Taiwan ADNI Progress Report

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TADNI

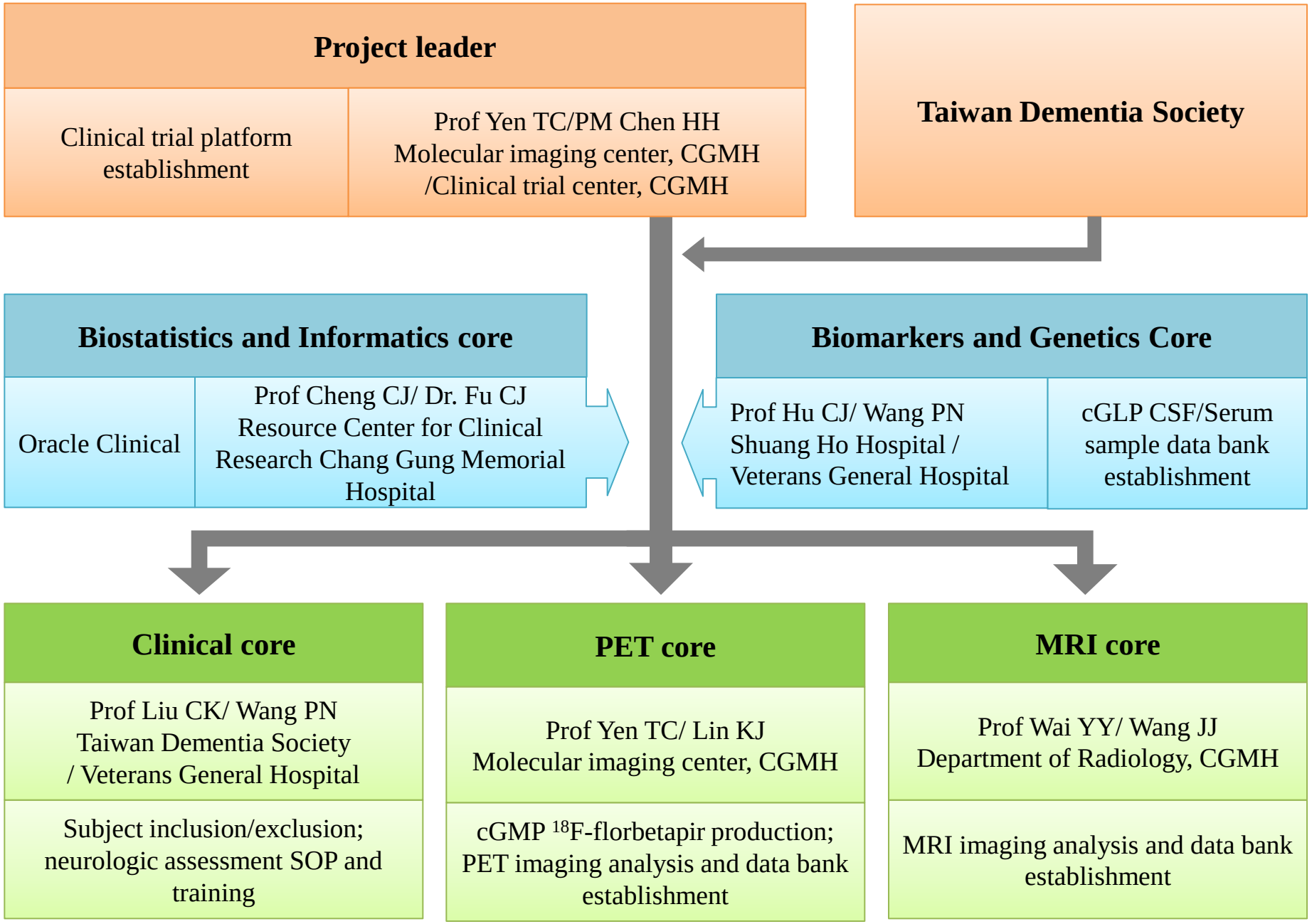
http://tadni.cgmh-mi.com/

TW ADNI

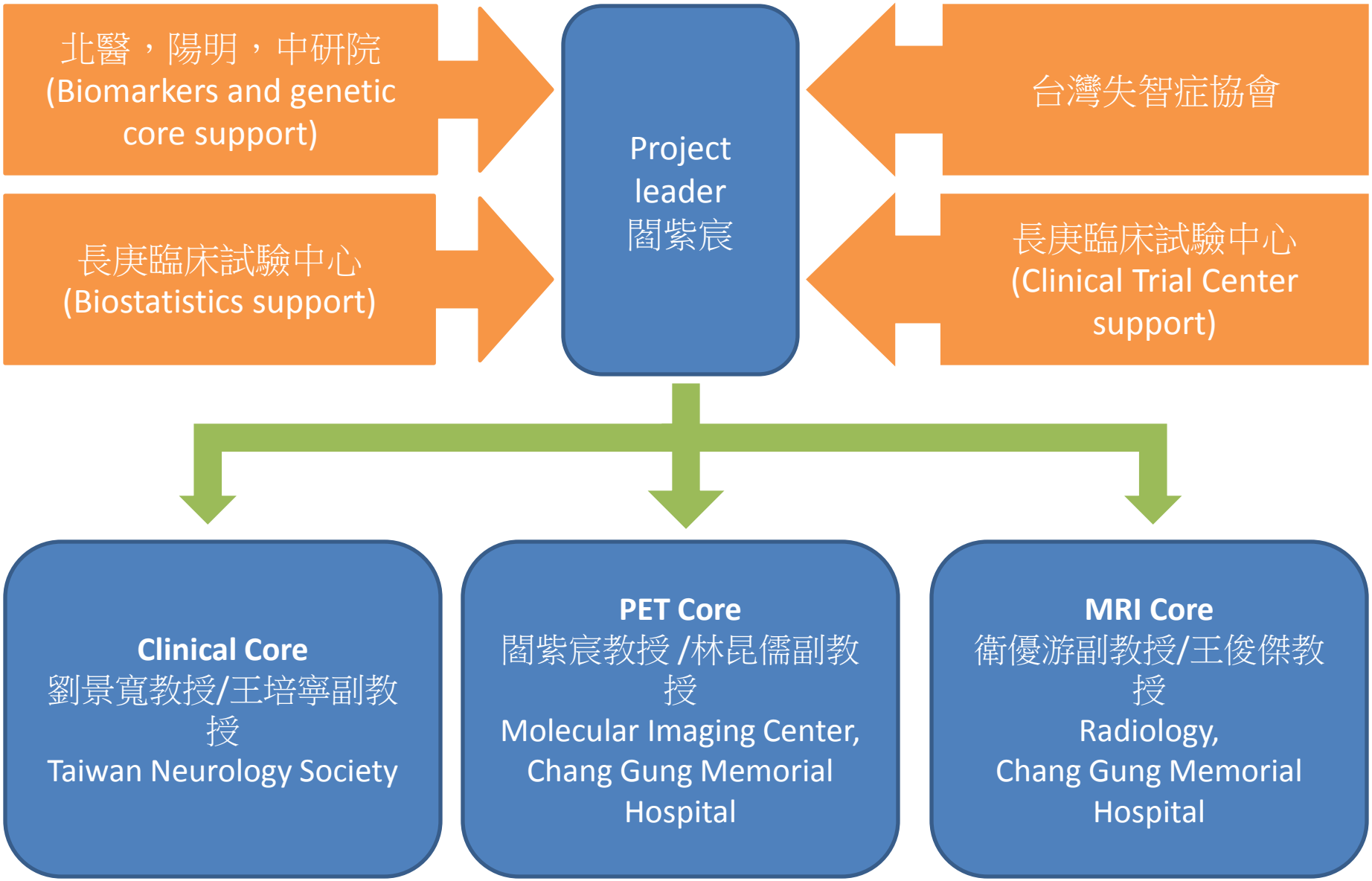
Home | News | Project | Research | Organization | Calendar

OVERVIEW

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by progressive decline in memory and other aspect of cognition and is the most common cause of dementia in the elderly. The average duration from onset of symptoms to nursing home placement is about 5 to 7 years. Accurate diagnosis of AD is sometimes difficult due to lack of reliable non-invasive biomarkers, although the diagnostic criteria have been proposed based on clinical presentation and history. A reliable or ideal biomarker should base on the presence of disease-specific pathology, and should be helpful in follow-up the disease course, evaluation of treatment effect and for presymptomatic identification of subjects at risk for developing AD.



Last update 2013-02-13



Last update 2013-02-13

Taiwan ADNI Project

在新視窗檢視醫院地圖

First stage	Second stage
1. 台北榮總, Veterans General Hospital-Taipei	1. 臺大醫院, National Taiwan University Hospital
2. 新光醫院, Shin Kong Wu Ho-Su Memorial Hospital	2. 台中榮總醫院, Veterans General Hospital-Taichung
3. 台北醫學大學, 行政院衛生署雙和醫院, Shuang Ho Hospital	3. 中國附醫, China Medical University Hospital
4. 三軍總醫院, Tri-service General Hospital	4. 彰化基督教醫院, Changhua Christian Hospital
5. 新店耕莘醫院, Cardinal Tien hospital	5. 成功大學附醫, National Cheng Kung University Hospital
6. 林口長庚, Chang Gung Memorial University Hospital-Linkou	6. 高雄長庚醫院, Chang Gung Medical Fundation, Kaohiung Branch
	7. 高醫中和附醫, Kaohsiung Medical University, Chung-Ho Memorial Hospital
	8. 高雄榮總醫院, Veterans General Hospital-Kaohsiung
	9. 花蓮慈濟醫院, Buddhist Tzu-Chi General Hospital

Hospital list updated on 2011-04-21

Under IRB review

ADNI: Alzheimer's Disease Neuroimaging Initiative

Taiwan ADNI: First Stage

- Start from north Taiwan
- 6 medical centers
- 200 subjects
- Inclusion and exclusion criteria follow the rules of

Normal	Early MCI	Late MCI	AD
50	50	50	50

Activities update for TADNI

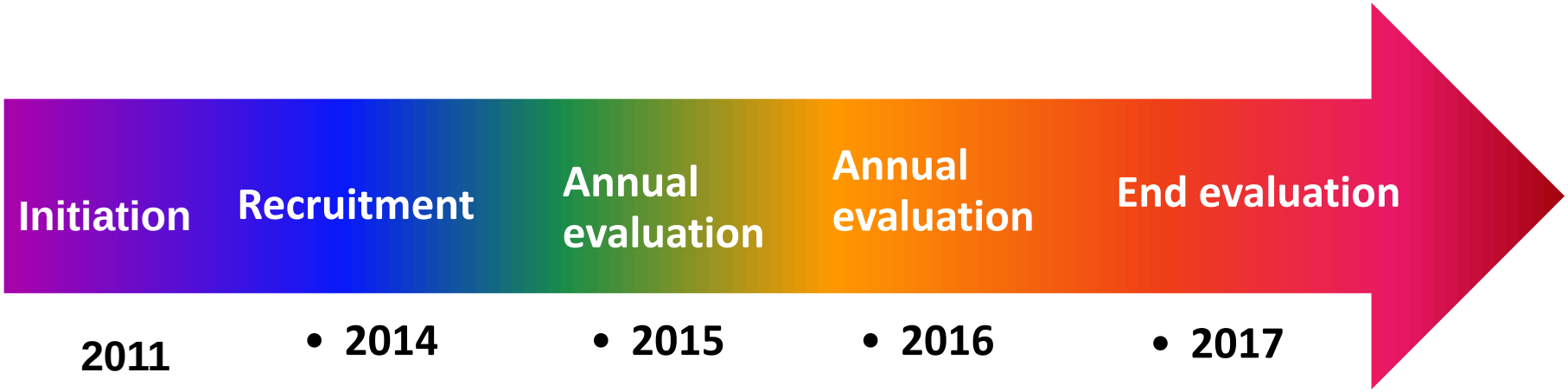
Date	Events
2011-07-21	Taiwan vascular dementia initiative (T-VADI) meeting update
2011-08-05	CDE PI meeting for TADNI PET core project
2011-08-27	PI meeting for TADNI project
2012-06-17	TADNI registration to ClinicalTrials.gov
2012-06-19	TADNI project approved by TFDA
2012-08-04	When AD meets PD conference
2012-11-09	PI meeting for TADNI project
2013-01-13	2013 Chang Gung Neurology & Neurosurgery Forum
2013-04-18	28th International conference of Alzheimer's disease international
2013-05-03	Frontier in Neurodegenerative diseases and beyond-from basic to translational

Diagnosis of NL, MCI and AD

	NL	EMCI	LMCI	AD
Memory complaints	−	+	+	+
MMSE	24-30	24-30	24-30	20-26
CDR	0	M≥0.5 Others 0	M≥0.5	0.5-1
Logic memory				
edu ≥16	≥9	9-11	≤8	≤8
edu 6-15	≥5	5-9	≤4	≤4

- **Age between 55-90**
- **Only subjects with ≥6 years education will be included**

TADNI
3-year longitudinal study



Neuropsychological Tests

Biomarker

- **Blood: Apo E polymorphism, amyloid, tau**
- **CSF**

Imaging studies

- **MRI**
- **PET: FDG-PET, F18-AV45-PET**

Visit name	Screen	Baseline	Month 6	Annual	End
Visit Type	In-Clinic	In-Clinic	In-Clinic	In-Clinic	LP
Explain study	X				
Obtain consent	X				
Demographic data	X				
Medical history	X				
Vital signs	X	X	X	X	
Screening Labs	X				
ApoE genotyping		X			
Collect and process biomarkers		X	X	X	
Concomitant Medications	X	X	X	X	
Neuropsychological tests	X	X	X	X	
Diagnostic Summary	X	X	X	X	
3T MRI Imaging (100%)		X		X	
FDG-PET Imaging (100%)		X		X	
F18-AV45 Amyloid PET Imaging (100%)		X		X	
Lumbar Puncture (LP) (optional)		X			X

Qualification of Neuropsychological tests

MMSE	Chinese Version Verbal Learning Test
CDR	Geriatric Depression Scale
WMS III Logical Memory story A recall	Clock drawing Test
Everyday Cognition (ECog)	Neuropsychiatric Inventory Q
Montreal Cognitive Assessment (MoCA)	ADAS-Cog 11 (with Delayed Word Recall)
Category Fluency (Animals)	Activities of Daily Living (FAQ)
Trails A & B	Chinese version Verbal Learning Test
Boston Naming Test (30-item)	

QC controls of Biofluids markers

- Setting of collection SOP
  - Barcode, collection tube, temperature requirement, sample tracking, shipping, storage
- Regulation of equipment and personnel
- Alarm system-SOP
- Barcode system
- GLP certification
- Test run-July, 2011

TW-ADNI MRI core - Aims

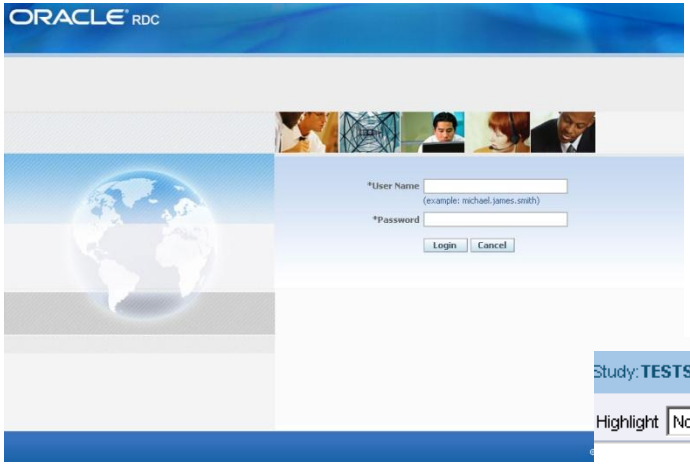
More than a neuroimaging repository for AD

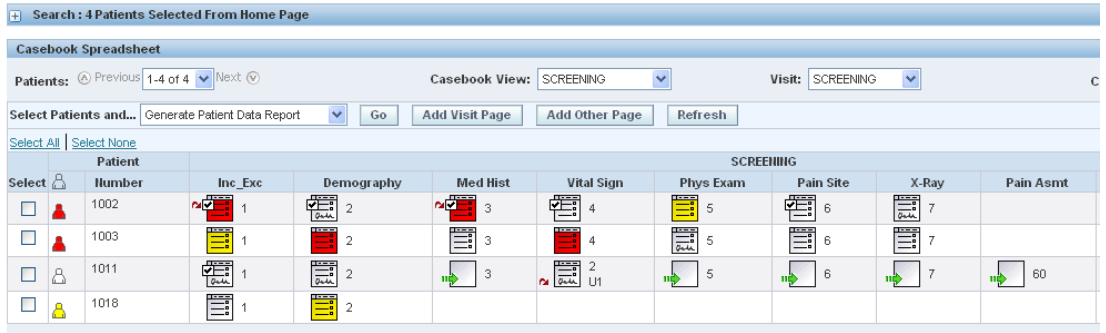
- Establish ***standard protocol*** for MRI acquisition
- Develop and implement ***methods for quality control*** of MR images
- Improve the ***post-processing methods***
- Investigate ***functional connectivity of brain***

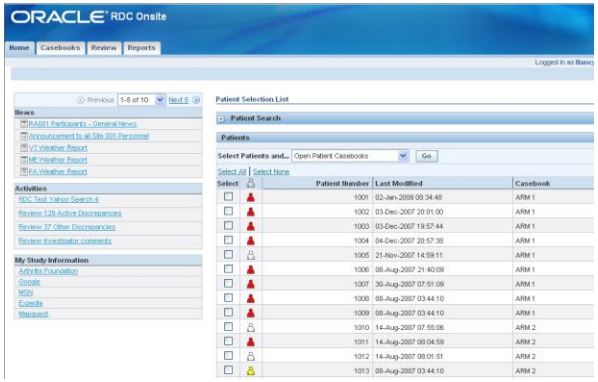
PET core protocol -Two scans

- All scans will be acquired in pairs of [^{18}F]FDG and [^{18}F]AV45 scans,
- performed on separate days, between 1 day and 2 weeks apart, with either scan performed first.

Data Management (Oracle)







Study Name: TESTSTUDY1 | Site: X001 | Patient: 101 | Visit Name: VISIT1

DEMOGRAPHIC DETAILS

Date of Birth
DD/MMM/YYYY

Initials
F/M/L

Gender
☐ Male ☐ Female

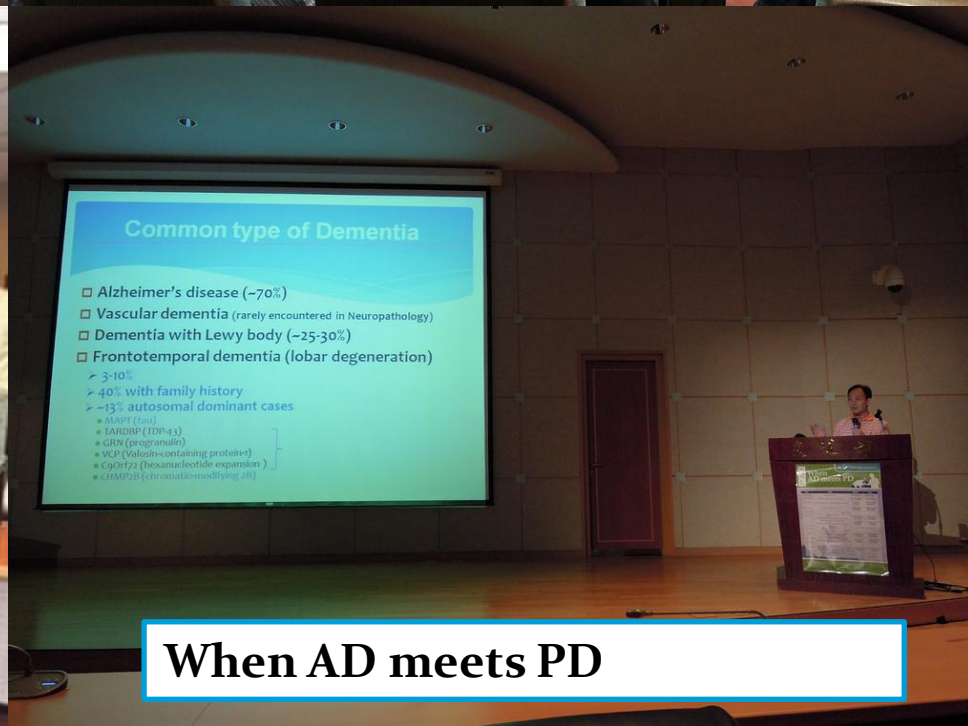
February 2010

SUN	MON	TUE	WED	THU	FRI	SAT
	1	2	3	4	5	6
7	8	9	10	11	12	13
14	15	16	17	18	19	20
21	22	23	24	25	26	27
28						

Race
☐ White
☐ Black or African American
☐ Asian
☐ Native Hawaian or Other Pacific Islander
☐ American Indian or Alaska Native
☐ Other
Other Specify _____

2013 Chang Gung Neurology & Neurosurgery Forum

Frontier in Neurodegenerative diseases and beyond-from basic to translational



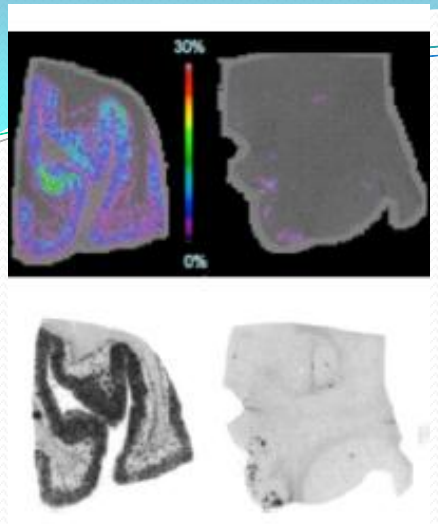
When AD meets PD

Peer Reviewed Articles from TW-ADNI (1)

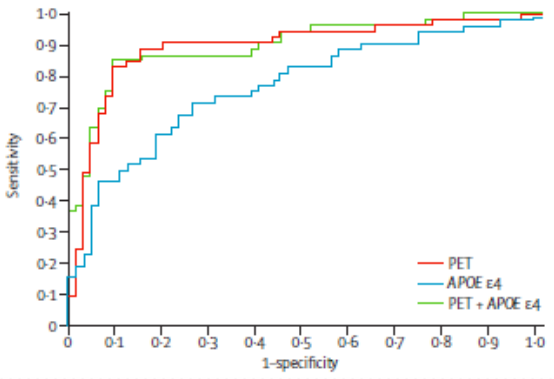
1. Wey SP, Weng CC, Lin KJ, Yao CH, Yen TC, Kung HF, Skovronsky D, Kung MP*. Validation of an 18F-labeled biphenylalkyne as a positron emission tomography imaging agent for β-amyloid plaques. Nucl Med Biol. 2009, 36(4): 411-417. (PMID:19423009)
2. Lin KJ^, Hsu WC^, Hsiao IT, Wey SP, Jin LW, Daniel Skovronsky, Wai YY, Chang HP, Lo CW, Yao CH, Yen TC*, Kung MP*. Whole-Body Biodistribution and Brain PET Imaging with 18F-AV-45, a Novel Amyloid Imaging Agent-a Pilot Study. Nucl Med Biol. 2010 May;37(4):497-508. (PMID:20447562)
3. Yao CH^, Lin KJ^, Weng CC, Hsiao IT, Ting YS, Yen TC, Jan TR, Daniel Skovronsky Kung MP, Wey SP*. GMP-compliant automated synthesis of [18F]AV-45 (Flobetapir F 18) for imaging beta-amyloid plaques in human brain. Appl Radiat Isot. 2010 Dec;68(12):2293-7. (PMID: 20638295)
4. Hsiao IT^, Huang CC^, Hsieh CJ, Hsu WC, Wey SP, Yen TC, Kung MP*, Lin KJ*. Correlation of early-phase F-18 Florbetapir (AV-45/Amyvid) PET images to FDG images: Preliminary studies. Eur J Nucl Med Mol Imaging. 2012 Apr;39(4):613-20. (PMID: 22270508)

Peer Reviewed Articles from TW-ADNI (2)

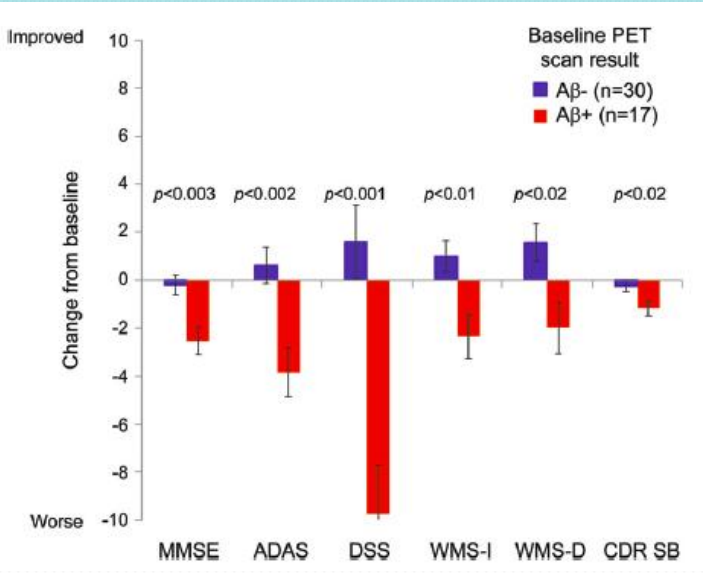
5. Huang KL^, Lin KJ^, Ho MY, Chang YJ, Chang CH, Wey SP, Hsieh CJ, Yen TC, Hsiao IT*, Lee TH*. Amyloid deposition after cerebral hypoperfusion: Evidenced on [(18)F]AV-45 positron emission tomography. J Neurol Sci. 2012 Aug 15;319(1-2):124-9. (PMID: 22572706)
6. Kung MP, Weng CC, Lin KJ, Hsiao IT, Yen TC, Wey SP. Amyloid plaque imaging from IMPY/SPECT to AV-45/PET. Chang Gung Med J. 2012 May-Jun;35(3):211-8. (PMID: 22735052)
7. Hsiao IT^, Huang CC^, Hsieh CJ, Wey SP, Kung MP, Yen TC*, Lin KJ*. Perfusion-like Template and Standardized Normalization based Brain Image Analysis: using F-18 florbetapir (AV-45/Amyvid) PET. Eur J Nucl Med Mol Imaging. 2013 Jun;40(6):908-20. (PMID: 23412134)
8. Huang KL^, Lin KJ^, Ing-Tsung Hsiao IT, Kuo HC, Hsu WC, Chuang WL, Kung MP, Wey SP, Hsieh CJ, Wa YY, Yen TC*, Huang CC*. Regional Amyloid Deposition in Amnestic Mild Cognitive Impairment and Alzheimer's Disease Evaluated by [18F]AV-45 Positron Emission Tomography in Chinese Population. PLoS One. 2013;8(3):e58974. (PMID: 23516589)



Semin Nucl Med 2011; 41:300-304

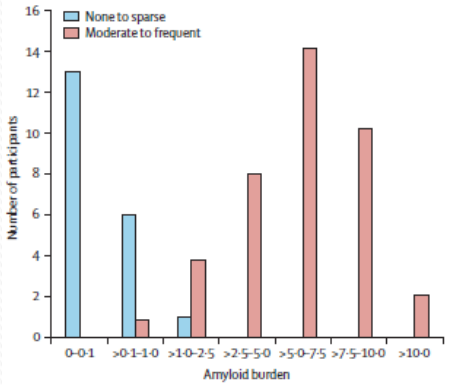


Lancet Neurol 2011; 10: 424–35



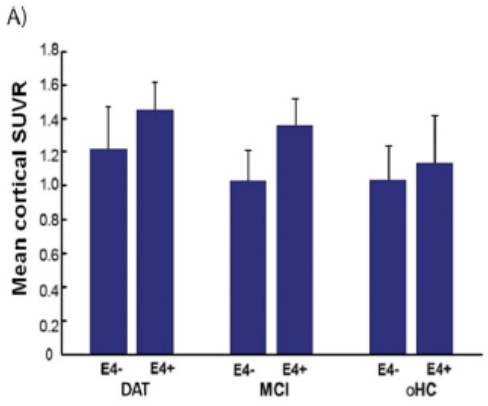
Neurology: 2012;79:1636–1644

Dx



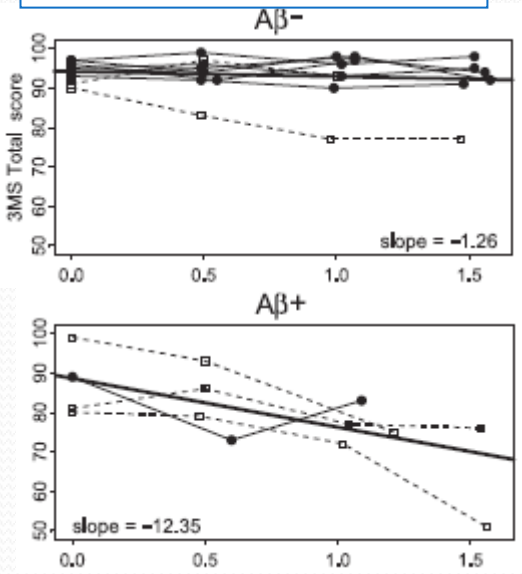
Lancet Neurol 2012; 11: 669–78

Monitor



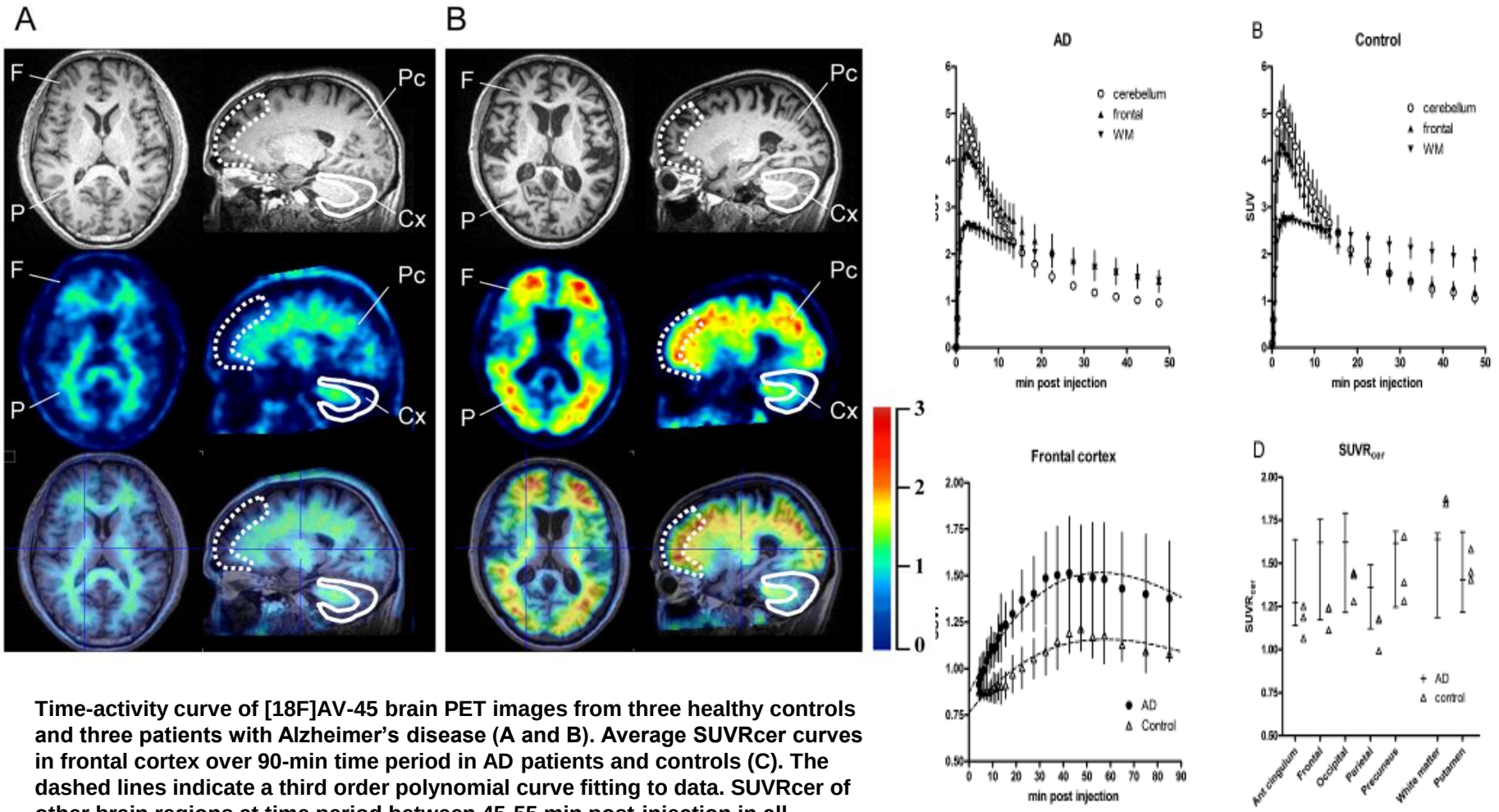
Neurobiology of Aging 34 (2013) 1–12

Prognosis



Alzheimer's & Dementia - (2012) 1–5

18F-AV-45 Brain Imaging (Phase I)



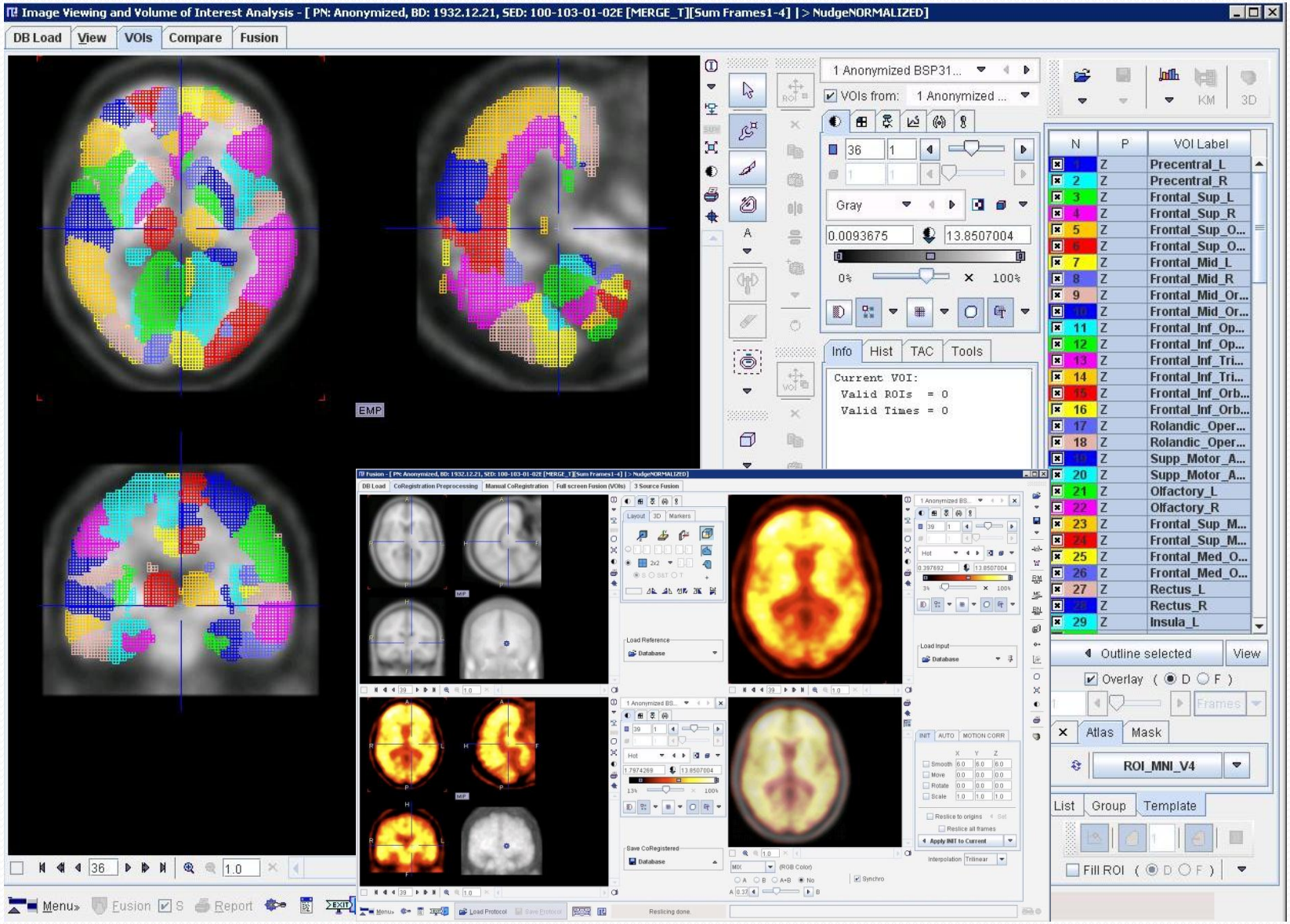
Time-activity curve of [18F]AV-45 brain PET images from three healthy controls and three patients with Alzheimer's disease (A and B). Average SUVRcer curves in frontal cortex over 90-min time period in AD patients and controls (C). The dashed lines indicate a third order polynomial curve fitting to data. SUVRcer of other brain regions at time period between 45-55 min post-injection in all subjects (D). Data were displayed in mean ± SD.

Different stage of AD

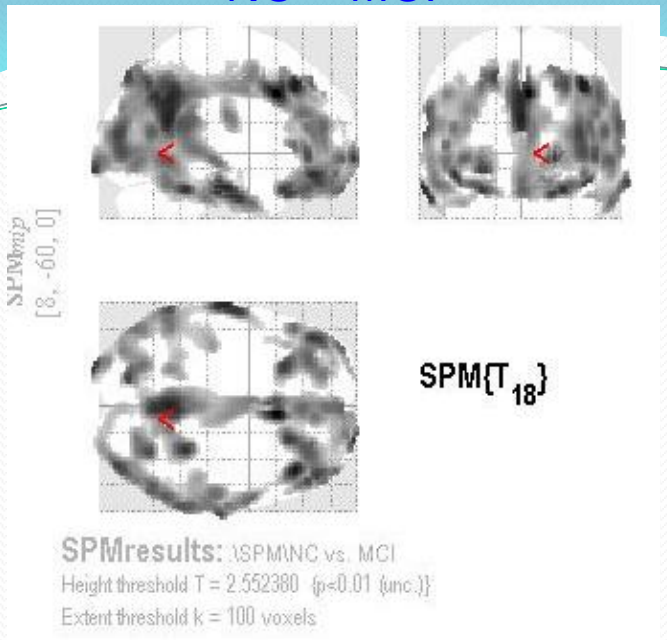
- NL: aMCI: AD (SUVR)
  - $1.08 \pm 0.08 : 1.27 \pm 0.06 : 1.34 \pm 0.13$, ($p = 0.0003$)
- NL: aMCI: AD (positive rate)
  - 9% : 62% : 92%
- aMCI (abnormal plaque deposition)
  - Precuneus, frontal and posterior cingulate gyrus
- MMSE scores and [^{18}F]AV-45 SUVRs among CN, aMCI and AD
  - Significance

Kuo-Lun Huang submitted to Plos One, 2012

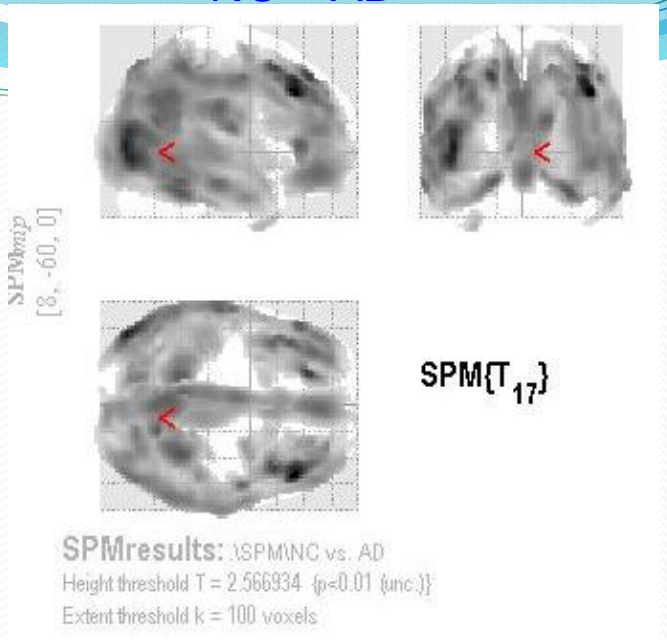
PET & MR correlated to AAL template



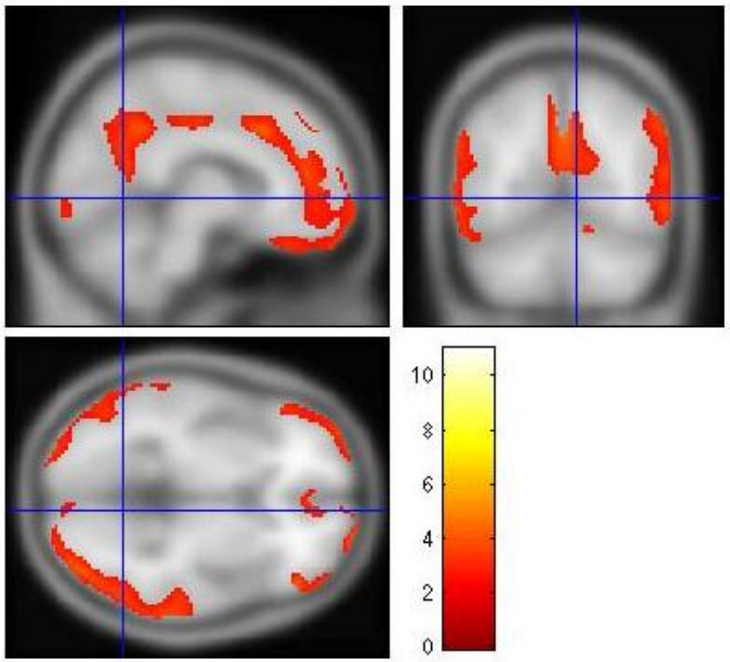
NC < MCI

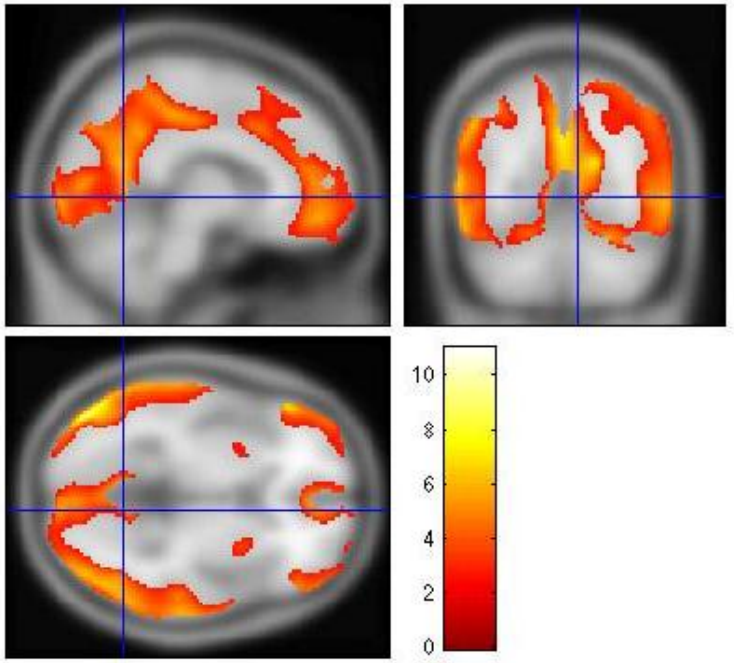


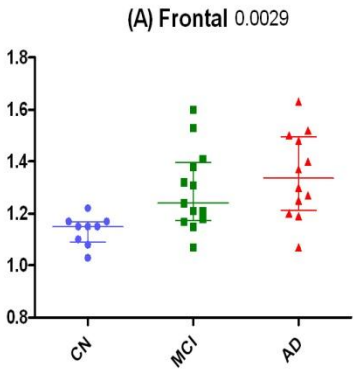
NC < AD

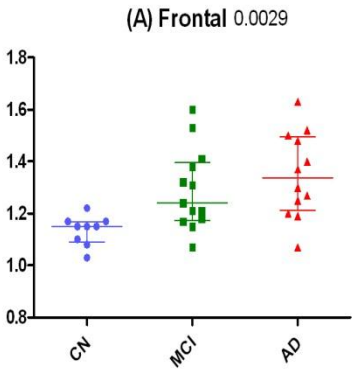


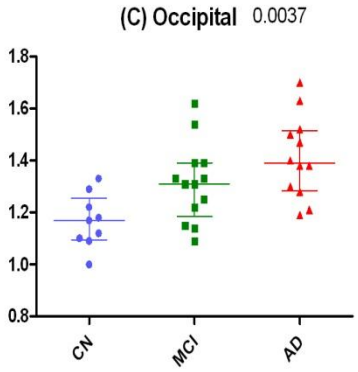
P<0.01, extent voxels = 100, no correction

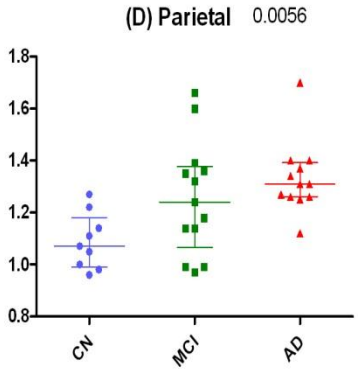


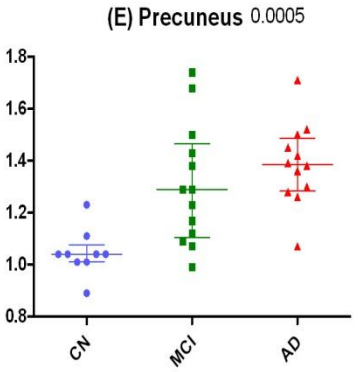


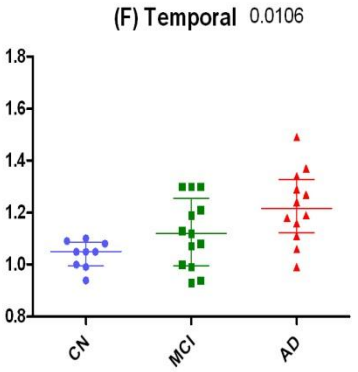

(A) Frontal 0.0029
1.8
1.6
1.4
1.2
1.0
0.8
CN
MCI
AD

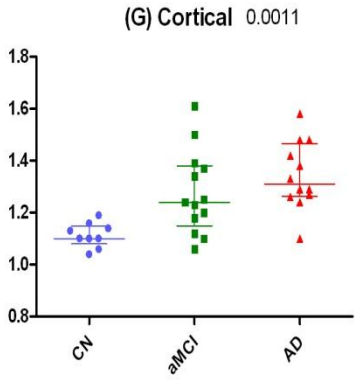

(A) Frontal 0.0029
1.8
1.6
1.4
1.2
1.0
0.8
CN
MCI
AD


(C) Occipital 0.0037
1.8
1.6
1.4
1.2
1.0
0.8
CN
MCI
AD

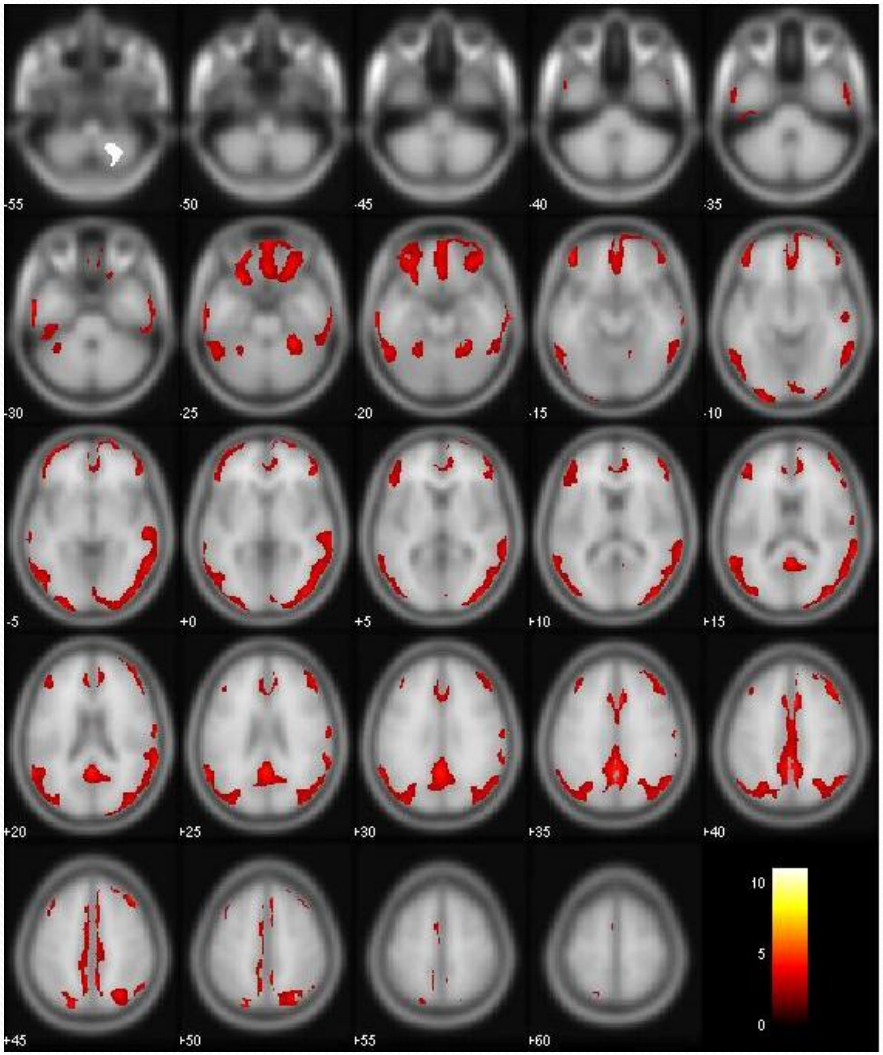

(D) Parietal 0.0056
1.8
1.6
1.4
1.2
1.0
0.8
CN
MCI
AD


(E) Precuneus 0.0005
1.8
1.6
1.4
1.2
1.0
0.8
CN
MCI
AD

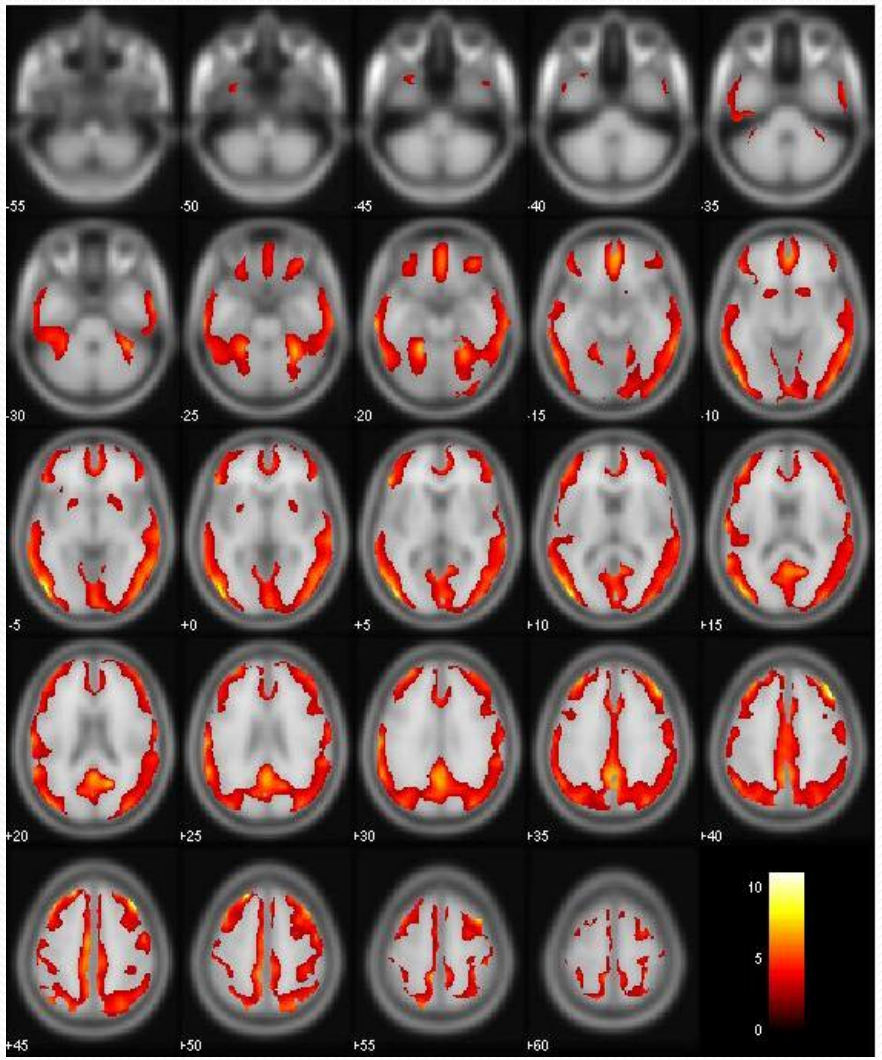

(F) Temporal 0.0106
1.8
1.6
1.4
1.2
1.0
0.8
CN
MCI
AD

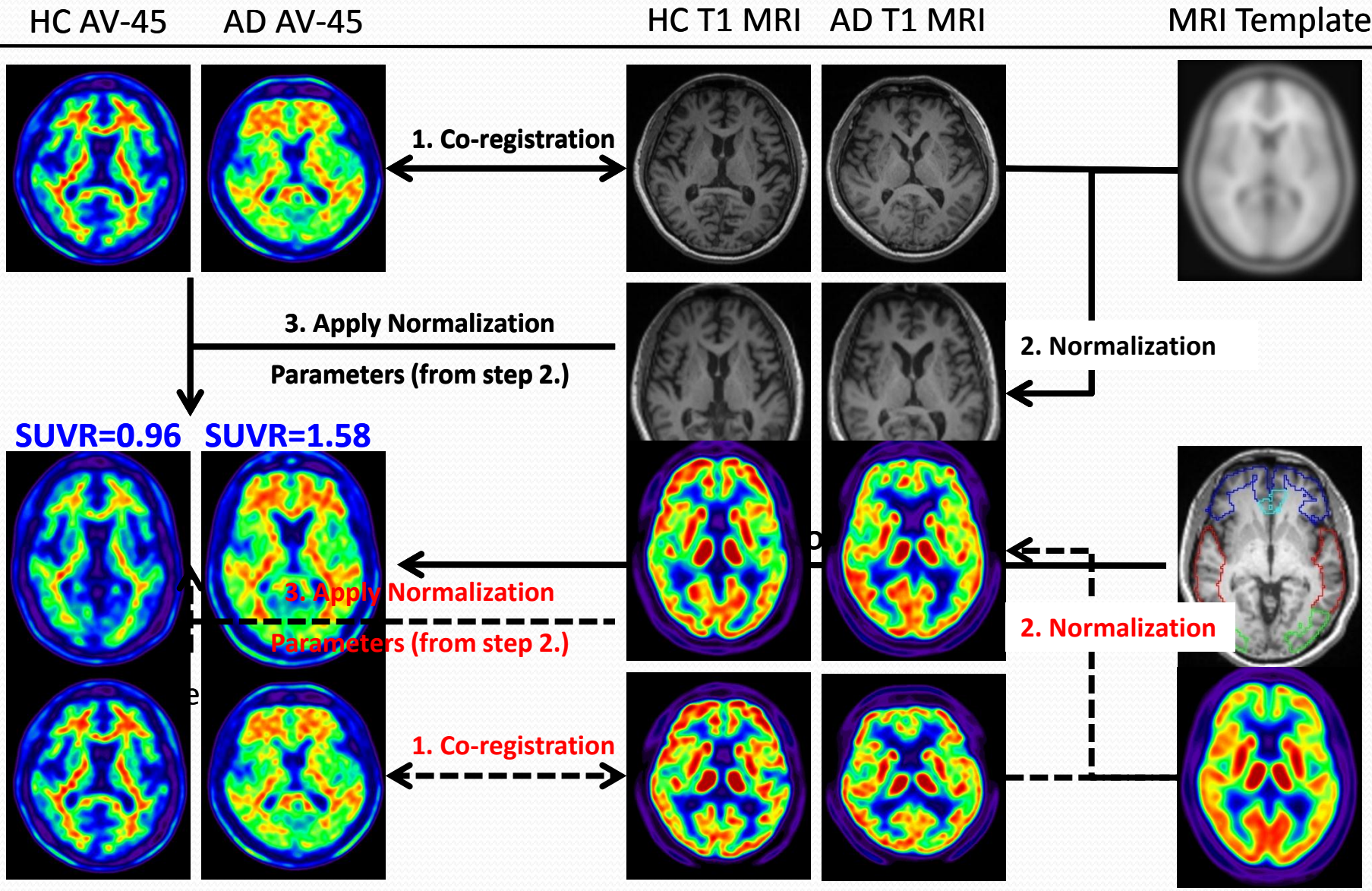

(G) Cortical 0.0011
1.8
1.6
1.4
1.2
1.0
0.8
CN
aMCI
AD

(A) aMCI > CN

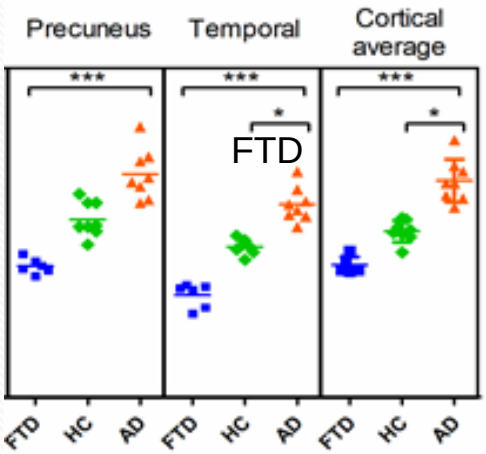


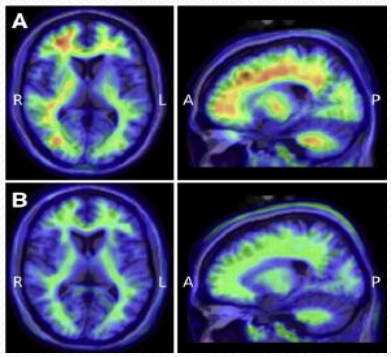
(B) AD > CN

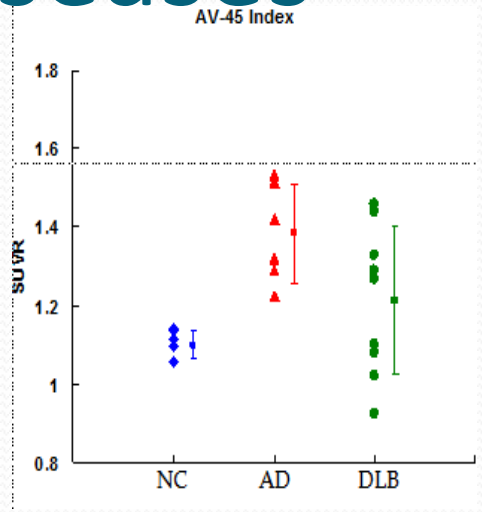



HC AV-45
AD AV-45
HC T1 MRI
AD T1 MRI
MRI Template
1. Co-registration
3. Apply Normalization
Parameters (from step 2.)
2. Normalization
SUVR=0.96
SUVR=1.58
3. Apply Normalization
Parameters (from step 2.)
2. Normalization
1. Co-registration
HC AV-45
AD AV-45
HC pAV-45
AD pAV-45
pAV-45 Template

Differentiate diagnosis for Patients with Co-morbid diseases

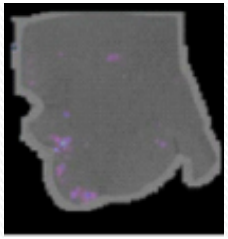


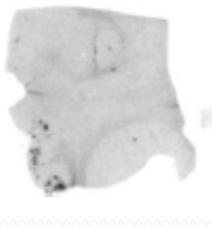




DLB

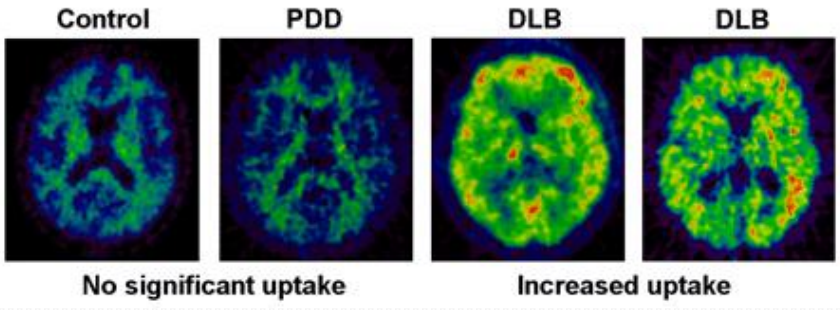
Traumatic brain injury

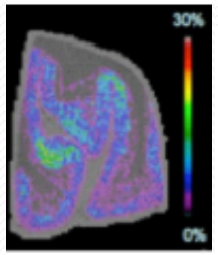




HC, Semin Nucl Med 41:300-304

Amyloid deposition after cerebral hypoperfusion





AD, Semin Nucl Med 41:300-304

Low

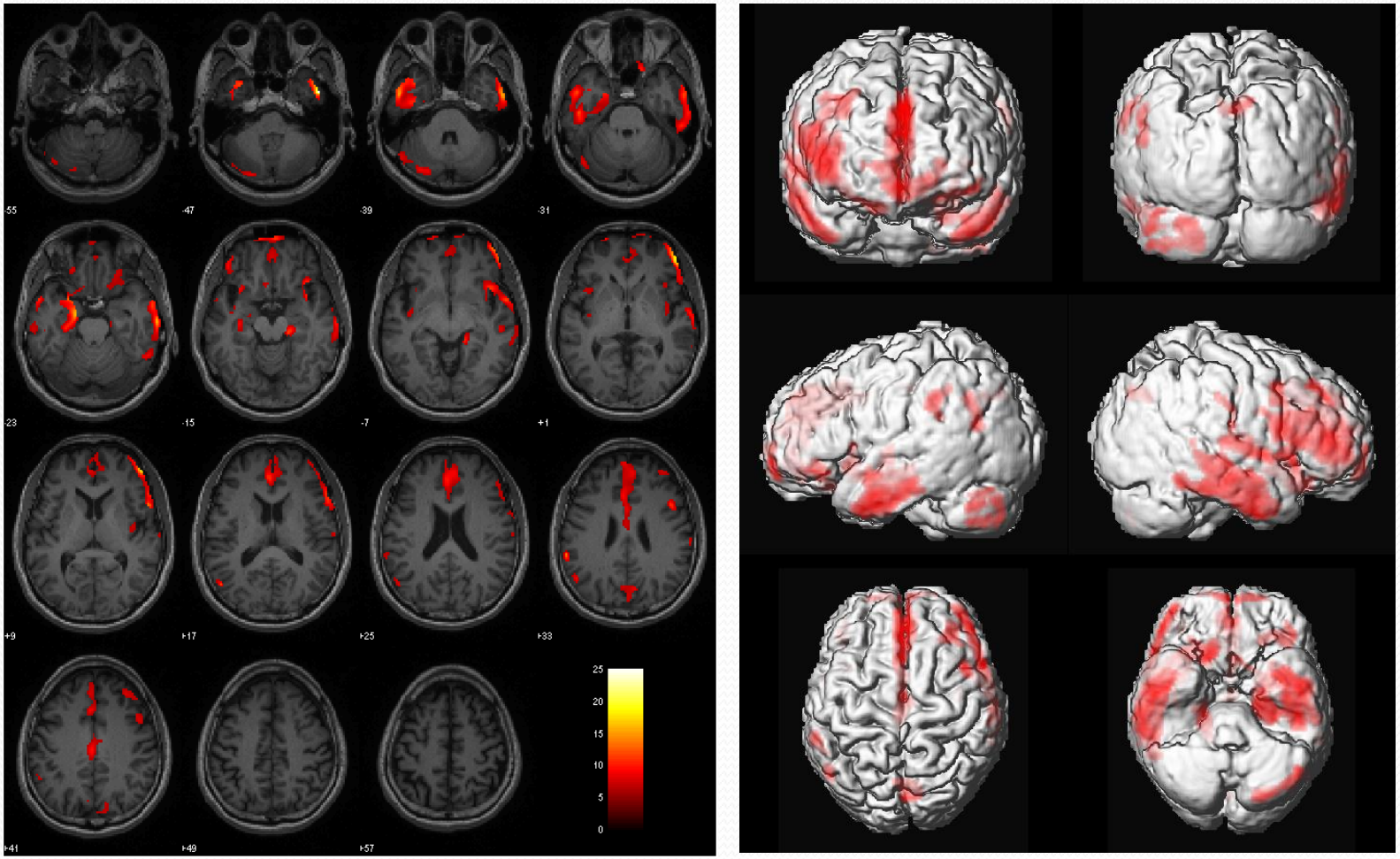
Moderate

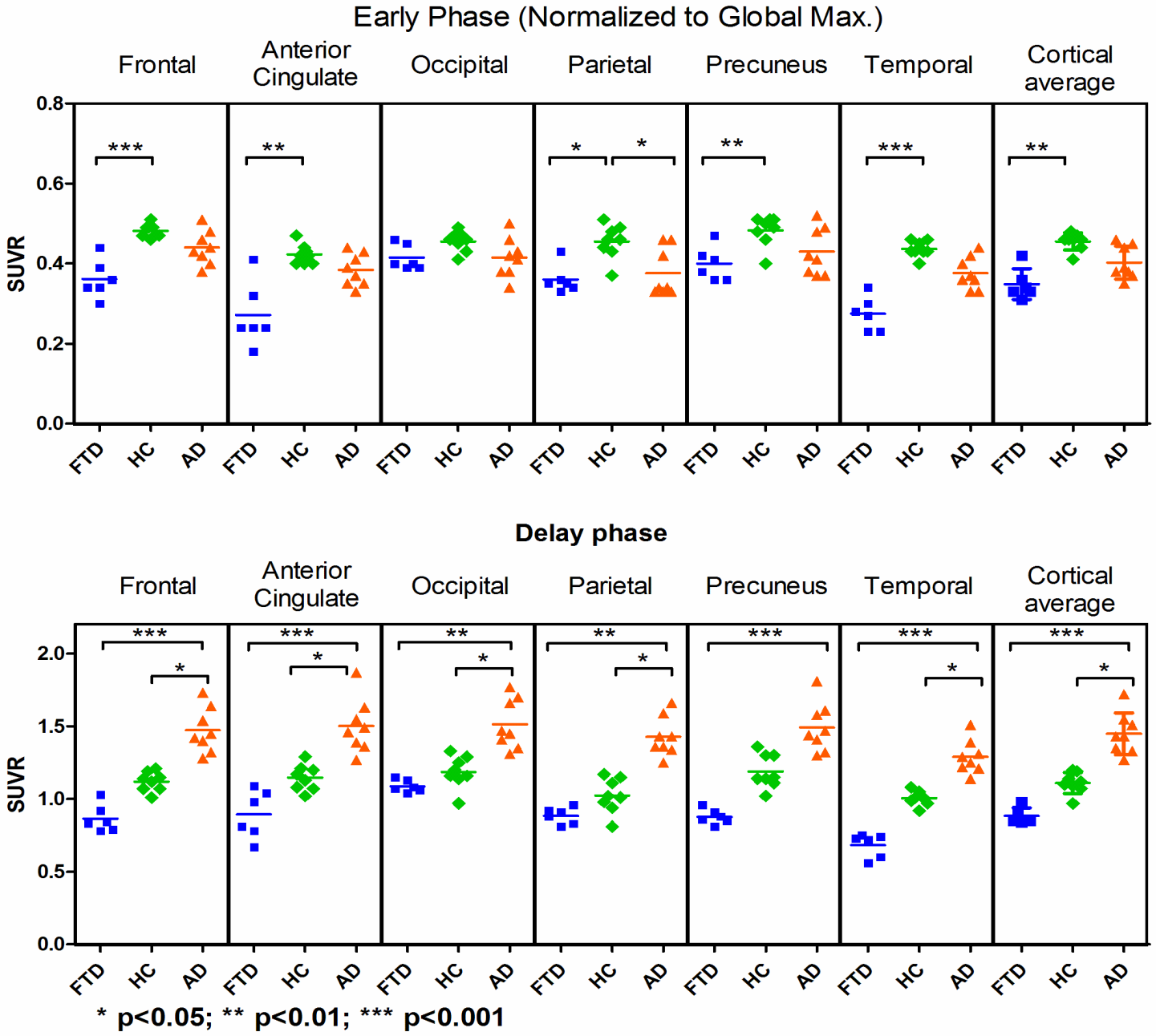
High

Amyvid

Differentiate diagnosis for Patients with Co-morbid diseases (1)

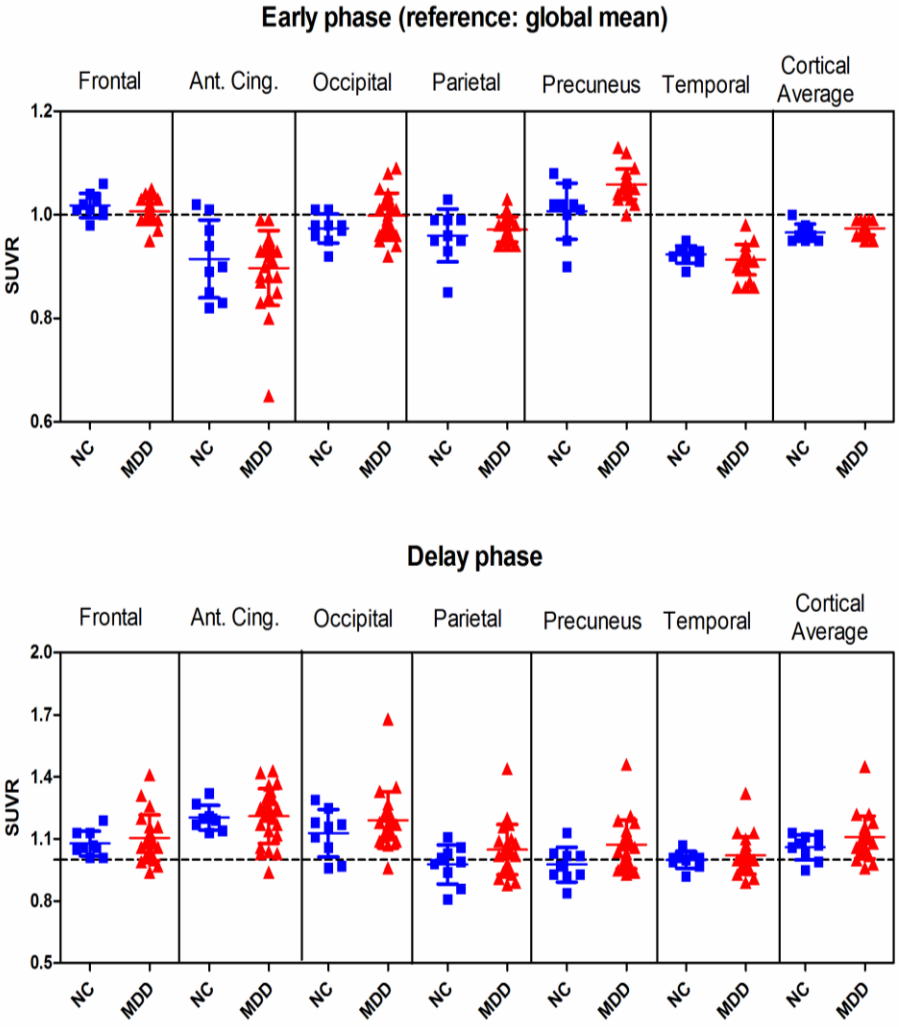
Early phase group comparison –
Frontotemporal Dementia vs. Healthy control

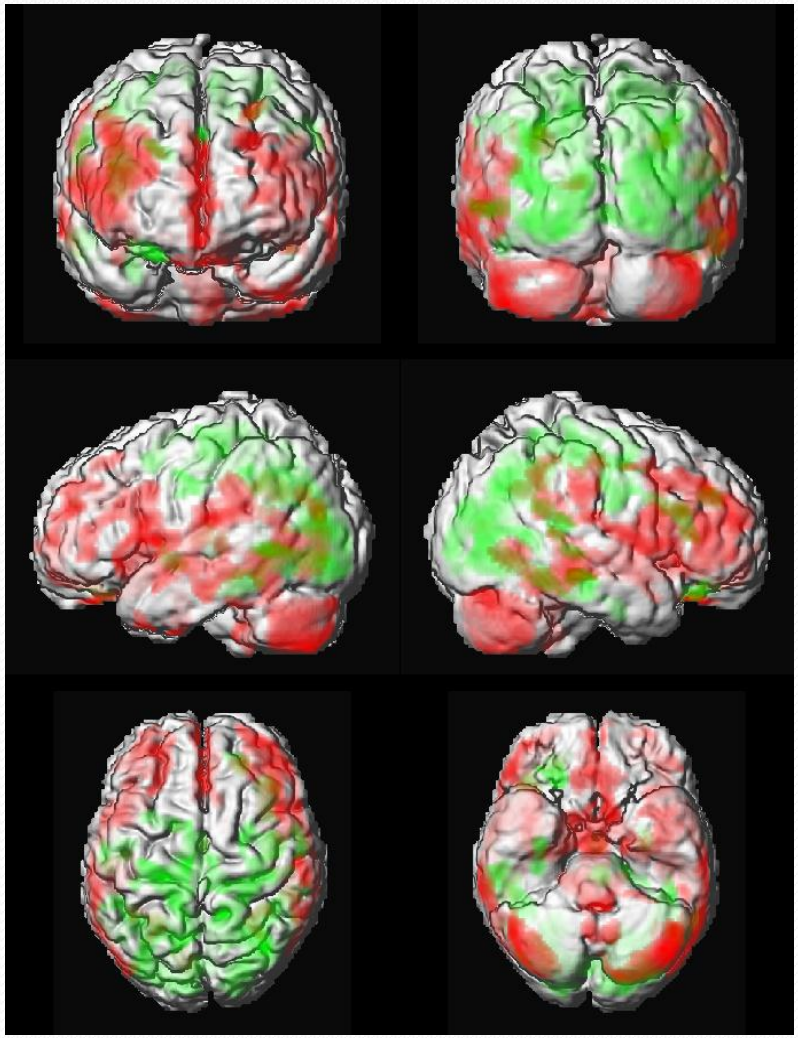



Early Phase (Normalized to Global Max.)
Frontal
Anterior Cingulate
Occipital
Parietal
Precuneus
Temporal
Cortical average
SUVR
0.8
0.6
0.4
0.2
0.0
***
**
*
*
**
***
**
FTD
HC
AD
Delay phase
Frontal
Anterior Cingulate
Occipital
Parietal
Precuneus
Temporal
Cortical average
SUVR
2.0
1.5
1.0
0.5
0.0
***
*
**
*
**
*
***
*
***
*
***
*
FTD
HC
AD
* p<0.05; ** p<0.01; *** p<0.001

Differentiate diagnosis for Patients with Co-morbid diseases (2)

Major Depression Disorder (MDD)





Red – Early phase – MDD < HC

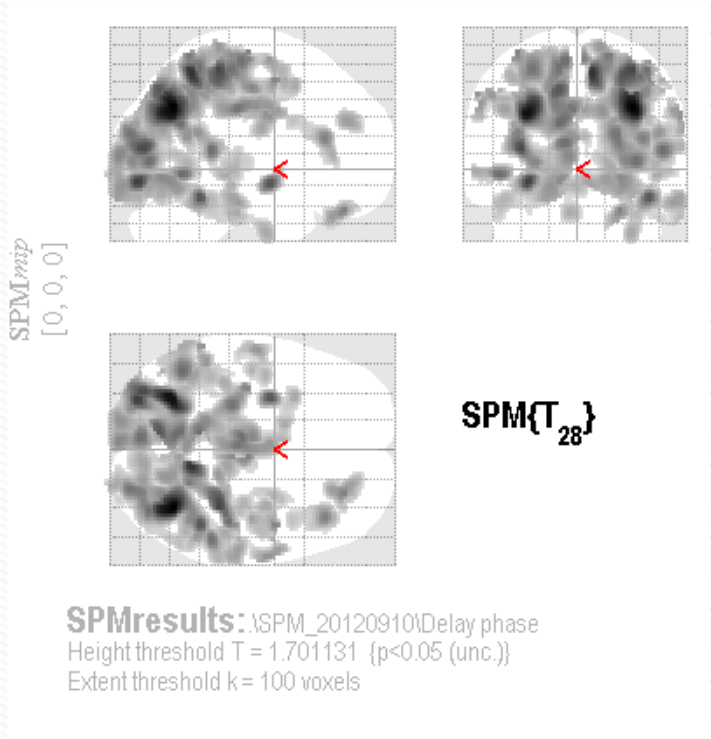
Green – Late phase – MDD > HC

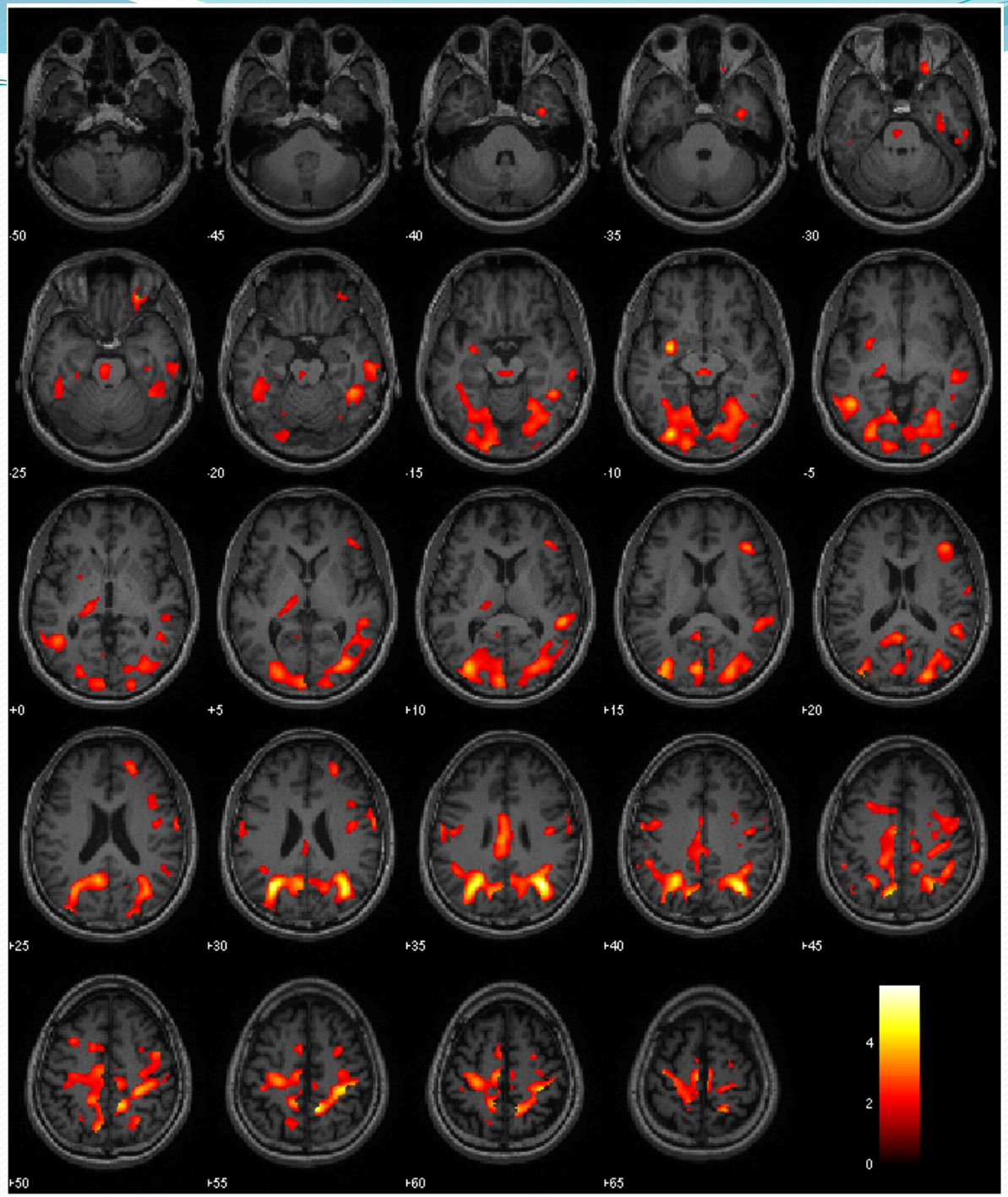
Late Phase

MDD > HC

P<0.05

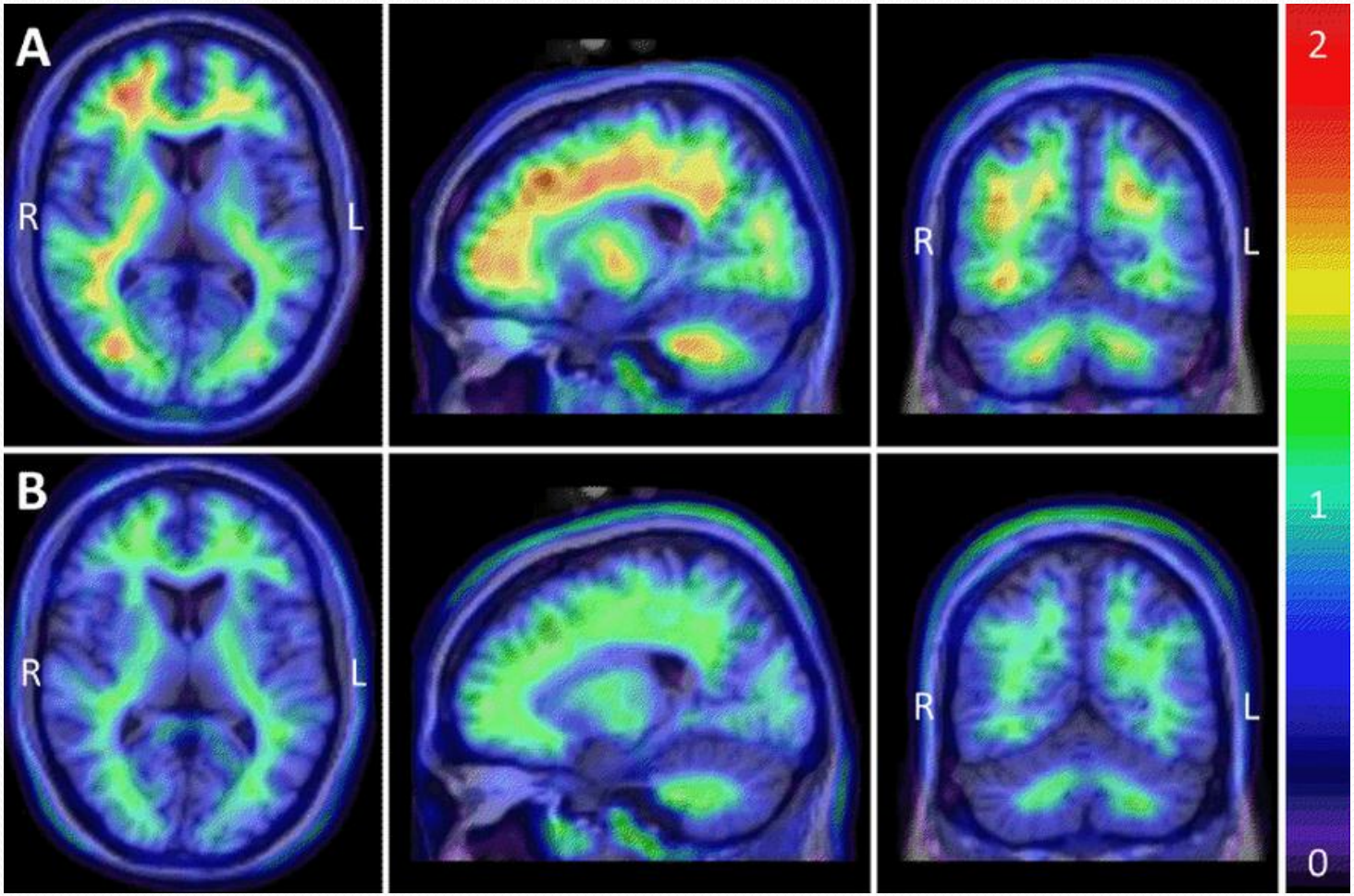
Extent voxel=100



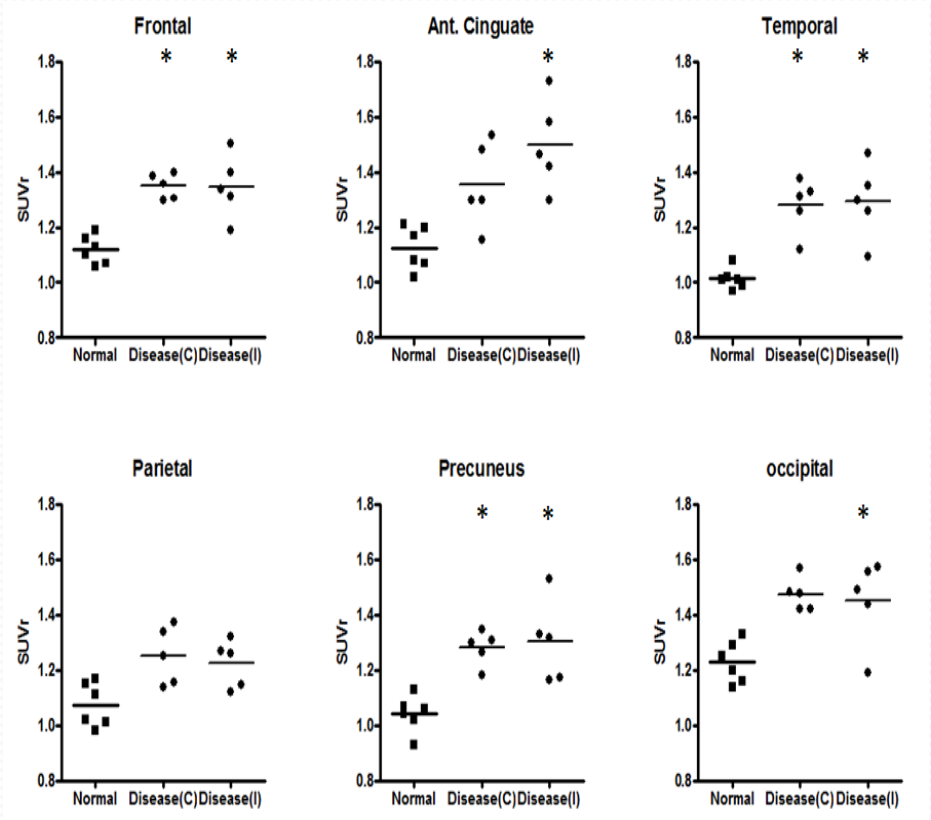


Differentiate diagnosis for Patients with Co-morbid diseases (3)

Amyloid deposition after cerebral hypoperfusion



Kuo-Lun Huang



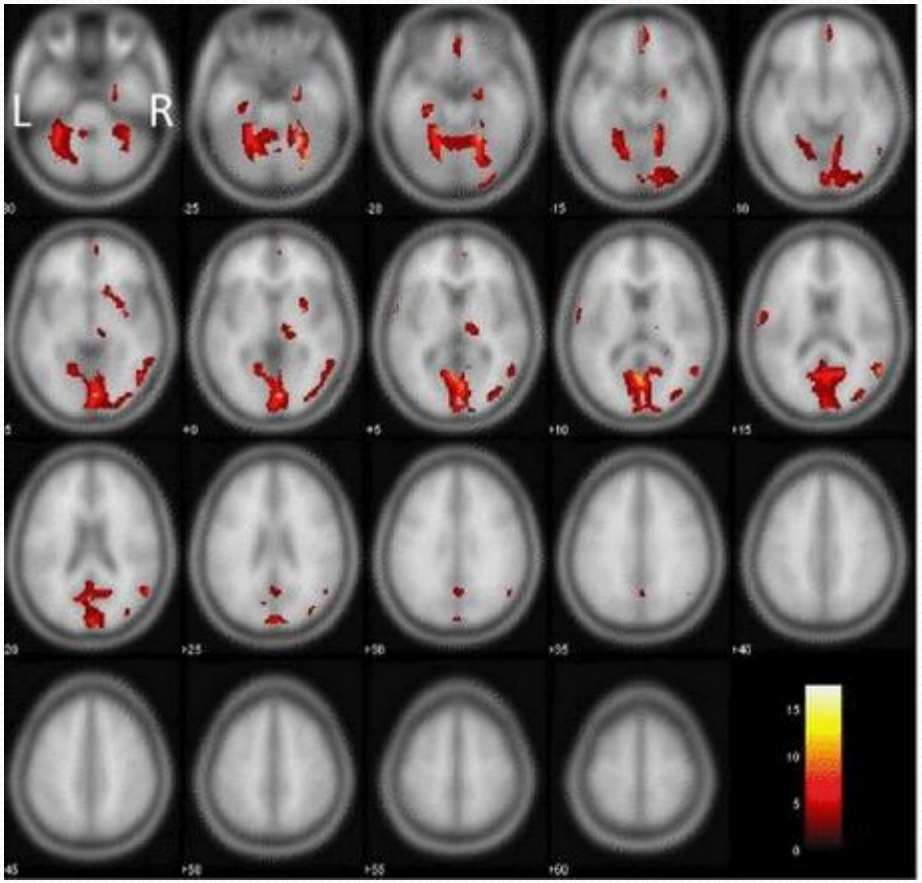


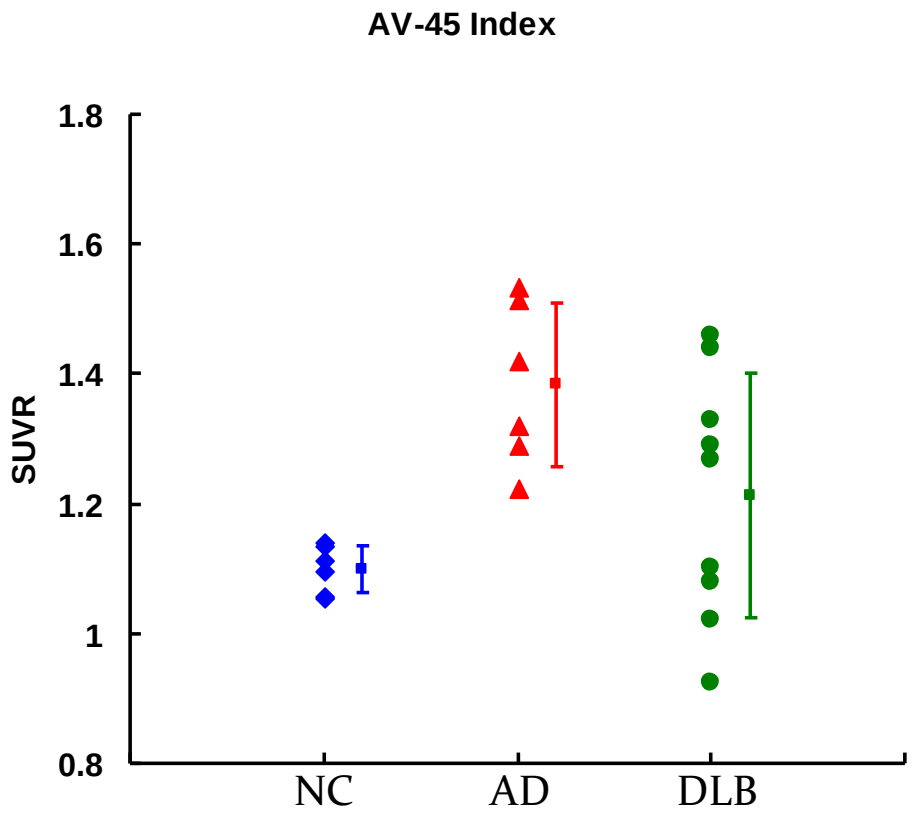
Fig. 3. [^{18}F]AV-45 SUVR in the contralateral (C) and ipsilateral (I) brain cortex of demented patients with carotid artery stenosis and the elderly controls. (* $p < 0.05$).

Differentiate diagnosis for Patients with Co-morbid diseases (4)

Dementia with Lewy bodies (DLB)

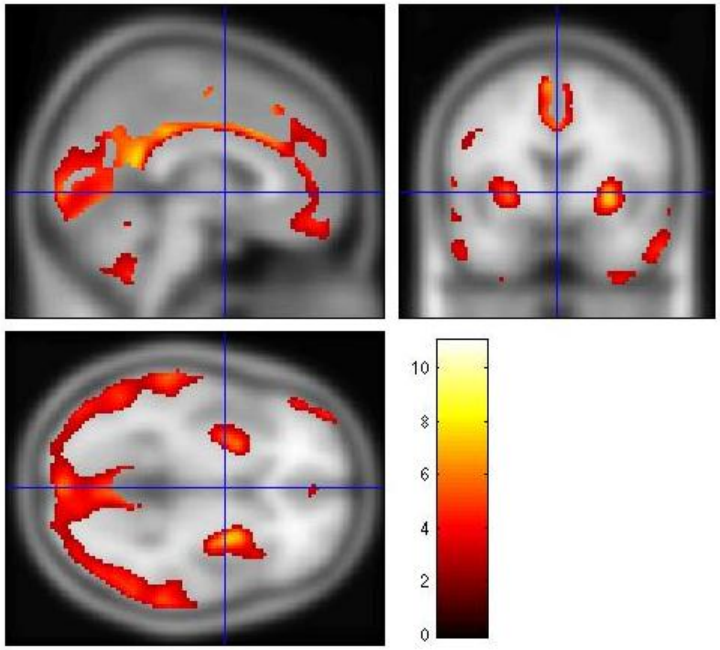
	DLB	NC	AD
Sup. Frontal	1.28±0.23*	1.04±0.07	1.38±0.24
Sup. Orb. Frontal	1.26±0.24	1.26±0.11	1.53±0.21
Med. Orb. Frontal	1.19±0.33^{+}	1.09±0.03	1.48±0.19
Frontal	1.21±0.21*	1.12±0.05	1.41±0.18
Ant. Cingulate	1.12±0.37**	1.12±0.08	1.43±0.15
Post. Cingulate	1.33±0.27*	1.35±0.10	1.52±0.13
Occipital	1.32±0.21*	1.23±0.08	1.46±0.19
Parietal	1.17±0.15	1.07±0.08	1.34±0.08
Precuneus	1.28±0.17	1.04±0.07	1.42±0.11
Temporal	1.14±0.19^{+}	1.01±0.04	1.23±0.13
Striatum	1.45±0.26*	1.25±0.09	1.53±0.16
Index	1.21±0.19^{+}	1.10±0.04	1.38±0.13

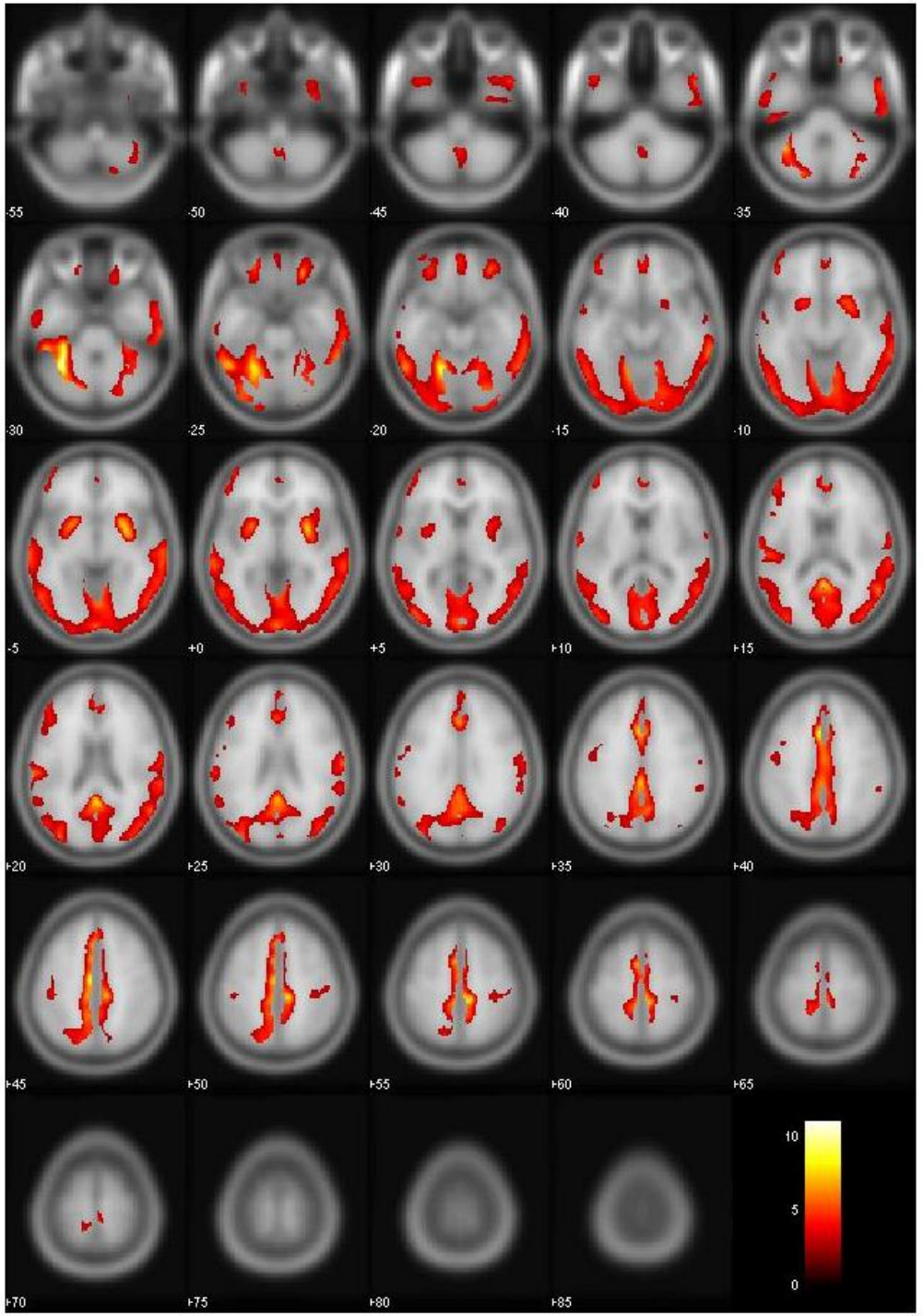
* Significant different from DLB to NC (* p<0.05, ** p<0.01, + p<0.005)



NC < DLB

P<0.05, extent voxels = 100
with FDR correction





Future work

- We have struggled for grant support and IRB approval.
- We already finished preparatory phase, establishing methodology and normative data for all tests.
- We will start recruiting patients and healthy controls form 2014.
- We will include centers from southern Taiwan.