

Signals from Gut Biome to Brain and Behavior

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Studies of the interrelation between microbes of the gastrointestinal tract and general health are increasingly focused on bidirectional links between that microbiota and mental health, mood and behavior.

Research has suggested that while physiological and behavioral changes such as pharmacological intervention, diet and chronic stress can affect the microbiota configuration, gut microbiota have been shown to affect the development and functioning of the brain.

Origins of gut biome signaling research

Neuroscientists first noticed that mice bred to be "germ-free" (GF) showed a behavioral phenotype, with exaggerated stress-reactivity and within 5 years experiments reduced their anxiety-like behavior through exposure to selected microbes.

Physiological mechanisms

An array of processes is postulated to facilitate signaling between the gut microbiota and brain. A relatively direct link is suggested by the neurochemicals produced by microorganisms of the gut, which can bind to host receptors, including dopamine, GABA, serotonin and norepinephrine.

A more circuitous path involves immune and inflammatory responses with the microbiota provoking pro-inflammatory cytokines, which also affect brain function. Their effects in the hypothalamus include an increase in corticotrophin releasing hormone (CRH), with subsequent cascade of events through the hypothalamic-pituitary-adrenal axis (HPA).

Clinical applications

A "leaky gut" hypothesis proposes that increased permeability in the intestinal barrier could precede mucosal inflammation, or enable translocation of bacteria from the gut, prompting systemic inflammation.

It is consistent with stress being associated with alterations in the integrity of the intestinal barrier and the composition of microbiota, and posits that subsequent inflammatory response can mediate the expression of neuropsychiatric symptoms.

One study showed that the brain's signaling of the inflammasome, a multiprotein complex expressed to activate the pro-inflammatory cytokines, has been determined to affect anxiety- and depressive-like behaviors in mice as well as the composition of their gut microbiota.

In another study, GF mice receiving transplantations of fecal microbiota from human patients with major depression fared worse in stress testing than those receiving transplantations from healthy controls. The samples of the two groups had been confirmed to have distinctly different microbiota composition.

References

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Reviewed by Jonas Wilson, Ing. Med.

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Last Updated: Jul 21, 2016