

# Words of Editor-in-Chief

*Psychosomatic Gastroenterology* (PG) is the official academic journal of Chinese Digestive Psychosomatic Union (CDPU), which was founded in April 2016 in Shanghai, China. It is the first global journal focusing on “psychosomatic gastroenterology”.

*Psychosomatic Gastroenterology* is an open access, peer-reviewed journal that covers basic and clinical research, therapeutics and education for all aspects of psychosomatic gastroenterology, including the mechanism research and therapeutic research. The accepted articles include original research, reviews, case reports, expert experience, academic event reports and so on. *Psychosomatic Gastroenterology* creates a novel interface between the fields of social, psychological and biological research.

We hope *Psychosomatic Gastroenterology* would play an important role in promoting the management of gastrointestinal diseases in which psychological mechanisms may be involved. And, we look forward to publishing more and more your papers with great importance in psychosomatic gastroenterology.



Chairman of Chinese Digestive Psychosomatic Union  
Chief of Chinese Association of Psychosomatic Digestive Diseases  
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Chinese Society of Gastroenterology; Psychosomatic Disease Collaborative Group

# Application of gut-directed neuromodulators in treatment of psychosomatic gastrointestinal disorders

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**Abstract:** Psychosomatic gastrointestinal disorders are a great challenge in the clinical practice of gastroenterology. The application of neuromodulators (particularly antidepressants) is one of the theoretical and practical breakthroughs to improve the therapeutic efficacy of these disorders. The clinical problems to be resolved are different in the specialty of gastroenterology and psychiatry. So, the targets, mechanisms, and efficacy of neuromodulators could be different. The application of neuromodulators in gastroenterology specialty emphasizes the gut-directing. This mini-review discussed the rational application of neuromodulators in the management of psychosomatic gastrointestinal disorders.

**Key words:** Neuromodulators; Drug selection; Dosage; Course of treatment.

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In recent years, the Chinese Digestive Psychosomatic Union (CDPU) has organized nationwide experts in the academic field of digestive psychosomatics to formulate a series of Expert Opinions and Consensus, and initiated them to publish review and experience articles in journals such as *Chinese Journal of Digestion*, *Chinese Journal of Gastroenterology*, and *Chinese Journal of Practical Internal Medicine*, and disseminated the concept of digestive psychosomatic holistic medicine through various academic activities [1-5]. Currently, gastroenterologists have made great improvements in recognizing and treating psychosomatic digestive disorders. However, there are still a lot to do to improve the precise use of neuromodulators, which are also called the central-acting medications antidepressants/antianxiotics, or psychotropic medications.

Given the different clinical problems needing to be resolved, the targets, mechanisms, and efficacy of neuromodulators used in the specialty of gastroenterology and psychiatry are different. The application of neuromodulators in gastroenterology specialty emphasizes the gut-directing. In other words, the aim of gastroenterologists to apply neuromodulators is focused on the management of psychosomatic gastrointestinal disorders, with a particular emphasis on the gut-related acting targets and mechanisms. This will improve the ability of gastroenterologists to apply neuromodulators, as well as facilitate doctor-patient communication and improve patient compliance. Experts in the academic field of digestive psychosomatics tend to refer to traditional terms such as “central-acting drugs” and “antidepressants/antianxiotics” as “neuromodulators” [6]. Here, we advocate that they can be called “gut-directed neuromodulators” to reflect the principle of individualized and precise use of neuromodulators in the field of gastroenterology.

In clinical practice, psychosomatic gastrointestinal disorders are classified into three categories [2, 5]: (i) Comorbidity of gastrointestinal and psychosomatic disorders; (ii) Gastrointestinal disorders with psychological stress as a major etiological factor; and (iii) Gastrointestinal disorders for which conventional gastrointestinal medications fail to achieve the desired efficacy and need the aid of psychosomatic

interventions or medications. They pose a great challenge to clinical practice in gastroenterology. Different from the aim of neuromodulators used in psychiatry specialty, the application of neuromodulators in the treatment of psychosomatic gastrointestinal disorders should emphasize on the efficacy achieved via gut-directing targets and mechanisms. The following issues need to be emphasized in clinical practice of gastroenterology.

### Indications

The indications of neuromodulators mainly include the above three categories of psychosomatic gastrointestinal disorders. The clinical goal of neuromodulators is regulating the key pathophysiological processes involving motility, secretion, sensation, mucosal barriers, and anti-infective/immune homeostasis.

### Pay attention to the connections between functional changes of specific brain regions caused by different psychological stress factors and gastrointestinal symptoms

When selecting drugs for psychosomatic gastrointestinal disorders, it is necessary to pay attention to the connections between functional changes of specific brain regions caused by different psychological stress factors and gastrointestinal symptoms. The principles for selection of gut-directing neuromodulators include:

(1) Choice of neuromodulators for psychosomatic gastrointestinal disorders triggered by transitory stressful events. These events can trigger dysfunction of emotion-regulating brain regions such as the frontal lobe, cingulate gyrus, and insula, which may affect gastrointestinal motility, secretion, and sensation. Enhanced functioning of these brain regions may elicit emotional responses such as anxiety, agitation, mania, irritability, etc., with corresponding incoordination of gastrointestinal motility and visceral hypersensitivity. This may play critical roles in the pathophysiology of gastroesophageal reflux, peptic ulcers, and autoimmune inflammation, as well as the development of gastrointestinal symptoms such as burning sensation, abdominal pain, bloating, rumbling and diarrhea. Antidepressants with significant anxiolytic and sedative

effects are appropriate in these conditions. On the other hand, impaired functioning of emotion-regulating brain regions may elicit negative emotional responses such as depression and low morale, which may cause gut dysmotility and discomfort, manifested as inappetite, post-meal fullness, dry hard stools, and lack of bowel movement. In these conditions, antidepressants able to enhance psychodynamic are preferred.

(2) Choice of neuromodulators for somatization symptoms triggered by long-term psychological stressful events (e.g. adolescence, fear of the internal and external environment, circadian disorders, etc.). These events often affect the function of brain regions such as orbitofrontal region, striatum, supraoptic nucleus, and amygdala, leading to cognitive dysfunction. When these patients consult in gastroenterology clinic, they usually show cognitive biases such as suspicion and fear of disease, communication difficulties, and describe some nearly non-existent feelings such as abnormal sense of taste, globus hystericus, wandering abdominal pain and bloating, anal obstruction, incomplete defecation, and anal pain. For these patients, antipsychotics or mood stabilizers are advisable.

### The peripheral effects on gastrointestinal tract

The peripheral effects on gastrointestinal tract is the basis for the selection of gut-directed neuromodulators [1-6]. Neuromodulators with an anti-dopamine effect is useful in alleviating gastroesophageal reflux and improving gastric emptying. Neuromodulators with an anti-cholinergic effect is beneficial for reducing the resistance to gastric emptying and improving intestinal spasms, thus alleviating the corresponding symptoms. Neuromodulators capable of increasing peripheral 5-hydroxytryptamine (5-HT) levels lead to enhancement of 5-HT<sub>4</sub> receptor excitability, and thus improve smooth muscle motility and reduce low-grade mucosal inflammation. Mood stabilizers can improve patients' perceptions and incorrect response behaviors. Tricyclic antidepressants can act centrally to exert antidepressant and anxiolytic effects, and simultaneously act peripherally to enhance 5-HT content and exert anticholinergic effect. Therefore, they are widely used for refractory functional gastrointestinal

disorders without constipation and other psychosomatic gastrointestinal disorders. Selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine, sertraline, and citalopram/escitalopram, are commonly used antidepressants. Via overt peripheral effect on gastrointestinal motility, they can be used for depression accompanied with gut dysmotility.

### Dosage and course of treatment

For disorders with psychological factors as the key etiology or clinical manifestations, dosage and course of treatment of neuromodulators should follow the guidelines or consensus of psychiatry, choosing high-grade neuromodulators and combined drug schemes with adequate dosage and regimen [1-5]. For disorders with gastrointestinal symptoms as predominating symptoms, a strategy of choosing low-grade neuromodulators with small dosage and short course, in combination with conventional gastrointestinal medications, is recommended. After obtaining satisfactory efficacy, neuromodulators can be used on demand. For rapid-acting tricyclic antidepressants, especially the flupentixol-melitracen combination, it is recommended to change to on-demand medication after obtaining satisfactory efficacy upon a short course of treatment. This strategy, along with psychological counseling and behavioral guidance, may achieve satisfactory clinical outcome. Moreover, it may also decrease the risk of drug dependence and adverse reactions caused by long-term medication [7].

### Use herbal medicine as a supplemental treatment option

Traditional Chinese medicine (TCM) is one of China's distinctive strengths in addressing psychosomatic gastrointestinal disorders [1]. The "five viscera" theory of TCM is helpful for doctors with Western medical education background to understand TCM's evidence-based treatment of psychosomatic gastrointestinal disorders. In TCM, the "five viscera" are divided according to their function (instead of the anatomy, morphology, and function in the context of Western medicine). From a TCM perspective, emotional problems are attributed to the dysfunction of the "liver" viscera, and cognitive and psychiatric disorders are attributed to the dysfunction of the "heart" viscera. Gastrointestinal dysfunction in modern medicine is

defined in TCM as spleen-stomach disharmony. In the treatment of psychosomatic gastrointestinal disorders, Chinese patent medicine capable of regulating the functions of the “liver”, “heart”, “spleen”, and “stomach” viscera can be chosen as complementary therapy to neuromodulators.

### Conflicts of interest statement

None declared.

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