



Eat your stress away!

Targeting the Microbiota-Gut-Brain Axis: Prebiotics Have Anxiolytic and Antidepressant-like Effects and Reverse the Impact of Chronic Stress in Mice.

The Microbiota-Gut-Brain Axis is a mysterious wonderland full of Nobel prize scientific discoveries to be made. Everything your body builds is dependent on what you ingest, from your energy supplies to the levels of hormones your brain has available to communicate with your body. Eating seems to have a greater undisclosed impact on our mood, motivation and accomplishments that we are just beginning to understand.

Vicente Chavez

The gut-brain axis is the term used for communication that occurs between our gut and brain. The microbiota-gut-brain axis specifically refers to the complex environment of microorganisms that inhabit our stomachs and its ability to communicate with our brain via the gut signaling pathways. The gut microbiota composition typically referred to as the gut microbiome (bacterial environment) has been implicated in a variety of central nervous system disorders, cancer, inflammation and obesity^{1,2,3}. A beneficial microbiome includes great diversity of species to effectively balance each other's many inflammatory and regulatory signaling chemicals⁴. The number of bacterial cells inside a "standard person's" gut is upwards of 3.8×10^{13} ^(5,6). This number is unfathomable for many and is a large reason the gut chemistry is so complex. A variety of substances can influence the microbiota including probiotics, prebiotics and antibiotics⁷. Probiotics are live beneficial bacteria that naturally occur in all-time favorite foods such as yogurt, miso soup and kimchi. Prebiotics are plant fibers found in the skins of fruit, vegetable roots and beans. Prebiotics are typically indigestible facilitating growth of our good anti-inflammatory bacteria^{8,9}. Antibiotic administration has proven to be a difficult task because it indiscriminately effects all bacteria¹⁰. The microbiome involves and impacts neural, humoral, immune and metabolic pathways¹¹. Modulating the microflora offers potentially new avenues to develop novel therapeutics for complex stress-related Central Nervous System (CNS) disorders where there is huge medical need present¹².

A recent study conducted over the course of ten weeks by Burokas et al., set out to investigate the impacts of prebiotics such as Fructo-oligosaccharides (FOS) and galacto-oligosaccharides (GOS) (both soluble fibers) as microbiome manipulators. These prebiotics are found in common food items, FOSs are in red onions, bananas and nutrition bars. GOSs can be found in cashews, hummus dip and soy milk^{13,14}. The study's aim was to understand their potential roles as an anxiolytics (anxiety-reducer) and as antidepressants¹⁵. Mice were given FOS, GOS or a combination of both for three weeks, with the goals of nurturing a beneficial microbiome. Anxiety, depression, cognition, stress response and social behavior were measurements of this study. Tests included marble burying, elevated plus maze, resident-intruder test and novel object recognition test^{16,17,18}. Many of the tests identified baseline anxiety, depression and stress levels by recording levels of certain chemicals such as corticosterone, IL-6 and TNF-Alpha implicated in the immune system and environmental stress¹⁹. Results indicated that chronic prebiotic FOS+GOS treatment exhibited both antidepressant and anxiolytic effects in response to stress.

FOS+GOS treatment reduced stress-induced corticosterone release and effected hippocampus and hypothalamus genetic expression indicating long-term brain changes (Figure 1,2 & 3).

These findings support our growing understanding of the impacts of what we choose to eat on our mental health and most notably physical health. It is evident that our societies fundamental lifestyle and diet changes occurred too quickly for our body to effectively adapt. Our bodies inability to adequately evolve have led to a rise in health problems coined “diseases of civilization”²⁰. The convenience of fast food and a high-sugar/sodium Western Diet has been implicated in a wide range of mental, physical and community-based health problems such as depression, obesity and lack of medical resources^{21,22,23}. There is a huge call to action to pay greater attention to one’s diet. There is no perfect diet for any particular individual, but more focus on vegetables, fruits and nuts is recommended as our body has evolved around these food sources²⁴. More research is needed to positively influence the direction of policy surrounding food, medicine and most importantly people’s decision making.

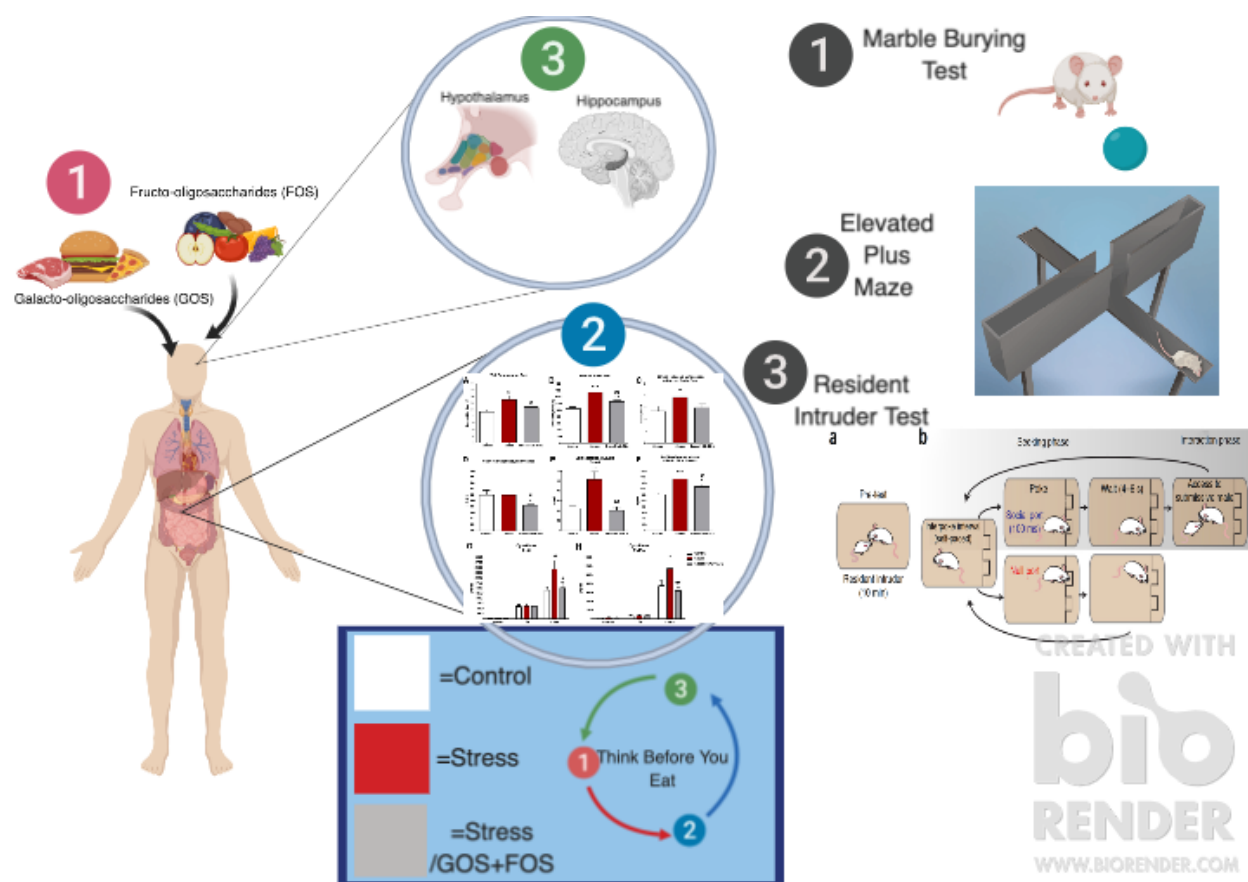


Figure 1. Representative outline of the study and tests employed to measure behavioral responses. Red 1 indicates the two compounds investigated in this study. Blue 2 represents the study results seen more clearly in Figure 2 below. Green 3 represents the long-term changes that occur in the brain in response to the types of food ingested. The take home message is Think Before You Eat. Black/White 1,2 and 3 are examples of the many behavioral tests included in this study (1,2 and 3; Marble Burying Test, Elevated Plus Maze and Resident Intruder Test respectively).

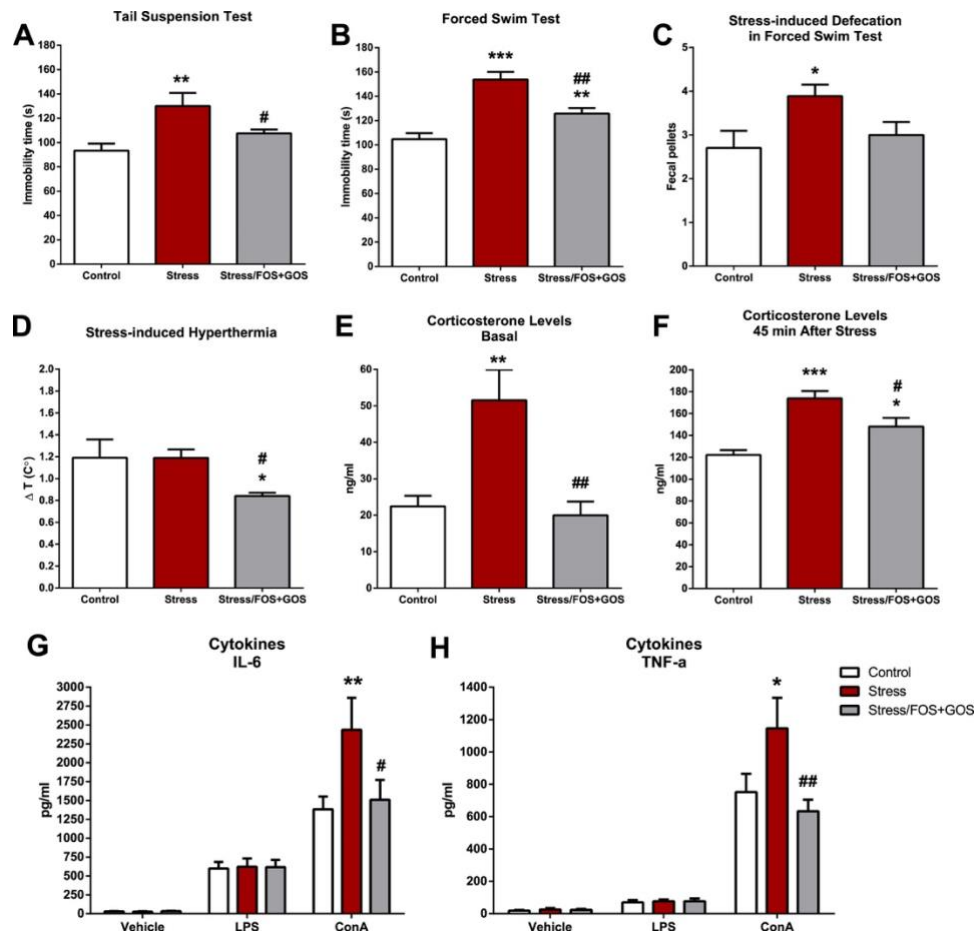


Figure 2. Closer look of the figure used in Figure 1. Test suspension test, forced swim test, stress-induced defecation in forced swim test, stress-induced hyperthermia, corticosterone levels basal, corticosterone levels 45 min after stress, cytokines IL-6, and cytokines TNF-alpha results included for a closer interpretation.

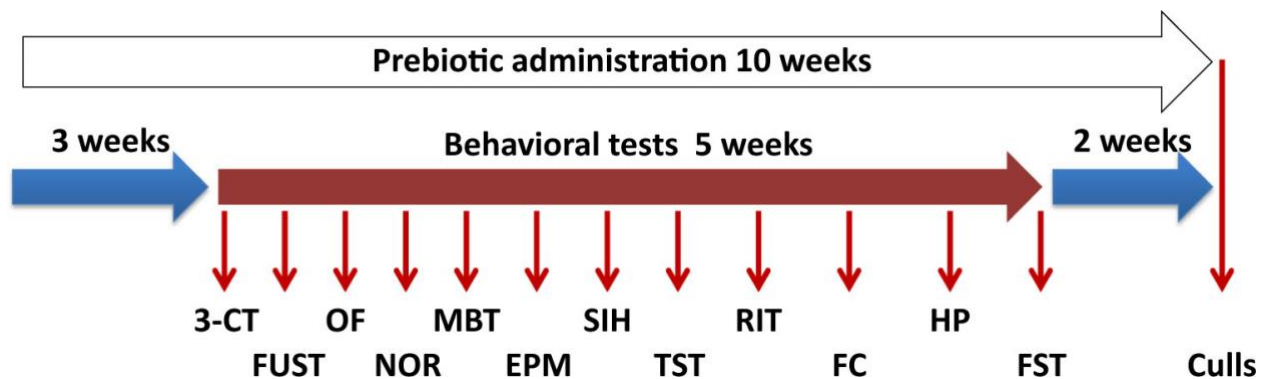


Figure 3. Supplemental methods. Total of 10 weeks prebiotic administration. Behavioral testing occurred on a gradient from least stressful to most. Stress-induced hyperthermia occurred 30 minutes before testing that occurred between 8 am and 4 pm (between 8 am and 12 noon for the forced swim test). "Week 4: 3-CT, three-chamber test; FUST, female urine sniffing test; OF, open field; NOR, novel object recognition test. Week 5: MBT, marble burying test; EPM, elevated plus maze; SIH, stress-induced hyperthermia. Week 6: TST, tail suspension test; RIT, resident-intruder test. Week 7: FC, fear conditioning. Week 8: HP, hot plate; FST, forced swim test and blood collection. Week 10: animals are culled and tissue is collected."

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