

# Research on gut bacteria may change the way we look at anxiety, depression, and behavioural disorders

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If aliens were to examine a human, they would think we were just slavish organisms designed to feed microbes and carry them around. Our bodies contain 10 times more bacteria than cells, and there are an estimated 3.3 million genes in the total bacteria DNA, which is 160 times the number of human genes. Our intestine hosts about one kilogram of bacteria, which help to digest and metabolise food, produce vitamins and protect us from infections.

The above is textbook knowledge, but many recent studies have uncovered new and unsuspected roles for these little companions. There is evidence that [gut bacteria](#) can protect or predispose us to pathologies ranging from inflammation to diabetes and obesity. And, as far-fetched as it sounds, a remarkable amount of data shows that they can even modify our mood and behaviour.

Microbes are hot on the scientific agenda. In May, the U.S. government launched a National Microbiome Initiative with an overall budget of a half-billion dollars, while the EU is funding more than 300 projects related to the microbiome.

Yolanda Sanz, a researcher at the Institute of Agrochemistry and Food Technology (IATA) of the Spanish National Research Council in Valencia, Spain, coordinates MyNewGut, the largest EU consortium in the field with 30 partners in 15 Countries. We asked Sanz about the perspectives of research and the intriguing connections between the microbiome and the brain.

## **What makes our gut flora, and how does it change over time?**

Our intestine hosts a complex ecosystem of bacteria; we call it the gut microbiota, which includes at least 1000 species. We get most of our gut

microbes soon after birth, although there is evidence of colonisation even during prenatal life.

Over the first two to three years of life, the microbiota is very unstable in its composition. This overlaps with a period in which the immune system is still immature. At this stage, the microbiota is greatly influenced by diet, for example whether you are breastfed or not.

With an adult diet, the composition of the gut microbiota becomes more stable and a microbiotic profile emerges. This usually prevails until old age when the diet diversity decreases and becomes more unstable, such as in babies. In some way, the evolution of microbiota reflects our growth and senescence.

## **Do we therefore have a sort of microbial identity, a bacterial fingerprint that is unique to an individual?**

Yes, each person has a different proportion of bacterial species and strains in his or her gut. If I had to put a figure on it, I would say that about a quarter of the microbiota is unique to each individual, but it's difficult to give a precise estimate. Also, we know that our genome influences our [gut flora](#). We don't know how it works, but at least some features of our microbiota are associated with our DNA.

## **What happens when people radically modify their diet?**

Studies show that dramatically altered diet—for instance, changed proportion of fiber, protein or fats—causes relatively quick changes in gut microbiota. About 30 to 40 percent of the bacterial strains will vary in their abundance. In this way, people get a new microbial identity until the diet changes again.

Drugs can also alter the microbiota. Recent studies point to antibiotics, of course, but also to proton pump inhibitors, anti-inflammatory drugs and other classes of medications that do not interact directly with bacteria. The picture is more complicated than what it looked a few years ago.

## **What is the connection between the microbiota, the brain, and mood?**

There is a growing evidence of a microbial gut-brain axis in which bacteria can influence the brain, and vice versa.

Researchers from Canada found that mice from a particularly shy species became more active and curious after receiving a gut microbial transplant from less inhibited mice. We know that some strains of intestinal bacteria produce compounds that have an effect on the nervous system—neurotransmitters, for example, or metabolites that alter the blood-brain barrier. We don't yet know the precise mechanisms, but it's quite clear that the gut microbes can influence mood and the behavioural patterns.

## **Do these findings apply to humans too?**

Most of the information comes from animal studies, but some data in humans are quite conclusive. People with primary depression, for example, show alterations in the microbiota.

In addition, transplanting the microbiota of depressed patients into mice can replicate the pathology in the animals.

A problem with human trials is that we can only analyse the patients' faeces, which are more representative of the bacteria from the lower

intestine. To get information about the other parts of the digestive tract, you would need to do biopsies and other invasive tests on healthy people, which would be unethical.

## **Can we imagine a probiotic therapy for brain disorders in humans, at least to alleviate some symptoms?**

There have been a few trials where patients with depression have been given probiotic treatments. The results are encouraging, but they are small studies, and there are many steps before we can say whether or not these interventions actually work.

To date, science has found many correlations between the [gut microbiota](#) and pathologies. To move toward therapy, researchers need to establish a causal relationship, and look closely at the mechanisms by which bacteria interact with the nervous system.

## **What are the next steps, and do you see interactions between the National Microbiome Initiative (NMI) in the US and the EU projects in the same field?**

To progress further, we need to study larger groups of patients and integrate different –omics approaches, such as genomics and proteomics. It's the philosophy behind the NMI and it's what we're doing with the European project MyNewGut. We have to recognise that the US is investing much more than Europe but there is plenty of room for collaboration. We try to make sure that most genomic data are open and available to the entire scientific community.

The NMI is open to partners from the EU, and many European

consortia, including ours, have partners from both sides of the Atlantic. The problem is that US partners cannot access any funding from the EU and vice versa. There are many future challenges we need to address together. It's not easy to transfer the mice findings on humans, but I think we're headed in a promising direction.

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