WWADNI MRI Core
Boston July 2013

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 – UCSF/VA
Paul Thompson – UCLA
Danielle Harvey - biostats

Major efforts over past year

- ingest and organize
  - methods documents, data dictionaries, numeric data submitted and viewable to public
  - 5 labs
  - 10 data streams covering different sets of subjects

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 grading

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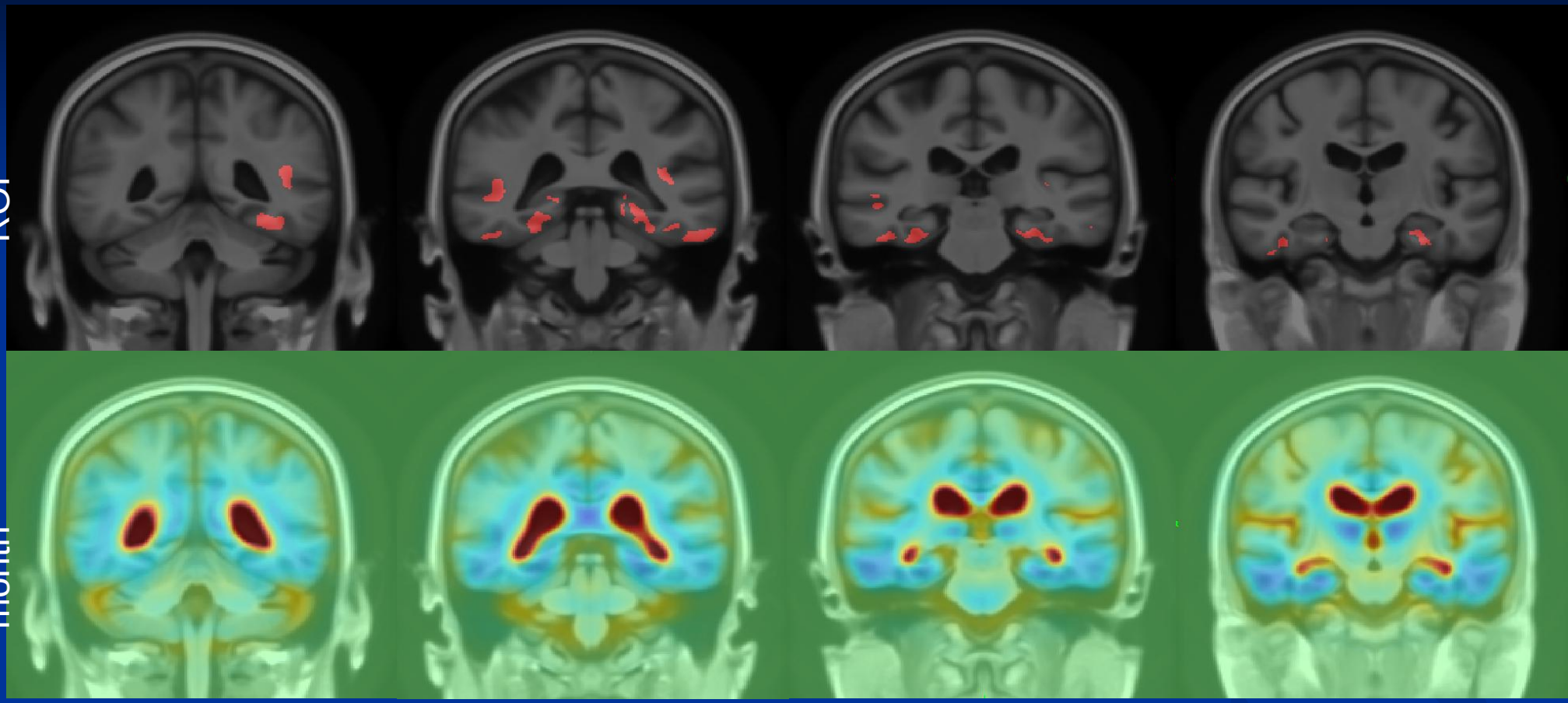
Structural MRI measures
3D T1 Volume - MPRAGE or IR SPGR

- BSI – UCL
- Freesurfer – UCSF/SFVA
- TBM – UCLA
- TBM-Syn - Mayo

TBM stat-ROI - Xue Hua, Paul Thompson



Coronal slices x=80, 90, 100, 100

T1 Based Measurements – Non-Accelerated Sample Size/arm for a 3 month trial (only n>20)

Variable	CN	EMCI	LMCI	AD
BBSI (UCL)	-	-	-	671
VBSI (UCL)	-	-	-	324
TBM-statROI (UCLA)	1038	1036	655	443
TBM-SyN (Mayo)	2293	2429	839	560
Inf. Lat. Vent. vol (UCSF)	26528	11435	2350	9293
Inf. Temp. vol (UCSF)	4647	363,043	9688	43,514
Lat. Vent. vol (UCSF)	1853	7517	908	719,222
Mid. Temp. vol. (UCSF)	40,456	21,380	7709	3609
Fusiform volume (UCSF)	7597	28,750	35,043	10,492

T1 Based Measurements – Non-Accelerated Sample Size/arm for a 6 month trial

Variable	CN	EMCI	LMCI	AD
BBSI (UCL)	899	706	513	220
VBSI (UCL)	718	782	290	202
Hippo BSI (UCL)	-	1667	-	-
TBM-statROI (UCLA)	504	516	244	-
TBM-SyN (Mayo)	561	1141	223	61
Inf. Lat. Vent. vol (UCSF)	5404	3175	1122	451
Inf. Temp. vol (UCSF)	2660	18,817	1470	1234
Lat. Vent. vol (UCSF)	999	1218	4201	272
Mid. Temp. vol. (UCSF)	2849	12,225	1270	662
Fusiform volume (UCSF)	5711	19,494	1420	1124

T1 Based Measurements – Non-Accelerated Sample Size/arm for a 12 month trial

Variable	CN	EMCI	LMCI	AD
BBSI (UCL)	116	213	-	-
VBSI (UCL)	160	271	-	-
Hippo BSI (UCL)	-	982	-	-
TBM-statROI (UCLA)	271	292	-	-
TBM-SyN (Mayo)	210	306	115	-
Inf. Lat. Vent. vol (UCSF)	1290	724	478	-
Inf. Temp. vol (UCSF)	988	1525	484	-
Lat. Vent. vol (UCSF)	275	636	218	-
Mid. Temp. vol. (UCSF)	1862	823	425	-
Fusiform volume (UCSF)	1591	1425	1098	-

T1 Based Measurements – Accelerated Sample Size/arm for a 6 month trial

Variable	CN	EMCI	LMCI	AD
BBSI (UCL)	1469	646	411	218
VBSI (UCL)	826	843	301	244
Hippo BSI (UCL)	-	1161	-	-
TBM-statROI (UCLA)	-	304	-	-
Inf. Lat. Vent. vol (UCSF)	-	1277	-	-
Inf. Temp. vol (UCSF)	-	132,737	-	-
Lat. Vent. vol (UCSF)	-	675	-	-
Mid. Temp. vol. (UCSF)	-	6938	-	-
Fusiform volume (UCSF)	-	96,619	-	-

T1 Based Measurements – Accelerated Sample Size/arm for a 12 month trial

Variable	CN	EMCI	LMCI	AD
BBSI (UCL)	105	249	-	-
VBSI (UCL)	145	305	-	-
Hippo BSI (UCL)	-	620	-	-
TBM-statROI (UCLA)	-	164	-	-

sMRI - summary

- Unaccelerated: 3 month trial sample sizes for AD ~ 300-600
- Unaccelerated: 6 month trial sample sizes for AD <100 - 200, for LMCI ~200, for CN and EMCI ~ 500
- Unaccelerated: 12 month trial sample sizes for LMCI and CN ~100-200, for EMCI ~ 200-300
- Accelerated: 6 month trial sample sizes AD ~ 200
- Accelerated: 12 month trial sample size EMCI ~ 100-300 and CN ~100
- Accelerated sMRI may be equivalent to unaccelerated. Further study, common lists, cross vendor

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Vascular Measurements
Presence of Infarcts (DeCarli)

Variable	CN	EMCI	LMCI	AD
Baseline	164 0.073 (0.26)	253 0.091 (0.29)	115 0.070 (0.26)	54 0.018 (0.14)
3 month change	115 0.017 (0.13)	199 0.050 (0.22)	69 0.014 (0.12)	27 0.037 (0.19)
6 month change	67 0.030 (0.17)	149 0.040 (0.20)	43 0.046 (0.21)	-
12 month change	-	94 0.042 (0.20)	-	-

EMCI look slightly more “vascular” (greater pathological heterogeneity?) than other groups, while AD less vascular

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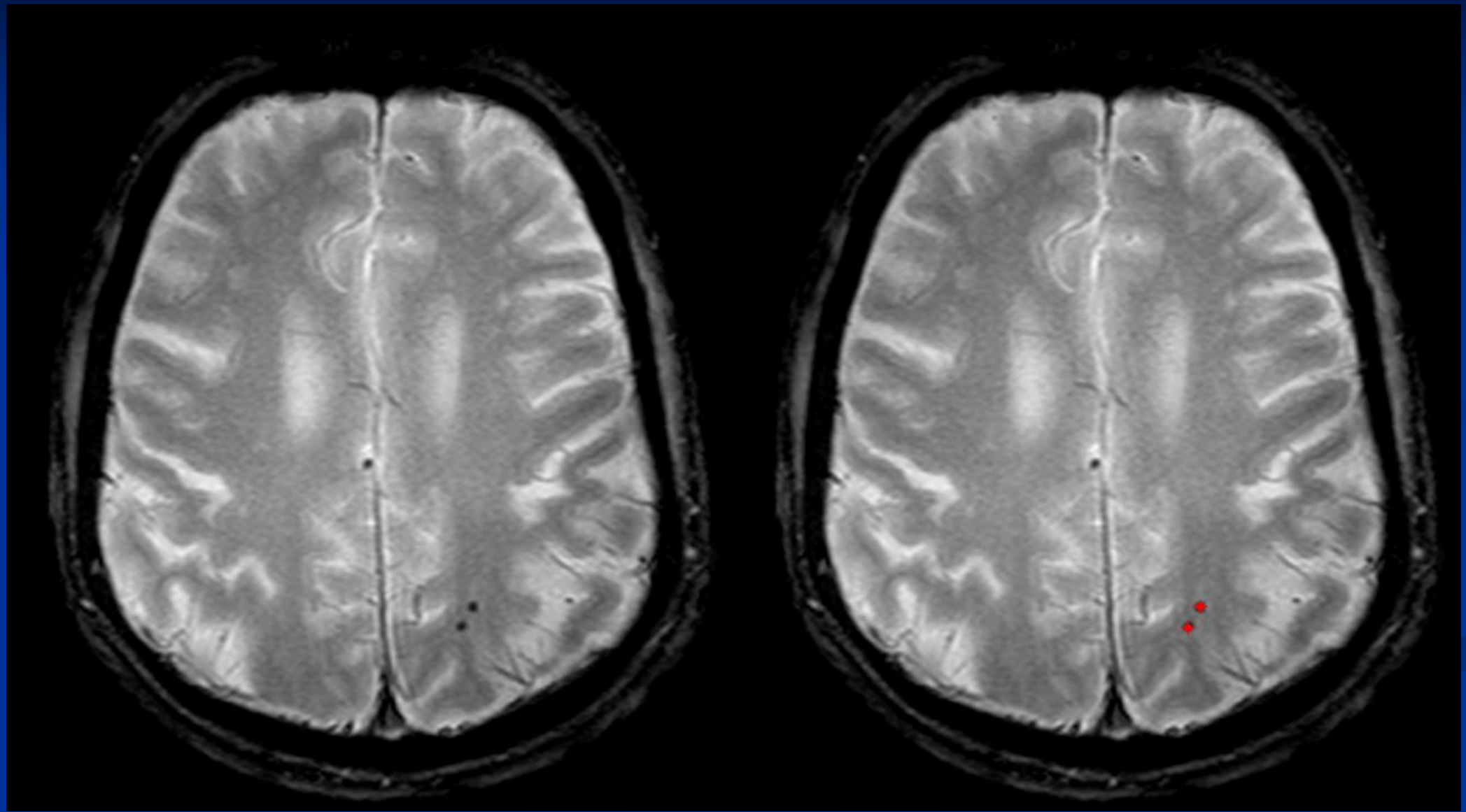
ARIA-H Marking SW application – Jeff Gunter and Dave Just

- Spatial registration and display of all volumes in subject time series
- Each MCH is tracked as an individual entity over time
- Definite vs possible at each time point
- x,y,x coordinates of each
- Marking done first by trained image analysts, all positive findings verified by MD

ARIA-H (MCH)



ARIA-H (MCH)

Variable	CN	EMCI	LMCI	AD
Baseline	184 0.42 (1.02)	298 3.37 (31.41)	156 1.00 (4.30)	116 1.25 (4.34)
3 month change	160 0.056 (0.32)	266 0.079 (0.41)	140 0.15 (0.67)	88 0.31 (1.67)
6 month change	160 0.087 (0.39)	235 0.15 (0.63)	128 0.30 (1.23)	58 0.5 (2.42)
12 month change	113 0.080 (0.33)	193 0.19 (1.01)	71 0.38 (1.09)	17 0.35 (0.61)

Baseline – increase with clinical severity (EMCI few very high outliers)
Rates – increase with clinical severity

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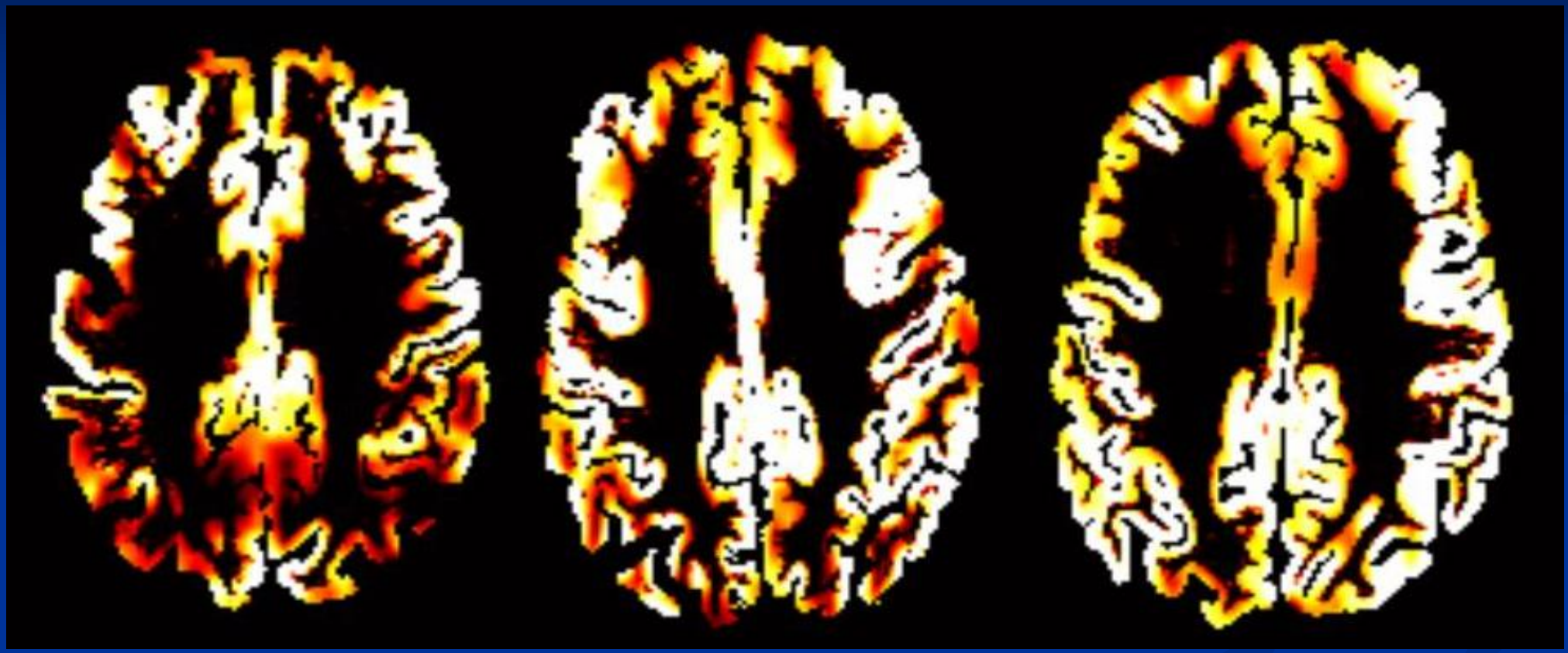
ASL – Alix Simonson, Diana Truran, Norbert Schuff.
Mike Weiner, SFVAMC/UCSF Lab



AD **eMCI** **Control**

ASL Numeric values

Precuneus	CN	EMCI	LMCI	AD
Baseline ($\times 10^4$)	40 32.3 (11.6)	46 31.9 (10.2)	35 31.9 (9.7)	22 26.5 (9.6)
0-3mo change ($\times 10^4$)	32 -1.74 (13.92)	34 -2.06 (8.34)	29 -2.17 (11.21)	11 -3.25 (9.68)
0-6mo change ($\times 10^4$)	24 -2.16 (10.6)	27 -0.24 (8.59)	23 -2.31 (6.67)	4 -3.27 (7.64)
0-12 mo change ($\times 10^4$)	5 -3.30 (8.00)	6 -7.21 (7.58)	-	-
Posterior Cing.				
Baseline ($\times 10^4$)	40 32.6 (13.0)	46 31.3 (12.2)	35 28.6 (9.9)	22 25.8 (10.5)
0-3mo change ($\times 10^4$)	32 -4.20 (12.03)	34 -2.07 (11.75)	29 -0.95 (10.33)	11 -3.85 (12.73)
0-6mo change ($\times 10^4$)	24 -2.60 (11.22)	27 -0.94 (7.49)	23 -2.22 (8.59)	4 -5.88 (8.38)
0-12mo change ($\times 10^4$)	5 1.53 (12.03)	6 -6.89 (7.82)	-	-

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

ADNI2 ADD-ON PROJECT: HIPPOCAMPAL SUBFIELDS*

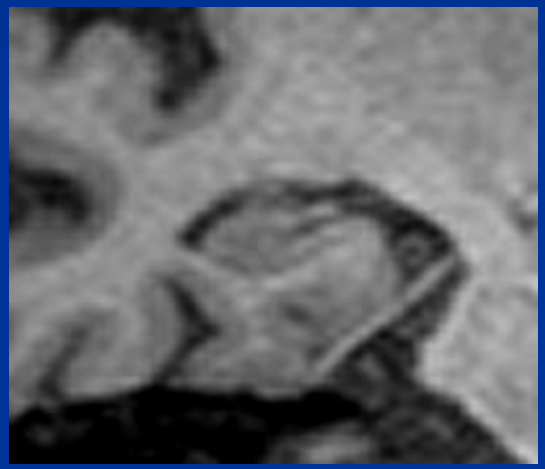
GOAL: Systematic comparison of the most common methods for subfield (subiculum, CA1, CA2, CA3, dentate) volumetry regarding their discriminative power for the detection of early Alzheimer's Disease in a common data set

T1 based methods

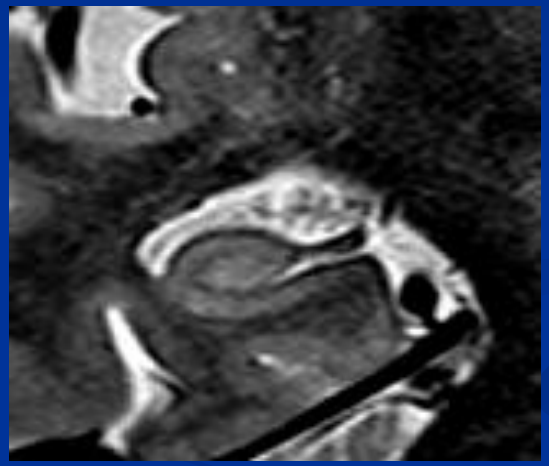
Shape Analysis
L. Wang, Northwestern U

Deformation Based Morphometry
P. Yushkevich, U Penn

Bayesian Inference Approach/Freesurfer
K. van Leemput, Harvard



T2 high resolution based methods



Manual Labeling
S. Mueller, UCSF

Multi-Atlas/Similarity Voting (ASHS)
P. Yushkevich. UPenn

Bayesian Inference Approach
K. van Leemput, Harvard

A high resolution T2 weighted hippocampal sequence optimized for ADNI will be acquired by Siemens sites.

All high resolution images will be made available to the scientific community via LONI website

*Sponsored by the Alzheimer's Association

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ADNI DTI

Talia Nir, Neda Jahanshad, Paul Thompson

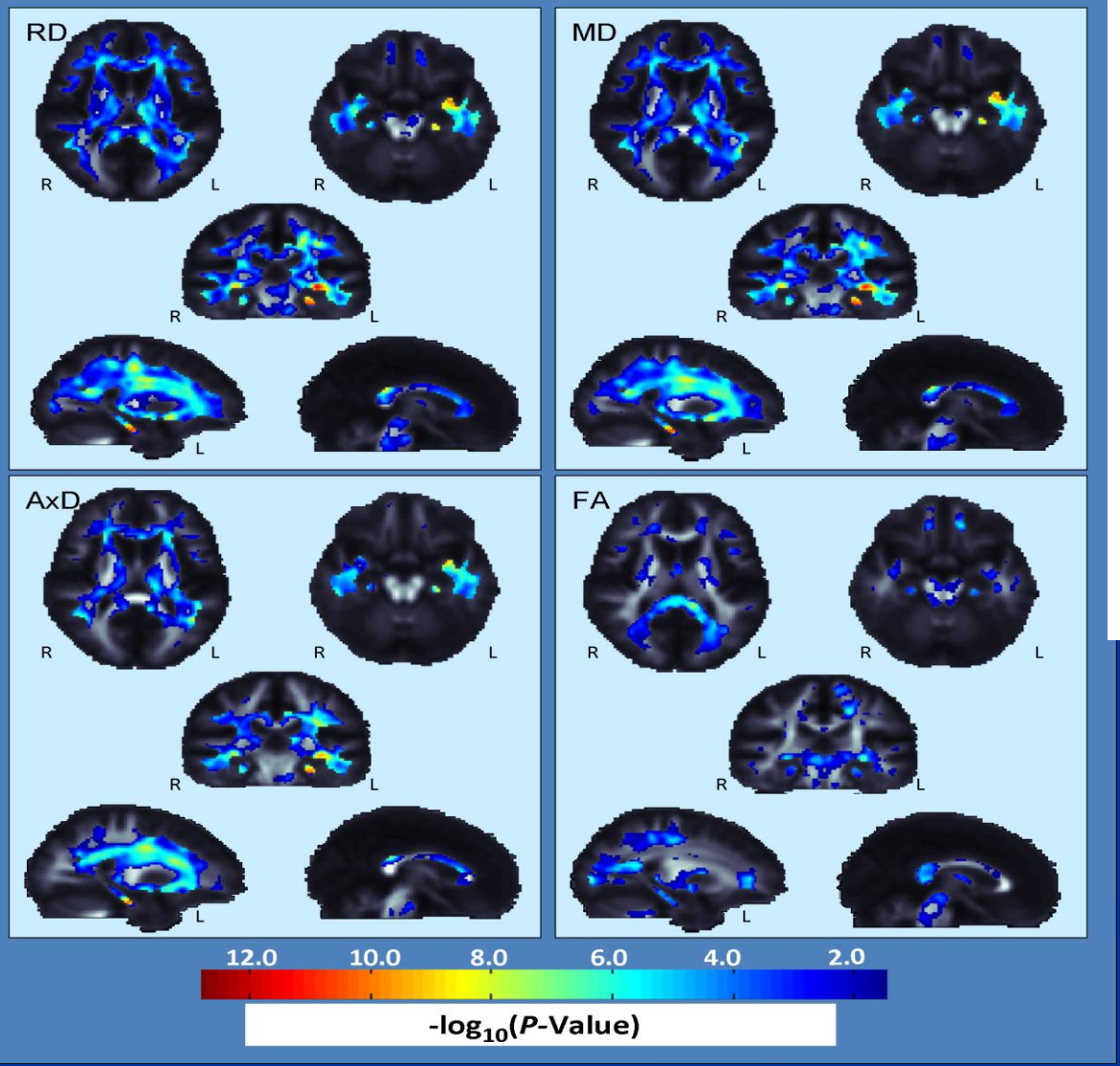
Imaging Genetics Center

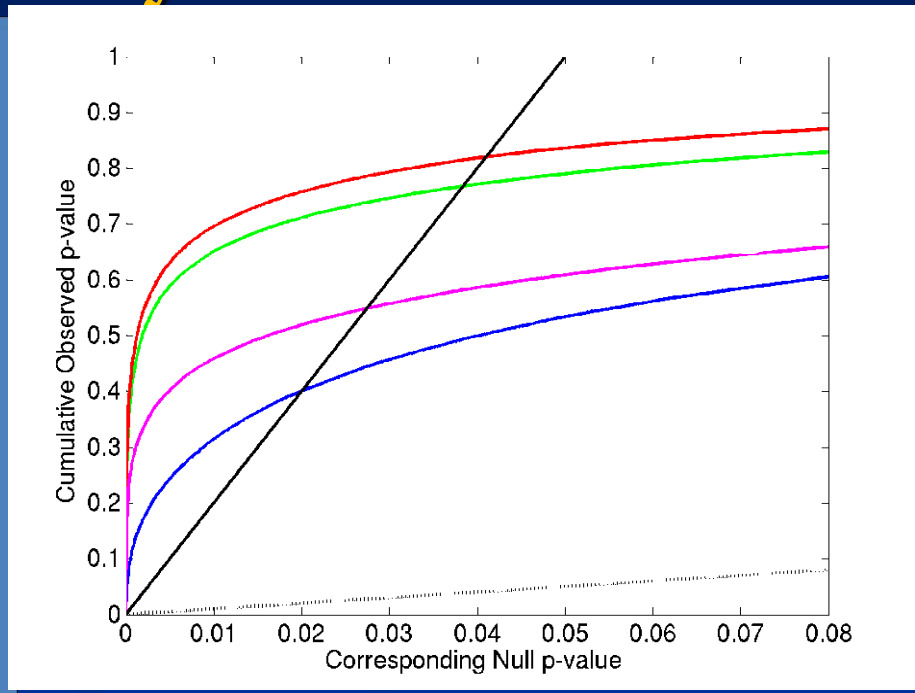
LONI

USC

AD versus CTL

Voxel Based Analysis





- AD is associated with widespread decreases in FA and increases in diffusivity
- RD followed by MD, pick up the largest effect sizes when comparing NC to AD
- The left temporal lobe shows the most significant differences

DTI numeric values

Mean diffusivity L cingulum (hippocampus)	CN	EMCI	LMCI	AD
Baseline ($\times 10^{-4}$)	53 8.87 (0.66)	61 9.58 (1.06)	34 9.73 (1.10)	39 10.50 (1.21)
0-3mo change ($\times 10^{-4}$)	31 0.08 (0.59)	51 -0.16 (0.63)	29 -0.066 (0.64)	24 -0.051 (0.70)
0-6mo change ($\times 10^{-4}$)	30 -0.039 (0.50)	42 -0.18 (0.99)	19 0.059 (0.51)	14 -0.066 (0.54)
0-12 mo change ($\times 10^{-4}$)	14 0.12 (0.46)	36 0.21 (0.59)	8 0.17 (0.53)	5 0.45 (0.47)

Baseline – MD increases with clinical severity
Rates – inconsistent < 12 months, but greater change in MD in AD vs CN at 12 mo

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TF- fMRI numeric values

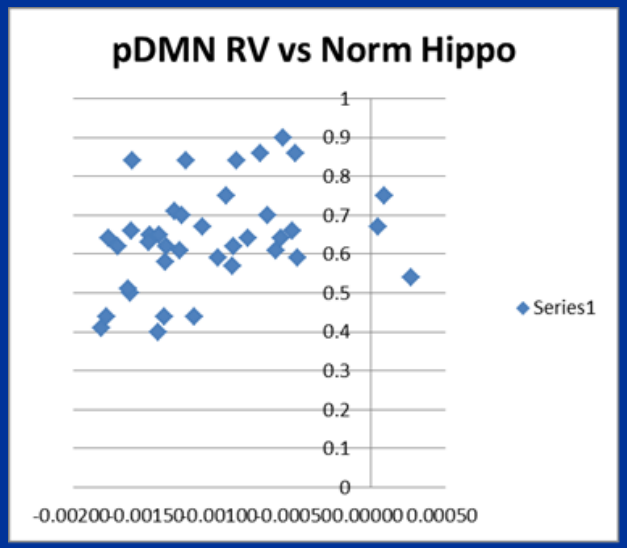
Functional coherence (similar to CoheReho), ratio aDMN/pDMN

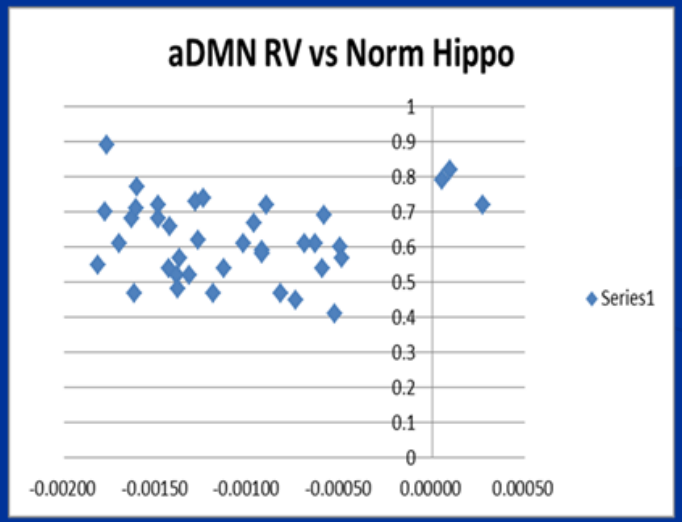
PDMN RV	CN	EMCI	LMCI	AD
Baseline	33 0.64 (0.15)	47 0.64 (0.10)	31 0.62 (0.10)	23 0.63 (0.13)
0-3mo change	31 -0.0087 (0.14)	43 0.023 (0.16)	30 0.0066 (0.097)	15 -0.0085 (0.17)
0-6mo change	28 0.0034 (0.20)	34 -0.0091 (0.11)	26 0.0069 (0.10)	13 -0.0085 (0.12)
0-12 mo change	16 0.02 (0.13)	28 -0.0014 (0.11)	14 0.01 (0.13)	6 -0.075 (0.16)

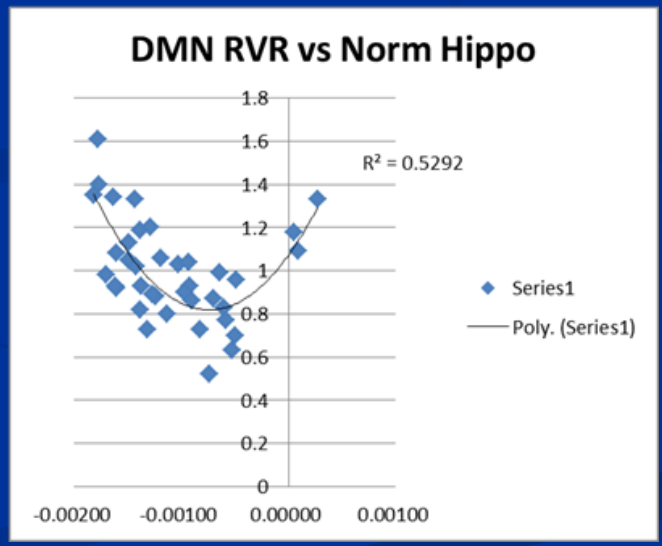
Baseline – little relationship to clinical severity
Rates – inconsistent by group (probably noise)

Non linear, non-monotonic relationship between TF-fMRI and hippocampal volume across all subjects

Functional coherence







Protocol changes under evaluation

- Optimize high performance sites
  - Add DTI with better spatial/angular resolution to GE sites with XRM gradients
  - Perhaps same for TF-fMRI – faster frame rate, longer time
- Perhaps add advanced DTI to Philips and advanced TF-fMRI to GE
- Change phantom scanning to site requalification rather than with each exam