Review of the theoretical basis of the heart-brain correlation

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Abstract. Despite rapid advancements in modern medicine, the treatment and prevention of cardiovascular diseases have achieved significant progress. However, issues such as high incidence, recurrence rates, and poor prognosis still profoundly threaten human life and quality of living. The correlation between the heart and brain in anatomy and function, supported by neurological regulation and pathological foundations, validates the association between them. Traditional medicine, characterized by holistic concepts and differential treatment, presents the therapeutic principle of treating different diseases similarly, offering new insights into the clinical treatment of cardiovascular diseases. This paper aims to summarize the theoretical basis of the heart-brain correlation from functional, material, neurologic, and pathological perspectives, aiming to provide more evidence for the theory of "treating the brain and heart simultaneously."

Keywords: Heart-brain correlation, Dominance of the spirit, Meridians, Autonomic nervous system, Atherosclerosis

1. Introduction

With the evolution of modern society, an increasing number of young individuals, due to factors like life stress, develop habits such as staying up late and irregularities in lifestyle and unhealthy dietary habits, leading to a trend of cardiovascular diseases (such as angina, acute myocardial infarction) occurring at younger ages. The "heart-brain correlation" theory embodies the traditional medicine's concise understanding of the relationship between the heart and brain. It represents the holistic concept of Chinese medicine and falls under the scope of treating different diseases similarly. It corresponds to the central-circulatory system in modern medicine and is often employed in the treatment of conditions like dizziness, insomnia, and dementia. This paper aims to summarize the correlation between the heart and brain, providing a basis and reference for future prevention and treatment of cardiovascular diseases.

2. Functional Correlation

As vital organs governing human life activities, both the heart and brain possess the ability to govern human consciousness and thinking. However, there remains ongoing debate about which organ dominates the spirit. The theory of "heart dominance of the spirit" was prevalent before the Ming and

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Qing Dynasties. The earliest text, “Nei Jing,” indicated that the heart is the sovereign organ, the abode of the spirit, the foundation of life, unchanging despite external alterations, capable of sustaining itself. Similarly, “Xunzi’s Explanation of Obscure Terms” also supports this viewpoint: “The heart is the ruler of form and the master of the spirit.” These assertions regarding the “heart’s dominance of the spirit” originate from the perspective of visceral function [1], positing that the heart harbors the spirit, governs consciousness and thinking, regulates other organs, and serves as the ruler of life—a notion consistent with the historical understanding of death: when an individual’s heart ceases beating and autonomous breathing ceases, the individual is declared dead.

Post-Ming and Qing Dynasties, with deepening comprehension of visceral functions and the infiltration of Western medicine, the theory of “brain dominance of the spirit” gradually gained prominence. Li Shizhen explicitly stated in “Compendium of Materia Medica”: “The brain is the abode of the original spirit; the spirit emanates from essence, which is the origin of life. Therefore, the original spirit in the brain is innate; when the spirit is present, life is present; when the spirit is absent, death ensues.” The brain dominates consciousness, memory, and all human recollections reside in the brain. “When people recall past events, they close their eyes and concentrate, which is focusing the spirit in the brain.” Wang Qingren, in “Correction of Medical Errors,” recorded, “The sharpness of memory and intelligence does not reside in the heart but in the brain,” affirming the theory of brain dominance from an anatomical perspective. As the supreme commander of life activities, the brain is pivotal for life. The concept of brain death in modern medicine posits that irreversible nerve damage leads to the loss of most or all brain functions; consequently, functions such as breathing and heartbeat cannot be sustained, ultimately leading inevitably to death.

Both viewpoints have their merits, yet neither should be universally applied. Whether from the perspective of visceral functions with the “heart’s dominance of the spirit” theory [1] or from the standpoint of physical location with the “brain’s dominance of the spirit” theory, both theories segment the functions of the heart and brain, contradicting the holistic concept of traditional medicine. The abilities of humans to contemplate, converse, move, sit, and lie down are all inseparable from either the heart or brain. In “Shuowen Jiezi,” the character for ‘think’ is interpreted as ‘the top part representing the brain and the bottom part representing the heart’. This illustrates that thought requires both the brain and the heart. Zhang Xichun, a renowned physician in both traditional Chinese and Western medicine, explicitly proposed in “Guidebook to Medical Knowledge Incorporating Western Medicine” that the heart and brain jointly govern the spirit. He believed that each has its own role—the original spirit in the brain is the essence, while the conscious spirit in the heart is its utility. “When individuals wish to employ their spirit, it travels from the brain to the heart. When the spirit is not in use, it returns from the heart to the brain.” This perspective has garnered recognition from many scholars, laying the foundation for the theory of “treating the heart and brain simultaneously.” Zhang Xi and others [2] argued that the original spirit governs the inherent activities of the body, endowing individuals with the abilities of sensation, movement, and perception, while the conscious spirit governs the application of these abilities and generates dynamic activities after the formation of the body [3]. When the heart and brain complement each other, the spirit manifests. However, some scholars do not entirely agree with this viewpoint. Piao Suncheon [4] believes that although the heart and brain reciprocally serve as essence and utility, the “heart dominates the spirit,” with the spirit as the root emanating from the brain’s functional base. Hence, the heart should be considered the essence, and the brain as the location where the spirit flows. Moreover, the brain is essentially a tool for the “kidneys to dominate essence.” The “kidneys dominating essence” serve as the brain’s material foundation and the root of the body. In essence, the heart, brain, and kidneys are “the heart and kidneys as essence, and the brain as utility.” Setting aside the disparities in the essence-utility viewpoint, the theory of “joint governance of the spirit by the heart and brain” integrates these organs into an organic whole. Both organs complement each other, jointly governing life activities.

3. Material Basis

3.1. Blood Foundation

The heart governs the blood vessels; it transforms the essence derived from the spleen and stomach into blood, propels blood circulation, nourishes internal organs, and permeates the muscles, delivering nutrients throughout the body. The brain, as the marrow reservoir, ensures clarity when filled; it is nourished by the essence and shares a common origin with blood. Thus, a strong qi in the heart propels robust blood circulation, nourishing the brain to enable its proper function.

From an anatomical perspective, the heart's aorta branches off from the aortic arch into the vertebral and carotid arteries, supplying blood to the cranial brain. Blood constitutes life's foundation, and the heart, as the body's blood-pumping organ, directly impacts the brain's oxygenation status. A momentary decrease in the heart's blood supply capability can cause irreversible damage to brain cells [5]. Liu Tongyun et al. [6] suggest that even lower ejection fractions lead to secondary issues like neurohormonal activation, inflammatory reactions, oxidative stress responses, and microvascular dysfunction, impairing cerebral autoregulation. Besides the heart's influence, blood vessel dilation and constriction affect blood supply. Nitric oxide (NO) serves as a critical endothelial vasodilator. Nitric oxide synthase (NOS) catalyzes NO production. NO widely distributes in the brain area. Research indicates that in rats with myocardial ischemia, acupuncture treatment improved symptoms and concurrently increased NO concentration and NOS activity within the RVLM (rostral ventrolateral medulla). When an NOS inhibitor pre-treated the RVLM area, the therapeutic effects after acupuncture were notably reduced [7]. This infers that acupuncture can activate the NO/NOS system in the RVLM, dilating blood vessels, increasing blood return volume, thus ameliorating myocardial ischemia.

3.2. Meridian Foundation

Meridians serve as channels for the circulation of qi and blood to nourish the limbs, sensory organs, and internal organs [8]. The brain resides in the highest part of the cranial cavity, connecting upward to the fontanelle and downward to the Fengfu, penetrating the spinal cord. "365 meridians all converge at the head," and the Heart Meridian is no exception [9]. The Heart Meridian, primarily responsible for eye connections, originates from the heart and travels alongside the throat, connecting with the ocular vessels before entering the brain. Additionally, the Governor Vessel acts as a connection between the heart and brain. On one hand, "The Governor Vessel... passes through the navel's center and ascends to the heart." On the other hand, the Governor Vessel ascends to the brain and marrow, enabling brain regulation of internal organs, balancing yin and yang, and coordinating the flow of qi, blood, and bodily fluids [10]. The interconnectedness of the heart and brain through meridians, ensuring smooth meridian circulation, governs the spirit, nourishes the brain, and promotes the prosperity of both the heart and brain, enhancing clarity of the mind [5].

4. Neurological Mechanism

From a neuroanatomical perspective, the heart's function is governed by both its autonomous regulation and the central nervous system [11].

4.1. Cardiac Autonomic Nervous System (ANS)

The Autonomic Nervous System (ANS) comprises the sympathetic and parasympathetic systems, collectively regulating cardiac activity.

The cardiac sympathetic nerves originate from the thoracic segment of the spinal cord, emitting preganglionic fibers through the white rami communicantes into the sympathetic trunk. After synapsing at the stellate ganglion and cervical sympathetic ganglion, they enter the pericardium, forming the cardiac plexus with the vagus nerve outside the heart's outer membrane. These nerves control the myocardium, the conduction system, and distribute along the vessel walls, regulating vascular smooth muscle, and modulating coronary blood flow [12]. Both left and right cardiac sympathetic nerves dominate different aspects of the heart. The left side mainly controls the junction between the atrium and ventricle, enhancing myocardial contractility and prolonging the QT interval, leading to various arrhythmias. The right side primarily affects the sinus node, resulting in accelerated heart rates. The cardiac parasympathetic nerves, the vagus nerves, have a simpler path. Originating from the dorsal and ambiguous nuclei of the vagus nerve, they directly enter the chest cavity after coursing through the neck, issuing cardiac branches that, after joining the sympathetic nerves, extensively distribute throughout the myocardium [12]. Similarly, both left and right vagus nerves exert different effects, with the right side mainly influencing the sinus node and the left side affecting the atrioventricular junction, predominantly slowing down conduction speed.

The ANS affects the heart's function through various pathways:

4.1.1. Neurotransmitters. The sympathetic nervous system primarily releases norepinephrine (NE), acting on β_1 receptors on the myocardial cell membrane, exerting a positive effect. An imbalance in the ANS with excessive sympathetic nervous system stimulation leads to NE over-secretion, resulting in heightened myocardial contractility, increased heart rate, potential arrhythmias, intense vasoconstriction causing vascular spasms, exacerbating inadequate perfusion, and leading to irreversible heart damage, eventually causing cardiac remodeling and dysfunction [13]. The parasympathetic nervous system primarily releases acetylcholine (ACh), which has actions opposing NE in the cardiovascular system. When the physiological balance between the two is disrupted, heightened vagal excitability reduces ACh secretion, diminishing its protective effect on myocardial cells and tissue systems.

4.1.2. Receptors. NE regulates cardiac function by activating adrenergic receptors (AR), comprising nine different subtypes expressed diversely across cells and tissues [14]. In the human heart, β_1-AR predominates [15]. Wang Yali et al. [16] suggest that excessive β_1-AR stimulation elevates intracellular Ca2+ concentration in myocardial cells, compromising cell integrity and damaging them. Under pathological conditions like heart failure, β_1-AR expression is desensitized, while α1-AR expression increases to about 25% (ranging from 9% to 45%) [17]. These receptors, through Gq protein coupling, activate phospholipase C to break down phosphatidylinositol 4,5-bisphosphate into inositol trisphosphate, elevating intracellular and extracellular Ca2+ concentration, causing myocardial damage [18]. ACh acting on receptors is categorized into muscarinic cholinergic receptors (mAChR) and nicotinic acetylcholine receptors (nAChR). The M-type receptors, particularly M2 receptors prevalent in the heart, exert negative effects on myocardial cells and tissues [19], counteracting sympathetic nervous activity. Additionally, Liu et al. [20,21] highlight the limited distribution of M3 receptors in the heart, which exert a protective effect on myocardial cells.

4.1.3. Neural Distribution. Wang Yao et al. [22] pointed out that the distribution density of the autonomic nervous system (ANS) can influence cardiac function. The neural distribution in the heart is affected by chemical adsorbents, such as nerve growth factors, and the balance between attractants and repellents. Chemical adsorbents in the heart can increase the density of sympathetic neural distribution, while chemical repellents have the opposite effect. Zhong Tao [23] indicated that differences in the distribution of the ANS in the coronary arteries can lead to coronary artery spasm, causing an imbalance in myocardial blood supply, ultimately resulting in abnormal cardiac electrophysiological activity and triggering various cardiac arrhythmias [24].

4.1.4. Coronary Arteries. Coronary arteries play a crucial role in nutrient supply to the heart during blood circulation. Liu Chengzhe et al. [25] note that the ANS regulates coronary arteries. Neurocrest cells, derived from the dorsal neural tube, are part of the ANS. Subtype cells—cardiac neural crest cells—play a significant role in cardiovascular development [26]. Excitation of the vagus nerve releases acetylcholine. Activation of muscarinic M3 receptors on vascular endothelial cells generates NO, while activation of M2 and M3 receptors on vascular smooth muscle inhibits vasoconstriction [27]. Moreover, the vagus nerve, inhibiting cardiac activity, reduces pumping, thereby having an unclear effect on coronary arteries. Sympathetic nerve excitation increases myocardial contractility, elevates the release

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of catecholamines like NE, increasing myocardial oxygen consumption. Activation of α-adrenergic receptors inhibits NO release, ultimately increasing coronary blood flow.

4.2. Cardiovascular Center

Within the nervous system lies a part responsible for regulating cardiovascular activity, namely the cardiovascular center.

4.2.1. Medulla Oblongata. The medulla oblongata serves as the fundamental center regulating cardiovascular activity, playing a vital role in blood pressure control. Numerous nuclei within the medulla, including the rostral ventrolateral medulla (RVLM), are involved in the baroreflex arc, such as the rostral ventrolateral and caudal ventrolateral medulla. The solitary nucleus acts as the primary center for pressure-sensitive reflexes, maintaining blood pressure homeostasis. Salusin-α [28,29], a novel cardiovascular peptide, when microinjected into the solitary nucleus, induces hypotensive and bradycardic effects, possibly linked to the inhibition of sympathetic neuronal activity within the RVLM [30]. Studies by Li Haoxu et al. [31] found that injecting Salusin-α into the caudal ventrolateral medulla (CVLM) in rats resulted in hypotensive effects and bradycardia mediated by M-cholinergic receptors [32]. The RVLM, a core center involved in regulating hypertension, is a pivotal pathway for various circuits [33,34]. Axons from the RVLM connect with sympathetic preganglionic neurons in the intermediolateral cell column of the spinal cord. Stimulating the RVLM excites the sympathetic nerves, exerting positive inotropic effects. According to research, stress-induced hypertensive rats exhibit increased expression of miR-335 and miR-674-3p in the RVLM. Injecting selective antagonists into the RVLM significantly reduces blood pressure, suggesting that miR-335 and miR-674-3p could be potential targets for treating stress-induced hypertension [35]. The nucleus ambiguous (NA) and the dorsal motor nucleus of vagus (DMV) contain the cell bodies of cardiac vagal preganglionic neurons, thus receiving sensory information from the NTS, exciting the cardiac vagus nerve, resulting in cardiac inhibition.

4.2.2. Hypothalamus. The hypothalamus serves as a higher center for regulating cardiovascular activity. Its anterior region can activate α-receptors to lower blood pressure, while the posterior region can stimulate β-receptors to raise blood pressure. The Paraventricular Nucleus (PVN) in the anterior hypothalamus, an integral part of the hypothalamus, directly controls sympathetic pre-ganglionic neurons, regulating cardiovascular activity [36,37]. Within the PVN, there are NOS-positive neurons capable of synthesizing and releasing NO, reducing sympathetic activity [38]. Electroacupuncture also suppresses sympathetic activity in the PVN to treat hypertension [39]. Moreover, research indicates [40,41] that NE and glutamate influence PVN's regulation of hypertension. Increased NE concentration in the PVN stimulates the release of adrenal cortical hormones, activating the HPA axis to regulate cardiovascular activity [42]. Glutamate activity in PVN exhibits a positive feedback effect on blood pressure regulation [43]. Yang Liping et al. [44] suggest that Substance P (SP) balances the discharge frequency of sympathetic and vagal nerves, enhancing myocardial contractility, increasing cardiac output, and improving cardiovascular activity. Apelin, widely distributed in the central nervous system, vessels, and vital organs like the heart, enhances cardiac contractility, promotes vasodilation, and stimulates vascular development [45]. Experimental findings [46] reveal increased expression of the inflammatory factor cyclooxygenase-2 (COX-2) in the PVN of rats with heart failure, indicating that inflammatory reactions during heart failure might be mediated by COX-2, subsequently activating the PVN to influence cardiovascular center activity.

The Ventromedial Hypothalamic Nucleus's lateral part (VMHVl) directly participates in regulating the autonomic nervous system [47]. Activation of VMHVl significantly stimulates sympathetic nerves [48], while ablating VMHvl leads to excessive activation of the vagus nerve [49]. Long-term depressive emotions exacerbate heart damage by exciting the PVN to activate the emotional nucleus VMHVL, causing autonomic nervous system imbalance and resulting in heart damage [13]. The Dorsomedial Hypothalamic Nucleus (DMH), an indispensable component in the sympathetic output pathway, may influence the cardiovascular system's sympathetic nerve output via signaling pathways involving leptin, glucagon-like peptide-1 (GLP-1), and neuropeptide Y (NPY) [50]. Additionally, stimulating neurons in the dorsolateral hypothalamus enhances myocardial contractility, increasing heart rate and output. The anterior part of the dorsomedial hypothalamus has an inhibitory effect on the sympathetic system and an excitatory effect on the vagus, disrupting this region affecting baroreceptor reflexes [34].

5. Pathological Correlation

Both Traditional Chinese Medicine and Western Medicine share a consistent view regarding the pathological connection between cardiovascular and cerebrovascular diseases. According to TCM, the pathogenesis of heart and brain diseases primarily involves phlegm, heat, stasis, and deficiency. These factors independently cause diseases or interact to obstruct Qi and Blood flow, damaging the heart and brain, leading to ischemic or hemorrhagic diseases. Western Medicine collectively terms this shared pathological basis as atherosclerosis (As) [5]. As predominantly affects major arteries, often causing luminal narrowing, decreased vascular elasticity, reduced compliance, insufficient blood supply, consequently resulting in angina, coronary heart disease, and cerebrovascular occlusions [51]. Several lifestyle factors influence As, including smoking, alcohol consumption, hypertension, diabetes, and hyperhomocysteinemia [52]. While these risk factors can induce As, they are also controllable. Actively controlling these factors is critical to alleviate As progression, preventing the occurrence and development of cardiovascular and cerebrovascular diseases [5].

6. Conclusion

In conclusion, the close physiological and pathological connection between the heart and brain influences each other. Considering cardiovascular diseases from both cardiac and cerebral aspects is beneficial not only for clinical treatment but also for improving patient prognosis, reducing complications, and the possibility of recurrence. Presently, there is a prevalence of focusing on treating brain diseases from a cardiac perspective, while there is a scarcity of approaches to treating heart diseases from a cerebral standpoint. Current cardiac rehabilitation primarily focuses on improving heart function through exercise, but the effectiveness of such methods is restricted by treatment duration, intensity, and patient compliance. Exploring a new treatment approach based on the correlation between the heart and brain would greatly benefit numerous cardiovascular disease patients.

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