

# Clues to autism's causes may lie in the gut

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Professor Alessio Fasano, a gastroenterologist at Massachusetts General Hospital in the US, has several relatives and friends raising children with autism—a neurological disorder characterized by impaired social behavior—so is keenly aware of the challenges faced by families that have children with autism.

Autism symptoms usually emerge during the first two years of a child's life, with the likely causes being a combination of genetic and [environmental influences](#). Environmental risk factors act during the embryonic stage and may include prenatal exposure to an infection or to toxic chemicals such as pollution and maternal diabetes.

"Parents find themselves living in a parallel world to their child where communication is enormously difficult and there is nothing they can do about it," said Fasano, who hopes to provide help.

He leads a research project that explores the links between [autism](#) and gut health. The six-year initiative, called [GEMMA](#), runs until the end of 2024.

Autism—formally known as [autism spectrum disorder](#) or ASD—is estimated to affect at least one in 100 people worldwide. Over the past three decades, reported cases have increased 'rapidly' in countries where prevalence studies have been carried out, according to advocacy group [Autism Europe](#).

"There's a huge increase in incidence worldwide," said Fasano, who suspects that broader diagnostic criteria have contributed to the reported rise in cases.

He believes it might be possible to treat some autistic behavioral traits by restoring balance to the ecosystem of myriad microorganisms in the [human gut](#)—often referred to as the microbiome.

"There's good evidence that communication between the gut and the brain influences many [neurological conditions](#) including autism," Fasano said. "It raises the possibility that gut microbial-based treatments may be useful as a safe therapeutic approach for the disorder."

## Gut check

While autism was first described in the 1940s, the underlying causes aren't clearly understood eight decades later.

What is known is that the condition has a strong genetic basis with multiple genes—maybe as many as 100—involved.

But inflammation of the nerve cells in the brain is also thought to play a role. And here it's believed that environmental factors—including gut health—could come into play.

In a healthy person, the semi-permeable wall of the intestine acts as a barrier. It controls the transport of essential ions, nutrients and water into the body while restricting the movement of harmful substances both into and out of the gut.

When a breach occurs in this barrier, substances from the gut leak into the body. This triggers an [immune response](#) that contributes to inflammatory diseases and metabolic disorders, which—it's speculated—in turn influence the brain.

This condition is commonly known as "leaky gut."

"What chronic [inflammatory diseases](#) have in common with autism is that they're caused by a combination of genetic predisposition and exposure to environmental triggers leading to inflammation," said Fasano. "With autism, it seems that the gut-brain axis communication is compromised and is letting things into the brain that cause neuroinflammation."

## Infant tracking

The GEMMA researchers are following 500 infants who range in age from zero to 36 months and are siblings of children with autism.

The likelihood of a child being born with autism is thought to [increase 10-fold](#) when an older sibling is on the spectrum.

The team is tracking—among other things—the microbial contents of the infants' stools. A balanced composition of bacteria in the intestine is known to maintain the integrity of the gut wall.

Gastrointestinal disorders ranging from stomach cramps to diarrhea are particularly common in people with autism. Furthermore, the condition is often associated with an imbalance of gut microbes: people with autism have less microbial diversity and a higher ratio of harmful-to-healthy bacteria.

GEMMA aims to restore balance to the microbiome and repair the gut barrier by finding a treatment that contains healthy bacteria, known as probiotics, along with prebiotics—non-digestible fiber that stimulates the growth of healthy bacteria.

"This could be a novel approach to improve both the intestinal problems that are so common in children with autism and [behavioral symptoms](#)," said Fasano.

## **Faster detection**

At present, the youngest age at which a child can be diagnosed with autism is 18 months. But most are diagnosed closer to three years of age.

Fasano dreams of a time when detection and treatment can occur before the onset of symptoms and after a simple stool analysis.

"We're aiming for precision medicine," he said.

Information from GEMMA suggests that autism may affect as many as one in 36 children.

Fasano suspects that a Western lifestyle, including poor diets, may be partly responsible.

"The environment we live in has probably changed too fast for our bodies to adapt," he said.

## **Other disorders**

The gut's connection to common neurological disorders is also the research focus of Jan Buitelaar, a professor of medical sciences at Radboud University in the Netherlands.

Buitelaar leads a project hunting for shared underlying characteristics in a range of seemingly distinct neurodevelopmental conditions. These include autism, attention-deficit hyperactivity disorder, intellectual disability and epilepsy.

Named [CANDY](#), the five-year project is due to end at the same time as GEMMA in December 2024.

It's no coincidence that a child with autism will frequently also have attention-deficit disorder or that someone with intellectual disability will have a sibling with epilepsy, according to Buitelaar.

"Often, several of these conditions occur together and, on top of that, go along with other illnesses—most commonly epilepsy," he said.

## Bacterial profiling

For this project, stool, urine, blood and saliva are being collected from three groups: children aged three to six, older ones and the mothers of young study participants.

Buitelaar and his colleagues are looking for common genetic abnormalities in people with differing neurodevelopmental conditions.

The team is also profiling the immune systems of study participants and collecting microbiome samples from both mice and humans. The aim is to explore links between microbiome composition, neurodevelopmental disorders and their varying symptoms.

"Our aim is to explore to what extent the microbiome plays a role in either mitigating or creating a vulnerability to an inflammatory response," said Buitelaar.

In addition, the researchers are seeking to determine whether certain types of bacteria are more present in people with severe forms of autism and, if so, how this information can be used for prevention and intervention.

Another objective of CANDY is, like GEMMA, to detect neurodevelopmental conditions more speedily.

"The hope is that early identification of autism can lead to prevention or treatment," said Buitelaar.

### **More information:**

- [GEMMA](#)
- [CANDY](#)

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