# Autism and ADHD are linked to disturbed gut flora very early in life

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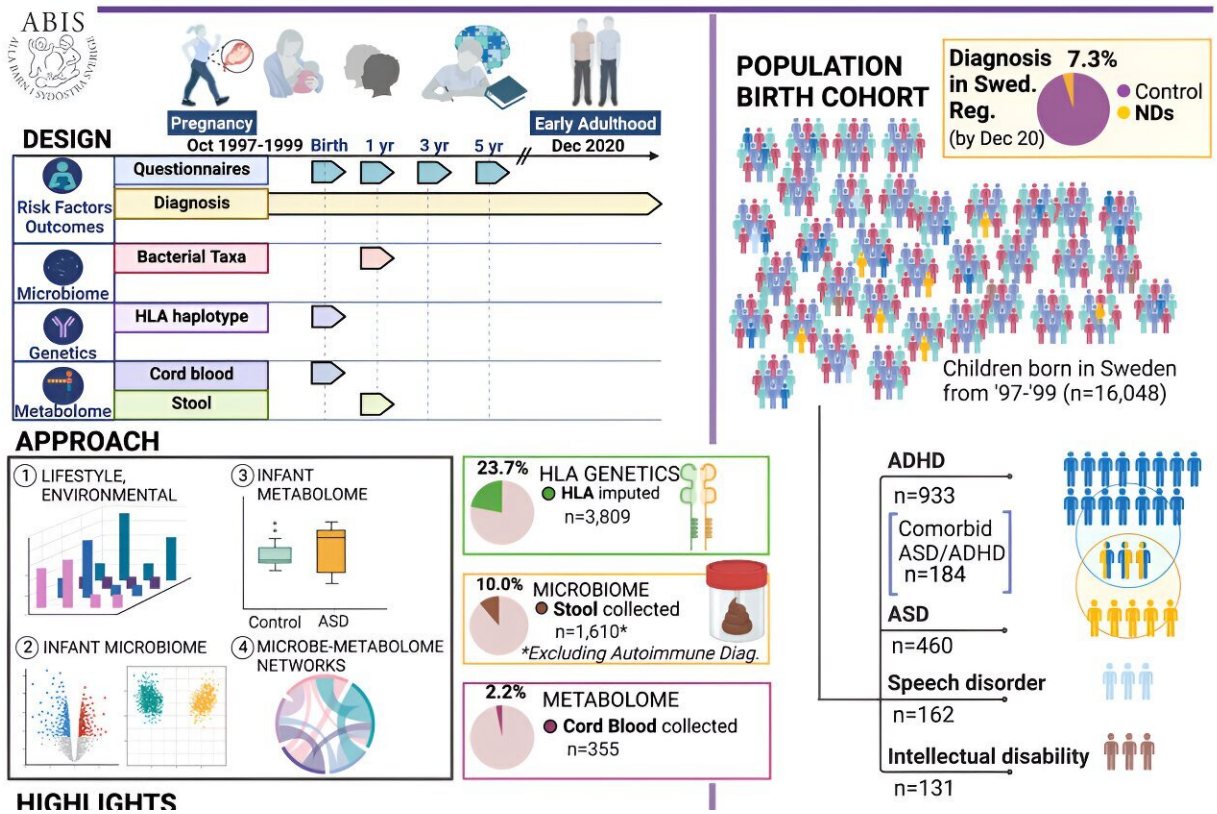


Credit: *Cell* (2024). DOI: 10.1016/j.cell.2024.02.035

Disturbed gut flora during the first years of life is associated with diagnoses such as autism and ADHD later in life. This is according to a study led by researchers at the University of Florida and Linköping

University and published in the journal *Cell*.

The study is the first forward-looking, or prospective, study to examine gut flora composition and a large variety of other factors in infants, in relation to the development of the children's nervous system. The researchers have found many biological markers that seem to be associated with future neurological development disorders, such as autism spectrum disorder, ADHD, communication disorder and intellectual disability.

"The remarkable aspect of the work is that these biomarkers are found at birth in cord blood or in the child's stool at one year of age over a decade prior to the diagnosis," says Eric W Triplett, professor at the Department of Microbiology and Cell Science at the University of Florida, U.S., one of the researchers who led the study.

The study is part of the ABIS (All Babies in Southeast Sweden) study led by Johnny Ludvigsson at Linköping University. More than 16,000 children born in 1997–1999, representing the general population, have been followed from birth into their twenties. Of these, 1,197 children, corresponding to 7.3%, have been diagnosed with autism spectrum disorder, ADHD, communication disorder or intellectual disability.

A large number of lifestyle and environmental factors have been identified through surveys conducted on several occasions during the children's upbringing. For some of the children, the researchers have analyzed substances in umbilical cord blood and bacteria in their stool at the age of 1.

"We can see in the study that there are clear differences in the intestinal flora already during the first year of life between those who develop autism or ADHD and those who don't. We've found associations with some factors that affect gut bacteria, such as antibiotic treatment during

the child's first year, which is linked to an increased risk of these diseases," says Ludvigsson, senior professor at the Department of Biomedical and Clinical Sciences at Linköping University, who led the study together with Triplett.

Children who had repeated ear infections during their first year of life had an increased risk of being diagnosed with a developmental neurological disorder later in life. It is probably not the infection itself that is the culprit, but the researchers suspect a link to antibiotic treatment. They found that the presence of Citrobacter bacteria or the absence of Coprococcus bacteria increased the risk of future diagnosis.

One possible explanation may be that antibiotic treatment has disturbed the composition of the gut flora in a way that contributes to neurodevelopmental disorders. The risk of antibiotic treatment damaging the gut flora and increasing the risk of diseases linked to the immune system, such as type 1 diabetes and childhood rheumatism, has been shown in previous studies.

"Coprococcus and Akkermansia muciniphila have potential protective effects. These bacteria were correlated with important substances in the stool, such as vitamin B and precursors to neurotransmitters which play vital roles orchestrating signaling in the brain. Overall, we saw deficits in these bacteria in children who later received a developmental neurological diagnosis," says Angelica Ahrens, Assistant Scientist in Triplett's research group at the University of Florida and the first author of this study.

The present study also confirms that the risk of developmental neurological diagnosis in the child increases if the parents smoke. Conversely, breastfeeding has a protective effect, according to the study.

In cord blood taken at the birth of children, the researchers analyzed the

amounts of various substances from the body's metabolism, such as fatty acids and amino acids. They also measured some harmful substances that come from outside, such as nicotine and environmental toxins. They compared substances in the umbilical cord blood of 27 children diagnosed with autism with the same number of children without a diagnosis.

It turned out that children who were later diagnosed had low levels of several important fats in the umbilical cord blood. One of these was linolenic acid, which is needed for the formation of omega 3 fatty acids that are anti-inflammatory and have several other effects in the brain.

The same group also had higher levels than the control group of a PFAS substance, a group of substances used as flame retardants and shown to negatively affect the immune system in several different ways. PFAS substances can enter the body via drinking water, food and the air we breathe.

It is not certain that the relationships that the research team found in the Swedish children can be generalized to other populations, but these issues need to be studied in other groups as well. Another question is whether gut flora imbalance is a triggering factor or whether it has occurred as a result of underlying factors, such as diet or antibiotics.

However, even when the researchers accounted for risk factors that might affect the gut flora, they found that the link between future diagnosis remained for many of the bacteria. This indicates that some of the differences in gut flora between children with and without future diagnosis are not explained by such risk factors.

The research is at an early stage and more studies are needed, but the discovery that many biomarkers for future developmental neurological disorders can be observed at an early age opens up the possibility of

developing screening protocols and preventive measures in the long term.

**More information:** Angelica P. Ahrens et al, Infant microbes and metabolites point to childhood neurodevelopmental disorders, *Cell* (2024). DOI: 10.1016/j.cell.2024.02.035

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