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Peer Reviewer of *World Journal of Clinical Cases*, Suman Baral, MD, Assistant Professor, Department of Surgery, Mediplus Hospital and Trauma Center, Pokhara 33700, Nepal. brylsuman.sur@gmail.com

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EDITORIAL

Traditional Chinese medicine treatment of insomnia based on microbial-gut-brain axis theory

Xue-Jian Wang

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Xue-Jian Wang, Department of Neurosurgery, The Second Affiliated Hospital of Nantong University, Nantong 226000, Jiangsu Province, China

Xue-Jian Wang, Department of Neurosurgery, Lueyang People's Hospital, Hanzhong 723000, Shaanxi Province, China

Corresponding author: Xue-Jian Wang, MD, PhD, Surgeon, Department of Neurosurgery, The Second Affiliated Hospital of Nantong University, No. 666 Shengli Road, Chongchuan District, Nantong 226000, Jiangsu Province, China. 6841441@163.com

Abstract

In recent years, insomnia has gradually become a common disease in society, which seriously affects people's quality of life. At present, with the deepening of research on intestinal microbiota-gut-brain axis in Western medicine, many studies suggest that regulating the gastrointestinal tract can treat brain-related diseases. It is found that brain-gut-bacteria axis plays an important role in the prevention and treatment of primary insomnia. At present, although the clinical treatment of insomnia with Western medicine can improve the insomnia symptoms of patients to a certain extent, there are still obvious adverse reactions, such as anxiety and depression, drug addiction, *etc.*, so long-term oral drug therapy cannot be carried out. Traditional Chinese medicine (TCM) and acupuncture techniques have certain therapeutic effects on insomnia. TCM believes that the brain and gastrointestinal system are connected through the meridian, and the pathophysiology is closely related. This paper will discuss the theory and feasibility of TCM for the treatment of insomnia from the pathological relationship between brain-gut axis, intestinal flora and insomnia.

Key Words: Insomnia; Microorganism; Microbial-gut-brain axis; Traditional Chinese medicine; Acupuncture and moxibustion

Core Tip: In recent years, insomnia has gradually become a common disease in society, which seriously affects people's quality of life. At present, with the deepening of research on intestinal microbiota-gut-brain axis in Western medicine, many studies suggest that regulating the gastrointestinal tract can treat brain-related diseases.

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INTRODUCTION

Insomnia is a condition in which the patient is dissatisfied with the duration and/or quality of sleep, thereby affecting daytime social functioning[1]. Cognitive decline, fatigue, or mood disorders associated with impaired daytime function occur[1]. Lack of sleep is the main cause of decreased daytime activity and cognitive ability. Chronic insomnia can lead to depression, anxiety, substance abuse, suicide, auto accidents, and immune disorders[2-4]. In today's increasingly competitive society, insomnia has become a common health problem. Studies have shown that brain activity is greatly affected by intestinal flora, and the mechanism may be related to neurotransmitters, immune factors and neuropeptides in the brain-gut axis[5].

BACKGROUND OF GUT MICROBIOTA-GUT-BRAIN AXIS

In the 1980s, the concept of "brain-gut axis" was first proposed, which refers to the bidirectional regulatory axis connecting the gastrointestinal tract and the central nervous system (CNS). The brain-gut axis consists of two pathways: (1) The descending pathway from the brain to the gut; and (2) The ascending pathway from the gut to the brain. Gut flora affects the brain primarily by secreting small molecules, but also by regulating immune, neuroendocrine, and vagal pathways. The gut microbiota-gut-brain axis (GBA) is a key regulatory pathway between the brain and the gastrointestinal tract[6,7].

BRAIN-GUT AXIS AND PRIMARY INSOMNIA

The GBA is a dynamic bidirectional neuroendocrine system. This bidirectional communication network consists of the CNS, autonomic nervous system, enteric nervous system (ENS), and hypothalamic-pituitary-adrenal (HPA) axis system. The outer branches of the glycemic index (GI) tract are connected to the enterobrain axis *via* the spinal cord and vagus nerve fibers, while the brain transmits outgoing parasympathetic and sympathetic nerves to the GI tract. According to recent studies on the pathophysiology of insomnia, one is that insomnia is related to the secretion disorder of cortisol and adrenalin releasing hormone caused by the dysfunction of HPA axis[8]. Secondly, insomnia is highly correlated with central neurotransmitters and inflammatory response factors, among which 5-HT, gamma-aminobutyric acid, tumor necrosis factor-α and interleukin-6 are dominant[9-11].

INTESTINAL FLORA AND PRIMARY INSOMNIA

The intestinal microbial community is composed of more than 1000 types of bacteria, most of which belong to *firmicutes*, *bacteroides*, *Proteus* and *actinomyces*[12]. Numerous studies have identified the microbial-GBA[13]. In this axis, the gut microbiota affects brain function and generates two-way information flow through three main pathways[14,15]. The first is the immunomodulatory pathway, in which the microbiota interacts with immune cells to influence the levels of cytokines, cytokinetic response factors, and prostaglandin E2[16]. The second is that insomnia is related to autonomic nervous dysfunction, autonomic nervous function is innervated by the pineal gland, in which the sympathetic god regulates the secretion of melatonin by the pineal gland, further affecting the quality of sleep. The third is the vagus nerve pathway, where the ENS plays a large role.

The ENS forms synaptic connections with the vagus nerve, which connects the gut to the brain, forming an information transmission pathway known as the enteric microbial-ENS-vago-brain pathway[17].

The CNS also affects intestinal flora. The HPA axis can regulate intestinal peristalsis, epithelial cell function and intestinal permeability, thus affecting the environment of intestinal microbiota and further changing the composition of intestinal microbiota[18-20].

DAMAGE OF INTESTINAL FLORA TO INSOMNIA

Chronic disturbance of host circadian rhythm and sleep loss will affect the metabolism of intestinal flora and trigger changes in its composition, usually reducing the total number of *Lactobacillaceae* organisms, but increasing the population of *bacteroides* polyformis and so on, resulting in microbial ecological imbalance[21-23].

Changes in the gut microbiome may mediate the harmful effects of insomnia, which are closely linked to inflammation. Modern studies have found that inflammation is a key mediator in the pathogenesis of metabolic and neurodegenerative diseases related to sleep deprivation[24,25]. Insomnia can cause elevated lipopolysaccharide (LPS), which in turn activates the Toll-like receptor 4/nuclear transcription factor-kappa B (TLR4/NF-κB) signaling pathway, thus promoting the production of inflammatory factors[26]. In addition, insomnia can also cause the imbalance of intestinal microflora, destroy the intestinal barrier, and increase the toxin content in peripheral blood, which indicates that microbial metabolites may participate in the inflammatory response induced by insomnia after entering the circulation[27,28]. Studies have suggested that insomnia can lead to the imbalance of intestinal microbial ecosystem, the destruction of intestinal barrier, and the influx of bacterial metabolites (LPS) into peripheral blood, thus activating the TLR4/NF-κB signaling pathway and ultimately promoting the development of inflammatory response[29].

TRADITIONAL CHINESE MEDICINE AND GBA

Sleep is an active process occurring in the CNS, which is regulated by the nervous, endocrine and immune systems, and there are various complex connections among these systems, which participate in the regulation of sleep-wake mechanism. Recent studies have shown that acupuncture can regulate the level of disturbed neurotransmitters, cytokines and hormones, promote the expression of biological clock genes, and maintain sleep-wake cycle. The types of studies include clinical studies and animal experiments, which have laid a foundation for revealing the specific mechanism of acupuncture in the treatment of insomnia and promoting clinical application[30].

CONCLUSION

At present, the mechanism of TCM treatment of insomnia is not clear, and the specific role of gut microbiota-GBA in it needs to be further studied. In future studies, it is necessary to further elucidate the mechanism and pathway of action of TCM in treating insomnia, so as to bring new breakthroughs for TCM to explore the nature of syndrome from the perspective of intestinal microecology.

FOOTNOTES

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Country of origin: China

ORCID number: Xue-Jian Wang 0000-0003-0389-5674.

Corresponding Author's Membership in Professional Societies: American Society for Peripheral Neurosurgery, 5300190.

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REFERENCES

1 **Qaseem A**, Kansagara D, Forciea MA, Cooke M, Denberg TD; Clinical Guidelines Committee of the American College of Physicians.

Management of Chronic Insomnia Disorder in Adults: A Clinical Practice Guideline From the American College of Physicians. *Ann Intern Med* 2016; **165**: 125-133 [PMID: 27136449 DOI: 10.7326/M15-2175]
2 **Ito E**, Inoue Y. [The International Classification of Sleep Disorders, third edition. American Academy of Sleep Medicine. Includes bibliographies and index]. *Nihon Rinsho* 2015; **73**: 916-923 [PMID: 26065120]
3 **Taylor DJ**, Lichstein KL, Durrence HH. Insomnia as a health risk factor. *Behav Sleep Med* 2003; **1**: 227-247 [PMID: 15600216 DOI: 10.1207/S15402010BSM0104_5]
4 **Sivertsen B**, Lallukka T, Salo P, Pallesen S, Hysing M, Krokstad S, Simon Øverland. Insomnia as a risk factor for ill health: results from the large population-based prospective HUNT Study in Norway. *J Sleep Res* 2014; **23**: 124-132 [PMID: 24635564 DOI: 10.1111/jsr.12102]
5 **Bathgate CJ**, Edinger JD, Krystal AD. Insomnia Patients With Objective Short Sleep Duration Have a Blunted Response to Cognitive Behavioral Therapy for Insomnia. *Sleep* 2017; **40**: zsw012 [PMID: 28364452 DOI: 10.1093/sleep/zsw012]
6 **Cryan JF**, Dinan TG. Mind-altering microorganisms: the impact of the gut microbiota on brain and behaviour. *Nat Rev Neurosci* 2012; **13**: 701-712 [PMID: 22968153 DOI: 10.1038/nrn3346]
7 **Moloney RD**, Desbonnet L, Clarke G, Dinan TG, Cryan JF. The microbiome: stress, health and disease. *Mamm Genome* 2014; **25**: 49-74 [PMID: 24281320 DOI: 10.1007/s00335-013-9488-5]
8 **Scott LV**, Dinan TG. Vasopressin and the regulation of hypothalamic-pituitary-adrenal axis function: implications for the pathophysiology of depression. *Life Sci* 1998; **62**: 1985-1998 [PMID: 9627097 DOI: 10.1016/s0024-3205(98)00027-7]
9 **Zhou Q**, An T, Pham KTM, Hu H, Li Z. The CIF1 protein is a master orchestrator of trypanosome cytokinesis that recruits several cytokinesis regulators to the cytokinesis initiation site. *J Biol Chem* 2018; **293**: 16177-16192 [PMID: 30171070 DOI: 10.1074/jbc.RA118.004888]
10 **Hu H**, An T, Kurasawa Y, Zhou Q, Li Z. The trypanosome-specific proteins FPRC and CIF4 regulate cytokinesis initiation by recruiting CIF1 to the cytokinesis initiation site. *J Biol Chem* 2019; **294**: 16672-16683 [PMID: 31540971 DOI: 10.1074/jbc.RA119.010538]
11 **Kurasawa Y**, Hu H, Zhou Q, Li Z. The trypanosome-specific protein CIF3 cooperates with the CIF1 protein to promote cytokinesis in Trypanosoma brucei. *J Biol Chem* 2018; **293**: 10275-10286 [PMID: 29764941 DOI: 10.1074/jbc.RA118.003113]
12 **Hills RD Jr**, Pontefract BA, Mishcon HR, Black CA, Sutton SC, Theberge CR. Gut Microbiome: Profound Implications for Diet and Disease. *Nutrients* 2019; **11**: 1613 [PMID: 31315227 DOI: 10.3390/nu11071613]
13 **Rutsch A**, Kantsjö JB, Ronchi F. The Gut-Brain Axis: How Microbiota and Host Inflammasome Influence Brain Physiology and Pathology. *Front Immunol* 2020; **11**: 604179 [PMID: 33362788 DOI: 10.3389/fimmu.2020.604179]
14 **Dinan TG**, Cryan JF. Gut instincts: microbiota as a key regulator of brain development, ageing and neurodegeneration. *J Physiol* 2017; **595**: 489-503 [PMID: 27641441 DOI: 10.1113/JP273106]
15 **Dinan TG**, Cryan JF. The Microbiome-Gut-Brain Axis in Health and Disease. *Gastroenterol Clin North Am* 2017; **46**: 77-89 [PMID: 28164854 DOI: 10.1016/j.gtc.2016.09.007]
16 **Agus A**, Planchais J, Sokol H. Gut Microbiota Regulation of Tryptophan Metabolism in Health and Disease. *Cell Host Microbe* 2018; **23**: 716-724 [PMID: 29902437 DOI: 10.1016/j.chom.2018.05.003]
17 **Powley TL**, Wang XY, Fox EA, Phillips RJ, Liu LW, Huizinga JD. Ultrastructural evidence for communication between intramuscular vagal mechanoreceptors and interstitial cells of Cajal in the rat fundus. *Neurogastroenterol Motil* 2008; **20**: 69-79 [PMID: 17931338 DOI: 10.1111/j.1365-2982.2007.00990.x]
18 **Leistner C**, Menke A. Hypothalamic-pituitary-adrenal axis and stress. *Handb Clin Neurol* 2020; **175**: 55-64 [PMID: 33008543 DOI: 10.1016/B978-0-444-64123-6.00004-7]
19 **Miller WL**. The Hypothalamic-Pituitary-Adrenal Axis: A Brief History. *Horm Res Paediatr* 2018; **89**: 212-223 [PMID: 29719288 DOI: 10.1159/000487755]
20 **Bian X**, Yang W, Lin J, Jiang B, Shao X. Hypothalamic-Pituitary-Adrenal Axis and Epilepsy. *J Clin Neurol* 2024; **20**: 131-139 [PMID: 38330420 DOI: 10.3988/jcn.2023.0308]
21 **Osório J**. Metabolism: Bacterial-host interplay in circadian regulation of metabolism. *Nat Rev Endocrinol* 2015; **11**: 2 [PMID: 25350063 DOI: 10.1038/nrendo.2014.194]
22 **Marcinkevicius EV**, Shirasu-Hiza MM. Message in a biota: gut microbes signal to the circadian clock. *Cell Host Microbe* 2015; **17**: 541-543 [PMID: 25974294 DOI: 10.1016/j.chom.2015.04.013]
23 **Ristori MV**, Quagliariello A, Reddel S, Ianiro G, Vicari S, Gasbarrini A, Putignani L. Autism, Gastrointestinal Symptoms and Modulation of Gut Microbiota by Nutritional Interventions. *Nutrients* 2019; **11**: 2812 [PMID: 31752095 DOI: 10.3390/nu11112812]
24 **Münzel T**, Daiber A, Steven S, Tran LP, Ullmann E, Kossmann S, Schmidt FP, Oelze M, Xia N, Li H, Pinto A, Wild P, Pies K, Schmidt ER, Rapp S, Kröller-Schön S. Effects of noise on vascular function, oxidative stress, and inflammation: mechanistic insight from studies in mice. *Eur Heart J* 2017; **38**: 2838-2849 [PMID: 28329261 DOI: 10.1093/eurheartj/ehx081]
25 **Lv X**, Fan C, Jiang Z, Wang W, Qiu X, Ji Q. Isoliquiritigenin alleviates P. gingivalis-LPS/ATP-induced pyroptosis by inhibiting NF-κB/NLRP3/GSDMD signals in human gingival fibroblasts. *Int Immunopharmacol* 2021; **101**: 108338 [PMID: 34794890 DOI: 10.1016/j.intimp.2021.108338]
26 **Zusso M**, Lunardi V, Franceschini D, Pagetta A, Lo R, Stifani S, Frigo AC, Giusti P, Moro S. Ciprofloxacin and levofloxacin attenuate microglia inflammatory response *via* TLR4/NF-kB pathway. *J Neuroinflammation* 2019; **16**: 148 [PMID: 31319868 DOI: 10.1186/s12974-019-1538-9]
27 **Gozal D**, Khalyfa A, Qiao Z, Akbarpour M, Maccari R, Ottanà R. Protein-Tyrosine Phosphatase-1B Mediates Sleep Fragmentation-Induced Insulin Resistance and Visceral Adipose Tissue Inflammation in Mice. *Sleep* 2017; **40** [PMID: 28651353 DOI: 10.1093/sleep/zsx111]
28 **Yang DF**, Huang WC, Wu CW, Huang CY, Yang YSH, Tung YT. Acute sleep deprivation exacerbates systemic inflammation and psychiatry disorders through gut microbiota dysbiosis and disruption of circadian rhythms. *Microbiol Res* 2023; **268**: 127292 [PMID: 36608535 DOI: 10.1016/j.micres.2022.127292]
29 **Gomes AC**, Hoffmann C, Mota JF. The human gut microbiota: Metabolism and perspective in obesity. *Gut Microbes* 2018; **9**: 308-325 [PMID: 29667480 DOI: 10.1080/19490976.2018.1465157]
30 **Pan LM**, Hong ZB, Guan RQ. Research progress on insomnia treated by traditional Chinese medicine and acupuncture based on microbial-gut-brain axis theory. *World J Clin Cases* 2024; **12**: 3314-3320 [PMID: 38983433 DOI: 10.12998/wjcc.v12.i18.3314]

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