Perfusion levels in the left hemisphere are associated with language outcomes in chronic post-stroke aphasia

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INTRODUCTION

- In stroke the disruption of cerebral blood flow (perfusion) is observed beyond the infarcted tissue even in chronic stages: in surrounding tissue, as well as in distal areas (Boukrina et al., 2019; Robson et al., 2017).
- Functional compensation following stroke relies on non-damaged tissue (Saur et al., 2006; Kiran & Thompson, 2019).
- However, structurally-preserved but suboptimally-perfused regions may contribute less to recovery (Fridriksson et al., 2012; Thompson et al., 2010, 2017); thus, the relationship between perfusion and cognitive functioning needs to be systematically established, especially in the context of language.

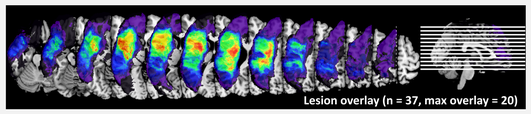
Aims of the current study

- **Determine how perfusion in perilesional tissue and different cortical areas are related to language outcomes in chronic aphasia.**

METHODS

Participants – 37 individuals with aphasia following LH stroke.

- 13 females, 24 males;
- M_{age} = 64.19 ± 11.17 years, age range: 43 - 84 years;
- $M_{months\ post\text{-}onset}$ = 54.24 ± 76.85 months, post-onset range: 2 - 290 months.



Language testing –
Western Aphasia Battery (Kertesz, 2007)
[mean (SD), max = 10]

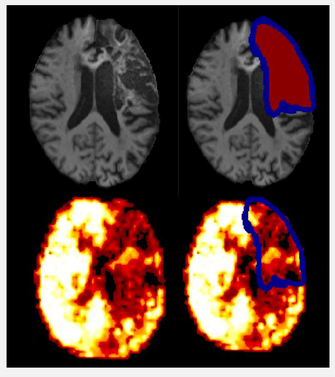
Fluency	Repetition	Naming	Aud. Comprehension	WAB AQ
8 (2.53)	7.87 (2.84)	7.7 (2.72)	9.06 (1.14)	82.72 (20.46)

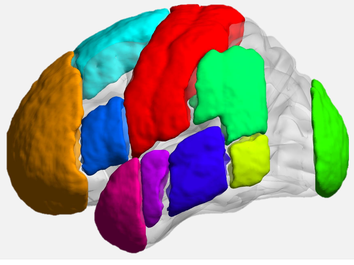
Neuroimaging data acquisition – Structural (T1) and perfusion data with Pseudo-Continuous Arterial Spin Labeling (PCASL) were acquired. PCASL data was based on two different sequences.

- Gradient echo, echo planar imaging single-shot readout sequence, TR/TE = 4000/12ms, flip angle = 90°, bandwidth = 2.6 KHz/pixel, FOV = 22cm, slice thickness = 5 mm, voxel size = 3.4x3.4x6 mm, slice-selective gradient = 6mT/m, 20 axial slices in ascending sequential acquisition order. The labeling duration was 1470ms with a post labeling delay of 1500ms. 80 images were acquired in the interleaved tag/control order for each subject. The first control image as a calibration image for the analysis of this cohort. *N = 29.*
- Gradient echo, echo planar imaging 4-shot spiral readout sequence, TR/TE = 4600/8.7ms, flip angle = 90°, bandwidth = 400Hz/Pixel, FOV = 24cm, slice thickness = 3mm, voxel size = 3×3×3 mm, slice-selective gradient = 6mT/m, 40 axial slices in ascending sequential acquisition order. The labeling duration was 1800ms with a post labeling delay of 2000ms. 16 images were acquired in the interleaved tag/control order for each subject. A M0 calibration image was automatically obtained. *N = 8.*

PCASL data processing

- Tag-control images were motion corrected using FSL's function MCFLIRT (Jenkinson, et al., 2012).
- Cerebral blood flow (CBF) maps were obtained using Oxford ASL (Chappell et al., 2009).
- CBF maps were quantified in standard physiological units (ml blood/100mg tissue/min) using a standard kinetic model (Alsop et al., 2015). Labeling efficiency was set to α=0.72 and the longitudinal relaxation time of the blood was set to T1_b=1650ms. No further smoothing was performed.





ROI analysis

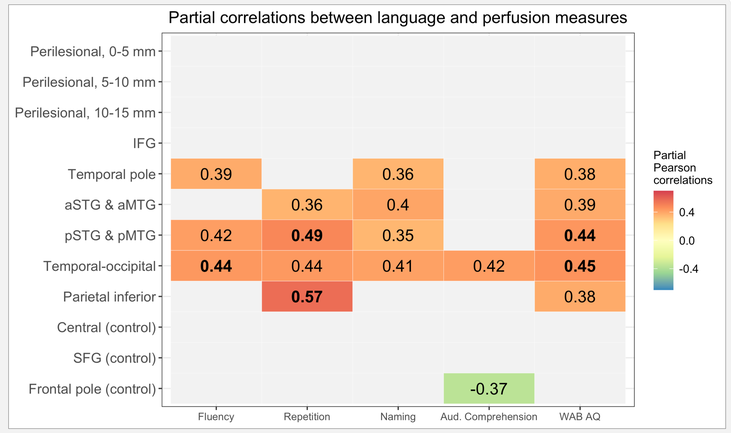
- **Perilesional ROIs –** were obtained by expanding the lesion mask drawn manually in native T1 space and then subtracting the original lesion mask from it.
  - The following perilesional ROIs were used: 0 – 5mm, 5 – 10 mm, 10 – 15 mm.
- **Atlas-based ROIs –** were taken from the Harvard-Oxford atlas in FSL. The ROIs covered different regions of the perisylvian cortex in the two hemispheres: inferior frontal gyrus (IFG), temporal pole, anterior temporal (including superior and middle temporal gyri; aSTG & aMTG), posterior temporal (pSTG & pMTG), temporal-occipital region, inferior parietal, along with several control regions (pre- and postcentral gyri, superior frontal gyrus, frontal pole, and occipital pole), that have not been implicated in language processing.
  - The lesion mask was parceled out from each atlas-based ROI in subject space and then mean perfusion values for each ROI were calculated.

CONCLUSIONS

- The findings highlight that slowed or reduced blood distribution is observed in regions beyond the lesion site in stroke, potentially impacting their functionality.
  - Hypoperfused neural tissue in critical language areas may not be fully able to support recovery, as previously suggested.
  - Currently, null results (lack of a relationship between perfusion and behavioral outcomes) should be interpreted cautiously, as they require further replication to eliminate the possibility of a type II error.
- Overall, the current results underscore the critical and general role that left hemisphere temporal regions play in various expressive and receptive language abilities, and in recovery in post-stroke aphasia.

RESULTS

- Hypoperfusion in the LH was observed.
  - Cerebral perfusion was significantly lower in all the ipsilesional LH regions compared to the contralesional RH regions.
- Residual perfusion in temporal language areas in the LH was significantly correlated with language outcomes even after controlling for type of scanning sequence, lesion volume and base-level perfusion of the occipital pole (see Figure on the right).
- Perfusion in the contralesional RH areas was not associated with language outcomes.



- Differential and specific contributions of residual perfusion in LH regions to language outcomes were explored further using regularized regression (lasso-type, R ver. 4.01, package glmnet; see Table below for standardized beta coefficients). This analysis shows which ROIs make unique contribution when perfusion in other regions is considered simultaneously.
  - Perilesional perfusion had an impact on **fluency** outcomes and **overall aphasia severity**.
  - Inferior parietal perfusion was associated with **repetition** abilities and **overall aphasia severity**.
  - **Naming** abilities were determined by perfusion in temporal areas.
  - **Comprehension** outcomes were not explained well by perfusion values, showing only temporal-occipital associations.
  - Overall, perfusion in anterior and posterior temporal areas had a significant impact on lexical-semantic abilities and general language impairment.

WAB score / ROIs	Fluency	Repetition	Naming	Aud. Comprehension	WAB_AQ
PCASL sequence (covariate)	*1.07*	*0.51*	*0.48*	*0.44*	*8.03*
Lesion volume (covariate)	*-1.16*	*-0.52*	*-1.33*	*-0.14*	*-6.75*
Occipital pole (covariate)	*-1.63*	*-1.97*	*-0.69*	*-0.16*	*-11.69*
Perilesional, 0-5 mm	0.74	0	0	0	1.49
IFG	-0.25	-0.76	-0.58	-0.35	-5.13
Temporal pole	0.96	0.48	0.37	0	5.19
aSTG & aMTG	-0.83	0	0.46	0.14	1.98
pSTG & pMTG	0.81	0.63	0	0	0
Temporal-occipital	0.58	0	0.50	0.30	3.74
Parietal inferior	0.04	1.95	0	0	6.21
R-squared	***0.64***	***0.63***	***0.54***	***0.30***	***0.59***

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