

Case 5: When amyloid imaging isn't enough

Tammie Benzinger, M.D., PhD.

Washington University School of Medicine in St. Louis

&

Nupur Ghoshal, M.D.

MCI Symposium 2014: Diagnostic Case Studies

Disclosure: Tammie L.S. Benzinger, M.D., Ph.D.

Research Support / Grants: NIH/NIA 5P01AG026276, 1U01AG032438, AG003991-27, 1R01NS066905-01, 1P01NS059560-01A1, UL1RR024992; Avid Radiopharmaceuticals (Eli Lilly), Alzheimer's Association, DIAN-TU Pharma Consortium

Stock/Equity (any amount): None

Consulting/Advisory Board: Eli Lilly (2011)

Speakers Bureau / Honoraria: None

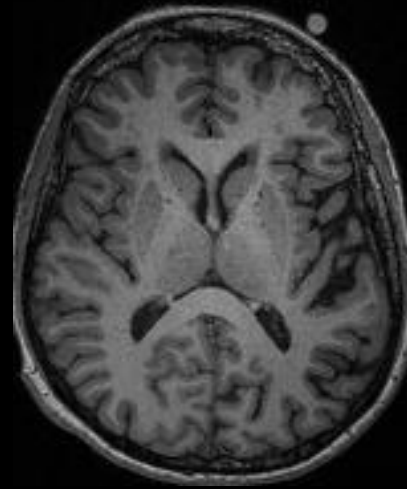
Other: Travel, National Multiple Sclerosis Society

Clinical background

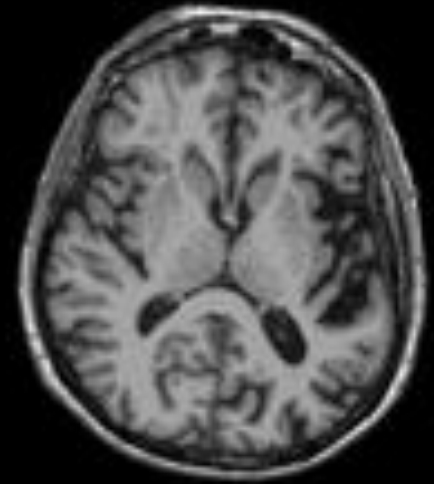
- A 73-year old cognitively normal, health woman presented for routine neuroimaging as part of an ongoing research study
- She had been a participant in longitudinal studies of memory and aging at our institution for 6 years, with serial imaging, CSF, and PET scans
- Clinical visit 12/2011:
 - Clinical dementia rating (CDR) 0.0, MMSE 26
- Imaging visits
 - 12/2012 MMSE 21
 - 9/2013 MMSE 14
 - Radiologist contacted to evaluate patient

PIB PET 12/2012

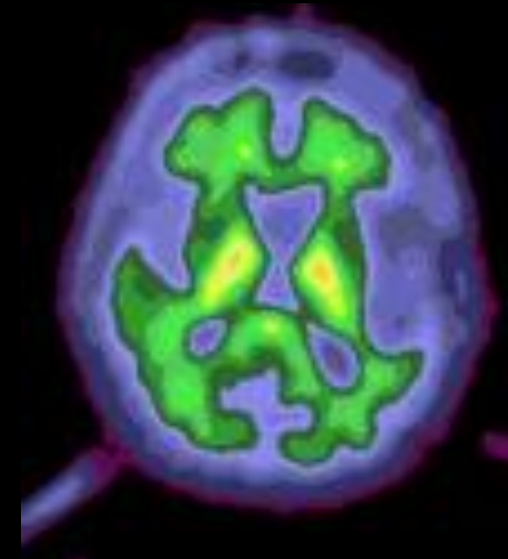
SUMMARY	BINDING POT.	SUVR
PREF	0.0707	1.1267
PREC	0.1683	1.2183
RAC	0.1267	1.2191
TEMP	0.0734	1.1883
GR	0.1266	1.1967
PAR	0.1027	1.1806
OCC	0.1322	1.1676
CAU	0.0514	1.1442
MCBP	0.1098	1.1825



2008

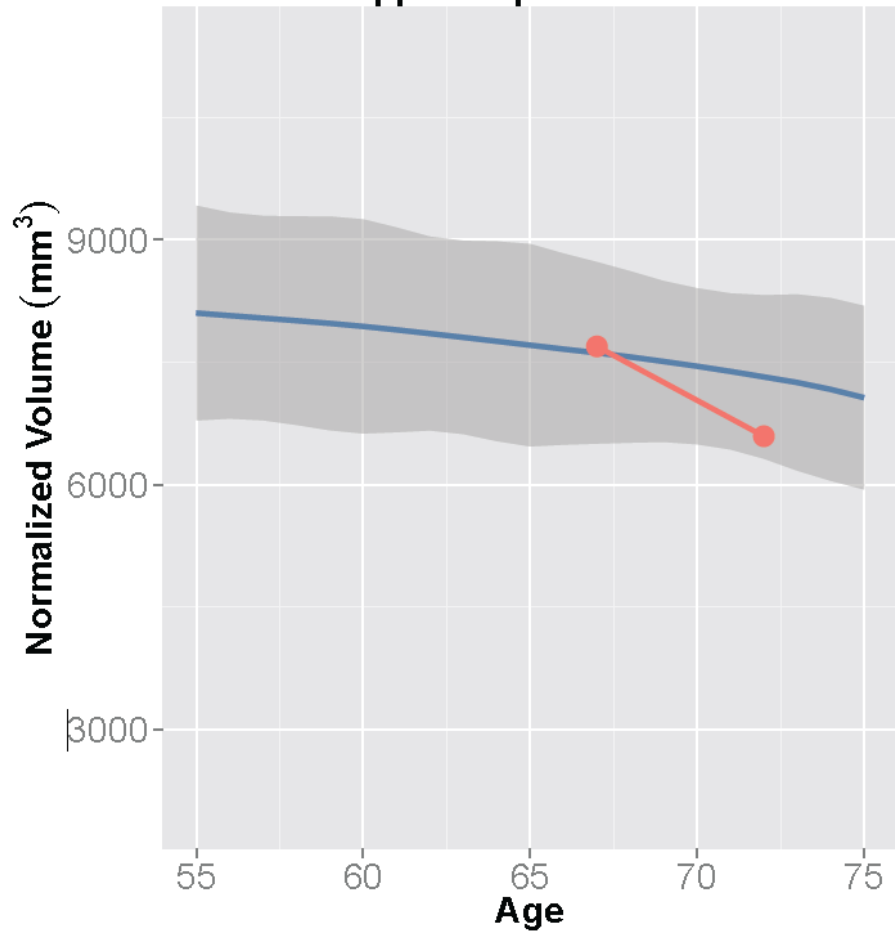


PIB PET & MRI
12/2012

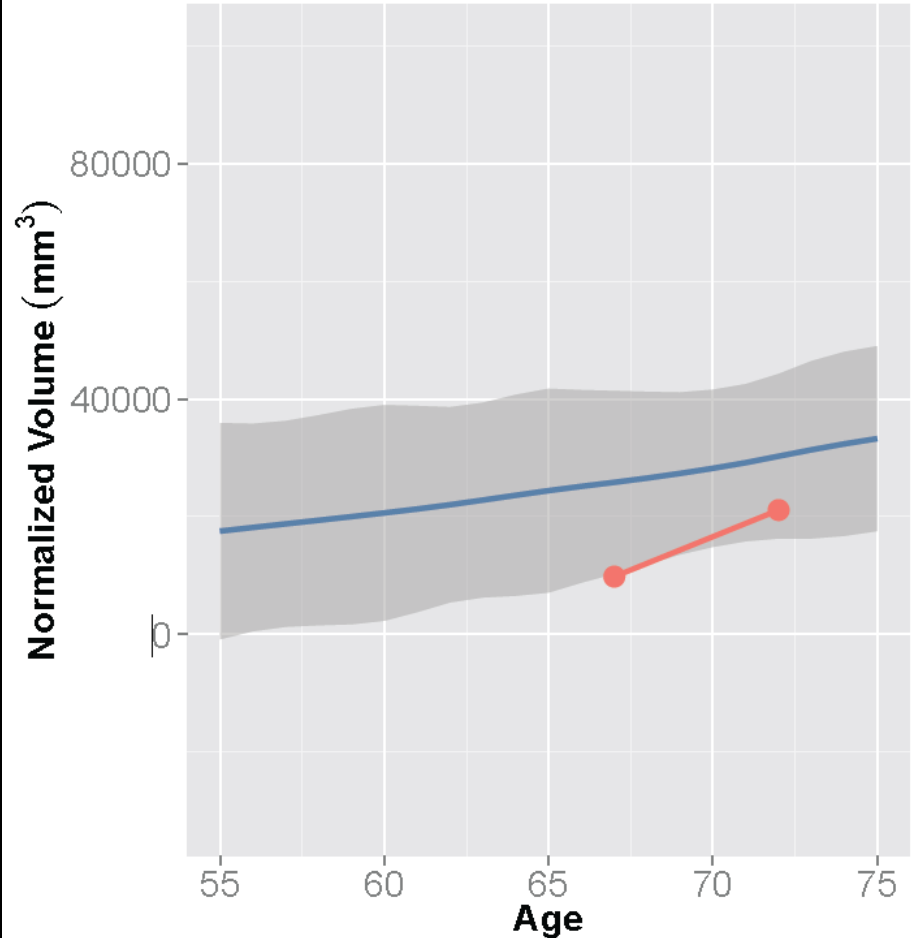


Longitudinal volumetric MRI results

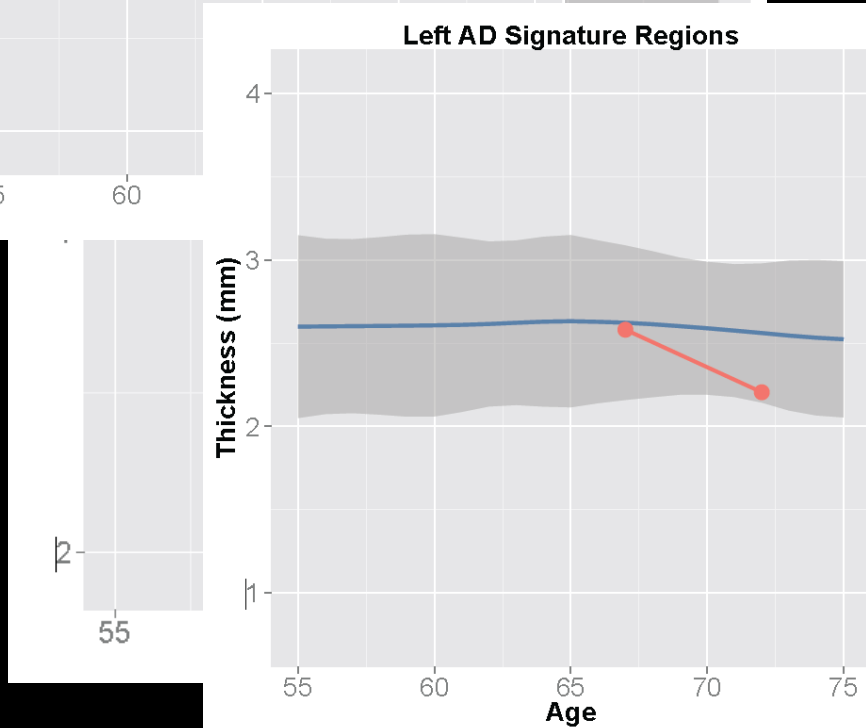
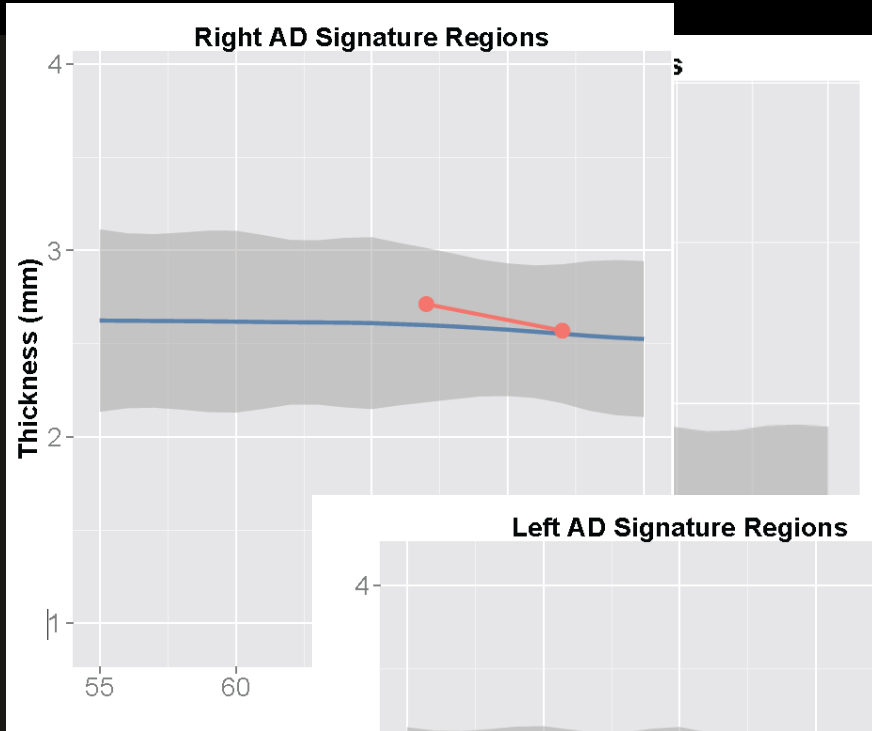
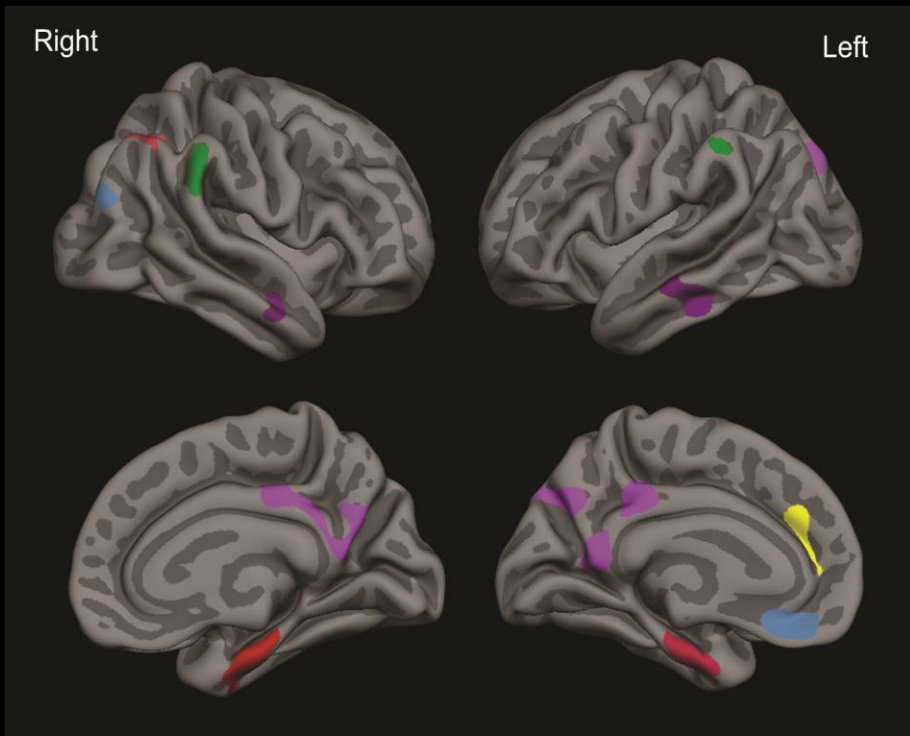
Hippocampal Volume



Lat. Ventricle Volume



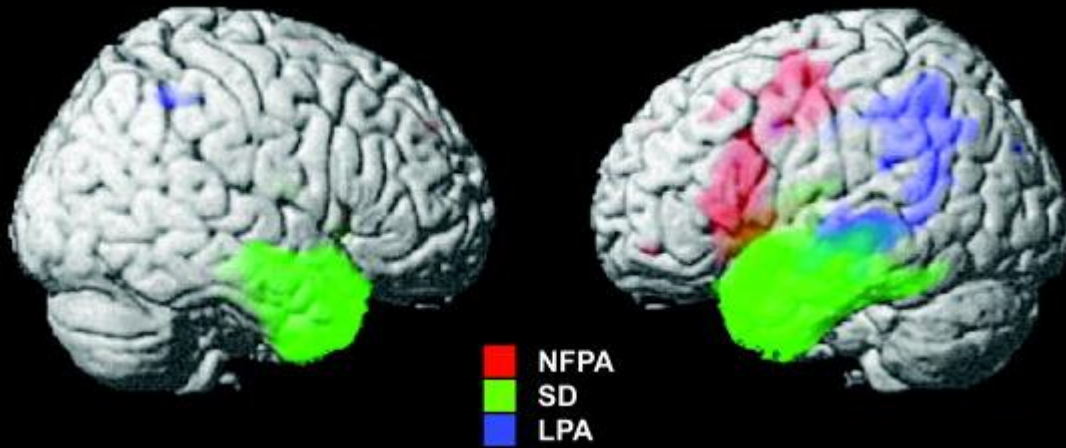
Liang, Refined Cortical Signature



Adapted from Bakkour A, *et al.*, *Neurology*. 2009;72(12):1048-55.

Putative regions of cortical thinning in primary progressive aphasia

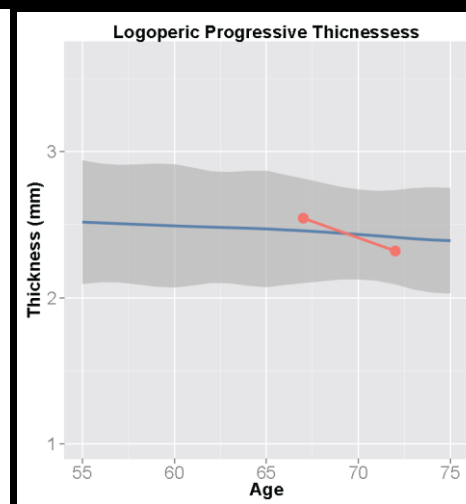
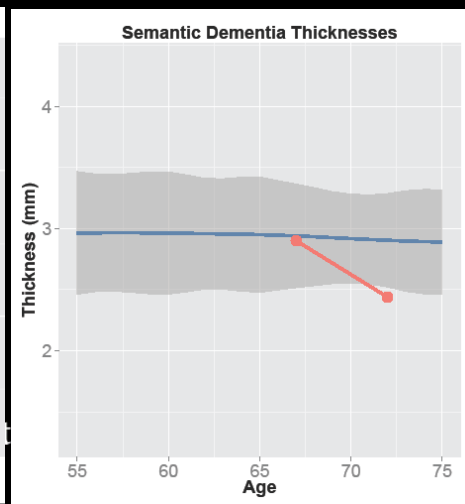
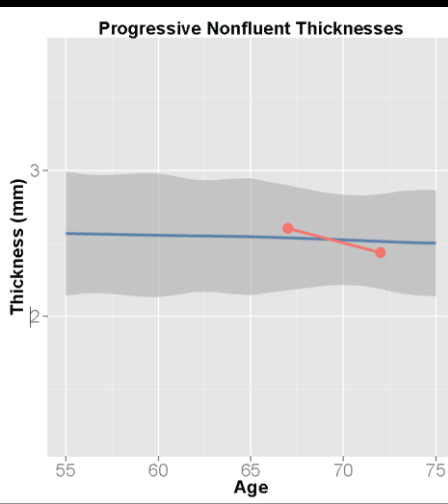
Gorno-Tempini *et al.*, *Annals of Neurology*, 2004)



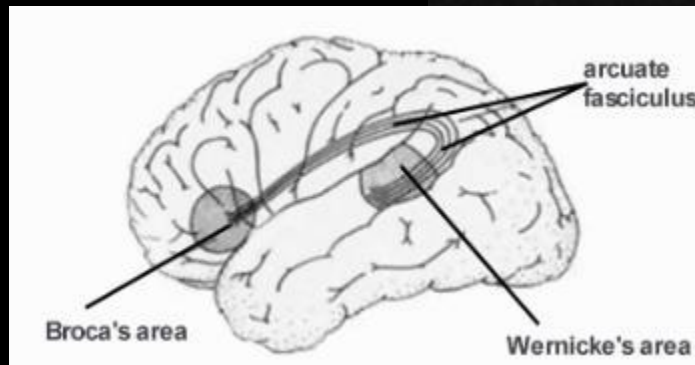
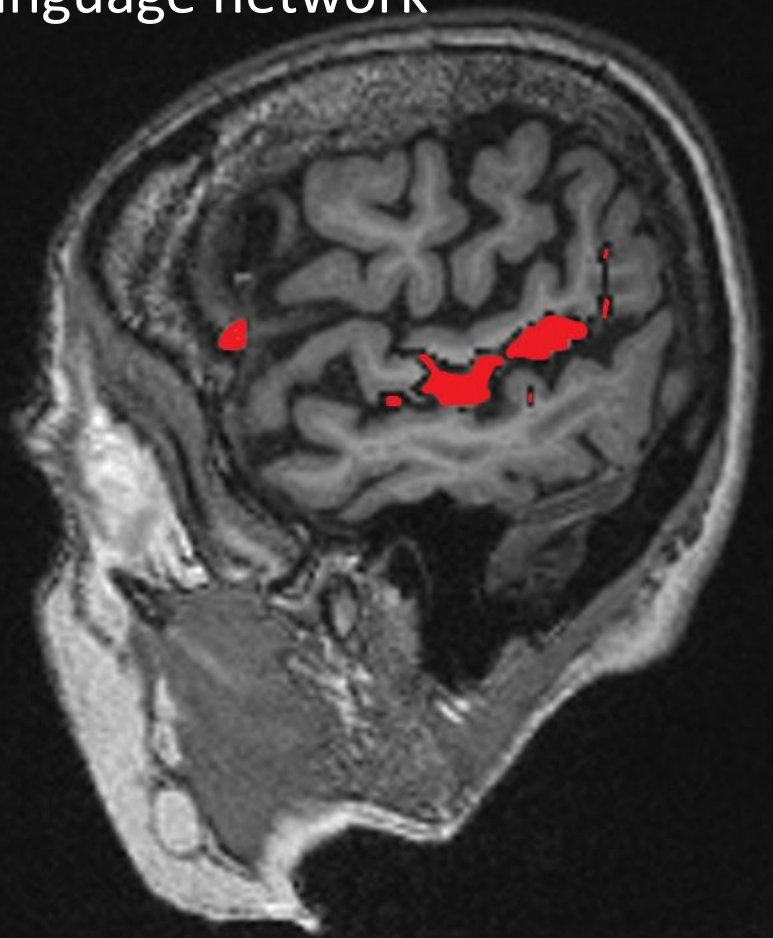
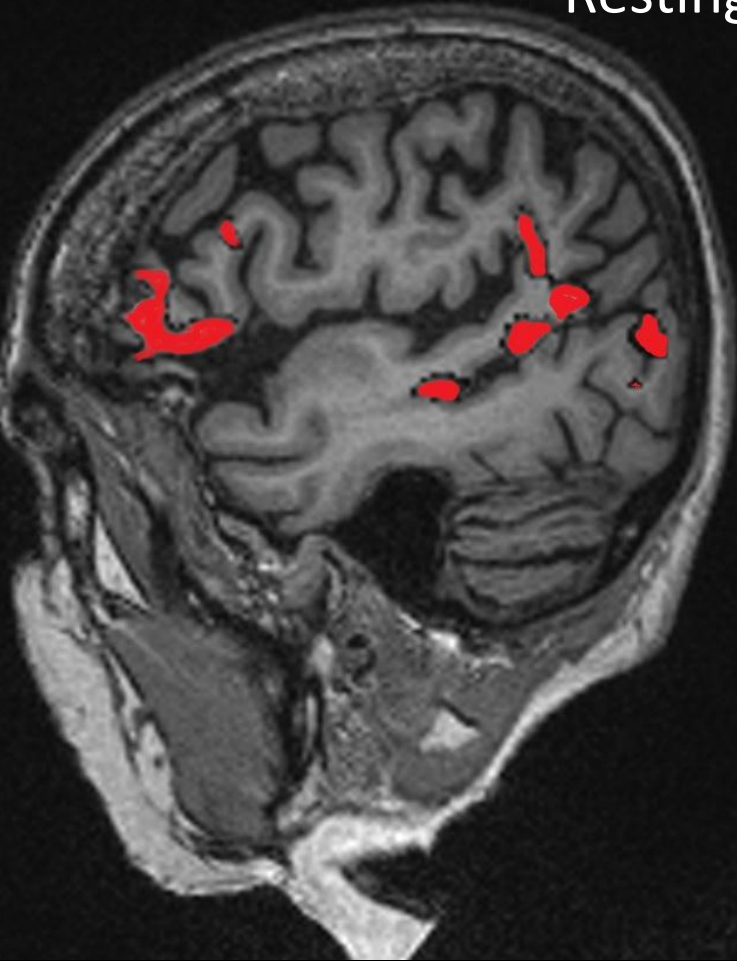
RED non-fluent progressive aphasia (NFPA)

GREEN semantic dementia (SD)

BLUE logopenic progressive aphasia (LPA)



Resting state fMRI language network



Clinical and CSF data

- 2007 clinical:MMSE 28, CDR 0, sum of boxes 0
- 2008 clinical:MMSE 25, CDR 0, sum of boxes 0.5 (judgment)
- **2008 CSF: Tau=410, p-Tau=58 AB42=372**
- 2009 clinical:MMSE 29, CDR 0, sum of boxes 0
- 1/2011 clinical MMSE 25, CDR 0, sum of boxes 0
- **2011 CSF: Tau=1604, p-Tau=22, AB42=307**
- 12/2011 clinical MMSE 26, CDR 0, sum of boxes 0
- 12/2012 MMSE 21 (at imaging)
- 1/2013 clinical MMSE 19, CDR 0.5, Sum of boxes 1.0
- 9/2013 MMSE 14 (at imaging)

Clinical consensus conference

- 1/2013 Clinical Assessment
 - Recent initiation of Aricept by the primary physician
 - Difficult with spelling and names of things began 1 year ago, with progression the last 6-9 months to difficulty with common words
 - Language difficulties are worst during stressful situations.
 - No difficulty recalling recent events, keeping appointments, paying bills, or with visuospatial tasks.
 - No sleep, movement, or mood symptoms
 - CDR 0.5, primarily due to language
 - Clinical diagnosis: **primary progressive aphasia**



Washington
University in St. Louis

SCHOOL OF MEDICINE

Primary progressive aphasia

- DDx
 - Alzheimer's disease (AD)
 - Frontotemporal lobar degeneration (FTLD)
 - Corticobasal degeneration
- Disability isolated to language
- Subtypes
 - Nonfluent progressive aphasia
 - Semantic dementia
 - Logopenic progressive aphasia
- Associated pathologies
 - AD
 - FTLD
 - Tau

References

1. Morris JC, Roe CM, Grant EA, Head D, Storandt M, Goate AM, Fagan AM, Holtzman DM, Mintun MA. Pittsburgh compound B imaging and prediction of progression from cognitive normality to symptomatic Alzheimer disease. *Arch Neurol*. 2009;66(12):1469-75. Epub 2009/12/17. doi: 10.1001/archneurol.2009.269. PubMed PMID: 20008650; PubMed Central PMCID: PMC2798814.
2. Feng L, Chong MS, Lim WS, Ng TP. The Modified Mini-Mental State Examination test: normative data for Singapore Chinese older adults and its performance in detecting early cognitive impairment. *Singapore medical journal*. 2012;53(7):458-62. Epub 2012/07/21. PubMed PMID: 22815014.
3. Fischl B. FreeSurfer. *NeuroImage*. 2012;62(2):774-81. doi: 10.1016/j.neuroimage.2012.01.021.
4. Bakkour A, Morris JC, Dickerson BC. The cortical signature of prodromal AD: Regional thinning predicts mild AD dementia. *Neurology*. 2009;72(12):1048-55. doi: 10.1212/01.wnl.0000340981.97664.2f.
5. Gorno-Tempini ML, Dronkers NF, Rankin KP, Ogar JM, Phengrasamy L, Rosen HJ, Johnson JK, Weiner MW, Miller BL. Cognition and anatomy in three variants of primary progressive aphasia. *Ann Neurol*. 2004;55(3):335-46. doi: 10.1002/ana.10825. PubMed PMID: 14991811; PubMed Central PMCID: PMC2362399.
6. Grossman M. Primary progressive aphasia: clinicopathological correlations. *Nature reviews Neurology*. 2010;6(2):88-97. doi: 10.1038/nrneurol.2009.216. PubMed PMID: 20139998; PubMed Central PMCID: PMC3637977.
7. Sutphen CL, Fagan AM, Holtzman DM. Progress Update: Fluid and Imaging Biomarkers in Alzheimer's Disease. *Biol Psychiatry*. 2013. Epub 2013/09/10. doi: 10.1016/j.biopsych.2013.07.031. PubMed PMID: 24012326.
8. Morris JC. The Clinical Dementia Rating (CDR): current version and scoring rules. *Neurology*. 1993;43(11):2412-4. PubMed PMID: 8232972.
9. Shimony JS, Zhang D, Johnston JM, Fox MD, Roy A, Leuthardt EC. Resting-state spontaneous fluctuations in brain activity: a new paradigm for presurgical planning using fMRI. *Academic radiology*. 2009;16(5):578-83. doi: 10.1016/j.acra.2009.02.001. PubMed PMID: 19345899; PubMed Central PMCID: PMC2818666.
10. Schummer G. The disconnection syndrome: futurehealth.org; 2009 [cited 2014 1/10/2014]. Available from: <http://www.futurehealth.org/populum/page.php?f=The-Disconnection-Syndrome-by-Gary-Schummer-090910-239.html>.

Research Imaging (KARI)

- Faculty
 - Beau Ances, MD, PhD
 - Dave Balota, PhD
 - Brian Gordon, PhD
 - **Nupur Ghoshal, MD**
 - Denise Head, PhD
 - Tammie Benzinger, MD, PhD
 - Dan Marcus, PhD
 - **John Morris, MD**
 - Jon McConathy, MD, PhD
 - Avi Snyder, MD
 - Yi Su, PhD
 - Marc Raichle, MD
 - Cathy Roe, PhD
 - Andrei Vlassenko, MD, PhD
 - Jeffrey Zachs, PhD
- Imaging Team
 - Darlene Dwyer, Russ Hornbeck, Trish Stevenson
 - Lisa Cash, Kelley Jackson, Angela Campbell
 - Jon Christensen, Tyler Blazey, Karl Friedrichsen, **Chris Owen**
 - Qing Wang, PhD; Nelly Joseph-Maturin, PhD, **Liang Wang, PhD**
- Funding
 - NIH/NIA Adult Children Study **P01AG026276**
 - Avid Radiopharmaceuticals (Eli Lilly)