STRATEGIC REGIONAL SUBCORTICAL HYPERINTENSITY VOLUMETRICS IN ALZHEIMER'S DISEASE AND NORMAL ELDERLY

Correlations with executive function, mental processing speed, and memory.

Joel Ramirez[a-c], Alicia A. McNeely[a-c], Christopher J.M. Scott[a-c], Donald T. Stuss[d-f], Sandra E. Black[a-g]

[a] LC Campbell Cognitive Neurology Research Unit, Toronto, Canada; [b] Heart & Stroke Foundation Centre for Stroke Recovery, Toronto, Canada; [c] Sunnybrook Health Sciences Centre, Brain Sciences Research Program, Sunnybrook Research Institute, Toronto, Canada; [d] University of Toronto, Institute of Medical Science, Faculty of Medicine, Toronto, Canada; [e] Rotman Research Institute, Baycrest, Toronto, Canada; [f] Ontario Brain Institute, Toronto, Canada, [g] Toronto Dementia Research Alliance, Toronto, Canada.

BACKGROUND

Subcortical hyperintensities (SH) are radiological entities commonly observed on MRI of Alzheimer's disease (AD) and normal elderly [1,2]. While the presence of SH is believed to indicate some form of small vessel disease, pathological heterogeneity, methodological differences, and the contribution of brain atrophy associated with AD pathology, have yielded inconsistent results in the literature.

PURPOSE

To examine the potential relationships between strategic regional signs of small vessel disease and cognitive function in a sample of AD patients and normal elderly controls.

MRI-derived regional SH volumes of interest were used to index small vessel disease burden. Performance on various neuropsychological tests were used to assess executive function, speed of mental processing, and memory.

DISCUSSION

In normal elderly, a 1% increase in medial middle frontal SH estimated a 0.24 SD decrease in executive performance. Previous studies have demonstrated patients with focal lesions in this frontal region perform poorly on the FAS task [5], a component of the Executive score in this study.

In AD patients, a 1% increase in pvSH estimated a 0.17 SD increase in time to complete the Trails(A). It has been suggested that SH burden in the periventricular region may affect communication between distant multiple cortical areas, resulting in an overall decrease in speed of processing [6]. Additionally, a subtle (2% of the variance) association was demonstrated with left temporal SH and memory. Future SABRE upgrades will include smaller temporal regions for future analyses.

Conclusion: Although the contribution of strategic regional SH was small relative to whole brain atrophy, these results suggest that signs of small vessel disease (as indexed by SH) may correspond with subtle cognitive deficits in the elderly, which may be exacerbated with AD pathology.

RESULTS

Table 1 – Participant demographics and volumetric imaging summary statistics.

	AD	NC	p value	Cohen's d Effect Size
Demographics				
n	265	100	-	
Age, y	72.8 (9.0)	69.5 (8.0)	p<0.001	
Sex, n (%) female	152 (57)	55 (55)		
Education, y	13.8 (3.8)	15.5 (3.0)	p<0.001	
MMSE/30 [a]	23.2 (4.5)	29.0 (1.1)	p<0.05	
Basic Tissue Volumetrics [b]				
ST-TIV	1211.8 (140.1)	1227.7 (112.5)	n.s.	
GM	509.9 (55.7)	560.8 (45.0)	p<0.0001	1.35
WM	363.6 (55.1)	403.1 (52.3)	p<0.0001	0.92
sCSF	274.8 (62.5)	224.2 (48.1)	p<0.0001	1.24
vCSF	52.9 (27.1)	34.1 (16.2)	p<0.0001	1.01
SH Volumetrics				
SH, Median (IQR)	5.4 (11.0)	2.5 (3.3)	p<0.01	0.54
pvSH, Median (IQR)	4.5 (9.9)	1.8 (3.0)	p<0.01	0.51
dwSH, Median (IQR)	0.6 (1.1)	0.3 (0.6)	<0.05	0.38
Lacunar (mm^3), Median (IQR)	32.8 (155.9)	10.3 (45.0)	p<0.0001	0.58

Values reported are mean (SD) unless otherwise specified. Data was normalized and converted to z-scores prior to analysis. Key: MMSE=Mini-Mental State Exam, ST-TIV=supratentorial total intracranial volume, GM=gray matter, WM=white matter, sCSF=sulcal cerebrospinal fluid, vCSF=ventricular CSF, SH=subcortical hyperintensity, pvSH=periventricular SH, dwSH=deep white SH, IQR=interquartile range.
[a] Available in 97 NC and 258 AD subjects.
[b] All volumes expressed in cubic centimeters (cc) unless otherwise indicated.

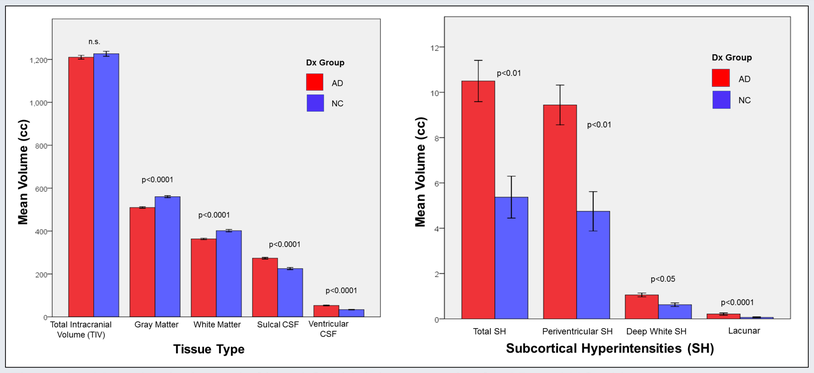

Figure 1 – Mean basic tissue (left) and SH (right) volumetrics for AD and NC with p-values.

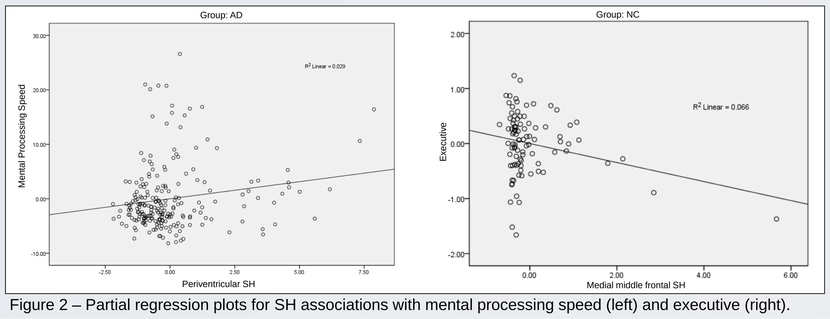

Figure 2 – Partial regression plots for SH associations with mental processing speed (left) and executive (right).

Table 2 – Regression results for regional SH and cognition.

	β Coefficient	R^2	p Value
Executive			
AD (n=223)			
BPF	0.26	0.07	p<0.0001
NC (n=94)			
Medial Middle Frontal SH	-0.24	0.07	p=0.01
Education, y	0.23	0.06	p<0.05
BPF	0.31	0.1	p<0.01
Mental Processing Speed			
AD (n=222)			
Periventricular SH	0.17	0.03	p=0.01
Age	-0.33	0.08	0<0.0001
BPF	-0.31	0.08	0<0.0001
NC (n=88)			
Age	0.24	0.06	p<0.05
Memory			
AD (n=236)			
Left Temporal SH	-0.13	0.02	p<0.05
Education, y	0.22	0.05	p=0.001
BPF	0.30	0.09	p<0.0001
NC (n=95)			
Education, y	0.25	0.08	0<0.01
Age	-0.40	0.18	p<0.0001

SH volumes were expressed as percentages and converted to z-scores prior to analysis. Key: BPF=brain parenchymal fraction. Cognitive domains are composite scores (see Table 3) generated from mean z-scores using NC data.

METHODS

PARTICIPANTS

A sample of probable/possible AD (NINCDS-ADRDA criteria) patients enrolled in the Sunnybrook Aging and Dementia study (n=265) and community dwelling normal elderly control participants (n=100). See Table 1 for additional demographic details.

MRI PROCEDURES

MRI Protocols: 1.5T GE Signa. T1-weighted (AX 3D SPGR, 1.2-1.4mm), proton density (PD) and T2-weighted (T2) (interleaved axial dual-echo spin echo, 3mm).

The Lesion Explorer (LE) image processing pipeline was used to obtain basic tissue and regional SH volumes of interest. LE is a reliable and comprehensive semi-automatic tool for segmentation and parcellation of MRI [3,4].

LESION EXPLORER

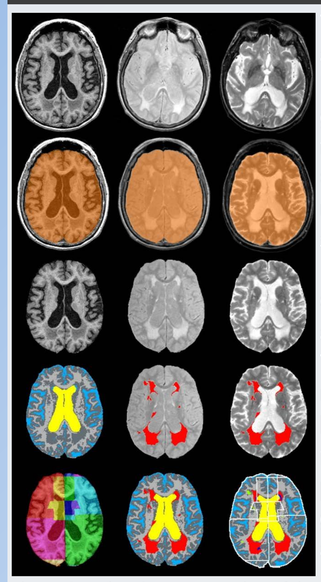

Figure 3 – Visual representation of the LE pipeline processing steps.

The LE pipeline was applied to coregistered T1, PD and T2 images to generate volumes for basic tissue classes: ST-TIV, GM, WM, sCSF, vCSF using an intensity based segmentation algorithm.

Quantification of SH was accomplished from a T1/PD/T2 segmentation using localized intensity-based histograms and a fuzzy clustering false positive minimization to generate: pvSH, dwSH, and lacunar volumes.

SABRE

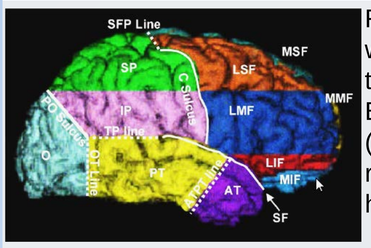

Figure 4 – 3D surface volume render with SABRE parcellations overlayed.

Regional parcellation was accomplished using the Semi-Automated Brain Region Extraction (SABRE) to generate 13 regions of interest per hemisphere.

NEUROPSYCHOLOGY

Table 3– Summary of cognitive domains and neuro-psychological tests used to generate composite scores.

Domain	Test	Measure
Executive	Verbal Fluency 'FAS' Test	Total words correct
	Wisconsin Card Sorting Test	Total correct
	Wisconsin Card Sorting Test	Perseverative errors to previous response
	Wisconsin Card Sorting Test	Perseverative errors to previous category
Mental Processing Speed	Trail Making Test (part A)	Time to complete (secs)
Memory	California Verbal Learning Test	Total correct at acquisition
	Wechsler Memory Scale Revised Visual Reproduction	Immediate recall
	Dementia Rating Scale	Memory

ACKNOWLEDGEMENTS

We gratefully acknowledge financial support from the Canadian Institute of Health Research (MT#13129), Alzheimer Society of Canada, Alzheimer's Association (USA), The L. C. Campbell Foundation and The Heart and Stroke Foundation Centre for Stroke Recovery.

REFERENCES

[1] O'Sullivan, M., 2008. Practical Neurology, 8:26-38.
[2] Pantoni, L., 2010. Lancet Neurology, 9:689-701.
[3] Ramirez et al., 2011. NeuroImage, 54(2):963-73.
[4] Ramirez et al., 2013. Brain Topography, 26(1):35-8
[5] Stuss et al., 1998. J Int Neuropsychol Soc, 4:265-278
[6] De Groot et al, 2000. Annals of Neurol, 47(2):145-51.

For more information or to download a copy of this poster, please visit brainlab.ca/posters or scan this QR code.