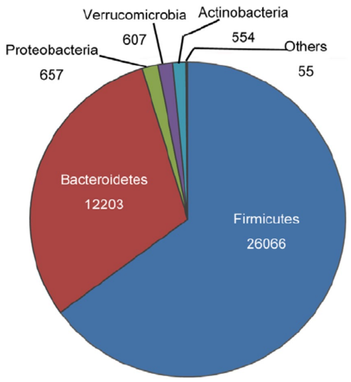
THE INFLUENCE OF NUTRITION ON THE GUT MICROBIOTA AND PSYCHIATRIC DISORDERS: A REVIEW

Megha Bhagavan, MS & Francis E. Jenney Jr., PhD, PCOM Georgia

ABSTRACT

The symbiotic harboring of gut microorganisms within the gastrointestinal tract has a profound influence on host physiology, well-being, and disease pathology. More specifically, the gut bacteria are able to interact with dietary components from foods chosen by the host and consequently relay their beneficial or precarious effects locally and systemically. The gut bacteria have the capacity to maintain a healthy gut microbiome or perpetuate intestinal imbalance, known as gut dysbiosis. Gut dysbiosis has both local effects in gastrointestinal pathologies, such as intestinal bowel syndrome (IBS) and intestinal bowel disease (IBD), as well as systemic pathologies, such as type II diabetes, obesity, and psychiatric disorders. The occurrence of psychiatric disorders may be further promoted by alterations of the gut microbiota via mechanisms of the gut-brain axis (*e.g.* microbial metabolites, neuroendocrine system, immune system). The risk of psychiatric disorders has been shown to be accelerated in university students due to their exposure to factors related to chronic stress such as academic workload, homesickness, and food insecurity (Beiter et al., 2015). Food insecure students tend to reach for foods low in nutritive value due to affordability and accessibility. These foods are high in unhealthy fats, sugars, and are processed. The dietary components of these unhealthy foods may detrimentally alter the gut microbiome resulting in both local pathologies and increasing the prevalence of psychiatric disorders. *The aim of this review is to study the physiological and biological role of the gut microbiota in modulating the mechanisms of the gut-brain axis to understand its influence, which is regulated by certain dietary patterns in university students in relation to the prevalence of their mental health.*

GUT MICROBIOME



- **The gut microbiome is an accumulation of a variety of gut microorganisms (*e.g.* protists, fungi, viruses, archaea, bacteria) called the gut microbiota, which perpetuate symbiotic relations with the body.**
- **The most abundant phyla of gut bacteria are *Bacteroidetes* and *Firmicutes*.**
- **The gut microbiota is found in abundance at the distal end of the digestive tube as the environment there is conducive to their productivity.**
- **Every individual has a different composition of the gut microbiome based on several factors not limited to: social interactions, environment, method of delivery from mother, hygiene, and diet.**

Figure 1. Gut bacteria composition and distribution.
Quantified by 16S rRNA sequences (Yang et al., 2009).

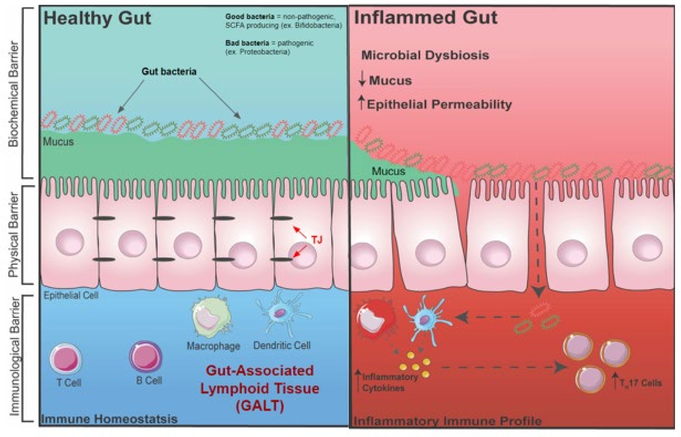


Figure 2. Healthy versus inflamed gut during intestinal homeostasis and dysbiosis. Image shows barriers intact preventing the gut bacteria from contacting the intestinal epithelium. Inflamed gut shows breached barriers with infiltration of activated immune cells such as cytokines promoting the inflammatory environment and leaky gut. (Cooney et al., 2021)

- **A healthy gut consists of a balance between good bacteria and bad bacteria**
  - **Good bacteria =** non-pathogenic, short-chain fatty acid (SCFA) producing bacteria (**ex. Bifidobacteria**)
  - **Bad bacteria =** pathogenic bacteria (**ex. Proteobacteria**)
  - Has proper ratios of particular phyla
  - SCFA production → increase tight junction protein expression (***Figure 4A***)
  - **Microbial SCFA metabolites:** propionate, acetate, butyrate
- **A dysbiotic gut consists of more bad bacteria than good bacteria**
  - Promotes the "leaky gut" phenomenon.
  - Leaky gut → local, intestinal inflammation → systemic inflammation
  - Restorative methods of the gut microbiome are available via diet (pre- and probiotics), drugs (antibiotics), and Fecal Microbial Transfer

GUT-BRAIN-AXIS

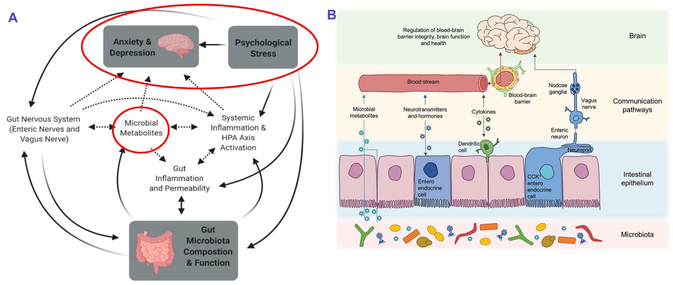


Figure 3 A-B. Mechanisms of the Gut-Brain-Microbiota Axis. A. The proposed ability of the gut microbial metabolites contributing to the onset of psychiatric disorders through different mechanisms (Bear et al., 2021). **B.** Different communication pathways between the gut and the brain (*i.e.* cytokines, hormones, neurotransmitters, etc.) (Ronaldson & Davis, 2020).

- **The gut-brain-axis consists of a bidirectional cross-talk between the gut and its microorganisms and the brain.**
- **There are several mechanisms of communication between the gut and the brain not limited to: neurotransmitters, hormones, vagus nerve, cytokines, hypothalamic-pituitary-adrenal (HPA) axis, microbial metabolites.**
- **Intestinal permeability may affect blood-brain-barrier (BBB) permeability via the presence or absence of microbial metabolites (*Figure 4B*).**
- **A dysbiotic gut environment can be a result of physiological stress → leaky gut → systemic inflammation → psychiatric disorders (anxiety and depression).**

PSYCHIATRIC DISORDERS

Definition: "a particular relationship between the person and the environment that is appraised by the person as taxing or exceeding his or her resources and endangering his or her well-being" (Lazarus and Folkman, 1984)

Acute Stress: "short-term stress"	**Chronic Stress:** "long-term stress"
Examples:	**Examples:**
→ Assignment due at 11:59pm	→ Poor sleep habits
→ Catching a flight on time	→ Academic environment
→ Capstone presentation	→ Food insecurity
	→ Homesickness

Depression: a mood disorder that causes a persistent feeling of sadness and loss of interest

Anxiety: an emotion characterized by feelings of tension and worried thoughts

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DIET TYPES

Refer to Figure 5 and 7B

Western Diet	Physiological response	Effect on psychiatric disorders
→ High fats → High sugar → Processed meats → Red meat Ex: fast food, sugary beverages, desserts	→ **increased** opportunistic bacteria and their metabolites ("bad" bacteria) → **increased** LPS and inflammatory cytokines → **decreased** beneficial bacteria and SCFAs	→ **increased** prevalence of anxiety → **increased** prevalence of depression

Refer to Figure 6 and 7A

Mediterranean Diet	Physiological response	Effect on psychiatric disorders
→ Plant-based diet → Whole foods → Fish, Seafood, Poultry (moderately) → Meats (less often)	→ **decreased** opportunistic bacteria and their metabolites → **decreased** LPS and inflammatory cytokines → **increased** beneficial bacteria and SCFAs	→ **decreased** prevalence of anxiety → **decreased** prevalence of depression

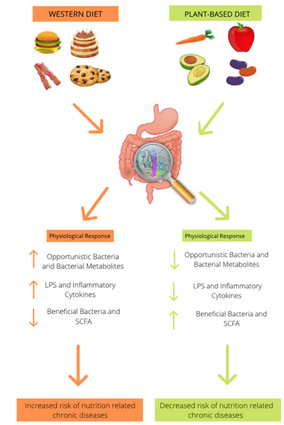

Figure 8. The effects of the western diet and plant-based (Mediterranean) diet on the gut and their resulting physiological response (Beam et al., 2021).

SUPPORTING DATA

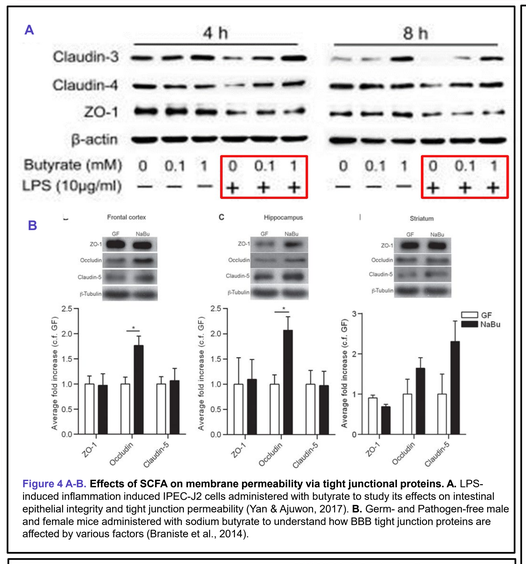

Figure 4 A-B. Effects of SCFA on membrane permeability via tight junctional proteins. A. LPS-induced inflammation induced IPEC-J2 cells administered with butyrate to study its effects on intestinal epithelial integrity and tight junction permeability (Yan & Ajuwon, 2017). **B.** Germ- and Pathogen-free male and female mice administered with sodium butyrate to understand how BBB tight junction proteins are affected by various factors (Braniste et al., 2014).

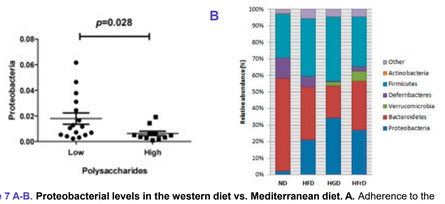

Figure 7 A-B. Proteobacterial levels in the western diet vs. Mediterranean diet. A. Adherence to the Mediterranean diet and its effect on Proteobacteria abundance (Garcia-Mantrana et al., 2018). **B.** HFD, HGD- or HFrD-induced changes in gut microbiome population with an interest in Proteobacteria (Do et al., 2018).

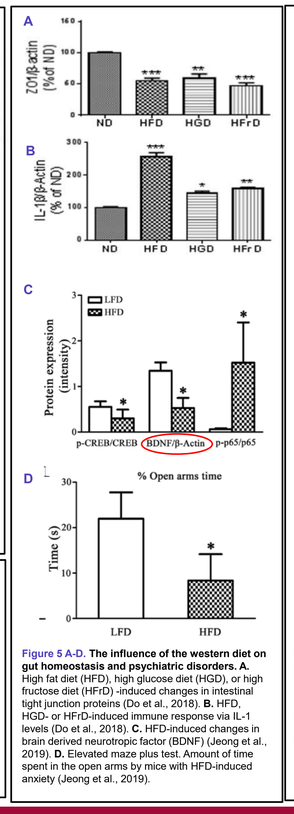

Figure 5 A-D. The influence of the western diet on gut homeostasis and psychiatric disorders. A. High fat diet (HFD), high glucose diet (HGD), or high fructose diet (HFrD) -induced changes in intestinal tight junction proteins (Do et al., 2018). **B.** HFD, HGD- or HFrD-induced immune response via IL-1 levels (Do et al., 2018). **C.** HFD-induced changes in brain derived neurotropic factor (BDNF) (Jeong et al., 2019). **D.** Elevated maze plus test. Amount of time spent in the open arms by mice with HFD-induced anxiety (Jeong et al., 2019).

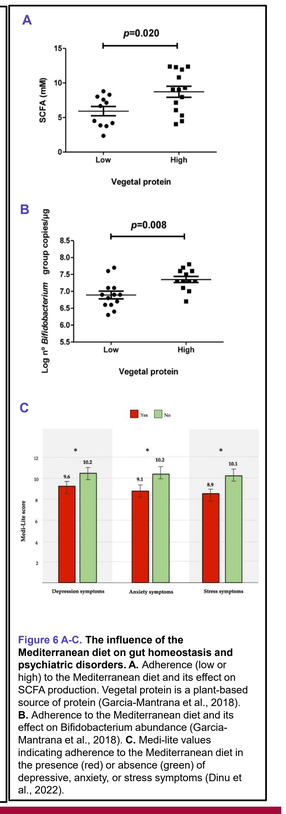

Figure 6 A-C. The influence of the Mediterranean diet on gut homeostasis and psychiatric disorders. A. Adherence (low or high) to the Mediterranean diet and its effect on SCFA production. Vegetal protein is a plant-based source of protein (Garcia-Mantrana et al., 2018). **B.** Adherence to the Mediterranean diet and its effect on Bifidobacterium abundance (Garcia-Mantrana et al., 2018). **C.** Medi-lite values indicating adherence to the Mediterranean diet in the presence (red) or absence (green) of depressive, anxiety, or stress symptoms (Dinu et al., 2022).

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