New research shows bowel habits are written in our DNA

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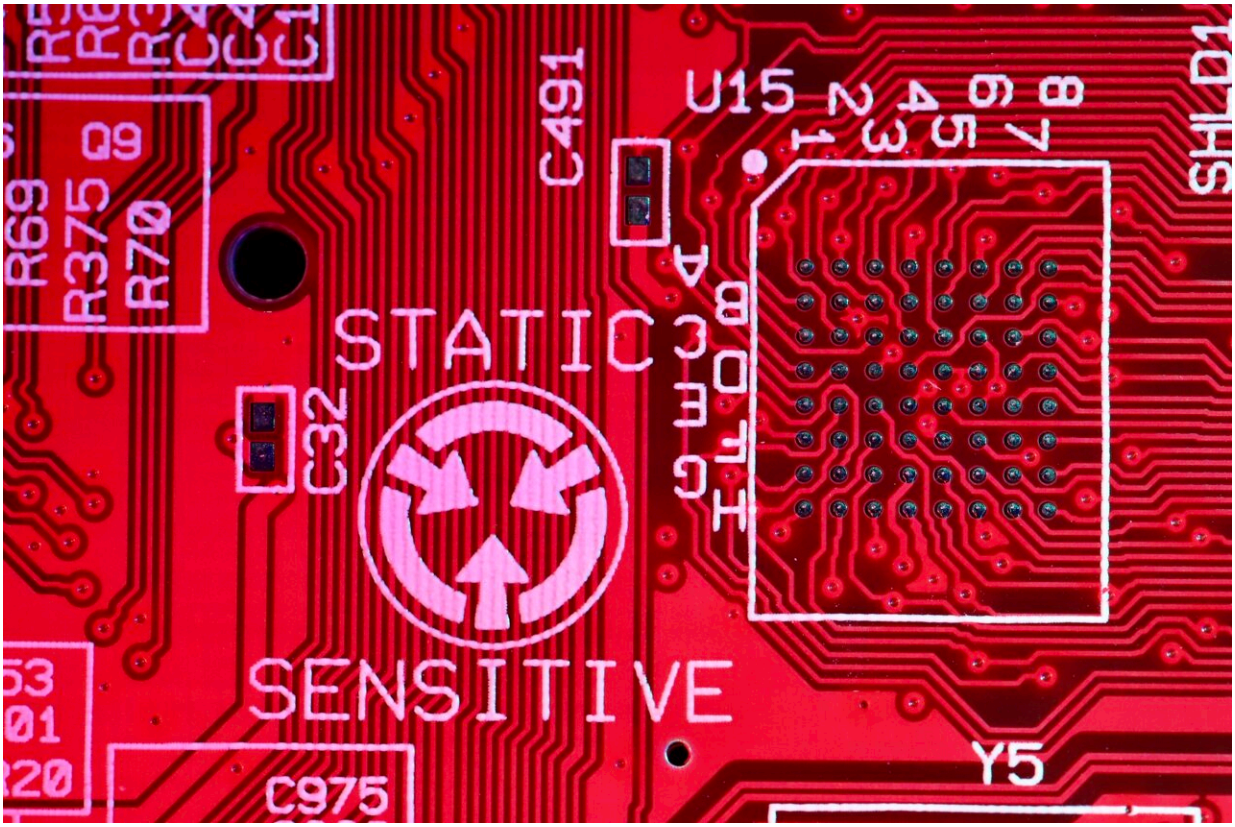

Credit: Nic Wood from Pexels

Do you "go" once a day? Maybe you go twice, or even three times? Or perhaps you only go a few times a week? Yes, we're talking about pooing. In our new study, we've found how often you go is, at least to

some degree, a function of your genetic make-up.

You might be wondering why this is something we chose to study. While many people rarely give a second thought to going when the urge presents itself, for others, common gastrointestinal conditions like irritable bowel syndrome (IBS) cause problems.

IBS affects up to 10% of people globally and is characterized by abdominal pain and bloating, irregular bowel habits, constipation and diarrhea. Although not life threatening, it can severely affect a person's quality of life.

We don't know exactly what causes IBS, which means therapeutic options are limited, mostly directed at treating the symptoms rather than targeting specific causes. We also don't have a way to tell who is at increased risk of IBS.

In this climate, our general research aims to identify genetic risk factors for IBS by looking at genomic information and health-related data across large groups of people. The idea is that our findings may, in time, pave the way towards better treatment options.

In our latest study, published in the journal *Cell Genomics*, we looked at how often people poo—or their "stool frequency"—and how this correlates with their genes. Our findings provide clues as to the genetic risk factors associated with IBS.

Investigating the genetic links for complex diseases such as IBS is challenging for a variety of reasons. One way to simplify things is to deconstruct the disease into individual biological components or traits related to the physiological processes disturbed during illness. These are called intermediate phenotypes or "endophenotypes". If you were looking at heart disease, blood pressure would be an example of an

intermediate phenotype.

We took this approach in our research, and opted to study intestinal motility, or gut motility, as a hallmark intermediate phenotype of IBS. By way of background, many people with IBS experience intestinal dysmotility, which is when the gut doesn't work properly at moving its contents (such as food and drink) through the digestive system. This may result in symptoms including constipation or diarrhea.

While direct measurement of gut motility in humans requires clinical procedures that are not suitable for large-scale studies, stool frequency has been shown to correlate with gut motility and may therefore be used as its proxy in big genetic studies.

On this basis, we analyzed data from 167,875 people (taken from the UK Biobank and four smaller groups in Europe and the US) who provided information on how often they move their bowels.

Alongside this data, we analyzed millions of DNA markers—the building blocks of our DNA which make each of us genetically unique. We demonstrated for the first time that stool frequency is, at least in part, a heritable characteristic.

We identified 14 regions of the human genome where specific DNA markers occur more often in people reporting higher or lower stool frequency compared to the rest of the population. This makes sense, because within these regions are multiple genes whose products (including neurotransmitters, hormones and receptors) are involved in the communication between the gut and the brain.

While some of these molecules were already known, and have even been the targets of drugs to influence gut motility, most represent potential new candidates for the treatment of diarrhea, constipation and IBS.

A common genetic denominator

We also found evidence of similar genetic architecture between stool frequency and IBS. In other words, the genetic factors important for controlling stool frequency appear to also be important when it comes to the risk of developing IBS.

Finally, we wanted to see whether what we learned in our study could be used to try to identify people at increased risk of IBS. We did this by calculating polygenic scores, which are numerical values summarizing genetic information, in this case relating to the probability of having altered stool frequency.

This was more informative for IBS primarily characterized by diarrhea. Using data from the UK Biobank, we showed that people with higher polygenic scores (therefore more likely to have higher stool frequency) are up to five times more likely to suffer from IBS with diarrhea than the rest of the population.

Some limitations

It's important to point out that our study doesn't account for lifestyle and dietary factors, which certainly have an effect on bowel habits.

And while we identified 14 regions containing DNA markers important for stool frequency, within most of these regions, individual genes and their specific biological functions still need to be characterized.

Further, stool frequency polygenic scores and their value in predicting IBS need to be tested and validated in independent studies and among people from different ethnic backgrounds (only individuals of European ancestry were included in this research).

Overall, however, these are important initial genetic findings, which could help us identify new treatment options. They also open up the possibility of using genetic information to identify IBS patients, as well as those falling into specific subtypes (such as IBS characterized by diarrhea). This in turn could help to stratify patients into appropriate treatment groups.

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