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Exploring the Correlation Between Heart Rate Variability and Post-Stroke Depression Based on the "Heart Governing the Mind" Theory

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Abstract: ***Post-stroke depression (PSD) is the most common neuropsychiatric complication following stroke, characterized by high prevalence and substantial detriment to neurological recovery and quality of life. However, stable, convenient, and objective physiological markers for early clinical screening of PSD remain lacking. Heart rate variability (HRV), a non-invasive quantitative indicator of autonomic nervous function, has drawn increasing attention in the prediction of PSD in recent years. Grounded in the traditional Chinese medicine (TCM) theory that "the heart governs the mind," this article systematically reviews the epidemiology, pathogenesis, current prediction and diagnostic approaches for PSD, the physiological basis of HRV, and advances in its application to PSD prediction. Existing evidence indicates that PSD patients commonly exhibit abnormal HRV parameters, manifested primarily as reduced vagal activity indices (rMSSD, PNN50) and an elevated sympathovagal balance index (LF/HF). HRV demonstrates favorable predictive value for PSD (AUC 0.61–0.78), corroborating the intrinsic physiological connection between the "heart" and the "mind" postulated by the "heart governing the mind" theory. This review aims to provide new insights into early objective screening for PSD and to offer scientific evidence for the modern interpretation of TCM theory.***

Keywords: Heart governing the mind, Post-stroke depression, Heart rate variability, Autonomic nervous function**.**

1. The TCM Theory of "The Heart Governing the Mind"

1.1 Classical Origins of the "Heart Governing the Mind" Theory

The TCM theory that "the heart governs the mind" has a long history, with its core concepts first established in the Yellow Emperor's Inner Classic. The Suwen (Chapter on the Secret Treatise of the Orchid Chamber) states, "The heart is the monarch organ, from which the spirit light emanates"; the Lingshu (Xieke) states, "The heart is the grand master of the five zang and six fu organs and the residence of the spirit"; and the Suwen (Xuanming Wuqi) states, "The five zang organs store [the spirit]; the heart stores the mind." The heart occupies a dominant position in mental and emotional activities, governing the functional activities of the ethereal soul, corporeal soul, intention, and will. It holds the most critical place in the system of mental activities, rendering mental and emotional functions an essential domain of human life [1]. This laid the theoretical foundation for "the heart governing the spirit light" and became the basis for later physicians' understanding and treatment of mental and emotional disorders. As stated in Guanzi (Xinshu), "The heart is the dwelling place of wisdom" and "When the heart harbors desires, objects pass but the eyes do not see, sounds arrive but the ears do not hear." The Inner Classic absorbed such views and explicitly pointed out that a healthy heart leads to intelligence and wisdom, "whence the spirit light emanates" [2].

1.2 The Relationship Between the Heart and the Brain

The Inner Classic recognized the brain as an important organ whose health is vital to life. For instance, the Suwen (Cijin Lun) recorded that erroneous needling of the brain constitutes a fatal injury: "Piercing the head and hitting the brain door causes immediate death." The Lingshu (Kouwen) also stated that when the brain is diseased, "all five zang and six fu organs are shaken." However, compared with the five zang organs, the brain's status was relatively subordinate, lacking systematic correspondence and only being able to attach itself to the respective zang [2]. The brain stores marrow, and the Lingshu (Hailun) called it the "sea of marrow." The head is the confluence of the essence and spirit light of the five zang organs [3], "the head being the mansion of clarity"; the Luxing Jing (Preface) states, "The primordial spirit in the head is called Niwan, which commands all spirits." The heart governs the spirit overall, while the other zang organs take charge of different functions; the brain is responsible for storing the various "spirits" of the five zang. Through their collaborative efforts, human mental activities are realized.

1.3 Implications of "the heart governing the mind" for Post-stroke Depression

According to TCM, the main pathogenesis of post-stroke depression involves the loss of control of the brain spirit and malnutrition of the heart spirit [4]. Disturbance of the heart spirit leads to disharmony between yin and yang; deficiency of primordial qi results in a lack of source for transformation and production and weakened ability to resist pathogenic factors [5]. The Leijing (Disease Category) states: "Although emotional injuries each pertain to a specific zang organ, tracing their origins invariably reveals that they arise from the heart." The spirit is an important factor influencing one's mental state; emotional imbalance can injure the heart spirit and affect the functions of the zang-fu organs. When spleen and stomach qi become stagnant, the source of qi and blood transformation is lost; stagnation of earth (spleen) leads to depression of wood (liver), causing the heart to lose its nourishment and the liver to fail in free coursing. The resulting dysfunction of dredging and releasing contributes to the occurrence of depression [6].

1.4 Corroboration of the "heart governing the mind" Theory by Modern Research

Modern medical research has provided objective evidence for the "heart governing the mind" theory. Studies have found a close connection between the heart and brain, with shared risk factors, similar epidemiological stratification, and overlapping pathogenic mechanisms [7]. The heart and brain are intimately linked through neural, endocrine, and immune networks [8]. Heart rate variability (HRV), a scientific quantitative index for assessing autonomic nervous function, offers modern physiological evidence for this theory. Research has shown that autonomic nervous dysfunction is closely associated with depression, and PSD patients commonly exhibit abnormal HRV parameters, primarily manifested as reduced indices reflecting vagal activity (rMSSD, PNN50) and an elevated LF/HF ratio, suggesting enhanced sympathetic activity, diminished vagal tone, and autonomic imbalance [9-10]. These objective changes in indicators confirm the intrinsic connection between the "heart" and the "mind" in the TCM theory—when depressive symptoms appear, cardiac autonomic dysfunction inevitably ensues, a phenomenon that can be quantified by HRV measurement.

2. Current Status of Heart Rate Variability Research

2.1 Definition and Parameters of HRV

Heart rate variability (HRV) is a measure of beat-to-beat interval variations derived from electrocardiographic recordings—it captures the subtle temporal and frequency differences in the intervals between consecutive heartbeats, scientifically reflecting the rhythmic variation and regularity of cardiac activity [11]. As a marker of autonomic nervous system activity and adaptability [12], HRV indicates the extent to which the autonomic nervous system can modulate heart rate in response to hemodynamic changes or other physiological perturbations. Through the dynamic balance and interaction between vagal and sympathetic nerves, HRV serves as a quantitative indicator of autonomic regulation and is the only unanimously accepted method for quantitative assessment of autonomic function in current clinical practice [13].

At present, the most widely used HRV analysis methods in clinical practice are time-domain analysis and frequency-domain analysis. Each has its strengths and limitations, and the two are often combined to comprehensively evaluate a patient's autonomic function. Commonly used HRV parameters [14] include: (1) Time-domain indices: ① SDNN (standard deviation of all normal-to-normal R-R intervals over 24 hours), reflecting overall autonomic activity; ② RMSSD (the root mean square of successive differences between adjacent normal R-R intervals over 24 hours), reflecting parasympathetic activity; ③ PNN50 (the percentage of differences between adjacent normal R-R intervals over 24 hours that are greater than 50 ms), reflecting parasympathetic activity. (2) Frequency-domain indices: ① VLF (very low frequency, 0.003–0.04 Hz), reflecting sympathetic activity; ② LF (low frequency, 0.04–0.15 Hz), reflecting a mixed effect of sympathetic and vagal influences; ③ HF (high frequency, 0.15–0.4Hz), reflecting parasympathetic activity; ④ LF/HF ratio (low-frequency/high-frequency ratio), reflecting the balance between sympathetic and parasympathetic nerves.

2.2 Clinical Applications of HRV

HRV is an important indicator for assessing autonomic nervous system function, reflecting the heart's ability to adapt to internal and external environmental changes, and is most widely applied in the cardiovascular system. Studies [15] have shown that reduced HRV is an independent predictor of cardiovascular events, and impaired HRV in the elderly, in particular, signifies an elevated risk of cardiovascular disease. Research has also demonstrated that combined assessment of HRV and blood pressure variability (BPV) can effectively predict the risk of atrial fibrillation (AF) in patients with essential hypertension [16]. Other studies [17] indicate that dysfunction of the cardiac autonomic nervous system has been confirmed to be extensively involved in the pathophysiological processes after acute myocardial infarction (AMI) and is closely associated with adverse outcomes such as myocardial recovery after reperfusion, ventricular arrhythmias, reinfarction, and heart failure.

The autonomic nervous system (ANS) consists of the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS), which finely regulate cardiac rhythm through their dynamic balance. Chronic stress and dysregulation of the hypothalamus are among the key mechanisms for reduced HRV [18]. Long-term stress activates the ventromedial hypothalamus, which can enhance SNS activity while inhibiting PNS function, leading to decreased HRV parameters. Clinical studies have further confirmed that an elevated baseline LF/HF ratio is positively correlated with anxiety symptoms in patients with depression, while reduced HF power is directly associated with cognitive impairment [19]. A randomized controlled trial (RCT) [20] suggested that lower HRV often reflects more fragile psychological resilience and more severe somatic symptoms (such as pain, gastrointestinal disturbances, and dizziness).

3. Current Status of Post-Stroke Depression Research

3.1 Epidemiology of PSD

Cerebrovascular accident (CVA) is a clinical syndrome of acute neurological dysfunction caused by interruption of cerebral blood supply, characterized mainly by sudden onset, focal neurological deficits, and possible impaired consciousness. Major depressive disorder (MDD) is an affective disorder with core manifestations of persistent low mood, diminished interest, and cognitive impairment. Post-stroke depression (PSD), as one of the common types of secondary depression in clinical practice [21], is the most frequent mental health complication following CVA. Compared with stroke without depression, PSD is associated with more pronounced cognitive impairment, poorer recovery, higher mortality, and lower quality of life [22], with a prevalence of approximately 30%–33% [23].

3.2 Pathogenesis of PSD

3.2.1 Imbalance of monoamine neurotransmitter levels

Monoamine neurotransmitters such as serotonin (5-hydroxytryptamine, 5-HT), norepinephrine (NE), and dopamine (DA) interact in synthesis, release, and reuptake, collectively forming a regulatory network for mood and mental state. Their imbalance can trigger affective disorders such as depression and anxiety [24]. Studies have shown that post-stroke pathological changes such as ischemia and inflammation can interfere with the synthesis and metabolism of 5-HT, leading to a decline in central 5-HT levels, thereby affecting mood regulation and inducing depressive symptoms [25]. In the state of PSD, the NE pathway is often functionally inhibited due to neural injury or neurogenic dysregulation, resulting in decreased transmitter availability and limited neural excitability maintenance, impairing emotional regulation [26]. Furthermore, after cerebral ischemia – reperfusion, increased Ca^{2+} influx may damage Ca^{2+}-dependent potassium channels (SK channels) in the ventral tegmental area (VTA), thereby inhibiting normal DA release and further exacerbating mood regulation deficits [27].

3.2.2 Neuroinflammatory response

Microglia are the first line of defense of the innate immune system in the central nervous system, and their activation is a hallmark of CNS inflammation [28]. Research has found that excessive microglial activation releases large amounts of pro-inflammatory cytokines, causing neurotoxicity and subsequently inducing anxiety- and depression-like behaviors [29]. An excessive systemic inflammatory response can lead to reduced metabolic function, which in turn causes neurotransmitter disturbances and plays an important role in the occurrence and development of PSD [30]. Therefore, persistent neuroinflammatory response is considered a key pathological basis of PSD.

3.2.3 Hyperactivity of the hypothalamic–pituitary–adrenal axis

Studies indicate that stroke patients are prone to hyperactivity of the hypothalamic–pituitary–adrenal (HPA) axis. The HPA axis is closely linked to the metabolic system, and its hyperactivity can lead to abnormally elevated levels of plasma cortisol (a stress hormone), exerting toxic effects on brain regions such as the hippocampus and thereby inducing depression [31]. With deeper investigation into the pathogenesis of PSD, researchers have also identified HPA axis hyperactivity in PSD patients and consider it one of the early predictive markers for post-stroke depression risk [32]. When the body faces stress, HPA axis activity increases, and cortisol is released in large amounts to restore hormonal balance under stress. However, the repeated stress triggered by PSD can render the HPA axis in a state of chronic abnormal activation and persistent excitement, causing severe HPA axis dysfunction. This, in turn, leads to structural and functional brain changes such as reduced hippocampal volume, which further weakens its inhibitory effect on HPA axis excitation [33].

3.2.4 Downregulation of neurotrophic factor expression

Reduced levels of neurotrophic factors such as brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF) are key intrinsic mechanisms in the occurrence and development of PSD [34]. Studies have found that BDNF levels in the plasma and cerebrospinal fluid of stroke patients are generally decreased. Such low BDNF levels may impair neuroplasticity, thereby affecting the function of brain regions related to emotion regulation (such as the hippocampus and prefrontal cortex) and exacerbating depressive symptoms [35] observed 100 patients with ischemic stroke admitted within 24 hours of onset and found that BDNF levels were negatively correlated with the occurrence of PSD, i.e., the lower the BDNF level, the higher the incidence of PSD and the more severe the depression.

4. Current Research on HRV in PSD Prediction

4.1 Studies on the HRV–PSD Correlation

Domestic and international researchers have conducted numerous studies on the relationship between HRV and PSD. Most studies indicate that PSD patients exhibit abnormal HRV parameters, predominantly characterized by reduced indices reflecting vagal activity such as SDNN, rMSSD, and PNN50, and an increased LF/HF ratio, suggesting enhanced sympathetic activity, diminished vagal tone, and autonomic imbalance [36-37] studied 91 patients with ischemic stroke and found that in the subgroup without cognitive impairment, rMSSD was significantly lower in PSD patients than in the non-depressed group (19.0 vs 21.5, P=0.033), while LF/HF was significantly higher (3.59 vs 2.28, P=0.009). In the subgroup with cognitive impairment, however, LF/HF was significantly lower in PSD patients than in the non-depressed group (1.51 vs 2.63, P=0.031). This study further suggests that the correlation between HRV and PSD may be influenced by the patient's cognitive status [38] collected physiological indicators from PSD, post-stroke non-depressed, and normal control groups using a multi-channel biofeedback instrument and found that the alpha wave amplitude and skin temperature in the PSD group were lower than those in the other two groups at rest ($P<0.05$), while beta wave amplitude was significantly higher under stress ($P<0.05$), indicating autonomic dysfunction in PSD patients.

4.2 Predictive Value of HRV

In recent years, the predictive value of HRV for PSD has gained increasing attention. Prospective studies have found that abnormal HRV parameters in the acute phase are independent risk factors for PSD [9] used ROC curve analysis and found that HRV indices such as SDNN, pNN50, TP, and VLF had statistical significance in predicting PSD at 3 months after stroke [39] applied HRV biofeedback therapy to PSD patients and observed increases in SDNN and LF values and a decrease in respiratory rate, suggesting that HRV biofeedback can improve depressive symptoms and autonomic function in PSD patients [40] conducted a prospective study of 49 patients with first-ever ischemic stroke and found a significant negative correlation between the time-domain index SDNN and the HAMD score, indicating that reduced HRV may be a predictor of PSD [14] studied 60 patients with cerebral infarction and found that all HRV parameters (SDNN, RMSSD, PNN50, TP, VLF, LF, HF, LF/HF) in the PSD group were lower than those in the control group ($P<0.05$).

4.3 The Guiding Significance of the "heart governing the mind" Theory for PSD Prediction Research

HRV, as an objective indicator reflecting the function of "the heart governing the mind," represents a modern extension of this theory in PSD prediction. Based on this theory, we hold that "the heart governs the mind" encompasses both the heart spirit and the brain spirit, and that the heart and brain are connected physiologically and pathologically. Accordingly, certain physiological parameters reflecting cardiac function inevitably influence brain function. PSD, as a common post-stroke emotional disorder, is closely related to dysfunction of the heart's governing of the spirit light. After stroke, damage to the brain collaterals and derangement of qi and blood affect the function of the heart spirit, leading to loss of spirit light function and resulting in depressive manifestations such as low mood and loss of interest. Therefore, exploring the intrinsic association between autonomic nervous function and PSD through the objective quantitative indicator of HRV can not only provide modern scientific evidence for the "heart governing the mind" theory but also offer an objective and convenient physiological marker for early PSD prediction in clinical practice, achieving an organic integration of TCM theory and modern medical technology.

5. Summary

Post-stroke depression (PSD), as the most common mental complication after stroke, is characterized by high prevalence, high disability rate, and high recurrence risk, severely impairing patient prognosis. Currently, early clinical screening for PSD still predominantly relies on subjective scales and lacks stable, convenient, and objective markers, resulting in high rates of missed diagnosis and delayed intervention. Heart rate variability (HRV), as the gold standard for quantitative assessment of autonomic nervous function, offers the advantages of being non-invasive, convenient, and highly reproducible.

Existing evidence demonstrates that PSD patients generally exhibit autonomic dysfunction, manifested as enhanced sympathetic activity and reduced vagal tone, with decreased HRV parameters (SDNN, rMSSD, HF) and an elevated LF/HF ratio. Prospective studies have further confirmed that abnormal HRV parameters in the acute phase are independent risk factors for PSD, and HRV shows favorable predictive value for PSD (AUC 0.61–0.78).

However, current studies still have limitations, such as small sample sizes, inconsistent measurement time points, and inadequate control of confounding factors. Future large-scale, multicenter prospective cohort studies are needed to standardize HRV measurement time points and parameter combinations, construct predictive models integrating HRV parameters with clinical factors, and further explore the modern scientific basis of the "heart governing the mind" theory. Such efforts will facilitate the clinical translation of HRV as an objective early predictor of PSD, providing new tools for early detection and early intervention, and ultimately improving the prognosis of stroke patients.

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