EasyChair Preprint

№ 6467

Defining Hypoperfusion in Chronic Aphasia: an Individualized Thresholding Approach

Noelle Abbott, Carolyn Baker, Conan Chen, Thomas Liu and Tracy Love

August 29, 2021

Defining hypoperfusion in chronic aphasia: an individualized thresholding approach

Noelle T. Abbott[1]*, Carolyn J. Baker[1], Conan Chen[2], Thomas T. Liu[2], and Tracy E. Love[1,3]

[1] Joint Doctoral Program in Language and Communicative Disorders, San Diego State University and University of California San Diego, San Diego, CA, USA
[2]Center for Functional MRI and Department of Radiology, University of California San Diego, San Diego, CA, USA
[3] School of Speech, Language, and Hearing Sciences, San Diego State University, San Diego, CA, USA

***corresponding author, ntodd6857@sdsu.edu**

Introduction

Individuals with chronic aphasia (IWA) exhibit variable patterns of language impairment, which makes it difficult to identify structure-function brain relationships[1,2]. This variability may be due to underlying alterations in brain *function*. Prior research has demonstrated that IWA have reduced cerebral blood flow (CBF; hypoperfusion) in areas of the brain that are structurally intact[3,4]. However, across these studies there is little consensus on how to best define hypoperfusion. Though standard CBF threshold values exist (healthy≥50mL/100g/min, hypoperfused=12-20mL/100g/min, necrotic≤12mL/100g/min), they do not fully capture tissue functionality in IWA[5-7]. Further, group-level analyses may overshadow important individual differences. In this exploratory study, we defined an individualized metric for hypoperfusion and used it (vs. standard approaches) to investigate (1) when perilesional tissue (often functionally compromised) returned to "normal" CBF levels and (2) how well our metric correlated with auditory comprehension.

Methods

Participants included 6 monolingual, right-handed (premorbid), chronic (>1 year) IWA who had a single, unilateral, left hemisphere stroke (Table 1). Aphasia subtype and severity were based on the Boston Diagnostic Aphasia Examination-3 and the Western Aphasia Battery-Revised[8-9]. Auditory comprehension was measured through the comprehension subtests of these assessments.

Neuroimaging Procedures: Anatomical and resting state CBF data were acquired using a 3T-GE scanner (pre-processing information can be found in Abbott et al. 2021[10]). All scans were co-registered and labeled using the Automated Anatomical Labeling Atlas[11]. To systematically define perilesional tissue, we created four 3mm perilesional bands (0-3mm, 3-6mm, 6-9mm, 9-12mm).

Analyses: **Group-** and **individual**-level analyses were performed to demonstrate the importance of an individualized approach. Here, we defined "normal" brain tissue based on each participant's right hemisphere average CBF (CBF_{RH}) and "functionally compromised" tissue as anything less than 1.5 standard deviations below CBF_{RH}. Hypoperfusion in LH-

perilesional bands and specific regions of interest (ROIs) were identified to explore the relationship between hypoperfusion and language behavior.

Results

Our individualized approach was more sensitive to differences in tissue functionality for each participant. While the **group-level** analysis showed no difference in the 0-3mm band from the calculated hypoperfusion threshold (t(5)=-1.18,p=0.15), **individual-level** analyses revealed additional information; there were differences *if and when* CBF values returned to “normal” in the remaining three bands (Fig.1).

Our individualized approach also picked up on hypoperfusion in ROIs that remained structurally intact, suggesting that our metric is more sensitive to individual patterns of brain function. Correlations between the two CBF metrics (standard/individual) and language behavior revealed a correlation between auditory comprehension and multiple temporal regions, which did not exist with standard thresholding. These results suggests that our individualized metric may better identify functionally compromised tissue on an individual basis.

Conclusions

We propose a new approach for measuring functionally compromised brain tissue in IWA. Standard cut-off values and group-level analyses often over- or under-estimate tissue functionality in IWA. These results underscore the necessity of considering not just the structural integrity of brain regions but also the functional integrity when investigating structure-function relationships. By adding in measures of functional integrity, researchers may be able to better account for some of the variability demonstrated by IWA.

References

1. Duncan, E. S., & Small, S. L. (2016). Increased modularity of resting state networks supports improved narrative production in aphasia recovery. Brain connectivity, 6(7), 524-529.

2. Lazar, R. M., Speizer, A. E., Festa, J. R., Krakauer, J. W., & Marshall, R. S. (2008). Variability in language recovery after first-time stroke. Journal of Neurology, Neurosurgery & Psychiatry, 79(5), 530-534.

3. Love, T., Swinney, D., Wong, E., & Buxton, R. (2002). Perfusion imaging and stroke: A more sensitive measure of the brain bases of cognitive deficits. *Aphasiology*, *16*(9), 873-883.

4. Brumm, K. P., Perthen, J. E., Liu, T. T., Haist, F., Ayalon, L., & Love, T. (2010). An arterial spin labeling investigation of cerebral blood flow deficits in chronic stroke survivors. *Neuroimage*, *51*(3), 995-1005.

5. Biagi, L., Abbruzzese, A., Bianchi, M. C., Alsop, D. C., Del Guerra, A., & Tosetti, M. (2007). Age dependence of cerebral perfusion assessed by magnetic resonance continuous arterial spin label-ing. Journal of Magnetic Resonance Imaging: An Official Journal of the International Society for Magnetic Resonance in Medicine, 25(4), 696-702.

6. Baron, J. C. (2001). Perfusion thresholds in human cerebral ischemia: historical perspective and therapeutic implications. Cerebrovascular Diseases, 11(Suppl. 1), 2-8.

7. Botteri, M., Bandera, E., Minelli, C., & Latronico, N. (2008). Cerebral blood flow thresholds for cerebral ischemia in traumatic brain injury. A systematic review. Critical care medicine, 36(11), 3089-3092.

8. Goodglass, H., Kaplan, E., & Barresi, B. (2001). BDAE-3: Boston Diagnostic Aphasia Examination–Third Edition. Philadelphia, PA: Lippincott Williams & Wilkins.

9. Kertesz, A. (2007). Western aphasia battery: Revised. Pearson.

10. Abbott, N. T., Baker, C. J., Chen, C., Liu, T. T., & Love, T. E. (2021). Defining Hypoperfusion in Chronic Aphasia: An Individualized Thresholding Approach. Brain Sciences, 11(4), 491.

11. Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., . . . Joliot, M. (2002). Automated Anatomical Labeling of Activations in SPM Using a Macroscopic Ana-tomical Parcellation of the MNI MRI Single-Subject Brain. NeuroImage, 15(1), 273-289. doi:10.1006/nimg.2001.0978

Acknowledgments
We thank Natalie Sullivan, David Shin, Frank Haist, Peter Pieperhoff, and Katrin Amunts for their assistance during various stages of data collection and processing, and all of our participants, their families, and our funding agencies for supporting this work. This research was funded by NIH NIDCD award numbers T32 DC007361, R21 DC015263, and R01 DC009272.

Table 1. [1]Based on WAB-R subtypes. [2]BDAE-3: Boston Diagnostic Aphasia Examination- 3rd edition severity rating scale (1=severe, 5=mild); [3]BDAE-AC: auditory comprehension composite (AC) score based on the BDAE-3 auditory comprehension subtests; [4]WAB-AQ: Western Aphasia Battery-Aphasia Quotient, measure of aphasia severity derived from the WAB-Revised (R) assessment (<50=severe, 51-70 = moderate, >71=mild); [5]WAB-AC: auditory comprehension composite (AC) score based on the WAB-R auditory comprehension subtests. [6]LH: left hemisphere; [7]RH: right hemisphere; cc^3: cubic centimeters; Percent (%) lesion in LH was calculated by dividing the lesion volume by the LH brain volume. *WAB-AQ score was low due to an inability to perform the repetition and overt naming tasks. Note: Education information was unavailable for S05. Tables combined from Abbott et al. 2021 [10]

Participant	Sex/Age/Years Post-Stroke	Education (Years)	Aphasia Subtype[1]	BDAE-3[2] Severity (1=Severe, 5=Mild)	BDAE-AC[3] Percentile	WAB-AQ[4] Max = 100	WAB-AC[5] Percentile	Lesion Location	LH[6] Brain Volume (cc^3)	RH[7] Brain Volume (cc^3)	Lesion Volume (cc^3)	% Lesion in LH
S01	M/55/15	17	Broca's	2	21	67.7	72	L inferior and posterior frontal lobe w/subcortical extension; anterior, superior and middle temporal lobe; inferior, anterior and posterior parietal lobe	540.90	619.85	172.52	31.90
S02	M/67/9	20	Broca's	3	65	82.6	91	L inferior and posterior frontal lobe w/subcortical extension; superior and middle temporal lobe; inferior and anterior parietal lobe	557.25	611.24	146.27	26.25
S03	F/65/7	16	Anomic	4	90	95.8	100	L posterior frontal lobe with subcortical structures	426.01	517.34	23.26	5.46
S04	M/59/4	12	Broca's	2	35	28.2*	80	L medial and posterior frontal lobe; superior and middle temporal lobe; anterior parietal lobe	544.43	580.05	66.03	12.13
S05	M/58/5	-	Broca's	2	11	50.8	72	L inferior and posterior frontal lobe w/subcortical extension; superior and middle temporal lobe; anterior, posterior, superior and inferior parietal lobe; middle and superior occipital lobe	436.17	487.67	180.60	41.41
S06	F/76/6	12	Anomic	3	78	88.2	89	L superior temporal lobe	352.06	389.63	12.06	3.43

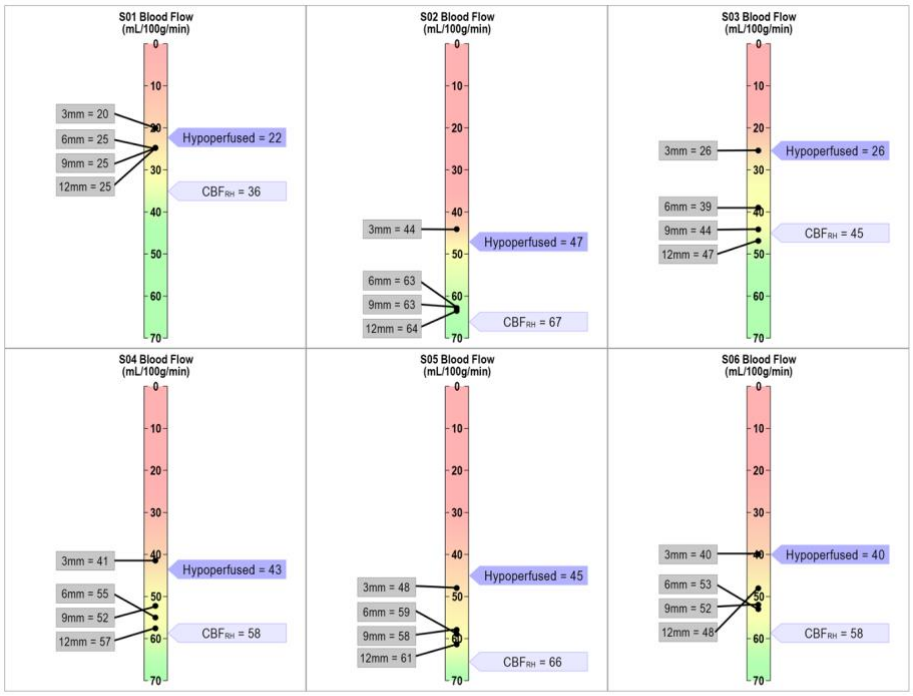

Figure 1. From Abbott et al., 2021. Individualized CBF threshold maps for each participant. The dark purple flag indicates when tissue is hypoperfused based on the individually defined approach of 1.5 SD below CBF_{RH}. The light purple flag indicates average CBF_{RH}. The gray boxes show CBF values for each of the four 3mm perilesional bands. As can be seen in the figure, the 0-3mm is either at or below the individually defined threshold for hypoperfusion for each participant.