

# NEWS

## HEALTH

# Autism spectrum disorders may be linked to air pollution

*Mouse studies reveal prenatal diesel exhaust exposure can render offspring vulnerable to autism spectrum disorder-like symptoms.*

BY HEATHER GERRIE

**T**he prevalence of autism spectrum disorder (ASD) has increased dramatically, rising from a diagnostic rate of one in every 10,000 children during the 1970s to one in 66 by 2018 [1].

Rising alongside the number of ASD cases are levels of air pollution. Research from neuroscientist Staci Bilbo at Duke University suggests the two may be linked. According to Bilbo, the surge in ASD cases strongly points to an environmental factor.

ASD is characterized by impairments in communication and stereotypic, repetitive behaviours. Though genetics – and a growing recognition of the disorder – account for a portion of cases identified each year, Bilbo says there are more cases than can be accounted for.

“All the genetic studies that have been done can only explain roughly 50 per cent of the cases of ASD,” Bilbo said. “There has to be some other culprit.”

Air pollution is the third leading cause of mortality worldwide and can affect us even before birth [2]. Maternal exposure to high levels of air pollution during pregnancy is linked to negative health outcomes in offspring, including premature birth and childhood asthma [2]. Diesel exhaust, which is the primary toxic component of air pollution, is particularly relevant. The



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**Prenatal exposure to air pollution may increase offspring risk of developing ASD.**

levels of diesel exhaust at the time and place of birth is one of the strongest and most consistent predictors of ASD [3].

According to Bilbo, the intersection between air pollution and ASD can be found at the level of the brain's immune system, which functions as the interface with the environment. In the brain, the immune system consists of microglial cells. Known as the watchdogs of the brain, microglia constantly survey the health of their environment and are the first responders to disruptions such as trauma, disease, and inflammation [3].

Microglia also play a critical

role in wiring the brain during development. They assist with connecting developing neurons – the messenger cells of the nervous system – and removing unnecessary or incorrect connections [4].

During pregnancy, maternal immune activation from exposure to inflammatory stimuli – such as air pollution – can cause hyperactive and abnormal immune function in developing offspring. Hyperactive microglia release neurotoxins and inflammatory mediators which affect neuron function and survival.

“The reason that we think

microglia are particularly important in autism, is that we increasingly think autism is of prenatal origins,” Bilbo said. “Microglia colonize the brain very early in development, so if you had an immune perturbation during pregnancy, this would alter microglial function, and therefore brain development.”

If air pollution alone could induce ASD, all babies born in urban

*“We need interventions that don’t rely on people packing up and moving to the countryside.”*

areas with high diesel exhaust exposure would be at high risk. However, Bilbo says the reality is more complicated, likely involving multiple genetic and environmental factors interacting with pollutants to result in ASD.

Initial research from Bilbo’s lab found that offspring of pregnant mice exposed to diesel exhaust particles throughout gestation had overly activated microglia, but no apparent behavioural abnormalities [4,5]. However, Bilbo noted a growing body of literature suggesting that psychological stress during pregnancy affects offspring brain development. Both stress and exposure to pollutants act on a common biological pathway – the immune system [4].

Bilbo then combined prenatal exposure to diesel exhaust particles with a psychological stressor, such as the restriction of nesting material during the final week of pregnancy. In addition to the predicted abnormal microglia, offspring now displayed behavioural and social deficits comparable to the ASD symptoms seen in humans [5,6].

The male offspring in these studies were more susceptible to developing ASD-like symptoms than females [6] In humans, males are diagnosed with ASD four times more than females [1].

Bilbo’s findings agree with the ‘two-hit model’ theory, where an initial

‘first hit’ to the immune system – such as prenatal exposure to air pollution – renders the developing immune system more reactive if a ‘second hit’ occurs [4]. In the case of ASD, if the first hit is an environmental toxin, the second hit is likely a social toxin.

“In humans, it’s not just pollutant levels, ASD is mediated by something else as well, which we very much

believe now to be socioeconomic status and social stress,” Bilbo said. Meaning that a ‘double hit’ of air pollution and maternal exposure to psychological stressors, such as violence or poverty, increases

offspring risk for ASD.

A study from the University of California investigating whether traffic-related pollution was related to ASD rates in Los Angeles found that amongst families living near highways, mothers from low socioeconomic backgrounds were more likely to have children with ASD [7]. The study reported that vulnerability, poverty and stress in mothers likely exacerbated the effects of pollution exposure during pregnancy.

“The people who are exposed to the highest levels of environmental toxins are also those that generally have the fewest resources to try and do anything about it,” Bilbo said. “It becomes an environmental justice issue, and at that point we need policy change. We need interventions that don’t rely on people packing up and moving to the countryside.”

It is difficult to show in human studies that an effect is more than just correlative, but “if we can show causality in a mouse, then we can demonstrate to the people who are making policy decisions that there is a real, causal mechanism,” Bilbo said.

Bilbo hopes that as we are forced to rely less on fossil fuels, the air quality in cities will improve. Even now, the transition to greener technology may begin to decrease risk of ASD in urban areas.

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