

# Psychobiotics: How gut bacteria mess with your mind

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What goes on in our gut may have profound effects on what goes on in our mind (*Image: Sven Paustian/Plainpicture*)

*Gut bugs can change the way our brains work, offering new ways to relieve problems like stress, anxiety and depression, say two leading professors*

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WE HAVE all experienced the influence of gut bacteria on our emotions. Just think how you felt the last time you had a stomach bug. Now it is becoming clear that certain gut bacteria can positively influence our mood and behaviour. The way they achieve this is gradually being uncovered, raising the possibility of unlocking new ways to treat neurobehavioural disorders such as depression and

obsessive-compulsive disorder (OCD).

We acquire our intestinal microbes immediately after birth, and live in an important symbiotic relationship with them. There are far more bacteria in your gut than cells in your body, and their weight roughly equals that of your brain. These bacteria have a vast array of genes, capable of producing hundreds if not thousands of chemicals, many of which influence your brain. In fact, bacteria produce some of the same molecules as those used in brain signalling, such as dopamine, serotonin and gamma-aminobutyric acid (GABA). Furthermore, the brain is predominantly made of fats, and many of these fats are also produced by the metabolic activity of bacteria.

In the absence of gut bacteria, brain structure and function are altered. Studies of mice reared in a germ-free environment, with no exposure to bacteria, show that such mice have alterations in memory, emotional state and behaviour. They show autistic patterns of behaviour, spending as much time focusing on inanimate objects as on other mice. This behavioural change is driven by alterations in the underlying brain chemistry. For example, dramatic changes in serotonin transmission are seen, together with changes in key molecules such as brain-derived neurotrophic factor, which plays a fundamental role in forming new synapses.

These findings give weight to the notion of probiotics – bacteria with a health benefit. Probiotics were first proposed by Russian biologist [Élie Metchnikoff](#) who, in the early 1900s, observed that people living in a region of Bulgaria who consumed fermented food tended to live longer. However, it now seems that certain bacteria – dubbed psychobiotics – might have a mental-health benefit, too.

Although the field of psychobiotics is in its infancy, there are already promising signs. Last year, for instance, researchers from the California Institute of Technology in Pasadena showed that when the bacterium *Bacteroides fragilis* was given early in life, it corrected some of the behavioural and gastrointestinal deficits in a mouse model of autism. And previous reports indicate that *Bifidobacterium infantis* is effective in an animal model of depression. How exactly do gut bacteria influence the brain? The mechanisms are becoming clear. The bacterium *Lactobacillus rhamnosus*, which is used in dairy products, [has potent anti-anxiety effects](#) in animals, and works by changing the expression of GABA receptors in the brain. These changes are mediated by the vagus nerve, which connects the brain and gut. When this nerve is severed no effect on anxiety or on GABA receptors is seen following psychobiotic treatment with *L. rhamnosus*.

*L. rhamnosus* has also been shown to [alleviate OCD-like behaviours](#) in mice. Interestingly, this bacterium not only alters GABA receptors in the brain but has been shown to synthesise and release GABA. Other evidence supports the view that gut bacteria may influence the brain in routes other than the vagus nerve – by altering the immune system and via the manufacture of short-chain fatty acids, for example.

Just as certain genes render bacteria pathogenic, it is likely that clusters of genes within gut bacteria provide mental health benefits. However, the essential genes for effective psychobiotics have yet to be established. It may be that, in the future, the ideal psychobiotic will be a genetically modified organism containing genes from several different bacteria. In the meantime, cocktails of bacteria are likely to be more effective than single strains in producing health benefits. For example, [a 2011 study](#) showed that a combination of *Lactobacillus helveticus* and *Bifidobacterium longum* reduced anxiety and depressive symptoms in healthy volunteers. [A 2013 neuroimaging study](#) showed that a fermented milk product containing four different probiotic bacteria was associated with the reduced response of a brain network involved in the processing of emotion and sensation. And certain strains of bacteria can reduce the symptoms of irritable bowel syndrome, a common stress-related disorder of the brain-gut axis. This is probably achieved through a reduction in levels of the "stress hormone" cortisol and of inflammatory molecules produced by the immune system.

These findings are promising, but we are still a long way from the development of clinically proven psychobiotics and it remains to be seen whether they are capable of acting like – or perhaps even replacing – antidepressants. At a time when prescriptions for antidepressants have reached record levels, effective natural alternatives with fewer side effects would be welcome. We are currently completing a study of the gut microbiota in people with severe depression. If we find consistent alterations, this will provide a strong rationale for targeting depression with a suitable psychobiotic. We are also about to start a placebo-controlled study of *Lactobacillus brevis* in treating anxiety in healthy volunteers. We must, however, sound a note of caution. Despite marketing claims to the contrary, most putative probiotics have no psychobiotic activity. Until recently, lax regulation in both the US and the European Union allowed manufacturers to make outlandish claims without supporting data. This situation is changing and will protect consumers from fraudulent marketing, but the reality is that only a small percentage of bacteria tested have positive neurobehavioural effects. Some bacteria fail to survive storage in the health food store or are eliminated by acidity in the stomach. Even if they do survive gut transit, they may be devoid of health benefits.

In the 20th century, the major focus of microbiological research was on finding ways to kill microbes via antibiotics. This century the focus has changed somewhat, with a recognition of the health benefits of bacteria, not just from an immunity perspective but from a mental health one. Today, in richer nations, the impact of stress on health is perhaps as great as the threat from harmful bacteria. Psychobiotics have enormous potential.

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