Podcast transcript: Autism and the Environment

[Theme music]

Ashley Ahearn (AA): You're listening to Environmental Health Chat – a show from the National Institute of Environmental Health Sciences that explores the connections between our health and our world.

I'm Ashley Ahearn.

[Music fades out]

Autism rates are rising. According to the Centers for Disease Control and Prevention, 1 in 36 children in the U.S. are diagnosed with the condition.

But it's a tough one to define and identify.

Staci Bilbo (SB): There's no biomarker, for instance, there's no brain scan that you can do and say, "Ah, yes, this is definitely autism or it's definitely not."

AA: Dr. Staci Bilbo is a professor of neurobiology at Duke University. She studies how environmental and social factors influence brain development and behavior in mice – and how that could inform our understanding of autism in humans.

Autism is a neurodevelopmental disorder, and it manifests in many different ways – that's why it's also referred to as autism spectrum disorder. People with autism may have difficulties with communication and social interaction and restricted interests or repetitive behaviors.

SB: There's no really defined pathology with autism. It's based on a pretty intense behavioral analysis by a trained psychologist or psychiatrist.

AA: It's unclear how autism develops, but many factors could be at play, from genetics to environmental factors to even our gut microbiome.

SB: There's a strong genetic component to autism, meaning that many, many different genes have been identified for their association with autism. But the majority of these genes are weakly predictive, suggesting that there may be multiple genes working in parallel, or that these genes are then interacting with other factors which we increasingly think are environmental factors.

AA: Hundreds of different environmental factors have been associated with autism. Air pollution, heavy metals, PCBs, endocrine disruptors like bisphenol A, the list goes on…

SB: But the same thing applies to these factors as to genetics in that each one alone is predictive, but fairly weakly predictive, of autism. So, there's no smoking gun, which, again, suggests it's the combination of different factors together, which are the most predictive.

AA: So, how to study those factors? How can scientists like Dr. Bilbo isolate certain factors and also look at them in combination?

Lab mice are the key.

Dr. Bilbo and her team wanted to zero in on two factors in particular: air pollution and maternal stress.

They divided their mice into four groups. One group was the control, so the mothers were kept under normal conditions. Another group was exposed to diesel particulate air pollution. A third group was exposed to maternal stress – which they modeled by limiting the housing materials available to pregnant mice. And the final group was exposed to a combination of air pollution and stress.

SB: And it became apparent pretty quickly, that it was really the combination of the two that was inducing these very striking behavioral changes and immune changes and brain changes in the offspring.

AA: Ok, so first – the behavioral changes. Mice that were exposed in utero to air pollution and maternal stress interacted with other mice differently. Dr. Bilbo would take a young mouse and put it in an enclosed area where it could either interact with another mouse or with a toy.

SB: And in our case, we had a rubber duck. And what you typically see in normal mice is that they are much more interested in the other mouse…and they might check out the object, but they're really not going to spend much time with it. But then our mice that were exposed to pollution and stress, they spent an equivalent amount of time – so it wasn't all of their time with the object – but they certainly were just as interested in the object as they were in the other mouse. Which was very, very different from what we saw in our control mice.

AA: Beyond the behavioral changes, Dr. Bilbo and her team designed the experiment to look at immune and brain changes. The immune system, she explained, is closely connected with neurological development. Basically, if you have an underperforming or overperforming immune system during key periods of brain development.

SB: Again, not all patients – there is no blanket term for autism – but certainly a significant subset have alterations in things like T cells or B cells, which are cells that are really important for fighting infections. But also in what we call innate immune cells, like macrophages, that are also important for infections. But the reason we care about them is that they are very important for brain development.

AA: Dr. Bilbo zeroed in on one type of immune cell in the brain, the microglia. These cells basically prune excess synapses between neurons as the brain develops.

SB: And so, what we found in this study is that we see in male mice that were exposed to the double hit of pollution and stress to their mom, when we looked at the male offspring, they had social deficits and they had changes in their microglia, and their microglia were not properly pruning synapses. Which means that you have sort of hyperconnectivity. And you can imagine why that might be problematic, where you're just not getting appropriate transmission of information, maybe you're getting too much information.

AA: And that could lead to behavioral changes that are commonly observed in people with autism. It's interesting that this outcome was only noted in male mice - not females. In humans, autism can manifest very differently between the sexes as well, which can make it hard to diagnose young girls with autism. In fact, in early life, three times more males are diagnosed with autism as females. But that doesn't mean females aren't being affected.

SB: We increasingly think that females are under-diagnosed because they are very good at mimicking social behaviors and therefore masking social deficits. But females often get diagnosed later in life when they present with other difficulties.

AA: Things like depression, anxiety, and eating and sleep disorders often co-occur with autism in females. Dr. Bilbo sees a parallel in her mice.

SB: In data that we haven't published yet, I can tell you that the females – very similar to what humans – seem to be presenting with other changes in their behavior later in life. And one of these is an increase in depressive-like behavior when they're young adults, which we don't see in the males.

AA: Finally, Dr. Bilbo wanted to explore the connections between the gut and the brain because another common characteristic of autism in humans is gut problems or food sensitivities.

SB: So, we thought, well, what if that's playing a role? Especially given a lot of increasing evidence over the past couple of decades of this sort of gut-brain cross talk, meaning that the microbes in the gut are essentially talking to the brain and also impacting the way the brain develops, and vice versa.

AA: So, with her mice, Dr. Bilbo wanted to see how factors like maternal stress and air pollution influenced their gut microbiomes. She analyzed the guts in the offspring from each group and sequenced the species of bacteria. She found reduced species diversity in the gut of the males who had been exposed to air pollution and stress in the womb. She also found that changing the gut microbiome reversed some of the behavioral and immune changes in the exposed mice.

Dr. Bilbo is excited about these results because they suggest that altering the microbiome after birth may have a positive impact on neurodevelopment.

SB: While we do think that autism is almost certainly prenatal in origin, meaning that these events are set in motion before birth, we can still rescue changes after birth by manipulating the microbiome. So, for therapeutic purposes, I think that's really encouraging.

AA (on tape): When I think about air pollution, you know, we know that communities of color are more likely to be situated near freeways or high pollution industrial activity. Talk to me a little bit about the environmental justice component of your research and what kind of conclusions we can make there.

SB: Absolutely, I think this is pointing directly to issues of environmental justice. When we came into this project, this was our first thought, that communities of color in particular that get exposed to the highest burden of toxicants also have the fewest resources on top of that. And so, this is a massive double hit that these communities face. And so, I think in terms of policy the message needs to be that we need to protect and clean up those communities.

AA: Dr. Bilbo's research shows us another way to look at this problem from a policy standpoint. She acknowledges that it's unlikely that we humans are going to eliminate all our exposures to air pollution. So, focusing on reducing stress might be a more immediately effective way to help pregnant human mothers.

SB: We found, at least in the mouse model and I can imagine this being the case in humans as well, that the stress component was extremely sensitive, meaning that it was almost like a stepwise increase in severity, depending on how much nest material these mice had to basically build their home. So, it's hard to just directly apply that back to people, but I think what it's telling us is that any sort of social support services that you could put in place to support pregnant mothers will have a huge impact on outcomes later in life.

[Music comes up]

AA: I'm Ashley Ahearn. Thanks for listening to Environmental Health Chat.