VENTRICULAR EXPANSION IN ALZHEIMER'S DISEASE: RELATIONSHIPS WITH SMALL VESSEL DISEASE AND COGNITION

UNIVERSITY OF TORONTO FACULTY OF MEDICINE Neuroscience Program

Sabrina Adamo[1,2], Joel Ramirez[1,2,3], Melissa F. Holmes[1,2], Fuqiang Gao[1,2,3], Mario Masellis[1,2,3,4], Sandra E. Black[1,2,3,4]

[1]L.C. Campbell Cognitive Neurology Research Unit, Toronto, Canada; [2]Hurvitz Brain Sciences Research Program, Sunnybrook Research Institute, Toronto, Canada; [3]Heart & Stroke Foundation Canadian Partnership for Stroke Recovery, Sunnybrook Health Sciences Centre, Toronto, Canada; [4]Department of Medicine, Division of Neurology, University of Toronto, Toronto, Canada.

Sunnybrook HEALTH SCIENCES CENTRE

HEART & STROKE FOUNDATION Canadian Partnership for Stroke Recovery

BACKGROUND

- Alzheimer's disease (AD) is the most common cause of dementia
- In 2016, it was estimated that over 500,000 Canadians are living with dementia [1]
- In addition to neuropsychological tests, MRI-based biomarkers measuring brain atrophy and small vessel disease (SVD) burden may be useful in tracking disease progression in prospective clinical trials of AD [2-3]

OBJECTIVE

Our study was aimed at determining the feasibility of using ventricular cerebrospinal fluid (vCSF) growth as an outcome measure for clinical trials in AD.

PARTICIPANTS

- Baseline & follow-up MRI and cognitive test scores from the Sunnybrook Dementia Study were examined
- AD patients (n=133) with varying degrees of SVD, meeting NINCDS-ADRDA criteria for probable/possible AD dementia [4], and NCs (n=47)

Table 1: Demographics and Volumetrics

	AD n=133	NC n=47	P-value	Cohen's *d*
Demographics				
Age				
Baseline	71.56 (8.61)	70.45 (7.27)	0.43	0.14
Follow-up	73.24 (8.66)	72.2 (7.13)	0.46	0.13
Sex, M/F	57/76	22/25	0.22†	
Education	13.3 (3.54)	15.85 (2.78)	0.00*	0.80
ISI	1.69 (0.87)	1.75 (0.78)	0.67	0.07
Volumetrics				
Ventricles				
Growth	10.59 (8.02)	5.63 (3.89)	0.00*	0.79
Shrinkage	3.18 (4.81)	3.36 (3.48)	0.82	0.04
Stable	44.9 (23.37)	32.2 (17.15)	0.00*	0.62

Data are presented as Mean (SD) unless otherwise indicated. All volumes are reported in cubic centimeters (cc).
†chi square test
$p > 0.01$

METHODS

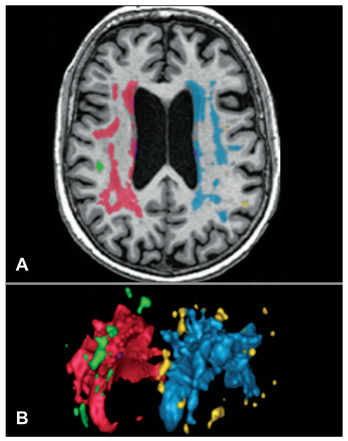


Figure 1: dWMH in green & yellow and pWMH in red & blue. A: Axial T1 B: 3-D rendering of WMH segmentation.

- **Cognition** was measured using the Mini-Mental State Examination (MMSE) at both time points
- **Brain Atrophy** was assessed using ventricular cerebral spinal fluid (vCSF) volumes
- **SVD** was assessed using periventricular and deep white matter hyperintensity (p/dWMH) volumes (Fig 1)
- Baseline and follow up MRI (mean ISI=1.7yrs) was acquired using a 1.5T GE Signa scanner
- Changes in MRI-based biomarkers were assessed using a previously validated method [5]
- ANCOVA was used to compare group dynamic progression
- Partial Pearson r correlations were used to examine relationships between changes in atrophy, SVD, and cognition
- All analyses accounted for baseline age, sex, and education

RESULTS

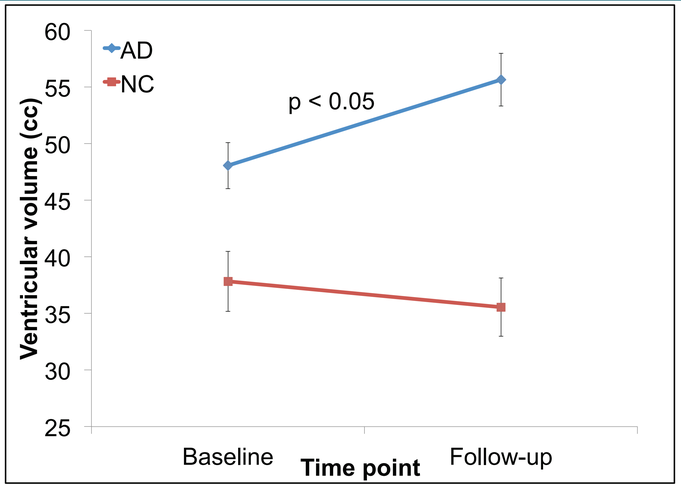
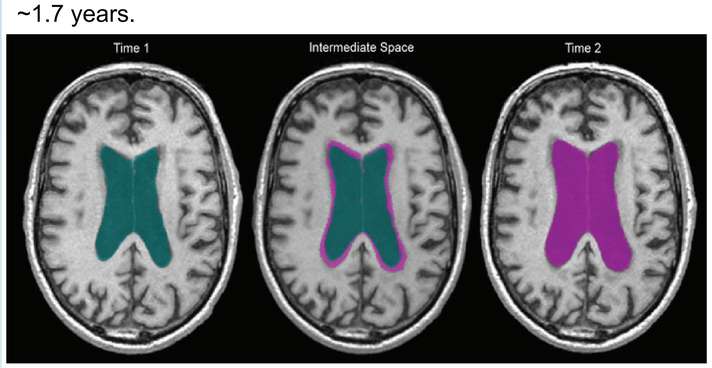


Figure 2: Mean (± SEM) ventricular change in Alzheimer's disease (AD; n=133) and normal controls (NC; n=47) after ~1.7 years.



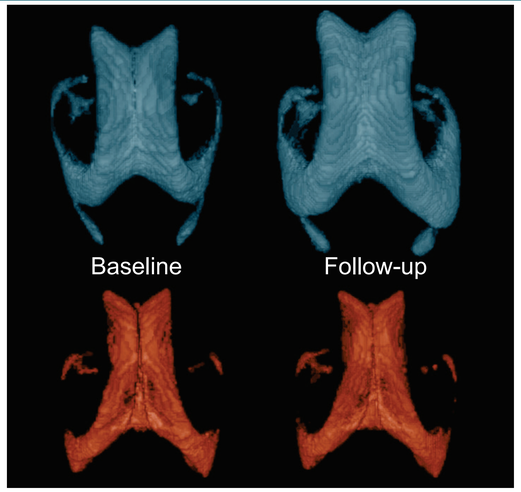


Figure 3: Shows top view of 3D volume surface renders of ventricles from an Alzheimer's disease patient (blue) and a normal elderly control (red). Left images show ventricles at baseline scanning and right images show after 1 year follow-up.

Figure 4: Two year ventricular expansion in a 60 year old man living with AD. Baseline vCSF = 83.6 cc, follow-up vCSF = 119.0 cc. Green indicates baseline vCSF voxels, pink indicates follow-up (right) and growth (middle). WMH within vCSF growth regions were subsequently removed to account for ventricular expansion.

RESULTS (CONT)

- Dynamic progression analyses revealed that in just under 2 years, AD patients exhibited significant increases in vCSF volume compared to NCs ($p<0.0001$; Fig 2)
- Pearson r analyses revealed vCSF volume growth was significantly correlated with pWMH ($r=0.4$, $p<0001$) but not dWMH ($p=0.285$, n.s.)
- vCSF volume growth exhibited a moderate correlation with change in MMSE score ($r=0.372$, $p<0.0001$) over the same time period

CONCLUSIONS

- Patients with AD showed greater vCSF progression than NCs (Fig 2)
- vCSF expansion in AD patients from their baseline to follow up scans was associated with SVD burden and cognitive decline (Fig 2)
- This suggests that vCSF growth is a promising biomarker that may be used as an outcome measure for clinical trials aimed at slowing progression and improving cognitive outcome
- Novel treatment strategies such as the use of anti-hypertensives, may use our MRI-based progression results as a tool to assess treatment outcomes [6]

REFERENCES

1. Alzheimer Society Canada (2016) *Report on Dementia*.
2. Nestor et al. (2008). *Brain*.
3. Iturria-Medina et al. (2016). *Nature Comm.*.
4. McKhann et al. (2011). *Alzheimer's Dement.*
5. Ramirez et al. (2016). *Front. Aging Neurosci.*
6. Edwards et al. (2017). *J. Alzheimers. Dis.*

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

ACKNOWLEDGEMENTS

Co-authors gratefully acknowledge funding support from the CIHR, L.C. Campbell Foundation, and the HSFCPSR. JR receives salary support from the CVN, OBI, and ONDRI. SEB receives financial support from the Dept of Medicine Sunnybrook HSC, SRI, Brill Chair in Neurology from U of T, and as Executive Director of the TDRA.