CHE Collaborative for Health & Environment

Webinar Highlights

Male Autism Spectrum Disorder & Prenatal BPA Exposure

Emerging research is shedding light on the relationship between prenatal exposure to environmental chemicals such as bisphenol A (BPA) and the development of neurodevelopmental disorders such as autism spectrum disorder (ASD). BPA, an endocrine-disrupting compound commonly found in plastics, may disrupt hormonal pathways critical for early brain development. A key player in this disruption appears to be the brain aromatase enzyme, which regulates the conversion of androgens to estrogens and influences neurodevelopment.

In this webinar, **Dr. Anne-Louise Ponsonby** presented findings from a study on the links between BPA exposure, aromatase function, and ASD-related behaviors and brain abnormalities.

Featured Speaker: Dr. Anne-Louise Ponsonby, epidemiologist and public health physician, speaking October 17, 2024.

This fact sheet has been created by CHE based on information presented in an EDC Strategies Partnership webinar. Selected quotes in bold are from the webinar speaker(s). For the full set of resources provided by the webinar presenter, see the webinar page, where you'll also find associated slides and resources.

The Problem

Numerous studies have shown a relationship between bisphenol exposures and neurodevelopmental disorders. For example, a review in 2021 found that prenatal exposure to bisphenols and phthalates may contribute to adverse neurodevelopmental outcomes in children. Despite this, regulation of these chemicals has been slow.

Dr. Ponsonby stressed that stronger causal evidence could help bolster efforts to regulate these chemicals and protect human health. This study set out to establish causal evidence by testing the hypothesis that BPA exposure in utero could be linked to autism through brain aromatase disruption, which would affect brain development. Aromatase is particularly

important in male brain development. As a result, following this hypothesis, males would be expected to be more affected by prenatal BPA exposure.

The study included analyses of BPA exposures and their effects in two human cohorts, the effects of BPA exposure on humans and mice, and the effects of BPA exposure at the cellular level, in vivo and in vitro.

Key findings:

- In mice, BPA reduced aromatase expression in the medial amygdala (which is involved in social behavior).
- Both male BPA-exposed mice and aromatase knockout (ArKO) mice demonstrated ASD-like behavioral and brain changes at structural and functional levels. (ArKO mice are mice that lack the gene to encode for aromatase).
- Boys with low aromatase activity have greater odds of ASD diagnosis at age 9 and ASD symptoms at age 2 when exposed to high levels of BPA in utero.
- Prenatal BPA exposure predicted higher methylation across a genetic region that is linked to aromatase gene activity. Laboratory studies found that this methylation mediates the association between prenatal BPA exposure and changes in brain-derived neurotrophic factor (BDNF) methylation, an essential component of neuroplasticity and synaptic function.

As predicted by the hypothesis, males were more likely to be affected by BPA exposure than females. However, not all males showed the same association. Instead, the association was found in males who were identified as genetically more vulnerable to the impacts of BPA. Autism, like other multifactorial diseases, results from a combination of genes and the environment.

These findings support an underlying causal relationship between prenatal BPA exposure and ASD. This study also points the way to potential therapies for reversing BPA's effects on aromatase.

Recommendations

BPA is the most studied bisphenol, but it is not the only concern. Substitute bisphenols, such as BPS and BPF, have similar chemical structures and therefore behave similarly at the molecular level. Phthalates have also been shown to have similar effects on aromatase.

Dr. Ponsonby expressed hope that the Global Plastics Treaty would take into account the human health impacts of early-life exposure to chemicals in plastics, and move to phase out these substances.

To Find Out More

- Watch the October 17, 2024 webinar: Male autism spectrum disorder & prenatal BPA exposure
- Read the presentation slides: Male autism spectrum disorder is linked to brain aromatase disruption by prenatal BPA
- Read the study: Male autism spectrum disorder is linked to brain aromatase disruption by prenatal BPA in multimodal investigations and 10HDA ameliorates the related mouse phenotype

About the Speaker

Dr. Anne-Louise Ponsonby is an epidemiologist and public health physician. She has extensive experience in the design, conduct and analysis of population-based studies, and public health translation. She is co-PI of a large birth cohort of over 10,000 infants that generated knowledge leading to a decline in sudden infant death syndrome (SIDS) incidence. In Australia, SIDS deaths declined by 80%, from 1.9 per 1,000 live births in 1990 to 0.2 live births in 2012 (Australian Bureau Statistics 2013). More recently, Ponsonby's work has been on combining population epidemiologic approaches with system biology, an approach she outlined in *Nature* (2014). Ponsonby is using this approach, within population-based studies, to investigate multiple sclerosis and early brain development. In particular, a current focus of her work is to use this comprehensive approach to better understand the possible adverse impact of some modern chemicals on brain development in early life. Ponsonby has 427 publications and has contributed to three patents. Ponsonby is on the research committee for the International Paediatric Multiple Sclerosis Study Group and part of several international collaborations.