-3>.
- FELICE, A. et al. Prenatal exposure to the organophosphate insecticide chlorpyrifos enhances brain oxidative stress and prostaglandin E2 synthesis in a mouse model of idiopathic autism. *Journal Of Neuroinflammation*, [s.l.], v. 13, n. 1, jun. 2016. Springer Nature. <http://dx.doi.org/10.1186/s12974-016-0617-4>.
- MORGAN, M. K. et al. The reliability of using urinary biomarkers to estimate children's exposures to chlorpyrifos and diazinon. *Journal Of Exposure Science & Environmental Epidemiology*, [s.l.], v. 21, n. 3, p.280-290, 26 maio 2010. Springer Nature. <http://dx.doi.org/10.1038/jes.2010.11>.
- BRAJIN, J. M. et al. Gestational Exposure to Endocrine-Disrupting Chemicals and Reciprocal Social, Repetitive, and Stereotypic Behaviors in 4- and 5-Year-Old Children: The HOME Study. *Environmental Health Perspectives*, [s.l.], 12 mar. 2014. Environmental Health Perspectives. <http://dx.doi.org/10.1289/ehp.1307251>.
- EL-BAZ, F.; ISMAEL, N. A.; EL-DIN, S. M. N. Risk factors for autism: An Egyptian study. *Egyptian Journal Of Medical Human Genetics*, [s.l.], v. 12, n. 1, p.31-38, maio 2011. Elsevier BV. <http://dx.doi.org/10.1016/j.ejmhg.2011.02.011>.
- BAVEYE, P.; LABA, M. Aggregation and Toxicology of Titanium Dioxide Nanoparticles. *Environmental Health Perspectives*, v. 116, n. 4, abr. 2008. Environmental Health Perspectives. <http://dx.doi.org/10.1289/ehp.10915>.
- ESKENAZI, B. et al. Organophosphate Pesticide Exposure and Neurodevelopment in Young Mexican-American Children. *Environmental Health Perspectives*, v. 115, n. 5, p.792-798, jan. 2007. Environmental Health Perspectives. <http://dx.doi.org/10.1289/ehp.9828>

### Acknowledgements

We thank the State University of Ceará and the Federal University of Ceará for the support for the development of this review, in addition to the members of the GENIT study group for valuable contributions to the conclusion of this study.