



Food Decision Making in Overweight Adults can be Manipulated by Prebiotic Diet

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Commentary

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Abbreviations: ENS: Enteric Nervous System; SCFAs: Short Chain Fatty Acids; VTA: Ventral Tegmental Area; rmOFC: Right Medial Orbitofrontal Cortex.

Commentary

In a recent issue of Gut, Medawar, et al. show that a prebiotic dietary intervention reduced reward-associated activation of brain during food decision-making via modulation of gut microbiome composition in humans (NCT03829189).

The gut is called the 'second brain' as it produces multiple neurotransmitters as the brain does. The enormous number of neurons lining the gastrointestinal tract and responsible for producing the neurotransmitters is called the enteric nervous system (ENS) [1]. Distortions in the ENS due to dietary and gut microbial alterations may lead to dysfunction of the gut-brain axis and the bidirectional communication between the central and peripheral nervous system affecting emotional and cognitive centers of brain [2]. Dietary intervention to modulate the gut microbiome and thus microbial metabolites to attenuate disease and improve quality of life is a trending area of research. Clinical trials investigating the effect of various probiotics and prebiotics reported the benefit of these dietary supplements in alleviating symptoms of inflammatory and nervous system associated diseases [3]. Microbiota derived short chain fatty acids (SCFAs) can cross the blood-brain barrier and modulate hypothalamic signaling [4,5]. The ability of SCFAs or SCFA-producing Akkermansia to reduce body weight has been shown in humans [6]. Prebiotic

or non-digestible oligosaccharides are reported to confer neuroprotective benefits. Galacto-oligosaccharide intake improved indices of preclinical anxiety of healthy females by reducing negative emotional bias and increasing positive bias leading to emotional well-being [7]. Prebiotic intake was reported to reduce subjective hunger and improve appetite management via regulation of plasma glucagon-like peptide and neuropeptide and ghrelin [8,9]. Inulin supplementation also led to weight loss and mood improvements in obese people which was correlated with increased relative abundance of Coprococcus genera [10].

In a recent randomized controlled cross-over study published in Gut, Medawar and colleagues investigated the effect of prebiotic fiber consumption on reward-related food decision-making in overweight subjects and analyzed the potential microbial and metabolic markers. The authors hypothesized that prebiotic intervention could alter the gut microbiota and hence neural stimulation patterns of food reward in the populace at risk for weight gain, and the subjects' desire for food, based on caloric density, may change following prebiotic consumption. In this within-subject cross-over study, the authors recruited 59 eligible, overweight young adults. The participants and staff were blinded regarding the prebiotics/placebo allocation. After 14 days of prebiotic (30 g inulin) or equal calory maltodextrin intake, SCFAs, glucose, lipid, inflammatory markers, and hormones were assayed in fasting blood. Gut microbiota and SCFAs were measured in stool. Functional MRI (fMRI) was performed before and after prebiotic intervention. Additionally, dietary habits and lifestyle behaviors were assessed at regular intervals. At behavioral level, the authors hypothesized that participants' ratings for wanting would be higher for food over art and that wanting would change

following prebiotic intake. They also expected activation of different regions of brain following food evaluation compared to art evaluation, at neural level. Authors first ascertained the food augmented activation of reward network in the brain by fMRI where they found that the liking and desire ratings following preference tasks were higher for food stimuli over art. The reward network of the brain was largely activated on food evaluation. Their exploratory analysis following prebiotic consumption revealed a significantly lower wanting score compared to placebo. In addition, participants following prebiotic consumption reported less subjective hunger in comparison with placebo. Gender-standardized body fat mass, serum lipid markers, and cholesterol significantly decreased in placebo.

Authors correlated the neurobehavioral changes after prebiotic intervention to a decrease in the genera of *Subdoligranulum*. A decrease in *Subdoligranulum* was significantly correlated with prebiotic intervention-induced drop in ventral tegmental area (VTA) brain activation towards wanting high-caloric food. In addition, an increase in *Lactiplantibacillus* was significantly associated with an increase in right medial orbitofrontal cortex (rmOFC) in some of the participants. No change in SCFAs was observed. KEGG analysis to disseminate the metabolic pathways disclosed the correlation of reduced VTA brain activation to the downregulation of pathways associated with flavonoid and stilbenoid biosynthesis, biofilm formation, amino and nucleotide sugar metabolism, and upregulation of ATP binding cassette transporters. Reduced rmOFC activation significantly correlated with upregulation of oxidative phosphorylation.

Multiple studies explored the effect of microbial therapeutics to improve emotional attention and memory paralleled by changes in linked brain activation [11-13]. In this proof-of-concept study, the authors explored the association of prebiotic dietary intervention with neurobehavioral changes, serum biomarkers as well as gut microbiota variations. This study provides instrumental evidence for the concept of microbiome-modulating high prebiotic diet can affect brain activation and decision-making related to high caloric food wanting in obese individuals. Although more investigations are required to validate the results across multiple populations, the study suggests the idea of making use of microbiome-changing dietary interventions to control unhealthy eating behavior. Original article: (<http://dx.doi.org/10.1136/gutjnl-2023-330365>)

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