MRI
WWADNI
Copenhagen 2014

Bret Borowski - Mayo

Matt Bernstein - Mayo

Jeff Gunter – Mayo

Clifford Jack - Mayo

David Jones - Mayo

Kejal Kantarci - Mayo

Denise Reyes – Mayo

Matt Senjem – Mayo

Prashanthi Vemuri - Mayo

Chad Ward – Mayo

Charlie DeCarli – UCD

Nick Fox – UCL

Norbert Schuff/Alix Simonson – UCSF/VA

Paul Thompson – USC

Danielle Harvey - biostats

MR measures performed

- Structural MRI measures
  - BSI – UCL
  - Freesurfer – UCSF/SFVA
  - TBM – USC
  - TBM-Syn – Mayo
- Cerebrovascuar disease – UC Davis
- AIRA H (CMB) – Mayo
- ASL - UCSF/SFVA
- Hipp subfields - UCSF/SFVA
- DTI - USC
- TF-fMRI - Mayo

sMRI - summary

- no consistent diff between accel vs unaccel (USC and Mayo)
- Change from unacccel to accel image pairs – no effect Siemens or Philips, but effect for GE (UCL)
- Overall recommendation - use accel, consistently
- Sample size est. 12 months
  - CN & EMCI: n ~ 200s per arm
  - LMCI: n ~ 100s per arm
  - AD: n ~ 50-100 per arm

CVD - Conclusions

- Normals have less WMH than other groups
- No WMH group differences amongst cognitively impaired groups
- WMH increase in volume with time
- Greater WHM volumes at baseline, greater cognitive decline over time

ELSEVIER

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Alzheimer's & Dementia

Focal hemosiderin deposits and β-amyloid load in the ADNI cohort

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- **Prevalence of superficial siderosis was 1%**
- **prevalence of microhemorrhages was 25%**
- **increasing with age and b-amyloid load**
- **Topographic densities of microhemorrhages were highest in the occipital lobes and lowest in the deep/infratentorial regions**
- **Greater number of microhemorrhages at baseline was associated with a greater annualized rate of additional microhemorrhages**

ASL Numeric values

Precuneus	CN	EMCI	LMCI	AD
Baseline ($\times 10^4$)	40 32.3 (11.6)	47 31.8 (10.1)	35 31.9 (9.7)	29 27.8 (9.5)
0-3mo change ($\times 10^4$)	33 -1.60 (13.72)	35 -1.90 (8.27)	29 -2.17 (11.21)	14 -1.24 (9.46)
0-6mo change ($\times 10^4$)	27 -2.62 (10.5)	32 -1.05 (8.38)	26 -2.88 (7.47)	-
0-12 mo change ($\times 10^4$)	12 -4.29 (9.26)	14 -6.37 (6.77)	-	-
Posterior Cing.				
Baseline ($\times 10^4$)	40 32.6 (13.0)	47 31.0 (12.2)	35 28.6 (9.9)	29 27.2 (11.4)
0-3mo change ($\times 10^4$)	33 -3.72 (12.17)	35 -1.58 (11.94)	29 -0.95 (10.33)	14 -2.83 (12.12)
0-6mo change ($\times 10^4$)	27 -2.90 (10.95)	32 -1.89 (7.51)	26 -2.44 (8.36)	-
0-12mo change ($\times 10^4$)	12 -2.68 (10.52)	14 -6.60 (7.12)	-	-

Baseline – decreasing perfusion with greater impairment
Rates – greater declines with greater impairment

Hipp subfield: group discrimination

Power to detect significant effect at alpha= 0.05

Comparison	Image	CIND 'Manual' HighRes	UPenn 'ASHS' HighRes	MGH 'Bayes' HighRes	NW 'Shape' T1	FS 'Subfield' T1	FS 'SubCort' T1
Controls vs MCI	Region	CA1-2 trans	CA1	Mol Layer Hippo	Subiculum	Fimbria	Hippocampus
	Power	0.46	0.38	0.73	0.46	0.46	0.08
MCI vs AD	Region	Subiculum	CA1	CA1	CA1	Presubiculum	Hippocampus
	Power	0.63	0.64	0.93	0.67	0.87	0.66
Controls vs AD	Region	Subiculum	CA1	Gran/Mol Layer Dentate	Subiculum	Presubiculum	Hippocampus
	Power	0.79	0.96	0.99	0.96	0.96	0.99
Amyloid Effect in Controls	Region	CA1-2 transition	Dentate	Subiculum	CA1	Tail	Hippocampus
	Power	0.70	0.39	0.88	0.56	0.54	0.50

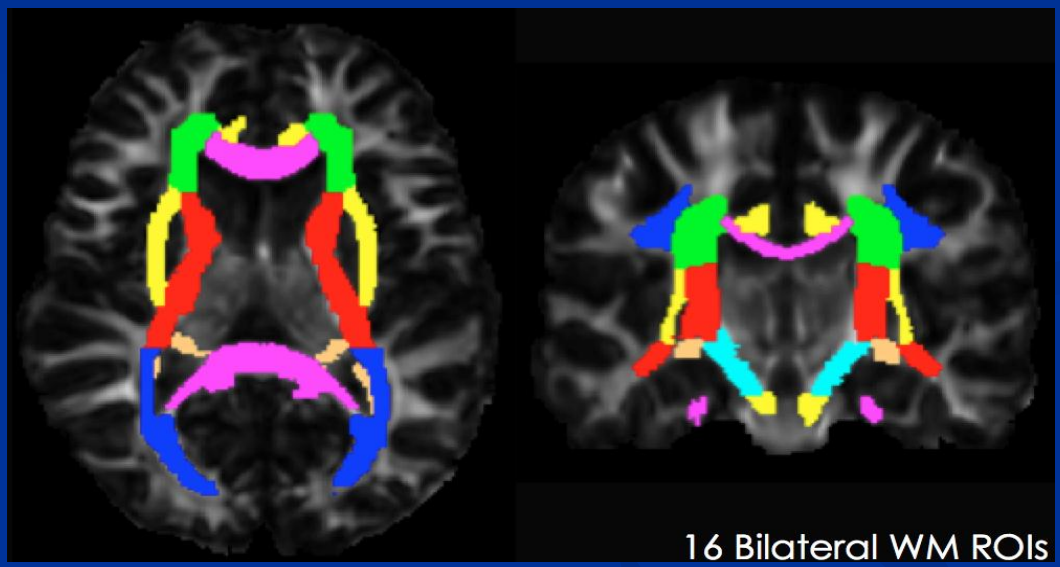
41 cases

Some ROIs have large group discrimination in each category

Not clear any advantage over standard hipp vol at this point

DTI ROI Summary Measures

- DTI summary measures include the 4 standard DTI measures:
  - fractional anisotropy (FA)
  - mean diffusivity (MD)
  - radial diffusivity (RD)
  - axial diffusivity (AxD)
- We compute these in 16 bilateral white matter (WM) regions of interest (ROIs) and 1 "total WM" ROI
  - JHU "Eve" atlas – standard



DTI n80s Similar to HV n80s

$$n = \frac{2s^2(z_{1-\frac{a}{2}} + z_{power})^2}{(0.25b)^2}$$

α=0.05
σ=mean of WM integrity changes
β=standard deviation of WM integrity changes
Desired power=80%

AD vs NC	
FA of WM ROI	**n80**
IFO	322
TOTAL_WM	626

AD	
FA of WM ROI	**n80**
IFO	191
TOTAL_WM	231

NC	
FA of WM ROI	**n80**
IFO	5096
TOTAL_WM	734

AD vs NC	
Structural ROI	**n80**
TOTAL_hippo	280

AD	
Structural ROI	**n80**
TOTAL_hippo	148

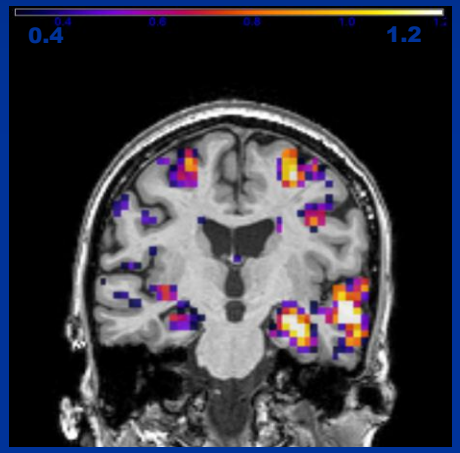
NC	
Structural ROI	**n80**
TOTAL_hippo	1279

AD vs NC	
cognitive score	**n80**
MMSE change	968

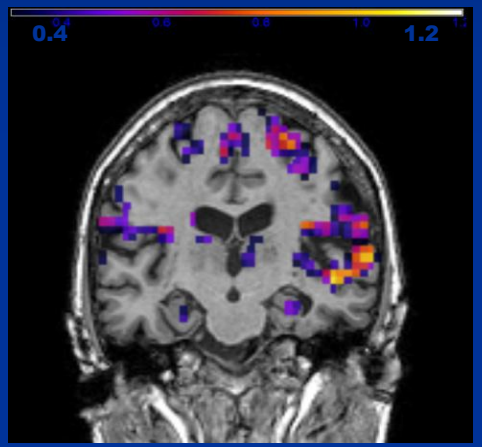
AD	
cognitive score	**n80**
MMSE change	854

NC	
cognitive score	**n80**
MMSE change	35898

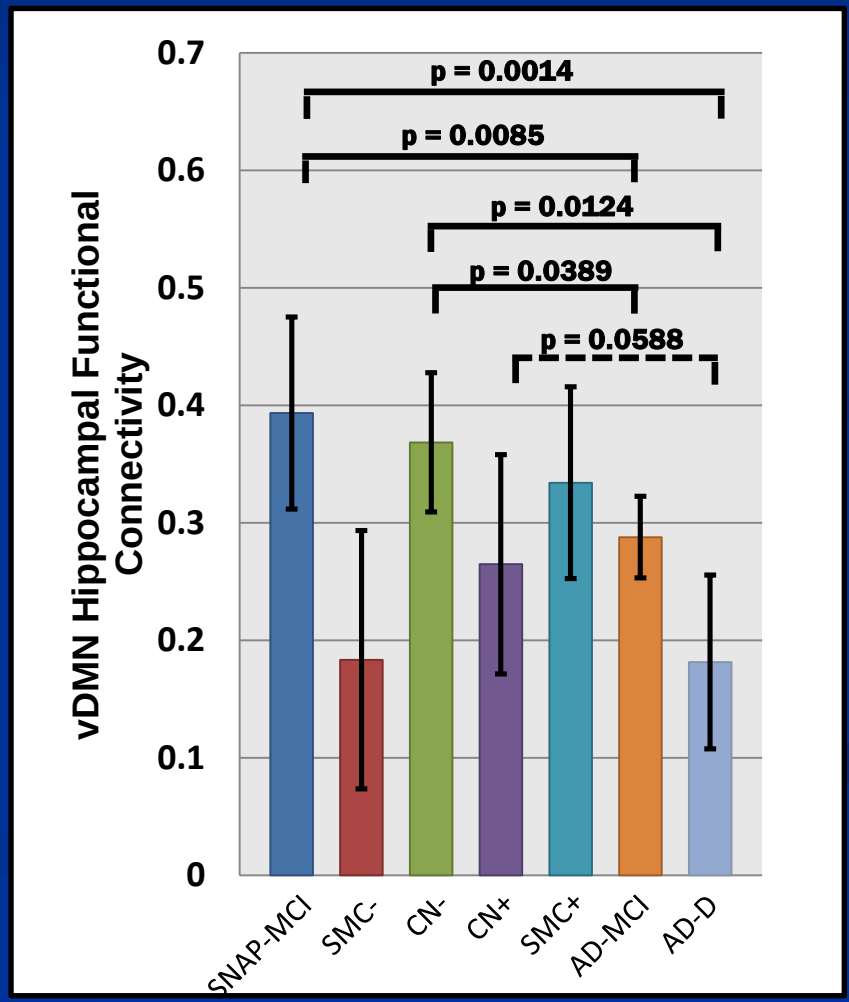
	SNAP-MCI	SMC-	CN-	CN+	SMC+	AD-MCI	AD-D	p
N	36	8	28	15	6	51	27	NA
Male (%)	17 (47)	5 (63)	9 (32)	9 (60)	1 (17)	27 (53)	13 (48)	0.38
Age (q1, q3)	70.5 (62, 75)	68 (67, 72)	73 (69, 77.5)	73 (70, 79)	69.5 (66, 73)	72 (68, 75.5)	74 (72.5, 76.5)	0.08
Educ (q1, q3)	16 (15, 18)	18 (17.5, 18)	16 (16, 16)	16 (16,17)	18.5 (16, 20)	16 (14, 18)	16 (14, 16)	0.17
ADASCOG13 (q1, q3)	12 (9.5, 15)	8.5 (5.5, 11)	8 (6, 10)	10 (9, 11)	10 (10, 10)	16 (10, 20)	32 (29, 38)	***2.60E-16***
AV-45 (q1, q3)	1.01 (0.98, 1.04)	0.99 (0.97 1.03)	1.00 (0.97, 1.02)	1.33 (1.22, 1.45)	1.37 (1.23, 1.44)	1.33 (1.23, 1.46)	1.46 (1.34, 1.58)	***4.78E-25***



Amyloid Negative Control Subject



Alzheimer's Dementia Subject



ADNI 3 Considerations for MRI protocol

- Unlike ADNI 2, in ADNI 3 will perform all sequence types on all scanners/subjects to the extent possible
- Favor fragmented vs standardized experimental sequences
  - Standardized → low end, least common denominator
  - Fragmented → use performance capability of high end systems
    - TF-fMRI - multi band Siemens
    - DTI - more diffusion encoding or 2 b-shell or comp SENSE DSI
- Rationale
  - 2016 state of art is 2021 routine
  - should test what advanced MR can add

ADNI 3

- Core sequences
  - 3D T1 volume (2X accel) – morphometrics
  - FLAIR – CVD, pathology detection
  - T2* GRE – MCH
  - T2 FSE with fat sat – TIV, distortion correction
- Experimental sequences
  - ASL – perfusion; pCASL, 3D, backgrond suppression
  - TF-fMRI – connectivity; low end 3sec TR; high end MB
  - DTI – diffusion; low end simple FA/MD; high end DKI, HARDI
  - Coronal high res T2 – hippocampal subfields?

ADNI GO/2 MRI 3T Protocol

CORE SEQEUNCES

- 3D T1 unaccelerated & 2x accelerated (MPRAGE on Siemens and Phillips, IR SPGR on GE) – morphometry
- FLAIR –cerebro vascular disease grading
- long TE 2D gradient echo – ARIA-H (CMB) grading

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EXPERIMENTAL SEQEUNCES

- Siemens (30 sites) - ASL perfusion (20), and high res T2 hipp subfield
- GE (14 sites) - DTI
- Phillips (12 sites) – task free-fMRI