Left temporal polar atrophy distinguishes Semantic Dementia from Alzheimer's disease

Breni Varatharajah[1,2], Benjamin Lam[1,2,3], Joel Ramirez[1,2,4], Manu J. Sharma[1,2], Vanessa Yhap[1,2], Melissa F. Holmes[1,2], Fuqiang Gao[1,2], Donald T. Stuss[1,2], Mario Masellis[1,2,3], Sandra E. Black[1,2,3,4]

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

BACKGROUND

- Alzheimer's Disease (AD) and Semantic Dementia (SD) are late-onset cognitive presentations with overlapping clinical features that can make distinguishing them difficult, particularly early in the course of illness.
- Studies have indicated that one feature of SD is anterior temporal atrophy, particularly on the left side[1].

OBJECTIVES

- The aim of this study was to determine whether left anterior temporal pole (LATP) atrophy can be used as an *in vivo* imaging biomarker to distinguish between the clinical phenotype of SD and AD in a sample reflective of the tertiary care setting.
- We first compared LATP volumes between a group of individuals with AD versus those with SD.
- We then examined whether LATP atrophy was associated with objective language impairment as measured by the Boston Naming Test (BNT) and Semantic Fluency (SeFlu).

METHODS

- We analyzed data from 88 participants from the Sunnybrook Dementia Study (clinicaltrials.gov NCT01800214) with clinical diagnoses of AD (n=44) or SD (n=44).
- Participants had undergone neuropsychological testing and structural MRI (1.5T), the latter of which was processed using a previously validated volumetric pipeline.
- BNT and SeFlu scores were not used in establishing the clinical diagnosis.
- Comparison of imaging and language test scores between AD and SD was done using the Mann-Whitney U.
- Association between LATP, expressed as percent brain parenchymal fraction (pBPF), and BNT, SeFlu, and the MMSE (as a global comparator of cognition) was done using Spearman's Rho.

	AD (n=44) Mean (SD)	SD (n=44) Mean (SD)	p-value
Age	68.0 (8.2)	68.0 (8.2)	1.0
Education, years	14.5 (3.2)	14.9 (3.8)	0.63
MMSE	24.2 (3.6)	22.4 (7.1)	0.92
LATP Raw parenchymal volume, cc	19.2 (4.2)*	15.8 (5.5)*	0.003
LATP Total intracranial capacity, cc	26.4 (5.4)	25.8 (4.0)	0.52
LATP brain parenchymal fraction, %	72.5 (5.8)*	60.2 (15.1)*	<0.001
BNT	22.7 (6.1)*	12.9 (8.4)*	<0.001
Semantic Fluency	11.0 (4.8)*	7.3 (4.9)*	0.001

Table 1: Comparison between AD and SD groups on demographic, imaging, and neuropsychological measures.
* Denotes significant difference p<0.05

	Spearman's rho	p-value
BNT x LAPT pBPF	0.58	<0.001
Semantic Fluency x LAPT pBPF	0.52	<0.001
MMSE x LAPT BPF	0.26	0.01

Table 2: Correlation between LAPT pBPF and cognitive measures in all participants

	Spearman's rho	p-value
BNT x LAPT pBPF	0.52	<0.001
Semantic Fluency x LAPT pBPF	0.38	0.01
MMSE x LAPT BPF	0.24	0.13

Table 3: Correlation between LAPT pBPF and cognitive measures in SD participants

	Spearman's rho	p-value
BNT x LAPT pBPF	0.36	0.02
Semantic Fluency x LAPT pBPF	0.54	<0.001
MMSE x LAPT BPF	0.24	0.12

Table 4: Correlation between LAPT pBPF and cognitive measures in AD participants

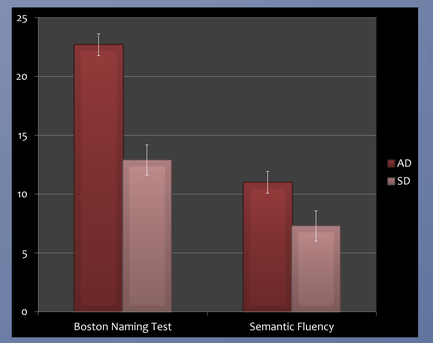

Figure 1: Comparison of language tests between AD and SD groups

RESULTS

- SD participants had smaller raw LATP volumes (15.8 cc vs. 19.2 cc, p=0.003), and smaller LATP pBPF (i.e. brain volumes controlled for intracranial capacity; 60.2 vs. 72.5, p<0.001; Cohen's *d* = 1.1). See Table 1
- SD participants scored lower on BNT (12.9 vs. 22.7, p<0.001) and SeFlu (7.3 vs. 11.0, p=0.001). See Table 1 and Figure 1
- When combining AD and SD participants, LATP pBPF moderately correlated with BNT (Spearman's rho = 0.58, p<0.001), and with SeFlu (Spearman's rho = 0.52, p<0.001), but not with MMSE (Spearman's rho = 0.26, p=0.01). See Table 2
- In SD participants only, LATP pBPF moderately correlated with BNT (Spearman's rho = 0.52, p<0.001) and with SeFlu (Spearman's rho = 0.38, p=0.01), but not with MMSE (Spearman's rho = 0.24, p=0.13). See Table 3
- In AD participants only, LATP pBPF moderately correlated with BNT (Spearman's rho = 0.36, p=0.02) and with SeFlu (Spearman's rho = 0.54, p=<0.001), but not with MMSE (Spearman's rho = 0.24, p=0.12). See Table 4

CONCLUSIONS

- We found that pBPF in the LATP distinguishes between SD and AD.
- pBPF specifically correlates with language function, but not global cognition when considering AD and SD participants together and separately.
- MMSE may not be a sufficient screening tool for either SD or AD.
- Limitations include lack of comparison to a control group.
- Future studies could examine relationships between pBPF and other areas of cognition, such as visual and verbal memory.

ACKNOWLEDGEMENTS

Co-authors gratefully acknowledge funding support from the CIHR, Linda C. Campbell Foundation, and the Heart & Stroke Foundation Canadian Partnership for Stroke Recovery. JR receives salary support from the Canadian Vascular Network, Ontario Brain Institute, and the Ontario Neurodegenerative Disease Research Initiative. SEB receives financial support from the Dept of Medicine Sunnybrook HSC, the Sunnybrook Research Institute, Brill Chair in Neurology from the University of Toronto, and as Executive Director of the Toronto Dementia Research Alliance

REFERENCES

1. D. Chan et al., (2001). *Annals of Neurology.*
2. J. Ramirez et al., (2011). *NeuroImage.*