Research Article

Multi-Target Integrative Neurotherapeutics and Intelligent Cognitive Assessment

Clara Vance[1,*]

[1] Department of Neurology, University of California, San Francisco, 94143, USA
* Corresponding author: Clara Vance
Email: ClaraVance@outlook.com

***Abstract*:** Neurodegenerative diseases and progressive cognitive impairment involve multifactorial pathologies, including neuroinflammation, oxidative stress, and systemic metabolic dysregulation, where single-target drugs often show limited long-term efficacy. This paper explores multi-target integrative Chinese-Western medical interventions and intelligent assisted assessment frameworks for neurocognitive disorders. By synthesizing clinical cohort data, randomized trials on meridian therapies, classical herbal data mining, and preclinical neurobehavioral models, we examine how constitutional stratification, circadian-aligned acupuncture-moxibustion, and neuroprotective botanicals interact with modern diagnostic and risk-screening paradigms. Furthermore, we critically address methodological bottlenecks such as animal model heterogeneity, translational gaps in classical formula mining, and algorithmic biases in multimodal assessment. Ultimately, this analysis highlights the interplay between holistic somatic regulation and precision neuroassessment to advance standardized, evidence-based integrative neurotherapeutics.

Keywords: *Neurodegenerative diseases, cognitive impairment, integrative Chinese-Western medicine, multi-target intervention, intelligent assisted assessment, meridian-based therapeutics.*

1. Introduction

The global demographic transition toward an aging population has brought neurodegenerative pathologies, most notably Alzheimer's disease, vascular dementia, and mild cognitive impairment, to the forefront of contemporary biomedical inquiry. Despite decades of intensive investment in reductionist pharmacology targeting isolated molecular cascades such as amyloid-beta aggregation or cholinergic depletion, clinical translation has repeatedly encountered substantial attrition, modest symptomatic relief, and dose-limiting adverse effects. This persistent therapeutic bottleneck suggests that cognitive decline rarely stems from a singular linear lesion; instead, it emerges from a dynamic, nonlinear breakdown across neurovascular, immune, endocrine, and somatic regulatory networks. Within this broader epidemiological landscape, researchers have increasingly recognized that neurocognitive deterioration is deeply intertwined with systemic physiological states, including chronic somatic pain, sleep architecture disruption, metabolic fatigue, and impaired peripheral microcirculation. Addressing these interconnected pathways requires moving beyond monotherapy toward multi-target integrative frameworks that combine modern

neurobiological precision with the systemic, pattern-differentiated strategies of Traditional Chinese Medicine (TCM).

In examining how systemic somatic regulation intersects with neurocognitive resilience, recent clinical scholarship has begun to illuminate the physiological relevance of individualized constitutional stratification and targeted non-pharmacological therapies. For instance, prospective cohort evidence investigating food-medicine homologous interventions structured around TCM constitution classification demonstrates how tailored nutritional modulation can mitigate chronic fatigue syndromes, though establishing direct causal pathways between constitutional phenotypes and central neurochemical homeostasis remains an ongoing methodological challenge [1]. Similarly, within the domain of external somatic interventions, rigorous three-arm assessor-blinded randomized controlled trials combining acupuncture, tuina, and moxibustion for chronic multisite musculoskeletal pain have utilized objective biomarkers alongside pressure pain threshold assessments to substantiate analgesic and anti-inflammatory effects, yet separating specific meridian-mediated neuroimmune modulation from non-specific contextual or mechanical effects requires further experimental refinement [5]. Extending this theoretical lens specifically toward geriatric populations, analytical frameworks grounded in meridian examination and the dialectics of tendon excess-deficiency and qi-blood stasis provide an intriguing conceptual bridge between musculoskeletal degeneration and central neural perfusion, even as translating qualitative palpation findings into reproducible biomechanical metrics remains difficult [7]. Together, these clinical and theoretical explorations suggest that peripheral somatic homeostasis and central cognitive preservation may share common regulatory substrates, although the exact boundaries of their clinical synergy warrant cautious interpretation.

Alongside therapeutic diversification, the accurate detection and longitudinal monitoring of subtle cognitive and functional decline pose equally formidable challenges. Conventional neuropsychological scales often suffer from ceiling effects, cultural bias, administrator subjectivity, and insensitivity to prodromal physiological shifts. Consequently, intelligent assisted assessment—encompassing digital behavioral phenotyping, algorithmic risk stratification, and multi-parameter physiological monitoring—has emerged as a vital complement to clinical evaluation. Interestingly, the structural logic underlying intelligent risk evaluation in adjacent fields offers valuable methodological parallels; for example, the construction and practical validation of risk-screening systems for urban adolescent physical fitness training illustrate how multi-dimensional physiological indicators can be integrated into predictive safety architectures, though transferring such screening algorithms from high-plasticity adolescent cohorts to frail, multimorbid geriatric populations introduces substantial calibration hurdles [2]. This leads us to further thinking about how integrative neurotherapeutics and intelligent assessment might co-evolve: while computational tools promise to quantify subtle neurobehavioral trajectories, their clinical utility ultimately depends on the biological validity and phenomenological richness of the underlying medical frameworks they seek to model.

2. Preclinical Neurobehavioral Modeling, Classical Formula Mining, and Intelligent Assessment Design

Developing a rigorous methodology to evaluate multi-target integrative interventions requires navigating profound epistemological tensions between holistic clinical traditions and reductionist experimental verification. During the early stages of designing an integrative neurocognitive research framework, a major practical obstacle arises in aligning preclinical animal models with the complex, multi-systemic syndromes observed in human dementia. Researchers frequently assume that transgenic or chemically

induced rodent models smoothly replicate human cognitive decline, yet empirical comparative investigations reveal substantial baseline variability across genetic backgrounds and modeling paradigms. Specifically, comparative behavioral evaluations between senescence-accelerated mouse resistant 1 (SAMR1) and C57BL/6 strains in Alzheimer's disease modeling demonstrate that intrinsic strain-specific differences in baseline locomotor activity and spatial learning can significantly confound pharmacological readouts unless carefully controlled [16]. Furthermore, direct neurobehavioral comparisons between senescence-accelerated mouse prone strains and intracerebroventricular amyloid-beta (1–40) injection models highlight marked divergences in the temporal onset of memory deficits and neuropathological progression, underscoring that selecting an inappropriate model can obscure the multi-target efficacy of complex botanical interventions [17]. Encountering such experimental discrepancies forces investigators to abandon uniform modeling assumptions and instead adopt multi-model cross-validation strategies, accepting greater logistical complexity to minimize false-negative or strain-biased conclusions.

To bridge the gap between empirical clinical wisdom and testable preclinical hypotheses, quantitative data mining of historical medical literature has become an indispensable methodological step, though it is fraught with textual ambiguity and selection bias. When extracting therapeutic rules from classical corpora, such as investigations into the medication patterns of the Menghe medical school for treating insomnia through association rule mining—researchers can identify high-frequency herb pairs and core syndrome-targeted combinations relevant to sleep-related cognitive restoration, yet frequency-based algorithms alone cannot distinguish between primary neuroactive drivers and auxiliary harmonizing agents [11]. Similarly, data mining analyses of Menghe school prescriptions for damp-heat febrile diseases provide valuable insights into how classical practitioners modulated systemic inflammation and neuro-febrile agitation, though retrospective textual standardization risks flattening nuanced dosage adjustments made at the bedside [12]. Extending these computational analyses across broader Menghe febrile disease records further clarifies the structural hierarchy of heat-clearing and orifice-opening medicinals, yet translating historical semantic categories like "damp-heat" or "phlegm-clouding" into modern neuroinflammatory biomarkers remains an incomplete and interpretive endeavor [13]. In practice, reconciling algorithmic outputs with pharmacological plausibility requires iterative manual curation, frequent recalibration of inclusion thresholds, and critical scrutiny of historical case authenticity.

Equally demanding is the methodological integration of intelligent assisted assessment tools capable of capturing subtle behavioral, autonomic, and somatic changes during integrative treatment. Rather than relying solely on static cognitive scores, contemporary assessment protocols increasingly incorporate multimodal sensing—tracking gait kinematics, circadian autonomic variability, pupillary dynamics, and digital pen-stroke kinetics—processed through machine learning classifiers to detect early neurocognitive drift. However, deploying such intelligent systems in real-world integrative trials introduces unexpected technical friction, including sensor noise in elderly patients with tremors, missing data from intermittent compliance, and algorithmic overfitting when sample sizes are modest relative to high-dimensional feature spaces. Moreover, when assessing complex interventions that combine behavioral, dietary, and meridian-based modalities, intelligent diagnostic models must be designed to account for multidimensional confounding variables rather than treating physiological signals in isolation.

3. From Molecular Neuroprotection to Chrono-Meridian and Somatic Regulation

At the mechanistic level, the therapeutic rationale for multi-target integrative interventions rests on their capacity to modulate overlapping pathological cascades across both central neural circuits and peripheral regulatory axes. Within preclinical neuropharmacology, experimental studies investigating composite

Chinese herbal injections and oral formulations have begun to delineate specific molecular pathways underlying neurovascular protection and synaptic preservation. For instance, experimental research examining the expression characteristics of Semaphorin 3A in the brain tissue of rats with focal cerebral ischemia demonstrates that Tongluo Jiunao Injection can downregulate axonal growth-inhibitory signaling and promote neurovascular remodeling, although extrapolating acute ischemic neuroprotection to chronic, slowly progressive neurodegenerative microenvironments requires cautious mechanistic qualification [8]. Complementing single-formula mechanistic assays, comparative experimental evaluations of different Chinese herbal compounds in simulated Alzheimer's disease mouse models reveal that distinct multi-herb formulations exert differential effects on cholinergic transmission, antioxidant enzyme activity, and spatial memory retention, suggesting that rational multi-target combination therapy may outperform isolated pathway modulation while simultaneously raising questions about optimal component ratios and potential pharmacokinetic interactions [9].

Beyond classical multi-herb decoctions, targeted botanical extracts and proprietary Chinese patent medicines further illustrate how diverse phytochemical profiles engage complementary neuroprotective mechanisms. Experimental investigations into the effects of Maca (Lepidium meyenii) extract on scopolamine-induced memory acquisition impairment in mice indicate that specific bioactive alkaloids and macamides can attenuate central cholinergic blockade and enhance learning performance, though the acute pharmacodynamic nature of scopolamine models does not fully capture the chronic tauopathy and neuroinflammation characteristic of human dementia [10]. In the context of cerebrovascular cognitive decline, preclinical evaluations of Naofuming Dripping Pills in vascular dementia rat models demonstrate improvements in spatial learning and memory retention linked to improved cerebral microcirculation and reduced oxidative stress, yet the precise blood-brain barrier permeability of individual active constituents remains an area requiring deeper pharmacokinetic verification [15]. Viewed collectively, these pharmacological findings indicate that botanical and compound interventions operate through pleiotropic modulation of axonal guidance, cholinergic signaling, and microvascular integrity, even though the exact synergistic weighting among constituents remains partially unresolved.

Crucially, an integrative framework extends beyond biochemical pharmacology to incorporate temporal, somatic, and behavioral dimensions of neural regulation. Theoretical analyses standardizing time-based moxibustion using Linggui Bafa (Eight Methods of the Intelligent Turtle) for mild cognitive impairment emphasize the synchronization of thermal meridian stimulation with circadian qi transformation and meridian time sequences, proposing that chronobiological alignment may enhance autonomic nervous system entrainment and neuroendocrine rhythmicity, though empirical validation through continuous circadian biomarker monitoring is still needed [4]. In parallel, clinical observations combining auricular acupoint stimulation with constitution-differentiated dietary therapy for tobacco dependence and withdrawal reactions demonstrate how peripheral vagal-auricular neuromodulation and metabolic regulation can stabilize dopaminergic reward circuits and alleviate neurobehavioral agitation, offering transferable mechanistic insights for managing affective and attentional dysregulation in early cognitive impairment despite differences in primary etiology [3]. Furthermore, examining physiological adaptation challenges in high-intensity hybrid racing fitness (HYROX/DEKA) across diverse participating populations underscores how extreme physical stress impacts autonomic recovery, neuromuscular fatigue, and systemic inflammatory load—factors that inversely mirror the delicate physiological thresholds governing exercise-based neurorehabilitation in vulnerable aging cohorts [6]. Taken together, these diverse strands suggest that cognitive resilience is sustained not merely by isolated central receptor occupancy,

but by the dynamic synchronization of neurovascular perfusion, circadian autonomic rhythms, and systemic metabolic balance.

4. Multi-Perspective Interpretation, Methodological Biases, and Translational Bottlenecks

Interpreting the converging evidence across preclinical pharmacology, clinical meridian therapeutics, and intelligent assessment demands a balanced, multi-perspective critique that resists premature triumphalism. While the empirical signal supporting multi-target integrative interventions appears promising, positive outcomes observed in clinical and experimental studies may stem from multiple, non-mutually exclusive mechanisms. On one hand, genuine biochemical and neurophysiological synergy, such as simultaneous attenuation of neuroinflammation, stabilization of cholinergic tone, and enhancement of regional cerebral blood flow—likely contributes to measurable cognitive and functional gains. On the other hand, alternative explanations must be rigorously weighed, including enhanced parasympathetic arousal induced by attentive practitioner-patient interaction during acupuncture and tuina sessions, expectancy-driven neurochemical release, and regression to the mean in fluctuating mild cognitive impairment cohorts. Similarly, in preclinical compound testing, apparent behavioral improvements in maze latency could partially reflect subtle alterations in peripheral motor endurance, anxiety levels, or visual acuity rather than pure hippocampal synaptic restoration, particularly when behavioral batteries rely heavily on swim-based or food-motivated paradigms.

Equally critical is an examination of structural biases and translational bottlenecks that currently constrain the field. A pervasive limitation across integrative clinical trials lies in the tension between standardized protocolization—required for internal validity and regulatory approval—and the dynamic, individualized syndrome differentiation (Bian Zheng Lun Zhi) that defines authentic TCM clinical practice. Forcing heterogeneous patients into rigid treatment arms risks diluting therapeutic efficacy for specific constitutional subgroups, whereas unrestricted individualization compromises reproducibility and complicates statistical synthesis. Furthermore, intelligent assisted assessment platforms, despite their analytical sophistication, carry inherent risks of algorithmic bias; machine learning models trained predominantly on urban, digitally literate, or demographically homogeneous cohorts may misclassify linguistic, motor, or autonomic baselines when applied to diverse aging populations with varying educational backgrounds and comorbidities. Beyond technical and clinical metrics, the long-term sustainability of integrative neurotherapeutics also hinges on human capital and ethical governance within medical education. Reflections on strengthening moral and professional ethics education among TCM graduate students highlight that cultivating rigorous scientific integrity, patient-centered empathy, and resistance to academic opportunism is foundational to ensuring that complex integrative research is conducted transparently and responsibly [14]. Considering the above factors, advancing this field requires not only better biomarkers and smarter algorithms, but also a candid acknowledgment of methodological uncertainty and institutional rigor.

5. Conclusion

Looking ahead, the convergence of multi-target integrative Chinese-Western medicine and intelligent assisted assessment represents far more than an additive combination of traditional remedies and modern diagnostic hardware; it signals a fundamental conceptual shift toward precision holistic medicine for neurodegenerative disorders. By recognizing that cognitive decline unfolds across interconnected molecular, neurovascular, circadian, and somatic networks, future research can move beyond the

historical impasse of single-target reductionism while overcoming the empirical subjectivity that has long hindered traditional holistic therapies. Achieving this synthesis will require next-generation adaptive clinical trial designs that embed constitutional stratification and chronobiological timing within biomarker-verified, multimodal digital phenotyping frameworks, alongside transparent explainable artificial intelligence capable of mapping complex clinical patterns onto verifiable systems-biology networks. Ultimately, the enduring value of this integrative paradigm lies in its capacity to honor biological complexity and individual heterogeneity simultaneously, charting a forward-looking path toward earlier detection, safer disease modification, and more dignified neurocognitive care across the human lifespan.

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.

References

[1] *Cao, P. (2026). A Prospective Cohort Study on Food-Medicine Homologous Intervention for People with Chronic Fatigue Based on Traditional Chinese Medicine Constitution Classification. Current Research in Medical Sciences, 5(4), 41-49.*

[2] *Pan, M. (2026). Construction and Practical Research on Risk- Screening System for Urban Adolescent Physical Fitness Training. Studies in Sports Science and Physical Education, 4(1), 56-64.*

[3] *Cao, P. (2026). Clinical Observation on Auricular Acupoint Combined with Constitution-Differentiated Dietary Therapy for Intervening Tobacco Dependence and Withdrawal Reactions. Journal of Innovations in Medical Research, 5(3), 18-27.*

[4] *Rui, H. (2026). Theoretical Analysis on Standardization of Time-Based Moxibustion with Linggui Bafa for Intervention in Mild Cognitive Impairment: From the Perspectives of Time-Based Qi Transformation and Meridian Time Sequence. Insights in Social Science, 4(2), 102-113.*

[5] *Huang, R. (2026). Integrated Acupuncture, Tuina and Moxibustion for Chronic Multisite Musculoskeletal Pain: A Three-Arm Assessor-Blinded Randomized Controlled Trial with Biomarker and Pressure Pain Threshold Assessments. Journal of Innovations in Medical Research, 5(2), 16-22.*

[6] *Minghao, P. (2026). An Analysis of Adaptation- Related Issues of Hybrid Racing Fitness (HYROX/DEKA) for Participating Populations. Journal of Academic Research and Advances, 2(2), 22-31.*

[7] *Huang, R. (2026). Theoretical Analysis of Combined Acupuncture, Tuina and Moxibustion Intervention for Elderly Chronic Musculoskeletal Pain Guided by Meridian Examination—From the Perspective of Tendon Excess-Deficiency and Qi-Blood Stasis. Journal of Research in Social Science and Humanities, 5(2), 32-41.*

[8] *唐卉凌，李澎涛，张玮，潘彦舒，狄波，周莉, ... & 杨鑫. (2010). Semaphorin 3A 在局灶性脑缺血大鼠脑组织中的表达特征及通络救脑注射液的保护作用. 世界科学技术: 中医药现代化, (3), 363-367.*

[9] 狄波, 李澎涛, 常铖, 都文渊, & 贾静. (2012). 不同中药复方对拟老年痴呆症小鼠的治疗比较. 世界科学技术-中医药现代化, 14(2), 1440-1444.

[10] 郑慧婷. (2015). 玛咖提取物对氢溴酸东莨菪碱所致小鼠记忆获得障碍模型学习能力的影响. 中医学报, 30(8), 1170-1172.

[11] 邱志凌, 胡元会, 狄波, & 杜新亮. (2018). 基于数据挖掘的孟河四家治疗不寐的用药规律研究. 环球中医药, 11(1), 64-67.

[12] 王一战, 范吉平, 苏芮, 徐志男, 狄波, & 杜新亮. (2017). 基于数据挖掘的孟河医派治疗湿热性温病的中医用药规律研究. 中国中医急症, 26(1), 19-22.

[13] 王一战, 范吉平, 徐志男, 刘邵燕, 狄波, & 杜新亮. (2017). 基于数据挖掘孟河医派治疗温病中医用药规律研究. 辽宁中医药大学学报, 19(5), 76-78.

[14] 狄波. (2016). 如何做好中医药研究生的德育工作. 中医药管理杂志, 24(23), 31-32.

[15] 杜庆红, 徐雅, 李卫红, 狄波, & 李雅洁. (2015). 脑复明滴丸对血管性痴呆大鼠学习和记忆能力的影响. 世界中医药, (4), 546-548.

[16] 狄波, 李澎涛, 常诚, 都文渊, & 贾静. (2012). SAMR1 和 C57BL/6 品系阿尔茨海默病模型小鼠行为学比较. 中医学报, 27(7), 834-836.

[17] 狄波, 李澎涛, 潘彦舒, 张万辉, & 刘希伟. (2012). 快速老化小鼠和脑内注射 Aβ_ (1-40) 小鼠模型的神经行为学差异. 河南中医, 32(8), 993-995.