

E-ADNI (PharmaCog WP5)

The pilot European Alzheimer's Disease Neuroimaging Initiative of the European Alzheimer's Disease Consortium

Giovanni B. Frisoni^{a,*}, Wouter J. P. Henneman^b, Michael W. Weiner^c, Philip Scheltens^d, Bruno Vellas^e, Emma Reynish^{e,f}, Jaroslava Hudecova^a, Harald Hampel^{g,h}, Katharina Burger^h, Kaj Blennowⁱ, Gunhild Waldemar^j, Peter Johannsen^j, Lars-Olof Wahlund^k, Giancarlo Zito^l, Paolo M. Rossini^l, Bengt Winblad^k, Frederik Barkhof^b, and the Alzheimer's Disease Neuroimaging Initiative

^a*IRCCS Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy*

^b*Department of Radiology, VU University Medical Centre, Amsterdam, The Netherlands*

^c*Center for Imaging of Neurodegenerative Diseases, Veterans Administration Medical Center and Departments of Radiology, Medicine, Psychiatry, and Neurology, University of California, San Francisco, San Francisco, CA, USA*

^d*Department of Neurology and Alzheimer Center, VU University Medical Centre, Amsterdam, The Netherlands*

^e*INSERM U. 558, Gerontopole, Pole Geriatrie, Centre Hospitalier Universitaire, Toulouse, France*

^f*Geriatric Medicine, Department of Clinical and Surgical Sciences, University of Edinburgh, Edinburgh, UK*

^g*Discipline of Psychiatry, School of Medicine and Trinity College Institute of Neuroscience, Trinity College Dublin, Trinity Centre for Health Sciences, The Adelaide and Meath Hospital Incorporating The National Children's Hospital, Dublin, Ireland*

^h*Department of Psychiatry, Alzheimer Memorial Center, Ludwig-Maximilian University, Munich, Germany*

ⁱ*Clinical Neurochemistry Laboratory, Sahlgrenska University Hospital, Mölndal, Sweden*

^j*Department of Neurology, Rigshospitalet, Section 2082, Copenhagen University Hospital, Copenhagen, Denmark*

E-ADNI / PharmaCog WP5

DESIGN

	MCI		T0	T6	T12	T18	T24	T30	T36
	Ab42+	Ab42-							
Clinical/Npsy	75	75	X	X	X	X	X	X	X
CSF	75	75	X			X			X
3T MR structural	75	75	X	X	X	X	X	X	X
diffusion	75	75	X	X	X	X	X	X	X
rest fMRI	75	75	X	X	X	X	X	X	X
Blood	75	75	X	X	X	X	X	X	X
EEG / P300	75	75	X	X	X	X	X	X	X

Qualification procedures

Clinical assessment & npsy

- Video and simulated case

MR qualification

Design

- 5 older local volunteers per centre
- Scan-rescan 2 weeks apart

Qualification markers

- stability of cortical thickness estim (FSsurf)
- stability of volume estimate via autom segment (FSsurf)
- stability of FA, MD
- stability of correlation between nodes
- stability of spatial activation

EEG & P300 qualification

Design

- 1 healthy volunteer per center

Analysis

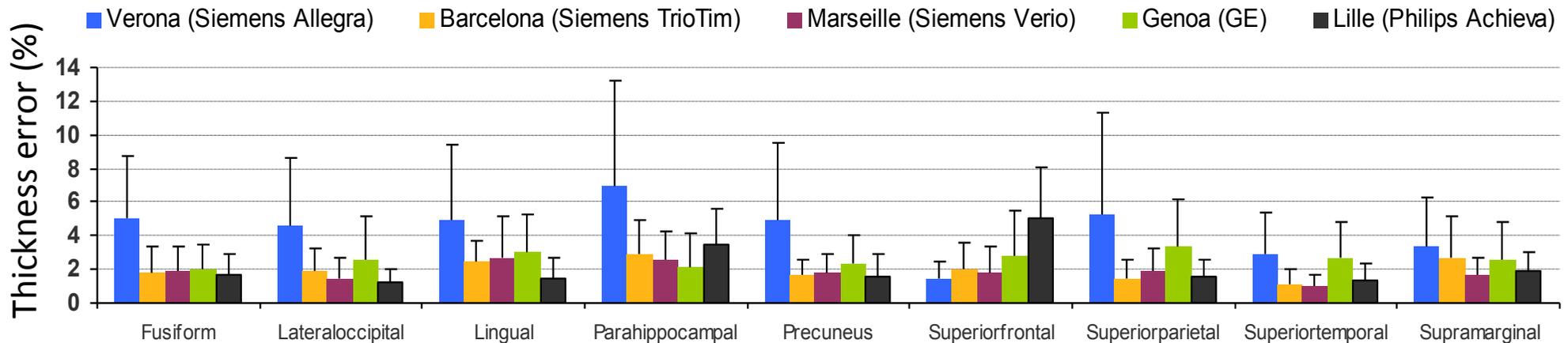
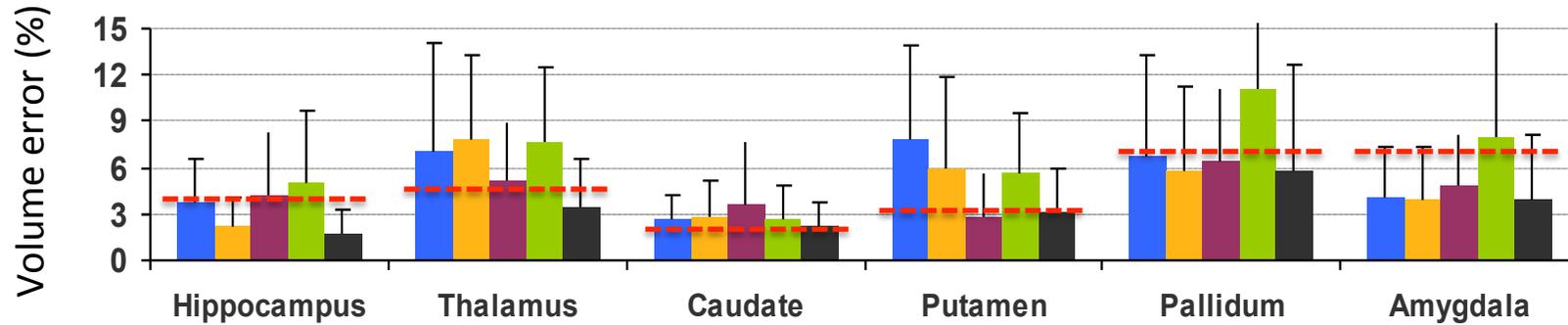
- α power eyes open-eyes closed
- detection of P300

CSF & Blood

- assays of $A\beta_{42}$, τ , $ph\text{-}\tau$ in CSF
- assays of putative markers in blood

Within site structural MR reproducibility

5 test-retest subjects (68 ± 10 years) per site (Freesurfer)



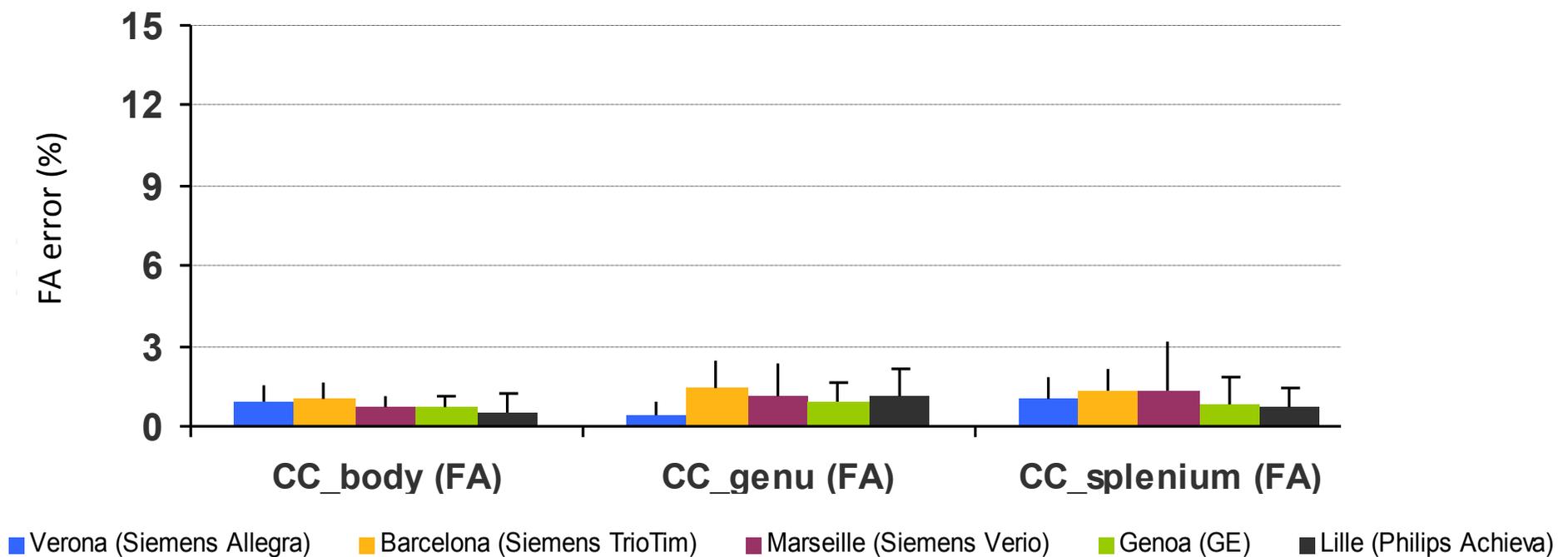
----- Literature data from Jovicic et al., Neuroimage. 2009; 46:177–192

Advancing science and treatment of Alzheimer's Disease



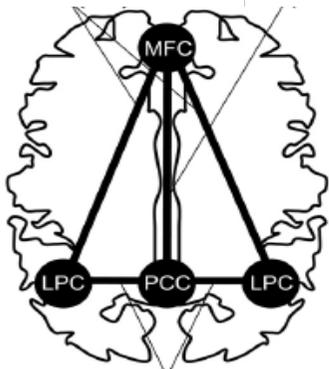
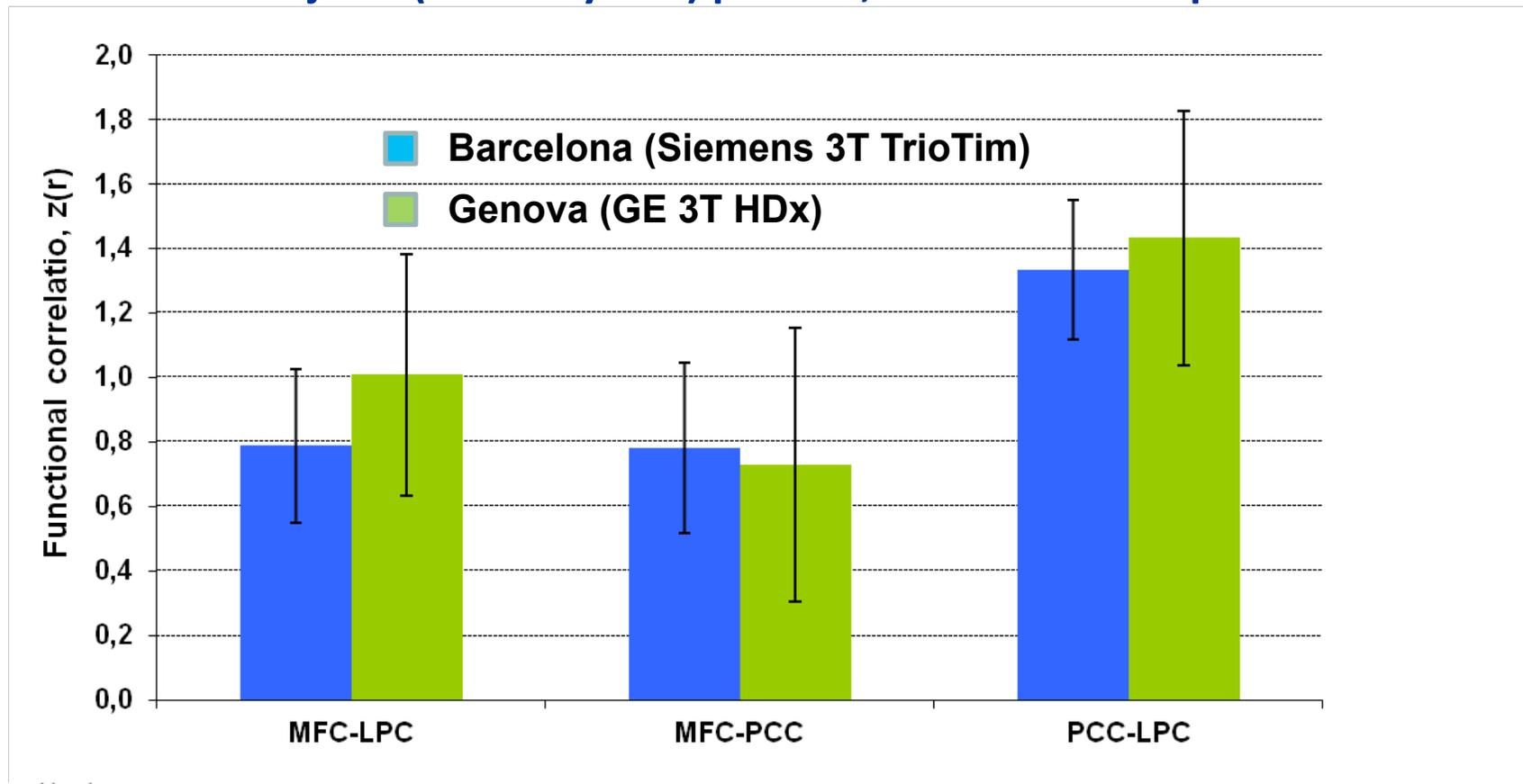
Within site diffusion MR reproducibility

5 test-retest subjects (68 ± 10 years) per site



Resting State Default Mode Network: Functional Correlation Between Key Nodes

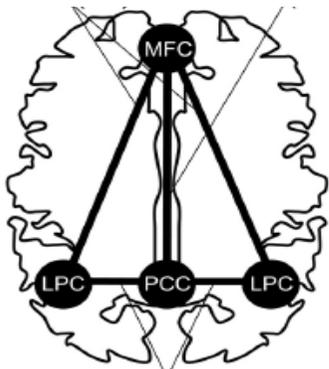
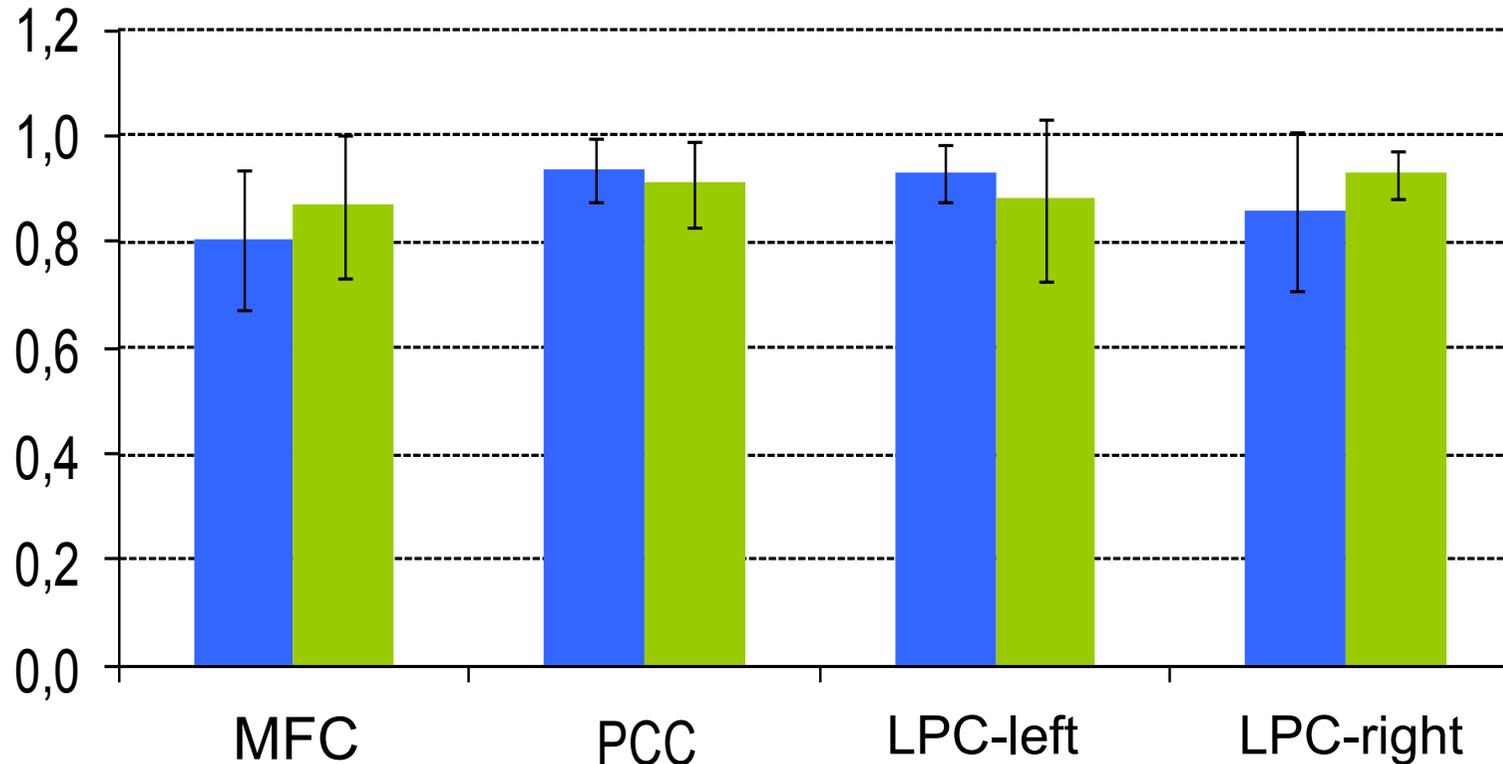
5 subjects (68 ± 10 years) per site, retest 1 week apart



- **MFC (medial frontal cortex)**
- **LPC (left and right lateral posterior cortex)**
- **PCC (posterior cingulate cortex)**
- **Defined by separate ICAs per site**

Resting State Default Mode Network: Reproducibility of Spatial Activation in Key Nodes

5 subjects (68 ± 10 years) per site, retest 1 week apart



MFC (medial frontal cortex)

PCC (posterior cingulate cortex)

LPC (lateral posterior cortex)

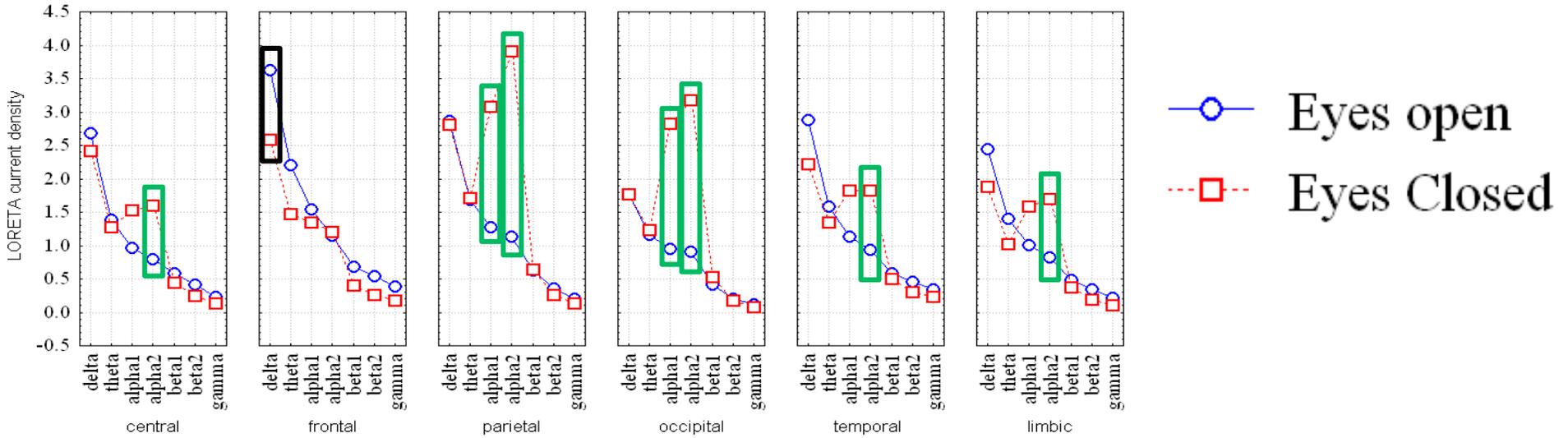
■ Barcelona (Siemens 3T TrioTim)

■ Genova (GE 3T HDx)

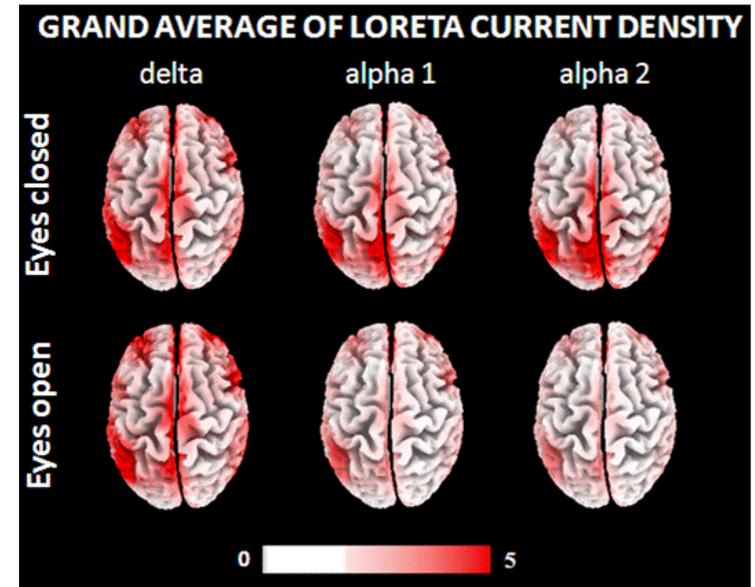
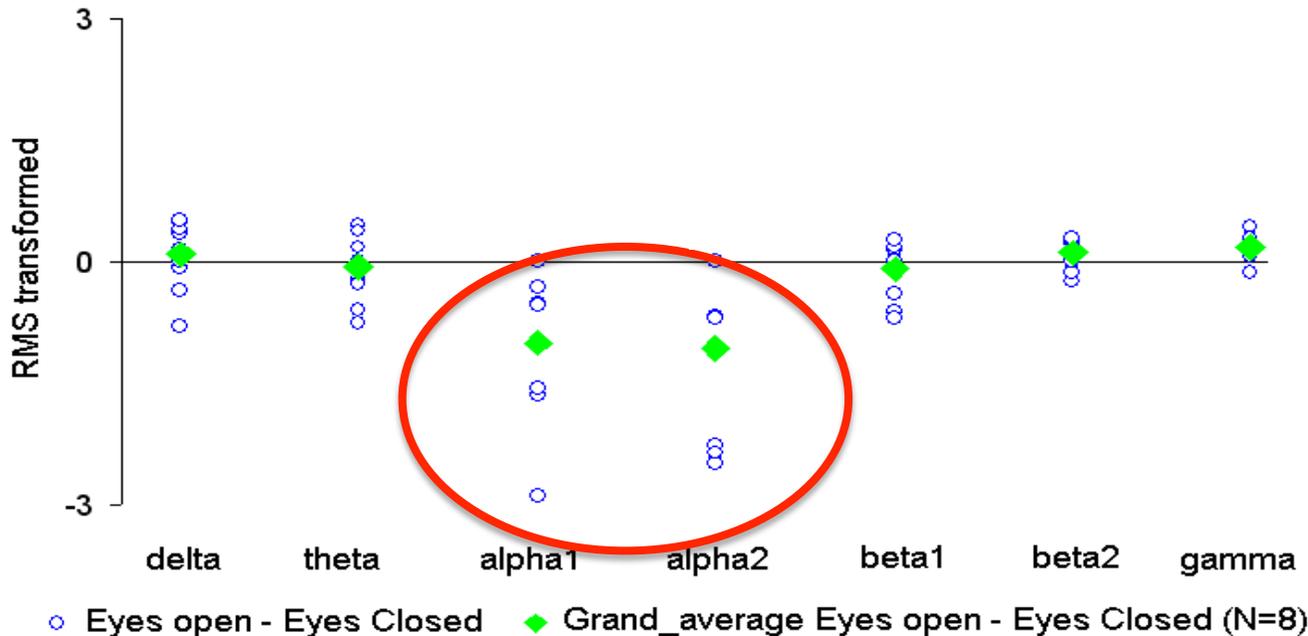
Results consistent with: Meindl et al. Human Brain Mapping, 2010. 31:237-246

Validation of EEG procedure: resting state eyes-open and eyes-closed in 8 healthy volunteers (1 per site)

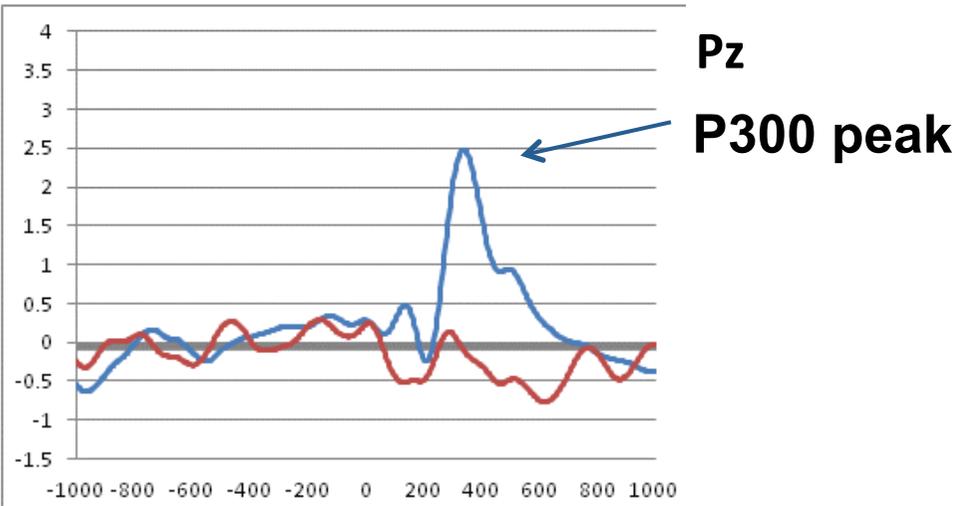
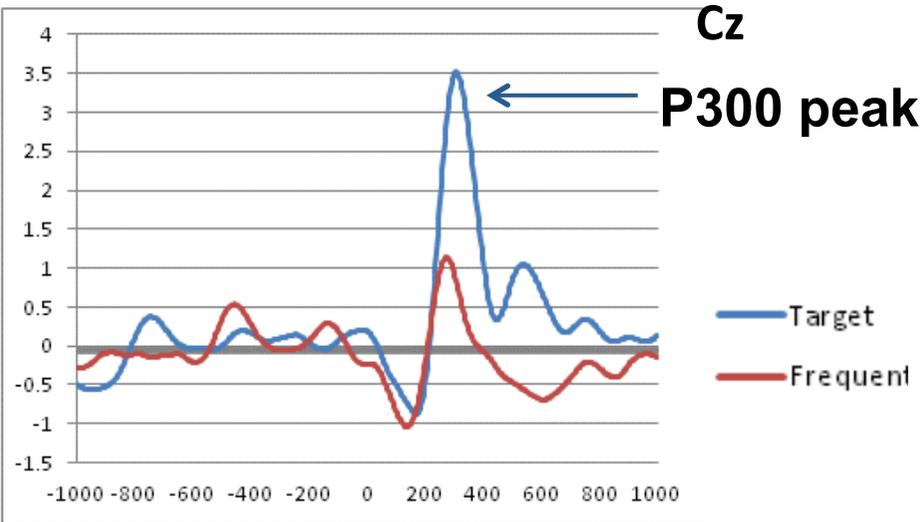
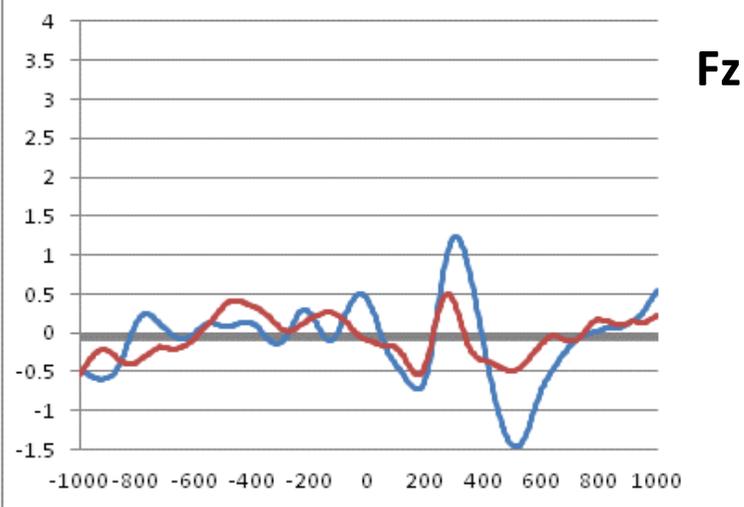
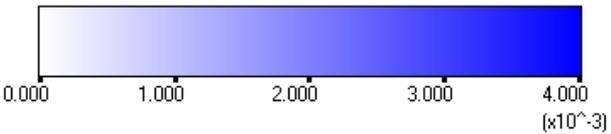
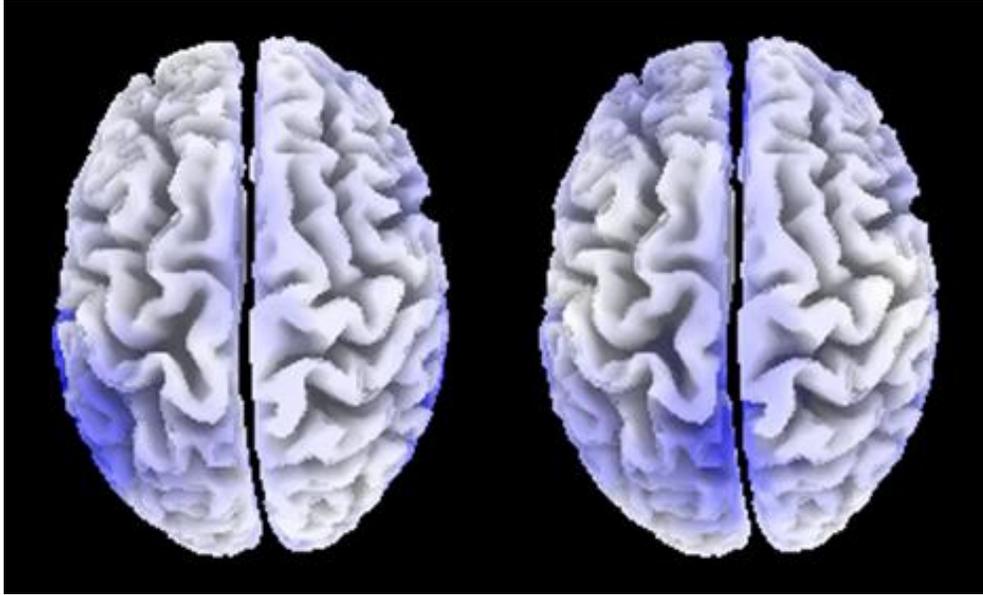
$F(30,210)=1.57; p<.0365$



Occipital LORETA power density



Validation of auditory P300 in 8 healthy volunteers (1 per site): grand average of ERP waveforms and LORETA sources of P300 peak



Patient characteristics



	e-ADNI (n=20)	Pilot-eADNI (n=19)	US-ADNI (n=394)
<i>Sociodemographics</i>			
Age	68.8+6.7	68.9+11.3	74.7+7.5
Sex (F)	13 (65%)	9 (47%)	141 (36%)
Education (years)	11.1+5.0	11.1+4.4	15.7+3.1
<i>Cognition</i>			
Mini Mental State exam	26.6+2.0	27.3+2.1	27.0+1.8
CDR-SOB	1.0+.6	1.3+1.0	1.6+.9
<i>Disability</i>			
Functional Assessment Quest.	2.4+1.7	1.6+1.8	3.8+4.5
<i>Depressive symptoms</i>			
Geriatric Depression Scale	2.5+1.4	2.5+1.9	1.6+1.4

Patient enrolment

