IJCSE International Journal of Computer Science and Engineering

ISSN 3107-7657 (Print) ISSN 3107-7657 (Online)

Research Article

# Multimodal Non-Pharmacological and Herbal Interventions for Neurodegenerative Cognitive Decline

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***Abstract*:** The progressive trajectory of neurodegenerative cognitive decline, encompassing mild cognitive impairment and Alzheimer's-type dementia, presents profound clinical and socio-technical challenges that single-target pharmacological regimens frequently fail to resolve. This paper investigates an integrative, multimodal paradigm that synthesizes chronotherapeutic Traditional Chinese Medicine interventions, preclinical neuroprotective herbal pharmacology, and digital health monitoring architectures. By critically examining the theoretical and empirical foundations of meridian time-sequence moxibustion alongside peripheral somatic-autonomic regulation, this study explores how non-pharmacological external therapies interact with systemic homeostatic pathways. Concurrently, preclinical neurobehavioral models and molecular analyses of herbal compounds are evaluated to illuminate underlying mechanisms involving axonal guidance proteins, cholinergic restoration, and cerebrovascular protection, while acknowledging the translational ambiguities inherent in rodent-to-human extrapolation. Furthermore, the integration of standardized clinical evaluation frameworks, data-mined classical prescription patterns, and smart sensor-driven wellness platforms is analyzed to address adherence barriers and ecological validity in geriatric care. Through a deliberately reflective synthesis that balances methodological rigor with epistemic humility, this work underscores the potential of combining ancient chronobiological wisdom with contemporary digital infrastructure, suggesting that multi-target, personalized interventions may offer a resilient, albeit still evolving, trajectory for mitigating cognitive deterioration.

***Keywords:*** *Neurodegenerative cognitive decline; Time-based moxibustion; Experimental herbal pharmacology; Digital wellness monitoring; Multimodal Traditional Chinese Medicine;*

## 1. Introduction

The escalating global prevalence of neurodegenerative disorders, particularly mild cognitive impairment (MCI) and vascular or Alzheimer's-type dementias, has exposed the structural limitations of reductionist, single-target therapeutic models. While contemporary neurology has invested heavily in amyloid-centric and cholinesterase-inhibiting pharmaceuticals, clinical outcomes remain modest, often accompanied by adverse systemic effects and an inability to halt the multifactorial cascade of neuroinflammation, synaptic loss, and cerebral hypoperfusion. Consequently, an urgent epistemological shift is occurring within translational medicine, moving away from isolated molecular interventions toward systems-level, multimodal frameworks capable of addressing both central neuropathology and peripheral somatic dysregulation. Within this evolving landscape, Traditional Chinese Medicine (TCM) offers a sophisticated, albeit historically under-standardized, repertoire of chronotherapeutic external modalities, herbal formulations, and constitutional dietary regimens. However, bridging the gap between traditional holistic theory



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ISSN 3107-7657 (Print) ISSN 3107-7657 (Online)

and contemporary evidence-based standards requires more than mere clinical juxtaposition; it demands rigorous methodological scrutiny, preclinical mechanistic validation, and the deployment of modern digital monitoring infrastructures.

Recent scholarly contributions have begun to lay the foundational stonework for this integrative architecture, particularly by formalizing the theoretical and operational parameters of non-pharmacological TCM interventions. For instance, the seminal theoretical work on time-based moxibustion utilizing Linggui Bafa (the Eight Methods of the Intelligent Turtle) provides an indispensable chronobiological framework for MCI intervention, demonstrating how aligning thermal stimulation with meridian time sequences and circadian Qi transformation may recalibrate neuroendocrine rhythms [5]. What makes this theoretical synthesis particularly compelling is its effort to translate abstract temporal metaphysics into replicable clinical protocols, though the precise neurophysiological correlates of meridian time-windows remain open to further empirical verification. Beyond direct central cognitive targeting, chronic neurodegenerative decline in aging populations is frequently compounded by somatic comorbidities, such as chronic musculoskeletal pain, metabolic fatigue, and sleep architecture disruption, which accelerate neuroinflammatory burden. In this regard, the rigorous three-arm assessor-blinded randomized controlled trial investigating integrated acupuncture, tuina, and moxibustion for chronic multisite pain establishes a high methodological benchmark by pairing subjective clinical scales with objective biomarker and pressure pain threshold assessments [7]. Similarly, the broader clinical viability of external modalities is reinforced by multicenter observational research on standardized TCM external therapy for chronic soft tissue pain, which highlights both the scalability of unified protocols across diverse clinical settings and the persistent challenge of controlling practitioner-dependent variance [8].

To elevate these clinical observations into a cohesive public health and geriatric care ecosystem, researchers have increasingly turned toward systemic standardization and digital health integration. The construction of a comprehensive standard system for traditional external therapies in TCM health preservation addresses a critical bottleneck in translational credibility—namely, the historical lack of uniform operational definitions and safety thresholds [10]. Building directly upon such standardization efforts, the pioneering development of a smart wellness model that fuses TCM health preservation industry standards with digital monitoring systems illustrates how continuous physiological tracking can extend clinical oversight into the patient's daily living environment [11]. Yet, as digital health infrastructures expand to capture longitudinal biometric and behavioral data, broader socio-technical questions regarding data governance and intellectual property emerge; even seemingly adjacent inquiries into digital archive management practices for intellectual property assets in cross-border ecosystems offer instructive parallels on how proprietary clinical algorithms and digital wellness frameworks must be safeguarded against fragmentation and unauthorized appropriation [1]. Considering the above factors, the integration of chronotherapeutic external stimulation, somatic pain management, and digital wellness architectures forms a promising macro-structural foundation, though its clinical efficacy ultimately depends on deeper mechanistic grounding in experimental pharmacology and tailored constitutional care.

## 2. Preclinical Mechanistic Foundations and Experimental Herbal Pharmacology

While non-pharmacological external therapies modulate systemic autonomic tone and circadian rhythms, the direct attenuation of neurodegenerative cascades requires biochemical agents capable of crossing the blood-brain barrier, mitigating oxidative stress, and promoting synaptic plasticity. Experimental herbal pharmacology provides vital mechanistic insights into these neuroprotective processes, yet interpreting preclinical animal studies demands a cautious, critical perspective due to the inherent limitations of rodent behavioral paradigms and interspecies metabolic differences. A foundational contribution in this domain is the investigation of Semaphorin 3A expression in focal cerebral ischemia rat models and the protective effects of Tongluo Jiunao injection, which illuminates how herbal preparations may modulate axonal guidance molecules to foster post-ischemic neural regeneration [15]. By identifying specific molecular targets within the neurovascular unit, this work moves herbal pharmacology beyond phenomenological observation, although the acute focal ischemia model only partially mirrors the chronic, insidious hypoperfusion seen in human vascular cognitive impairment.

Further complexity arises when comparing the efficacy of multi-herb compounds across distinct neurodegenerative phenotypes. In a pivotal comparative study evaluating different traditional Chinese herbal compounds in senile dementia mouse models, researchers demonstrated that multi-component formulations exert differential effects on spatial learning and memory retention, underscoring the necessity of matching specific phytochemical profiles to distinct pathological stages [16]. However, the



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ISSN 3107-7657 (Print) ISSN 3107-7657 (Online)

translational validity of such findings is heavily contingent upon the fidelity of the underlying animal models themselves. Addressing this fundamental methodological concern, rigorous behavioral comparisons between SAMR1 and C57BL/6 mouse strains in Alzheimer's disease modeling have provided crucial baseline parameters, revealing how genetic background significantly influences baseline locomotor activity and cognitive performance, which could otherwise confound pharmacological assessments [29]. Extending this critical refinement of experimental paradigms, subsequent neurobehavioral analyses contrasting senescence-accelerated mice (SAMP8) with intracerebroventricular injected models have clarified the distinct temporal trajectories of endogenous aging versus acute amyloid toxicity [30]. These comparative model studies are exceptionally valuable to experimental neuropharmacology because they prevent researchers from over-interpreting behavioral rescue in acute toxicity models as definitive cures for chronic human neurodegeneration.

Alongside complex multi-herb formulas, targeted phytochemical extracts and standardized patent medicines have also yielded illuminating, if nuanced, preclinical evidence. For example, experimental evaluation of maca (Lepidium meyenii) extract in scopolamine-induced memory acquisition impairment mouse models demonstrates that specific botanical extracts can counteract central cholinergic blockade and restore learning capacity [18]. Nevertheless, because scopolamine induces a transient, purely pharmacological amnesia rather than progressive neuronal death, such findings should be interpreted as evidence of symptomatic cholinergic support rather than disease modification. Conversely, investigations into the effects of Naofuming dripping pills on learning and memory abilities in vascular dementia rats address chronic cerebrovascular pathology more directly, suggesting that composite herbal formulations can ameliorate hypoperfusion-induced cognitive deficits through multi-pathway vascular and neuroprotective mechanisms [27]. Taken together, these preclinical pharmacological and model-validation studies establish a rigorous, albeit complex, biochemical rationale for herbal intervention, prompting us to examine how classical clinical wisdom and constitutional differentiation can be systematically harnessed in human populations.

## 3. Clinical Synthesis, Constitutional Differentiation, and Data-Driven Prescription Mining

Translating preclinical pharmacological insights and standardized external therapies into personalized human care requires bridging classical diagnostic heuristics with modern epidemiological and computational methodologies. In TCM clinical practice, neurodegenerative decline and its prodromal states are rarely viewed as isolated cerebral events; rather, they are conceptualized through systemic patterns such as tendon excess-deficiency, Qi-blood stasis, and constitutional vulnerability. A profound theoretical contribution to this clinical synthesis is the analysis of combined acupuncture, tuina, and moxibustion for elderly chronic musculoskeletal pain guided by meridian examination, which elucidates how resolving peripheral Qi-blood stagnation and tendon-channel imbalances can alleviate the somatic stressors that frequently precipitate geriatric cognitive and functional decline [13]. While the theoretical coherence of meridian palpation and combined external therapy is compelling, its clinical execution relies heavily on practitioner diagnostic acumen, which introduces potential inter-rater variability that future pragmatic trials must carefully quantify.

To systematize individualized internal interventions, contemporary researchers have increasingly paired traditional constitutional theory with prospective epidemiological designs and computational data mining. A notable advancement in preventive metabolic and neuro-supportive care is the prospective cohort study examining food-medicine homologous interventions for individuals with chronic fatigue based on TCM constitution classification [12]. By stratifying participants according to baseline constitutional phenotypes before administering dietary-herbal regimens, this study mitigates the dilution of treatment effects often seen in unstratified trials, though observational cohort designs remain susceptible to residual lifestyle confounding. Similarly, clinical observations combining auricular acupoint stimulation with constitution-differentiated dietary therapy for managing tobacco dependence and withdrawal reactions demonstrate how non-pharmacological neuromodulation and tailored nutrition can synergistically regulate neurochemical craving and autonomic agitation—mechanisms highly relevant to managing behavioral and psychological symptoms in early cognitive decline [14].

At the same time, extracting actionable herbal regimens from centuries of accumulated clinical records necessitates rigorous computational scrutiny to separate reproducible therapeutic patterns from idiosyncratic prescribing. Here, data-mining investigations into the medication rules of the Menghe medical school for treating insomnia (bumei) offer an exemplary methodological template, revealing core herb pairings that nourish heart-kidney Yin and calm the spirit—pathways intimately



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ISSN 3107-7657 (Print) ISSN 3107-7657 (Online)

linked to glymphatic clearance and sleep-dependent memory consolidation [19]. Equally instructive are parallel data-mining studies examining the Menghe school's pharmacological strategies for damp-heat febrile diseases [20] and broader warm-pathogen (wenbing) syndromes [23], which collectively demonstrate how association rule mining and cluster analysis can decode complex multi-herb synergies and latent inflammatory-clearing strategies. Yet, as we integrate these data-mined prescriptions and external therapies into modern healthcare delivery, patient receptivity and cross-cultural perception play decisive roles in real-world adherence. Empirical surveys assessing domestic and international cognitive awareness of acupuncture for constipation [26] and herbal medicine for gastrointestinal dysfunction [31] reveal substantial disparities in public understanding, mechanistic skepticism, and cultural familiarity across global populations. These findings serve as a sobering reminder that even the most rigorously mined prescription or standardized moxibustion protocol will face implementation bottlenecks unless accompanied by culturally sensitive patient education and transparent communication of clinical evidence.

## 4. Socio-Technical Ecosystems, Hardware Telemetry, and Historical-Educational Contexts

The long-term sustainability of a multimodal cognitive intervention framework depends not only on biological efficacy and clinical standardization, but also on the surrounding socio-technical infrastructure, hardware reliability, and human capital that support daily execution. In home-based and community geriatric care, continuous monitoring of behavioral patterns, sleep-wake cycles, and somatic agitation requires unobtrusive, wearable, and ambient sensor architectures. Remarkably, valuable engineering insights for low-power, reliable biometric telemetry can be drawn from adjacent cyber-physical domains. For instance, algorithmic research on acoustic event recognition utilizing Mel-Frequency Cepstral Coefficients (MFCC) and lightweight neural networks demonstrates how subtle vocal and acoustic biomarkers can be extracted with minimal computational overhead [3]—a methodological approach directly adaptable to detecting nocturnal vocalizations, agitation, or respiratory irregularities in cognitively impaired elders. Similarly, the architectural design of multi-sensor fusion control systems in wearable devices illustrates how combining accelerometer, acoustic, and physiological inputs can trigger real-time closed-loop feedback while minimizing false positives [4]. However, deploying continuous wearable sensors among vulnerable populations introduces non-trivial physical safety risks, particularly concerning lithium-ion battery degradation and thermal hazards. Consequently, engineering research on thermal runaway early warning and safety management systems for polymer lithium-ion batteries in wearable devices provides indispensable design principles for ensuring hardware integrity and patient safety during prolonged, unsupervised monitoring [6].

Beyond wearable telemetry, preserving physical mobility and preventing frailty are essential components of multimodal neuroprotection, yet structured physical training carries inherent musculoskeletal and cardiovascular risks if improperly calibrated. In this context, the construction and practical evaluation of risk-screening systems for urban adolescent physical fitness training offer a rigorous methodological blueprint for pre-exercise physiological stratification and dynamic load adjustment [2], while parallel validations of such risk-screening frameworks underscore the importance of iterative real-world calibration to balance sensitivity and specificity [9]. Adapting these algorithmic risk-screening architectures to geriatric cohorts could substantially reduce fall and overexertion risks during integrative somatic-cognitive rehabilitation.

Ultimately, however, technological platforms and clinical algorithms are only as effective as the clinicians, researchers, and historical epistemologies that guide them. Examining the human factor within academic and clinical TCM institutions reveals critical structural dynamics that shape translational capacity. Empirical surveys investigating the mental health status and influencing factors among incoming graduate students at the China Academy of Chinese Medical Sciences highlight the psychological pressures and cognitive demands placed on emerging clinician-scientists [17], while SWOT analyses of graduate employment trajectories illuminate the institutional bottlenecks and interdisciplinary skill gaps facing the next generation of TCM researchers [28]. Addressing these educational challenges requires intentional pedagogical cultivation, as explored in studies on fostering core values [24] and strengthening moral and professional ethics education among TCM postgraduates [25], which together argue that scientific integrity and humanistic empathy are foundational to clinical excellence. Finally, situating this entire multimodal enterprise within a broader historical-comparative perspective prevents parochialism and fosters genuine interdisciplinary dialogue. Comparative historical analyses of Sino-European medical traditions through the lens of "sympathetic understanding" (liaojie zhi tongqing) [21], alongside critical examinations of how the European Renaissance and the Chinese New



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ISSN 3107-7657 (Print) ISSN 3107-7657 (Online)

Culture Movement reshaped medical modernity [22], remind us that biomedical reductionism and traditional holism are not irreconcilable binaries, but historically contingent epistemologies whose thoughtful synthesis may yield more humane and effective care for the aging mind.

## 5. Integrative Outlook and Future Translational Horizons

Considering the convergence of chronotherapeutic external modalities, experimental neuropharmacology, data-driven constitutional medicine, and sensor-enabled wellness architectures, the path forward for mitigating neurodegenerative cognitive decline lies neither in uncritical adherence to traditional dogma nor in narrow pharmacological reductionism, but rather in a deliberately calibrated, self-correcting multimodal ecosystem. While the integration of time-based Linggui Bafa moxibustion, targeted herbal neuroprotectants, and continuous digital monitoring offers a compelling theoretical and empirical response to the multifactorial nature of cognitive deterioration, substantial methodological work remains to be done before such frameworks can achieve universal clinical adoption. Specifically, future research must transition from parallel, single-modality validations to adaptive, multi-arm pragmatic trials that utilize wearable telemetry and standardized biomarker panels to capture dynamic interactions between circadian Qi modulation, peripheral somatic relief, and central neuroplasticity, thereby transforming these foundational scholarly contributions into a resilient, personalized, and globally accessible standard of neurodegenerative care.

**Data Availability Statement**

Data will be made available on request.

**Funding**

This work was supported without any funding.

**Conflicts of Interest**

The author(s) declare no conflicts of interest.

### Ethical Approval and Consent to Participate

Not applicable.

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