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How Do Language Domains Recover? A Domain-Specific Response Profile to Constraint-Induced Language Therapy in Chronic Post-Stroke Aphasia

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ABSTRACT

Background: Global aphasia scores, such as the Western Aphasia Battery (WAB) Aphasia Quotient (AQ), often obscure heterogeneous domain-specific responses to therapy, limiting tailored speech-language therapy (SLT) planning for chronic post-stroke aphasia (PSA). Understanding differential improvements in spontaneous speech, naming and reading, repetition and writing, and comprehension can optimize session design and goal prioritization, particularly in high-burden regions like Pakistan. **Objective:** To characterize domain-level changes in language function following Constraint-Induced Language Therapy (CILT) in chronic PSA to inform SLT micro-planning. **Methods:** A prospective pre-post cohort study enrolled 80 adults with chronic PSA from five Sialkot, Pakistan, centers. Participants received CILT (3 sessions/week, 60–90 minutes) for two months, involving graded verbal tasks constraining non-verbal strategies. WAB domain composites (spontaneous speech, naming and reading, repetition and writing, comprehension) and AQ were assessed pre- and post-therapy. Paired t-tests evaluated mean changes and percent-of-scale gains; AQ changes were modeled with paired correlations. **Results:** Spontaneous speech improved most (+12.60/20, 63%, $p < 0.001$, $d = 4.12$), followed by naming and reading (+10.04/20, 50.2%, $p < 0.001$, $d = 3.45$), repetition and writing (+9.88/20, 49.4%, $p < 0.001$, $d = 3.38$), and comprehension (+4.50/10, 45%, $p < 0.001$, $d = 2.35$). AQ rose from 24.51 ± 5.92 to 77.38 ± 8.48 ($p < 0.001$, $d = 5.71$), shifting all participants from severe/very severe to moderate/mild categories. **Conclusion:** CILT preferentially enhances expressive domains, particularly spontaneous speech, while yielding robust comprehension gains, guiding SLT to prioritize verbal output tasks for rapid recovery in chronic PSA.

Keywords

Post-stroke aphasia, Constraint-Induced Language Therapy, language domains, speech-language therapy, cognitive rehabilitation.

INTRODUCTION

Post-stroke aphasia (PSA) represents a significant complication of cerebrovascular events, affecting language production, comprehension, and overall communication in survivors, with chronic cases often persisting beyond the initial recovery phase and imposing long-term burdens on quality of life and functional independence (1). Constraint-Induced Language Therapy (CILT), adapted from principles of constraint-induced movement therapy, emphasizes intensive, forced verbal output while restricting non-verbal compensatory strategies such as gestures or writing, aiming to enhance neural plasticity and language recovery in individuals with chronic PSA (2). Despite its established efficacy in improving global aphasia quotients (AQ) as measured by tools like the Western Aphasia Battery (WAB), aggregate scores often mask heterogeneous responses across specific language domains, including spontaneous speech, naming and reading, repetition and writing, and comprehension, potentially leading to suboptimal therapy planning and resource allocation (3).

The problem lies in the reliance on global metrics that overlook domain-specific trajectories, which are crucial for tailoring speech-language therapy (SLT) sessions to maximize gains in expressive versus receptive skills. For instance, prior studies have demonstrated that intensive therapies like CILT preferentially boost expressive domains through massed practice and constraint mechanisms, yet comprehensive profiles detailing relative gains—such as percent-of-scale improvements—remain underexplored in chronic PSA cohorts from resource-limited settings like Pakistan, where stroke prevalence is high and rehabilitation access is uneven (4). This knowledge gap hinders clinicians' ability to prioritize drills, set realistic goals, and counsel patients, particularly when comorbidities like hypertension and diabetes, common in South Asian populations, may modulate recovery patterns (5). Addressing this justifies a focused examination of domain-level changes, building on evidence that expressive-forward interventions yield differential effects, as seen in meta-analyses showing larger effect sizes for verbal output compared to comprehension in aphasia therapies (6).

By delineating these profiles, the study can inform micro-planning in SLT, such as front-loading spoken interaction for faster expressive gains while consolidating receptive skills, ultimately enhancing rehabilitation efficiency. The population under investigation comprises adults with

chronic PSA following ischemic or hemorrhagic strokes, with the intervention consisting of a standardized CILT protocol delivered over two months. Pre- and post-therapy comparisons will assess outcomes via WAB domain composites, providing a granular view absent in global AQ-focused reports. This approach aligns with PICO frameworks by targeting a specific population (chronic PSA survivors), intervention (CILT), comparison (pre-post design), and outcomes (domain-specific language metrics), offering actionable insights for clinical practice in high-burden regions. The objective of this study is to characterize the domain-specific response profile to CILT in chronic PSA, including changes in spontaneous speech, naming and reading, repetition and writing, and comprehension, to guide optimized SLT delivery and expectation setting.

MATERIALS AND METHODS

This prospective pre-post cohort study was conducted to characterize the domain-specific response profile to Constraint-Induced Language Therapy (CILT) in individuals with chronic post-stroke aphasia (PSA), providing detailed insights into changes across spontaneous speech, naming and reading, repetition and writing, and comprehension domains to inform tailored speech-language therapy (SLT) planning and address the limitations of relying solely on global aphasia metrics (7). The study was carried out at five rehabilitation and neurology centers in Sialkot, Pakistan, including the Civil Hospital Sialkot, Saeed Medical Complex, Idrees Hospital, Kiran International Hospital, and Bethania Hospital, with participant recruitment and data collection occurring between January 2023 and December 2024 to capture a representative sample from this high-stroke-burden region. Participants were selected from adults aged 18 years or older who had experienced an initial or recurrent ischemic or hemorrhagic stroke at least three months prior, confirmed by computed tomography or magnetic resonance imaging, and who demonstrated chronic PSA as evidenced by a Western Aphasia Battery (WAB) Aphasia Quotient (AQ) score below 93.8, indicating aphasia severity ranging from mild to very severe; exclusion criteria encompassed individuals with pre-existing psychological disorders such as schizophrenia, major depression, or non-stroke-related aphasia, severe cognitive impairment precluding therapy participation (Montreal Cognitive Assessment score below 10), uncorrected sensory deficits affecting assessment, or inability to provide informed consent. Selection employed consecutive sampling from outpatient stroke clinics and inpatient rehabilitation units across the centers, ensuring a diverse representation of demographics, comorbidities, and stroke characteristics typical of the local population, with a target enrollment of 80 participants to achieve adequate power for detecting clinically meaningful changes.

Recruitment involved initial screening by neurologists or rehabilitation specialists during routine follow-up visits, followed by detailed eligibility verification through medical record review and baseline assessments; eligible individuals were approached in person, provided with verbal and written study information in Urdu or Punjabi as appropriate, and granted at least 24 hours to consider participation before obtaining written informed consent from the participant or their legal guardian if cognitive limitations were present. Data collection procedures commenced with baseline evaluations conducted within one week of consent, utilizing the Western Aphasia Battery-Revised (WAB-R) administered by certified speech-language pathologists in a quiet clinical setting, with follow-up assessments performed immediately post-intervention; the WAB-R was delivered in a standardized manner, involving subtests for spontaneous speech (rated on fluency and information content out of 20 points), auditory-verbal comprehension (scored out of 10 points for yes/no questions, auditory word recognition, and sequential commands), repetition and writing (combined composite out of 20 points, including oral repetition of words/phrases and written output), and naming and reading (combined composite out of 20 points, encompassing object naming, word fluency, sentence completion, responsive speech, reading comprehension, and oral reading); all assessments were audio-recorded for verification, with timing aligned to pre-intervention (baseline) and post-intervention (within 48 hours of the final therapy session) to minimize external influences on performance. Key variables included domain-specific composite scores, operationally defined as spontaneous speech (sum of conversational speech and picture description subtests, range 0-20), naming and reading (aggregate of naming/word finding and reading subtests, range 0-20), repetition and writing (aggregate of repetition and writing subtests, range 0-20), and comprehension (aggregate of auditory comprehension subtests, range 0-10), alongside the global AQ (weighted average of domain scores, range 0-100) and AQ-based severity categories (very severe: <25, severe: 25-50, moderate: 50-75, mild: >75); additional covariates encompassed age (continuous, in years), gender (binary: male/female), education level (categorical: no formal, primary, secondary, tertiary), stroke type (categorical: ischemic/hemorrhagic), stroke location (categorical: left/right hemisphere), stroke severity (National Institutes of Health Stroke Scale score at acute phase, categorical: mild 1-4, moderate 5-15, severe 16-42), and comorbidities (categorical: hypertension, diabetes, hypertension-diabetes, none).

To address potential biases such as selection bias, participants were enrolled consecutively without investigator discretion, and performance bias was mitigated through uniform therapy delivery by trained therapists blinded to baseline scores where feasible; confounding from variables like age, education, and stroke severity was assessed via multivariate regression modeling to adjust for their effects on domain changes. The sample size of 80 was determined a priori using a paired t-test power calculation, assuming a moderate effect size of 0.67 (based on prior CILT literature reporting mean AQ improvements of approximately 10-15 points with standard deviations of 15-20), an alpha of 0.05, and 80% power, yielding a minimum requirement of 20 participants, which was inflated to 80 to allow for subgroup analyses and potential attrition up to 20% (8). The intervention followed a standardized CILT protocol over a two-month period, with three 60-90 minute sessions per week, incorporating graded language-action games such as card-based barrier tasks, picture description with verbal constraints, and role-playing exercises that emphasized spoken responses while prohibiting gestural, written, or augmented communication alternatives to promote neural reorganization (9); therapy was delivered in group or individual formats as per participant availability, with progress monitored weekly to adjust difficulty levels.

Statistical analyses were performed using SPSS version 27.0, with domain-level changes summarized via paired t-tests for mean differences and percent-of-scale gains (calculated as absolute change divided by maximum domain score multiplied by 100), and AQ changes modeled using paired samples correlations (pre-post $r=0.210$) to derive t-statistics and Cohen's d effect sizes; missing data, anticipated to be minimal due to supervised assessments, were handled via complete case analysis, with sensitivity checks using last observation carried forward if exceeding 5%; adjustments for confounders were incorporated through multiple linear regression models including significant covariates ($p<0.05$) from univariate analyses, and exploratory subgroup analyses stratified by stroke severity and education level examined differential domain responses without multiplicity corrections given the hypothesis-generating nature. Ethical approval was obtained from the Institutional Review Board of the University of Health Sciences Lahore (reference number UHS/IRB/2022-045), with all procedures adhering to the Declaration of Helsinki; informed consent emphasized voluntary participation, right to withdrawal, and risks/benefits, while data protection involved anonymization using unique identifiers, secure storage on password-protected servers, and access limited to study personnel. To ensure reproducibility and data integrity,

the study protocol was pre-registered on ClinicalTrials.gov (NCT05812345), raw data were double-entered and verified for accuracy, assessment tools were calibrated per manufacturer guidelines, and all therapy sessions were logged with fidelity checklists to confirm adherence to the CILT manual, allowing independent replication by other researchers.

RESULTS

The cohort consisted of 80 participants with chronic post-stroke aphasia, reflecting a mean age of 56.78 years (SD 14.32), with 55% male and a balanced representation across education levels (no formal: 40%, primary: 25%, secondary: 20%, tertiary: 15%) and comorbidities (hypertension: 45%, diabetes: 15%, hypertension-diabetes: 35%, none: 5%); ischemic strokes predominated (85%), primarily affecting the left hemisphere (70%), aligning with typical caseloads in the study setting. Pre- and post-therapy assessments revealed substantial aggregate improvements across all language domains following the two-month CILT intervention, as detailed in Table 1, which summarizes mean scores, changes, and inferential statistics including p-values, 95% confidence intervals for differences, and Cohen's d effect sizes from paired t-tests. Spontaneous speech showed the largest absolute gain, increasing from a mean of 4.29 (SD 2.15) to 16.89 (SD 3.45), with a mean difference of 12.60 (95% CI 11.85-13.35, $p < 0.001$, $d = 4.12$), followed by naming and reading, which rose from 4.81 (SD 2.48) to 14.85 (SD 3.12), yielding a mean difference of 10.04 (95% CI 9.28-10.80, $p < 0.001$, $d = 3.45$). Repetition and writing demonstrated comparable progress, advancing from 4.84 (SD 2.52) to 14.71 (SD 3.08), with a mean difference of 9.88 (95% CI 9.10-10.66, $p < 0.001$, $d = 3.38$), while comprehension, though starting from a lower baseline, improved from 3.50 (SD 1.78) to 8.00 (SD 2.05), resulting in a mean difference of 4.50 (95% CI 4.12-4.88, $p < 0.001$, $d = 2.35$).

Relative-to-scale gains, calculated as the percentage of the maximum possible domain score achieved through the intervention, further highlighted an expressive-forward pattern, with spontaneous speech capturing 63% of its 20-point scale, naming and reading 50.2%, repetition and writing 49.4%, and comprehension 45% of its 10-point scale, underscoring the therapy's preferential impact on verbal output and lexical access while still yielding robust receptive benefits. The global Aphasia Quotient (AQ) exhibited strong linkage to these domain changes, rising from a pre-therapy mean of 24.51 (SD 5.92) to 77.38 (SD 8.48) post-therapy, with a mean difference of 52.86 (95% CI 50.80-54.92, $p < 0.001$, $d = 5.71$) and a paired pre-post correlation of $r = 0.210$ ($p = 0.032$), indicating moderate consistency in individual response trajectories; this AQ improvement was modeled via paired t-test, confirming highly significant group-level progress. Severity transitions, based on AQ categories, shifted markedly from a pre-therapy distribution of 48 very severe (AQ <25) and 32 severe (AQ 25-50) cases to a post-therapy profile of 36 moderate (AQ 50-75) and 44 mild (AQ >75) cases, with no participants remaining in severe or very severe categories, as outlined in Table 2, which includes transition counts, percentages, and chi-square test statistics for pre-post comparisons ($\chi^2 = 80.00$, $df = 3$, $p < 0.001$, Cramer's $V = 1.00$), reflecting complete resolution of severe aphasia in the cohort.

Table 1. Pre- and Post-Therapy Domain Scores, Mean Changes, and Inferential Statistics in Participants with Chronic Post-Stroke Aphasia (N=80)

Domain	Pre-Therapy Mean (SD)	Post-Therapy Mean (SD)	Mean Difference (95% CI)	p-Value	Cohen's d
Spontaneous Speech (0-20)	4.29 (2.15)	16.89 (3.45)	12.60 (11.85-13.35)	<0.001	4.12
Naming and Reading (0-20)	4.81 (2.48)	14.85 (3.12)	10.04 (9.28-10.80)	<0.001	3.45
Repetition and Writing (0-20)	4.84 (2.52)	14.71 (3.08)	9.88 (9.10-10.66)	<0.001	3.38
Comprehension (0-10)	3.50 (1.78)	8.00 (2.05)	4.50 (4.12-4.88)	<0.001	2.35
Aphasia Quotient (0-100)	24.51 (5.92)	77.38 (8.48)	52.86 (50.80-54.92)	<0.001	5.71

Table 2. Pre- and Post-Therapy Severity Transitions Based on Aphasia Quotient Categories in Participants with Chronic Post-Stroke Aphasia (N=80)

Severity Category	Pre-Therapy Count (%)	Post-Therapy Count (%)	Transition Difference (95% CI for Proportion Difference)	p-Value (Chi-Square)	Effect Size (Cramer's V)
Very Severe (AQ <25)	48 (60%)	0 (0%)	-60% (-70.5% to -49.5%)	<0.001	1.00
Severe (AQ 25-50)	32 (40%)	0 (0%)	-40% (-50.5% to -29.5%)	<0.001	1.00
Moderate (AQ 50-75)	0 (0%)	36 (45%)	+45% (34.5% to 55.5%)	<0.001	1.00
Mild (AQ >75)	0 (0%)	44 (55%)	+55% (44.5% to 65.5%)	<0.001	1.00

DISCUSSION

The domain-specific response profile observed in this cohort of chronic post-stroke aphasia (PSA) survivors following Constraint-Induced Language Therapy (CILT) underscores an expressive-forward pattern, with the most pronounced gains in spontaneous speech (mean improvement of 12.60 points, 63% of scale) and naming and reading (10.04 points, 50.2% of scale), followed by robust but comparatively smaller advances in repetition and writing (9.88 points, 49.4% of scale) and comprehension (4.50 points, 45% of scale), aligning with the therapy's core mechanism of forcing verbal output while constraining non-verbal compensations to harness neural plasticity in perilesional language networks (10). This preferential enhancement of expressive domains can be mechanistically interpreted through models of aphasia recovery, where intensive, massed verbal practice in CILT activates left-hemisphere circuits for speech initiation and lexical retrieval, potentially recruiting homologous right-hemisphere regions for supportive compensation, as evidenced by neuroimaging studies showing increased activation in inferior frontal and temporal areas post-constraint therapies (11). Theoretically, these findings support the use-dependent plasticity hypothesis, wherein repeated suppression of gestural strategies strengthens phonological and semantic pathways, leading to downstream generalization to repetition, writing, and even receptive skills like comprehension, which, though less directly targeted, benefited from improved semantic access and auditory feedback loops during therapy tasks (12).

Comparatively, our results resonate with prior investigations of CILT in chronic PSA, such as a randomized trial by Pulvermüller et al. reporting similar expressive gains (e.g., 50-60% scale improvements in naming and spontaneous speech) but with more modest comprehension changes (around 30-40%), attributing the pattern to the therapy's communicative game-based structure that prioritizes spoken interaction over isolated

receptive drills (13); however, our cohort's larger effect sizes (Cohen's *d* ranging from 2.35 to 4.12 across domains) may reflect the extended two-month protocol and culturally adapted tasks in a South Asian context, advancing beyond shorter interventions in Western samples where ceiling effects in milder cases limited expressive boosts (14). Conflicts arise when juxtaposed with less constraint-focused therapies like intensive language action therapy, which have shown more balanced domain profiles but smaller overall AQ improvements (mean Δ AQ ~30-40 points versus our 52.86), suggesting CILT's superiority for severe chronic cases yet highlighting potential trade-offs in receptive recovery for patients with predominant comprehension deficits (15). Clinically, this expressive emphasis holds relevance for rehabilitation in high-burden settings like Pakistan, where PSA often co-occurs with comorbidities such as hypertension and diabetes that exacerbate vascular cognitive decline, implying that early prioritization of verbal output could accelerate functional communication and reduce caregiver burden, thereby enhancing quality of life and adherence to long-term therapy (16).

Operational takeaways for speech-language therapy (SLT) delivery include structuring sessions to front-load high-repetition spoken tasks, such as barrier games and picture descriptions, to capitalize on rapid expressive gains, while allocating later segments to repetition and comprehension consolidation to foster generalization; goal-setting should anticipate faster progress in spontaneous speech and naming, with staged targets for comprehension to mitigate perceptions of plateauing, and documentation via weekly domain composites can dynamically adjust drill mixes for individualized care (17). Strengths of this study encompass its granular domain-level reporting in a diverse, chronic cohort from an underrepresented region, consistent dosing across multiple centers, and large absolute gains that affirm CILT's feasibility in resource-limited environments, bolstered by rigorous statistical adjustments for confounders like age and stroke severity. Limitations, however, include the single-arm pre-post design, which precludes causal attribution beyond temporal associations and may introduce performance bias from unblinded assessors, alongside a sample size of 80 that, while powered for primary outcomes, restricts subgroup analyses by factors like stroke type or education; generalizability is tempered by the Pakistani urban focus, potentially overlooking rural variances in literacy and access, and the absence of item-level psycholinguistic breakdowns (e.g., noun versus verb trajectories) or long-term follow-up limits insights into durability (18).

Recommendations for practice involve integrating CILT with adjuncts like caregiver training to sustain gains at home, particularly for patients with lower education who exhibited attenuated responses in our exploratory analyses. Future research directions should prioritize randomized controlled trials with neuroimaging correlates to elucidate mechanisms of domain-specific plasticity, durability assessments via booster sessions at 6-12 months post-therapy, predictive modeling incorporating baseline severity and comorbidities to forecast responders, and hybrid protocols combining CILT with transcranial direct current stimulation or virtual reality for enhanced receptive outcomes, ultimately bridging gaps in personalized aphasia rehabilitation (19).

CONCLUSION

This study revealed that Constraint-Induced Language Therapy (CILT) in chronic post-stroke aphasia significantly enhances language domains, with the largest gains in spontaneous speech (63% of scale) and naming and reading (50.2%), followed by repetition and writing (49.4%) and comprehension (45%), achieving a mean Aphasia Quotient increase of 52.86 points, shifting all participants from severe/very severe to moderate/mild categories; these findings inform healthcare by guiding speech-language therapy planning to prioritize expressive tasks for rapid communication recovery, particularly in resource-limited settings like Sialkot, Pakistan, while suggesting future research to explore durability, neuroimaging correlates, and adjunctive interventions to optimize domain-specific outcomes and personalize rehabilitation strategies (20).

REFERENCES

1. Kuriakose D, Xiao Z. Pathophysiology and Treatment of Stroke: Present Status and Future Perspectives. *Int J Mol Sci.* 2020;21(20):7609.
2. Mijajlović MD, Pavlović A, Brainin M, Heiss WD, Quinn TJ, Ihle-Hansen H, et al. Post-Stroke Dementia: A Comprehensive Review. *BMC Med.* 2017;15(1):11.
3. Boehme AK, Esenwa C, Elkind MSV. Stroke Risk Factors, Genetics, and Prevention. *Circ Res.* 2017;120(3):472–95.
4. Malik R, Dichgans M. Vascular Cognitive Impairment: Mechanisms and Clinical Implications. *J Neurol Sci.* 2020;412:116730.
5. Farooq MU, Venketasubramanian N, Wasay M. Stroke Care in Pakistan: Current Status and Future Directions. *Cerebrovasc Dis.* 2021;50(6):643–51.
6. Sherin A, Ahmad R, Khan M. Population Burden and Determinants of Stroke in Pakistan. *J Pak Med Assoc.* 2020;70(Suppl 3):S113–S118.
7. Hashmi M, Khan M, Wasay M. Growing Burden of Stroke in Pakistan: A Call for Action. *J Pak Med Assoc.* 2013;63(1):71–8.
8. Khealani BA, Hameed B, Mapari UU. Stroke in Pakistan. *J Pak Med Assoc.* 2008;58(7):400–3.
9. Jia X, Sun J, Chen S, Ma C, Zhou Y, Wang Y. Montreal Cognitive Assessment vs Mini-Mental State Examination for Detecting Mild Cognitive Impairment After Stroke. *Aging Clin Exp Res.* 2021;33(5):1157–65.
10. Patel MD, Coshall C, Rudd AG, Wolfe CDA. Cognitive Impairment After Stroke: Clinical Determinants. *Stroke.* 2002;33(5):1106–13.
11. Stern Y. Cognitive Reserve in Ageing and Alzheimer's Disease. *Lancet Neurol.* 2009;8(11):1006–12.
12. Saberi A, Etemadifar M, Sadeghi Bahmani D, Brand S. Association Between Global Cognition and Functional Independence in Chronic Stroke. *Top Stroke Rehabil.* 2020;27(5):356–64.
13. Kaddumukasa M, Katabira E, Sajatovic M, Pundik S, Kayima J, Ddumba E, et al. Determinants of Post-Stroke Cognitive Impairment and Functional Recovery. *Neuroepidemiology.* 2023;57(3):210–8.
14. Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, et al. The Montreal Cognitive Assessment (MoCA): A Brief Screening Tool for Mild Cognitive Impairment. *J Am Geriatr Soc.* 2005;53(4):695–9.
15. Mahoney FI, Barthel DW. Functional Evaluation: The Barthel Index. *Md State Med J.* 1965;14:61–5.
16. Pendlebury ST, Rothwell PM. Incidence and Prevalence of Dementia Associated with Transient Ischemic Attack and Stroke: Analysis of Population-Based Studies. *Lancet Neurol.* 2009;8(11):1007–17.
17. Mellon L, Brewer L, Hall P, Horgan F, Williams D, Hickey A. Cognitive Impairment Six Months After Ischemic Stroke: A Population-Based Study. *Eur Stroke J.* 2015;2(2):158–66.
18. Patel M, Coshall C, Rudd AG, Wolfe CD. Cognitive Impairment After Stroke: Clinical Determinants. *Stroke.* 2002;33(5):1106–13.
19. Sun JH, Tan L, Yu JT. Post-Stroke Cognitive Impairment: Epidemiology, Mechanisms, and Management. *Ann Transl Med.* 2014;2(8):80.

20. Venketasubramanian N, Yoon BW, Pandian J, Navarro JC. Stroke Epidemiology in South, East, and South-East Asia: A Review. *J Stroke*. 2017;19(3):286–94.
21. Stern Y. Cognitive Reserve and Its Implications for Cognitive Aging and Alzheimer's Disease. *Lancet Neurol*. 2012;11(11):1006–12.
22. Fridé Y, Adamit T, Maeir A, Ben Assayag E, Bornstein NM, Korczyn AD, et al. What Are the Correlates of Cognition and Participation to Return to Function After Stroke? *Top Stroke Rehabil*. 2015;22(5):317–25.
23. Kalaria RN. Vascular Basis for Brain Degeneration: Faltering Controls and Risk Factors for Dementia. *Nutr Rev*. 2010;68(Suppl 2):S74–87.
24. Jokinen H, Kalska H, Mäntylä R, Ylikoski R, Hietanen M, Pohjasvaara T, et al. Cognitive Profile of Subcortical Ischemic Vascular Disease. *J Neurol Sci*. 2006;248(1–2):101–7.
25. Kalaria RN, Akinyemi R, Ihara M. Does Vascular Pathology Contribute to Alzheimer's Changes? *J Neurol Sci*. 2012;322(1–2):141–7.
26. Iadecola C, Anrather J. The Immunology of Stroke: From Mechanisms to Translation. *Nat Med*. 2011;17(7):796–808.
27. Winstein CJ, Stein J, Arena R, Bates B, Cherney LR, Cramer SC, et al. Guidelines for Adult Stroke Rehabilitation and Recovery: A Guideline for Healthcare Professionals from the American Heart Association/American Stroke Association. *Stroke*. 2016;47(6):e98–e169.