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# Cerebral Small Vessel Disease Burden: a Biomarker for Post-Stroke Aphasia Recovery

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# Cerebral small vessel disease burden: A biomarker for post-stroke aphasia recovery

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## Introduction

Cerebral small vessel disease (cSVD) is a disorder of microvessels that causes a range of abnormalities seen on brain imaging. cSVD is a common neuropathological processing in the elderly, causing two principle, potentially devastating, outcomes in this population: stroke and vascular cognitive impairment and dementia (Wardlow et al., 2019; Zanon Zotin et al, 2021). Despite the high prevalence of cSVD in stroke survivors, its role on post-stroke aphasia recovery has not been systematically examined. In this study we systematically assessed the clinical significance of the global burden of cSVD through a neuroimaging evaluation of white matter hyperintensities (WMH), enlarged perivascular spaces (EPVS), lacunes and global cortical atrophy (GCA) in people with aphasia (PWA) that underwent language therapy.

## Methods

Thirty chronic PWA (10F, age: mean=61years, range=40–80 years, education: mean=15 years, range=12–18, time post stroke: mean=52 months, range=8–170 months) due to single left hemisphere stroke (volume: mean=135.21cm$^3$, range=11.66–317.07cm$^3$) completed up to 12 weeks of semantic feature analysis treatment for word retrieval deficits (Gilmore et al., 2018). Mean baseline aphasia severity from the Western Aphasia Battery–Revised (WAB-AQ quotient) was 59.83 (range=11.7–95.2). Baseline T1- and T2–FLAIR-weighted MRI scans were rated for four major cSVD biomarkers, including WMH, EPVS, lacunes and GCA, using validated visual rating scales (see Figure 1A). Total cSVD burden was rated on an ordinal 0-4 scale, by counting the presence and severity of each of the four biomarkers (see Figure 1B). To determine the role of cSVD burden on treatment-induced aphasia recovery, we used mixed effects logistic regression with binary naming accuracy as the predicted variable. Our main predictor was the interaction between total cSVD score and session, WAB-R AQ, stroke lesion volume, months post onset and age were included in the model as covariates, and participant and item were included as random factors.

## Results

Our participants presented with various degrees of brain changes associated with cSVD. The regression model showed a significant interaction among total cSVD burden and session ($p<0.0001$). Follow up analyses showed that the predicted probability of accurate naming increased over time more for participants with less severe cSVD (see Figure 1C).

This interaction was significant after controlling for aphasia severity, an also significant predictor ($p<0.001$), and stroke related factors, including total lesion volume and months post onset.

## Conclusions

This work indicates that the severity of cSVD may predict how well PWA will respond to language treatment independent of demographic and stroke-related factors, including initial aphasia severity, such that patients with less severe cSVD are expected to exhibit better treatment outcome compared to patients with more severe cSVD. This is in line with the general premise of neuroplasticity, that is, structural integrity influences language recovery (Kiran & Thompson, 2019), and provides evidence that cSVD, an index of brain reserve (i.e., individual differences in brain structure due to chronic brain pathological changes) constitutes a clinically relevant predictor not only of post-stroke dementia (Mok et al., 2017; Wong et al., 2016) but also of post-stroke aphasia recovery (Varkanitsa et al., 2020).

## References


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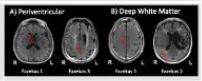
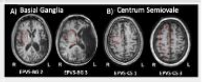
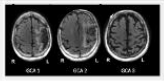
**(A)**

| Marker | Description | Visual assessment | Example |
|---|---|---|---|
| White Matter Hyperintensities (WMH) | White matter lesions characterized by bilateral, mostly symmetrical hyperintensities on T2-weighted MRI | Fazekas et al. 1987 |  |
| Enlarged Perivascular Spaces (EPVS) | Fluid-filled spaces (CSF-like signal) that follow the typical course of a vessel | Wardlaw et al. 2013 |  |
| Lacunes | Round or ovoid, subcortical, fluid-filled cavity, with a central CSF-like hypointensity and a surrounding rim of hyperintensity | Wardlaw et al. 2013 |  |
| Global Cortical Atrophy (GCA) | Lower brain volume that is not related to a specific macroscopic focal injury such as trauma or infarction | Harper et al. 2015 |  |

**(B)**

| MRI feature | Definition | Score |
|---|---|---|
| WMH | Periventricular WMH Fazekas 3 and/or deep WMH Fazekas 2-3 | 1 point |
| EPVS | Moderate to severe perivascular spaces in basal ganglia (EPVS-BG ≥ 2) | 1 point |
| Lacunes | ≥ 1 Lacune | 1 point |
| GCA | Moderate to severe GCA (GCA ≥ 2) | 1 point |

**(C)**

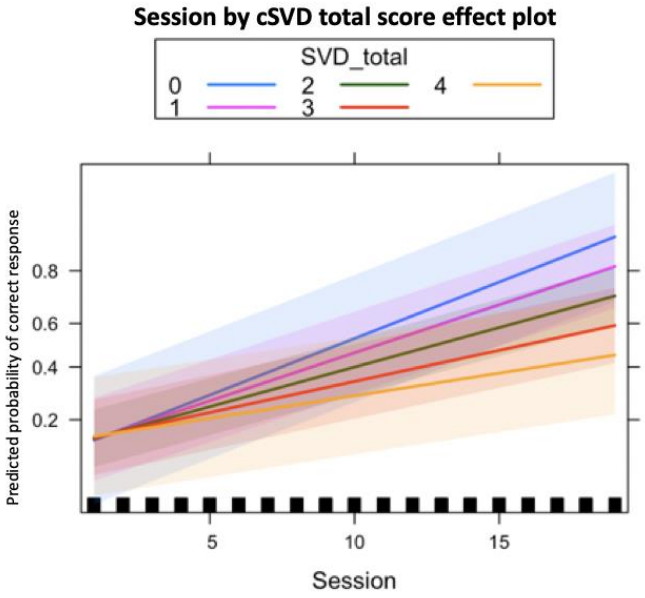



*Figure 1*. (A) Definitions and representative examples of the four neuroimaging markers of cSVD burden, (B) Scoring system for total cSVD burden, (C) Session by cSVD total score effect plot: 0 (blue line) indicates absence of cSVD, whereas 4 (orange line) indicates severe cSVD (i.e., maximum score).