

**World Wide Alzheimer's Disease Neuroimaging Initiative
Teleconference Agenda
May 2/ May 1**

I. Welcome

Heather Snyder from the Alzheimer's Association welcomed attendees to the spring touch base worldwide ADNI teleconference. Maria Carrillo will be unable to join the call, and sends her apologies.

II. Progress Updates

a) NA-ADNI, ADNI GO, ADNI2

Michael Weiner shared an update from the North American ADNI efforts. ADNI is fully enrolled and there are 2.5 years in ADNI2. They have run into some budget difficulties and are going to cut some studies, including FDG-PET, and stop seeing the AD dementia and decreasing the number of visits for the MCI individuals. The real exciting right now is the addition of tau imaging to the field. To date, there have been two large grants (DoD and NIH) to add multi-site PET on a major scale in ADNI over the next year. The NIH has also suggested we submit a competitive renewal – this would start in 2016 – and it would run until 2022 with an emphasis on tau PET longitudinal. If there are questions, Michael is happy to be touch; his email is mweiner@ucsf.edu.

b) AIBL/Australia ADNI

Chris Rowe gave an overview of ongoing activities in Australia. Right now, AIBL is between government funding sources and there is hope that some will be designated to AIBL. They are starting the 90 month / 7.5 year subject follow up. There are 519 who have completed 6 year follow up. Recruited 400 new subjects in 2013; trying to keep to 1000.

Over 500 publications to date, and significant downloads from LONI. They have switched to all F18 tracers for the study. In addition, they are adding tau imaging into 200 AIBL subjects and expect approval in the next month.

There is also a small study in Vietnam Vets to investigate risk of Alzheimer's disease, modeling on the ADNI-Veterans study. Chris visited with the team in India about a proposed Alzheimer's study; it is waiting funding decision. In addition, they have used the AIBL

infrastructure and to collaborate with the A4 study in Melbourne. In addition, they have also used the infrastructure to initiate several drug trials. AIBL is establishing a network throughout Melbourne and offering the clinicians a free scan for their MCI individuals.

c) European ADNI/NEUGRID

Giovanni Frisoni shared an update on European ADNI efforts; slides are included. European ADNI is a project in the context of a larger project funded in the context of PharmaCog (funded under IMI Innovative Initiatives). In PharmaCog, there is a section with an ADNI design. They enrolled 150 subjects and following every 6 months, including fMRI and MRI. Chris asked Giovanni to confirm whether everyone will have amyloid imaging; not everyone will be able to receive due to geographical restrictions.

d) Korean ADNI

Seong Yoon Kim provided an update on the Korean ADNI. Since last year, we are starting to recruit subjects. The first subject will be recruited in June or July of 2014. They are working on setting up the electronic data system and testing the feasibility/ reliability. Flutametamol will be used and it is being supplied by GE Healthcare. They will have about 300 people; 50 controls. The Ministry of Health and Welfare started a large cohort study of normal subjects and over 1000 subjects will be recruited; these individuals will be recruited in the same way that Korean ADNI will screen volunteers. In addition, Korean government is setting up biomarker centers for neurodegenerative diseases and is planning to standardize measurements of t-CSF metabolites and bio-metabolites. This establishment will take some time (1-2 years) and will also be helpful infrastructure for Korean ADNI. In September, 2014, Korean ADNI members are planning to meet with J-ADNI and China ADNI (sponsored by Ministry of Korean Health and Welfare). Through this meeting, we hope to get experience and advice from other Asian ADNI members. Heather asked about the availability of the normal control cohort data is undetermined

e) Argentina ADNI

To date, Argentina ADNI has recruited 60; 54% had lumbar puncture. They have also developed several manuscripts. They are having discussions around funding from the Ministry of Science in Argentina for collaborations around Argentina ADNI. They have

worked with Dr. John Morris at Wash University for training around the DIAN trial. They are looking forward to Copenhagen.

III. Discussion: *WW-ADNI Face to Face Meeting*

After last year's AAIC Worldwide ADNI meeting, there was some discussion about adjusting future face to face meeting formats. These teleconferences serve as a way to touch base on the activities and progress of the different country efforts, and the face to face meeting give us an opportunity to approach the collaborations and data in a different way. Since our November teleconference, there have been several ideas shared and discussed in a variety of venues.

Topics suggested to date include:

- Genetic analyses across the sample sets – looking at analyses done and to be done; identify needs in the different WW-ADNI efforts
- At the recent ADNI PPSB meeting, there was a discussion about generating iPSC on global populations as a derived model systems
- WW-ADNI inspired studies or studies leveraging WW-ADNI
 - Korean Sub-cortical Vascular Dementia
 - Canadian white matter study
 - WHAP study in Australia
- Where are resubmissions in process; what are the next generation of studies being proposed; how to leverage synergies
- WW-ADNI-focused big data to smart data
 - AdNeuroMed
 - EMIF
 - GAAIN
 - Other efforts/ collaborations
- Featuring a junior investigator from each ADNI to present their work – focus on innovative studies / data analysis
- Any effort to synergize different works around WW-ADNI is precisely the thing we should be doing; one of the major achievements of US ADNI are the harmonized procedures. Giovanni likes the idea of discussion around synergizing data analysis that pools the information.

IV. New Business

All

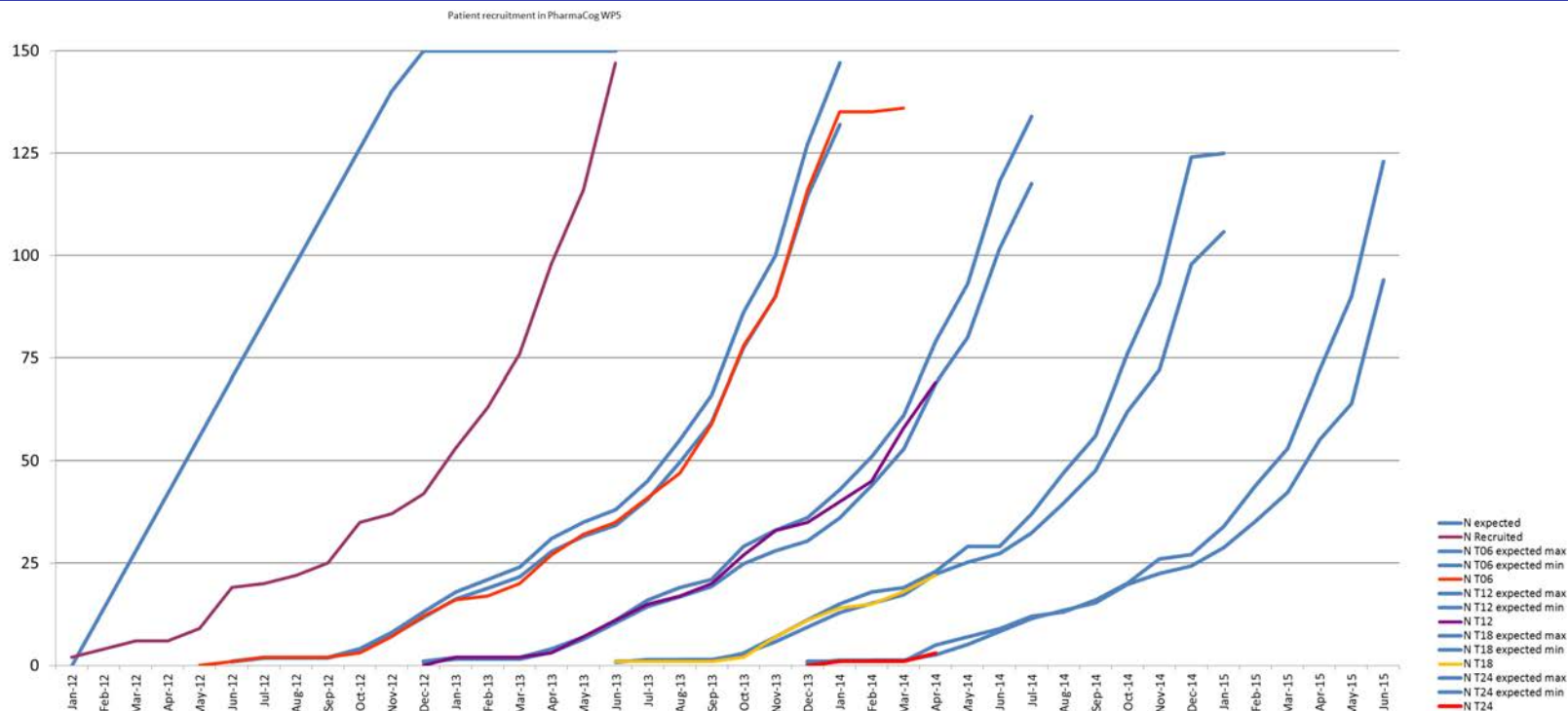
Heather shared that the Association is looking to update the alz.org/wwadni website with individual trial sites, as we have heard from industry partners and other ADNI efforts that this information

would be helpful to have on hand. To that end, we will be contacting each of the PIs to both review the data on the website for accuracy/ updates and to provide (if willing) an updated list of trial sites within your country.

V. Save the Date Face to Face meeting at AAIC:

Friday, July 11, 2014 in Copenhagen – 9:00 am

Enrollment and follow-ups as of April 30, 2014



End of recruitment	150 pats expected	147 pats enroled COMPLETED
Follow-up as of April 30 2014	147-132 pats expected	136 pats T06 COMPLETED
	79-69 pats expected	69 pats T12 ONGOING
	23-22 pats expected	22 pats T18 ONGOING
	3-5 pats expected	3 pat T24 ONGOING

Clinical characteristics of 145 MCI by Abeta42 status

CSF-pos Abeta42 <550 pg/mL (Mulder et al., 2010, Hulstaert et al., 1999)



	All	CSF-positive (n=55)	CSF-negative (n=90)	p
<i>Sociodemographics</i>				
Age	69.2 _± 7.3	69.8 _± 6.7	68.8 _± 6.7	.40
Education	10.6 _± 4.4	11.3 _± 4.5	10.1 _± 4.3	.11
Sex (F)	83 (57%)	31 (56%)	52 (58%)	.87
<i>Clinical features</i>				
Onset of cognitive symptoms (years)	3.0 _± 2.6	2.6 _± 1.7	3.3 _± 3.0	.12
Mini Mental State Examination	26.6 _± 1.8	26.1 _± 1.7	27.0 _± 1.8	.005
Functional Assessment Questionnaire	2.6 _± 2.5	2.6 _± 2.5	2.6 _± 2.6	.82
Geriatric Depression scale	2.4 _± 1.8	2.4 _± 1.8	2.5 _± 1.9	.72
Neuropsychiatric Inventory	8.6 _± 10.5	9.6 _± 11.0	8.1 _± 10.2	.43

Neuropsychological characteristics of 145 MCI by Abeta42 status (1/2)



	All	CSF-positive (n=55)	CSF-negative (n=90)	p
Verbal memory				
AVLT, immediate recall	31.2 _± 9.7	29.2 _± 8.4	32.4 _± 10.3	.05
AVLT, delayed recall	4.3 _± 3.2	3.7 _± 3.1	4.6 _± 3.3	.11
Visual memory				
Paired associates learning test (n. of errors)*	19.2 _± 11.6	19.8 _± 11.9	18.7 _± 11.4	.63
Delayed match to sample (% correct all del.) *	68.0 _± 16.5	62.7 _± 16.9	72.0 _± 15.1	.002
Pattern recognition memory test (% correct) *				
immediate	77.4 _± 15.4	75.5 _± 14.7	79.0 _± 15.9	.23
delayed	65.0 _± 18.0	63.5 _± 17.6	66.1 _± 18.3	.44
Spatial recognition memory test (% correct) *	63.8 _± 13.3	58.8 _± 12.9	67.5 _± 12.5	<.0005
Working memory				
Digit Span forward	5.4 _± 1.1	5.4 _± 1.1	5.3 _± 1.2	.78
Digit Span backward	3.8 _± 1.1	3.8 _± 1.0	3.8 _± 1.1	1.00
Spatial working memory test (n. of errors) *	43.2 _± 21.4	48.3 _± 21.3	39.4 _± 20.8	.02

*Tests from the CANTAB battery

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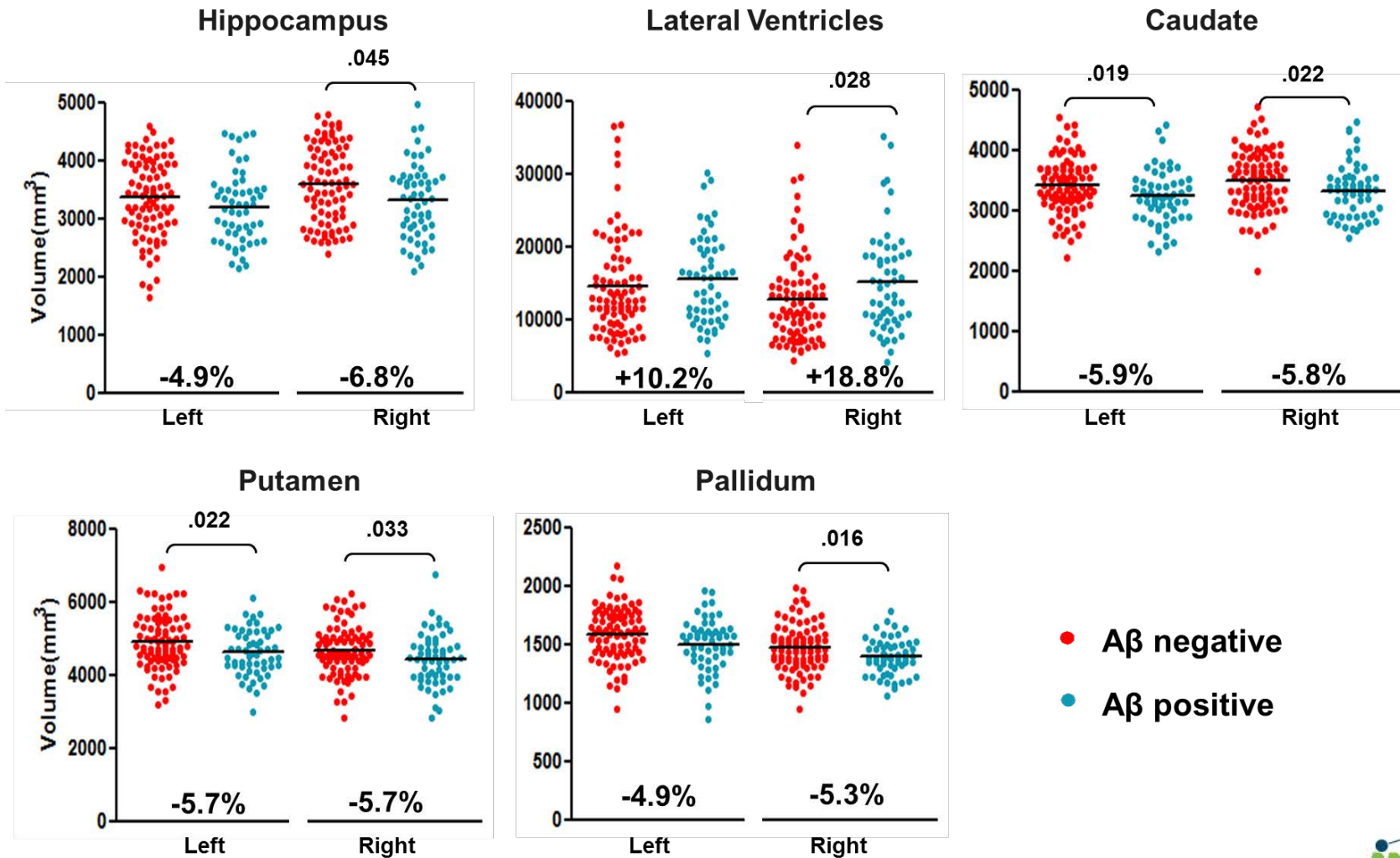
Genetic and CSF features of MCI by Abeta42 status



	CSF-positive (n=55)	CSF-negative (n=90)	p
<i>ApoE</i>			
E2 carriers	3 (8%)	5 (9%)	.88
E3 carriers	27 (75%)	54 (100%)	<.0005
E4 carriers	29 (81%)	17 (32%)	<.0005
<i>CSF</i>			
Tau (pg/ml)	556+335	426+346	.03
p-tau (pg/ml)	79+38	61+31	.002

MRI – Brain volume estimates in 145 MCI by Abeta42 status

Task force leaders: Jorge Jovicich and Moira Marizzoni

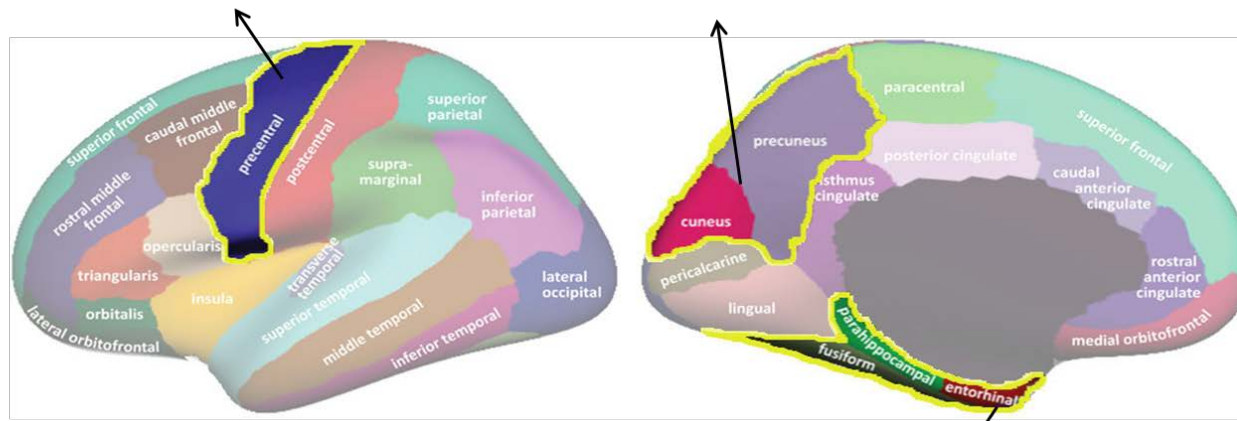
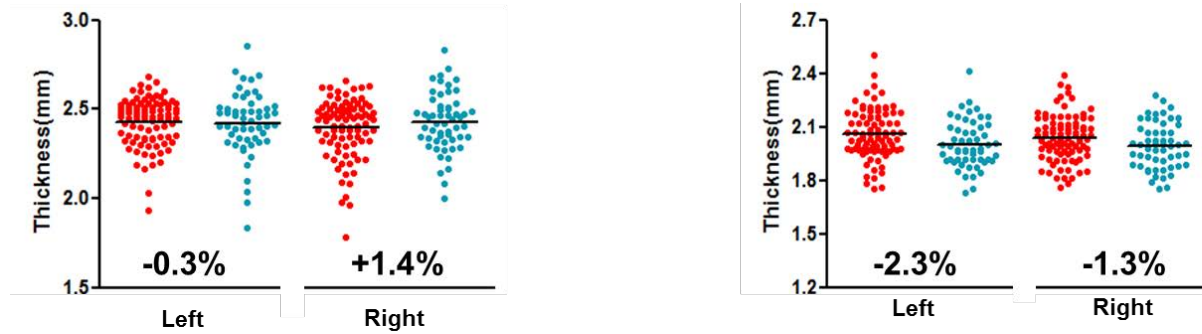


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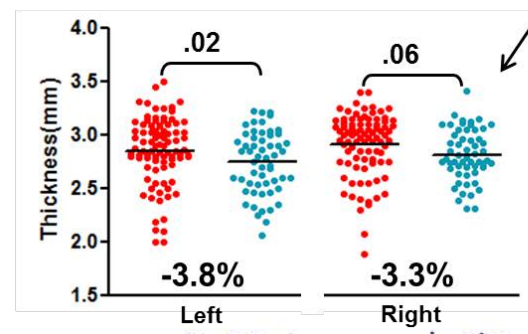


MRI – Cortical thickness estimates in 145 MCI by Abeta42 status

Task force leaders: Jorge Jovicich and Moira Marizzoni



- Aβ negative
- Aβ positive

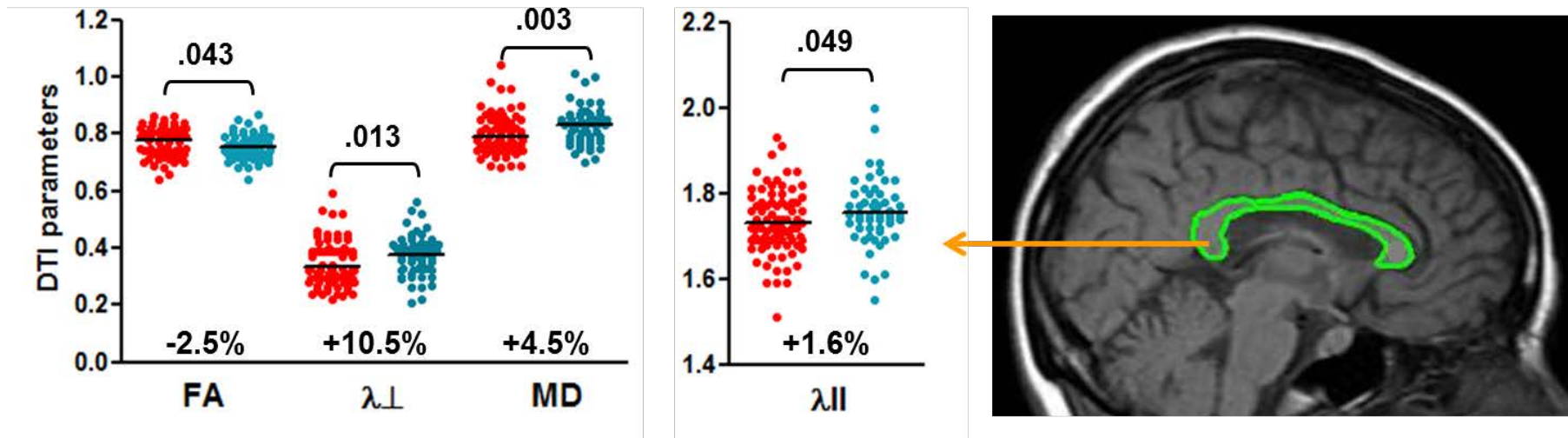


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MRI – Brain diffusion estimates in 145 MCI by Abeta42 status

Task force leaders: Jorge Jovicich and Moira Marizzoni

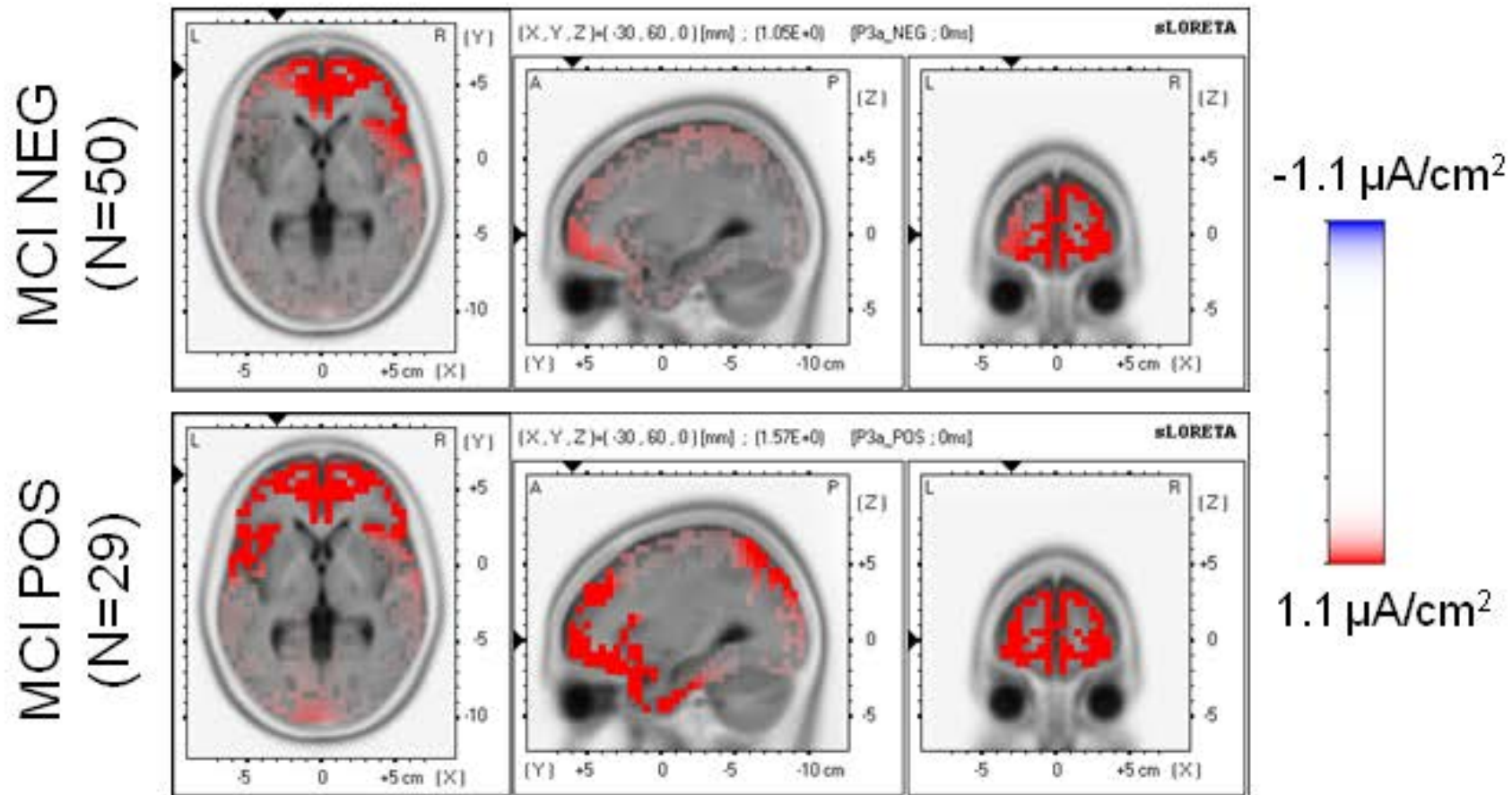


● Aβ negative ● Aβ positive

Relationship between cortical sources of EEG auditory oddball event-related potentials (P3) and CSF A β level



P3a sLORETA SOLUTION



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Dissemination: papers



Journal	Title	Status	Author
Journal of Alzheimer's Disease	Disease tracking markers for Alzheimer's disease at the prodromal (MCI) stage	Published on Aug 2011	Drago et al.
NeuroImage	Brain morphometry reproducibility in multi-center 3T MRI studies: A comparison of cross-sectional and longitudinal segmentations	Published on Dec 2013	Jovicich et al.
Drug Discovery Today: Therapeutic Strategies	A new paradigm for testing AD drugs – neuroimaging biomarkers as surrogate outcomes homologous in animals and humans	In press. E-pub: Dec 2013	Marizzoni et al.
NeuroImage	Multisite Longitudinal Reliability of Tract-Based Spatial Statistics in Diffusion Tensor Imaging of Healthy Elderly Subjects	In review	Jovicich et al.
Brain	Striatum and entorhinal cortex common neuropathological targets in Alzheimer's disease mouse models	submitted	Micotti et al.

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