

# Gut–brain interaction: scope of neuromodulation techniques

Sujita K. Kar<sup>1\*</sup>, Vikas Menon<sup>2</sup> and Aditya Agarwal<sup>1</sup>

<sup>1</sup>Department of Psychiatry, King George's Medical University, Lucknow, India, and <sup>2</sup>Department of Psychiatry, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, India

## Letter to the Editor

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### Author for correspondence:

\*Sujita K. Kar, MD  
Email: [drsujita@gmail.com](mailto:drsujita@gmail.com)

To the Editor,

The complex bidirectional association between the gastrointestinal system and brain is denoted in the gut–brain axis. Brain pathologies may cause disturbances in the gut and vice versa, which indicates that gut pathology may be a cause or effect of brain pathology.<sup>1</sup> Indeed, there is now evidence for increased cortical excitability and impaired motor conduction in disorders of gut such as celiac disease.<sup>2</sup> These changes in the brain may cause alterations in cognition, commonly referred to as “brain fog.”<sup>2</sup> Dietary modifications (eg, restriction of gluten in diet) may restore the cortical homeostasis to some extent.<sup>2</sup> Similarly, it has been reported that there is alteration in immunological parameters (cytokines, oxidative stress radicals, nitrosative stress parameters, autoimmune activation, amine catabolism, and gut–brain axis alteration) in patients of depression.<sup>3</sup> These parameters have been found to be associated with inflammatory bowel disease too. These changes are likely to alter neuroplasticity. The elevated inflammatory cytokines are known to cause cognitive dysfunctions, which is evident in a spectrum of psychiatric disorders ranging from schizophrenia, bipolar affective disorder, depression, and obsessive compulsive disorder to Alzheimer's disease.<sup>4</sup>

The activity of gut–brain axis can be modulated by broadly two approaches. The first being the top-down approach, where cortical neuromodulation will regulate the activity of gut and the second being bottom-up approach, where modulating the gut activity (by altering the gut microbiota) will signal the brain through immune regulation and production of microbial metabolites as well as microbial neural substrates. Supplementation with probiotics causes regulation of gut flora thereby reducing the release of cytokines and its subsequent consequences of cortical neuronal alterations (bottom-up approach). Similarly, practicing complementary therapies such as yoga and meditation helps in reduction of stress and anxiety, thereby reducing the sympathetic overdrive and gut activity (top-down approach). The latter approach has been followed in several researches however the former approach by using neuromodulation techniques is less studied. For the management of functional gastrointestinal disorders, life style modification measures including dietary modification, stress, anxiety management, and medications affecting the serotonergic or cholinergic system are often recommended. These treatment measures exert their action by either or both of these approaches (top-down and bottom-up).

Neuromodulation techniques like vagus nerve stimulation, transcranial direct current stimulation, and repetitive transcranial magnetic stimulation, which are capable of altering cortical excitability, increasing vagal tone, and consequently inhibiting cytokine production may be of use in modulating the gut activity. The neuromodulation techniques also facilitate neuroplasticity.<sup>5</sup> There is an association between microglial activity and hippocampal neuroplasticity.<sup>4</sup> As the microglial cells release cytokines and there is a close association between gut microbiota in release of cytokines by the microglial cells, possibly neuromodulation technique may alter the microglial activity and consequent cytokine production. This may prevent the alteration in neuroplasticity mediated by the cytokines. There is a need to study the role of various neuromodulation techniques in the management of functional gastrointestinal disorders.

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