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A Narrative Review of Integrative Management for Upper Limb Spasticity After Stroke: The Synergistic Role of Acupuncture and Botulinum Toxin A Monitored Through Biomarkers

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Abstract

Post-stroke upper limb spasticity (PULS) is a disabling condition that severely limits motor function and quality of life. While botulinum toxin A (BTX-A) injection is a standard treatment, its benefits are often partial and temporary. Traditional Chinese acupuncture (TCA) is increasingly used as an adjunct therapy. Concurrently, there is growing interest in identifying objective biomarkers to monitor recovery and elucidate treatment mechanisms.Combining acupuncture with BTX-A is more effective than BTX-A monotherapy for PULS rehabilitation. The therapy induces favorable changes in biomarkers related to muscle repair, neural plasticity, and neuroendocrine adaptation, providing a molecular basis for the observed clinical synergy. This integrated, biomarker-informed approach offers a promising direction for personalized neurorehabilitation in stroke survivors.

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Introduction

Stroke is a primary contributor to persistent disability globally, frequently resulting in lasting motor deficits [1]. Post-stroke upper limb spasticity (PULS) is a prevalent and debilitating sequela, marked by heightened muscle tone, hyperreflexia, and involuntary contractions that impair arm and hand function, cause discomfort, and reduce independence and quality of life [2]. This condition arises from damage to descending motor pathways, leading to disinhibited spinal reflexes and altered muscular responses to stretch [3].

The standard pharmacological intervention for focal spasticity involves intramuscular injections of Botulinum Toxin A (BTX-A), which acts by blocking acetylcholine release at the neuromuscular junction, thereby temporarily reducing excessive muscle activity [4]. Although effective for decreasing tone, the functional improvements from BTX-A are often inconsistent and short-lived, typically waning within 3 to 6 months [5]. This has prompted exploration into adjunctive therapies capable of augmenting and prolonging its benefits.

Traditional Chinese Acupuncture (TCA) is a complementary modality grounded in principles of energy (Qi) and blood flow regulation [6]. Contemporary research suggests its mechanisms involve modulation of neural plasticity, regulation of neurochemical and neurotrophic factors, enhancement of local circulation, and anti-inflammatory actions [7, 8]. Accumulating evidence supports its utility in improving motor outcomes and alleviating spasticity after stroke [9, 10].

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Alongside clinical measures, there is a growing emphasis on identifying objective biological markers to track recovery and clarify therapeutic mechanisms. Relevant biomarkers include molecules involved in tissue repair, neural growth inhibition, and neuroendocrine function. This narrative review examines the combined application of acupuncture and BTX-A for PULS, focusing on concomitant changes in specific biomarkers—Follistatin-like 1 (FSTL1), Nogo-A, Secretogranin II (SCG2), and Dehydroepiandrosterone sulfate (DHEA-S)—as potential indicators of treatment efficacy and underlying recovery processes.

Rationale for a Combined Therapeutic Strategy

Managing PULS necessitates a multifaceted approach. While BTX-A effectively reduces peripheral muscular hyperactivity, it does not directly remediate the central nervous system dysfunction central to spasticity. In contrast, acupuncture is proposed to exert effects both centrally and peripherally, potentially influencing cortical reorganization, modulating spinal cord excitability, and promoting the release of endogenous neuromodulators [7, 8]. A synergistic interaction is plausible: BTX-A mitigates the peripheral manifestation of spasticity, while acupuncture fosters central nervous system adaptation and functional reorganization. This aligns with contemporary neurorehabilitation paradigms that advocate combining targeted impairment reduction with activity-based training.

Clinical Evidence

Recent research, including a pivotal randomized controlled trial (RCT), offers strong support for the integrated approach [15]. This trial serves as a focal point for this narrative synthesis.

In this RCT of 62 individuals with PULS, participants were assigned to receive either BTX-A monotherapy or BTX-A supplemented with a 12-week regimen of acupuncture at points including Jianyu (LI15) and Quchi (LI11) [15]. Both groups underwent standard rehabilitation. Outcomes were evaluated using validated clinical scales and surface electromyography (EMG).

Results consistently favored the combination therapy group. Greater reductions in muscle spasticity (Modified Ashworth Scale) and more substantial gains in motor function (Fugl-Meyer Assessment for Upper Extremity) were observed [15, 16]. Notably, improvements in activities of daily living (Modified Barthel Index) and upper limb functional capacity (Carroll Upper Extremity Function Test) were significantly enhanced in the combined treatment group, indicating more clinically meaningful recovery [17]. Additionally, this group experienced greater pain reduction (Visual Analog Scale) and demonstrated lower levels of baseline muscle electrical activity (EMG RMS), suggesting improved normalization of neuromuscular control [15, 18].

The combination therapy demonstrated a favorable safety profile, with adverse event rates comparable to BTX-A alone, confirming that the addition of acupuncture is generally well-tolerated [15].

Biomarkers: Insights into Molecular Mechanisms

A novel dimension of recent investigation is the analysis of serum biomarkers, providing a window into the biological processes modulated by treatment [15]. In the referenced trial, biomarker profiles diverged markedly between groups after the 12-week intervention.

The combination group showed a 32.6% increase in FSTL1, a protein associated with muscle regeneration and suppression of fibrosis [11]. This suggests an active promotion of a restorative muscular environment. Concurrently, a 41.8% decrease in Nogo-A was observed. Nogo-A is a key myelin-derived inhibitor of axonal growth and CNS plasticity [12]. Its pronounced reduction implies a downregulation of growth-inhibitory signaling, potentially facilitating neural circuit reorganization.

Levels of SCG2 increased by 27.4%. SCG2 is a precursor to active peptides such as secretoneurin, involved in blood vessel formation, neuroprotection, and synaptic function [13, 26]. Its elevation may indicate an enhanced adaptive neuroendocrine response to therapy. Finally, DHEA-S levels rose by 21.5%. This neurosteroid possesses neuroprotective, anti-inflammatory, and plasticity-promoting properties, and its increase may contribute to a more supportive neural environment for recovery [14, 27].

Importantly, these biomarker shifts were significantly correlated with clinical improvements. For example, increases in FSTL1 and decreases in Nogo-A were associated with better motor and functional scores [15], reinforcing the potential functional relevance of these molecular changes.

Discussion

The concordance of enhanced clinical outcomes and beneficial biomarker alterations suggests a coherent, multi-mechanistic model of action for the combined therapy:

- **Peripheral-Muscle Interface:** BTX-A directly diminishes muscle overactivity, while acupuncture may potentiate this effect and independently promote muscle repair, as suggested by elevated FSTL1 [11, 24].
- **Central Nervous System Plasticity:** Acupuncture may encourage neural rewiring by reducing

expression of inhibitory proteins like Nogo-A and by fostering a neurotrophic milieu, thereby complementing BTX-A's peripheral action [12, 25, 36].

- **Systemic and Neuroendocrine Modulation:** The treatment appears to stimulate a beneficial systemic adaptation, reflected in raised SCG2 and DHEA-S levels, which may support neural health, mitigate inflammation, and enhance stress resilience [13, 14, 26, 27].

This multi-targeted framework offers a plausible biological explanation for the superior functional gains observed with combination therapy compared to either modality alone [19, 20, 28], representing a shift from purely symptomatic management toward active promotion of recovery mechanisms.

While promising, the current evidence base has constraints. The primary RCT had a limited sample size and a 12-week observation period [15]. Studies with longer follow-up are required to assess the sustainability of clinical and biomarker effects. Future work should also aim to optimize treatment protocols, including the timing, dosage, and specific acupuncture point selection for maximal synergy with BTX-A. The integration of advanced neuroimaging techniques with longitudinal biomarker assessment could provide a more comprehensive understanding of neuroplastic changes [29]. Furthermore, validating this biomarker panel in larger, multi-center cohorts could facilitate the development of personalized rehabilitation strategies guided by individual molecular profiles [30].

Conclusion

The integration of Traditional Chinese Acupuncture with Botulinum Toxin A injections presents a promising, multi-modal strategy for managing post-stroke upper limb spasticity. Current evidence synthesized in this review indicates that this combination yields superior outcomes in reducing spasticity, enhancing motor function, and improving daily living activities compared to BTX-A alone [15, 19, 37]. Significantly, these clinical benefits are accompanied by measurable, favorable alterations in a panel of biomarkers related to muscle repair, neural plasticity, and neuroendocrine function [15]. This molecular evidence provides a novel rationale for the observed therapeutic synergy. Moving forward, this biomarker-informed, integrative approach holds considerable potential for progressing toward more individualized and effective neurorehabilitation for stroke survivors.

AI Use Declaration

Artificial intelligence (AI) tools were used in a limited capacity (~15%) during the editing phase to improve linguistic fluency. All intellectual conception, critical evaluation, data interpretation, and substantive writing were undertaken by the author. AI was not employed for content generation, data analysis, or scientific inference.

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Authors Contributions

The authors contributed to the data analysis. Drafting, revising and approving the article, responsible for all aspects of this work.

Conflict of Interest

None

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