

Investigating Grey Matter Volume and Cerebral Blood Flow as Biomarkers of Cognitive Resilience in a Population At Risk for Vascular Cognitive Impairment and Dementia



Melissa Wong, HBS¹; Guocheng Jiang, BMS¹; Damien Gallagher, MD¹; Bradley J. MacIntosh, PhD¹; Sandra E. Black, MD¹; Fuqiang Gao, MD¹; Joel Ramirez, PhD¹; Nathan Herrmann, MD¹; Mark J. Rapoport, MD¹; Yejin Kang, BHS¹; Kate Survilla, HBS¹; Danielle Vieira, HBS¹; Krista L. Lanctôt, PhD¹
1. Hurvitz Brain Sciences Program, Sunnybrook Research Institute, Toronto (Canada)



INTRODUCTION

- Reductions in grey matter volume (GMV) and cerebral blood flow (CBF) are observed in vascular cognitive impairment (vMCI) and dementia.
- However, differences in GMV and CBF between individuals with normal cognition and cognitive impairment with similar vascular burden have yet to be examined.

OBJECTIVES

- To investigate cognitive resilience in individuals at a higher risk for dementia due to vascular contributions using neuroimaging biomarkers.

METHODS

- Participants:
 - 57 cognitively normal non-cardiovascular disease (CVD) controls (NCN) from the Alzheimer’s Disease Neuroimaging Initiative (ADNI; adni.loni.usc.edu)
 - No history of cardiovascular disease
 - 20 cognitively normal CVD controls (CCN) from the MOVE-IT trial
 - History of CVD
 - 59 individuals with vMCI from the MOVE-IT trial
 - History of CVD and/or vascular risk factors and demonstrated modest cognitive deficits on a neuropsychological battery

- Structural and perfusion images were acquired at 3T
- Voxel-based morphometry and voxelwise CBF (CCN and vMCI only) analyses were conducted to determine differences in GMV and CBF between groups.
- Sensitivity analyses were conducted in age- (within 5 years) and sex-matched subgroups
- Multiple regressions were conducted to determine the association between significant CBF regions-of-interest and cognitive status, adjusting for GMV.

RESULTS

Table 1 Baseline demographics [mean (SD) or count (%)].

	NCN (n = 57)	CCN (n = 20)	vMCI (n = 59)
Age (years)	68.7 (7.6)	66.4 (7.9)	68.0 (7.8)
Sex (male)	39 (68%)	16 (80%)	41 (69%)

Table 2 VBM analysis of the full sample. GMV differences were thresholded at $p < 0.05$ (cluster-level FWE corrected).

	x	MNI Coordinates y	z	(Z (E))	Brain Region (Harvard-Oxford Atlas)	Yeo 7-Network
NCN > CCN	4	-12	4	4.29	Right Thalamus	
	48	-63	-9	5.13	Right Lateral Occipital Cortex, inferior division	Visual
	48	-64	3	4.68	Right Lateral Occipital Cortex, inferior division	Visual
	57	-72	4	4.25	Right Lateral Occipital Cortex, inferior division	Visual
NCN > vMCI	-69	-45	6	4.99	Left Middle Temporal Gyrus, temporooccipital part	Default
	-68	-27	15	4	Left Superior Temporal Gyrus, posterior division	Somatomotor
	-69	-28	0	3.46	Left Middle Temporal Gyrus, posterior division	Somatomotor
	-50	32	-3	4.57	Left Inferior Frontal Gyrus, pars triangularis	Default
	-42	38	-8	3.98	Left Frontal Pole	Default
	-42	48	2	3.87	Left Frontal Pole	Control
	64	3	6	4.39	Right Precentral Gyrus	Saliency/Ventral Attention
	72	-21	4	4.12	Right Superior Temporal Gyrus, posterior division	Somatomotor
	69	-10	9	3.96	Right Postcentral Gyrus	Somatomotor
	58	12	-18	5.09	Right Temporal Pole	Default
	46	12	28	4.29	Right Inferior Frontal Gyrus, pars opercularis	Dorsal Attention
	36	3	58	4.23	Right Middle Frontal Gyrus	Control
CCN > NCN	48	8	48	3.35	Right Middle Frontal Gyrus	Control
	52	9	40	3.16	Right Middle Frontal Gyrus	Dorsal Attention

Table 3 VBM sensitivity analysis of the age- and sex-matched subgroup. GMV differences were thresholded at $p < 0.05$ (cluster-level FWE corrected).

	x	MNI Coordinates y	z	(Z (E))	Brain Region (Harvard-Oxford Atlas)	Yeo 7-Network
NCN > vMCI	52	15	24	4.88	Right Inferior Frontal Gyrus, pars opercularis	Control
	62	15	20	4.85	Right Inferior Frontal Gyrus, pars opercularis	Saliency / Ventral Attention
	64	4	4	4.35	Right Precentral Gyrus	Saliency / Ventral Attention
	-48	30	26	4.68	Left Middle Frontal Gyrus	Control
	-52	33	18	4.47	Left Inferior Frontal Gyrus, pars triangularis	Control
	-52	42	14	4.15	Left Frontal Pole	Control
	24	20	60	4.28	Right Superior Frontal Gyrus	Control
	28	6	68	3.71	Right Superior Frontal Gyrus	Dorsal Attention
	15	30	63	3.6	Right Superior Frontal Gyrus	Default

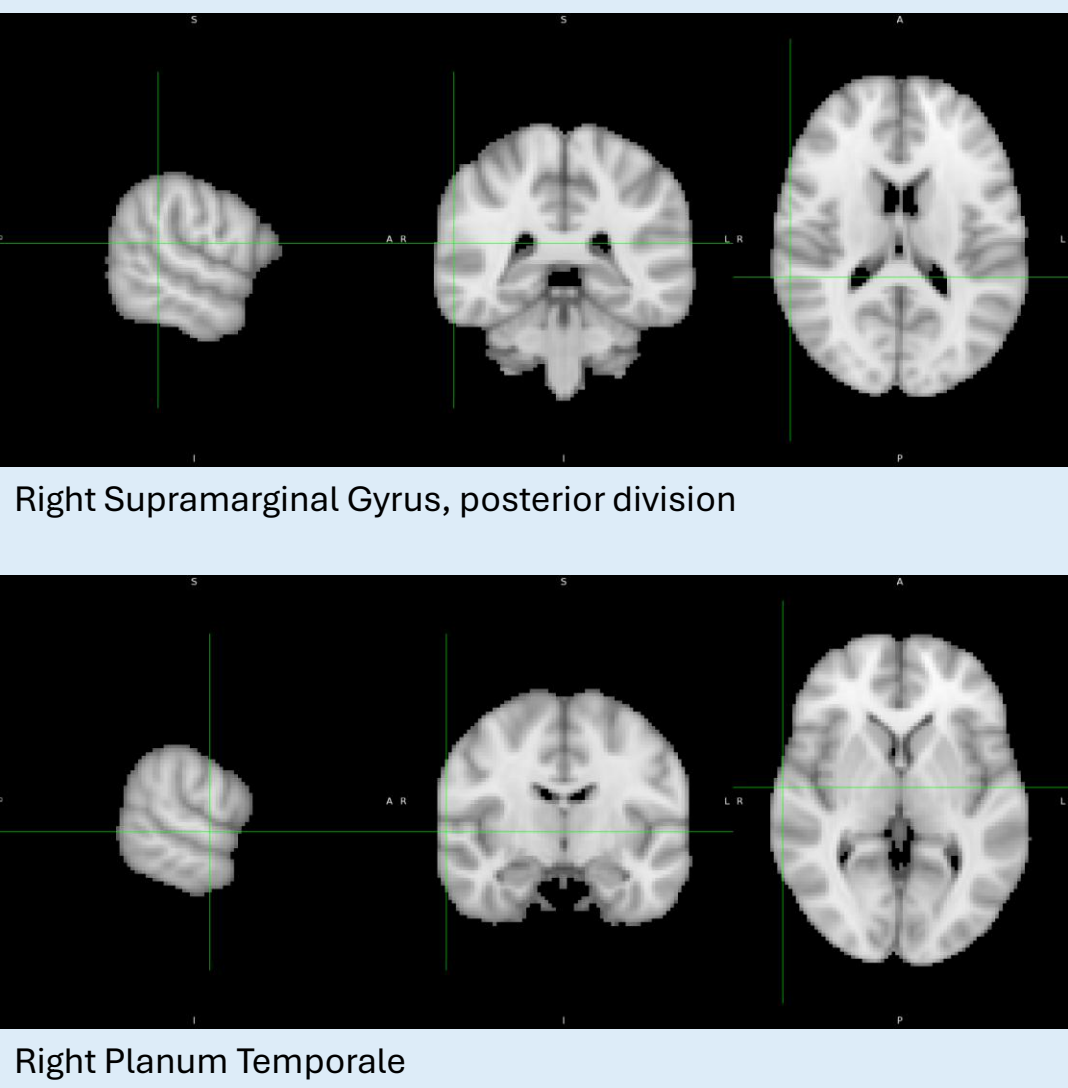
Table 4 CBF voxelwise sensitivity analysis of the age- and sex-matched subgroup. Results were thresholded at $p < 0.05$ FWE-corrected).

	Brain Region (Harvard-Oxford Atlas)	x	MNI Coordinates y	z	# Voxels
NCN > vMCI	Right Supramarginal Gyrus, posterior division	60	-38	16	76
	Right Planum Temporale	64	-10	2	52

Table 5 Associations between the significant CBF regions-of-interest and cognitive status, adjusting for GMV and white matter hyperintensity volume.

Brain Region	Coefficient	B	SE	t	p
Right Supramarginal Gyrus, posterior division	Intercept	28.15	16.83	1.67	0.1139
	Cognitive Status	-6.68	3.79	-1.76	0.0968
	Grey Matter Volume (cm ³)	0.006	0.004	1.46	0.1629
	White Matter Hyperintensity Volume (cm ³)	-0.55	0.20	-2.74	0.0144
Right Planum Temporale	Intercept	45.34	10.24	4.43	0.0004
	Cognitive Status	-10.56	3.10	-3.40	0.0036
	Grey Matter Volume (cm ³)	0.02	0.01	1.89	0.0772
	White Matter Hyperintensity Volume (cm ³)	-0.82	0.20	-4.21	0.0007

Figure 1 Significant voxels identified from the voxelwise CBF sensitivity analysis.



CONCLUSION

- Regional cerebral blood flow reductions in the right planum temporale remained independently associated with cognitive status, suggesting that this reduction is a distinct process from grey matter atrophy and WMH.
- The central executive network and dorsal attention network may be implicated in this vascular at-risk stage.
- Vascular mild cognitive impairment may be an optimal window for therapeutic intervention before further atrophy occurs.

ACKNOWLEDGEMENTS

We would like to thank all the participants for their participation in the MOVE-IT study.



MW has received funding from the CIHR Canada Graduate Research Doctoral Scholarship, CAN-TAP-TALENT Doctoral Award, Peterborough K.M. Hunter Charitable Foundation Graduate Award, SCACE Graduate Fellowship in Alzheimer’s Research, and Toronto Rehabilitation Institute Student Scholarship



Contact: Dr. Krista Lanctôt, Sunnybrook Health Sciences Centre, 2075 Bayview Avenue, Room FG21, Toronto, Ontario, M4N 3M5, Canada
Email: krista.Lanctot@sri.utoronto.ca