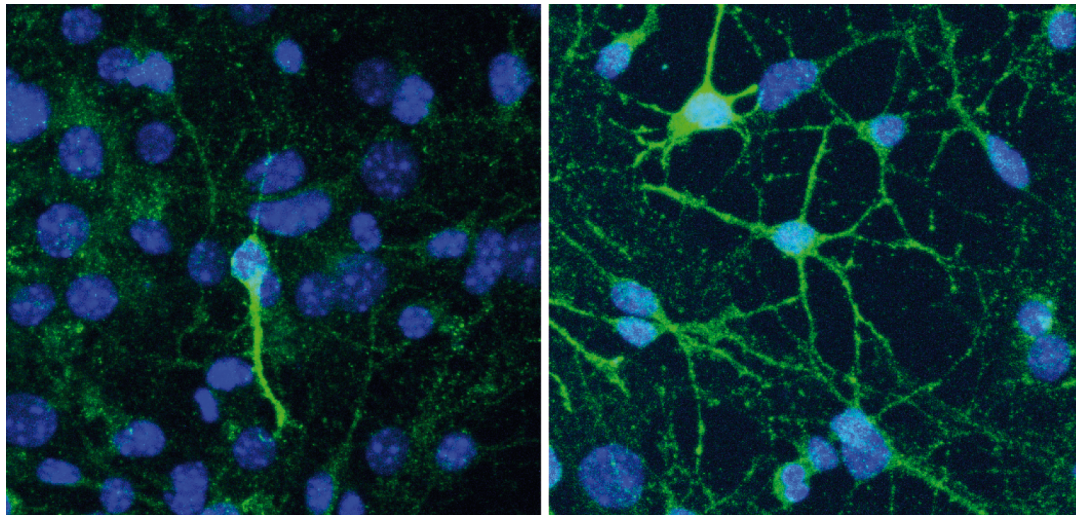


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Depression and the efficacy of antidepressants depend on the composition of the gut microbiota

The production of new neurons highlights the inefficacy of fluoxetine (on the left). Increased biosynthesis of serotonin helps boost neurogenesis (on the right) and treat symptoms of depression. © Institut Pasteur

Does a healthy microbiota lead to a healthy mind? A joint study between the Institut Pasteur, the CNRS and Inserm has revealed the highly specific profile of the gut bacterial population in a mouse model used to study depression. When the bacterial population is transferred to healthy mice, they exhibit behaviors associated with depression within a few days. This can be explained by the fact that the bacterial community in the stressed mice produces very few of the precursors needed to synthesize serotonin – thereby rendering a class of antidepressants such as fluoxetine ineffective. The findings were published in [Cell Reports](#) on March 17, 2020.

The bacterial population in the gut, known as the gut microbiota, performs many vital functions for the body. A number of studies in recent years have established strong links between the brain and the microbiota. Several neurological and psychiatric disorders are thought to be caused by an imbalance in the gut bacterial population, but little was previously known about the underlying mechanisms.

Scientists from the Institut Pasteur, the CNRS and Inserm recently discovered that after transferring the microbiota of stressed, anxious mice to healthy mice, the psychological traits of the former could soon be transferred in the latter. Within a few days, the recipient mice exhibited all the characteristic symptoms of depression (reduced motivation, absence of

pleasure, apathy, etc.). It was notable that the recipient mice with an unbalanced bacterial population had very low levels of amino acids – especially tryptophan – in the blood and the gut. Tryptophan is a precursor for the synthesis of serotonin, a cerebral neurotransmitter associated with positive mood. In the mice whose depression was caused by an imbalance in the gut microbiota, the scientists demonstrated the inefficacy of an antidepressant such as fluoxetine.¹ But the same antidepressant became effective again when the diet of the mice was supplemented with metabolites produced naturally by gut bacteria (like *5-Hydroxytryptophane*) but lacking in the recipient mice.

This research shows that some forms of depression may be transmitted by a simple microbiota transfer. Pierre-Marie Lledo, CNRS Director of Research and Head of the Perception and Memory Unit (Institut Pasteur/CNRS), adds: "We demonstrated that eliminating some families of gut bacteria may reduce the level of amino acids in the host's bloodstream, that a simple imbalance in the gut microbiota is all it takes to bring about depression, and that this depression is resistant to the action of a class of antidepressants (selective serotonin reuptake inhibitors, or SSRIs)." "We ultimately managed to restore the efficacy of the antidepressants by supplementing the mice's diet with metabolites derived from bacterial activity," concludes Gérard Eberl, Head of the Microenvironment and Immunity Unit at the Institut Pasteur.

By revealing the beneficial role of some gut bacteria on mental health, this study in animals identified a family of gut bacteria that could be referred to as "psychobiotics." The research may help explain why 30% of those treated with antidepressants experience no beneficial effects from the treatment. The theory now needs to be tested in humans.

source

Changes in gut microbiota by chronic stress impair the efficacy of fluoxetine, [Cell Reports](#), 17 mars 2020

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¹ A selective serotonin reuptake inhibitor that increases the level of serotonin in the synapses.