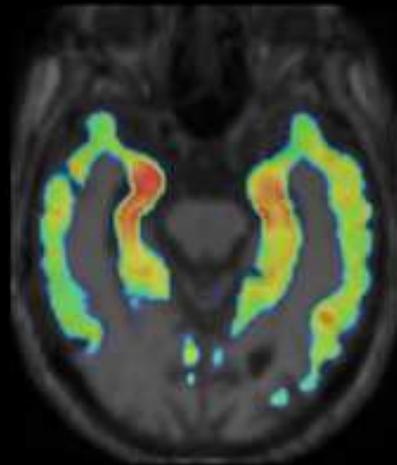
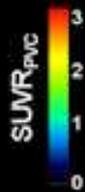


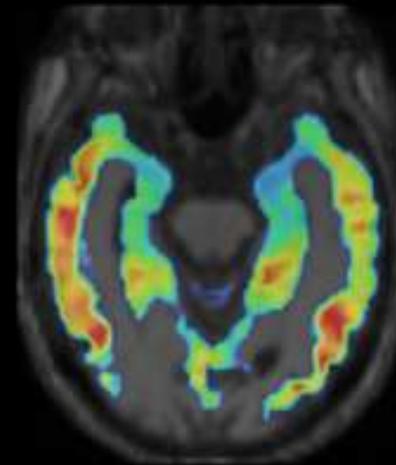
# Nuclear Neurology

Tau and amyloid imaging in Alzheimer's disease

SUVR<sub>PVC</sub>



$^{18}\text{F}$ -THK5117



$^{11}\text{C}$ -PiB

SNM 2014 Image of the Year



彭南靖

民國105年10月17日



# Aducanumab trial

OUTLOOK  
Stem-cell  
activation?

# nature

THE INTERNATIONAL WEEKLY JOURNAL OF SCIENCE



## TARGETING AMYLOID

Antibody aducanumab reduces Alzheimer's disease-associated amyloid in human brain PAGES 36 & 50

**COMPUTING**  
DNA MEMORIES  
Genomic technology tackles big data  
PAGE 22

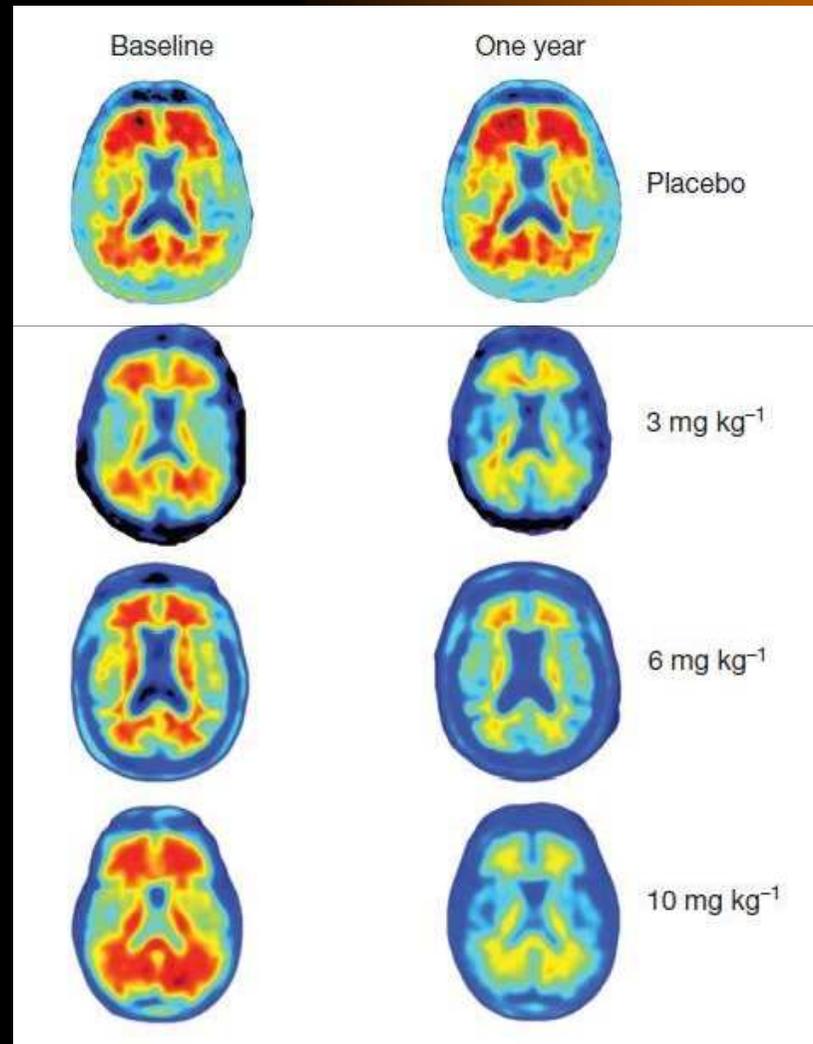
**RESEARCH MISCONDUCT**  
CHEATING HAPPENS  
Don't ignore the fraud factor in irreproducibility  
PAGE 29

**ATOMIC THEORY**  
SPHERES OF INFLUENCE  
How John Dalton's wooden models defined the atom  
PAGE 32

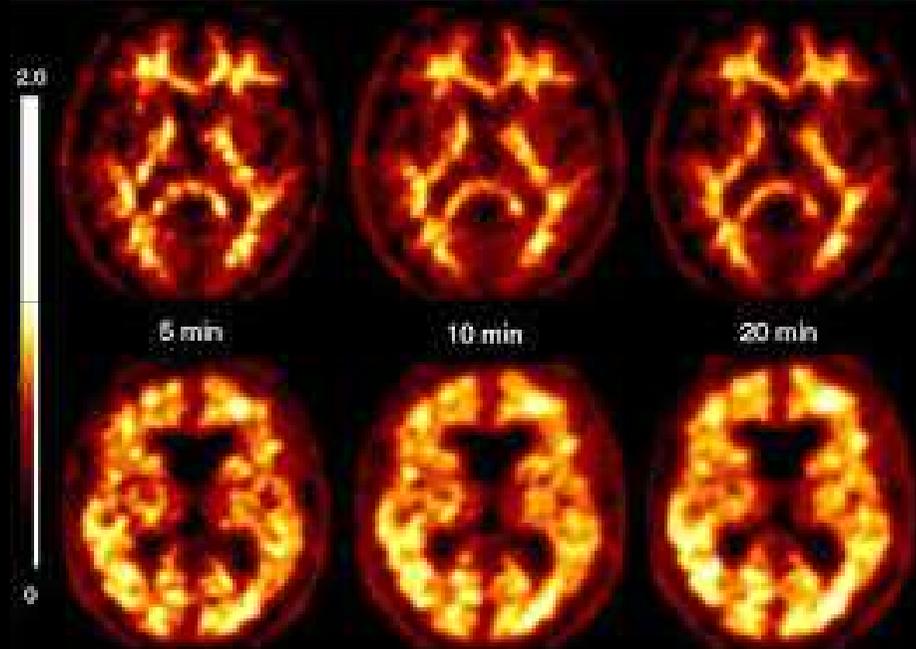
NATURE.COM/NATURE  
1 September 2016 A10  
Vol. 537, No. 7618



9 770028 083093



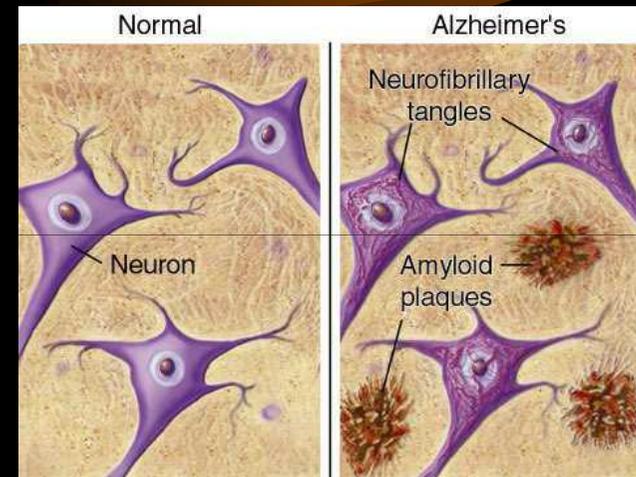
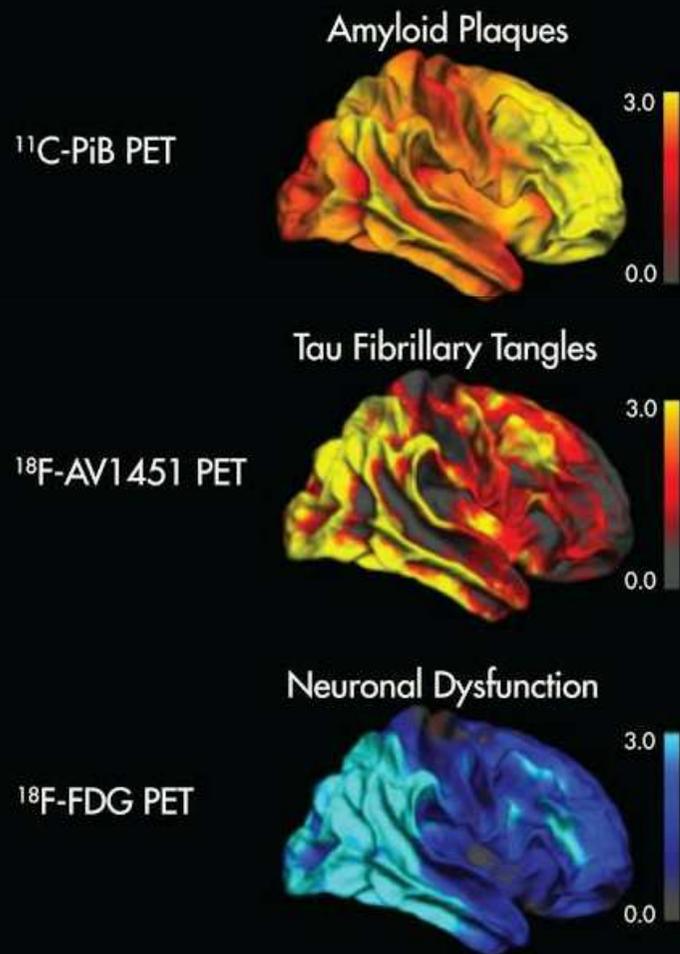
# Florbetaben (NeuraCeq)



Clin Transl Imaging (2015) 3:13–26

2014/3 FDA approved. The other 2 PET drugs approved by FDA: **florbetapir** (Amyvid, Eli Lilly and Company) and **flutemetamol** (Vizamyl, GE Healthcare) in FDA in 2012 and 2013, respectively.

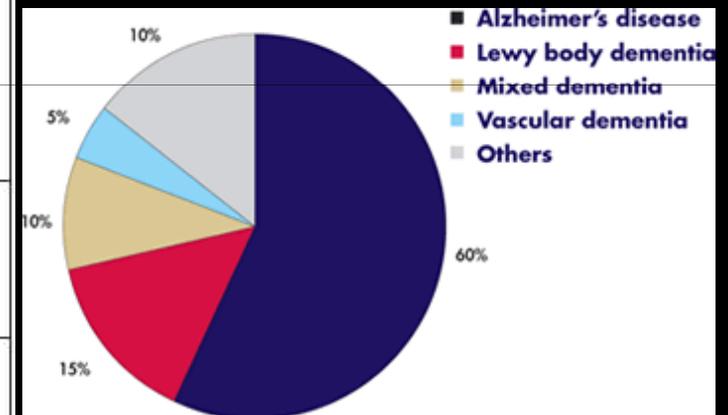
# SNM 2016 Image of the Year



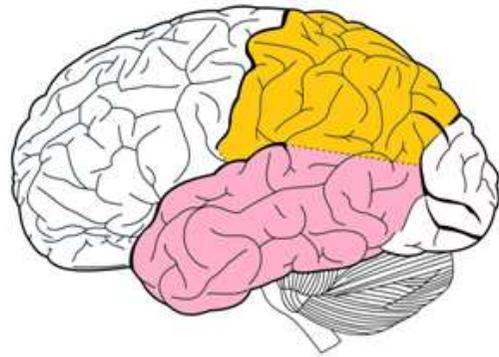
Topographical  
Correspondence of Tau --  
but not Amyloid-  
Pathology with Neuronal  
Dysfunction in AD

# Types of Dementia

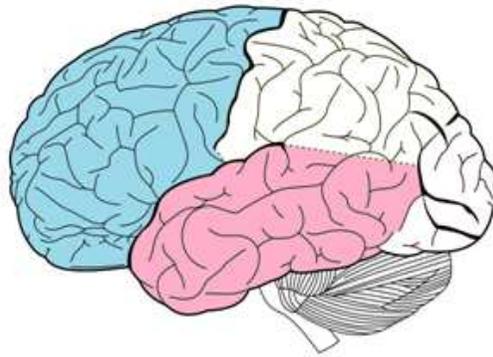
Types of Dementia			
Type of Dementia	History	Signs and Symptoms	Pathology/Imaging
Alzheimer's Disease (50–80% of all dementia cases)	Gradual, progressive onset	<ul style="list-style-type: none"> <li>• Memory loss, especially for names and recent events</li> <li>• Language deficits</li> <li>• Rapid forgetting</li> <li>• Impaired visuospatial skills</li> <li>• Normal gait and neuro exam early</li> <li>• Later affective disturbances; behavioral symptoms such as aggression</li> </ul>	<ul style="list-style-type: none"> <li>• Generalized atrophy (esp. medial temporal)</li> <li>• Beta amyloid plaques</li> <li>• Neurofibrillary tangles</li> </ul>
Vascular (20–30%)	Abrupt or gradual onset	<ul style="list-style-type: none"> <li>• Focal neurological signs</li> <li>• Signs of vascular disease</li> </ul>	<ul style="list-style-type: none"> <li>• Strokes</li> <li>• Lacunar infarcts</li> <li>• White matter lesions</li> <li>• Vulnerable to cerebrovascular events</li> </ul>
Lewy Body (10–25%)	Insidious onset, progressive with fluctuations	<ul style="list-style-type: none"> <li>• Fluctuating cognition</li> <li>• Visual hallucinations</li> <li>• Neuroleptic sensitivity</li> <li>• Shuffling gait</li> <li>• Increased tone</li> <li>• Tremors</li> <li>• Falls</li> </ul>	<ul style="list-style-type: none"> <li>• Generalized atrophy</li> <li>• Lewy bodies in cortex and midbrain</li> </ul>
Frontotemporal (10–15%)	Insidious onset, typically in 50s–60s; rapid progression	<ul style="list-style-type: none"> <li>• Disinhibition</li> <li>• Socially inappropriate behavior</li> <li>• Poor judgment</li> <li>• Apathy, decreased motivation</li> <li>• Poor executive function</li> </ul>	<ul style="list-style-type: none"> <li>• Frontal and temporal atrophy</li> <li>• Pick cells and pick bodies in cortex</li> </ul>



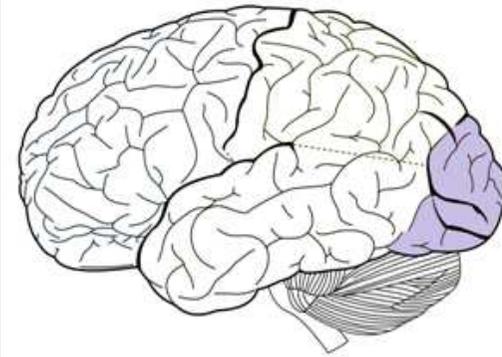
# FDG-PET in 3 Major Dementias



阿茲海默症

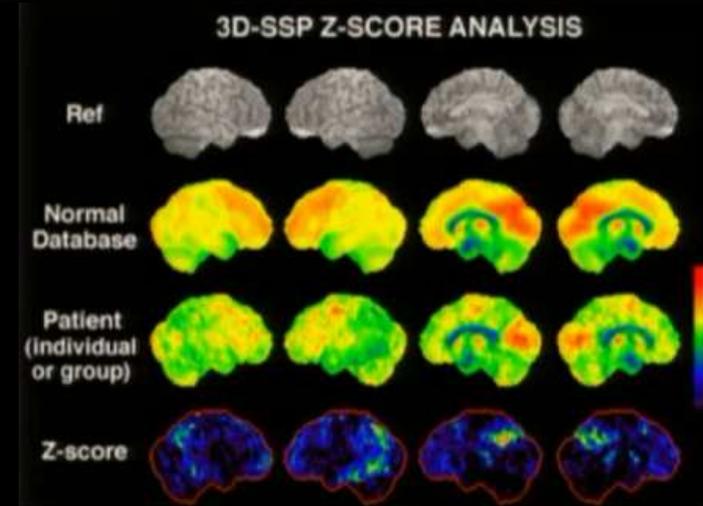
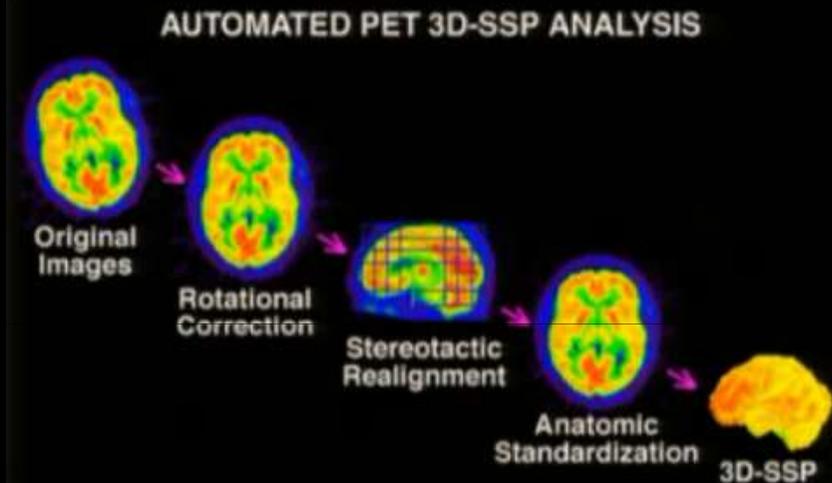
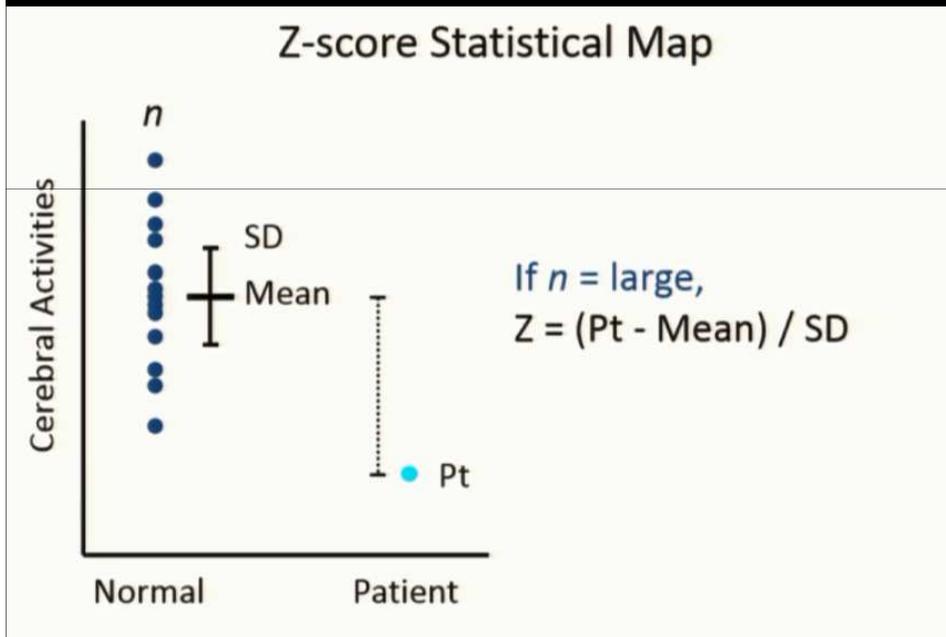


額顳葉型失智症



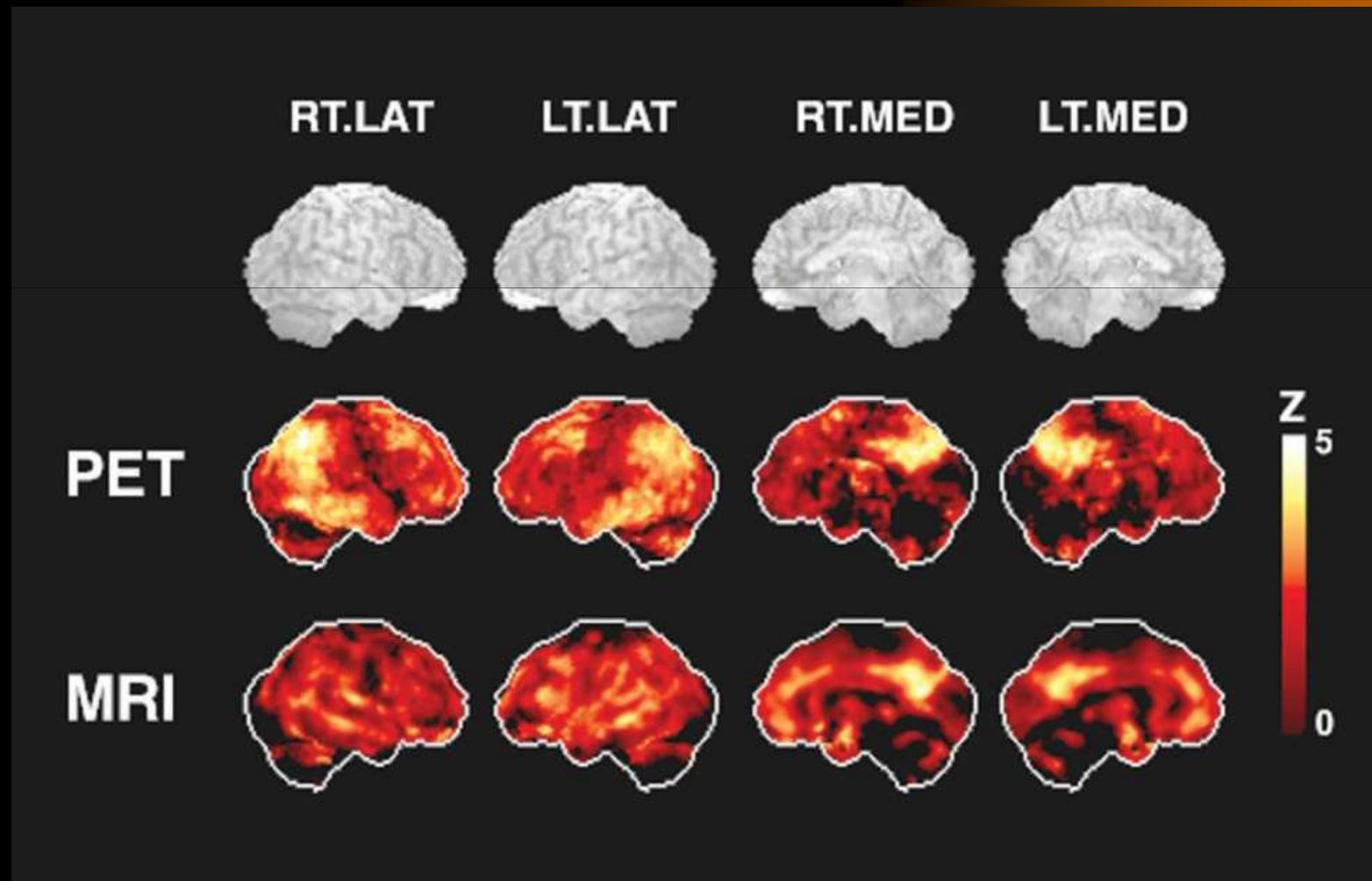
路易氏體型失智症

# eZIS (easy Z-score imaging system)

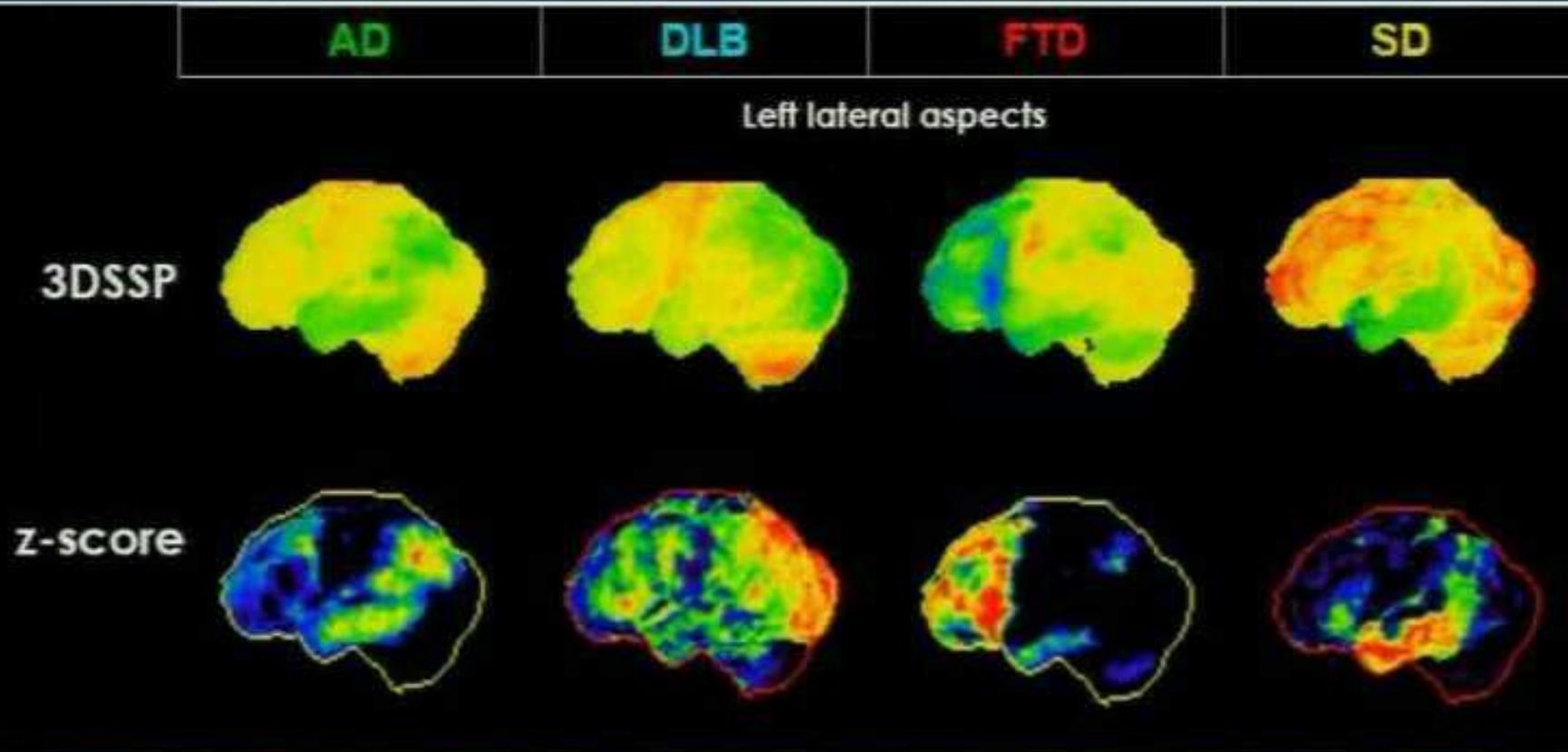


J Nucl Med 1995; 36:1238-1248

# SNM 2004 Image of the Year



## FDG-PET: Differential diagnosis of neurodegeneration

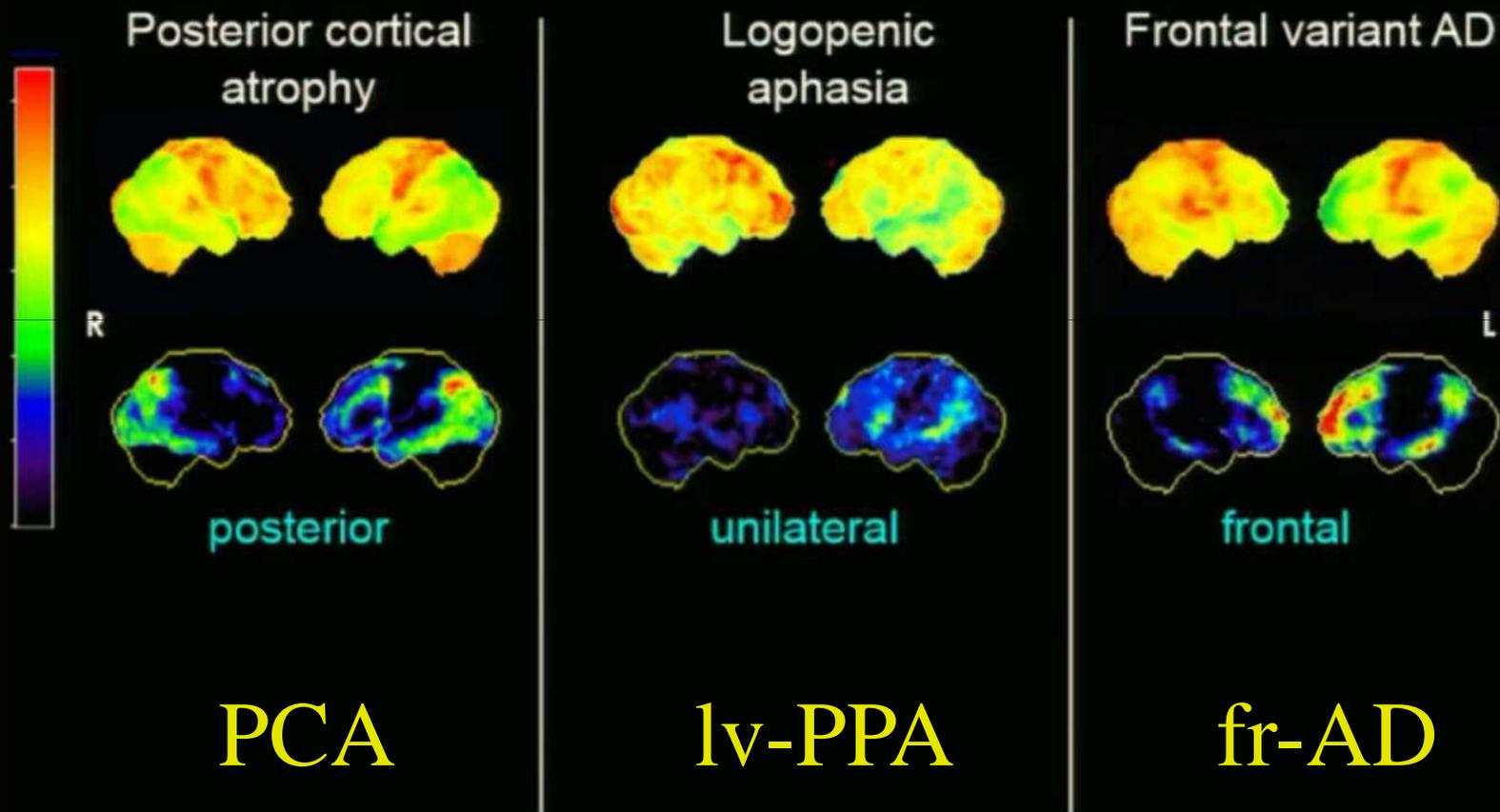


- Specific disease patterns in the individual subjects, reflect symptomatic deficits and correlate with the degree of cognitive decline
- But: some overlap, sometimes equivocal patterns

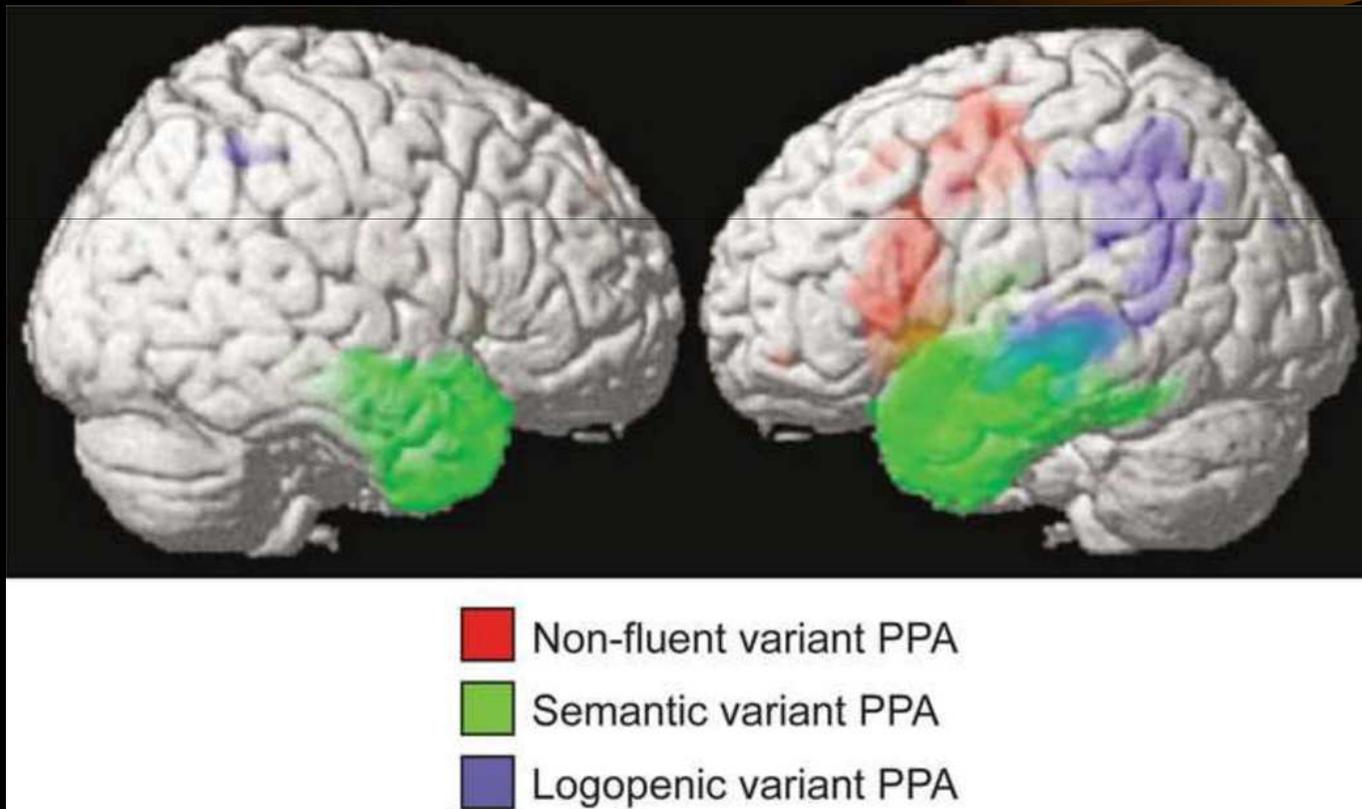


## Atypical variants of Alzheimer's disease

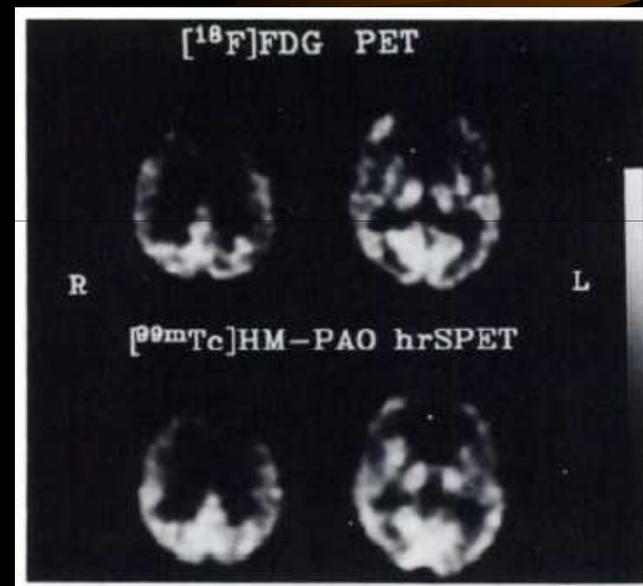
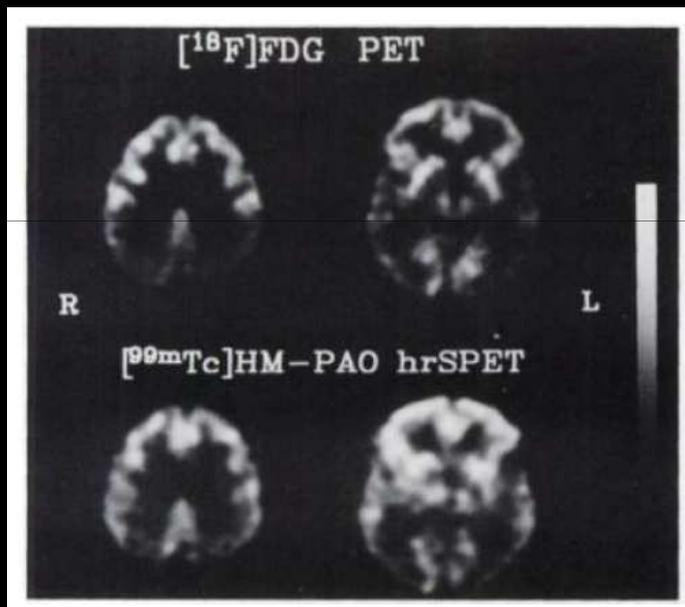
### Glucose metabolism [18F]FDG PET



# PPA (primary progressive aphasia)



# PET vs. SPECT

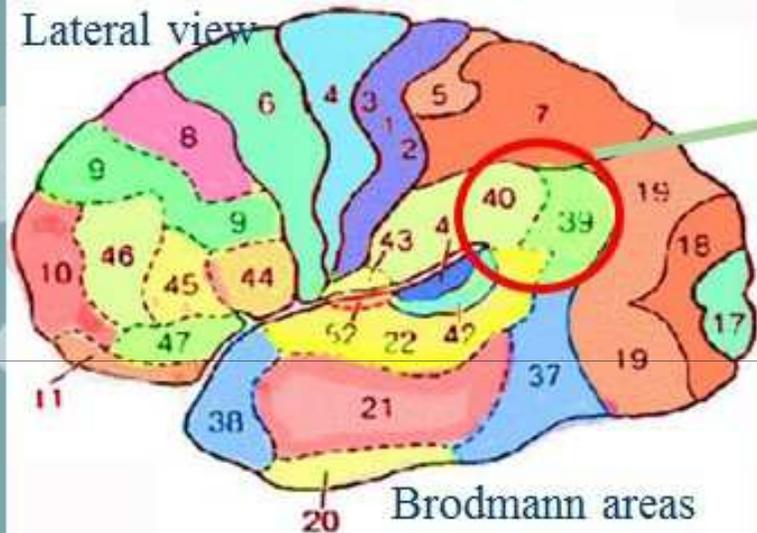


PET and SPECT had **similar abilities** for delineating reductions in perfusion and metabolism in the temporoparietal cortex (left) and frontal cortex (right).

J Nucl Med 1994;35:210-216.

# Three major neuroimaging findings in early Alzheimer's disease

Lateral view

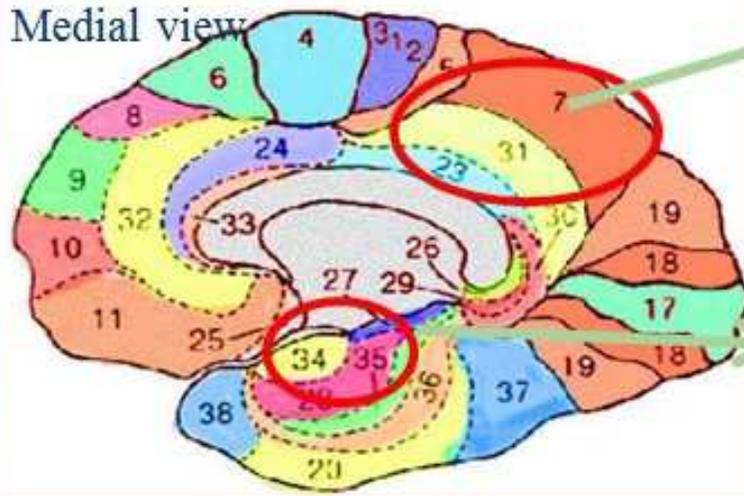


Parietal cortex (supramarginal and angular gyri)

SPECT  
FDG-PET

Apraxia, agnosia, acalcuria,  
aphasia, disorientation

Medial view



Posterior cingulate gyrus ~ precuneus

Disturbance in episodic memory

Medial temporal areas  
(hippocampus, entorhinal cortex)

MRI

# Circuit for Cognition and Memory

---

## ■ Circuit for Cognition and Execution

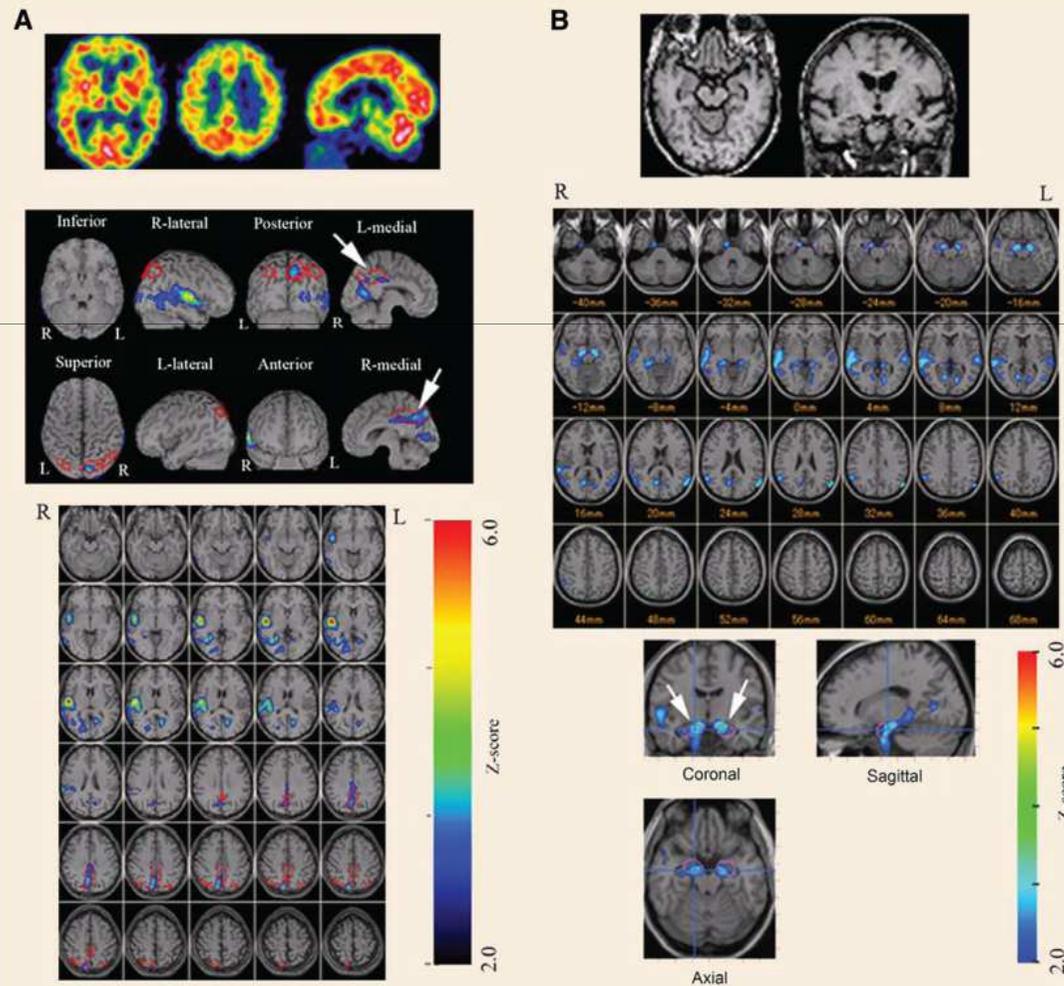
- ◆ Frontal – Striatum – Pallidum – Thalamus

## ■ Circuit for Memory

- ◆ Hippocampus – Mammillary body – ant Thalamus – Cingulate (Papez)
- ◆ Amygdala – dm Thalamus – Prefrontal – ant Temporal (Yakovlev)

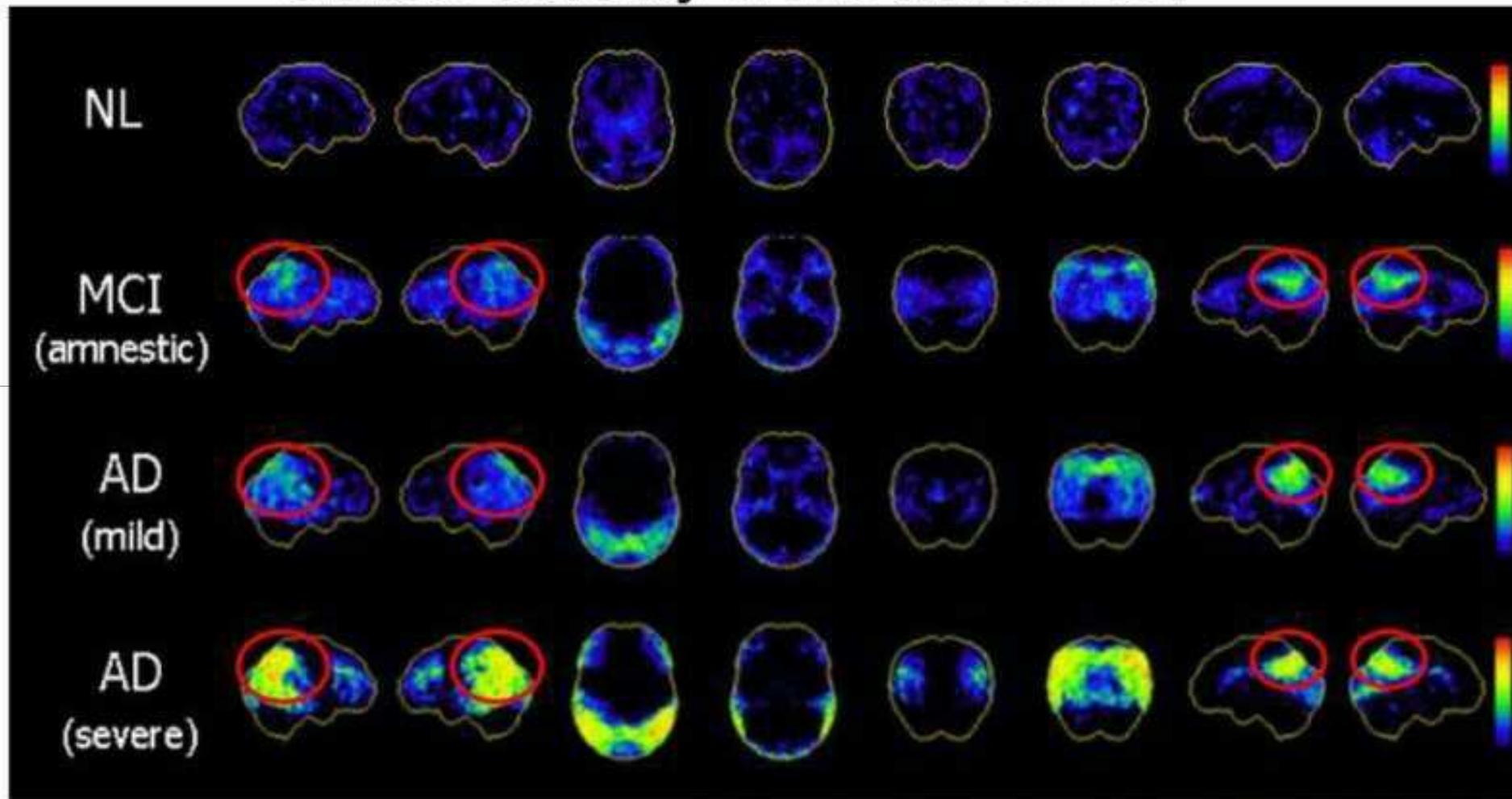


# Very early AD: PET vs. MRI



J Nucl Med 2007;  
48:1289-1300

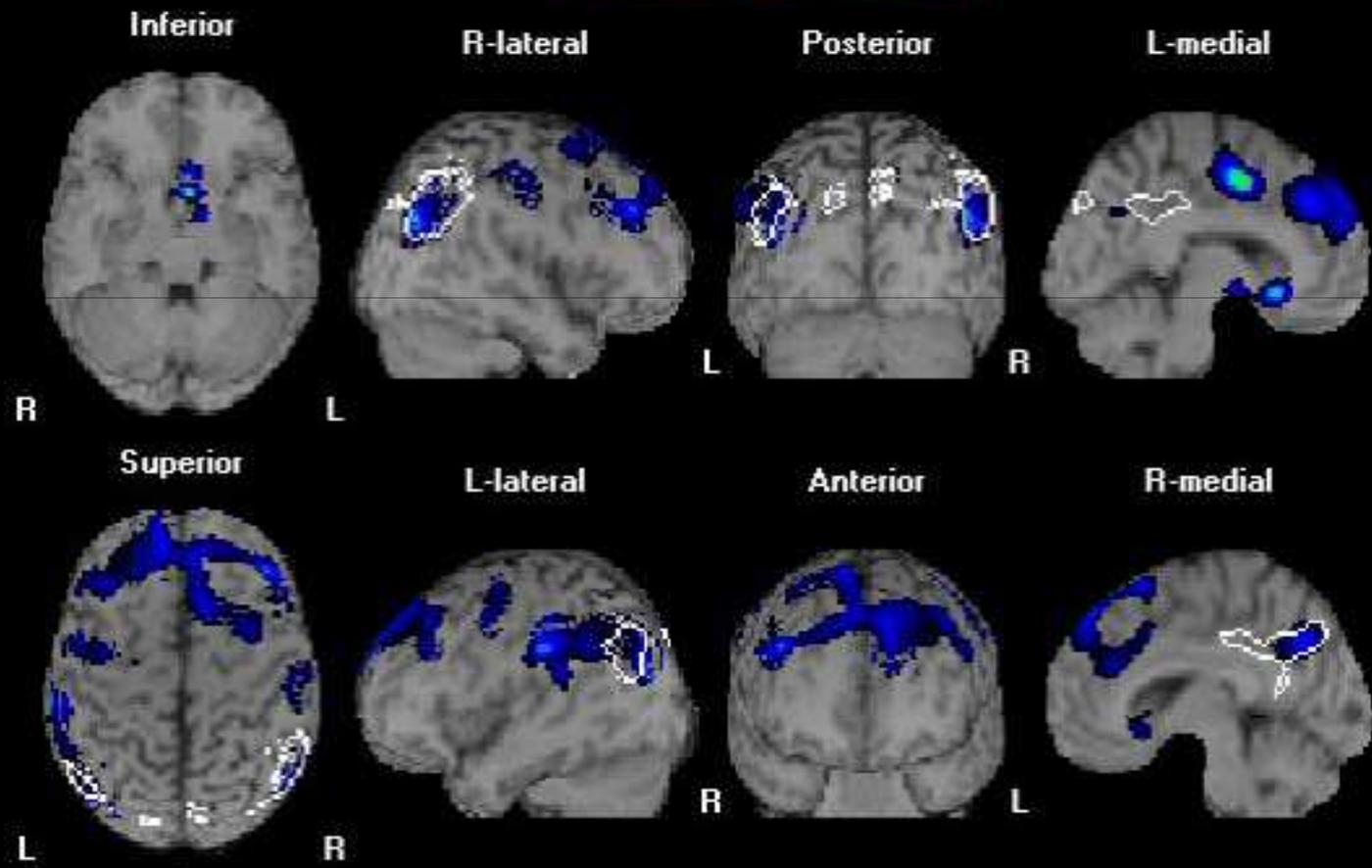
## Clinical Severity of AD and SPECT



*L. Mosconi et al. / Experimental Gerontology 42 (2007) 129–138*

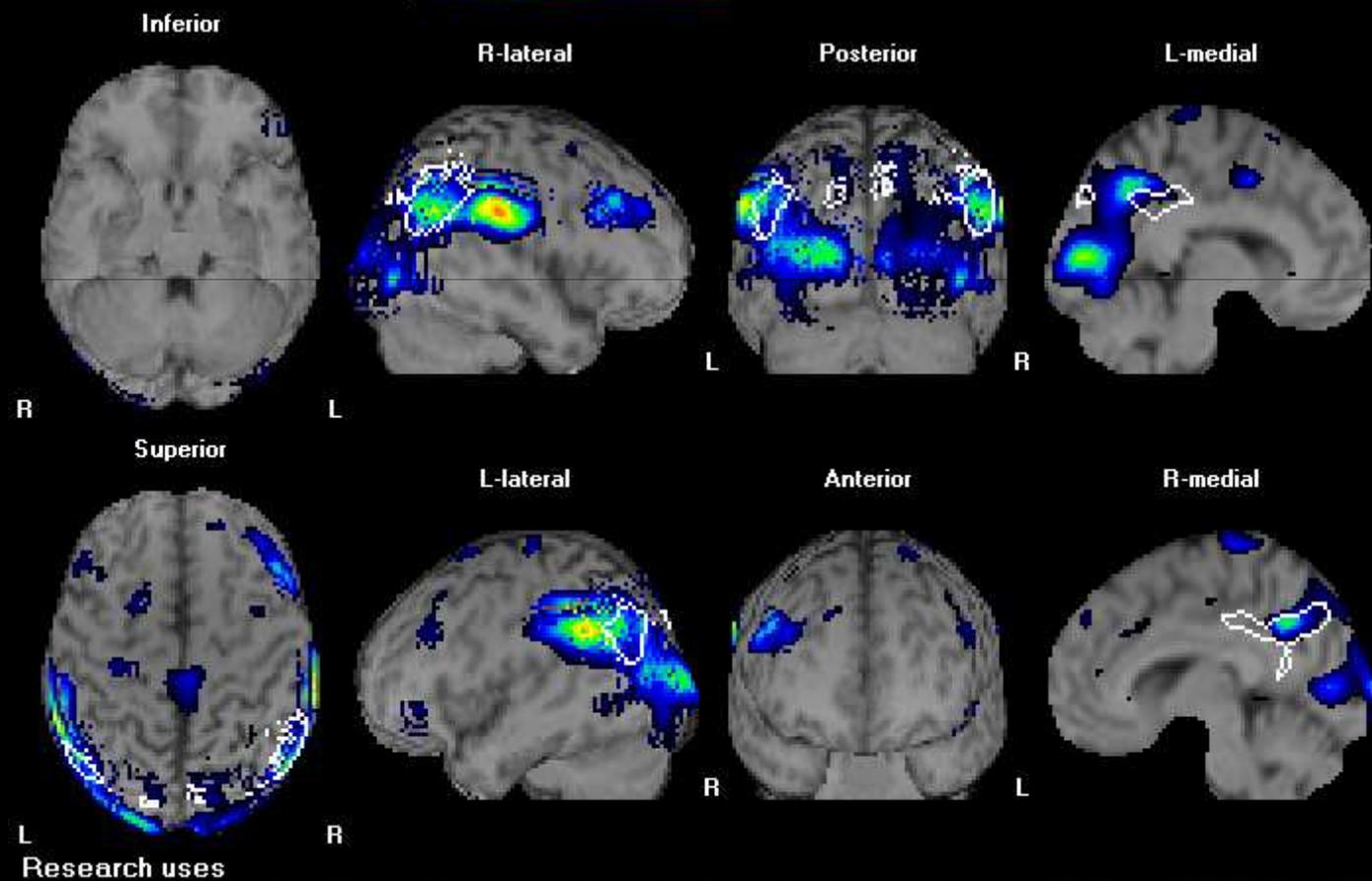
# Early AD

Zoom: x1.5  Label 2.0  6

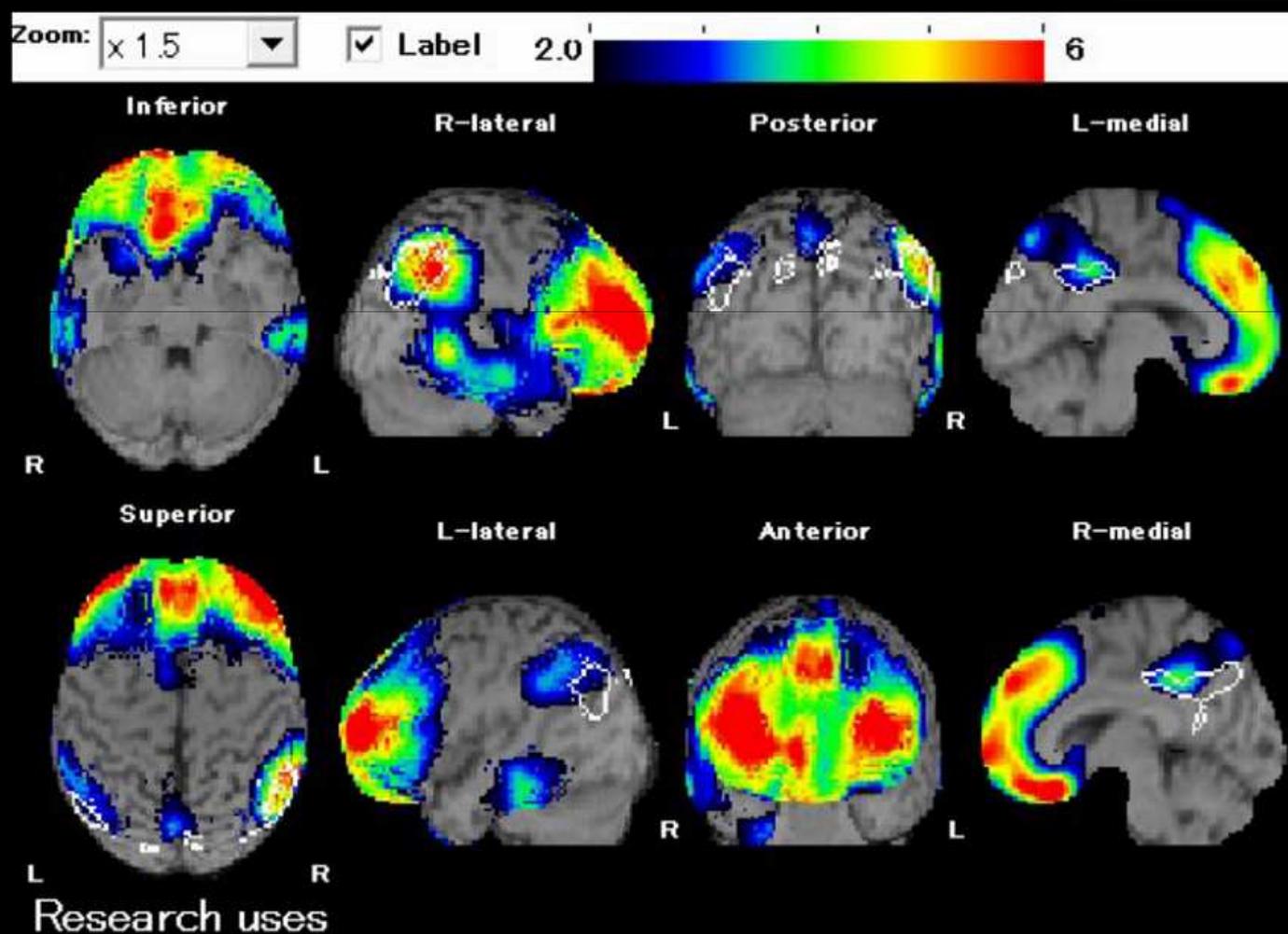


Research uses

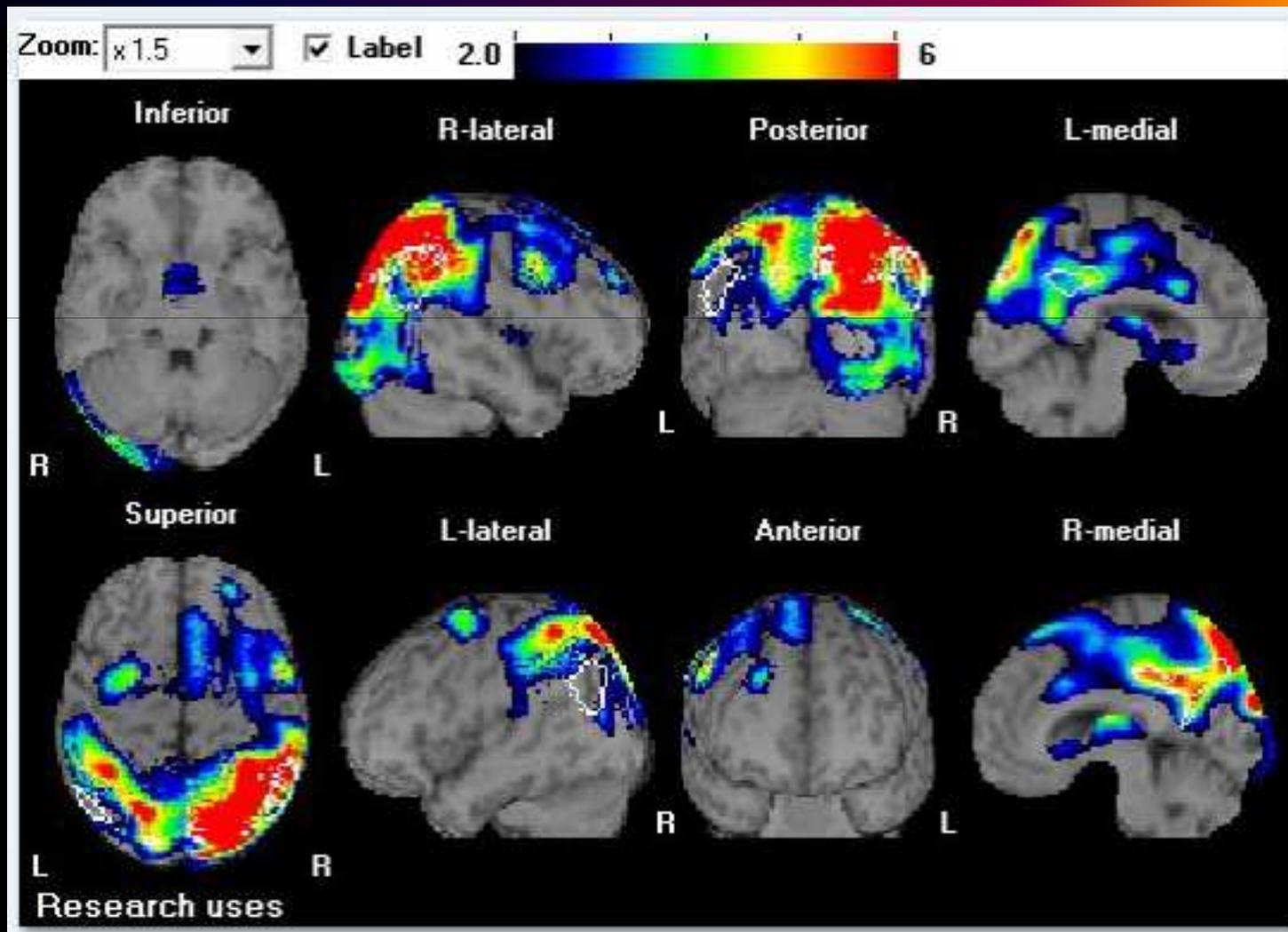
# Dementia with Lewy Body



# Frontal variant Alzheimer's disease

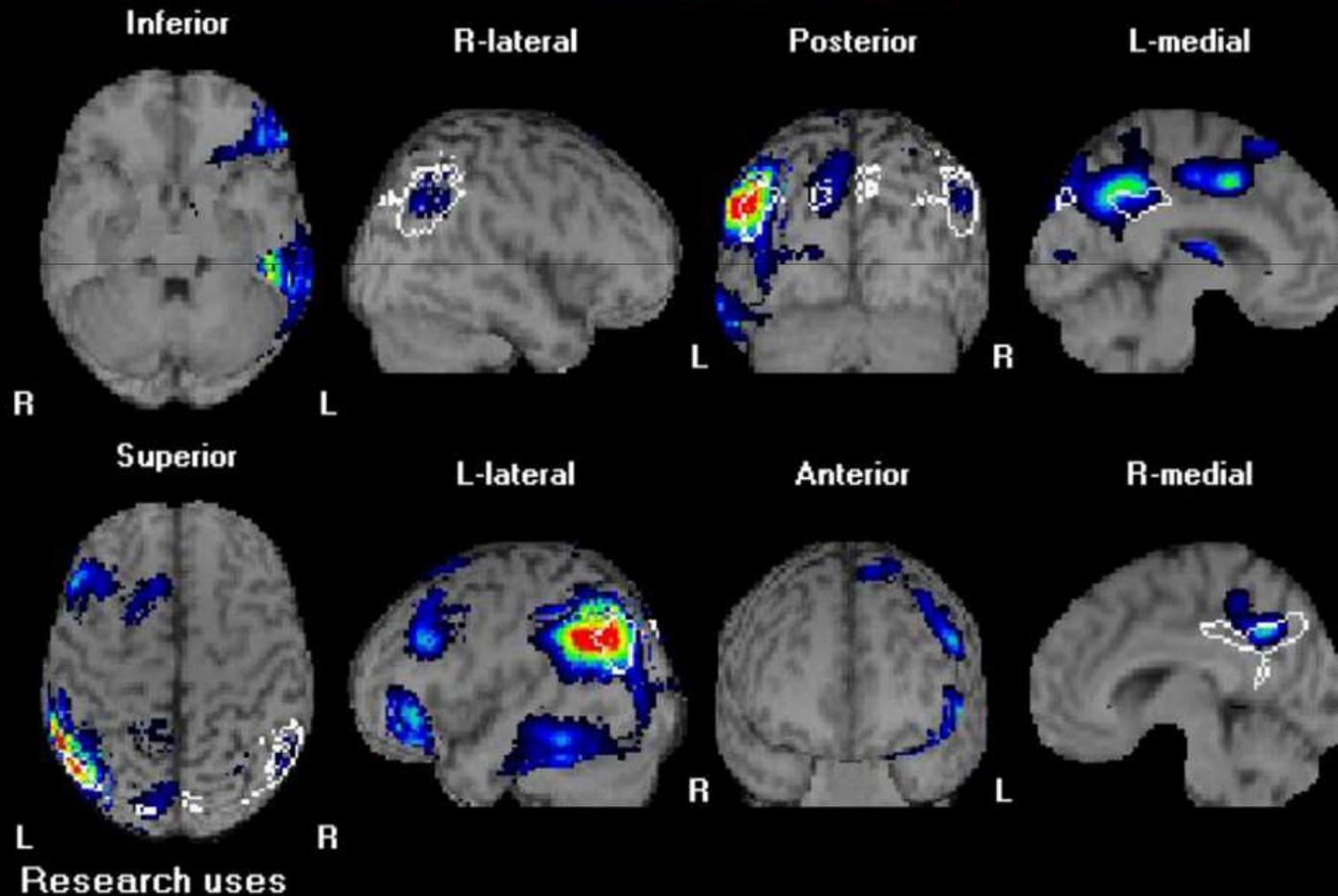


# Posterior Cortical Atrophy



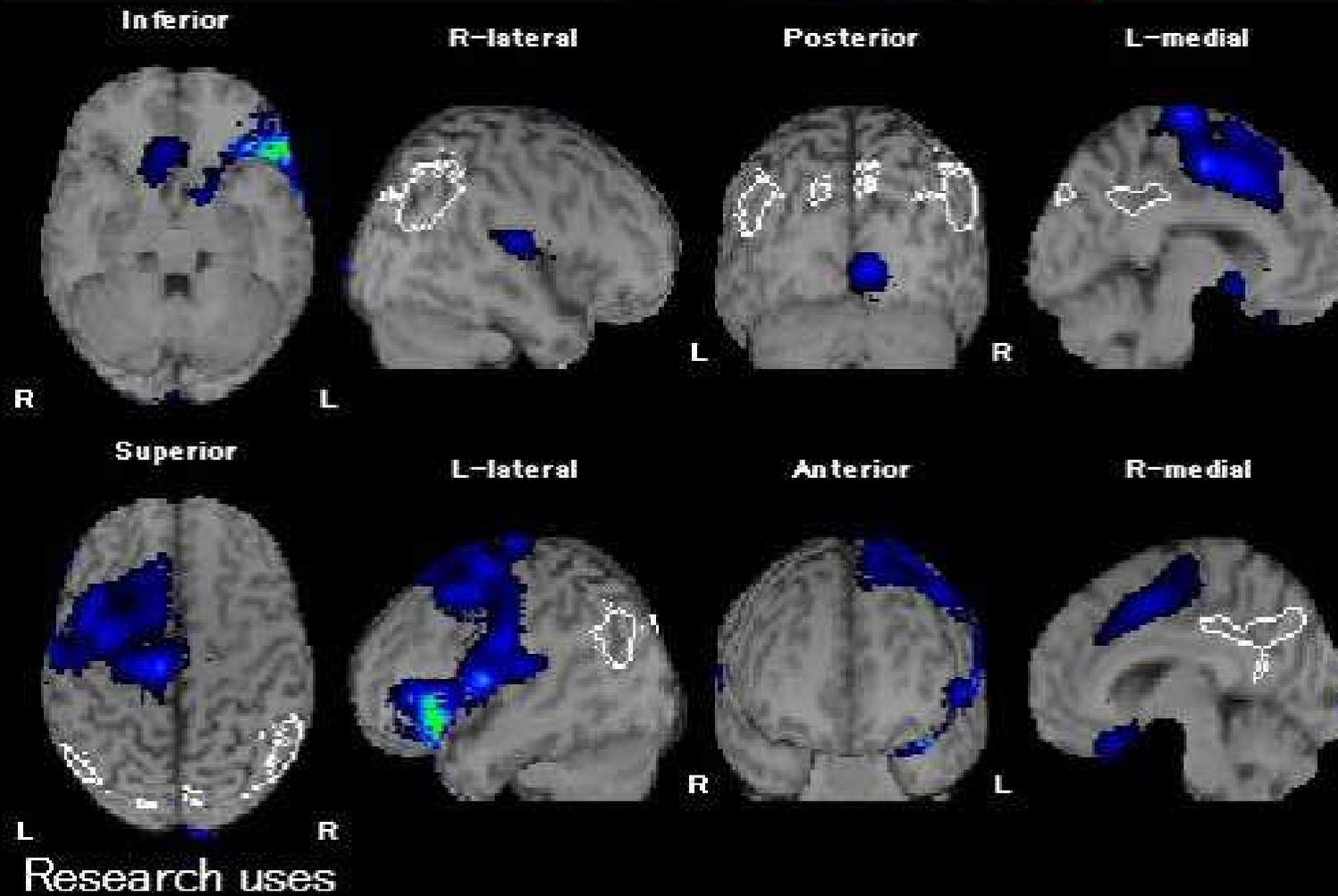
# Logopenic PPA

Zoom: x1.5  Label 2.0 

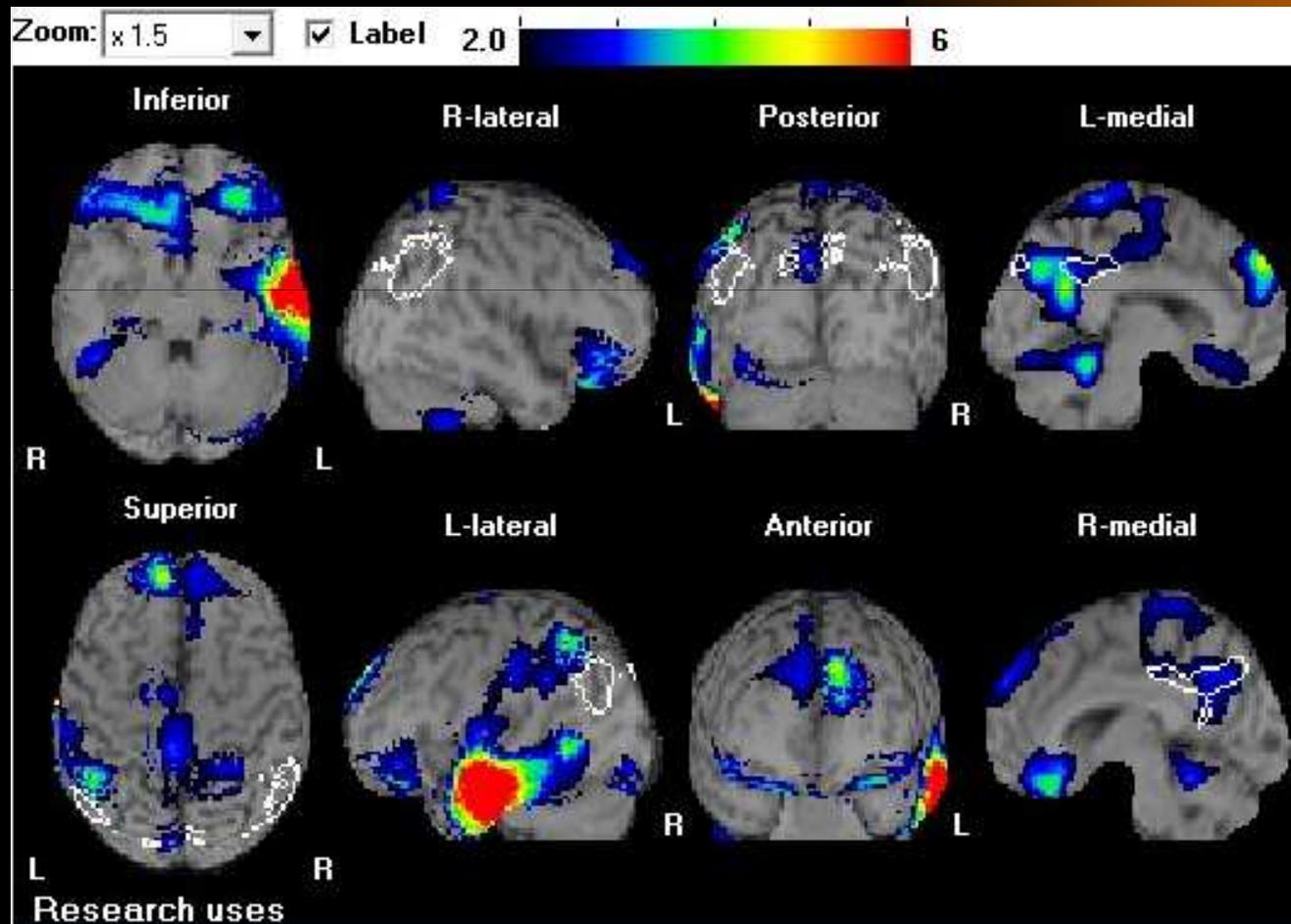


# Non-fluent PPA

Zoom: x 1.5  Label 2.0  6



# Semantic PPA



### Brain FDG PET Patterns of Hypometabolism in Neurodegenerative Disorders

Brain Region	Disorder				
	Alzheimer Disease	DLB	PCA	FTD	Corticobasal Degeneration
Bilateral posterior parietotemporal	↓	↓	↓	Initially preserved, later ↓	Preserved to asymmetric reduction
Posterior cingulate	↓	↓	↓	Initially preserved, later ↓	Asymmetric ↓
Anterior cingulate	Preserved	Variable	Preserved	↓	↓
Frontal lobe	Mild ↓ (more with advanced disease)	↓ (more with advanced disease)	Preserved	↓	Asymmetric ↓
Anterior temporal lobe	Relatively preserved	Variable	Preserved	↓	Preserved
Basal ganglia	Preserved	↓ (caudate)	Preserved	Variable to preserved	Asymmetric ↓
Primary sensorimotor cortex	Preserved	Preserved	Preserved	Variable to preserved	Asymmetric ↓
Primary and associative visual cortex	Preserved	↓ in medial occipital cortex (primary visual)	↓ in lateral occipital cortex (visual association)	Preserved	Preserved

Note.—↓ = hypometabolism.

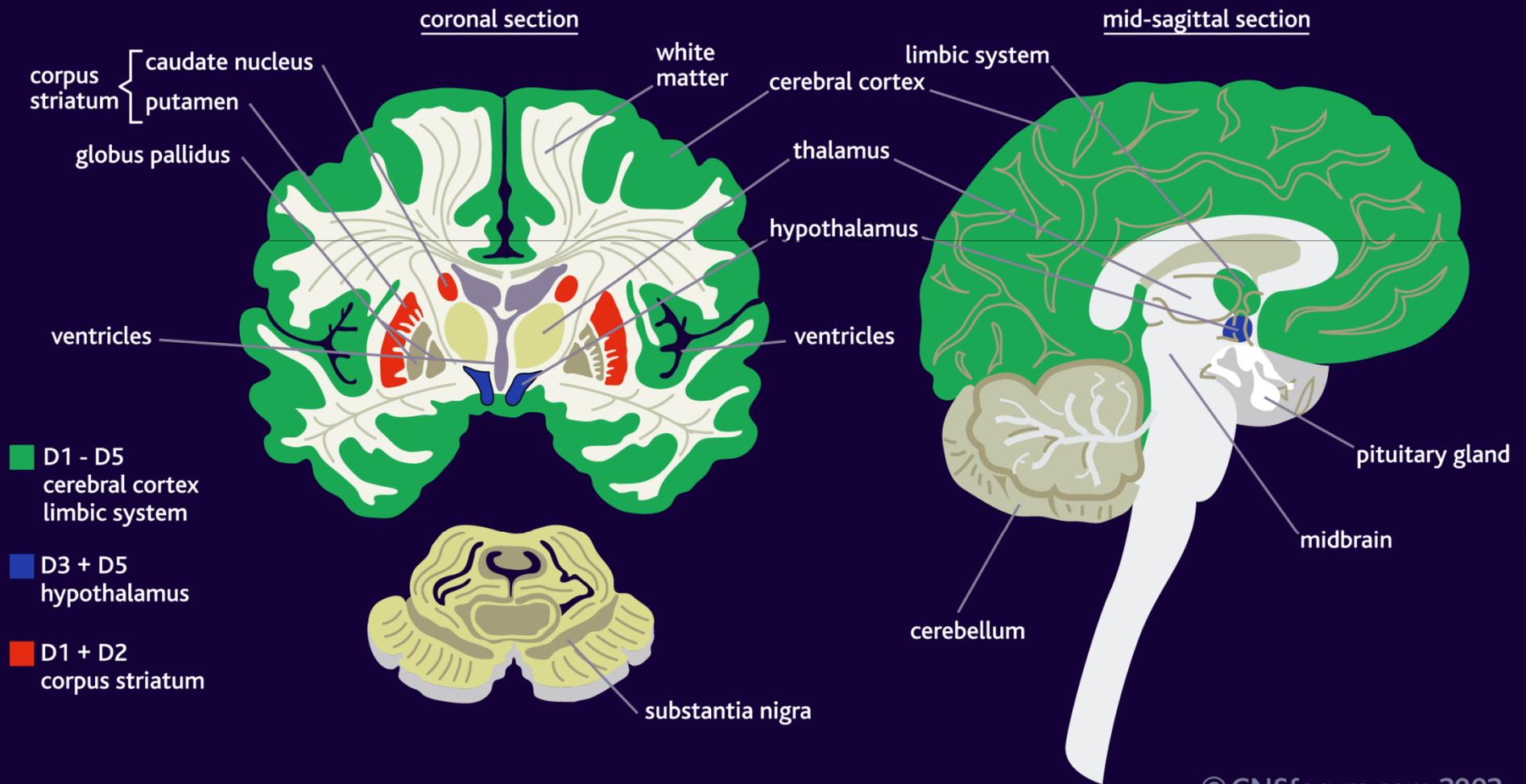
# MOU (memorandum of understanding



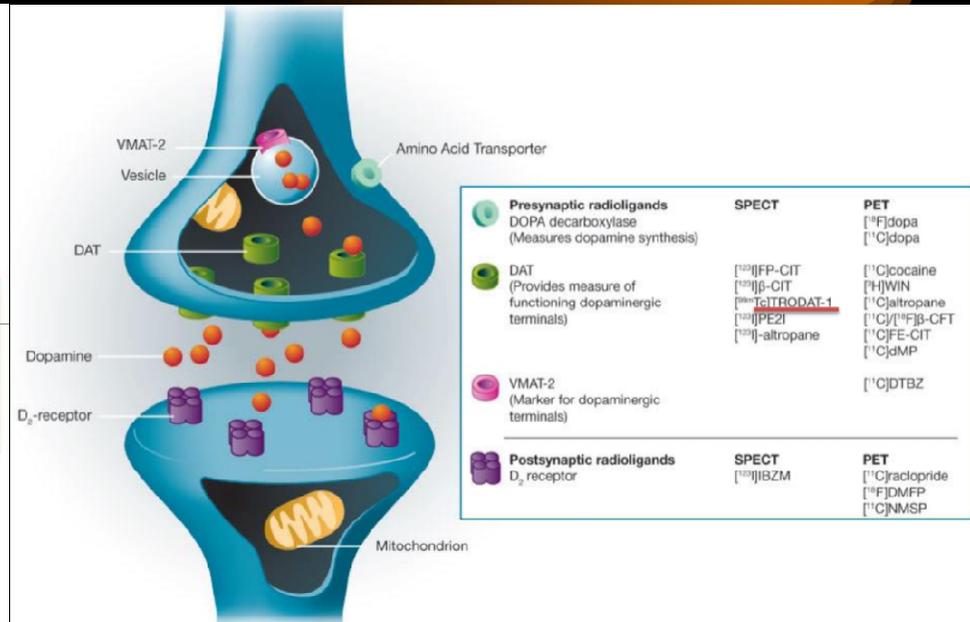
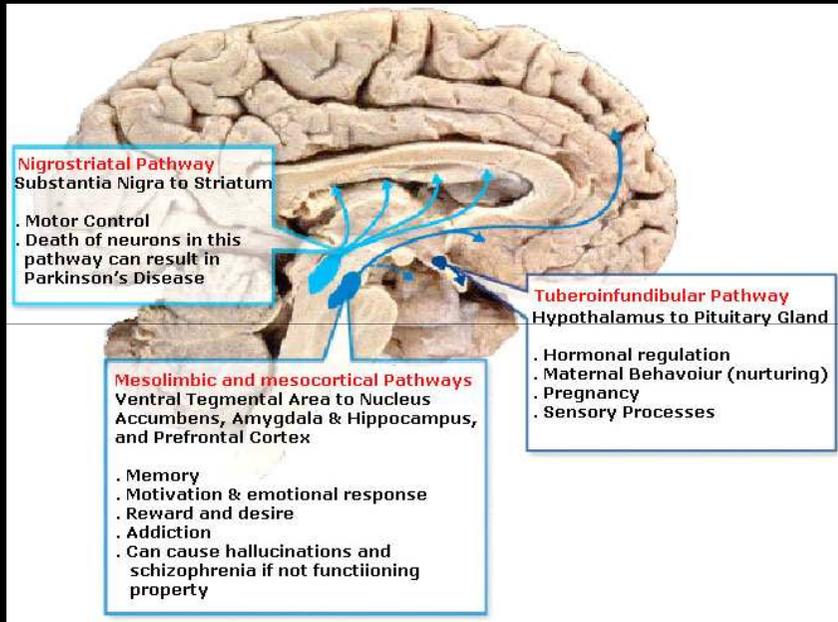
神經影像常模研究小組第一次會議  
台灣臨床失智症學會(TDS)、中華民國核醫學學會(TSNM) 台中 2016.9.3



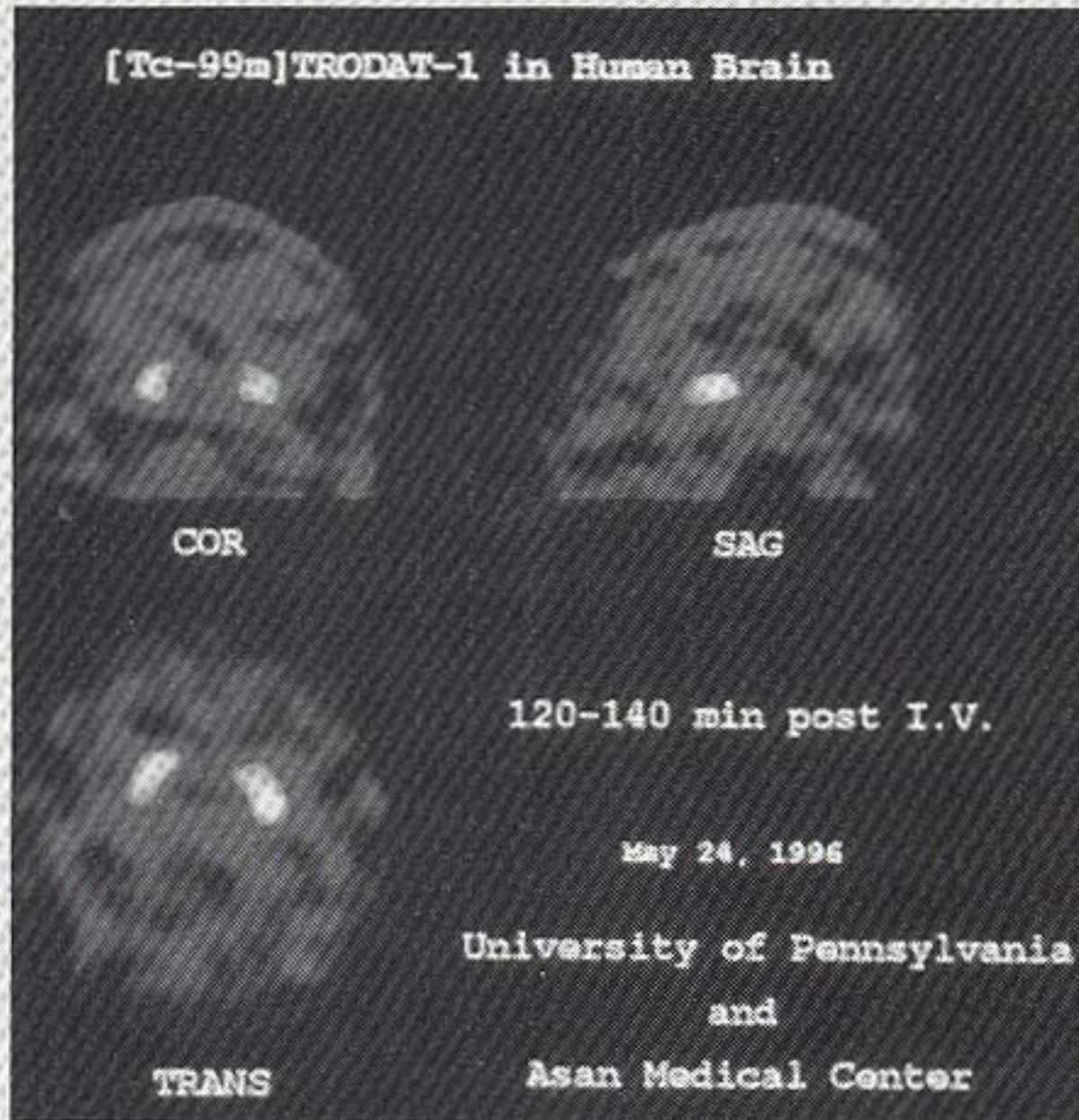
# Dopamine receptors



# Dopamine Transporter (DAT)



# Image of the Year



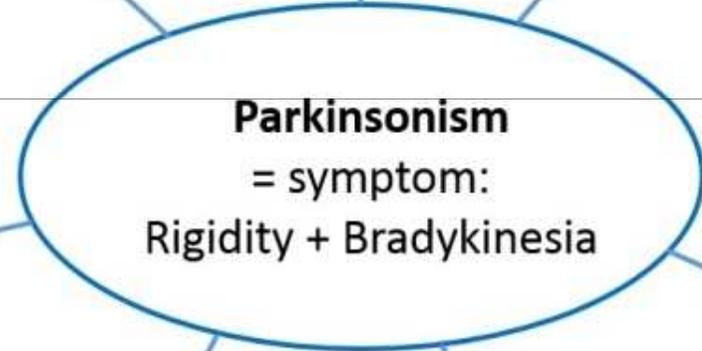
This year, I have selected the image of the dopamine transporter, accomplished with a  $^{99m}\text{Tc}$ -labeled tracer to be the "Image of the Year." The dopaminergic system continues to be one of the most active areas of research in nuclear medicine.

**$\alpha$ -synucleinopathies**

**Parkinson's disease (PD)**

Multisystem atrophy (MSA)

Dementia with Lewy Bodies (DLB)



(advanced Alzheimer's disease (AD))

Progressive supranuclear Palsy (PSP)

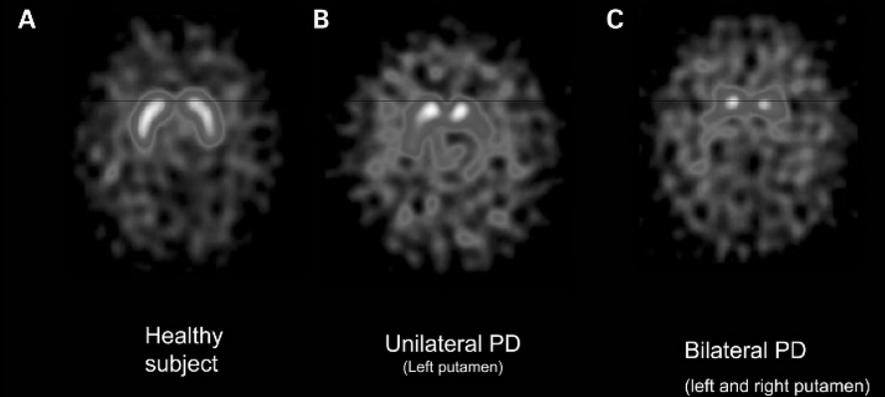
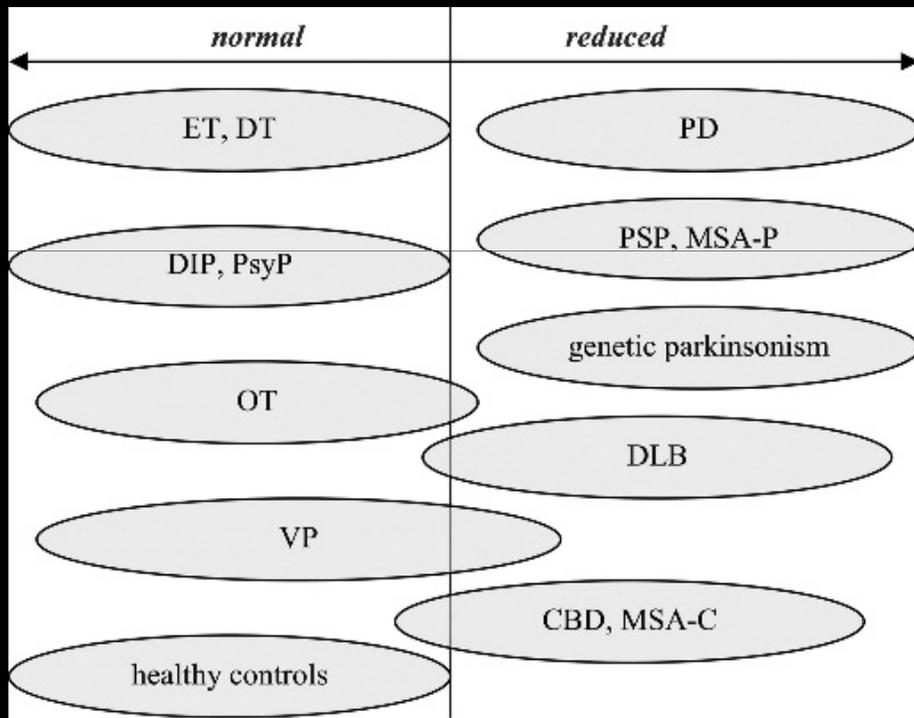
Non-degenerative:  
-Ischaemia (stroke)  
-Medication

Corticobasal degeneration (CBD)

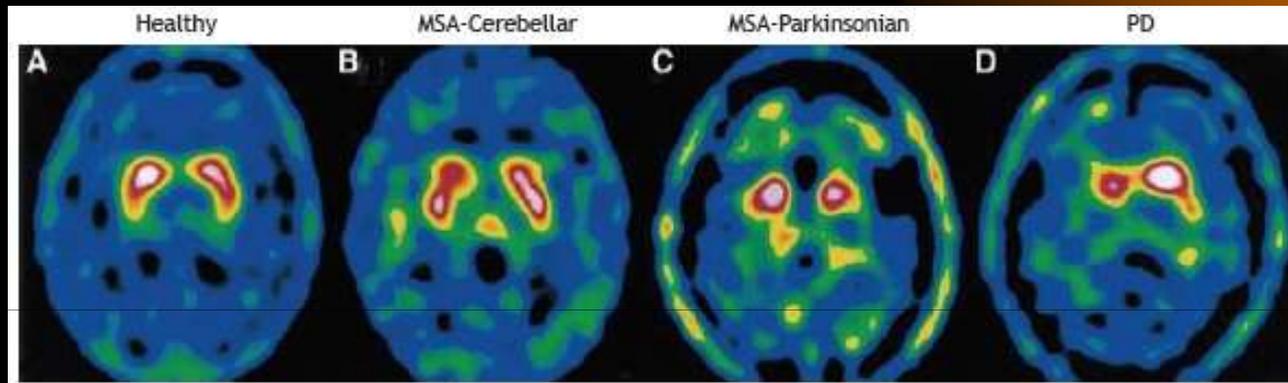
(advanced frontotemporal dementia (FTD))

**tauopathies**

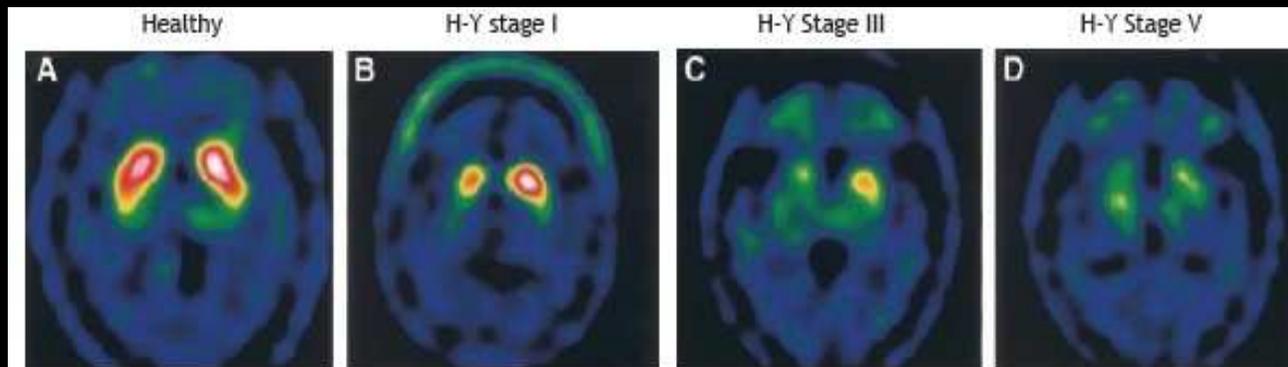
# DAT- SPECT in movement disorders



# Dopamine Transporter (DAT)



<sup>99m</sup>Tc -TRODAT-1 SPECT images of 4 similarly aged individuals

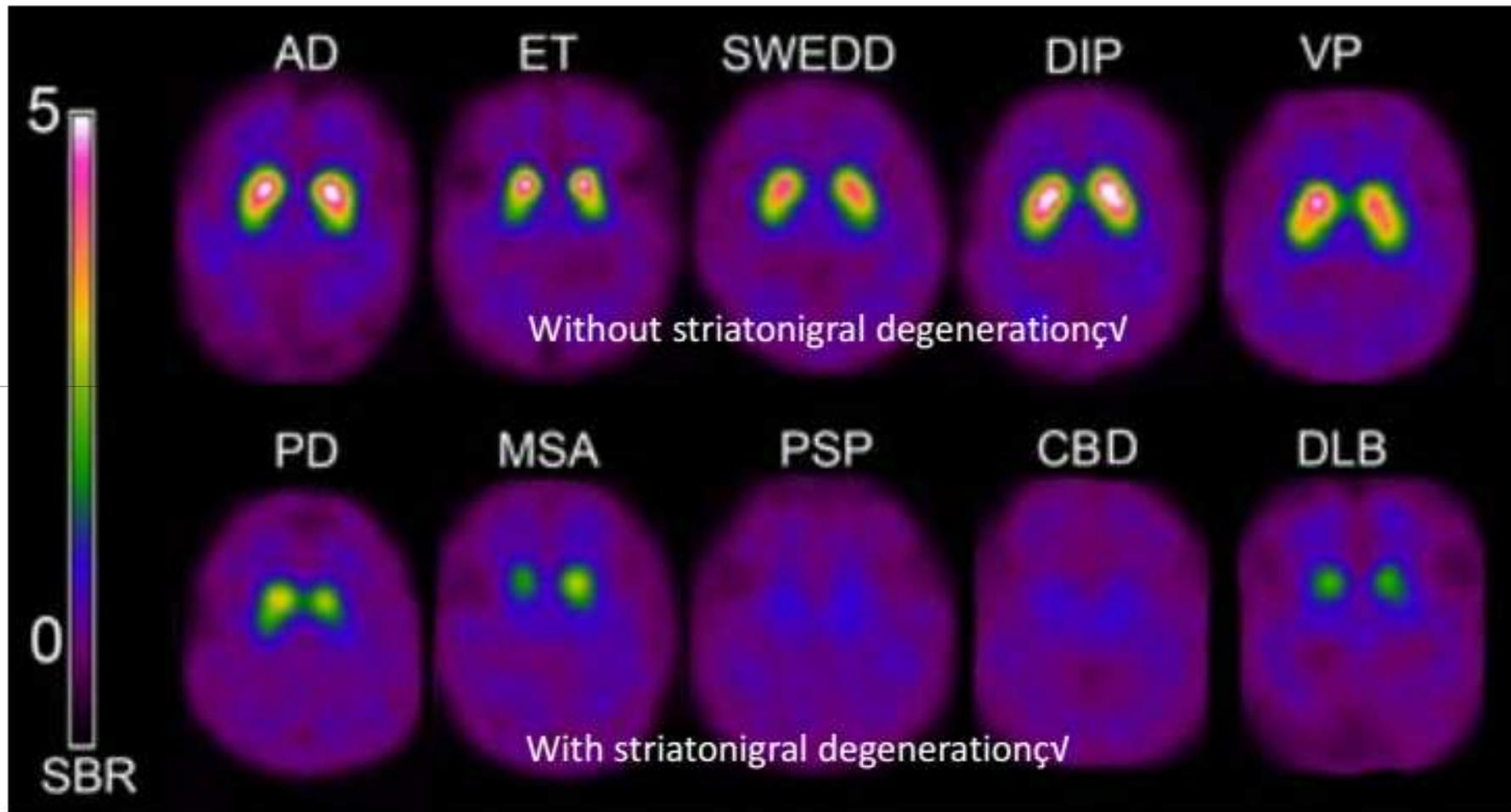


(A) Healthy volunteer (B) H-Y stage I with left side tremor and bradykinesia (C) H-Y stage III with bilateral bradykinesia, dominant in the left side (D) H-Y stage V with severe bilateral akinesia

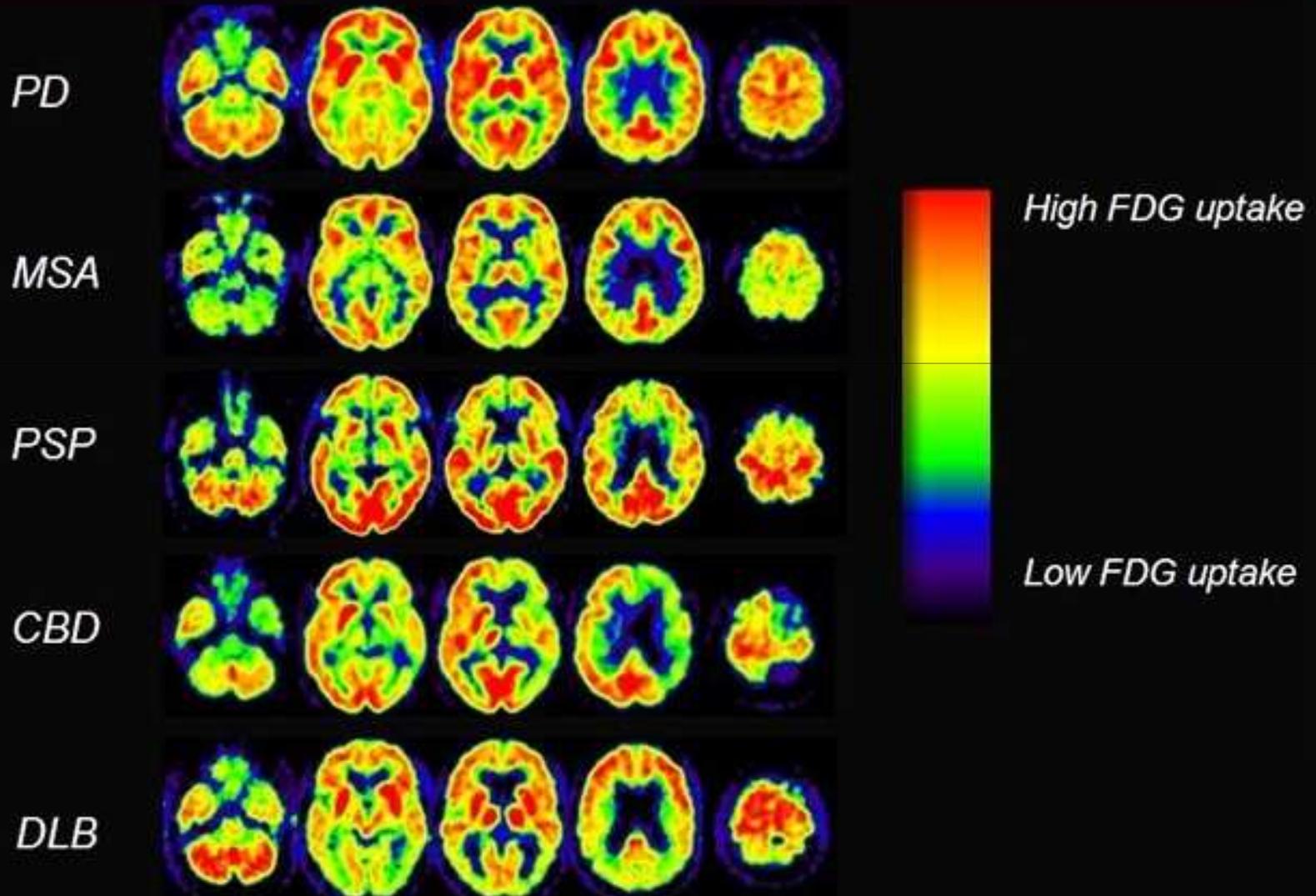
## Reference:

1. Lu CS et al. J Nucl Med 2004;45(1):49-55
2. Weng YH et al. J Nucl Med 2004;45(3): 393-401

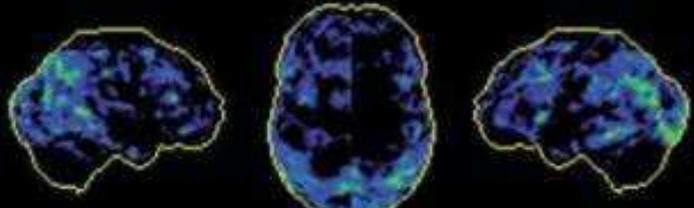
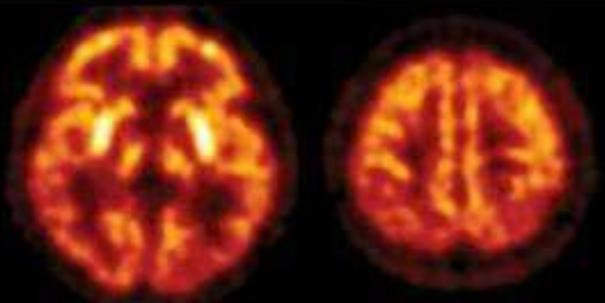
# Quantitative images



# Visual assessment individual FDG-PET scan

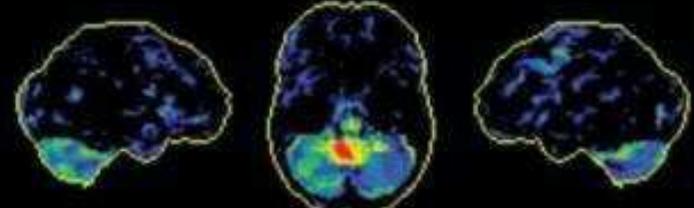
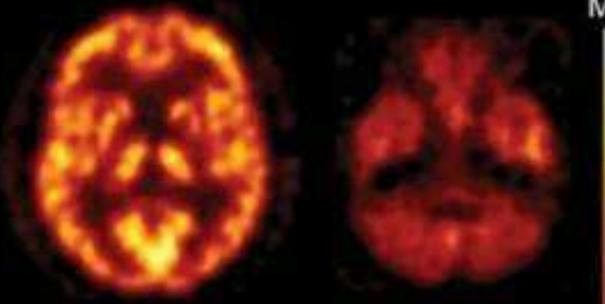


LBD  
(PD)



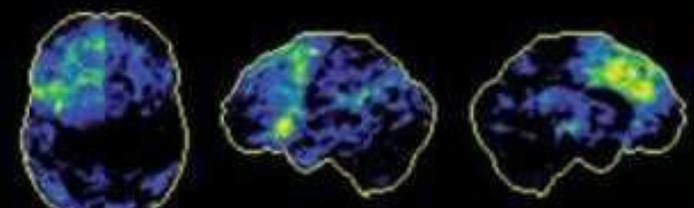
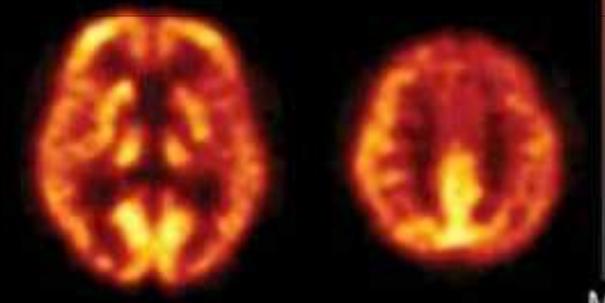
Right lateral Superior Left lateral

MSA



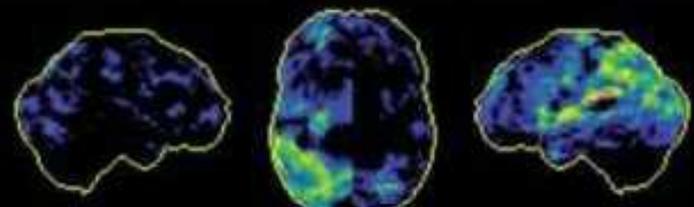
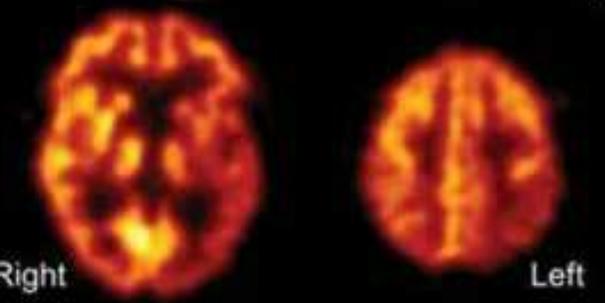
Right lateral Inferior Left lateral

PSP



Superior Left lateral Left mesial

CBD



Right lateral Superior Left lateral

Max

Min

[<sup>18</sup>F]FDG uptake

7

6

5

4

3

2

1

0

z-score

Right

Left

# アルツハイマー型認知症と鑑別が必要な認知症疾患の画像所見

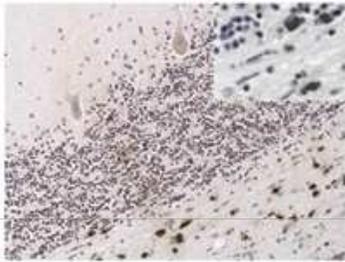
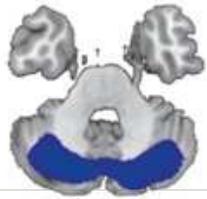
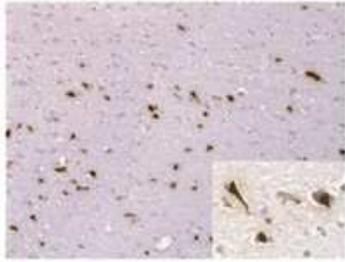
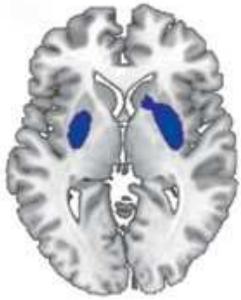
MRI	IMP 脳血流SPECT・3D-SSP解析 (Z-score画像)	ドパミントランスポートSPECT (正規化画像)
<b>アルツハイマー型認知症 (AD)</b> 側脳室下角の拡大、海馬を含む側頭葉内側の萎縮 右 冠状断像 横断像 左	頭頂葉、後方連合野、後部帯状回、楔前部の血流低下 右外側面 左外側面 右内側面 左内側面	集積正常 右 左
<b>レビー小体型認知症 (DLB)</b> 側脳室下角の拡大、海馬を含む側頭葉内側の萎縮はADより軽度 右 冠状断像 横断像 左	後頭葉、一次視覚野、頭頂葉の血流低下 後頭葉や一次視覚野の血流低下が無いAD様の症例もあります 右外側面 左外側面 右内側面 左内側面	集積低下 右 左
<b>進行性核上性麻痺 (PSP)</b> 中脳被蓋の萎縮 ハチドリサイン 前 矢状断像 右 横断像 左	前頭葉、前部帯状回の血流低下 中脳の血流低下を認める例もあります 右外側面 左外側面 右内側面 左内側面	集積低下 右 左
<b>大脳皮質基底核症候群 (CBS)</b> 中心前回、頭頂葉の左右差のある萎縮 右 横断像 左	中心前回、頭頂葉の左右差のある血流低下 右外側面 左外側面 左 上面 右 左 後面 右	左右差のある集積低下 右 左
<b>前頭側頭型認知症 (bvFTD)</b> 前頭葉、側頭葉の萎縮 右 横断像 左	前頭葉、側頭葉の血流低下 右外側面 左外側面 右内側面 左内側面	集積低下と集積正常の両方の報告があります。
<b>意味性認知症 (SD)</b> 側頭葉外側(含側頭葉極)および/側の、左右差のある(主に左)萎縮 右 冠状断像 横断像 左	側頭極を主とする側頭葉の左右差のある(主に左)血流低下 右外側面 左外側面 右 下面 左 右 前面 左	特徴的な所見は報告されていません。

小 ← 血流低下 → 大      小 ← 線条体集積 → 大

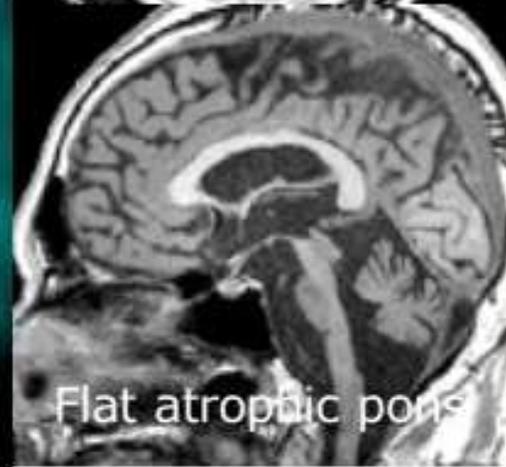
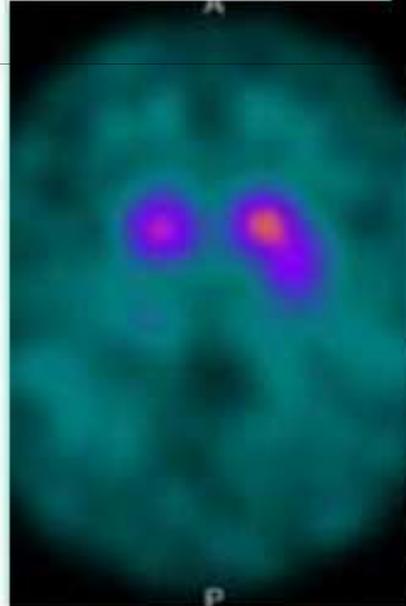
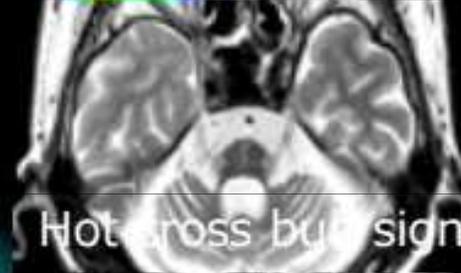
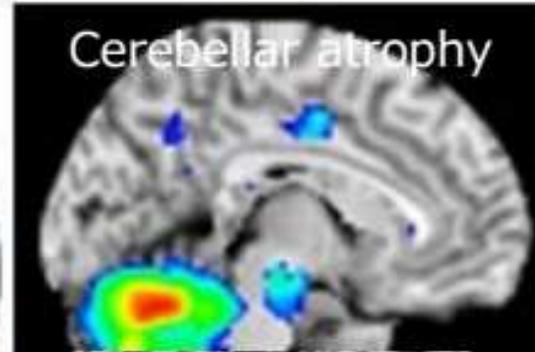
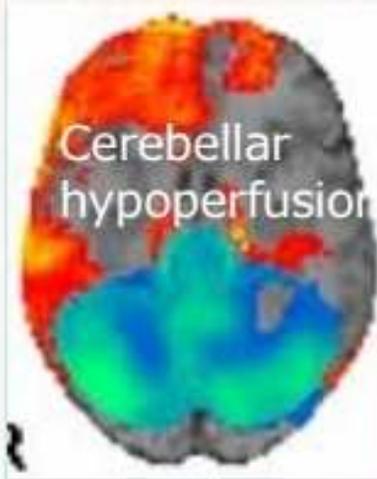
MRI・脳血流SPECT・ドパミントランスポートSPECTの疾患ごとの代表的な画像所見を提示するため、異なる被験者の画像を組み合わせている例もあります。 症例提供: 日本医科大学大学院医学研究科 神経内科学分野 石渡 明子 先生

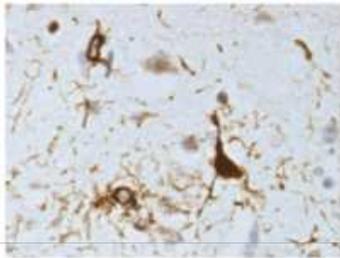
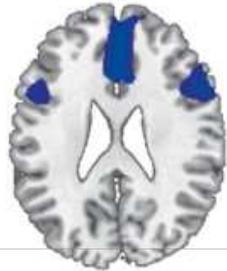
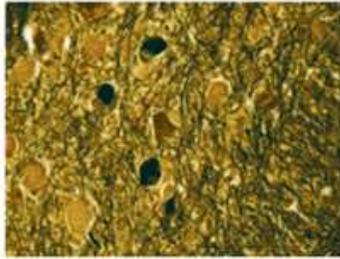
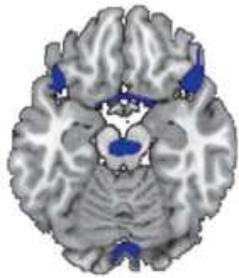
# Parkinsonian syndromes

Tracer	Parkinson's disease	PSP	MSA	CBGD
Trodat	Asymmetric reduction	Symmetrical reduction	Symmetrical reduction	Asymmetric reduction
	putamen > caudate	caudate = putamen	caudate = putamen	caudate = putamen
<sup>18</sup> FDG	Normal/raised in Striatum and cerebellum	Reduced in Bilateral striatum and midline frontal cortices	Reduced in striatum and cerebellum	Asymmetric reduction in striatum, thalamus, frontal and parietal cortices

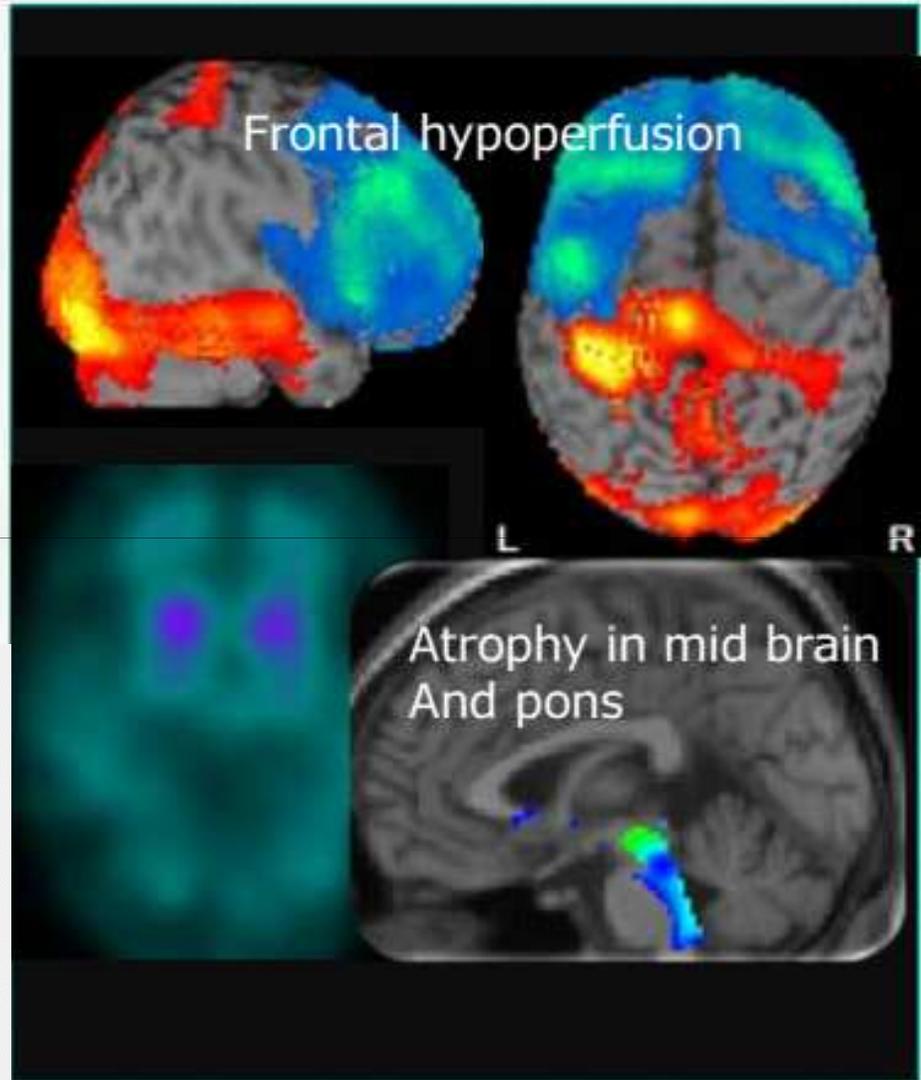
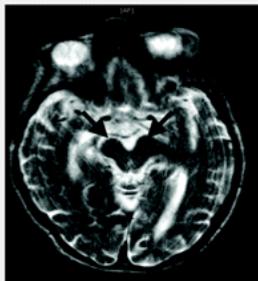
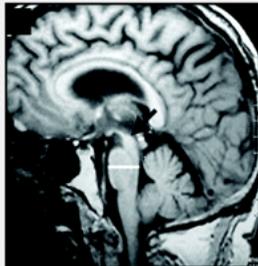


MSA

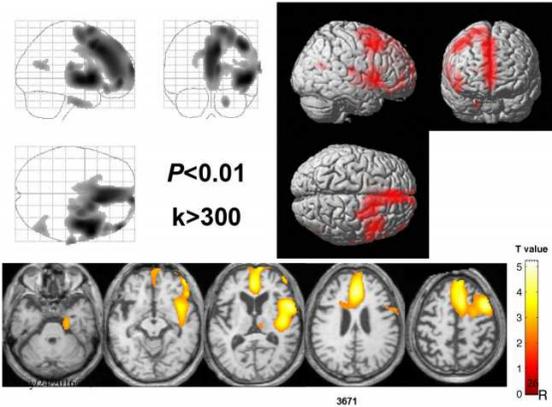




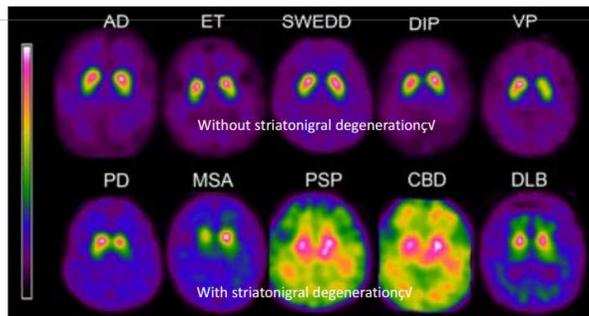
PSP



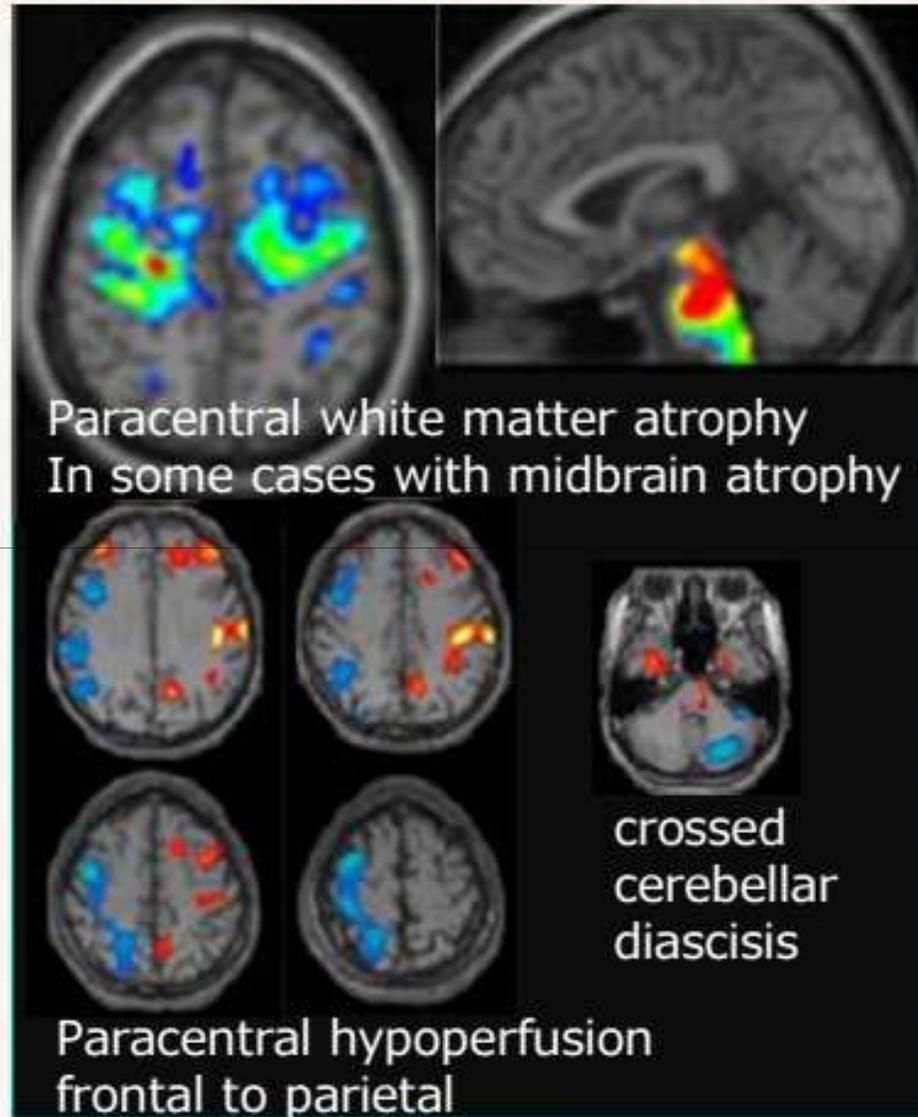
### CBD 79 M



### Qualitative images



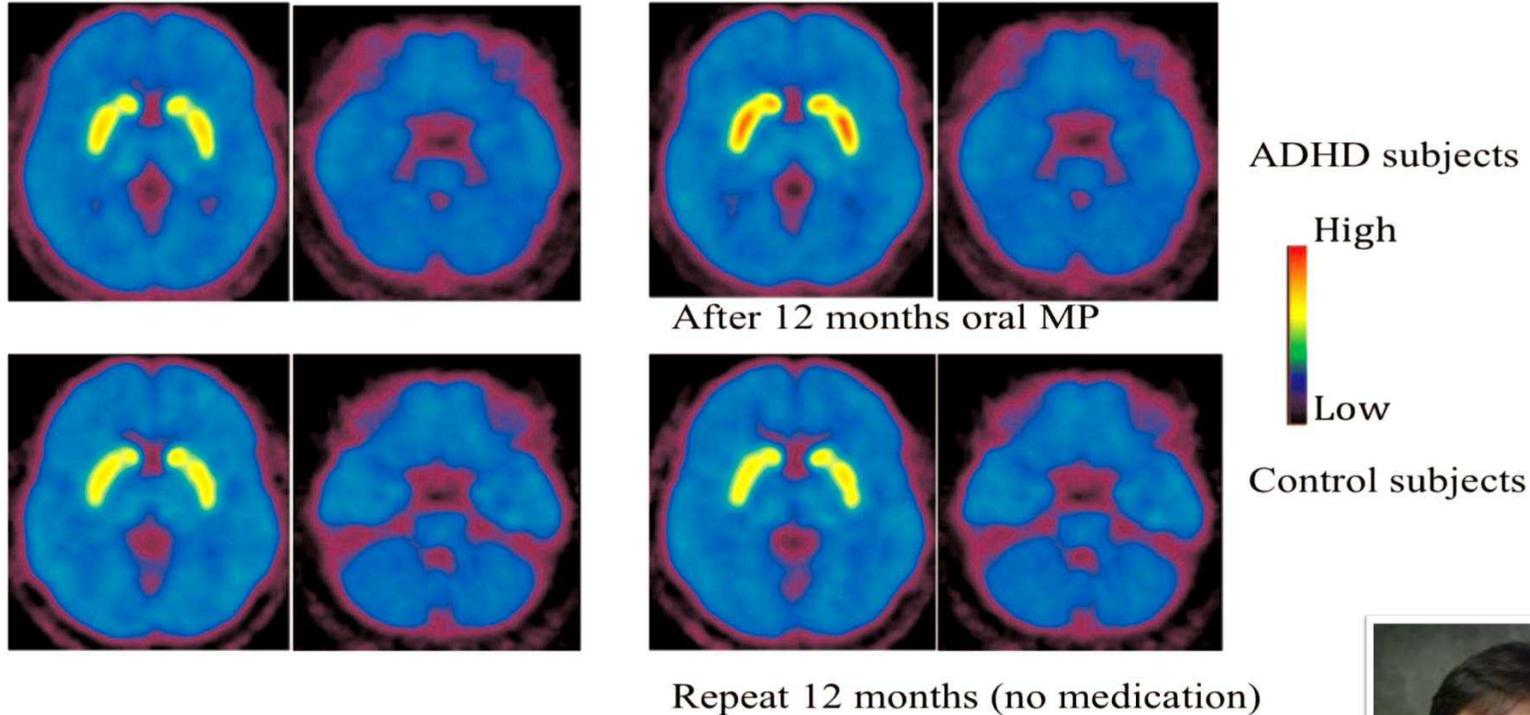
### CBD



*TOPIC: Brain Dopamine and  
Attention Deficit Hyperactive Disorder*

Baseline visit

Follow up visit



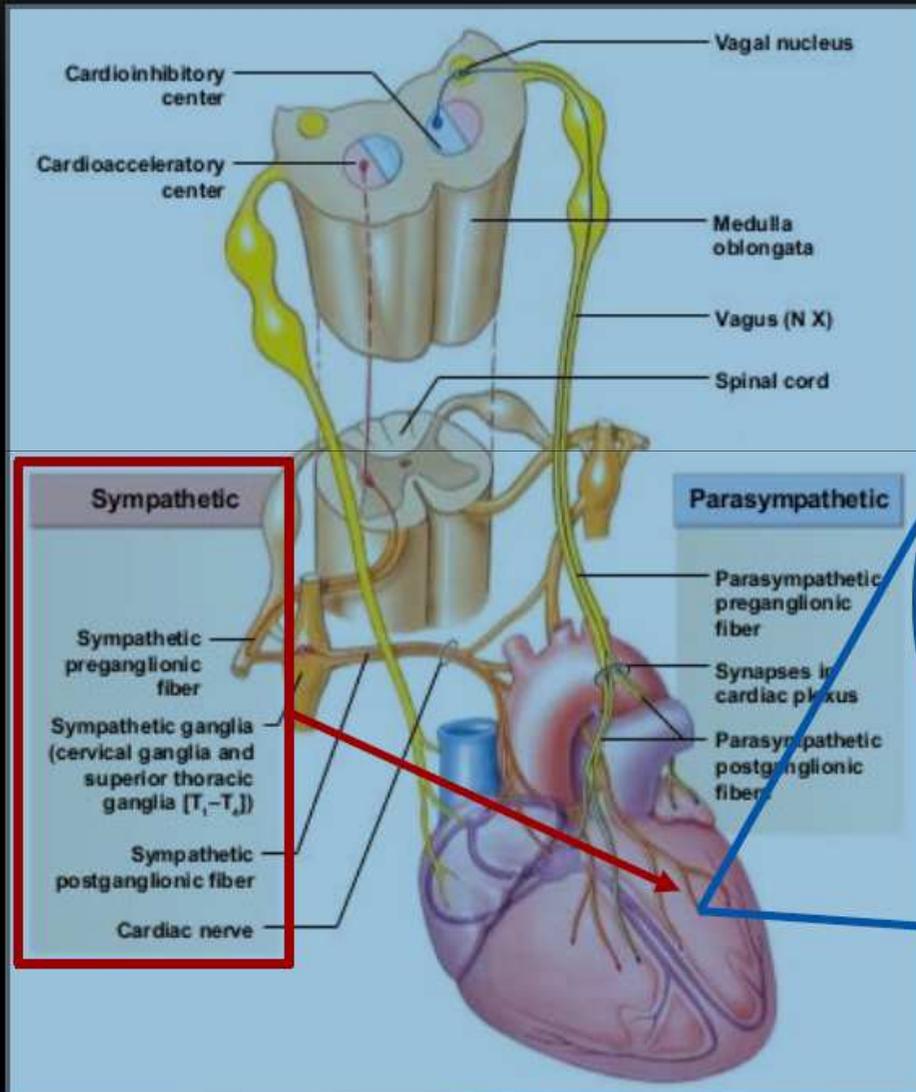
2015年9月11日 16:00  
醫學院四樓大會議室

*Professor  
Gene-Jack Wang, M.D.*

Adjunct Professor of Radiology, SBU, Stony Brook, NY  
Clinical director, Laboratory of Neuroimaging (LNI),  
National Institute on Alcohol Abuse and Alcoholism (NIAAA)

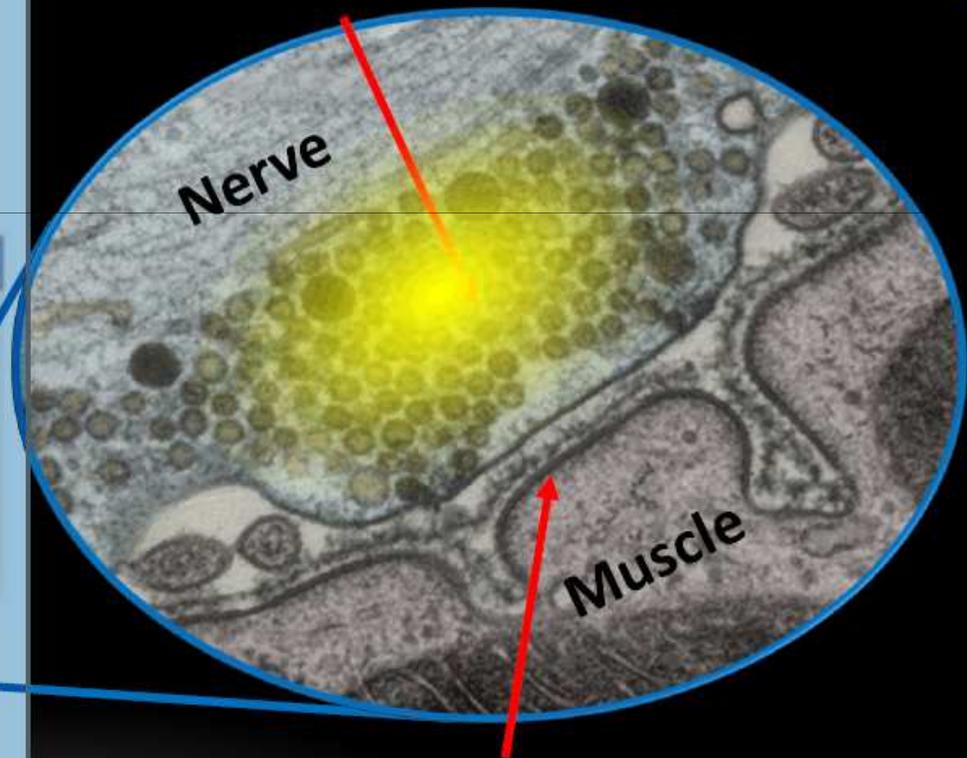


# Cardiac autonomic innervation



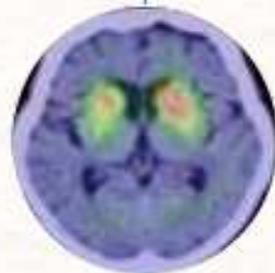
Pre-synaptic vesicles

filled with **NE** ← <sup>123</sup>I-*m*IBG

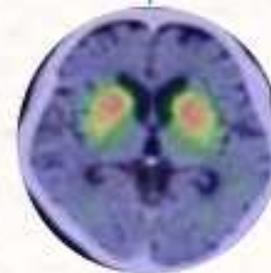


Adrenoceptors

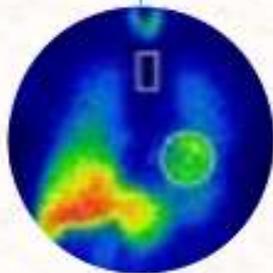
# parkinsonism



Degenerative disease

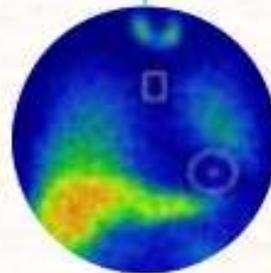


Not degenerative



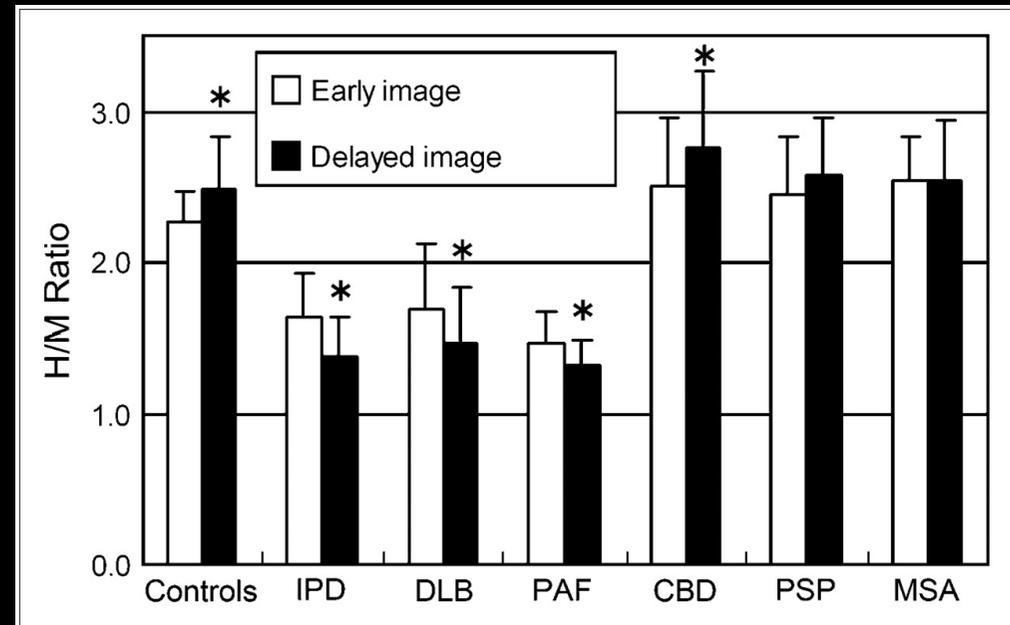
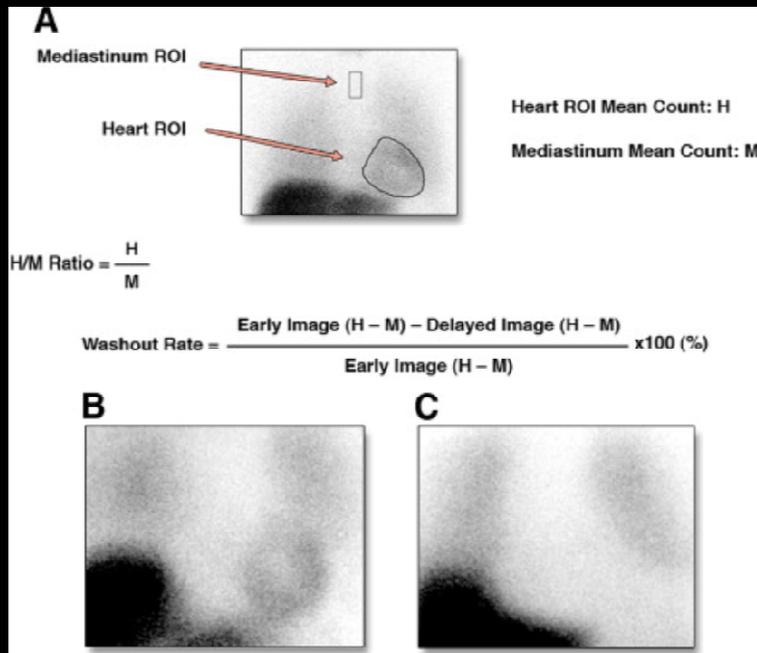
MSA, PSP, CBD, or  
the other

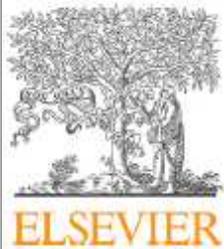
Not like PD or DLB



PD, DLB or MSA

# Parkinsonian's Syndrome





Contents lists available at SciVerse ScienceDirect

# Sleep Medicine

journal homepage: [www.elsevier.com/locate/sleep](http://www.elsevier.com/locate/sleep)



## Original Article

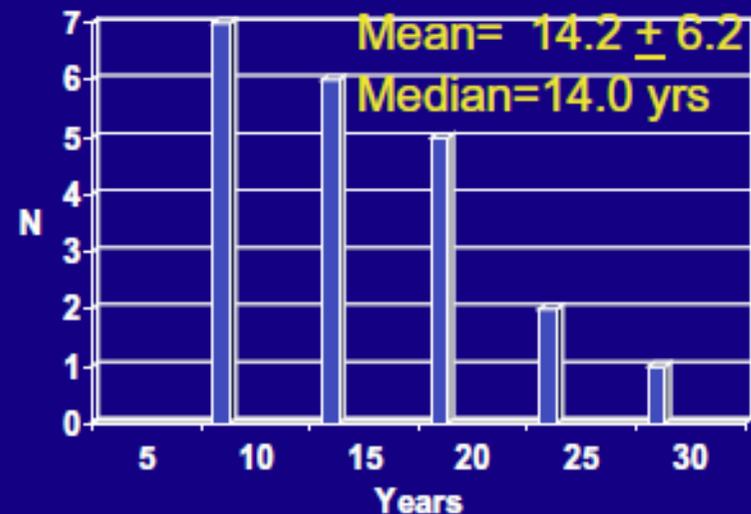
### Delayed emergence of a parkinsonian disorder or dementia in 81% of older men initially diagnosed with idiopathic rapid eye movement sleep behavior disorder: a 16-year update on a previously reported series

Carlos H. Schenck<sup>a,\*</sup>, Bradley F. Boeve<sup>b</sup>, Mark W. Mahowald<sup>c</sup>

**Table 1**

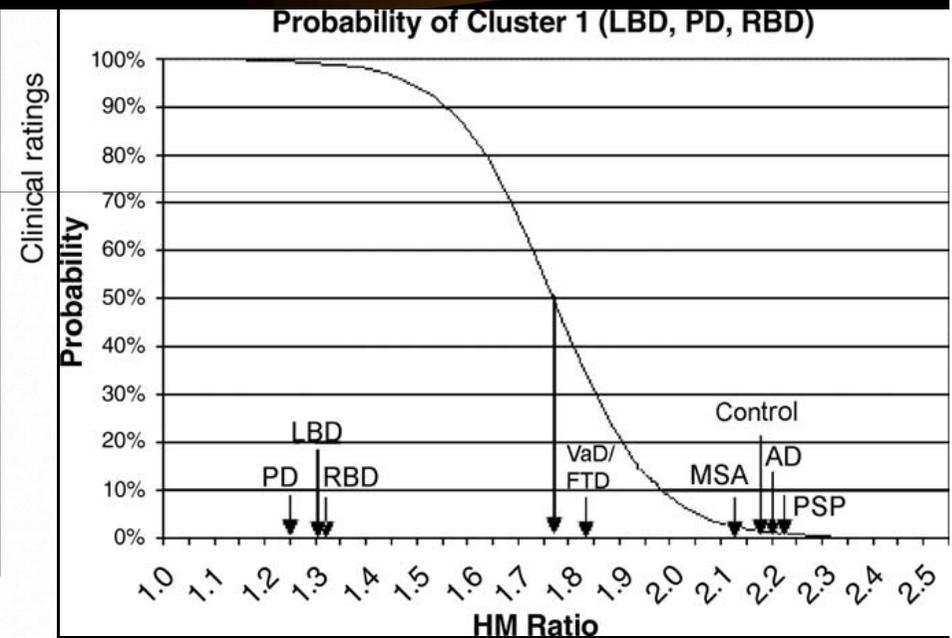
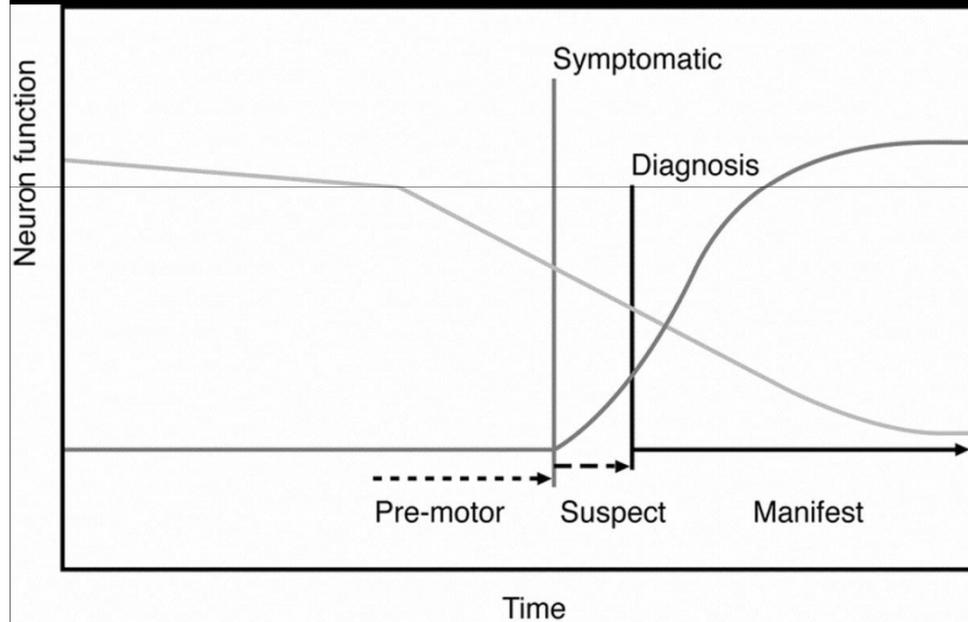
Eventual parkinsonian disorders/dementia in a series of middle-aged and older males initially diagnosed with idiopathic RBD (iRBD).

N = 13 Parkinson's disease	
N = 3 Dementia with Lewy bodies	
N = 1 Dementia (unspecified; profound)	
N = 2 Multiple system atrophy	
N = 2 Clinically diagnosed Alzheimer's disease with autopsy-confirmed combined Alzheimer's disease plus Lewy body disease pathology	
N = 21 iRBD "converters"	
Mean age ( $\pm$ SD), years, iRBD onset	57.7 $\pm$ 7.7
Mean age ( $\pm$ SD), years, parkinsonism/dementia onset	71.9 $\pm$ 6.6
Mean interval ( $\pm$ SD), years, iRBD onset to parkinsonism/dementia onset (range: 5–29 years)	14.2 $\pm$ 6.2



Sleep Med 2013; 14:744-748

# Lewy body Disease



Movement disorders 2011; 26:7



The End

*Thanks for your attention !*