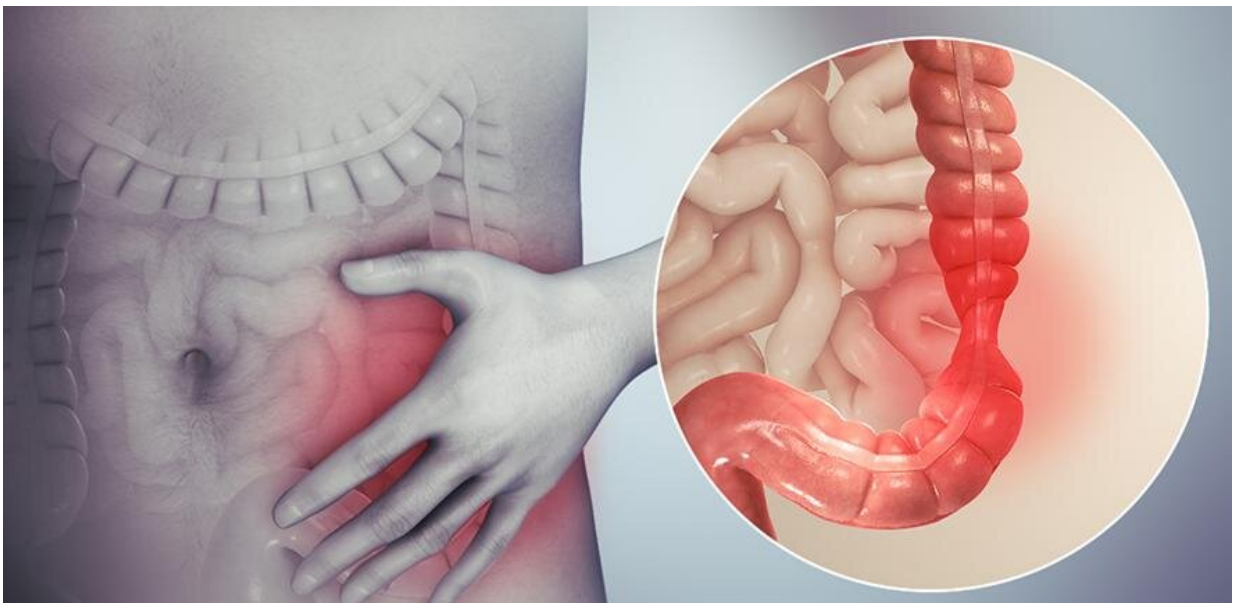


Genetic study reveals possible shared origins of irritable bowel syndrome and mental health disorders

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3D still showing Irritable bowel syndrome. Credit: [Scientific Animations](#)

An international study of more than 50,000 people with irritable bowel syndrome (IBS) has revealed that IBS symptoms may be caused by the same biological processes as conditions such as anxiety. The research highlights the close relationship between brain and gut health and paves the way for development of new treatments.

IBS is a common condition world-wide, affecting around 1 in 10 people and causing a wide range of symptoms including abdominal pain, bloating and bowel dysfunction that can significantly affect people's lives. Diagnosis is usually made after considering other possible conditions (such as Crohn's disease or bowel cancer), with clinical tests coming back "normal." The condition often runs in families and is also more common among people who are prone to anxiety. The causes of IBS are not well understood, but an international team of researchers has now identified several genes that provide clues into the origins of IBS.

The research team, including more than 40 institutions and coordinated by scientists in UK and Spain, looked at [genetic data](#) from 40,548 people who suffer with IBS from the UK Biobank and 12,852 from the Bellygenes initiative (a world-wide study aiming to identify genes linked to IBS) and compared them to 433,201 people without IBS (controls), focusing on individuals of European ancestry. The findings were repeated with de-identified data from the genomics company 23andMe Inc., provided by customers who have consented to research, by comparing 205,252 people with IBS to 1,384,055 controls.

The results showed that overall, heritability of IBS (how much your genes influence the likelihood of developing a particular condition) is quite low, indicating the importance of environmental factors such as diet, stress and patterns of behavior that may also be shared in the family environment.

However, six [genetic differences](#) (influencing the genes NCAM1, CADM2, PHF2/FAM120A, DOCK9, CKAP2/TPTE2P3 and BAG6) were more common in people with IBS than in controls. As IBS symptoms affect the gut and bowel, it would be expected that genes associated with increased risk of IBS would be expressed there—but this is not what the researchers found. Instead, most of the altered genes appear to have more clear-cut roles in the brain and possibly the nerves

which supply the gut, rather than the gut itself.

Researchers also looked for overlap between susceptibility to IBS and other physical and mental health conditions. They found that the same genetic make-up that puts people at increased risk of IBS also increases the risk for common mood and anxiety disorders such as anxiety, depression, and neuroticism, as well as insomnia. However, the researchers stress that this doesn't mean that anxiety causes IBS symptoms or vice versa.

Study co-senior investigator and consultant gastroenterologist Professor Miles Parkes from the University of Cambridge explained: "IBS is a common problem, and its symptoms are real and debilitating. Although IBS occurs more frequently in those who are prone to anxiety, we don't believe that one causes the other—our study shows these conditions have shared genetic origins, with the affected genes possibly leading to [physical changes](#) in brain or nerve cells that in turn cause symptoms in the brain and symptoms in the gut."

The study also found that people with both IBS and anxiety were more likely to have been treated frequently with antibiotics during childhood. The study authors hypothesize that repeated use of antibiotics during childhood might increase the risk of IBS (and perhaps anxiety) by altering the 'normal' gut flora (healthy bacteria that normally live in the gut) which in turn influence nerve cell development and mood.

Current treatments for IBS vary widely and include dietary changes, prescription medications targeting the gut or brain, or behavioral interventions. Lead author Chris Eijsbouts from the University of Oxford suggests that discovering genes which contribute to IBS may aid in the development of new treatments in the long term. He said: "Even genetic changes that have only subtle effects on IBS can provide clues about pathways to target therapeutically. Unlike the individual genetic

changes themselves, drugs targeting the pathways they tell us about may have a considerable impact on the condition, as we know from other disease areas."

Co-senior investigator Dr. Luke Jostins from the University Oxford commented: "We anticipate that future research will build on our discoveries, both by investigating the target [genes](#) identified and exploring the shared genetic risk across conditions to improve understanding of the disordered brain-gut interactions which characterize IBS."

"IBS represents a remarkable challenge for genetic studies. These initial findings have been long awaited, and finally tell us this type of research is worth the struggle," added Ikerbasque Professor Mauro D'Amato from CIC bioGUNE, co-senior investigator and coordinator of the Bellygenes initiative.

More information: Chris Eijsbouts et al, Genome-wide analysis of 53,400 people with irritable bowel syndrome highlights shared genetic pathways with mood and anxiety disorders, *Nature Genetics* (2021). [DOI: 10.1038/s41588-021-00950-8](https://doi.org/10.1038/s41588-021-00950-8)

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