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Original Article

Acorus tatarinowii volatile oil inhalation combined with Fengchi (GB20) acupuncture enhances cognitive recovery in post-stroke patients

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Abstract: Objective: To evaluate the efficacy of Acorus tatarinowii volatile oil inhalation combined with Fengchi (GB20) acupuncture on cognitive function in post-stroke cognitive impairment (PSCI) patients and clarify its role in cognitive improvement. Methods: This single-center retrospective cohort study included 235 PSCI patients (January 2023-December 2024), divided into acupuncture group (routine rehabilitation + Fengchi electroacupuncture, n = 125) and combination group (additionally Acorus tatarinowii volatile oil inhalation, n = 110). After 1:1 propensity score matching, 92 patients per group were analyzed. The primary outcomes were changes in the Mini-Mental State Examination (ΔMMSE) and Montreal Cognitive Assessment (ΔMoCA) scores before and after treatment. Secondary outcomes included changes in the Modified Barthel Index (ΔMBI) and mean flow velocity (ΔMFV) in cerebral arteries measured by transcranial Doppler (TCD). Multivariate linear/logistic regression and model validation were performed. Results: Baseline characteristics were balanced after matching. At 3 months both groups improved on MMSE, MoCA, and MBI (all $P < 0.001$), with greater gains in the combination group ($P < 0.01$). Combination therapy produced larger increases in MFV across major cerebral arteries (all $P < 0.05$). Combined therapy was an independent positive predictor of cognitive improvement (multivariate linear regression: ΔMMSE $\beta = 1.84$, $P < 0.001$; ΔMoCA $\beta = 1.27$, $P = 0.006$; logistic regression: odds ratio [OR] = 2.19, 95% confidence interval [CI]: 1.05-4.56, $P = 0.036$). The predictive model demonstrated good discrimination, with an area under the receiver operating characteristic curve (AUC) of 0.83. Conclusion: Acorus tatarinowii volatile oil inhalation combined with Fengchi acupuncture is superior to acupuncture alone in promoting cognitive recovery and functional independence in patients with post-stroke cognitive impairment. The benefits are associated with improved cerebral hemodynamics and warrant further validation in prospective randomized controlled trials (RCTs).

Keywords: Post-stroke cognitive impairment, acupuncture, Fengchi (GB20), Acorus tatarinowii volatile oil, cerebral hemodynamics

Introduction

Stroke remains one of the leading causes of long-term disability worldwide. A substantial proportion of stroke survivors develop varying degrees of cognitive impairment, collectively referred to as post-stroke cognitive impairment (PSCI), which markedly compromises quality of life and imposes a considerable socioeconomic and healthcare burden [1]. Stroke-related cognitive decline tends to appear early - most cases emerge within the first three months after the index event - and its likelihood rises with age, stroke severity and coexisting cardiovascular risk factors [2]. Current treatment options are varied but none has gained universal acceptance. Drug therapies, notably cholinesterase inhibitors, help some patients but are beset by tolerability issues (for example, gastrointestinal symptoms and bradycardia) and do not provide a reliable, widely applicable solution [3]. Non-pharmacological cognitive rehabilitation programs can be effective, yet they demand sustained patient engagement and consider-

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able clinical or caregiver resources, which limits how broadly they can be implemented [4]. Given these gaps, there is a clear rationale for evaluating adjunctive, low-risk interventions that might support neural recovery after stroke [5].

Acupuncture has attracted renewed research interest in this context. Preclinical and clinical work points to several possible mechanisms: modulation of neurovascular coupling, dampening of post-stroke inflammation, facilitation of synaptic plasticity, and changes in cerebral blood flow [6, 7]. Meta-analyses of trials in stroke populations report modest but consistent gains on standard cognitive scales such as the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) after acupuncture-based interventions [8]. Among the acupoints used in practice, Fengchi (GB20) is notable because of its proximity to vertebrobasilar vessels and brainstem structures; stimulation at this site has been associated with transient increases in cerebral blood velocity and functional improvements in ischemic models and some small clinical series [9]. For mechanistic studies and objective outcome assessment, transcranial Doppler (TCD) indices offer a practical way to quantify changes in cerebral hemodynamics and to link those changes to clinical effects [10].

Aromatherapy and other smell-based interventions are increasingly being tested as low-burden additions to standard care for cognitive disorders. Their attraction in clinical settings is straightforward: they are non-invasive, simple to deliver, and generally well accepted by patients. Olfactory input projects directly to limbic structures and can therefore influence networks involved in memory and emotion; it also has downstream effects on neuroendocrine and immune signaling, which may be relevant to recovery after brain injury [11]. *Acorus tatarinowii (Acorus calamus)* yields a volatile oil whose main active constituents, α-asarone and β-asarone, have shown antioxidant, anti-inflammatory and neuroprotective actions in animal and cellular studies. Preclinical work reports that these constituents improve learning and memory across several experimental models [12]. Mechanistic investigations suggest that such effects may be mediated through the regulation of key signaling pathways, including phosphoinositide 3-kinase/protein kinase B (PI3K/AKT) and inhibition of the NOD-like receptor family pyrin domain containing 3 (NLRP3) inflammasome [13]. More recent investigations further indicate that inhaled *Acorus* oil can dampen neuroinflammation, support neuronal repair processes and influence pathways related to insulin resistance, findings that strengthen its biological plausibility as an adjunctive neuroprotective agent after stroke [14].

Viewed together, acupuncture and *Acorus* oil address post-stroke cognitive impairment from different angles: needling is thought to influence regional perfusion and neural plasticity, while inhaled volatile compounds may act through anti-inflammatory and neuroprotective mechanisms. Yet clinical data on the two therapies used in combination are scarce, and it remains unclear whether any clinical benefit is accompanied by measurable changes in cerebral haemodynamics. To explore this question, we designed the present retrospective cohort study to compare Fengchi (GB20) electroacupuncture alone with the same acupuncture plus *Acorus tatarinowii* oil inhalation, assessing cognitive outcomes (MMSE, MoCA), daily function (Modified Barthel Index, MBI) and transcranial Doppler-derived flow indices. If the combined approach proves effective, it would offer a practical, well-tolerated adjunct to existing PSCI rehabilitation strategies and provide a rationale for testing the intervention in prospective randomized trials.

Materials and methods

Study design and grouping

This retrospective cohort study was conducted at Zhejiang Provincial People's Hospital and enrolled patients treated between January 2022 and December 2024. Selection of the rehabilitation approach was made by the attending physician according to each patient's clinical status, traditional Chinese medicine (TCM) syndrome differentiation and individualized rehabilitation needs. Before initiating therapy, clinicians discussed with patients (or their legal representatives) the two treatment options - Fengchi (GB20) electroacupuncture alone or Fengchi electroacupuncture combined with inhalation of *Acorus tatarinowii* essential oil - including expected effects, limitations and procedural steps. Because treatment assignment reflected routine clinical practice and was documented in the electronic medical record (EMR), group allocation was non-randomized. The study complied with the Declaration of Helsinki and was approved by the Zhejiang Provincial People's Hospital Ethics Committee (Approval No. ZJPPH-ER-2024-(040)). Given the retrospective design, the committee waived the need for re-consent.

Data retrieval

Study subjects were identified by cross-referencing the hospital EMR with the rehabilitation assessment database. We screened all stroke patients who underwent continuous rehabilitation for at least three months during the study interval (January 2022-December 2024) and included those who satisfied our predefined inclusion and exclusion criteria for post-stroke cognitive impairment (PSCI). Extracted data were anonymized prior to analysis to protect patient confidentiality.

Inclusion and exclusion criteria

Inclusion criteria: 1. Diagnosis of PSCI in accordance with the Chinese Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke (2014) [15]. 2. Diagnosis of "phlegm-stasis interlocking" pattern based on TCM syndrome differentiation for PSCI, characterized by primary symptoms including memory loss, irritability, insomnia, limb weakness, dizziness, poor appetite, constipation, pale complexion, greasy tongue coating, and rapid pulse [16]. 3. No exposure to other cognitive-enhancing drugs or rehabilitation therapies within the previous 3 months. 4. Patients and their families were fully informed and consented to the treatment. 5. Complete and traceable medical records and treatment documentation.

Exclusion criteria: 1. Pre-existing cognitive impairment or neurodegenerative disease prior to stroke onset. 2. Severe cardiac, hepatic, or renal dysfunction. 3. Presence of immune system disorders or active infections. 4. Needle phobia or skin lesions at acupuncture sites. 5. Missing treatment records exceeding 20% or interruption of therapy for ≥ 7 consecutive days.

Interventions

Based on the actual rehabilitation regimen recorded in the electronic medical records, patients were assigned to one of the following two groups: the acupuncture group (n = 125) and the combined essential oil-acupuncture group (n = 110).

Acupuncture group: Patients received routine rehabilitation therapy in combination with bilateral Fengchi (GB20) electroacupuncture. All acupuncture treatments were performed by licensed acupuncturists with at least five years of clinical experience. Fengchi (GB20) was localized according to the National Standard for Acupoint Location (GB/T 12346-2021). Sterile disposable needles (0.30 × 40 mm) were inserted obliquely toward the tip of the nose to a depth of 20-25 mm. Upon achieving deqi, the needles were connected to a KWD-808 Series I pulse acupuncture device, using a sparse wave pattern with slight head movement. Each session lasted 30 minutes, administered once daily, five times per week, for a continuous duration of three months.

Combined essential oil-acupuncture group: In addition to the electroacupuncture protocol described above, patients received inhalation therapy with Acorus tatarinowii essential oil. The essential oil was prepared by hospital pharmacists, with 0.4 mL diluted in 20 mL of room-temperature purified water and placed in the diffuser tray within a 50 × 40 × 30 cm enclosed plastic chamber. For aromatherapy administration, the Acorus tatarinowii preparation was placed in a gently warmed reservoir and the resulting vapour was delivered to the patient via a nasal cannula. Each inhalation session, lasted 30 minutes, was performed three times per day, and was scheduled to coincide with the electroacupuncture treatments. Every application was recorded in the nursing and treatment charts to ensure full traceability.

Routine rehabilitation program: Both treatment arms received the same standardized post-stroke rehabilitation package, comprising cognitive retraining, motor exercises, balance and gait re-education, occupational therapy, psychological support, and guideline-directed secondary prevention medications (for example, antiplatelet agents, statins, antihypertensives and glucose-lowering drugs as indicated). All rehabilitation sessions were delivered in a dedicated rehabilitation unit by therapists who had completed standardized training.

Data extraction

Extraction procedure: Two trained researchers independently abstracted data from the electronic medical record into a prespecified data collection form, following a written extraction manual to promote consistency. Collected variables included demographic and clinical characteristics (age, sex, and years of education), stroke subtype (ischemic or hemorrhagic), interval from stroke onset to enrollment (days), and comorbidities or exposures (hypertension, diabetes mellitus, coronary heart disease, smoking and alcohol use). Baseline clinical scores comprised the National Institutes of Health Stroke Scale (NIHSS), Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA). Primary outcomes at three months after treatment included MMSE, MoCA, the Modified Barthel Index (MBI) and TCD-derived cerebral hemodynamic indices.

Data integrity and discrepancy handling: Two trained researchers independently extracted data and compared their entries. Any disagreement was settled by a third reviewer who checked the source records. Records lacking essential information (for example, baseline or three-month cognitive assessments) or without adequate follow-up were removed from the analysis.

Outcome measures

Timing: All outcomes were collected at baseline and at three months after treatment, with a ±14-day allowance; assessments outside this window were excluded. Cognitive testing was performed by rehabilitation therapists who had completed standardized training and was entered directly into the electronic record at the time of assessment. All transcranial Doppler (TCD) studies were acquired by a single qualified neurosonographer who remained blinded to group assignment.

Primary outcomes: Primary outcome measures focused on changes in Mini-Mental State Examination (ΔMMSE) and Montreal Cognitive Assessment (ΔMoCA) scores from baseline to the 3-month post-treatment follow-up. The MMSE consists of 30 items, with a total score ranging up to 30; lower scores correspond to more severe cognitive deficits [17]. The MoCA assesses eight distinct cognitive domains, also with a maximum total score of 30, and scores of ≥ 26 are regarded as within the normal cognitive range [18].

Secondary outcomes. Secondary endpoints comprised functional ability, assessed by the Modified Barthel Index (MBI; 10 items, maximum score 100, higher score = greater independence), and cerebral hemodynamic indices obtained by TCD [19]. TCD was performed with a DWL-P system (DWL, Germany) while the patient lay supine and rested. Mean flow velocities (MFV, cm/s) were sampled from standard acoustic windows in the middle (MCA), anterior (ACA) and posterior (PCA) cerebral arteries and the intracranial vertebral artery (VA); the higher MFV from either side was used for the analysis.

Data handling. Two trained researchers entered data independently and cross-checked entries; a third investigator adjudicated any discrepancies against source records. Records with missing key variables (for example, baseline or three-month cognitive scores) or inadequate follow-up were excluded from the final dataset.

Statistical analysis

Sample size calculation for ΔMMSE was based on the assumption of equal variances between the groups, with a pooled standard deviation of 3.5 [20, 21]. The control group (acupuncture alone) was assumed to have a baseline ΔMMSE of 4.0 [20], and the minimum clinically meaningful additional improvement for the combination therapy group was set at 1.5 points, as an increase of 1-2 MMSE points can significantly enhance patients' daily cognitive function [20]. Using a two-sided $\alpha = 0.05$ and a two-sample t-test assuming equal variances, the estimated sample sizes were 86 per group for 80% power and 115 per group for 90% power. Following 1:1 propensity score matching, each group included 92 patients, corresponding to an estimated statistical power of approximately 82.8%, which was sufficient to detect the prespecified 1.5-point difference.

1:1 propensity score matching (PSM) was conducted via logistic regression. Propensity scores (probability of assignment to the combination group) were estimated incorporating covariates: age, sex, years of education, stroke subtype (ischemic/hemorrhagic), onset-to-enrollment time, baseline NIHSS/MMSE/MoCA scores, and comorbidities (hypertension, diabetes, coronary artery disease, smoking, alcohol consumption). Nearest neighbor matching was used with a caliper width of 0.2 × standard deviation (SD) of the logit propensity score. After propensity-score matching, baseline covariate balance was evaluated using standardized mean differences (SMDs); an SMD < 0.10 was taken to indicate acceptable balance and thus adequate attenuation of baseline imbalance. Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS, version 26.0; IBM Corp., Armonk, NY, USA) and R (version 4.2.1, R Foundation for Statistical Computing). Continuous variables were screened for normality with the Shapiro-Wilk test and for equality of variances with Levene's test. Variables meeting the assumptions of normality and homoscedasticity are reported as mean ± standard deviation and compared with independent-samples t tests. Non-normally distributed measures are presented as median (interquartile range) and compared using nonparametric tests (Mann-Whitney U for between-group comparisons; Wilcoxon signed-rank or paired t as appropriate for within-subject comparisons). Categorical data are summarized as counts (percentages) and analyzed by χ^2 tests (or Fisher's exact test when cell counts were small). All hypothesis tests were two-sided, and P < 0.05 was considered statistically significant.

To quantify the relationship between treatment and cognitive change, we fitted multivariable linear regression models with change scores (ΔMMSE or ΔMoCA) as the dependent variable. The main predictor was treatment assignment (combination therapy versus acupuncture alone), and covariates included age, sex, years of education, stroke subtype, baseline cognitive score, NIHSS, hypertension, diabetes, coronary artery disease, smoking, and alcohol use. Regression coefficients (β) with associated t statistics and *P* values are reported; coefficient plots and residual diagnostics were used to inspect model fit and verify assumptions.

For dichotomous endpoints - defined a priori as a clinically meaningful improvement (ΔMMSE ≥ 2, and as a stricter criterion ΔMMSE ≥ 2 together with ΔMoCA ≥ 2) - we first ran univariate logistic regressions to screen candidate predictors. Variables with suggestive associations were entered into multivariable logistic regression models to estimate adjusted odds ratios (ORs) with 95% confidence intervals. All models were examined for plausibility and multicollinearity, and results are presented with two-sided *P* values.

Results

Baseline characteristics

Prior to propensity score matching (PSM), the study included 125 patients in the acupuncture group and 110 in the combined treatment group. There were no significant differences between groups regarding age, years of education, or baseline MMSE, MoCA, and MBI scores (all P > 0.05). However, the time from stroke onset to enrollment was significantly longer in the acupuncture plus *Acorus tatarinowii* essential oil group compared with the acupuncture-only group [49.0 (41.0-58.0) vs 44.0 (36.0-53.0) days; Z = -2.79, P = 0.005]. Baseline NIHSS scores were also slightly higher in the combined treatment group [6.0 (5.0-7.0) vs 5.0 (5.0-7.0); Z = -2.33, P = 0.020] (**Table 1**).

Following 1:1 PSM, 92 patients remained in each group (**Figure 1**). Post-matching comparisons indicated no significant differences in demographic or clinical characteristics, including age, years of education, baseline cognitive and functional scores (MMSE, MoCA, MBI), time from stroke onset to enrollment, NIHSS, or comorbidity distribution (all P > 0.05). Standardized mean differences (SMDs) for all covariates were < 0.1, demonstrating adequate balance between the groups (**Table 2**).

Effects of treatment on cognitive function, daily living ability, and cerebral hemodynamics

At baseline, there were no significant differences between the groups in MMSE, MoCA, or MBI scores (all P > 0.05), confirming comparable cognitive and functional status prior to intervention. At the 3-month follow-up, both treatment arms demonstrated clear improvements across all outcome measures when compared with baseline values (all P < 0.001).

In patients receiving acupuncture alone, MMSE scores increased by an average of 4.66 ± 3.92 points, while MoCA and MBI scores rose by 5.84 ± 3.71 and 13.68 ± 9.74 points, respec-

Table 1. Baseline characteristics before propensity score matching

Variable	Acupuncture (n = 125)	Combined (n = 110)	Statistic	*P*	SMD
Age, Mean ± SD	62.39 ± 7.74	63.36 ± 7.59	t = -0.963	0.337	0.127
Education years, Mean ± SD	8.99 ± 2.77	8.72 ± 2.73	t = 0.769	0.442	-0.101
MMSE baseline, Mean ± SD	18.62 ± 3.54	17.93 ± 3.45	t = 1.515	0.131	-0.201
MoCA baseline, Mean ± SD	16.81 ± 3.63	16.98 ± 3.37	t = -0.372	0.71	0.051
MBI baseline, Mean ± SD	62.10 ± 9.03	61.27 ± 9.50	t = 0.687	0.493	-0.087
Onset-to-enrollment time, M (Q_1, Q_3)	44.00 (36.00, 53.00)	49.00 (41.00, 58.00)	Z = -2.79	0.005	-0.335
NIHSS, M (Q_1, Q_3)	5.00 (5.00, 7.00)	6.00 (5.00, 7.00)	Z = -2.33	0.02	-0.25
Sex, n (%)			X^2 = 0.104	0.748	
Female	48 (38.40)	40 (36.36)			-0.042
Male	77 (61.60)	70 (63.64)			0.042
Ischemic stroke, n (%)	101 (80.80)	94 (85.45)	χ^2 = 0.897	0.343	0.132
Hypertension, n (%)	73 (58.40)	71 (64.55)	χ^2 = 0.931	0.335	0.128
Diabetes, n (%)	79 (63.20)	82 (74.55)	χ^2 = 3.491	0.062	-0.26
Coronary heart disease, n (%)	23 (18.40)	12 (10.91)	χ^2 = 2.590	0.108	-0.24
Smoking, n (%)	28 (22.40)	23 (20.91)	χ^2 = 0.077	0.782	-0.037
Drinking, n (%)	22 (17.60)	29 (26.36)	χ^2 = 2.645	0.104	0.199

t: t-test, Z: Mann-Whitney test, χ^2: Chi-square test, SD: standard deviation, M: median, Q_1: first quartile, Q_3: third quartile; SMD: standardized mean difference; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment; MBI: Modified Barthel Index; NIHSS: National Institutes of Health Stroke Scale.

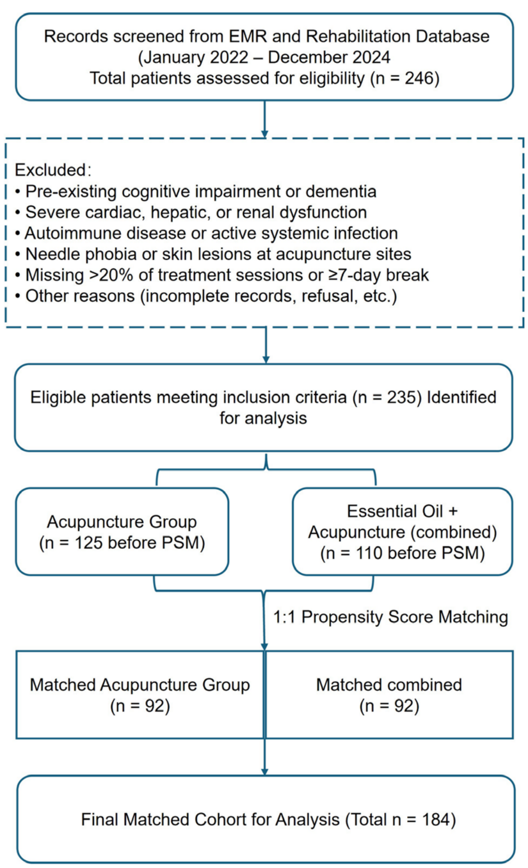

Figure 1. Flow diagram of patient enrollment and grouping.

tively. In contrast, participants treated with the combined regimen achieved larger gains, with mean increases of 6.41 ± 3.96 points in MMSE, 7.04 ± 3.85 points in MoCA, and 22.07 ± 12.05 points in MBI. Direct comparisons between groups showed that improvements in cognitive performance and daily functioning were significantly greater in the combined treatment group (MMSE: P < 0.001; MoCA: P < 0.01; MBI: P < 0.001; **Figure 2**).

With respect to cerebral hemodynamics, mean flow velocities (MFVs) of the major intracranial arteries were comparable between the groups at baseline, with no statistically significant differences detected (all P > 0.05). After three months, MFVs increased significantly in both groups (all P < 0.001). In the acupuncture-only group, ΔMFVs were as follows: MCA, 7.07 ± 8.71 cm/s; ACA, 5.48 ± 8.90 cm/s; PCA, 5.87 ± 7.89 cm/s; VA, 5.90 ± 6.57 cm/s. In the combined treatment group, corresponding ΔMFVs were 9.74 ± 8.47, 8.34 ± 9.23, 9.32 ± 7.29, and 8.20 ± 7.13 cm/s. Between-group comparisons demonstrated significantly greater MFV improvements in the combined treatment group for all four arteries (MCA: P = 0.036; ACA: P = 0.034; PCA: P = 0.002; VA: P = 0.024), suggesting that adjunct *Acorus tatarinowii* essential oil

Table 2. Baseline characteristics after propensity score matching

Variable	Acupuncture (n = 92)	Combined (n = 92)	Statistic	P	SMD
Age, Mean ± SD	62.58 ± 7.62	63.50 ± 7.75	t = -0.814	0.416	0.08
Education years, Mean ± SD	9.04 ± 2.85	8.91 ± 2.68	t = 0.309	0.757	0.06
MMSE baseline, Mean ± SD	18.13 ± 3.66	18.15 ± 3.30	t = -0.036	0.971	0.02
MoCA baseline, Mean ± SD	16.98 ± 3.62	17.10 ± 3.44	t = -0.225	0.822	0.03
MBI baseline, Mean ± SD	62.89 ± 9.42	61.18 ± 10.04	t = 1.191	0.235	0.09
Onset-to-enrollment time, M (Q_1, Q_3)	46.50 (39.00, 55.50)	45.00 (38.75, 52.00)	Z = -0.694	0.488	0.08
NIHSS, M (Q_1, Q_3)	6.00 (5.00, 7.00)	5.00 (5.00, 6.25)	Z = -1.915	0.055	0.09
Sex, n (%)			χ^2 = 0.214	0.644	
Female	34 (36.96)	31 (33.70)			-0.069
Male	58 (63.04)	61 (66.30)			0.069
Ischemic stroke, n (%)	75 (81.52)	81 (88.04)	χ^2 = 1.516	0.218	0.08
Hypertension, n (%)	57 (61.96)	59 (64.13)	χ^2 = 0.093	0.76	0.05
Diabetes, n (%)	26 (28.26)	24 (26.09)	χ^2 = 0.110	0.74	0.04
Coronary heart disease, n (%)	11 (11.96)	11 (11.96)			
Smoking, n (%)	21 (22.83)	20 (21.74)	χ^2 = 0.031	0.859	0.03
Drinking, n (%)	16 (17.39)	24 (26.09)	χ^2 = 2.044	0.153	0.09

t: t-test, Z: Mann-Whitney test, χ^2: Chi-square test, SD: standard deviation, M: median, Q_1: 1st quartile, Q_3: 3st quartile; SMD: standardized mean difference; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment; MBI: Modified Barthel Index; NIHSS: National Institutes of Health Stroke Scale.

therapy produced a more pronounced enhancement of cerebral perfusion (**Table 3**).

To visualize cerebral hemodynamic alterations following intervention, representative transcranial Doppler (TCD) waveforms were selected. Before treatment, patients in the acupuncture-only group showed suboptimal signal penetration through the right temporal acoustic window, together with relatively low baseline blood flow velocities (**Figure 3A**). After the intervention, flow velocity increased slightly, indicating a limited but detectable improvement in cerebral circulation (**Figure 3B**). In the combined therapy group, the mean flow velocity (MFV) of the right vertebral artery was likewise reduced at baseline (**Figure 3C**). In contrast, post-treatment TCD recordings demonstrated a marked rise in MFV in several intracranial arteries (**Figure 3D**). These findings suggest that the combined intervention produced a more pronounced enhancement of cerebral perfusion compared with electroacupuncture alone.

Multiple linear regression analysis: independent effect of combined therapy on cognitive improvement

To further evaluate the independent contribution of the combined intervention to cognitive outcomes, multivariable linear regression models were constructed using changes in cognitive scores (ΔMMSE and ΔMoCA) as dependent variables. Treatment modality (combined therapy vs acupuncture alone) was entered as the primary explanatory variable, while potential confounders - including age, sex, educational attainment, stroke subtype, baseline NIHSS score, and other clinically relevant factors - were included as covariates. After adjustment, patients receiving combined therapy exhibited significantly greater improvement in MMSE scores compared with those treated with acupuncture alone (β = 1.84, t = 4.32, P < 0.001). Educational level was positively associated with MMSE change (β = 0.16, t = 1.99, P = 0.048), as was a history of smoking (β = 1.03, t = 1.99, P = 0.048). Baseline MMSE score showed an inverse relationship with the magnitude of improvement (β = -0.75, t = -12.2, P < 0.001), indicating that individuals with poorer initial cognitive performance tended to achieve larger absolute gains (**Figure 4A**). Examination of model residuals revealed no obvious deviation from normality or heteroscedasticity, supporting the robustness of the regression assumptions (**Figure 4B**).

A similar pattern emerged for MoCA. Combined therapy remained a significant positive correlate of ΔMoCA (β = 1.27; t = 2.78; P = 0.006),

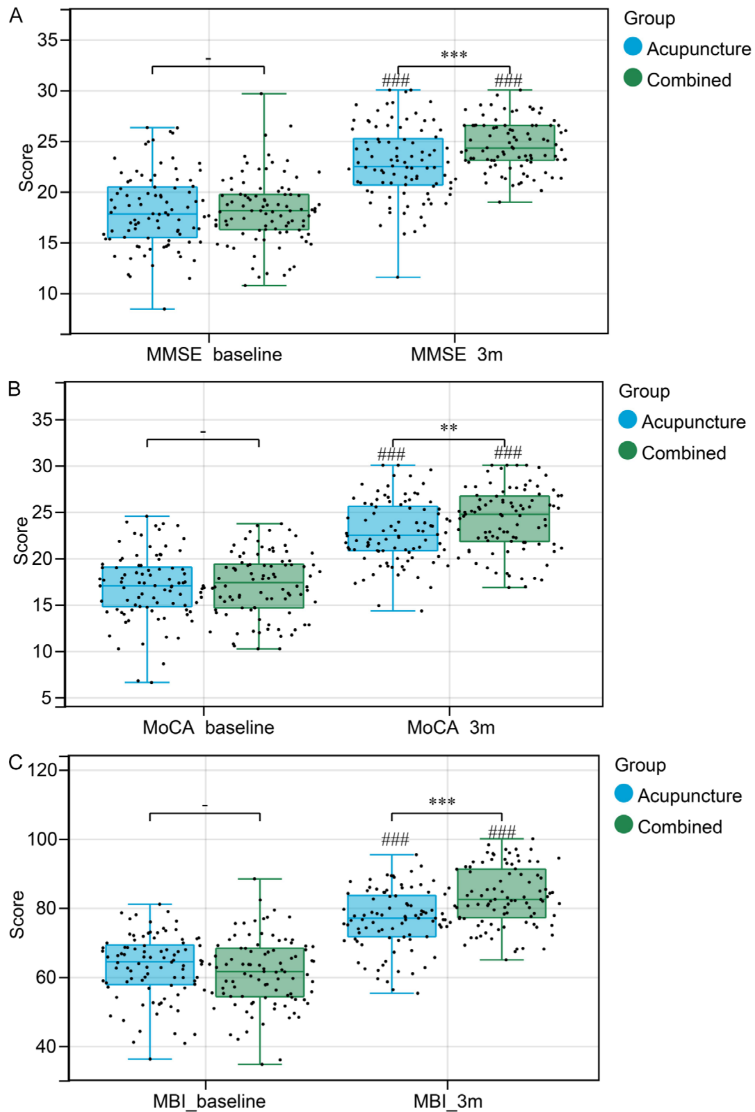

Figure 2. Changes in Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), and Modified Barthel Index (MBI) scores before and after treatment. A: MMSE. B: MoCA. C: MBI. **P < 0.01, ***P < 0.001 between-group comparisons; ###P < 0.001 within-group comparisons.

whereas baseline MoCA was inversely related to the amount of change (β = -0.61; t = -9.38; P < 0.001). Residual plots for the MoCA model did not reveal obvious departures from homoscedasticity or normality (**Figure 5A**, **5B**).

Multiple logistic regression: independent predictors of clinically effective cognitive improvement

We next examined binary endpoints defined as clinically meaningful improvement (ΔMMSE ≥ 2, and the combined criterion ΔMMSE ≥ 2 with ΔMoCA ≥ 2). In univariate logistic screens (**Table 4**), intervention group, baseline MMSE, baseline MCA mean flow velocity, and smoking history were associated with effective cognitive recovery (all P < 0.05). Other candidate variables showed no significant univariate relationships.

In the multivariable logistic model (**Table 5**), assignment to the combined therapy increased the odds of achieving clinically meaningful improvement (OR = 2.19; 95% CI: 1.05-4.56; P = 0.036). Higher baseline MMSE reduced the likelihood of such improvement (OR = 0.79 per point; 95% CI: 0.70-0.89; P < 0.001), consistent with the regression results that participants with lower baseline scores had larger absolute gains. Baseline mean flow velocity in the middle cerebral artery was also inversely associated with the outcome (OR = 0.95 per unit; 95% CI: 0.91-0.99; P = 0.045), suggesting that initial cerebral perfusion status influenced recovery. Other covariates did not retain significance after the adjustment (all P > 0.05).

To evaluate the predictive accuracy of the multivariable logistic model, we constructed a receiver operating characteristic (ROC) curve (**Figure 6A**). The area under the curve was 0.83 (95% CI, 0.77-0.89), indicating good discriminative ability. A waterfall chart (**Figure 6B**) decomposed individual risk estimates and highlighted that treatment group and baseline MMSE accounted for the largest shifts in predicted risk. Calibration assessment (**Figure 6C**) showed close concordance between predicted probabilities and observed event rates; the bias-corrected calibration curve closely followed the 45° identity line. Decision curve analysis (**Figure 6D**) further demonstrated net clinical benefit of the model over both “treat-all” and “treat-none” approaches across a wide span of deci-

Table 3. Comparison of transcranial Doppler (TCD) parameters between the two groups

Variables	Acupuncture (n = 92)	Combined (n = 92)	Statistic	*P*
MCA baseline, Mean ± SD	53.81 ± 8.42	54.30 ± 7.59	t = -0.42	0.678
MCA 3m, Mean ± SD	60.87 ± 8.32***	64.04 ± 8.48***	t = -2.56	0.011
ΔMCA, Mean ± SD	7.07 ± 8.71	9.74 ± 8.47	t = -2.11	0.036
ACA baseline, Mean ± SD	50.28 ± 8.44	49.83 ± 7.55	t = 0.38	0.707
ACA 3m, Mean ± SD	55.76 ± 8.12***	58.17 ± 7.23***	t = -2.13	0.035
ΔACA, Mean ± SD	5.48 ± 8.90	8.34 ± 9.23	t = -2.13	0.034
PCA baseline, Mean ± SD	47.65 ± 7.61	47.04 ± 7.85	t = 0.54	0.59
PCA 3m, Mean ± SD	53.52 ± 7.10***	56.35 ± 6.93***	t = -2.74	0.007
ΔPCA, Mean ± SD	5.87 ± 7.89	9.32 ± 7.29	t = -3.08	0.002
VA baseline, Mean ± SD	42.88 ± 7.36	44.00 ± 7.20	t = -1.05	0.297
VA 3m, Mean ± SD	48.78 ± 7.42***	52.20 ± 7.22***	t = -3.17	0.002
ΔVA, Mean ± SD	5.90 ± 6.57	8.20 ± 7.13	t = -2.28	0.024

MCA: middle cerebral artery; ACA: anterior cerebral artery; PCA: posterior cerebral artery; VA: intracranial segment of the vertebral artery; unit: cm/s; Δ = post-treatment - pre-treatment; t = t-test; SD = standard deviation; ***P < 0.001, within-group comparison.

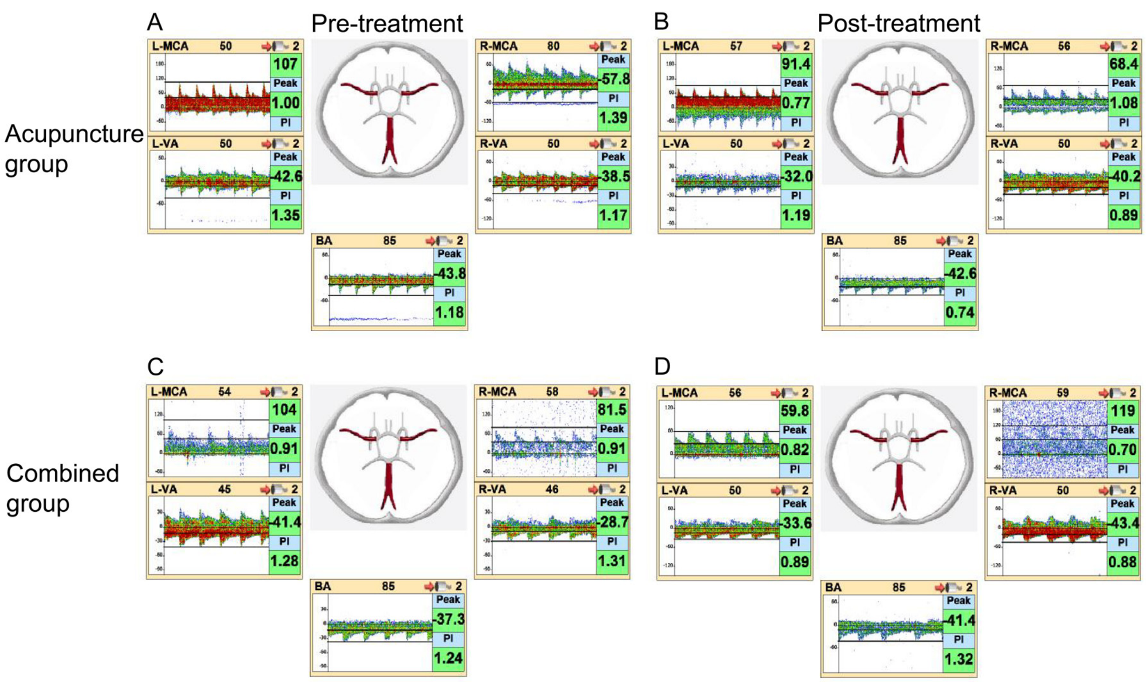

Figure 3. Representative transcranial Doppler (TCD) tracings of cerebral arterial flow velocity in different groups and time points. A: Acupuncture group, pre-treatment. B: Acupuncture group, post-treatment. C: Combined treatment group, pre-treatment. D: Combined treatment group, post-treatment.

sion thresholds, supporting its potential applicability in clinical decision making.

Discussion

Propensity score matching produced well-balanced groups with respect to demographic and clinical baseline variables, thereby reducing the chance that post-treatment differences simply reflected preexisting imbalance. Over the three-month rehabilitation course both arms showed measurable improvements in global cognition (MMSE, MoCA) and activities of daily living (MBI); however, gains were consistently larger in patients who received acupuncture together with inhalation of *Acorus tatarinowii* essential oil. This pattern suggests an incremental benefit when the herbal volatile oil is added to elec-

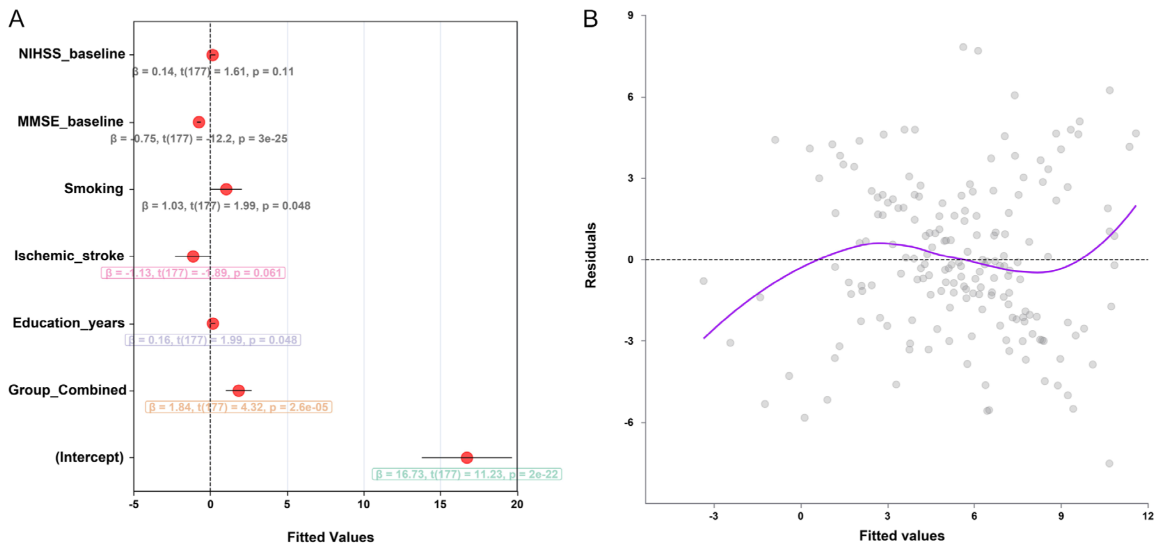

Figure 4. Multiple linear regression analysis for changes in Mini-Mental State Examination (ΔMMSE). A: Coefficient plot displaying regression coefficients (β), t values, and *P* values for each independent variable. B: Residual plot showing fitted values (x-axis) versus residuals (y-axis).

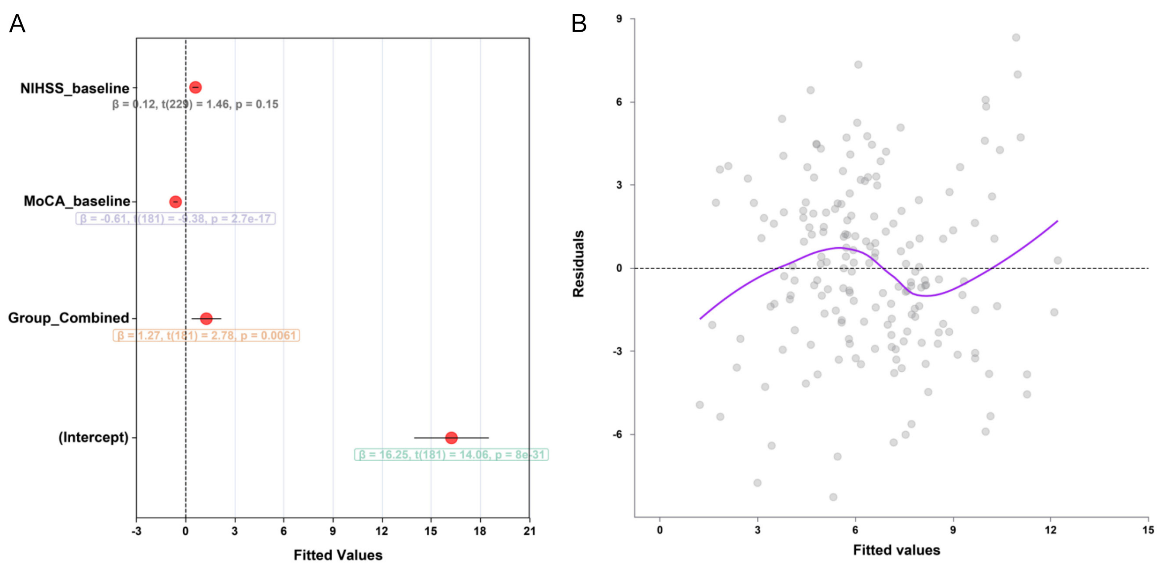

Figure 5. Multiple linear regression analysis for changes in Montreal Cognitive Assessment (ΔMoCA). A: Coefficient plot displaying β coefficients, *t*-values, and *P*-values. B: Residual plot showing fitted values (x-axis) versus residuals (y-axis).

troacupuncture. These findings are concordant with randomized trials and meta-analyses that report modest but reproducible cognitive gains after acupuncture in post-stroke populations, effects commonly ascribed to improved cerebral perfusion, promotion of neuroplasticity, and dampening of post-stroke inflammatory processes [20, 22]. Our data reinforce acupuncture's role in rehabilitation [23] and extend the literature by providing clinical evidence that adjunctive administration of *Acorus tatarinowii* - delivered by inhalation or topical application - may amplify those therapeutic effects.

Mechanistically, *Acorus tatarinowii* contains lipophilic volatile components, notably α-asarone and β-asarone, which can cross biological barriers and reach central nervous system targets. Preclinical work indicates that these compounds can limit neuronal apoptosis, reduce pathological aggregates (amyloid-β, phosphorylated tau), and promote synaptic function,

Table 4. Univariate logistic regression analysis of factors associated with cognitive improvement

Variables	β	S.E	Z	P	OR (95% CI)
Intercept	2.05	0.68	2.99	0.003	7.78 (2.01-30.12)
Group	-	-	-	-	-
Acupuncture	-	-	-	-	1.00 (Reference)
Combined	0.85	0.37	2.3	0.028	2.35 (1.16-4.76)
Male (vs Fmale)	-0.26	0.38	-0.68	0.496	0.77 (0.36-1.65)
Ischemic stroke (vs Hemorrhagic stroke)	-0.08	0.52	-0.15	0.88	0.92 (0.34-2.51)
Hypertension (Yes vs No)	-0.55	0.39	-1.41	0.158	0.58 (0.27-1.26)
Diabetes (Yes vs No)	0.01	0.42	0.02	0.984	1.01 (0.44-2.33)
Coronary heart disease (Yes vs No)	0.22	0.61	0.36	0.718	1.25 (0.38-4.12)
Smoking (Yes vs No)	-0.79	0.43	-1.84	0.068	0.45 (0.19-1.06)
Drinking (Yes vs No)	0.1	0.44	0.23	0.817	1.11 (0.46-2.68)
Age	-0.01	0.03	-0.33	0.741	0.99 (0.94-1.04)
Education years	-0.06	0.07	-0.86	0.39	0.94 (0.82-1.08)
MMSE baseline	-0.25	0.06	-4.2	< .001	0.78 (0.69-0.88)
MoCA baseline	-0.11	0.06	-1.83	0.067	0.90 (0.80-1.01)
MBI baseline	-0.01	0.02	-0.5	0.616	0.99 (0.96-1.03)
MCA baseline (cm/s)	-0.06	0.02	-2.1	0.032	0.94 (0.90-0.99)
ACA baseline (cm/s)	0.01	0.02	0.5	0.617	1.01 (0.97-1.06)
PCA baseline (cm/s)	-0.01	0.03	-0.33	0.741	0.99 (0.94-1.04)
VA baseline (cm/s)	-0.02	0.03	-0.67	0.502	0.98 (0.93-1.03)
Onset-to-enrollment time	0.01	0.01	0.67	0.502	1.01 (0.98-1.04)
NIHSS baseline	0.01	0.08	0.12	0.904	1.01 (0.86-1.18)

β: regression coefficient; S.E: standard error; Z: Z statistic; P: probability value; OR: odds ratio; CI: confidence interval; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment; MBI: Modified Barthel Index; NIHSS: National Institutes of Health Stroke Scale; MCA: middle cerebral artery; ACA: anterior cerebral artery; PCA: posterior cerebral artery; VA: intracranial segment of the vertebral artery. The dependent variable of the regression analysis is cognitive improvement efficacy, coded as: effective = 1 (both MMSE and MoCA scores increased by ≥ 2 points), ineffective = 0 (did not meet the criteria of simultaneous ≥ 2-point increase in MMSE and MoCA scores).

thereby improving learning and memory in animal models [24, 25]. Aromatherapy more broadly has been associated with improvements in mood, sleep, and certain cognitive domains in clinical and experimental settings, effects plausibly mediated by olfactory-limbic and neuroimmune pathways [26]. Putting these pieces together, a plausible explanation for our findings is the complementary action at different levels: acupuncture may modulate regional blood flow and cortical excitability when applied to points such as Baihui (GV20) or Fengchi (GB20), while *Acorus* oil may exert neuroprotective and anti-inflammatory effects after central uptake [14, 27]. The combination could therefore target both hemodynamic and cellular contributors to post-stroke cognitive impairment, which would account for the larger improvements in MMSE, MoCA and MBI observed in the combined group [28].

From a hemodynamic standpoint, patients who received acupuncture plus *Acorus tatarinowii* oil showed larger rises in mean flow velocity (MFV) across the major intracranial vessels (MCA, ACA, PCA and VA) than those treated with acupuncture alone. Earlier work using transcranial Doppler reported that acupuncture can raise bilateral cerebral arterial velocities in stroke cohorts [29]; our data suggest that adding *Acorus* oil augments that response. The mechanism is uncertain, but several routes are plausible. The volatile constituents of *Acorus* may improve endothelial responsiveness and thus facilitate vasodilation (for example via nitric oxide pathways), or they may blunt perivascular inflammation and sympathetic drive, both of which would tend to increase regional perfusion. Meanwhile, needling at scalp and cervical points (e.g., Fengchi [GB20], Baihui [GV20]) has been linked to local vasomotor

Table 5. Multiple logistic regression analysis of predictors of effective cognitive improvement

Variables	β	S.E	Z	*P*	OR (95% CI)
Intercept	2.13	0.72	2.96	0.003	8.42 (2.10-33.74)
Group					
Acupuncture					1.00 (Reference)
Combined	0.78	0.37	2.09	0.036	2.19 (1.05-4.56)
Male	-0.24	0.39	-0.62	0.535	0.78 (0.36-1.69)
Ischemic stroke	-0.05	0.53	-0.09	0.93	0.95 (0.34-2.68)
Hypertension	-0.58	0.4	-1.44	0.149	0.56 (0.25-1.23)
Diabetes	0.03	0.43	0.08	0.94	1.03 (0.44-2.41)
Coronary heart disease	0.25	0.62	0.40	0.69	1.28 (0.38-4.33)
Smoking	-0.76	0.44	-1.71	0.087	0.47 (0.20-1.12)
Drinking	0.12	0.45	0.27	0.789	1.13 (0.46-2.74)
Age	0	0.03	-0.02	0.984	1.00 (0.95-1.05)
Education years	-0.05	0.07	-0.63	0.526	0.96 (0.83-1.10)
MMSE baseline	-0.24	0.06	-4.00	< .001	0.79 (0.70-0.89)
MoCA baseline	-0.1	0.06	-1.80	0.073	0.91 (0.81-1.01)
MBI baseline	-0.01	0.02	-0.53	0.594	0.99 (0.95-1.03)
MCA baseline	-0.05	0.02	-2.00	0.045	0.95 (0.91-0.99)
ACA baseline	0.01	0.02	0.33	0.738	1.01 (0.96-1.06)
PCA baseline	-0.01	0.03	-0.53	0.594	0.99 (0.94-1.04)
VA baseline	-0.02	0.03	-0.66	0.512	0.98 (0.93-1.04)
Onset-to-enrollment time	0.01	0.01	0.65	0.517	1.01 (0.98-1.04)
NIHSS baseline	0.02	0.08	0.21	0.832	1.02 (0.87-1.19)

β: regression coefficient; S.E: standard error; Z: Z statistic; P: probability value; OR: odds ratio; CI: confidence interval; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment; MBI: Modified Barthel Index; NIHSS: National Institutes of Health Stroke Scale; MCA: middle cerebral artery; ACA: anterior cerebral artery; PCA: posterior cerebral artery; VA: intracranial segment of the vertebral artery. The dependent variable of the regression analysis is cognitive improvement efficacy, coded as: effective = 1 (both MMSE and MoCA scores increased by ≥ 2 points), ineffective = 0 (did not meet the criteria of simultaneous ≥ 2-point increase in MMSE and MoCA scores).

changes and microcirculatory remodeling [24]; the oil's effects could therefore act in concert with acupuncture at vascular and cellular levels. Importantly, the combined treatment remained an independent predictor of cognitive gain after adjustment for age, education and other confounders, and participants with lower baseline cognitive scores showed the largest absolute improvements. This pattern - greater perfusion change accompanied by larger clinical gains in those most impaired - is consistent with the idea that enhanced blood flow may contribute to recovery, although causality cannot be established from the present data [30].

The main practical contribution of this study is to test a simple, low-risk adjunct to standard acupuncture: inhaled or topically applied *Acorus tatarinowii* oil. As a natural product, the oil delivers lipophilic bioactives that can reach the central nervous system via olfactory routes or transdermal absorption at treated sites, and it is inexpensive and easy to deploy in routine rehabilitation settings [31]. Over three months the integrative protocol produced larger gains in cognition and daily function than acupuncture alone, suggesting a value for clinical translation. Looking ahead, aromatherapy could be combined with cognitive training and motor rehabilitation within a multimodal program designed to address the multiple drivers of post-stroke cognitive impairment; however, randomized, placebo-controlled trials and mechanistic studies are needed to define optimal dosing, delivery, and the specific biological pathways involved.

There are several important limitations to note. First, this was a single-center retrospective cohort study rather than a randomized trial. Although we used propensity score matching to even out baseline characteristics, unmeasured

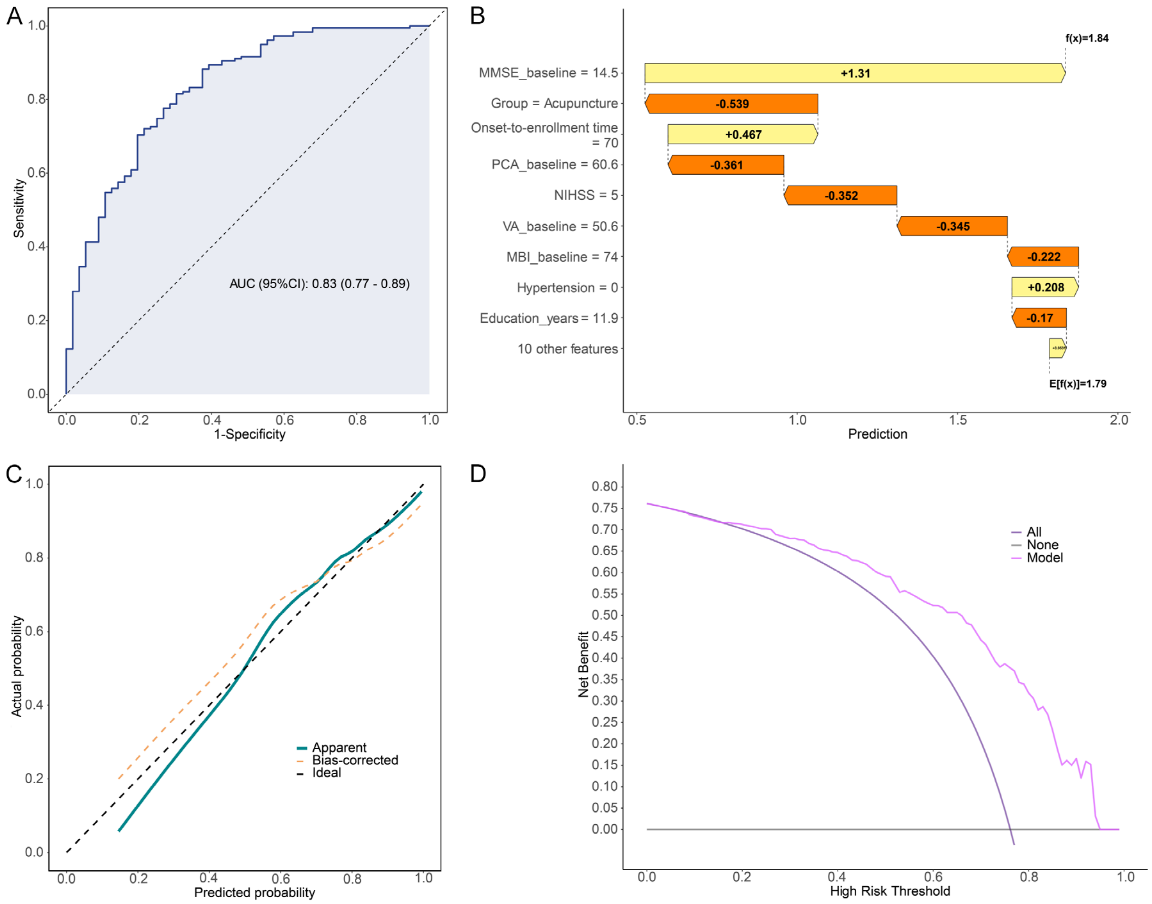

Figure 6. Validation of the multiple logistic regression model for predicting clinically effective cognitive improvement. A: Receiver operating characteristic (ROC) curve of the model, with an area under the curve (AUC) of 0.83 (95% confidence interval [CI]: 0.77-0.89). B: Individual-sample waterfall plot displaying the contribution magnitude of each predictor to single-sample predictions. positive/negative values indicate promoting/inhibiting effects on effective cognitive improvement. C: Calibration curve: the apparent curve (observed vs predicted probabilities), bias-corrected curve (after bootstrap adjustment), and the ideal 45° line (representing perfect calibration). D: Decision curve analysis: comparison of the model's net benefit with the "treat all" and "treat none" strategies across different high-risk thresholds.

confounders and residual selection bias - such as differences in patient adherence, unrecorded concurrent therapies, or incomplete documentation of baseline clinical data inherent to retrospective designs - cannot be completely ruled out. Retrospective data collection relies on existing medical records, which may introduce information bias due to inconsistent recording standards or missing data that were not prospectively tracked. Second, despite matching, the sample remained modest in size (n = 92 per group), and follow-up lasted only three months. These constraints limit our ability to comment on the durability of benefit or on longer-term safety, a limitation that is further amplified in retrospective studies where extended follow-up data may be less complete or harder to verify. Third, cognitive function was assessed using clinical scales (MMSE and MoCA) but we did not include objective neuroimaging or molecular biomarkers (for example, functional magnetic resonance imaging (fMRI), perfusion single-photon emission computed tomography (SPECT), amyloid-β or tau). In a retrospective setting, such objective measures are often not routinely collected in standard clinical records, which would have strengthened mechanistic inferences and reduced reliance on subjective measures if available. Fourth, given the retrospective nature of the study, we were unable to measure plasma or tissue levels of Acorus tatarinowii constituents nor systematically capture inhalation dose information from existing records. As a result, dose-response relationships remain uncharacterized and the intervention protocol cannot be fully standardized based on retrospective data alone.

Future work ought to prioritize multicenter, randomized, double-blind trials with larger samples and longer follow-up to validate the findings of this retrospective study. Incorporating multimodal imaging, inflammatory and neurodegenerative biomarkers, and pharmacokinetic assessments of the essential oil will be important next steps to clarify mechanisms and to optimize administration (dose, delivery route, frequency). Additionally, prospective data collection focused on standardized intervention protocols and detailed outcome measurements will help address the limitations inherent to retrospective analyses.

Conclusion

In this retrospective cohort study, adding Acorus tatarinowii essential oil inhalation to acupuncture produced larger short-term gains in cognition (MMSE, MoCA), activities of daily living (MBI), and cerebral mean flow velocities than acupuncture alone. The combined regimen remained an independent positive predictor of cognitive improvement after adjustment for key covariates. Taken together, the retrospective data support the feasibility of this integrative approach and provide a rationale for further prospective testing. Definitive recommendations will require randomized, placebo-controlled trials that examine dose, mechanism, and long-term outcomes, as these will help overcome the inherent limitations of retrospective observational designs.

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Disclosure of conflict of interest

None.

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