



Perspective of Brain-Heart Axis (BHA) with Research on Autonomic Nervous System (ANS)

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Abstract

For the autonomic nervous system (ANS), several studies have been reported on heart rate variability (HRV), the central autonomic network (CAN), the brain-heart axis (BHA), and heart-brain interactions (HBI). Regarding the BHA, three distinct pathways have been proposed: neural, mechanical, and biochemical. HBI includes two categories: cardiac effects of neurological disease and neurological effects of cardiac disease. The BHA functions as a sophisticated communication system that connects central nervous system (CNS) operations with cardiovascular regulation through the ANS, neurohumoral, and neuroanatomical connections. Future research on the BHA includes electrophysiological methods, enhanced neuroimaging, interdisciplinary teamwork, artificial intelligence (AI), and machine learning applications in brain-heart research.

Keywords

Autonomic Nervous System, Heart Rate Variability, Central Autonomic Network, Brain-Heart Axis, Heart-Brain Interactions, Artificial Intelligence

Abbreviations

AI: Artificial Intelligence; ANS: Autonomic Nervous System; BHA: Brain-Heart Axis; CAN: Central Autonomic Network; CNS: Central Nervous System; HBI: Heart-Brain Interactions; HRV: Heart Rate Variability

Commentary

For integrative medicine (IM), research on the autonomic nervous system (ANS) has recently advanced, incorporating methods such as the measurement of heart rate variability (HRV). The authors have been conducting research in these areas, as well as in music therapy. Alongside progress in investigating the functions of the sympathetic and parasympathetic nervous systems, research into the

relationship between the brain and the heart has also advanced. This paper provides an overview of concepts such as the brain-heart axis (BHA) and heart-brain interactions (HBI) [1]. Regarding the activity of the ANS, HRV has been widely used as a key physiological marker for non-invasive measurement. HRV is applied in a wide range of fields, including diabetes, cardiovascular disease, sleep medicine, and psychiatry, to evaluate sympathetic and parasympathetic activities [2].

However, with the progress in the BHA perspective, HRV has become not only an autonomic index but also an important marker reflecting the integrated network of the brain and heart in a bidirectional manner.

Complex bidirectional interactions have been recognized between the cardiovascular and nervous systems. They are integrated through the BHA, a physiological pathway that controls both the neural regulation of cardiovascular function and the cardiovascular influences on the brain [3]. The term BHA refers to the connections between the heart and the brain. It is bidirectional and occurs through a complex network of autonomic nerves, hormones, and cytokines, playing important roles in common disorders. The BHA is a physiological system that includes the mutual exchange of various types of information among the peripheral ANS, the cardiovascular system, and the central autonomic network (CAN). The CAN comprises the prefrontal cortex, anterior cingulate cortex, insular cortex, hypothalamus, amygdala, and brainstem [4]. The CAN regulates blood pressure and heart rate through the sympathetic and vagus nerves. In contrast, sensory stimuli are transmitted from cardiac chemoreceptors and baroreceptors to the brain through afferent vagal pathways. This information influences cognition, emotion, stress responses, and decision-making. Consequently, the BHA has been recognized as a bidirectional network that involves both efferent control from the brain to the heart and afferent feedback from the heart to the brain.

Regarding the BHA, the neural and cardiovascular systems have been pivotal in regulating human physiological, emotional, and cognitive states, which always interact through anatomical, functional, and medical connections. Regarding the details of the BHA, three distinct pathways have been proposed for its integrated function [5]. They include the neural, mechanical, and biochemical pathways. The neural pathway centers on the CAN and ANS. The mechanical pathway involves baroreception and mechanotransduction mediated by Piezo channels. Furthermore, the biochemical pathway links the brain and heart through inflammatory cytokines, neurotransmitters, and hormones. The breakdown of these multilayered networks is observed not only in

heart failure, arrhythmia, and stroke but also in depression, anxiety disorders, dementia, sleep disorders, chronic inflammation, frailty, and aging. Such an understanding may form the foundation of a new field of neurocardiology, extending beyond traditional ANS research.

From a neurocardiological perspective, attention has also been focused on abnormalities in the BHA. Some examples include myocardial damage or arrhythmias resulting from epilepsy or stroke. Conversely, an elevated risk of cognitive decline and cerebral infarction is associated with atrial fibrillation and heart failure. In the future, ongoing research is expected to advance the multifaceted assessment of BHA function, together with HRV analysis, electroencephalography (EEG), functional magnetic resonance imaging (fMRI), functional near-infrared spectroscopy (fNIRS), and artificial intelligence (AI) analysis [5]. As a core metric in BHA research, HRV will maintain its position and continue to grow in importance as a translational biomarker that can bridge the fields of neuroscience, cardiology, psychiatry, and geriatrics.

The BHA involves complex interactions between the cardiovascular and nervous systems. HBI may be categorized into two types: i) cardiac effects of neurological disease and ii) neurological effects of cardiac disease. In the former, a neurogenic cascade may be involved as a trigger, in which sudden shifts in autonomic balance lead to an exaggerated catecholamine release. Examples include epilepsy, intracranial hemorrhage, ischemic stroke, stroke-heart syndrome, cardiomyopathy, and neurogenic pulmonary edema [6]. In the latter, cardiac conditions can adversely affect the neurological system. Atrial fibrillation and left ventricular thrombus can cause cardioembolic stroke, whereas heart failure and severe aortic stenosis are associated with the development of cognitive impairment.

HRV has been positioned as a "trans-diagnostic surrogate marker" for assessing BHA integrity [7]. In other words, HRV has also been regarded as a "trans-diagnostic proxy" for assessing BHA abnormalities. Based on this concept, HRV appears to have the potential to serve as a comprehensive biomarker

reflecting brain-heart network dysfunction across a wide range of conditions. HRV is also anticipated to serve as a common evaluation metric linking three dimensions: mechanistic understanding, physiological measurement, and clinical application. Its clinical value continues to expand through recent integration with AI analysis and multimodal physiological measurements. These applications may include not only cardiovascular diseases but also anxiety disorders, depression, dementia, aging, epilepsy, and inflammatory diseases. HRV is expected to have promising applications in disease prediction, assessment of treatment efficacy, and personalized medicine. Under these circumstances, future challenges include the standardization of measurement conditions and validation through large-scale prospective studies.

An umbrella review was performed for HRV studies.

The investigators summarized HRV differences between patients with mental disorders and controls, as well as HRV changes before and after treatment in patients [8]. The review included 442 papers involving 35,625 subjects and covered a broad range of diseases, in which decreased HRV levels were observed in dementia, post-traumatic stress disorder (PTSD), functional somatic syndromes, somatic symptom disorder, and schizophrenia. In their HRV research, the authors proposed the "HRV-5 axis" framework. Historically based on the Circulation Task Force guidelines [9], this physiological model is organized around the following five axes: (1) total autonomic activity (Total Power), (2) sympathetic dominance (LF/HF), (3) parasympathetic activity (HF), (4) autonomic balance (LFnu/HFnu), and (5) autonomic adaptability (SD1/SD2). Detailed research parameters, including these metrics, are summarized in **Table-1**.

Table-1: Several Metrics for Heart Rate Variability

Domain	Metrics	Description	Unit
Time	HR	Average heart rate (HR) per minute. It can reflect the vagal activity.	/min
	RMSSD	Root mean square of successive inter-beat interval (IBI) differences. Reflects vagal activity.	ms
	SDNN	Standard deviation of NN intervals. It reflects overall autonomic activity.	ms
Frequency	LF	Absolute power of the low-frequency power (0.04-0.15 Hz). Reflects overall autonomic activity.	ms ²
	HF	High-frequency power (0.15-0.40 Hz). It reflects vagal activity.	ms ²
	LF/HF	Ratio of LF-to-HF absolute power. It reflects vagal activity.	—
Non-linear	SD1	Poincaré plot standard deviation perpendicular to the line of identity. It reflects vagal activity.	ms
	SD2	Poincaré plot standard deviation along the line of identity. Reflects overall autonomic activity.	ms
	SD1/SD2	Ratio of SD1-to-SD2 standard deviation. It reflects overall autonomic activity.	—

As reported recently, HBI has been recognized for its role in autonomic regulation, attentional control, perceptual salience, decision-making, and affective reactivity [10]. HBI has been consistently implicated in clinical investigations involving neurological, cardiovascular, and psychiatric conditions. Under these circumstances, the perspective of HBI may be valuable for understanding autonomic regulation and attentional control. Clinical research on HBI has attracted attention in areas including human-computer interfaces, affective computing, and sensorimotor evaluation [11]. These studies have demonstrated considerable potential for neuroscientific research and biomarker development. Different frameworks can

employ signal-processing techniques, ranging from estimating brain responses to individual heartbeats to analyzing interactions that may link the heart to changes in brain organization.

Aspects related to human emotions, psychology, and cognition are also important. Intricate bidirectional communication between the brain and the heart has been recognized. It is mediated by neural, autonomic, and hemodynamic pathways and plays a crucial role in neurovisceral integration (NVI) and the regulation of emotional and cognitive processes in the brain. Three background factors have been proposed: HRV, cross-frequency coupling (CFC), and heartbeat-evoked

responses (HERs) [12]. CFC can facilitate the synchronization of low-frequency (LF) cardiac rhythms with higher-frequency (HF) brain oscillations. These processes support cognitive functions such as decision-making, memory, and emotional regulation. From a psychological point of view, the brain and the mind have several regulatory aspects. These are summarized in **Table-2**, which presents the directions of regulation and their associated psychological characteristics.

Table-2: Regulating the Brain and Mind

Direction of Adjustment	Psychological Characteristics
Focusing on the Present Experience	Breathing, Body Sensations
Reducing Stressful Responses	Suppression of Amygdala Activity
Enhancing Prefrontal Cortex Function	Attention, Emotional Regulation
Stabilizing the Default Mode Network	Creativity and Insight
Improving Psychological Responses	Flexibility and Resilience

The BHA can function as a sophisticated communication system that connects central nervous system (CNS) operations with cardiovascular regulation through ANS pathways and neurohumoral and neuroanatomical connections [13]. Some research limitations remain, and future directions include electrophysiological methods, enhanced neuroimaging, interdisciplinary teamwork, AI, and machine learning applications in brain-heart research. In summary, this article has discussed several issues related to the BHA and HBI. These medical studies will help elucidate the mechanisms underlying the ANS, the CNS, and their associated functions. Furthermore, these findings are expected to contribute to the future advancement of clinical practice utilizing AI and to the well-being of individuals.

Conflict of Interest

The authors have read and approved the final version of the manuscript. The authors declare no conflicts of interest.

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References

[1] Habibi P, Chen LY, Sorond FA, Shroff GR, Sabayan B. Heart-Brain Axis: Subclinical Cardiovascular Changes and Brain Health. *J Am Heart Assoc.* 2026 Feb 3;15(3):e047458. [PMID: 41614273]

[2] Bando H, Wago H, Tanaka N, Okubo T, Bando M. Experience with multisensory relaxation interventions using Solfeggio frequencies and visual stimuli with related perspectives. *Res J Sport Health Psychol.* 2026;8(1):177.

[3] Hu JR, Abdullah A, Nanna MG, Soufer R. The Brain-Heart Axis: Neuroinflammatory Interactions in Cardiovascular Disease. *Curr Cardiol Rep.* 2023 Dec;25(12):1745-58. [PMID: 37994952]

[4] Li H, Guo W, Nie Q, Wang Z, Li H. Central autonomic network dysfunction in Stroke-Heart Syndrome: mechanistic roles of the insula and limbic system. *Front Neurosci.* 2026 Feb 18;20:1690302. [PMID: 41788541]

[5] Valenza G, Matic Z, Catrambone V. The brain-heart axis: integrative cooperation of neural, mechanical and biochemical pathways. *Nat Rev Cardiol.* 2025 Aug;22(8):537-50. [PMID: 40033035]

[6] Goh FQ, Tan BYQ, Yeo LLL, Sia CH. The Heart-Brain Axis: Key Concepts in Neurocardiology. *Cardiol Discov.* 2025 Jun;5(2):162-77. [PMID: 40535756]

[7] Liu S, Cui Y, Chen M. Heart rate variability: a multidimensional perspective from physiological marker to brain-heart axis disorders prediction. *Front Cardiovasc Med.* 2025 Nov 6;12:1630668. [PMID: 41282340]

[8] Wang Z, Zou Y, Liu J, Peng W, Li M, Zou Z. Heart rate variability in mental disorders: an umbrella review of meta-analyses. *Transl Psychiatry.* 2025 Mar 28;15(1):104. [PMID: 40155386]

[9] Heart rate variability: standards of measurement, physiological interpretation and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. *Circulation.* 1996 Mar 1;93(5):1043-65. [PMID: 8598068]

[10] Sadoun SN, Boutin A, Cottin F, Laleg-Kirati TM. Modeling Brain-Heart Interaction: A Review of Mechanistic Dynamical Models. *IEEE Rev Biomed Eng.* 2025 Dec 23;PP. [PMID: 41433159]

[11] Candia-Rivera D, Faes L, De Vico Fallani F, Chavez M. Measures and Models of Brain-Heart Interactions. *IEEE Rev Biomed Eng.* 2026;19:24-40.

[PMID: [40031285](#)]

[12] Ashrafpour S, Mahmoudjanloo M, Ashrafpour M. Beyond the Beating: The Dynamic Interplay between Heart and Brain in Emotion and Cognition. *Int J Mol Cell Med.* 2026;15(1):1261-84.

[13] Tuama RM, Mustafa AA, Yahya ZS. A review on brain-heart axis physiology and its clinical implications. *Int J Med Sci.* 2025;7(1):41-51.



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5

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