Gene mutations associated with autistic behavior are also responsible for disturbances in the gastrointestinal tract

Human geneticists from Heidelberg discovered that behavioral defects in autism and functional problems of the esophagus and gastrointestinal tract have common genetic causes / Publication in *PNAS*

Individuals with autism often also show disturbances of the gastrointestinal tract. Scientists from Heidelberg, Würzburg, and Ulm have shown for the first time that the behavioral features and digestive problems in autism might be directly related. As reported in the scientific journal *PNAS*, they provided evidence that gene mutations in *Foxp1* affect not only the brain but also gastrointestinal function using a mouse model. Congenital defects in *Foxp1* can therefore cause typical autistic phenotypes such as social deficits, stereotypic behavior, and reduced cognitive skills, but can also impair bowel activity and esophagus function.

“This discovery has an immediate effect on the consultation of patients and their relatives,” says senior author Prof. Dr. Gudrun Rappold, Director of the Department of Human Molecular Genetics at the Institute of Human Genetics of Heidelberg University Hospital. “Restricted esophagus- and bowel function may be treated with an adapted diet and medication. But above all, it is now clear that gastrointestinal problems are neither caused by patients’ medication alone nor by their deviant eating habits, as frequently assumed.”

Digestive problems occur with above-average frequency in individuals with autism spectrum disorders. However, these complaints have not been assessed to date. Furthermore, some affected individuals have only limited communicative or intellectual skills and their ability to report on digestive or swallowing problems is limited. Many patients with the so-called FOXP1 syndrome, for instance, are diagnosed with gastrointestinal problems. Prof. Dr. Gudrun Rappold at the Institute of Human Genetics and Prof. Dr. Andreas Friebe at the Physiological Institute of Würzburg University and their teams have systematically examined these interrelationships in mice bearing the same genetic defect as humans.

The majority of genes associated with autism are active in the brain *and* gastrointestinal tract

These mice showed an abnormal feeding behavior and less food and water intake compared with those without this genetic alteration. The colon and esophagus had thinner muscle layers. Disturbed sphincter function at the gastric entrance reduced opening during swallowing (achalasia). This disrupts the passage of food, which can damage and enlarge the esophagus. Additionally, passage of food through the intestine was significantly slower. Dr. Henning Fröhlich, first author of the study, concludes that “achalasia combined with changes in intestinal peristalsis are most likely the cause of swallowing problems and constipation that frequently occur in patients with FOXP1 syndrome”.

The *Foxp1* gene is a blueprint for a protein that regulates the functional activity of other genes. The scientists found out that some genes that had already been identified in the brain are also regulated by *Foxp1* in the esophagus. “In fact, the vast majority of genes directly related to autism are active in both the brain and gastrointestinal tract. Therefore, we assume that defects in these genes interfere with the function of both the brain and the gut. This remains to be clarified”, concludes Prof. Rappold. Prof. Niesler, who works on the genetics of neurogastroenterologic disorders, adds “Understanding the role of these genes during the development of bowel dysfunctions in autism can also help us clarify the genetic causes of functional gastrointestinal diseases in people, in which the communication between the gut and the brain is disturbed”.

Literature:

Fröhlich H*, et al.* (2019) Gastrointestinal dysfunction in autism displayed by altered motility and achalasia in *Foxp1*$^{+/-}$ mice. *Proceedings of the National Academy of Sciences of the United States of America.*

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