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Research Progress on the Association Between Heart Rate Variability Based on the Theory of "Heart Governing Spirit" and Ischemic Brain White Matter Hyperintensity with Mild Cognitive Impairment

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Abstract: ***With the acceleration of population aging, dementia has become a major global public health crisis. Vascular dementia (VD) is one of the most prevalent dementia subtypes, and the identification and intervention of its prodromal stage—mild cognitive impairment (MCI)—are of great clinical significance. Heart rate variability (HRV), the gold standard non-invasive biomarker for evaluating cardiac autonomic nervous function, has been proven to be closely correlated with cognitive function in recent studies. Ischemic white matter hyperintensities (WMH) represent the core imaging manifestation of cerebral small vessel disease, and serve as an important early marker of vascular cognitive impairment. Patients co-occurring with WMH and MHI carry a high risk of progression to dementia. Based on the traditional Chinese medicine (TCM) theory of "the heart governing the spirit", this paper systematically reviews the physiological basis of HRV and clinical research progress of WMH combined with MCI, deeply explores the potential mechanisms linking HRV and WMH-related cognitive impairment, analyzes the clinical value of HRV as an early warning biomarker for this patient population, and proposes future research directions in response to existing research limitations. This review proposes that HRV can act as a quantitative objective indicator for the theory of "the heart governing the spirit", providing a non-invasive, dynamic early warning tool for the highly heterogeneous population with WMH complicated by MCI, and offering novel research ideas for integrated traditional Chinese and Western medicine prevention and treatment of cognitive disorders.***

Keywords: Heart rate variability (HRV), Mild cognitive impairment (MCI), Ischemic white matter hyperintensities (WMH), The heart governing the spirit, Heart-brain axis, Autonomic nervous function.

1. Introduction

Dementia, particularly Alzheimer's disease (AD) and vascular dementia (VD), has become a serious challenge threatening the health and quality of life of elderly individuals. According to the World Health Organization report, the global number of dementia patients was estimated at 35.6 million in 2010 and is projected to reach 65.7 million by 2030 and 115.4 million by 2050 [1]. In China, the prevalence of dementia among individuals aged 60 and above was approximately 12% in 2010, rising to 33% by 2050, imposing a significant economic burden on society [2].

The pathogenesis of vascular dementia (VD) is a dynamically evolving process, progressing from subjective cognitive decline and mild cognitive impairment (MCI) to dementia, which provides a valuable "time window" for early intervention [3–5]. MCI represents a transitional state between normal aging and dementia, characterized by a high risk of progression. Numerous studies indicate that the rate at which MCI progresses to dementia ranges from 10% to 20% annually, ten times faster than the rate observed in healthy elderly individuals of the same age [5]. Therefore, the MCI stage constitutes a critical entry point for dementia prevention and treatment.

Ischemic white matter hyperintensities (WMH) represent one of the most hallmark imaging features of cerebrovascular diseases (CSVD). Their prevalence rises from 50% to 95% in individuals aged 45–80 years and are nearly ubiquitous in those over 80 years old [28]. WMH disrupts cortical-subcortical neural fiber connections, leading to slowed information processing and impaired executive function, and are closely associated with the onset and progression of mild cognitive impairment (MCI) [29, 30]. Patients with WMH combined with MCI exhibit both well-defined imaging markers and clinical manifestations of cognitive dysfunction, making them an ideal model for investigating early detection and intervention strategies for vascular dementia (VD).

In traditional Chinese medicine theory, cognitive function falls within the realm of "shen" (spiritual essence). The Huangdi Neijing proposes the core concept that "the heart governs shen," asserting that the heart controls both vital and mental activities in the human body [6]. Modern medical research has demonstrated a close physiological and pathological relationship between the heart and the brain, with shared risk factors and mechanisms such as inflammation, oxidative stress, and ischemia linking them closely together [7, 8]. Heart rate variability (HRV), as a key indicator reflecting cardiac autonomic nervous system function, quantifies the dynamic balance between the sympathetic and vagus nerves [9]. Investigating the relationship between HRV and cognitive function in patients with white matter hyperintensities (WMH) combined with mild cognitive impairment (MCI) not only aids in elucidating the scientific rationale behind the "heart-governing-shen" theory but may also provide new objective evidence for early warning and prevention of cognitive disorders.

Based on the core concept of the “heart governs consciousness” theory, this paper systematically reviews the research evidence regarding the association between HRV, WMH, and mild cognitive impairment (MCI), explores its underlying mechanisms, analyzes existing limitations, and outlines future research directions, aiming to provide new theoretical perspectives and clinical insights for the integrated prevention and treatment of cognitive disorders through traditional Chinese and Western medicine.

2. The Connotation and Extension of the Traditional Chinese Medicine Theory that “The Heart Governs the Spirit”

2.1 Theoretical Implications of “The Heart Governs Spirit”

“The heart governs the spirit” is one of the core tenets of traditional Chinese medicine’s foundational theory, encompassing both the broad concept of spirit (the external manifestation of all human life activities) and the narrow concept of spirit (spiritual, conscious, and cognitive functions) [6]. The *Suwen·Linglan Midian Lun* states: “The heart is the sovereign organ from which spiritual clarity emanates,” while the *Lingshu·Xieke* notes: “The heart is the supreme commander of the five zang and six fu organs and the abode of the spirit” —both emphasizing the heart’s dominant role in mental processes [6]. The *Suwen·Liujie Zangxiang Lun* further clarifies: “The heart is the foundation of life and the manifestation of spirit,” underscoring its fundamental role in both physiological and psychological activities.

From the perspective of Traditional Chinese Medicine’s theory of visceral manifestations, the function of “the heart governing spirit” relies on its material foundation in regulating blood circulation. When heart blood is abundant and vascular pathways are unobstructed, the spirit receives adequate nourishment, manifesting as mental vitality, sharp cognition, and robust memory. Conversely, when heart blood is deficient or blood flow is impaired, the spirit lacks proper nourishment, leading to cognitive decline such as forgetfulness, slowed response, and poor concentration. This understanding aligns fundamentally with the modern medical concept that “cerebral perfusion depends on cardiac pumping function.”

2.2 The Academic Debate Between “The Heart Governs Spirit” and “The Brain Governs Spirit”

Since the introduction of Western medical knowledge to China, the debate between “the heart governs consciousness” and “the brain governs consciousness” has persisted for a long time. Some scholars argue that modern anatomy has localized cognitive and conscious activities to the brain, making the notion of “the brain governing consciousness” more consistent with scientific facts; others adhere to the traditional TCM perspective that “the heart governs consciousness,” considering it one of the core pillars of the TCM theoretical system [10]. Modern scholars have gradually recognized that the essence of this debate lies in the fact that the concept of the “heart” in Traditional Chinese Medicine (TCM) is not entirely equivalent to the modern anatomical concept of the “heart.” TCM visceral theory emphasizes functional units rather than anatomical organs; the heart and brain are functionally closely interconnected, rather than being opposed, but rather interacting and collaborating with each other [10, 11]. Modern medical research has also confirmed the existence of a complex bidirectional regulatory network between the heart and the brain, wherein changes in cardiac function can directly affect cerebral perfusion and brain function, and vice versa [7, 8]. Some scholars have proposed that the TCM concept of the “heart” actually encompasses certain functions of the brain in modern medicine, reflecting a comprehensive understanding of life activities based on an holistic perspective [11]. Therefore, the dispute between “the heart governs spirit” and “the brain governs spirit” fundamentally reflects differences in epistemological approaches between Western and TCM medicine, and should be addressed through theoretical integration rather than opposition.

2.3 Modern Scientific Interpretation of the Theory That “The Heart Governs Spirit”

Modern research demonstrates that the heart and brain are closely interconnected through a neuro-endocrine-immune network [7]. The heart is not merely a blood-pumping organ; it also participates in regulating the central nervous system by secreting hormones such as atrial natriuretic peptide [8]. The brain, being a highly metabolically active organ that receives one-fifth of cardiac output, is particularly susceptible to hypoxia caused by reduced blood flow [7]. Studies indicate that decreased cerebral perfusion is the primary cause of cognitive decline in patients with heart failure, while cognitive function in dementia patients can be improved by increasing blood flow to the brain [8].

More critically, the heart transmits rhythmic signals to the nucleus accumbens via vagal afferent fibers, thereby regulating the locus coeruleus, hypothalamus, and prefrontal cortex. This “cardio-brain axis” pathway constitutes the neuroanatomical basis for how heart rate variability (HRV) serves as a bridge between cardiac function status and cognitive functions (“mind”). As the central integration hub of the autonomic nervous system, the nucleus accumbens receives afferent signals from peripheral organs such as the heart and blood vessels; after integration, these signals are projected to the limbic system and higher cortical regions, influencing cognitive processes including emotional regulation, attention, and executive functions. Furthermore, cardiac rhythmic signals can directly modulate the neuroelectrophysiological foundations of cognitive processing by affecting rhythmic brain activities (e.g., θ-wave and α-wave oscillations).

Based on the aforementioned theory, the modern scientific interpretation of “the heart governs consciousness” can be summarized as follows: The heart systematically regulates cerebral perfusion, metabolism, and neural electrical activity through three mechanisms—blood pumping function, neuroendocrine signaling, and autonomic nervous rhythm—thereby influencing cognitive function. HRV, as an external quantitative measure of cardiac autonomic rhythm, objectively reflects the functional state of the heart; linking it to cognitive function ("consciousness") provides a solid theoretical foundation and empirical validity.

3. Research Progress in Heart Rate Variability (HRV)

3.1 Definition and Historical Development of HRV

In 1965, Hon and Lee in the United States observed during fetal heart monitoring that intrauterine fetal distress could attenuate variations in heart rate variability [12]. In 1978, Wolf et al. first termed this phenomenon "heart rate variability" and noted its reflection of autonomic cardiac function [13]. In 1996, the European Society of Cardiology and the North American Society of Cardiac Pacing and Electrophysiology jointly developed the first HRV guidelines, establishing standardized detection criteria and analytical methods for HRV [14]. Subsequently, HRV research has expanded from the cardiovascular field to encompass multiple disciplines such as neuroscience, psychiatry, and endocrinology, becoming a pivotal tool for assessing autonomic nervous system function.

3.2 Analytical Parameters and Clinical Significance of HRV

HRV refers to the minute variations between successive cardiac beats and serves as a non-invasive indicator for assessing cardiac autonomic function [15]. Its analytical methods primarily include time-domain analysis, frequency-domain analysis, and nonlinear analysis.

Commonly used indicators in time-domain analysis include [16]: SDNN (standard deviation of 24-hour normal RR intervals, reflecting overall autonomic function; normal reference value: 141 ± 39 ms), rMSSD (root-mean-square deviation of adjacent RR intervals, reflecting vagal nerve function; normal reference value: 27 ± 12 ms), and PNN50 (percentage of adjacent RR intervals with differences greater than 50 ms; a normal reference value <50% indicates diminished vagal nerve activity). Among these, SDNN provides the most comprehensive assessment of overall autonomic function, whereas rMSSD and PNN50 are more sensitive to changes in vagal nerve function.

Frequency domain analysis decomposes heart rate fluctuation signals into distinct frequency components, with commonly used parameters including [17]: LF (low frequency, 0.04–0.15 Hz, reflecting the combined activity of the sympathetic and vagus nerves), HF (high frequency, 0.15–0.40 Hz, representing vagal nerve activity), and the LF/HF ratio (indicating the balance between sympathetic and vagus nerves). Generally, an elevated LF/HF ratio suggests predominant sympathetic dominance, whereas a reduced ratio indicates dominant vagal activity. Under resting conditions, vagal tone prevails; in contrast, under stress or pathological states, sympathetic activity is relatively enhanced.

Nonlinear analysis methods (such as sample entropy and trend-free fluctuation analysis) have garnered increasing attention in recent years, as they can capture the complex dynamic characteristics of HRV signals and may provide more comprehensive physiological information than traditional time-domain or frequency-domain metrics; however, their standardization for clinical applications remains inadequate.

3.3 Clinical Applications of HRV

Heart rate variability (HRV) is most widely utilized in cardiovascular diseases, with its reduction serving as an independent predictor of heart failure, malignant arrhythmias, and sudden cardiac death [18]. Studies have demonstrated that patients with coronary artery disease, acute myocardial infarction, essential hypertension, and heart failure exhibit significant decreases in both time-domain and frequency-domain HRV parameters, which are correlated with disease severity [19–22].

In recent years, the application of HRV in other diseases has garnered increasing attention. In the field of neuropsychiatric disorders, studies have demonstrated significantly reduced HRV levels in patients with stroke, anxiety, and depression, suggesting that central nervous system pathologies can lead to autonomic dysfunction [23, 24]. In pain medicine, chronic pain patients also exhibit abnormalities in HRV parameters. Furthermore, HRV abnormalities are associated with various conditions including diabetes, functional dyspepsia, and rheumatoid arthritis [25–27], highlighting its potential as a comprehensive biomarker for assessing autonomic nervous function.

Of particular note, HRV measurement offers advantages such as being non-invasive, convenient, and highly reproducible, making it suitable for widespread adoption in primary healthcare institutions and community settings. This underscores its practical feasibility as a tool for early screening of cognitive impairment.

4. Vascular Cognitive Impairment and Ischemic white Matter Hyperintensities (WMH)

4.1 Vascular Cognitive Impairment and Mild Cognitive Impairment (MCI)

Vascular cognitive impairment (VCI) is a broad spectrum of syndromes ranging from mild cognitive dysfunction to dementia, caused by cerebrovascular risk factors or cerebrovascular diseases, encompassing the entire disease spectrum from mild cognitive impairment (MCI) to vascular dementia (VD) [4]. The concept of VCI underscores the central role of vascular factors in cognitive impairment; unlike Alzheimer's disease (AD), which is characterized primarily by Aβ deposition and tau protein hyperphosphorylation, VCI is more closely associated with vascular pathological changes such as white matter injury, lacunar infarcts, and microbleeds.

MCI represents the early stage of VCI, characterized by age-unrelated decline in cognitive function while daily living abilities remain adequate [5]. Since its introduction by Petersen et al., the concept of MCI has been widely adopted in clinical research and practice. Based on the nature of cognitive impairment, MCI can be classified into amnestic MCI (primarily involving memory deficits) and non-amnestic MCI (mainly affecting executive functions, language, or other cognitive domains); the former is more likely to progress toward Alzheimer's disease (AD), whereas the latter is more closely associated with vascular dementia (VD). Addressing MCI holds significant clinical importance for reversing or delaying the onset of dementia.

4.2 Imaging Characteristics and Epidemiology of Ischemic white Matter Hyperintensities (WMH)

Ischemic white matter hyperintensities (WMHs) represent one of the hallmark imaging features of cerebrovascular small vessel disease (CSVD), appearing as hyperintense signals on T2/FLAIR sequences [28]. Based on anatomical location, they are classified into periventricular white matter hyperintensities (PWMH) and deep white matter hyperintensities (DWMH). PWMH predominantly occur around the lateral ventricles and are associated with ischemic changes in the subependymal region; DWMH are distributed in deep white matter areas such as the central semicircular fossa and more strongly reflect chronic ischemic damage caused by small vessel lesions.

The prevalence of WMH increases significantly with age, rising from 50% to 95% in individuals aged 45–80 years. DWMH is nearly universal in those over 80 years old, while PWMH is present in 95% of cases [28]. Risk factors for WMH include advanced age, hypertension, diabetes, hyperlipidemia, and smoking; these factors also represent traditional risk factors for vascular disease (VD). The severity of WMH is typically assessed semi-quantitatively using scales such as the Fazekas scale (grades 0–3) or the ARWMC scale; in recent years, voxel-based quantitative analysis methods have been increasingly applied in clinical research.

4.3 The Mechanism of Association Between WMH and Cognitive Disorders

White matter in the brain is highly sensitive to ischemia; its blood supply primarily derives from perforating arteries with limited collateral circulation, making it particularly vulnerable to reduced perfusion. White matter hyperintensities (WMHs) disrupt cortical-subcortical neural fiber connections, slowing information processing and impairing executive functions, thereby leading to cognitive dysfunction [29, 30]. Specifically, WMHs can damage critical white matter tracts such as the frontal-subcortical circuits and long connectivity fibers (e.g., the superior longitudinal fasciculus and cingulocoronal tract), which serve as essential anatomical foundations for maintaining cognitive functions including executive control, attention, and working memory.

Studies indicate that compared to Alzheimer's disease (AD), cognitive impairments associated with white matter hyperintensities (WMH) are more pronounced in attention, semantic memory, executive function, and information processing [31]. The severity of WMH correlates positively with cognitive decline, and increased WMH burden predicts future risk of dementia [30, 31]. Longitudinal studies further demonstrate a significant correlation between the progression rate of WMH and the rate of cognitive deterioration, suggesting that WMH is not merely a static imaging feature but its dynamic changes also hold substantial clinical significance.

4.4 WMH Combined with MCI: a Distinct Clinical Subgroup

WMH combined with MCI refers to a patient population that simultaneously meets both the clinical diagnostic criteria for MCI and imaging findings of WMH. This group exhibits the following characteristics: (1) presence of objective cognitive impairment while maintaining largely preserved daily living abilities; (2) cranial MRI reveals WMH that cannot be explained by other neurological disorders; (3) presence of high-risk factors for vascular disease (VD), such as hypertension or diabetes; (4) being in the early stage of VD progression, which represents a critical window for intervention.

Compared with mild cognitive impairment (MCI) of other etiologies, patients with white matter hyperintensities (WMHs) coexisting with MCI exhibit cognitive impairments predominantly characterized by executive dysfunction and slowed information processing speed, while memory deficits are relatively mild [31]. This feature facilitates clinical identification of WMH-associated MCI. However, systematic studies specifically targeting this population remain limited, and its clinical features, prognostic patterns, and biomarker profile require further clarification.

4.5 Current Treatment Status of WMH Combined with MCI and Its Association with HRV

The current treatment strategies for WMH combined with MCI primarily include the following aspects: (1) Control of vascular risk factors, such as strict management of blood pressure, blood glucose, and lipid levels; (2) Pharmacological interventions targeting cognitive symptoms, including cholinesterase inhibitors (donapexine, carbalazine), memantine, and butylphthalide [32]; (3) Traditional Chinese medicine therapy, which employs principles of kidney-tonification, essence-replenishment, blood circulation promotion, stasis resolution, phlegm elimination, and orifice dredging, with commonly used formulations such as Buyang Huanwu Decoction and Tongluo Yizhi Decoction [33, 34].

It is noteworthy that certain therapeutic agents inherently exert regulatory effects on HRV. For instance, donepezil enhances the HF component and increases vagal tone, while butylphthalide may indirectly influence autonomic balance by improving cerebral perfusion. In traditional Chinese medicine, herbs such as Astragalus membranaceus, Angelica sinensis, and Ligusticum chuanxiong—active components of Buyang Huanwu Decoction—exert dual effects in improving microcirculation and regulating autonomic function. This suggests a potential bidirectional interaction between therapeutic interventions and HRV. Monitoring HRV changes during treatment could provide objective electrophysiological indicators for efficacy evaluation and offer new insights for optimizing integrated traditional Chinese and Western medical treatment regimens. Utilizing HRV as an objective metric for assessing treatment efficacy in patients with WMH complicated by MCI may facilitate a closed-loop management approach of TCM's "diagnosis – treatment – evaluation."

5. Study on the Correlation Between HRV and Cognitive Dysfunction

5.1 Exploration of the Mechanisms Linking HRV to Cognitive Function

The mechanisms linking HRV to cognitive function primarily include the following aspects [35, 36]:

1) Vascular mechanism: Reduced HRV reflects autonomic dysfunction, where excessive sympathetic activation can induce spasms and sclerosis of intracranial small arteries, leading to demyelination changes in periventricular and central white matter regions of the brain. Chronic imbalance between sympathetic and parasympathetic nerves may further accelerate atherosclerosis by impairing vascular endothelial function, ultimately resulting in cognitive impairment. This mechanism is directly associated with the formation of white matter hyperintensities (WMHs) and likely represents the core pathway linking HRV alterations, WMHs, and mild cognitive impairment (MCI).

2) Hypoperfusion mechanism: HRV rhythm imbalance can increase blood pressure variability and reduce pressure reflex sensitivity, leading to cerebral hypoperfusion. The white matter of the brain is located in regions distal to arterial blood supply and is particularly sensitive to decreases in perfusion pressure. When autonomic regulation function declines, blood pressure fluctuations intensify and the brain's automatic blood flow regulation capacity is impaired, resulting in recurrent ischemia and hypoxia of brain tissue, which subsequently causes white matter damage and cognitive decline [7, 8].

3) Inflammation and oxidative stress: Autonomic dysfunction can activate inflammatory responses, with peripheral blood inflammatory markers such as interleukin-6 (IL-6) and C-reactive protein (CRP) being closely associated with white matter injury [36]. Reduced vagal tone diminishes the inhibitory effect of the "cholinergic anti-inflammatory pathway"—the vagus nerve releases acetylcholine, which binds to α7 nicotinic acetylcholine receptors on the surface of immune cells such as macrophages, thereby suppressing the release of pro-inflammatory factors (e.g., TNF-α, IL-6, IL-1β). When vagal activity is diminished, this anti-inflammatory pathway is impaired, leading to increased release of pro-inflammatory factors, further exacerbating vascular endothelial damage and blood-brain barrier disruption, and promoting the formation and progression of white matter hyperintensities (WMHs).

4) Neurodegenerative mechanisms: Intracranial hypoperfusion, ischemia, and hypoxia can enhance the production and deposition of β-amyloid protein (Aβ), while also altering the phosphorylation status of tau protein, potentially accelerating the pathological progression of Alzheimer's disease (AD). Furthermore, chronic hypoperfusion may directly impair cognitive function by suppressing the expression of brain-derived neurotrophic factors and disrupting hippocampal neurogenesis.

The aforementioned four stages do not operate independently but rather form a cascading amplification effect: "autonomic nervous system imbalance → hemodynamic disturbance → inflammatory cascade reaction → accelerated neurodegeneration." This process begins with autonomic dysfunction and progresses through multiple pathological mechanisms, ultimately leading to cognitive decline. As a quantitative indicator of autonomic function, HRV can provide early signals at the initiating stage of this cascade reaction.

5.2 Correlation Between HRV and Different Types of Dementia

Numerous studies have demonstrated a correlation between HRV and various types of dementia. A meta-analysis incorporating 27 studies revealed significantly reduced resting HRV and overall variability in dementia patients, particularly those with Lewy body dementia and mild cognitive impairment (MCI) [37]. In patients with vascular dementia (VD), decreased HRV is closely associated with cerebrovascular risk factors, white matter injury, and impaired autonomic regulation centers [35, 38]. In mouse models of Alzheimer's disease (AD), an HRV pattern characterized by enhanced sympathetic activity and suppressed parasympathetic activity has been observed, whereas HRV alterations in AD patients vary depending on disease progression, medication use, and other factors, yielding inconsistent results [39]. Research indicates that parasympathetic activity in Lewy body dementia patients is markedly lower than in healthy individuals, and HRV changes are more pronounced compared to AD patients [37], which may align with the more prominent autonomic dysfunction clinical manifestations observed in these patients (e.g., orthostatic hypotension, constipation, abnormal sweating).

The differences in HRV changes across different types of dementia suggest that the parameter spectrum of HRV may exhibit certain etiological specificity. For example, an HRV pattern characterized by an elevated LF/HF ratio is more prevalent in patients with vascular dementia (VD), whereas one marked by a significant reduction in HF is more common in Lewy body dementia. These findings provide insights into the potential application of HRV in the differential diagnosis of dementia.

5.3 Clinical Study of HRV and Mild Cognitive Impairment (MCI)

Although the relationship between HRV and dementia has been preliminarily established, systematic research on its association with mild cognitive impairment (MCI) remains insufficient. Existing findings are inconsistent: Kim et al. [40] reported a linear correlation between HRV indices and cognitive function, as well as negative correlations between time-domain parameters (SDNN and RMSSD) and memory performance in patients with Alzheimer's disease (AD) and Lewy body dementia. In contrast, Zeki Al Hazzouri et al. [41], studying 2, 118 participants, demonstrated a nonlinear relationship between SDNN and the Stroop cognitive test, characterized by an asymmetric inverted U-shaped pattern, where both extremely low and extremely high HRV values were associated with poorer cognitive performance. These discrepancies may stem from differences in study subjects, sample size, HRV analysis methods, and cognitive assessment tools employed.

However, growing evidence suggests that reduced HRV may serve as an early biological marker of cognitive decline in non-demential populations [42, 43]. Liu Liyun et al. [42] found significant correlations between HRV parameters and MoCA scores in patients with coronary heart disease, indicating that decreased HRV is associated with cognitive impairment even in individuals who do not meet the diagnostic criteria for mild cognitive impairment (MCI). More critically, the longitudinal decline rate of HRV may hold greater predictive value than single measurement values—some studies have demonstrated that the LF/HF ratio exhibits significant shifts 2–3 years prior to the transition from MCI to dementia, suggesting that dynamic HRV monitoring can be an effective strategy for identifying high-risk individuals at risk of progression.

5.4 Imaging Correlation Study Between HRV and WMH

In recent years, a limited number of studies have begun to investigate the direct relationship between HRV and WMH. Kang Liyuan et al. [35] conducted HRV measurements and cranial MRI assessments in patients with ischemic cerebrovascular disease, finding that the HRV time-domain parameters SDNN and rMSSD were negatively correlated with WMH severity, suggesting a close association between autonomic dysfunction and the extent of white matter injury. The study also demonstrated that an elevated LF/HF ratio was associated with increased risk of WMH progression, further supporting the hypothesis that autonomic imbalance plays a role in WMH formation.

These findings provide preliminary clinical evidence for the association between HRV and WMH, although existing studies have limitations such as small sample sizes, predominantly cross-sectional designs, and inadequate control of confounding factors. Future large-scale, prospective studies are required to further validate the causal relationship between HRV parameters and WMH progression, as well as to clarify their temporal sequence.

5.5 HRV and WMH in MCI: Current Research Status and Prospects

Although previous studies have separately examined the associations between HRV and MCI as well as between HRV and WMH, research on HRV characteristics in the specific population of patients with both WMH and MCI remains in its infancy. To date, there is no systematic literature report specifically addressing HRV parameters in patients with WMH combined with MCI. This research gap is primarily reflected in the following aspects:

1) Lack of descriptive characteristics for HRV parameters: Do patients with WMH combined with MCI exhibit specific alterations in HRV parameters compared to those with isolated WMH or isolated MCI? What is the relationship between these alterations and the characteristics of cognitive domain impairments (e.g., executive function versus memory function)? This remains unclear.

2) Lack of stratified analysis: WMH patients with mild cognitive impairment (MCI) exhibit significant heterogeneity, and different risk factors (e.g., hypertensive, age-related, or metabolic types) may correspond to distinct HRV parameter profiles. For instance, patients with predominant executive function impairments may demonstrate more pronounced elevation of the LF/HF ratio, whereas those with predominant memory deficits may show more marked reductions in HF. To date, no systematic study has conducted HRV stratified analysis for these subtypes.

3) Lack of research linking to TCM syndrome patterns: The theory of "the heart governing the spirit" emphasizes the intrinsic relationship between the heart and the spirit. Whether different TCM syndromes (e.g., phlegm-obstructed orifices, blood stasis retention, kidney essence deficiency) correspond to distinct HRV parameter profiles has not been investigated in existing studies.

4) Lack of longitudinal follow-up data: Can HRV predict the rate of cognitive decline in patients with WMH and MCI? Does improvement in HRV indicate better clinical outcomes? These critical questions remain unanswered.

These identified gaps represent crucial directions for future research; addressing them could lead to the development of more specific biomarkers for early VCI detection and provide a quantitative basis for the objectification of TCM syndrome differentiation.

6. Summary and Prospects

In conclusion, HRV serves as an effective tool for assessing autonomic nervous function and exhibits a close correlation with cognitive function. Grounded in the Traditional Chinese Medicine (TCM) theory that "the heart governs spirit," HRV can be regarded as an external quantitative manifestation of cardiac function; investigating its relationship with "spirit" (cognitive function) holds dual theoretical and practical significance. This systematic review demonstrates that examining the association between HRV and white matter hyperintensity (WMH) combined with mild cognitive impairment (MCI) from the perspective of the "heart-governing-spirit" theory not only enhances the modern scientific interpretation of TCM principles but also provides novel approaches and tools for early detection of cognitive disorders.

The core innovation of this study lies in systematically proposing that HRV can serve as a quantitative bridge for the theory of "the heart governing spirit," bridging traditional Chinese medicine's holistic perspective with modern research on the heart-brain axis, thereby providing a non-invasive, dynamic early warning tool for the highly heterogeneous population comprising WMH patients with MCI. This perspective is relatively rare in existing domestic and international reviews, demonstrating significant originality and translational potential.

The current research gaps and future directions primarily include:

1) Mechanism Exploration: Further elucidate the neurobiological and pathophysiological mechanisms by which HRV affects cognitive function (particularly WMH-related cognitive impairment), with a focus on validating the hierarchical pathway of "autonomic imbalance → cerebral perfusion fluctuations → inflammatory cascade → white matter damage → cognitive decline," and clarifying the causal relationships and temporal sequence among each component.

2) Clinical validation: Conduct large-scale, prospective cohort studies to elucidate the value of HRV (particularly its longitudinal trajectory) in predicting cognitive decline in patients with WMH complicated by MCI, and identify sensitive and specific parameter indicators as well as warning thresholds. A follow-up period of at least 3–5 years is recommended to observe the endpoint event of progression from MCI to dementia.

3) Stratified study: Patients with white matter hyperintensities (WMH) coexisting with mild cognitive impairment (MCI) were stratified by risk factors (hypertension, diabetes, hyperlipidemia, etc.) and types of cognitive domain impairment to investigate the HRV characteristic profiles of different subtypes, enabling precise early warning and personalized assessment.

4) Integrated Traditional Chinese and Western Medicine Research: Utilizing HRV as an objective indicator of the TCM theory that "the heart governs spirit," this study explores characteristic variations in HRV under different TCM syndromes to provide an objective basis for syndrome differentiation and treatment in TCM. Further research will investigate the regulatory effects of traditional Chinese herbal formulations (e.g., Buyang Huanwu Decoction, Tongluo Yizhi Decoction) on HRV and their correlation with cognitive improvement, thereby establishing a tripartite research paradigm encompassing "syndrome – HRV – therapeutic efficacy."

5) Early intervention strategies: Leveraging the early warning value of HRV, we explore novel approaches to delay cognitive decline by modulating autonomic nervous function (e.g., vagus nerve stimulation, heart rate variability biofeedback, exercise training, traditional Chinese medicine interventions), establishing a closed-loop management model of "HRV monitoring – warning – intervention" to achieve comprehensive integrated management of cognitive impairment combining Western and traditional Chinese medicine approaches.

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