PERFUSION IN AGING: QUANTIFICATION OF CEREBRAL PERFUSION IN HEALTHY AGING AND MILD COGNITIVE IMPAIRMENT USING PERFUSION MRI

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Background

- By 2050, it is estimated that >21.7 million Americans aged 65+yrs will have AD[1]
- Mild Cognitive Impairment is increasingly common in older adults. MCI is considered a prodromal form of AD. Adults with MCI are at high risk for AD.[2]
- Previous studies have shown AD is associated with decreased cerebral perfusion[3]
- Perfusion can be quantified using MRI with Dynamic Susceptibility Contrast (DSC)
  - Perfusion metrics include cerebral blood volume (CBV) and flow (CBF)
- Advanced DSC methods allow measurement of global and microvascular perfusion
  - Unique vascular sensitivity via the Spin and Gradient Echo (SAGE) method[4]
- ***Objective:*** *Gather preliminary measurement of total and microvascular perfusion in healthy aging (HC) and mild cognitive impairment (MCI) cohorts.*
- ***Hypothesis:*** *Microvascular dysfunction is an early indicator of cognitive changes than morphological and macrovascular changes.*

Methods

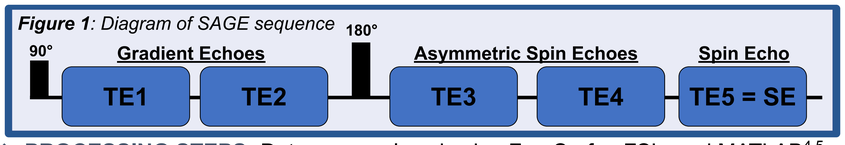
- **SUBJECTS:** *Two cohorts*: Healthy controls (HC, n = 3) and MCI (n = 3) participants
- **COGNITIVE TESTS:** Montreal Cognitive Assessment (MoCA) and Hopkins Verbal Learning Test (HVLT) to assess memory and other cognitive domains

	Age (years)	Sex (#)	MoCA	HVLT
HC	67 (∓ 6.9)	1 M / 2 F	27.33 (SD ±2.52)	67.78 (±1.92)
MCI	67 (∓ 6.9)	1 M / 2 F	21.67 (SD±1.53)	107.41 (±12.83)

Table 1*: Group Demographics and Cognitive Test Scores for HC and MCI cohorts*

- **MRI ACQUISITION:** 3T Philips MRI (Barrow Neuroimaging Innovation Center)
  - T_1-weighted structural image (MPRAGE)
    - TR: 7.0ms / TE: 3.2ms
    - Voxel Size: 1.0 mm x 1.0 mm x 1.0 mm, 176 sagittal slices
  - Perfusion imaging (SAGE-DSC)
    - TR: 1.8s / $TE_{1\text{-}5}$: 0.08 ms/0.26ms/0.50ms/0.68ms/0.86ms / FA: 90 °
    - Voxel size: 2.5 mm x 2.5 mm x 5 mm; 15 axial slices
    - Dynamic scan time: 7.5 minutes, injection of Gd-based contrast after 60 s

Figure 1*: Diagram of SAGE sequence*



- **PROCESSING STEPS:** Data was analyzed using FreeSurfer, FSL, and MATLAB[4,5]
  - Segmentation was performed using FreeSurfer on T1w images
  - Voxel-wise dynamic relaxation rates (R_2^* and R_2) were quantified using non-linear least squares fit of the following piecewise function[7] using all echoes

[1] $$S(TE) = \begin{cases} S_0^I \cdot exp[-TE \cdot R_2^*] & 0 < TE < \frac{TE_{SE}}{2} \\ S_0^{II} \cdot exp[-TE_{SE} \cdot (R_2^* - R_2)] \cdot exp[-TE \cdot (2R_2 - R_2^*)] & \frac{TE_{SE}}{2} < TE < TE_{SE} \end{cases}$$

  - CBF and CBV were quantified according to standard perfusion methods[6].
  - Mean Transit Time (MTT) maps were calculated from the central volume theorem (MTT = CBV/CBF)
- **ANALYSIS:**
  - Regions of Interest (ROIs) were selected from segmentation (see Table 2)
  - Mean perfusion parameters were quantified for each ROI (see Table 3-5)

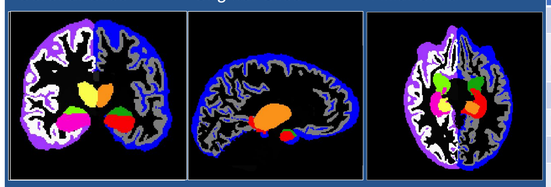


Figure 2: *Single Subject (healthy control) T1w Segmentation*

Table 2: *ROIs color-coded to subject's T1w segmentation*

ROI	Color
Left Amygdala	Green
Left Cerebral Cortex	Blue
Left Hippocampus	Red
Left Thalamus	Orange
Right Amygdala	Lime
Right Cerebral Cortex	Purple
Right Hippocampus	Pink
Right Thalamus	Yellow

Results

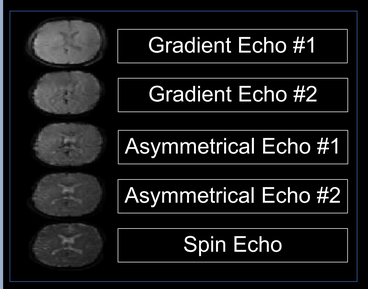


Figure 3: *Single subject (healthy control) Sample Slice of SAGE sequence*

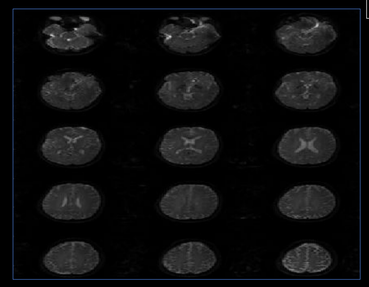


Figure 4: *Single subject (healthy control) DSC-MRI image of Spin Echo*

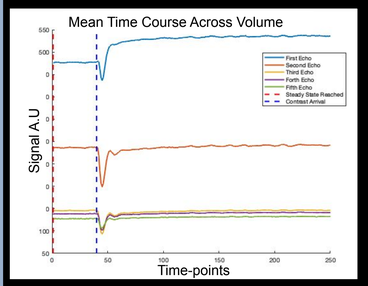


Figure 5: *Single subject (healthy control) Signal Across Volume*

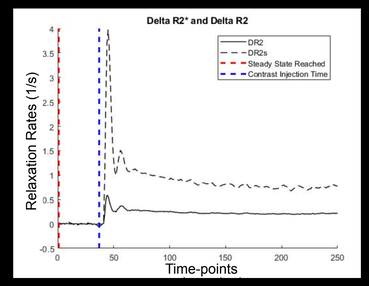


Figure 6:*Single subject (healthy control) Δ R_2*- and R_2 Curves*

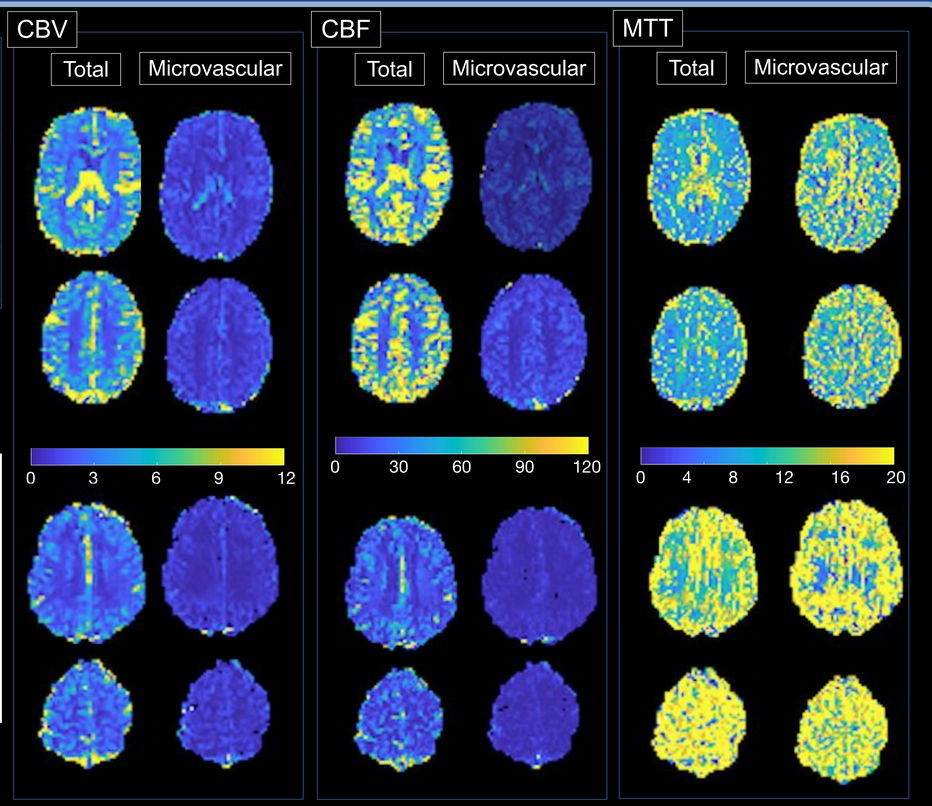


Figure 7:*Single HC subject (top) and MCI subject (bottom) SAGE T2*-weighted and T2-weighted whole-brain CBV, CBF, and MTT maps*

Group Analysis

- Preliminary analysis shows HC has higher values than MCI for CBV and CBF but lower for MTT.
- Left and Right Thalamus showed the greatest differences across all metrics
- Left and Right Amygdala showed the smallest differences across all metrics

Table 3: *CBV across HC and MCI*

	ROI	HC	MCI
Total *(ml/100g brain tissue *100)*	Left Amygdala	9.03	9.68
	Left Cerebral Cortex	6.56	6.07
	Left Hippocampus	6.81	6.31
	Left Thalamus	10.04	7.42
	Right Amygdala	7.04	7.47
	Right Cerebral Cortex	6.31	5.83
	Right Hippocampus	9.98	7.90
	Right Thalamus	10.01	8.19
Microvascular *(ml/100g brain tissue*100)*	Left Amygdala	1.29	1.82
	Left Cerebral Cortex	1.70	1.55
	Left Hippocampus	1.58	1.47
	Left Thalamus	2.02	1.52
	Right Amygdala	1.25	1.70
	Right Cerebral Cortex	1.58	1.45
	Right Hippocampus	2.01	1.75
	Right Thalamus	1.90	1.70

Table 4: *CBF across HC and MCI*

	ROI	HC	MCI
Total *(ml/min/100g brain tissue *1000)*	Left Amygdala	8.46	8.71
	Left Cerebral Cortex	6.02	5.32
	Left Hippocampus	6.10	5.84
	Left Thalamus	7.64	5.48
	Right Amygdala	7.10	7.56
	Right Cerebral Cortex	5.79	5.18
	Right Hippocampus	6.78	6.46
	Right Thalamus	7.33	6.30
Microvascular *(ml/min/100g brain tissue *1000)*	Left Amygdala	1.24	1.37
	Left Cerebral Cortex	1.25	1.05
	Left Hippocampus	1.12	0.96
	Left Thalamus	1.32	0.95
	Right Amygdala	1.16	1.50
	Right Cerebral Cortex	1.12	0.97
	Right Hippocampus	1.32	1.15
	Right Thalamus	1.37	1.28

Table 5: *MTT across HC and MCI*

	ROI	HC	MCI
Total *(1/min)*	Left Amygdala	13.38	28.41
	Left Cerebral Cortex	14.54	19.84
	Left Hippocampus	13.68	17.6
	Left Thalamus	15.41	3.4
	Right Amygdala	12.08	19.98
	Right Cerebral Cortex	14.12	19.63
	Right Hippocampus	16.52	19.78
	Right Thalamus	14.85	18.12
Microvascular *(1/min)*	Left Amygdala	15.24	29.72
	Left Cerebral Cortex	17.24	21.6
	Left Hippocampus	17.29	20.51
	Left Thalamus	17.91	5.4
	Right Amygdala	12.77	20.52
	Right Cerebral Cortex	17.37	21.39
	Right Hippocampus	17.1	21.54
	Right Thalamus	15.97	19.01

Discussion / Conclusions

- In this study, we assessed differences in perfusion between healthy aging and mild cognitive impairment cohorts by analyzing mean CBV and CBF.
- Total perfusion was higher than microvascular perfusion in all metrics for both cohorts.
- Thalamus showed the most remarkable difference in CBV and CBF, indicating that it could be a promising biomarker.
- Limitations include small sample sizes (n=6) and lifestyle differences affecting perfusion measurements.
- Future steps include the standardization of perfusion values for those diagnosed with AD.
- Our research could be used in the development of biomarkers for AD and the assessment of drug efficacy.

References & Funding

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6. *Willats, L., & Calamante, F. (2013). NMR in Biomed, 26(8), 913.*

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