Horizon
The EU Research & Innovation Magazine

European Commission

Autism cures may be closer as focus turns to early treatment

Fresh insights into the genes that cause the neurological disorder could open new routes for the prevention and perhaps even reversal of symptoms.

31 July 2023 - By VITTORIA D'ALESSIO

Autism Spectrum Disorder (ASD) is a complex neurodevelopmental condition that has been intensely investigated since the mid-20th century. It's estimated that ASD affects around 1 in 100 children and mainly boys.

Studies suggest that ASD is closely linked to genetics. The basic challenge is untangling the relationships between the many genes involved and the symptoms.

Genes and symptoms

A focus on these links has the potential to enhance understanding of the condition and treatments for it.

For instance, children born with a rare genetic mutation – on a gene called BCKDK – are more likely to develop impairments that, left untreated, would likely result in lifelong autism. Symptoms can include intellectual disability, epilepsy and a condition – microcephaly – where a baby's head is smaller than expected.

The faulty gene in question disrupts the way the brain can process essential nutrients known as "branched-chain amino acids" and creates the conditions for delayed neurological development.

'This got us thinking: now we know what causes this neurodevelopmental disorder, can we reverse it once the brain has developed?' said Gaia Novarino, a neuroscience professor whose team discovered the BCKDK mutation and its link to autism in 2012. 'Can we go back in time?'

Award winner

Novarino is a high-profile neuroscientist from Italy who has received numerous awards for her work in the field of autism research, including the Order of Merit of the Italian Republic.

‘I have always been interested in genetic disorders and was struck by the general lack of understanding of paediatric, neurodevelopmental disorders,’ she said. ‘We know too little about these diseases.’

Because autism shapes the developing brain long before birth, many assume it’s irreversible – a lifelong condition that, at best, can be managed with psychological support paired with speech and physical therapy.

Some people prefer to forgo treatment because they don’t believe autism needs to be cured, regarding it as an integral part of personality.

‘Not everyone wants their ASD, or their child’s ASD, to be treated,’ said Novarino. ‘If symptoms aren’t profound, a person can live with the condition with minimal support and they may come to see their autism as an essential part of who they are.’

In any case, more recent research has led scientists to assess whether some forms of ASD may be treatable – either fully or in part.

Mice tests

Novarino’s team, based at the Institute of Science and Technology Austria (ISTA) near Vienna, turned to mice for answers under a five-year European research project called REVERSEAUTISM that ended in September 2022.

Backed by EU funding, the researchers genetically engineered mice to be unable to process essential amino acids correctly, similarly to children with the BCKDK genetic mutation.

Amino acids are protein building blocks needed for vital reactions within and between nerve cells. The body can’t make amino acids itself and instead must find them from foods such as meat, fish, grains and nuts.

The team found that rodents with the mutation developed both motor and social difficulties after birth.

‘These mice have behavioural issues,’ said Novarino. ‘They also move in a strange way, with coordination problems.’

REVERSEAUTISM then took this research one step further to see whether, by injecting the missing amino acids directly into the brains of affected mice, their autism-like symptoms could be reversed.

‘The answer was yes,’ said Novarino. ‘Not all symptoms disappeared, but there was considerable improvement in both social behaviour and coordination in mice that received injections. In other words, some signs of the disorder were reversed.’

Study of 21 infants

REVERSEAUTISM’s findings so intrigued Dr Angeles García-Cazorla of Spain that she decided to study whether children with a BCKDK deficiency showed symptom improvements after taking the missing amino acids as a food supplement in conjunction with a high-protein diet.

García-Cazorla is head of Metabolic Diseases Unit at the Hospital Sant Joan de Déu in Barcelona. The missing amino acids are leucine, valine and isoleucine.

The study was based on 21 patients, aged between eight months and 16 months, recruited from centres around the world. The results were very promising.

‘In general, all patients improved, in particular regarding the growth of their head, which means there was a proliferation of neurons,’ said García-Cazorla. ‘They also showed improved motor function. Infants who weren’t

able to walk could now walk and infants who couldn't speak developed some basic language.'

Sooner the better

The earlier treatment was begun, the better the outcomes were.

'In the three children who started supplementation before the age of two, the evolution was much better and the child who started at eight months did best – she had normal brain development, with no signs of autism, by the age of three,' said García-Cazorla.

The study was carried out under an EU-initiated health alliance called the European Reference Network for Rare Hereditary Metabolic Disorders (MetabERN), which is led by patients and experts.

If future studies involving a larger cohort of BCKDK-deficient infants validate the results of the MetabERN investigation, García-Cazorla and Novarino hope national health policies will be changed to require all babies to be tested for BCKDK deficiency at birth.

This would form part of the newborn "heel prick" test, which checks up to 25 rare but serious health conditions.

'One of the challenges in the field of autism is that diagnosis is usually done quite late – rarely before the age of three or four – and at that point it becomes hard to treat,' said Novarino. 'Our work shows that starting supplementation early can make a real difference to people's lives.'

She and her team are pursuing this line of research in a European project called SecretAutism that began in December 2022 and will run through November 2027. They received EU funding to grow brain tissue in the laboratory using human stem cells.

By studying these "organoids", the researchers hope to gain further insights into what exactly the many different genes associated with autism are doing in the body, the stages at which problems develop and how to interrupt the process.

'We're approaching this from many angles, trying to understand how else we can treat patients with ASD,' said Novarino. 'It's very complex research, but that won't put us off.'

Research in this article was funded by the EU via the European Research Council (ERC). If you liked this article, please consider sharing it on social media.

More info

- REVERSEAUTISM
- SecretAutism
- EU-funded research and innovation in the area of the brain