BERG SYMPOSIUM WASHINGTON UNIVERSITY SEPT 2003

MICHAEL W WEINER MD

CURRENT FOCUS OF MOST IMAGING RESEARCH

- Improved methods to detect treatment effects in clinical trials
 - Reduce sample size
 - Shorten length of trial
- Early detection of AD

NICK FOX UNIVERSITY OF LONDON

Brain volume as % of intracranial volume vs time



CLIFFORD JACK

MAYO CLINIC

Sample size estimates to detect differences equaling 50% or 25%

of observed median

with 90% probability and an alpha level of 0.05 using two-sided *t*-tests among MCI patients

			Sample	Sample
		SD (on	size to	size to
	Observed	transforme	detect	detect
	median	d scale)	effect size	effect size
			of 50%	of 25%
Hippocampus	-2.55	16.13	24	102
Entorhinal cortex	-5.97	72.72	21	91
Whole brain	-0.63	1.91	32	130
Ventricle	3.29	0.44	16	69
CDR	0.54	0.33	311	1277
MMSE	-0.47	1.31	658	2628
			1	

<u>Neurology</u> in review

IMAGING THE TREATMENT AND EARLY DETECTION OF AD WITH: sMRI, pMRI, MRSI

> Michael W Weiner MD Norbert Schuff PhD Nathan Johnson MD Linda Chao PhD

Sample Size/Arm for 20% treatment effect One year trial

	80% power (One tail)	80% power (Two tail)	90% power (One tail)	90% power (Two tail)
ERC Rate	64	82	89	109
HP Rate	52	66	71	88
BSI_VENT	58	74	81	99

Entorhinal cortex (ERC), hippocampus (HP), ventricular BSI (BSI_VENT). Calculated from data on 20 AD subjects. Interscan interval = 1.8

Effects of AD and CIND on Hippocampal NAA



EFFECTS OF AD AND CIND ON CORTICAL



Perfusion MRI: MCI v NC

rCBF



GM concentration



P<0.05; cluster-level correction

Diffusion-weighted MRI and fMRI of Aging and Dementia

Randy Buckner Washington U. St Louis Mo

AGING CHANGE IN WHITE-MATTER

YNG vs OLD YNG vs DAT OLD vs DAT



3.09

Head, Buckner et al., in press, Cerebral

Functional NeuroimagingYOUNGOLD



Logan et al, Neuron 2002

Do words represent living/non living: Deactivations







_ustig et al., in press, PNAS

Functional MRI studies in early Alzheimer's disease

Reisa Sperling, M.D., M.MSc. Brigham and Women's Hospital Massachusetts General Hospital Harvard Medical School

Functional MRI - Face-Name Association Fusiform Activation





Sperling

Test-Retest Reliability of fMRI in AD for Pharmacological studies



Sperling

SCOTT SMALL Columbia U New York NY

- Aging predominately reduces LTP in the granule cells of the dentate gyrus;
- In contrast, AD causes deficits in basal synaptic transmission in pyramidal cells of the entorhinal cortex and CA subfields.
- Taken together, these studies suggest that AD and aging are separate and dissociable processes.

FDG PET in the Study of Cognitively Normal Persons at Genetic Risk for Alzheimer's Disease

Eric M. Reiman, MD

Banner Good Samaritan Medical Center University of Arizona Translational Genomics Research Institute Arizona Alzheimer's Disease Consortium Phoenix, Arizona, USA

CMRgl Abnormalities in Probable Alzheimer's Dementia



PC

Number of AD Patients per Treatment Group Needed to Detect an Effect with 80% Power in One Year

	Treatment Effect					
	20%	30%	40%	50%		
Frontal	85	38	22	14		
Parietal	217	97	55	36		
Temporal	266	119	68	44		
Cingulate	343	153	87	57		
Combined	62	28	16	10		

P=0.01 (two-tailed)

No adjustment for normal aging effects or subject attrition

CMRgI Abnormalities in 50-65 y.o. ε 4/ ε 4's



Correlations Between APOE ε4 Gene Dose and Reductions in Regional CMRgI (36 HM, 46 HT, 78 NC)









APOE ε 4 Gene Dose is Correlated with Reductions in Regional CMRgI



P < 0.0005

IMAGING PATHOLOGICAL PROTEINS WITH PET

Update on In Vivo Imaging of Plaques and Tangles

Gary W. Small, M.D. University of California, Los Angeles



Gary Small, UCLA School of Medicine





MMSE Scores vs. Residence Time (RT) Values



Gary Small, UCLA School of Medicine

Imaging Amyloid in Alzheimer's Disease with PIB

William E. Klunk. MD. PhD

Laboratory of Molecular Neuropharmacology Department of Psychiatry, Western Psychiatric Institute & Clinic University of Pittsburgh Medical Center

[¹¹C]6-OH-BTA-1 (PIB) Retention in Controls & AD



Retention of [¹¹C]6-OH-BTA-1 (PIB) in AD and Controls – SUV



Correlation of [¹¹C]6-OH-BTA-1 (PIB) Retention and rCMRglu



SUMMARY

- Accumulating evidence that structural MRI will play a major role in
 - Clinical trials for AD etc
 - Early detection of AD
- fMRI sheds light on mechanism of cognitive impairments and compensatory response. May play a role in drug trials and early detection

SUMMARY

- Molecular imaging with PET shows exciting potential to detect amyloid, and possibly other proteins
- The future role of these methods in clinical trials and early detection remains unknown