Gut-Brain Axis and Behavior

Clair R. Martin and Emeran A. Mayer

There has been growing interest in the interactions between the gut microbiome, the brain, and behavior [1, 2]. Even though the interest has been fueled by a series of provocative studies in rodent models, there is growing evidence that some of the reported preclinical findings may translate into human behavior and disorders. Preclinical evidence supports a role of the gut microbiome in behavioral responses associated with pain, emotion, social interactions, and food intake. In humans, the regular intake of a probiotic consortium in healthy women was associated with changes in brain networks involved in emotion recognition [3], and recent studies performed in patients with depression and mouse models generated by fecal microbial transfer from such patients suggest possible causation [4]. On the other hand, data indicating an effect of acute gut microbial alterations induced by probiotics or antibiotics on adult human behavioral and clinical parameters are very limited. Based on currently available data, it is likely that the brain and the gut microbiota are in bidirectional communication. While the reported dysbiotic states in depression, chronic stress, and autism may reflect altered brain signaling to the gut associated with these brain disorders, altered gut microbial signaling back to the brain may play a role in reinforcing brain alterations. On the other hand, diet-induced alterations in the gut microbiome may signal to the brain and alter brain networks involved in ingestive behavior resulting in craving for high fat and sugar intake. A major period of vulnerability and plasticity of brain-gut microbiome interactions occurs during the first few years in life, when both gut microbial systems and brain networks are developing. Plausible explanations for the apparent discrepancy between dramatic results in rodent models and the lack of conclusive evidence for the translatability of these findings into human disease populations include the limited homology of the human and mouse brains in terms of brain networks relevant for human brain disorders and the limitations of the gnotobiotic mouse models. Furthermore, there is good evidence that brain-gut microbiome interactions in the adult are fairly stable once they have been established during the first 3 years of life. There are many factors during this developmental period which have been shown to
influence the assembly of the gut microbial architecture, including the diet and stress level of the pregnant mother, the mode of delivery, breast feeding, early adverse life events, and antibiotic exposure. Epigenetic effects occurring during this developmental period could program the nature of brain-gut microbiome interactions for the adult period. In order to overcome the current limitations and uncertainties in this field, there is a need for large-scale, longitudinal human studies in well-phenotyped populations (including pediatric populations) [5]. Such studies should include interventions targeted at the gut microbiome (pre- and probiotics) while monitoring brain and behavioral responses, and at the brain (mind-based therapies) while monitoring the gut microbiota and their metabolites. It is only through these studies that it will be possible to establish causality between brain and gut microbial influences, and to develop novel therapies for human brain disorders aimed primarily at the gut microbiome.

References