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Il ruolo di nuove tecniche di imaging per la diagnosi precoce di demenza

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PET AND SPECT STUDIES OF THE BRAIN

Molecular Imaging has substantially contributed to characterizing and better understanding the brain pathology underlying the motor and cognitive manifestations of ND

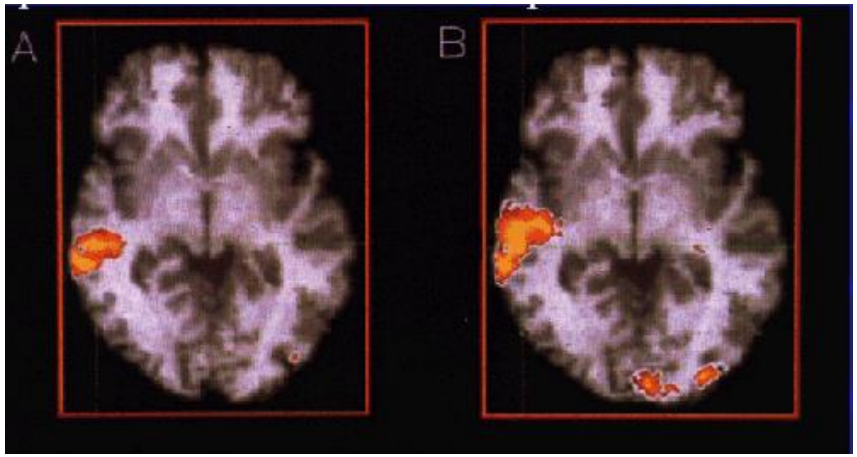
A. Different tracers to determine

- Perfusion
- Glucose utilization
- Dopaminergic function
- Neuroreceptors ligands behaviour
- Aminoacide transport

B. Kinetic model of tracer

C. Quantitative maps of regional in vivo

- physiology
- biochemistry
- pharmacology



MOLECULAR IMAGING IN NEURODEGENERATIVE DISEASES

✓ Setting

- disease severity as reflected by presynaptic dopamine terminal dysfunction or amyloid load → decision making
- subclinical dysfunction in subjects who are at risk for ND
- management and follow-up
- disease progression and monitoring drug efficacy

✓ Imaging tools with increasing complex application (hybrid imaging)

SPECT → SPECT/CT → PET/CT → PET/MRI fusion

✓ Adding CT/MRI enhances accuracy and interobserver agreement

SPECT

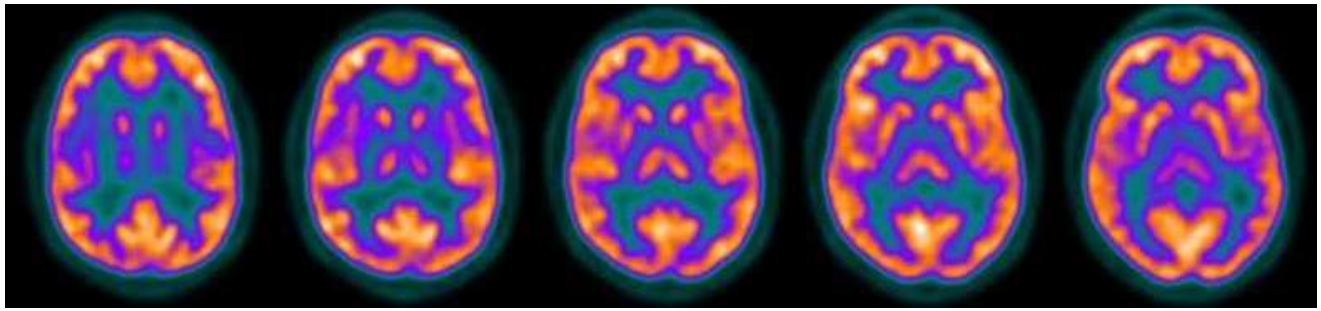
Advantages

✓ Quantifies specific molecular targets down to sub-nanomolar levels
✓ Links biological processes to symptoms and other clinical outcomes
✓ Enables treatments to be evaluated and monitored
✓ Enable translational approaches

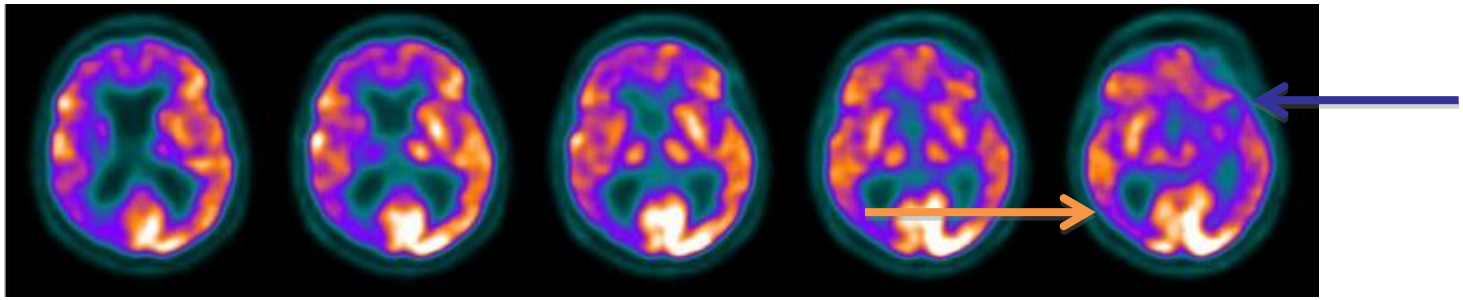
PET

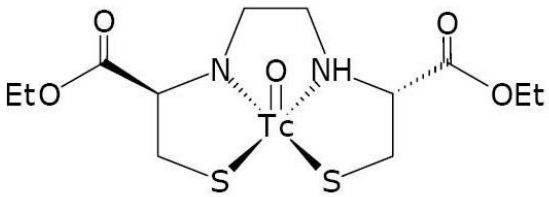
Brain perfusion: [99mTc]HMPAO, [99mTc]ECD SPECT

normal

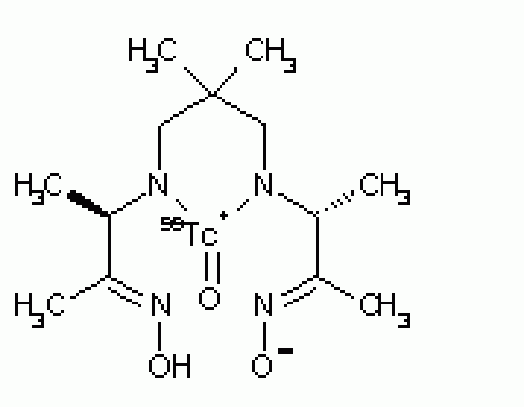


Vascular disease





[99mTc]ECD

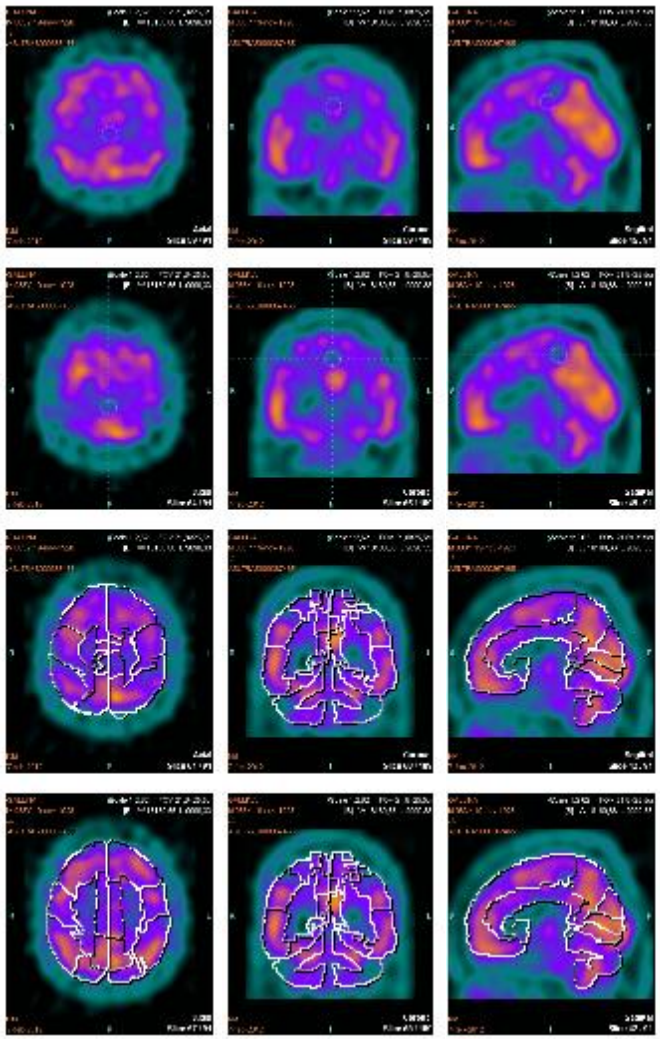


[99mTc]HMPAO

QUANTITATIVE ANALYSIS

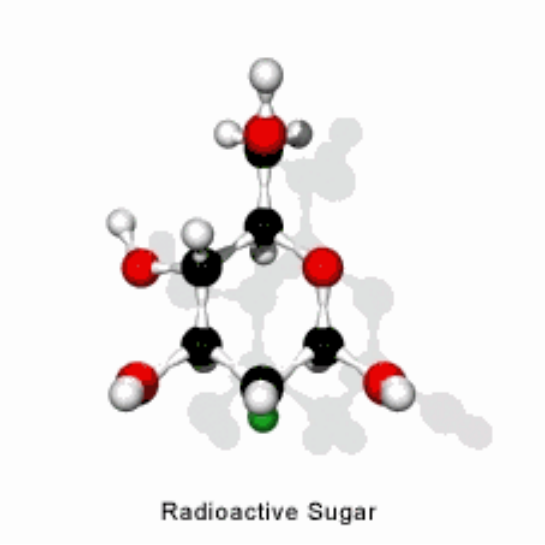
Method: Siemens Scenium analysis

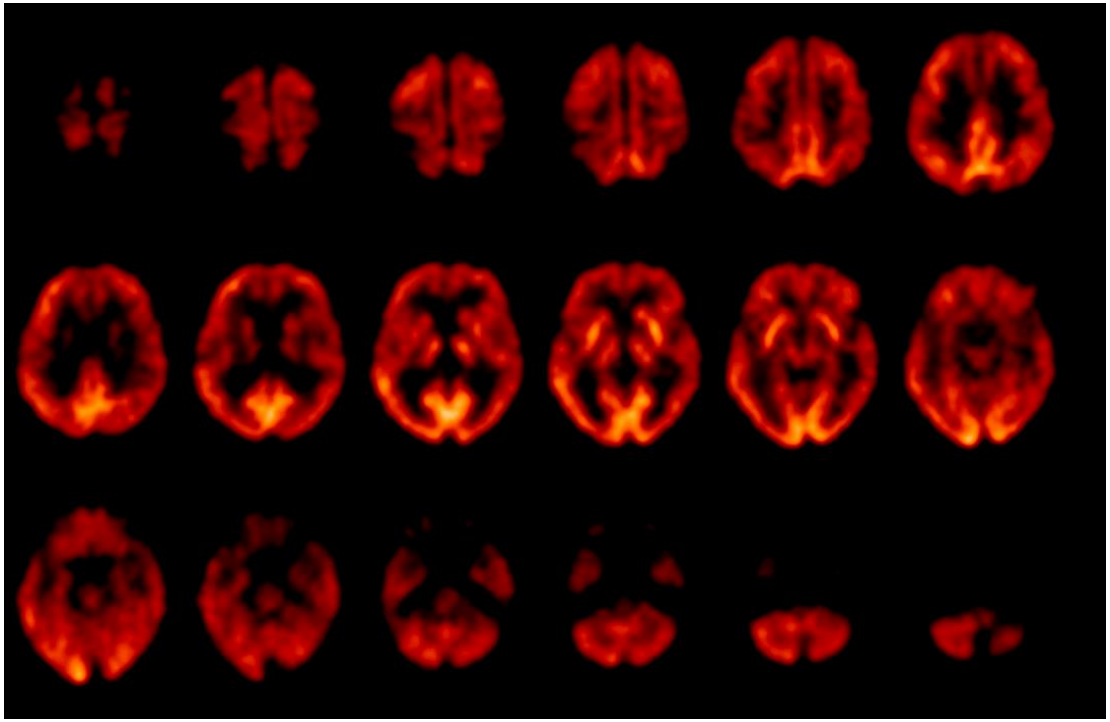
✓ **Voxel segmental analysis**



Region of Interest	Side	Min Uptake	Mean Uptake	Max Uptake	Mean # Std. Dev.
Basal ganglia	L	4.552	9.549	12.992	0,7
Basal ganglia	R	3.216	9.025	13.593	-0,3
Central region	L	4.607	9.649	13.074	2,1
Central region	R	4.436	9.614	13.701	3,2
Cerebellum	L	1.286	10.162	15.361	-0,3
Cerebellum	R	1.804	10.315	16.184	0,9
Cingulate and paracingulate gyri	L	5.516	10.247	14.464	3,8
Cingulate and paracingulate gyri	R	5.311	9.728	14.331	2,8
Frontal lobe	L	3.587	10.334	15.061	3,6
Frontal lobe	R	3.873	10.534	14.869	4,7
Mesial temporal lobe	L	6.060	8.627	11.193	1,1
Mesial temporal lobe	R	2.663	8.778	11.935	1,4
Occipital lobe	L	4.505	11.384	14.907	3,4
Occipital lobe	R	3.436	10.927	14.461	3,3
Parietal lobe	L	3.527	10.227	14.830	2,0
Parietal lobe	R	2.515	9.899	14.504	2,3
Temporal lobe	L	4.506	10.575	13.673	3,0

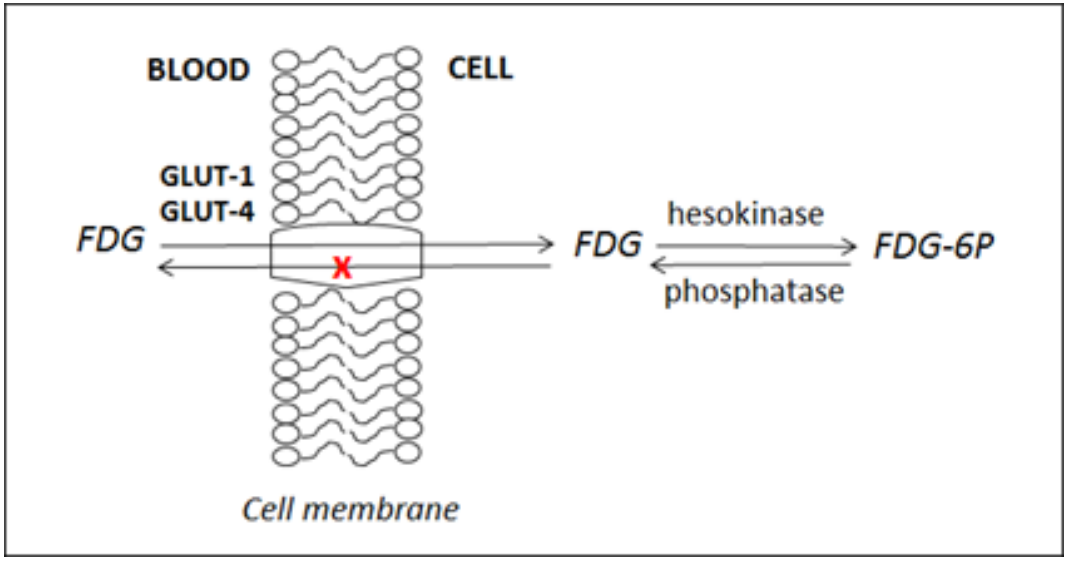
Cellular glucose utilization: [18F]FDG PET

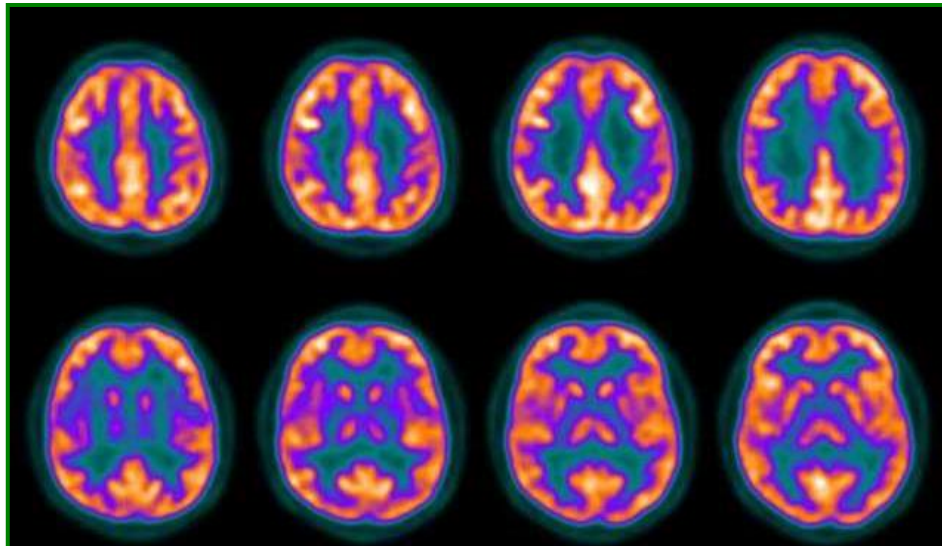




Normal brain and glucose consumption

Neuronal glucose utilization: FDG PET



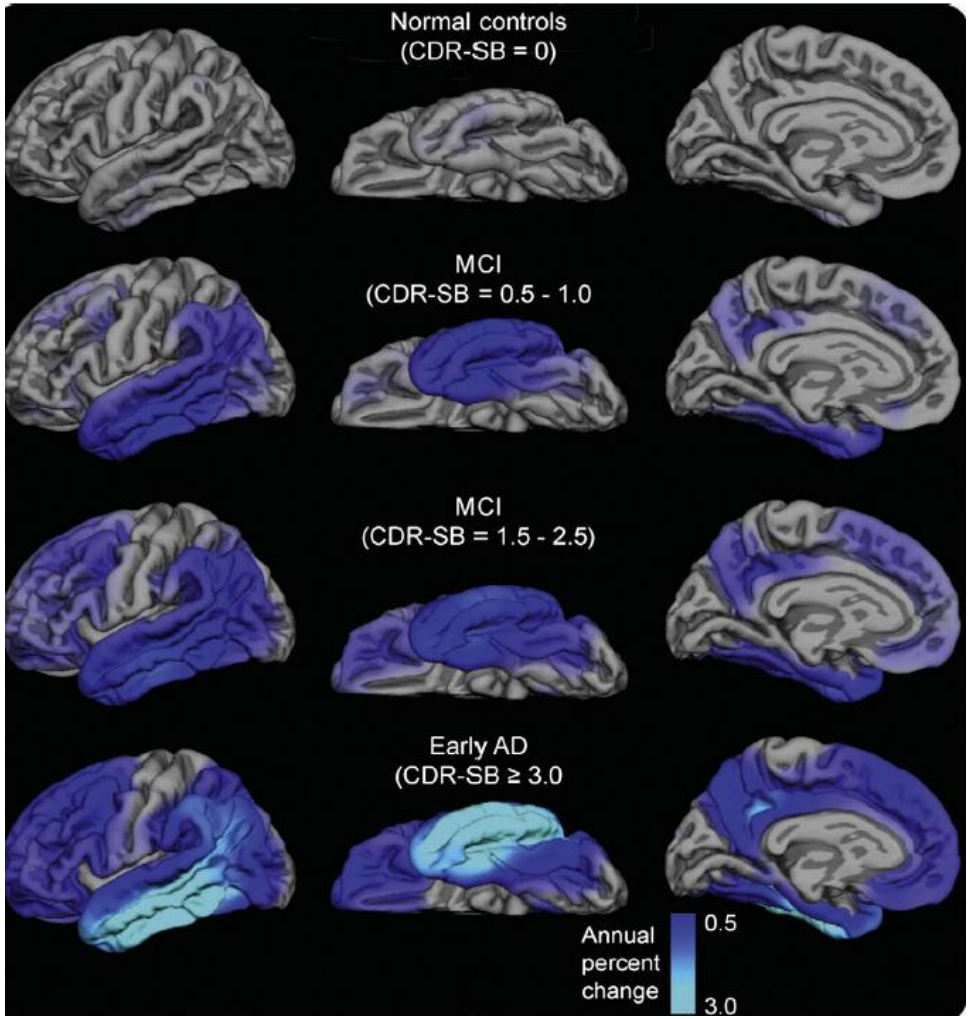


- FDG PET images are most often normal in the early stage and by visual assessment

QUANTITATIVE ANALYSIS

The most widely used FDG PET analysis methods for neurology research include, among others:
Neurostat (University of Washington, Seattle)
T-SUM tool implemented in PMOD hypometabolic convergence indexes
Statistical Parametric Mapping procedures (SPM; Wellcome Department of Cognitive Neurology, London, U.K.)

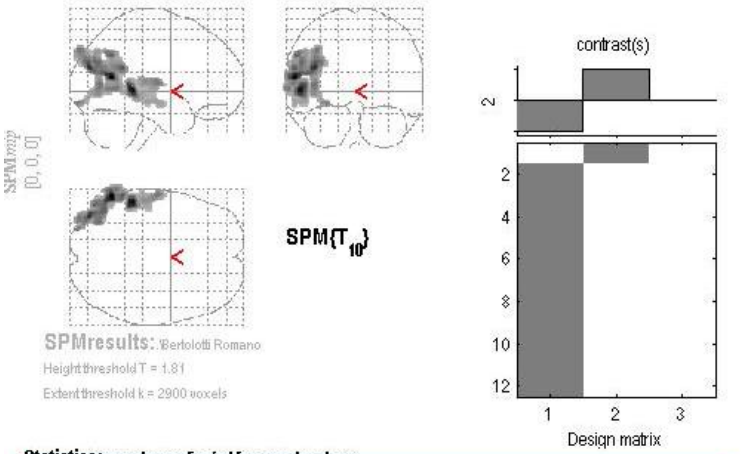
→ Spatial normalization procedures to enable voxel-based comparison of a patient's scans to a normative reference database
→ Yield statistical maps depicting deviations from norms at the individual voxel level, on a subject-by-subject basis



Annual atrophy rates as a function of degree of clinical impairment. Atrophy rates are most prominent in posterior brain regions early in the course of disease, spreading to anterior regions as the level of impairment increases, with relative sparing of sensorimotor regions

QUANTITATIVE ANALYSIS

Method: PET-SPM5, SPM8 dedicated Software



Statistics: *p-values adjusted for search volume*

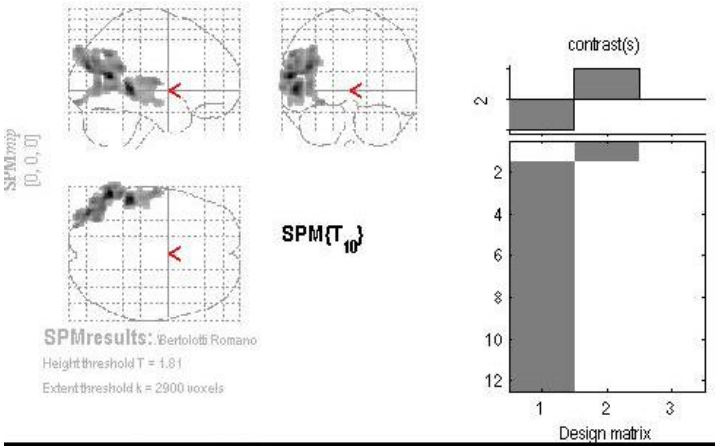
cluster-level			voxel-level					x,y,z (mm)		
$p_{corrected}$	k_E	$p_{uncorrected}$	$p_{FWE-corr}$	$p_{FDR-corr}$	T	$(Z_=)$	$p_{uncorrected}$			
0.070	2985	0.000	1.000	0.861	4.85	3.40	0.000	-60	-58	14
			1.000	0.861	4.51	3.26	0.001	-54	-38	0
			1.000	0.861	3.93	2.99	0.001	-40	-82	24

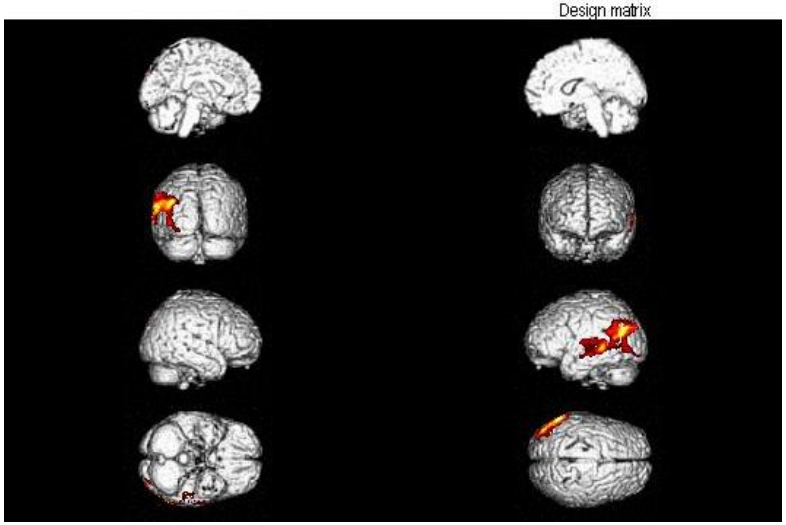
table shows 3 local maxima more than 8.0mm apart

Height threshold: T = 1.81, p = 0.049 (1.000)
Extent threshold: k = 2900 voxels, p = 0.000 (0.081)
Expected voxels per cluster, <k> = 181.228
Expected number of clusters, <c> = 0.08
Expected false discovery rate, <= 0.86

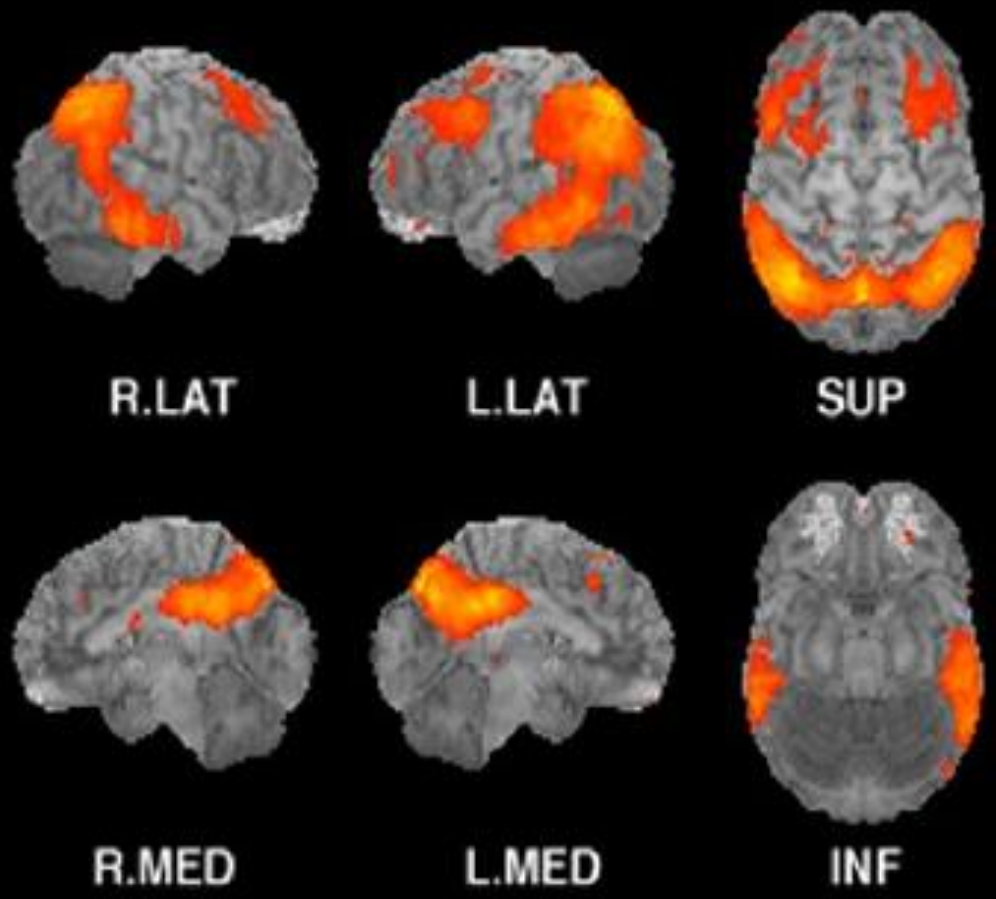
Degrees of freedom = [1.0, 10.0]
Smoothness FWHM = 11.4 12.2 13.2 (mm) = 5.7 6.1 6.6 (voxels)
Search vol: 4058312 cmm; 507289 voxels; 2113.0 resels
Voxel size: [2.0, 2.0, 2.0] mm (1 resel = 230.98 voxels)

- ✓ **Comparison of uptake value with normal control database**
- ✓ *P* value < 0.01

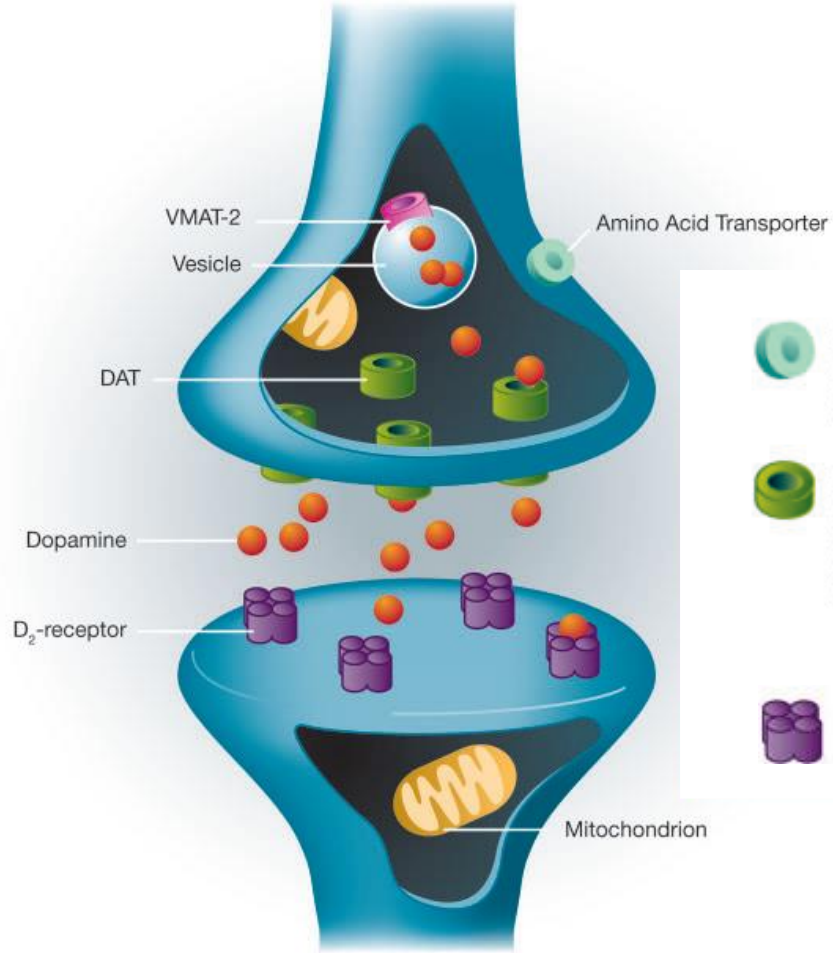




Quantitative evaluation of glucose rate uptake

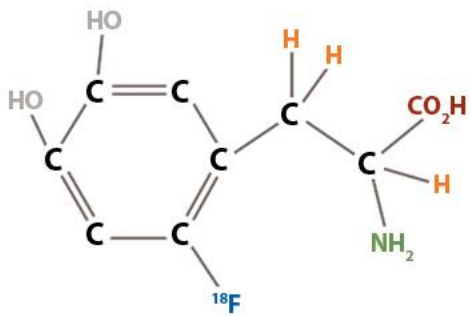


DOPAMINERGIC IMAGING



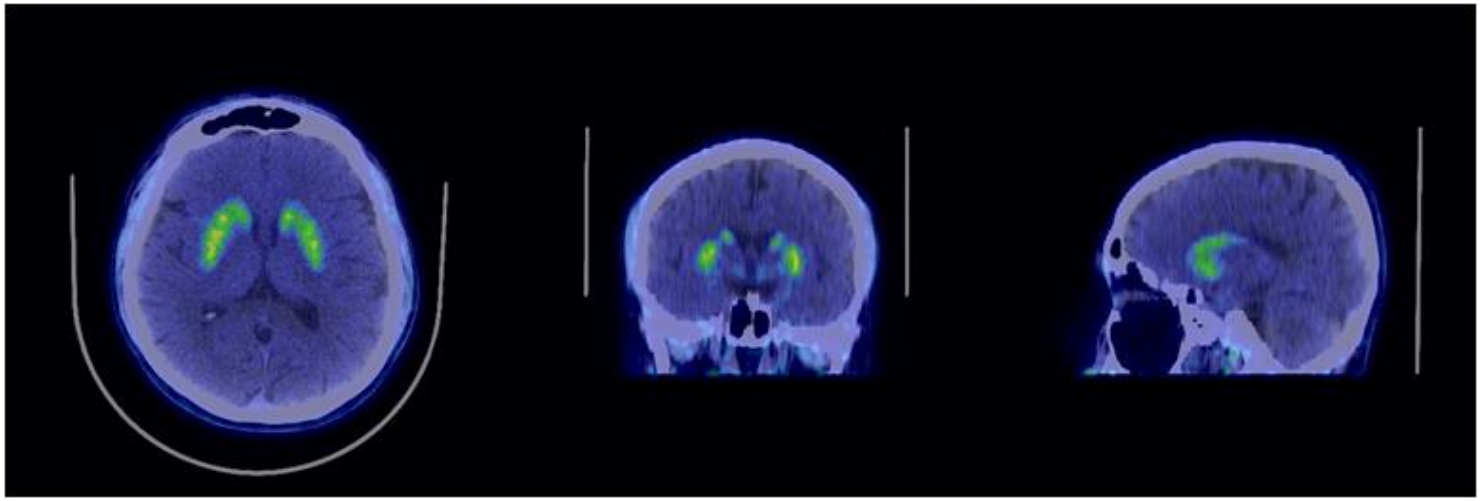
Presynaptic radioligand	SPECT	PET
DOPA decarboxylase activity (measures dopamine synthesis)		[^{18}F]dopa
DAT Ligand for dopamine transporter (provides measures of functioning dopaminergic terminals)	[^{123}I]FP-CIT	
Postsynaptic radioligands D2 receptor	[^{123}I]IBZM	

DOPA decarboxylase activity: [^{18}F]DOPA PET



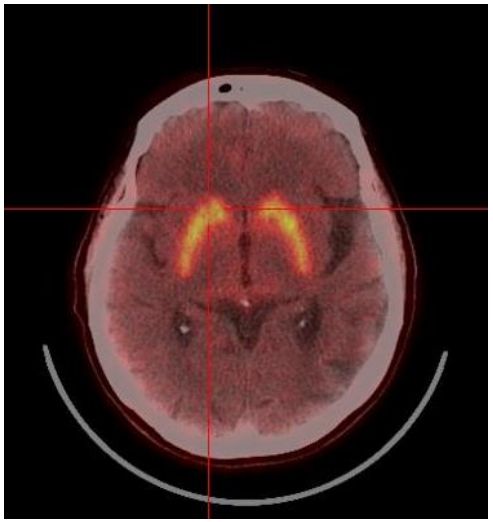
Functional state of dopamine innervations in living brain
Pre-synaptic radioligand

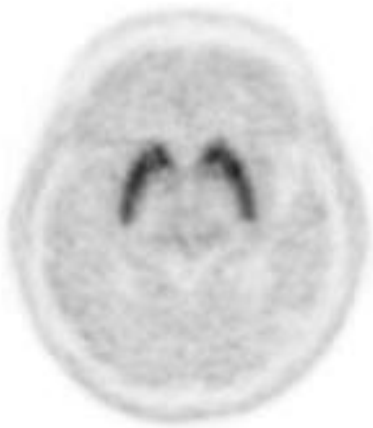
PET/CT



- Striatal [18F]DOPA uptake has been shown to correlate with dopaminergic cell densities in the substantia nigra and with striatal dopamine levels.
- Uninfluenced by dopaminergic medication, suggesting the usefulness of [18F]DOPA PET as a biomarker for monitoring the progression.

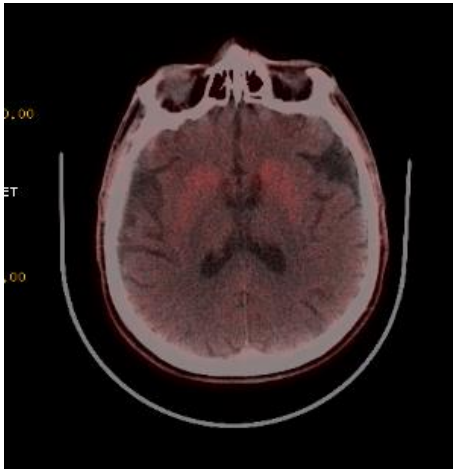
DOPA decarboxylase activity: [^{18}F]DOPA PET/CT

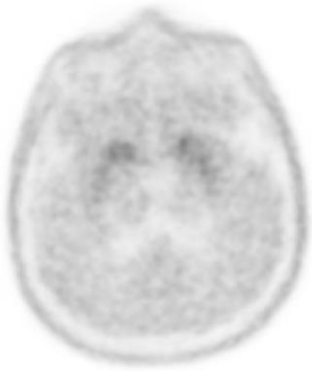




Drug induced tremor
Normal uptake

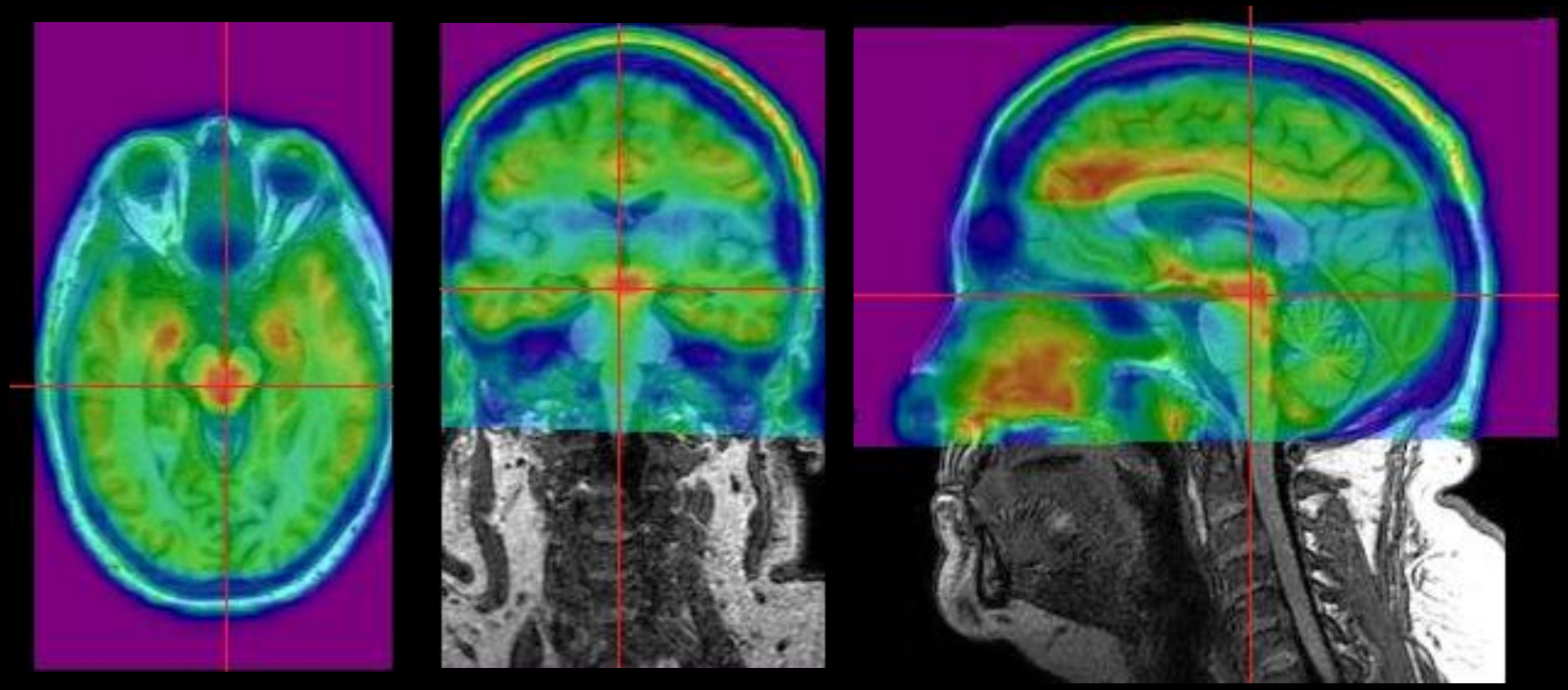
Lower [18F]DOPA uptake in the putamen has also been correlated with greater severity of motor symptoms and greater severity of bradykinesia and rigidity in PD





Advanced Parkinson's disease

[^{18}F]dopa PET/MR fusion
Dynamic PET imaging

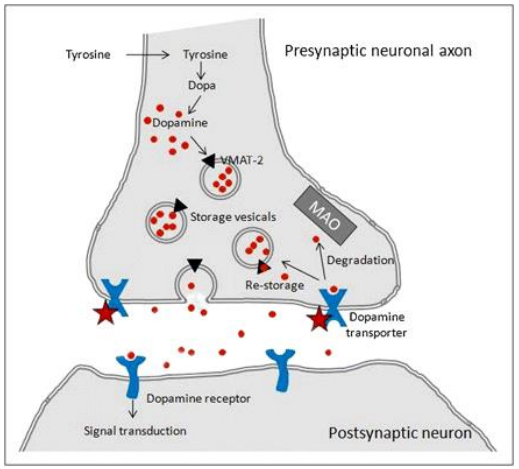


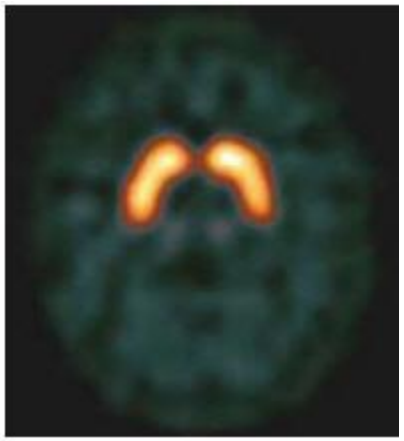
PD
Restless leg syndrome

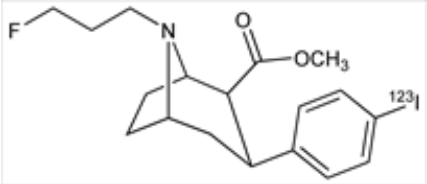
Dopamine transporter (DAT): [^{123}I]FP-CIT SPECT (DatScan)

- ✓ DAT is a sodium chloride–dependent transmembrane protein
- ✓ DAT controls dopamine levels by active reuptake of dopamine from the synaptic cleft after its interaction with the postsynaptic receptor
- ✓ Striatal 123I-FP-CIT uptake is correlated with DAT density

Visualization of the presynaptic DAT distribution in the striatum







Europe

2000 authorized for clinical use for the differential diagnosis of patients with clinically uncertain Parkinsonian syndrome

2006 expanded for the differential diagnosis of probable dementia with Lewy bodies from Alzheimer disease

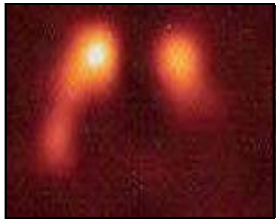
USA

2011 FDA approval of 123I-FP-CIT for clinical use

Dopamine transporter (DAT): [^{123}I]FP-CIT SPECT

Functional integrity of dopaminergic nerve terminals in the striatum
Pre-synaptic radioligand

Normal



H&Y 1

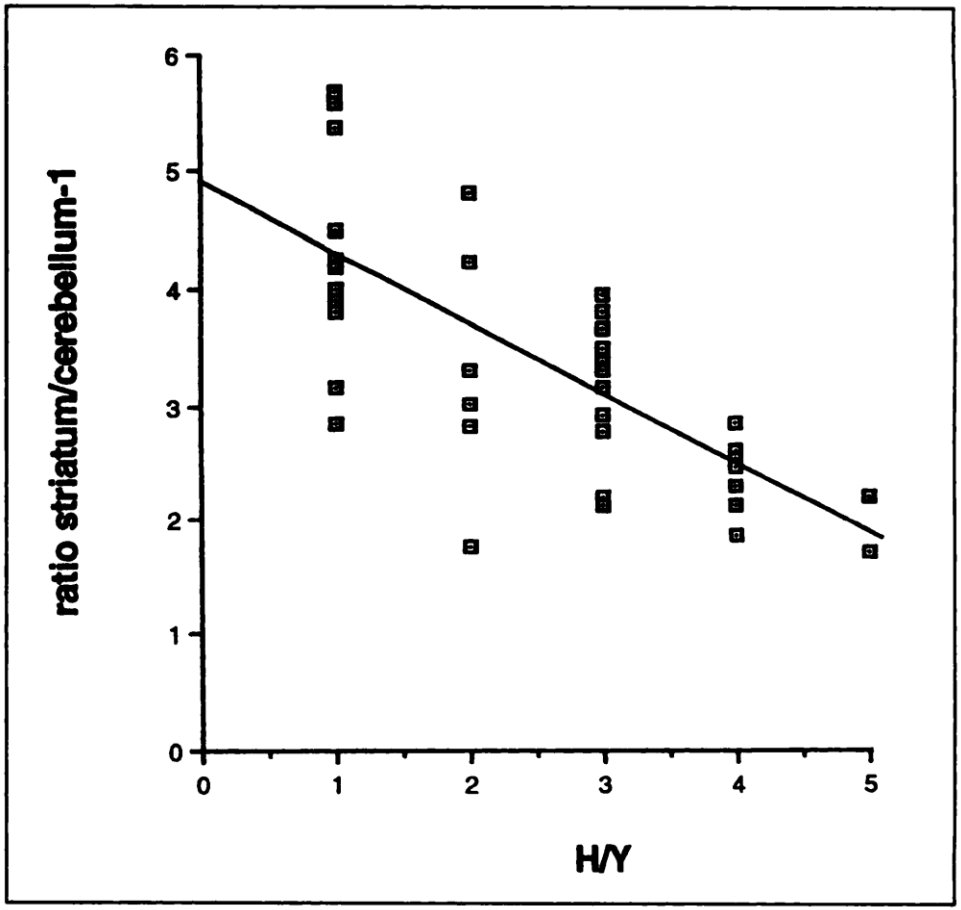
H&Y 2

H&Y 3

Biomarker of Parkinson disease progression (related to the Hoehn & Yahr rating scale)

Annual rate of reduction of striatal DAT uptake 6 - 13% in PD patients
(versus 0 to 2.5% in healthy controls)

Correlation between [123I]FP-CIT binding ratio and clinical severity of locomotor disability

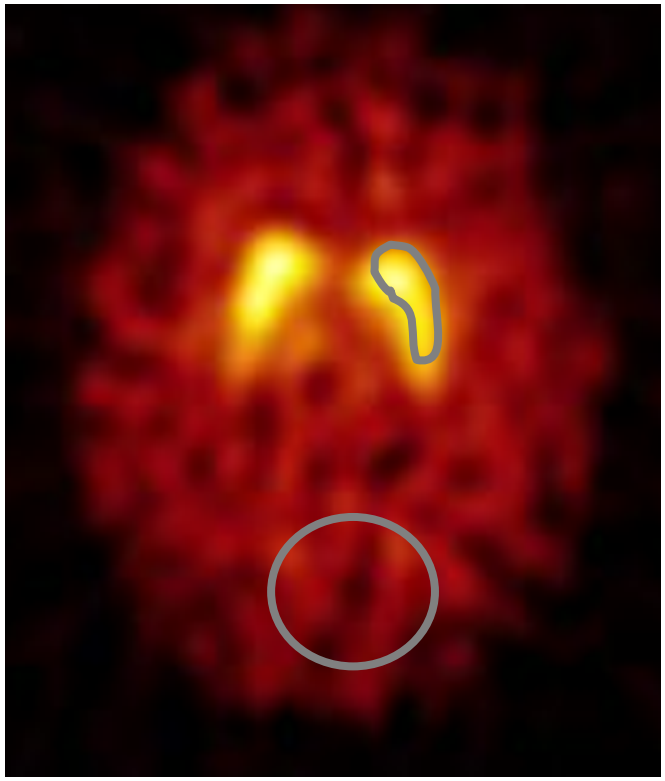


Putamen uptake of [123I]FP-CIT inversely correlates with Unified Parkinson's Disease Rating scale (UPDRS)

ROI (Region of Interest) method for quantification

Striatum/posterior cortex binding ratio

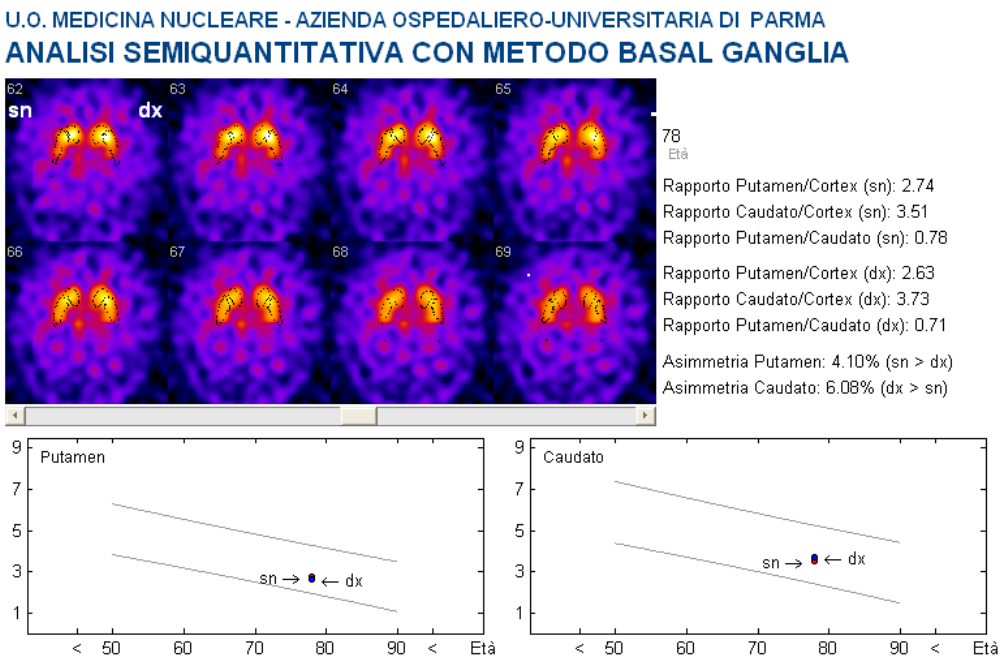
Striatum ROI cnts/ occipital ROI cnts %



QUANTITATIVE ANALYSIS

Method: Basal Ganglia dedicated Software

Eur J Nucl Med Mol Imaging (2007)

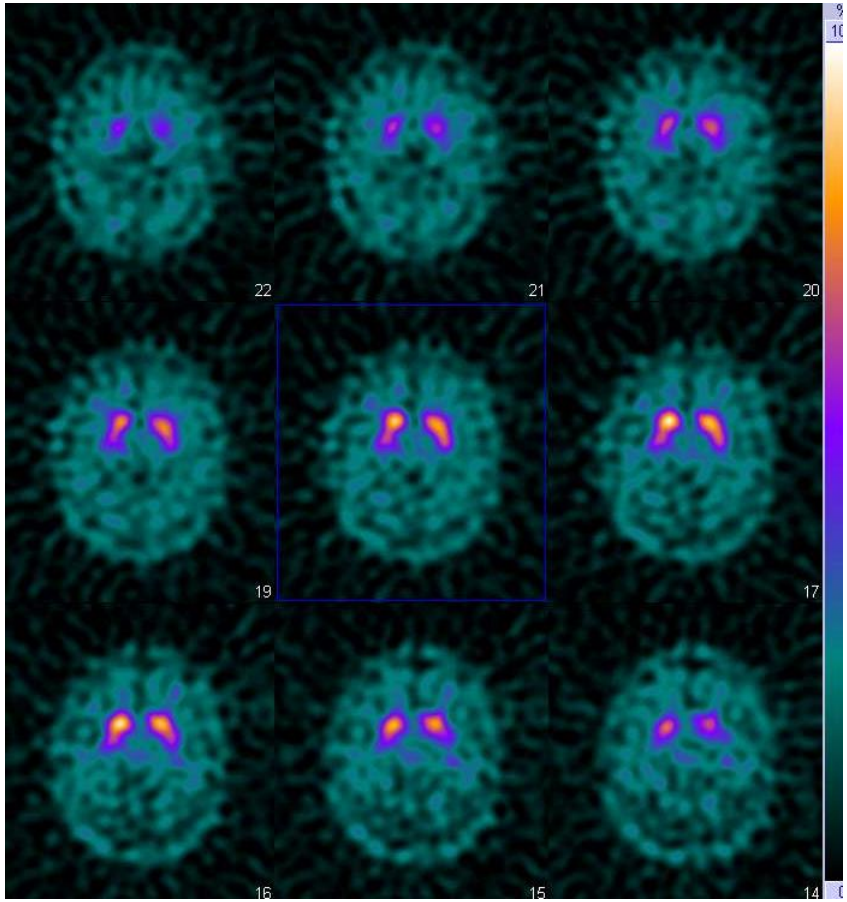


I risultati dell'esame del paziente sono rappresentati su di un grafico costruito analizzando con il metodo *Basal Ganglia* una popolazione non parkinsoniana di 50 soggetti (studio multicentrico). Le linee grigie rappresentano, all'interno della fascia di età tra 50 e 90 anni, i limiti di normalità con una confidenza del 90%.

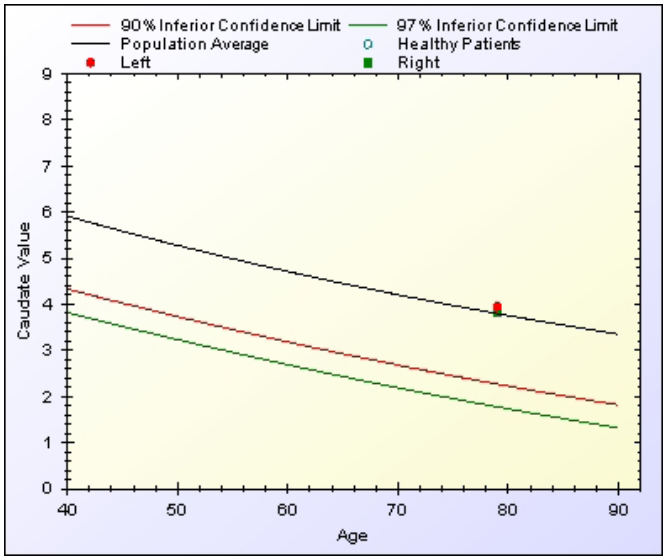
- ✓ 3D method for striatal authomatic segmentation with anatomical reference in the Talairach e Tournoux atlas
- ✓ **Comparison of uptake value with normal control database**.

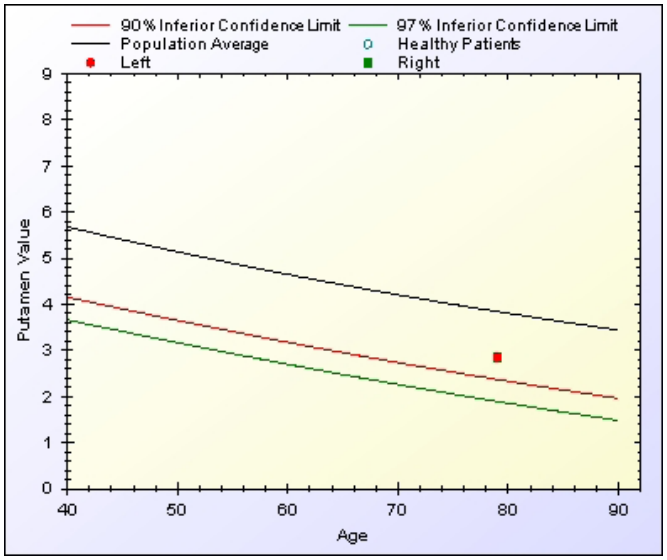
QUANTITATIVE ANALYSIS

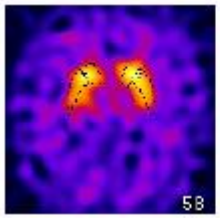
Method: Basal Ganglia dedicated Software

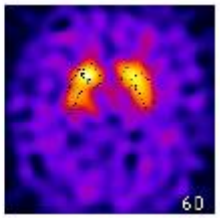


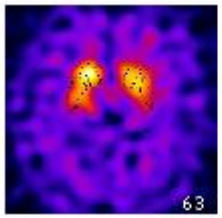
M, 64 yr
Right hand
tremor

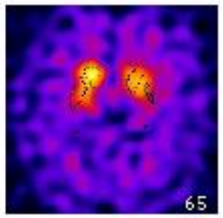






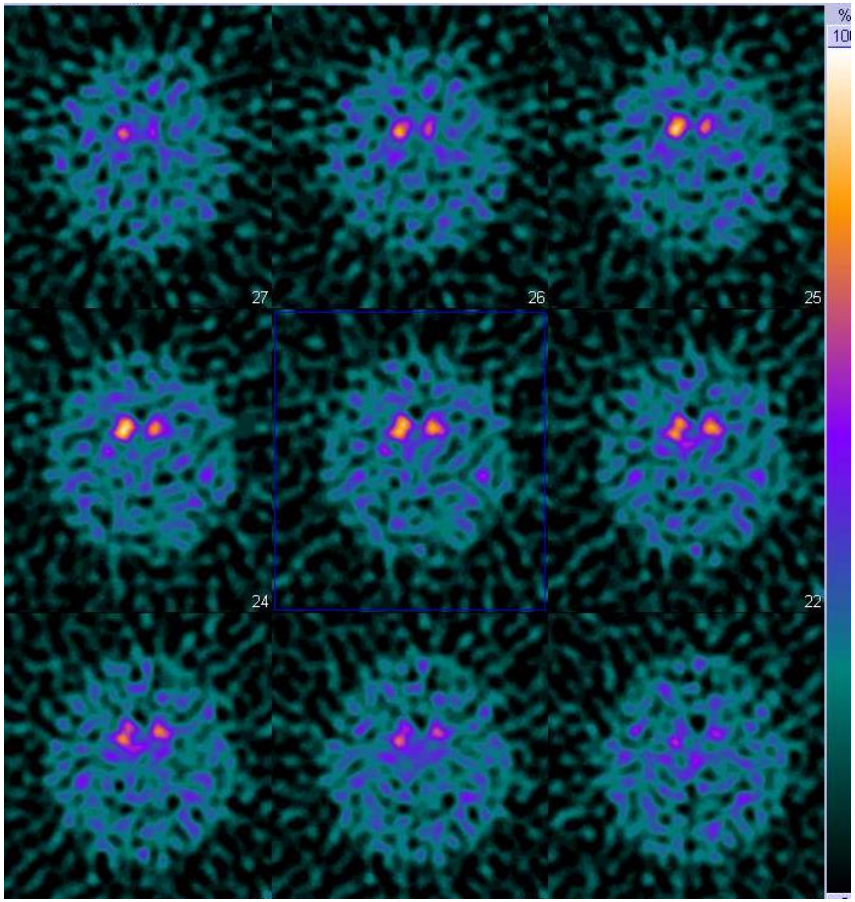




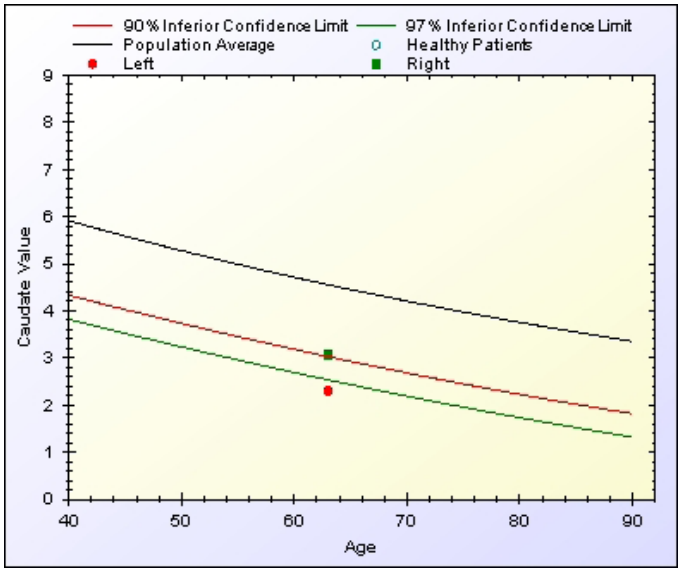


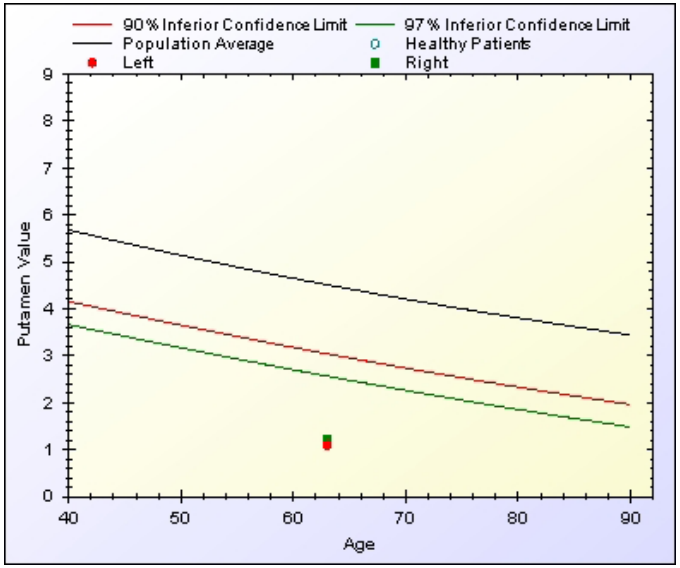
QUANTITATIVE ANALYSIS

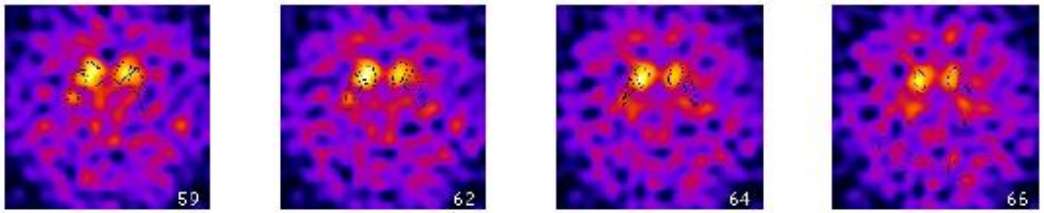
Method: Basal Ganglia dedicated Software



M, 60 yr
Hands tremor and bradikinesia

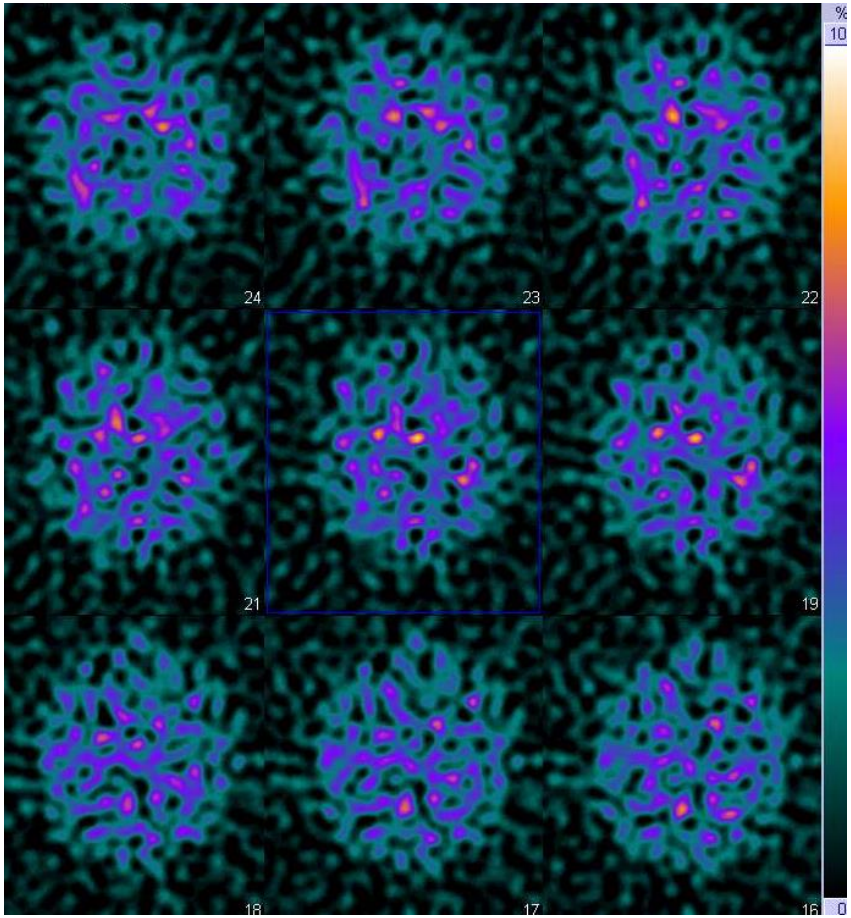




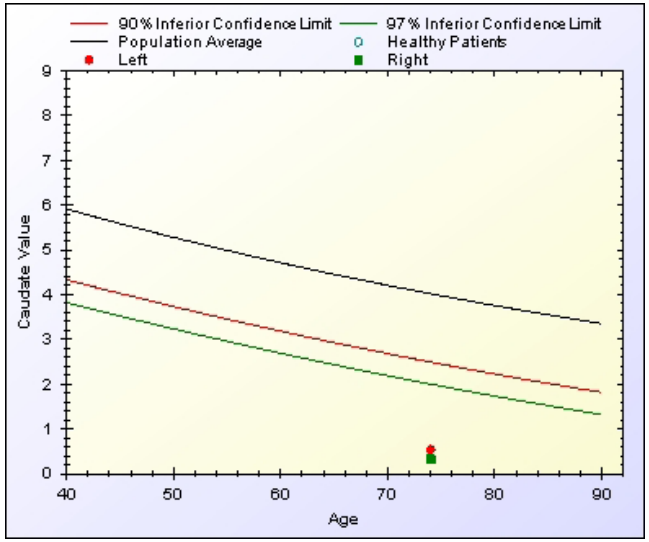


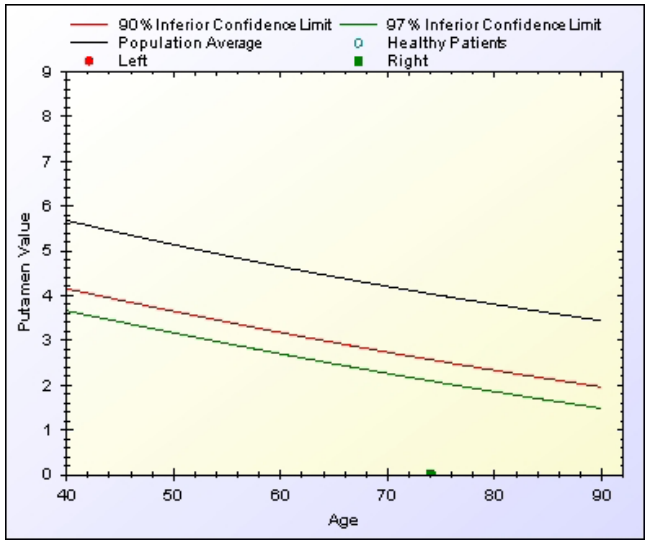
QUANTITATIVE ANALYSIS

Method: Basal Ganglia dedicated Software



M, 71 yr
Advanced
PD

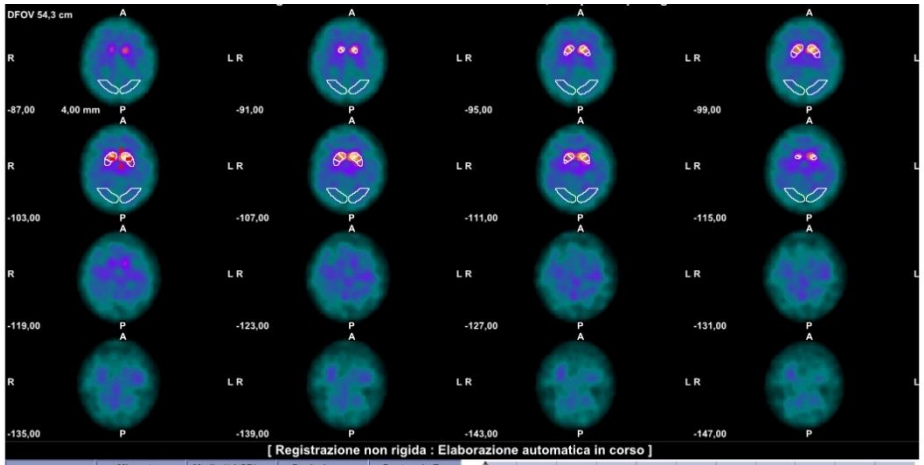




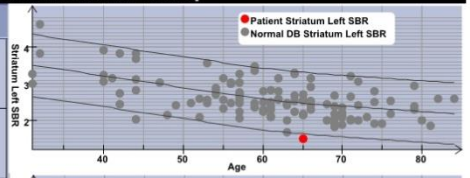
QUANTITATIVE ANALYSIS

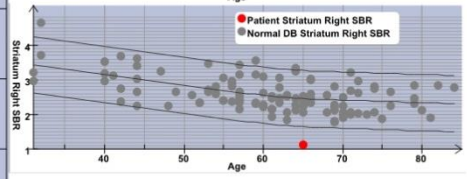
Method: DatQuant® (GE Healthcare)

Certified for clinical trials
Normal population: 18-85 yrs



	Misurato	Media (±1 SD)	Deviazione	Punteggio Z
Striatum Right SBR	+1,12	+2,46 (±0,40)	-54%	-3,30
Striatum Left SBR	+1,49	+2,47 (±0,42)	-40%	-2,33
Putamen Right SBR	+0,98	+2,38 (±0,39)	-59%	-3,58
Putamen Left SBR	+1,31	+2,36 (±0,41)	-45%	-2,58
Caudatus Right SBR	+1,46	+2,66 (±0,48)	-45%	-2,48
Caudatus Left SBR	+1,85	+2,70 (±0,50)	-31%	-1,69





M, 68 yr
Right arm tremor and
rest leg syndrome

	Misurato	Media (±1 SD)	Deviazione	Punteggio Z
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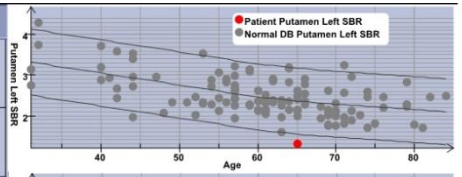

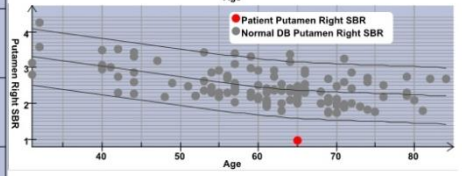

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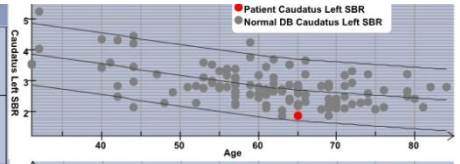
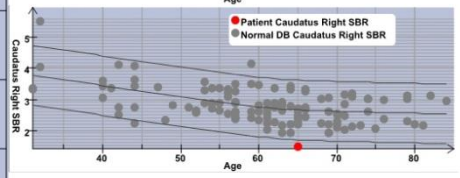




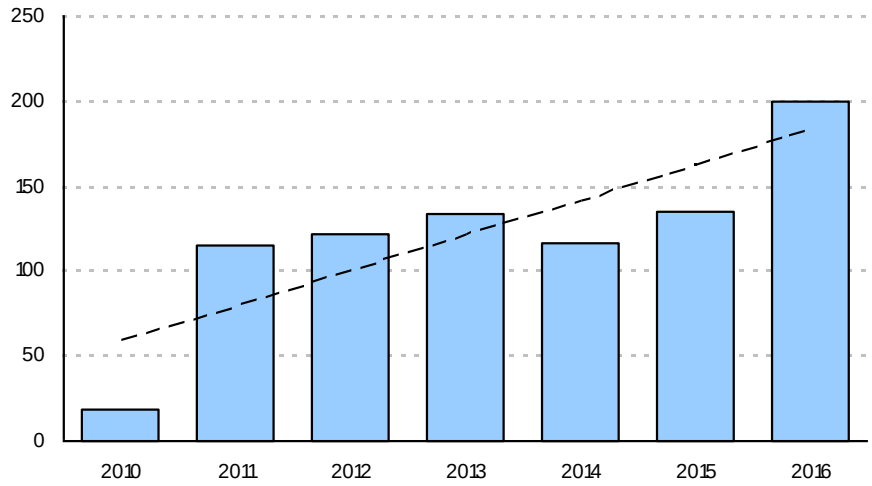
Drugs to be stopped for 4 wk before [123I]FP-CIT SPECT

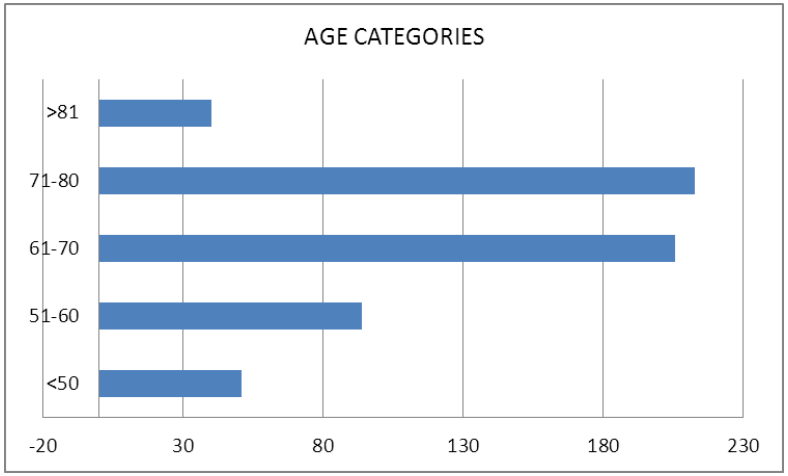
DRUG CLASS	DRUG NAME	EFFECT ON [^{123}I]FP-CIT binding
COCAINE		↓
AMPHETAMINES	d-Amphetamine methamphetamine methylphenidate	↓
CNS STIMULANTS	Phentermine or ephedrines	↓ influences are likely when used as tablets
MODAFINIL		↓
ANTIDEPRESSANTS	Mazindol bupropion radafaxine	↓
ADRENERGIC AGONISTS	Phenylephrine or norepinephrine	↑ influences are likely when infused at high doses
ANTICHOLINERGIC DRUGS		Benztropine ↓ Other anticholinergics ↑ (which will likely not affect visual assess)
OPIOIDS	Fentanyl	↓
ANESTHETICS	Ketamine PCP Isoflurane	↓

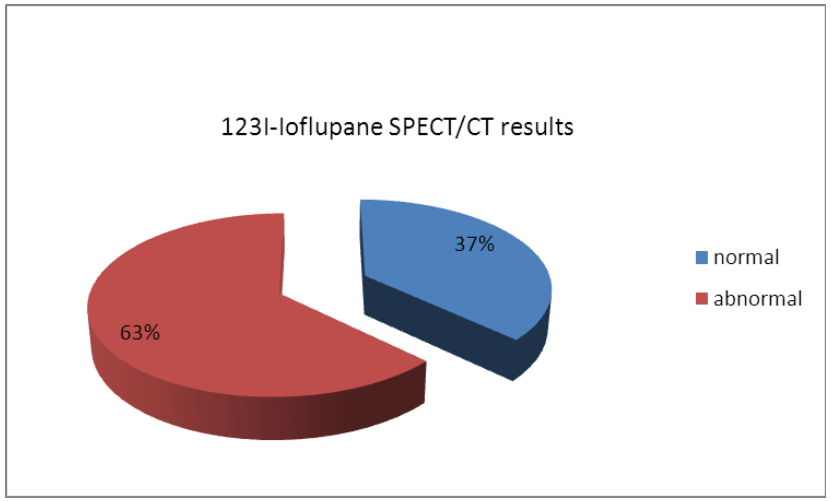
Antiparkinsonian drugs including L-dopa, dopamine agonists, monoamine oxidase-B inhibitors, and catechol-O-methyl transferase inhibitors do not need to be discontinued.

They showed no significant effect on the striatal 123I-FP-CIT uptake.

DAT imaging at AOU-PR

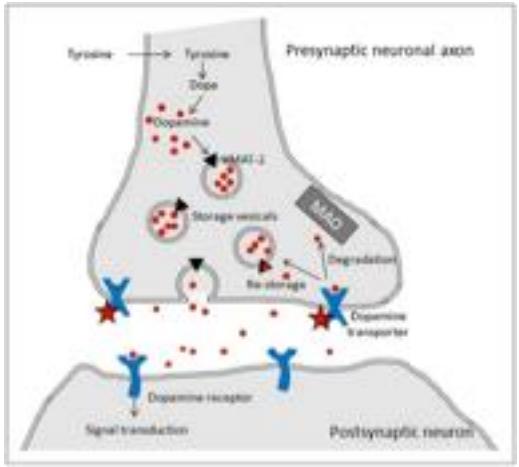


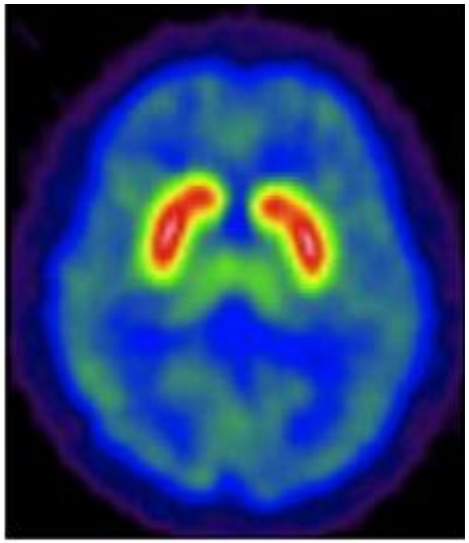


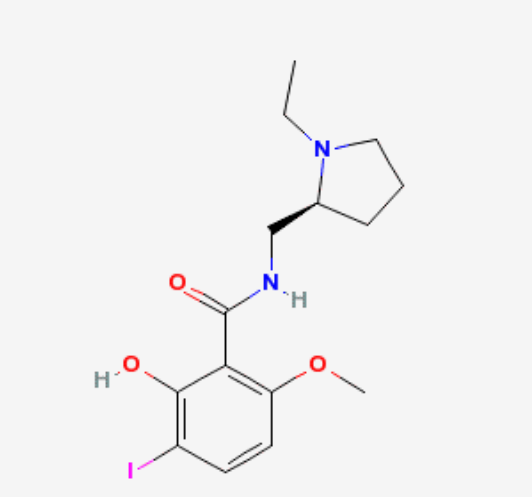


Dopamine receptor imaging D2/3R receptor: [^{123}I]IBZM SPECT

Postsynaptic radioligand
Selective D2/3R antagonist

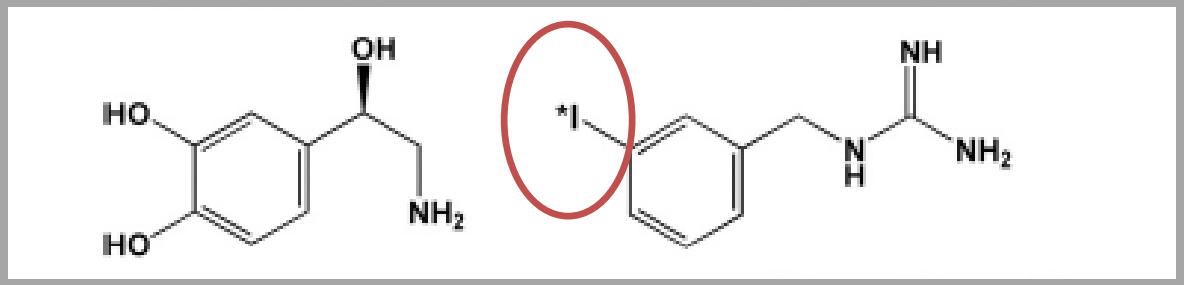






- Upregulation of D2/3R in early PD
- Biomarker of the striatal dopaminergic reward system in obesity

Cardiac adrenergic innervation: 123I-mIBG SPECT



*I = I-131 o I-123 o I-124

NE

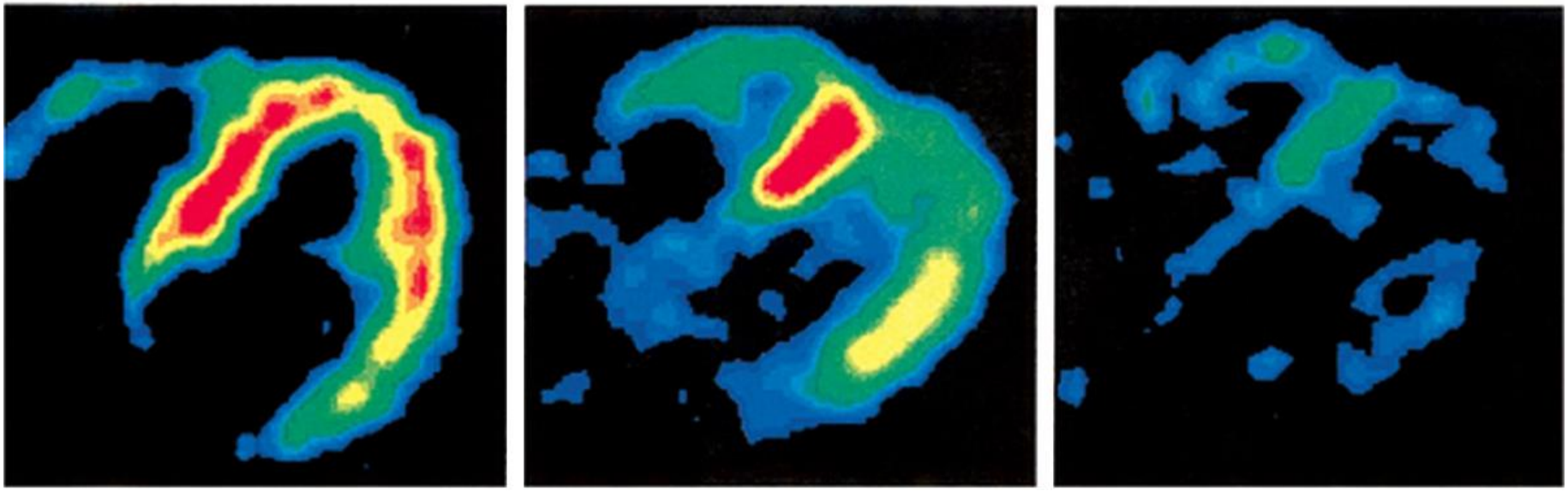
Metaiodobenzylguanidine

- **1994** [131I]MIBG received Food and Drug Administration (FDA) approval (NDA 20-084) as an imaging agent
- **2008** [123I]MIBG approved by FDA (NDA 22-290) as a tumor imaging agent (Adreview; GE Healthcare, Little Chalfont, UK).
- In Europe and Japan [123I]MIBG and [131I]MIBG were approved for tumor imaging more than 10 years ago

Progressive loss of uptake in Parkinson's disease

123I-*m*IBG SPECT

Normal **Parkinson**

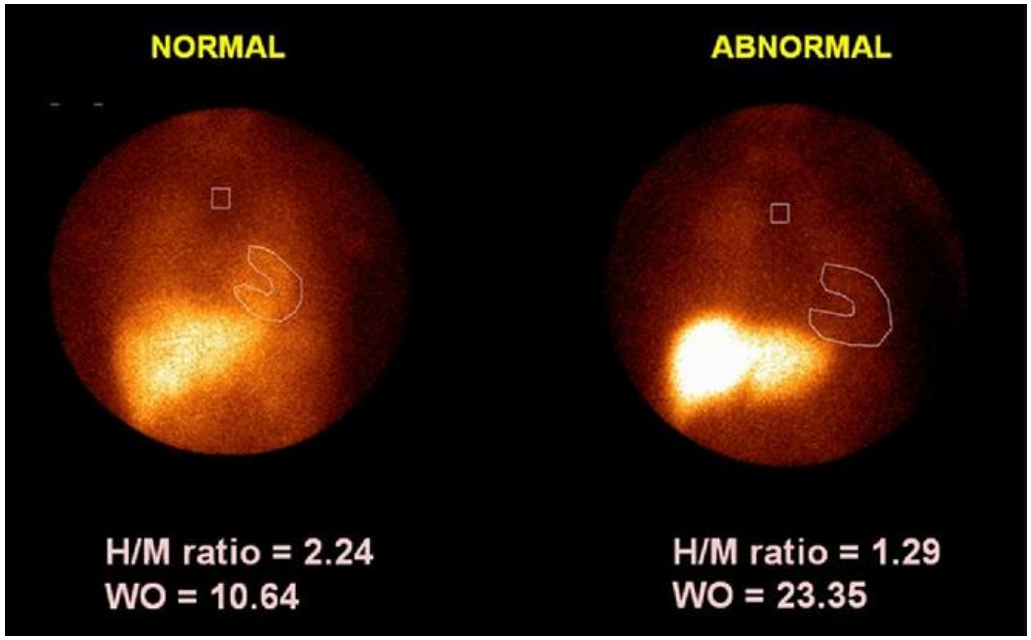


Baseline After 2 years

mIBG scanning

Early imaging
(15 min after injection)

Late imaging (4 hrs)

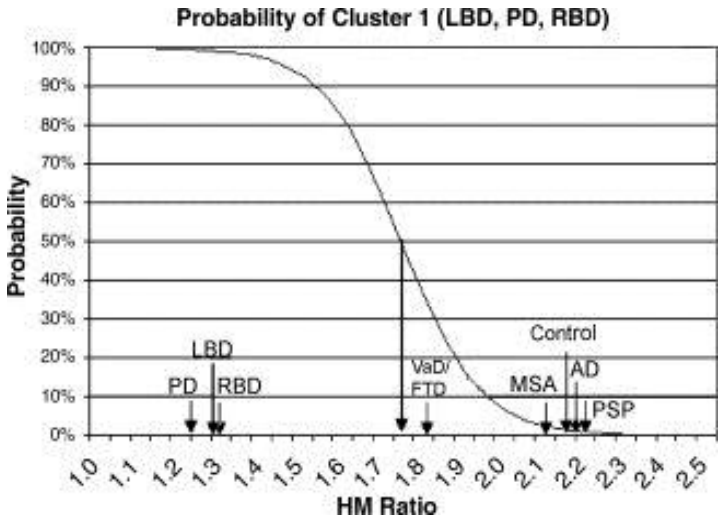


Early H/M reflects the integrity of presynaptic nerve terminals and uptake-1 function.

Late H/M combines information on neuronal function from uptake to release through the storage vesicle at the nerve terminals.

Washout is an index of the degree of sympathetic drive. Increased adrenergic drive is associated with high myocardial 123I-MIBG washout and low myocardial 123I-MIBG delayed uptake.

Meta-analysis of 123I-mIBG cardiac scintigraphy for the diagnosis of Lewy body–related (DLB and PD) disorders and non-LB-related diseases (ie, AD and MSA)

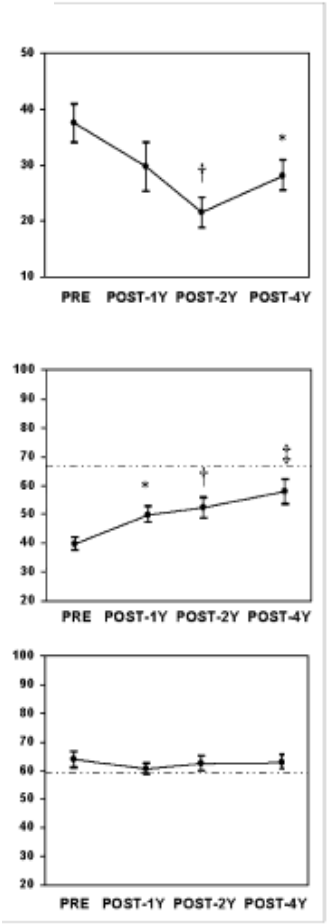


- 124 clinical samples drawn from 47 published studies.
- Data from 2965 subjects

- 123I-mIBG cardiac scintigraphy can accurately distinguish between ***2 movement disorders***, ***Parkinson's disease and multiple system atrophy***, and between ***2 common causes of dementia, Alzheimer's disease and dementia with Lewy bodies***.
- H/M ratio threshold of 1.77 yielded 94% sensitivity and 91% specificity for the discrimination of these diagnostic clusters
- RBD's (rapid eye movement sleep behavior disorder) inclusion in the LB-related cluster suggests that it, too, may be an LB-related condition.

2011 Movement Disorder Society

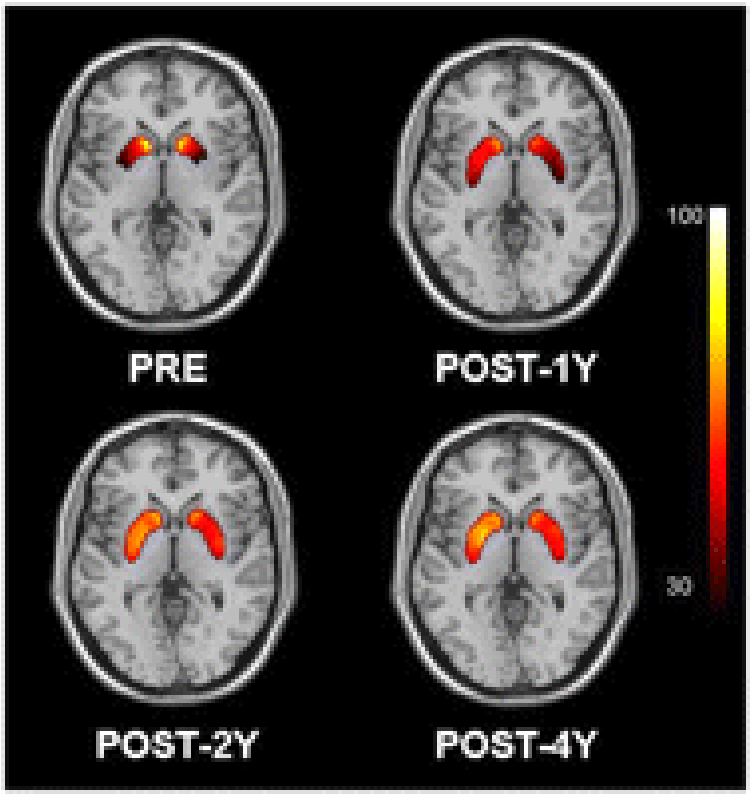
Dopamine Cell Implantation in Parkinson's Disease: Long-Term Clinical and ^{18}F-FDOPA PET Outcomes



UPDRS motor ratings

Striatal 18F-FDOPA uptake at baseline (pre) and at 1 (post 1 y), 2 (post 2 y), and 4 (post 4 y) years after bilateral implantation of fetal dopaminergic cells into putamen of PD patients.

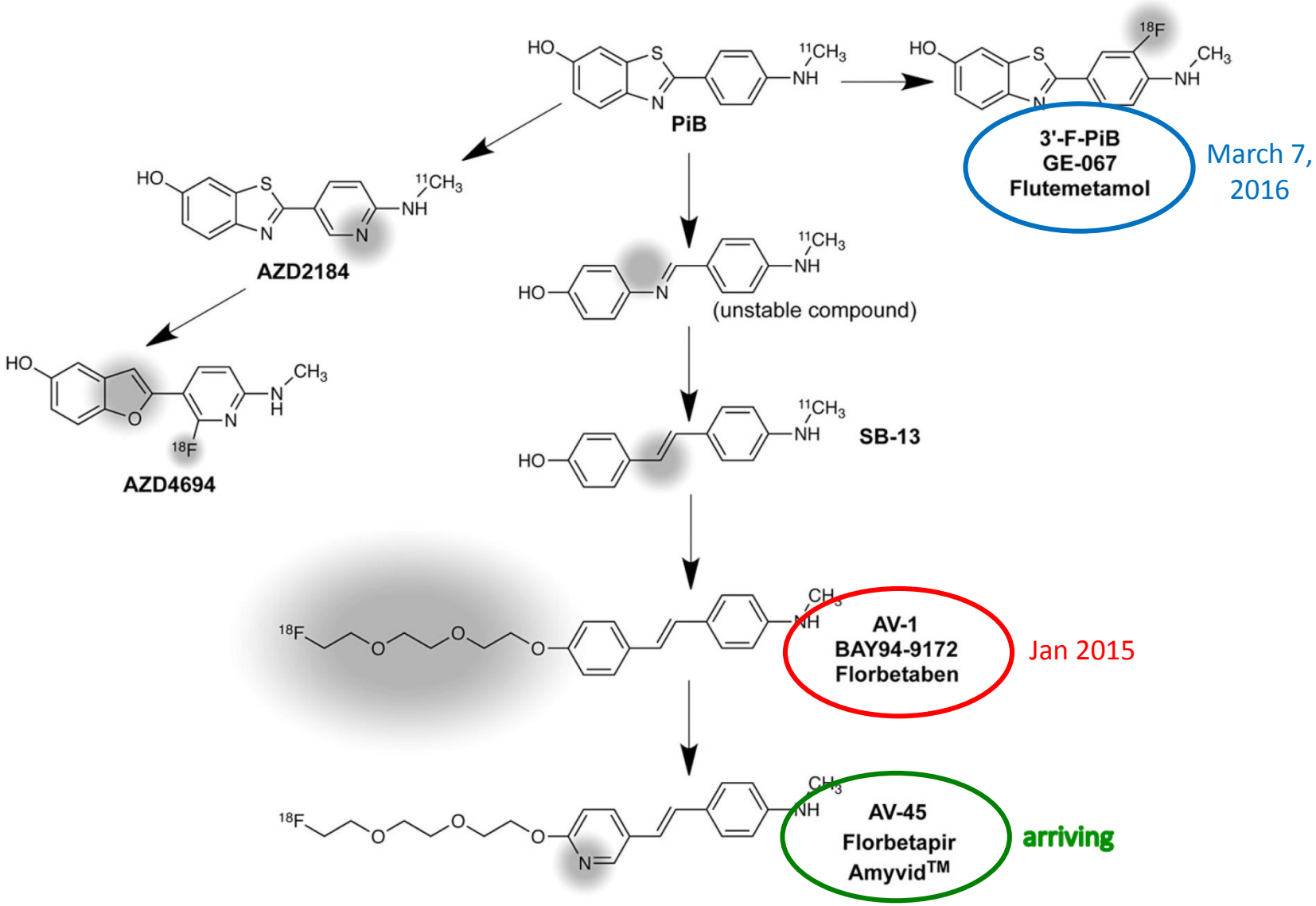
Nongrafted caudate after implantation



Significant treatment effect was noted over 2 y

JNM 2010

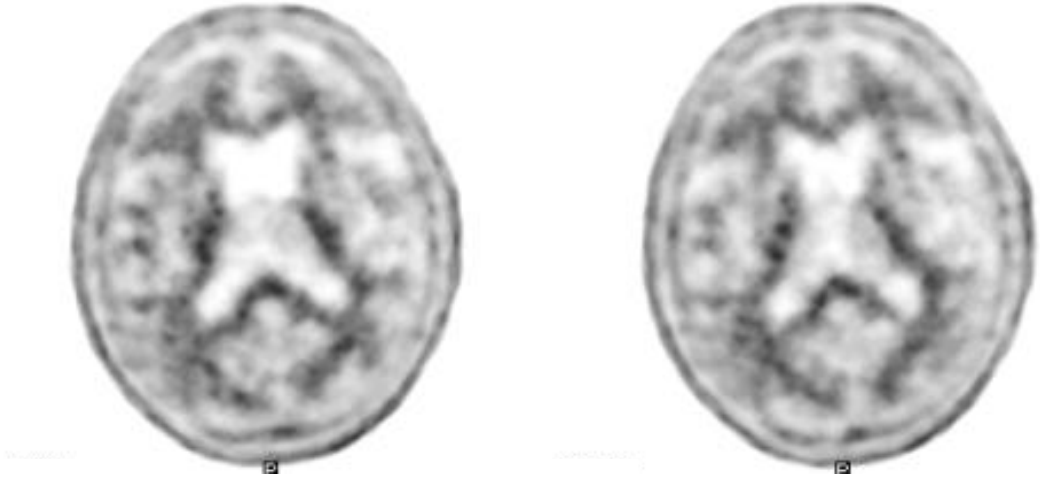
PET amyloid tracers: fibrillar Aβ-amyloid deposition (Jan 2015)



PET amyloid tracers

18F-Fluorbetaben

Normal distribution (phisiological uptake in white matter)
Regional retention reflects the regional density of amyloid plaques



BAPL 1 (β Amyloid Plaque Load)

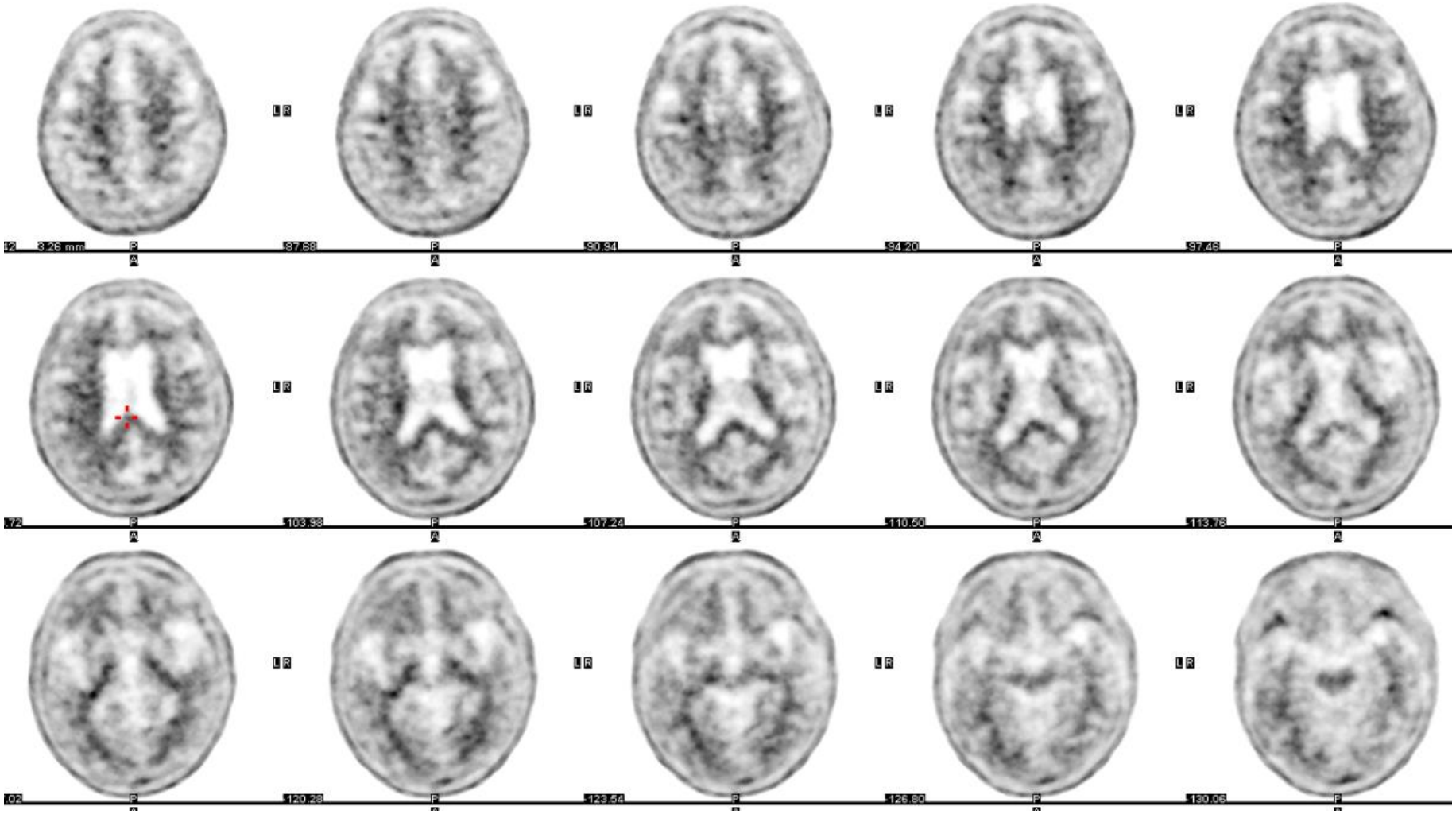
→ Qualitative regional grading score 1-4

- Temporal
- Parietal
- Precuneus
- Frontal

→ Global assessment (BAPL) score 1-3

PET amyloid tracers

18F-Fluorbetaben



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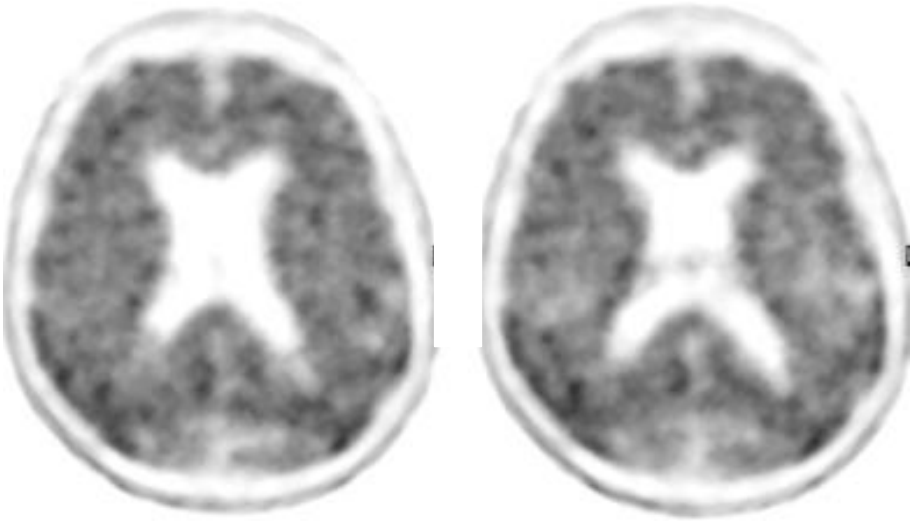
Regional retention reflects the regional density of amyloid plaques

PET amyloid tracers

18F-Fluorbetaben

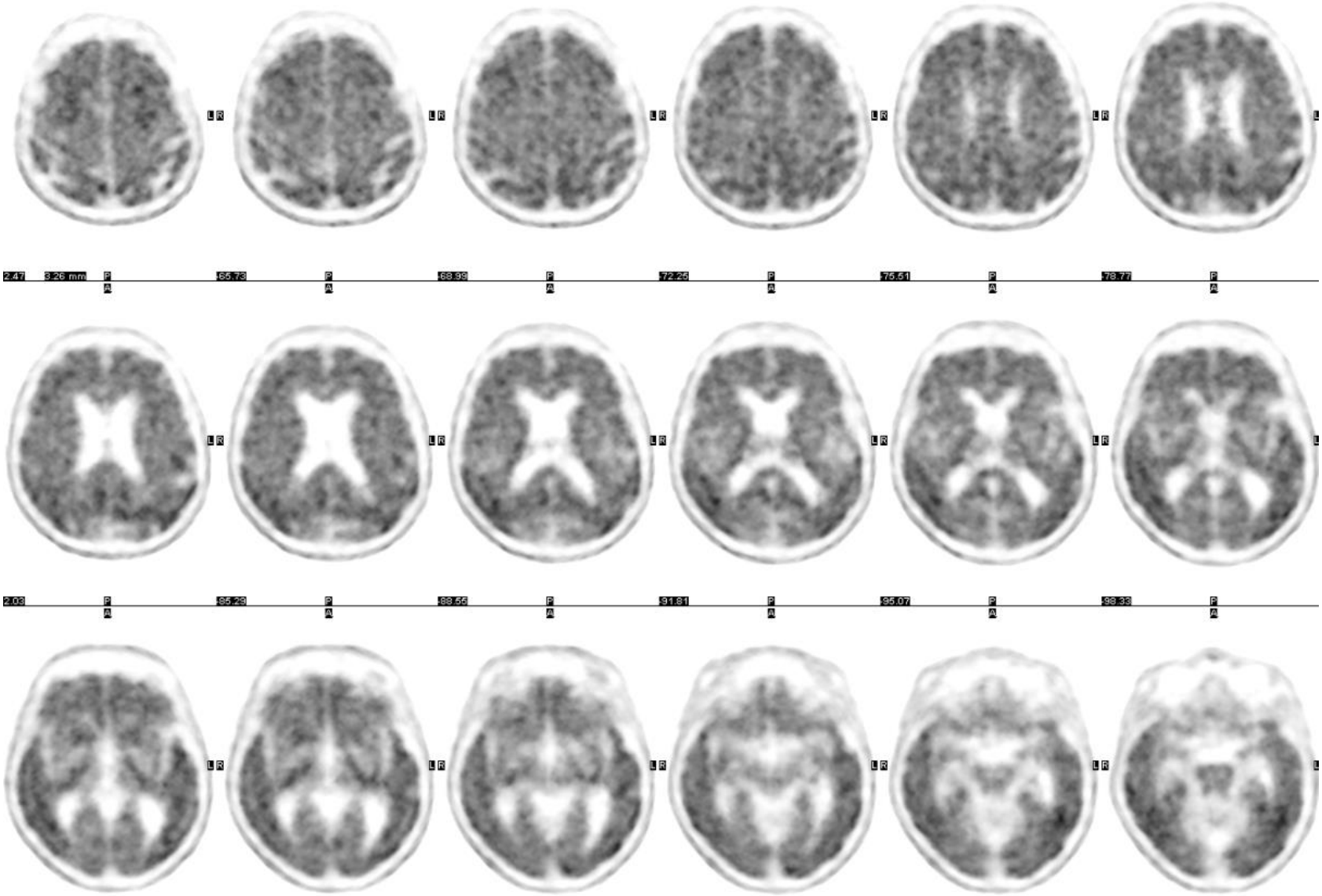
Cortical binding equal to or greater than white matter binding



BAPL 3 (β Amyloid Plaque Load)

PET amyloid tracers

18F-Fluorbetaben

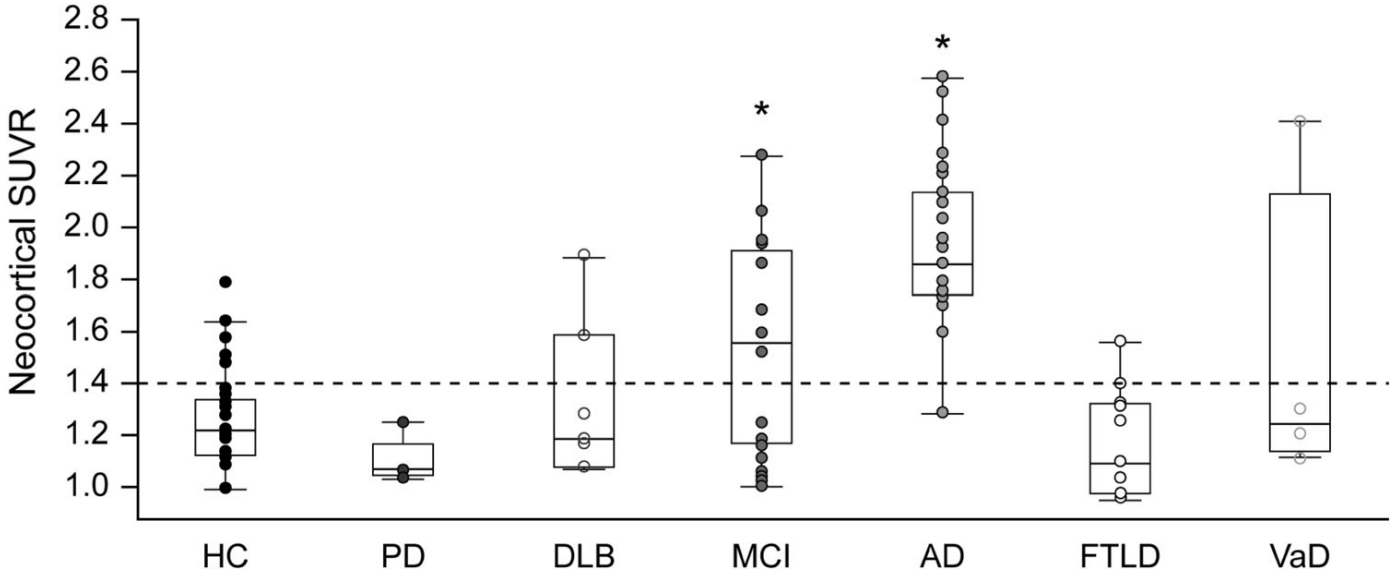


BAPL 3 (β Amyloid Plaque Load)
Crtical binding equal to or greater than white matter binding

PET amyloid tracers

18F-Fluorbetaben

- Robust separation between AD patients and healthy age-matched control (HC) subjects both by visual image interpretation and simple quantitative measures
- Recently completed phase II clinical studies further confirmed these results.
- Matching the reported post-mortem distribution of Aβ plaques, FBB allows detection of AD pathology in the brain of subjects with a wide spectrum of neurodegenerative diseases



Clin Transl Imaging (2015)

ELSEVIER
CrossMark
Alzheimer's & Dementia 11 (2015) 1050-1068
Alzheimer's & Dementia

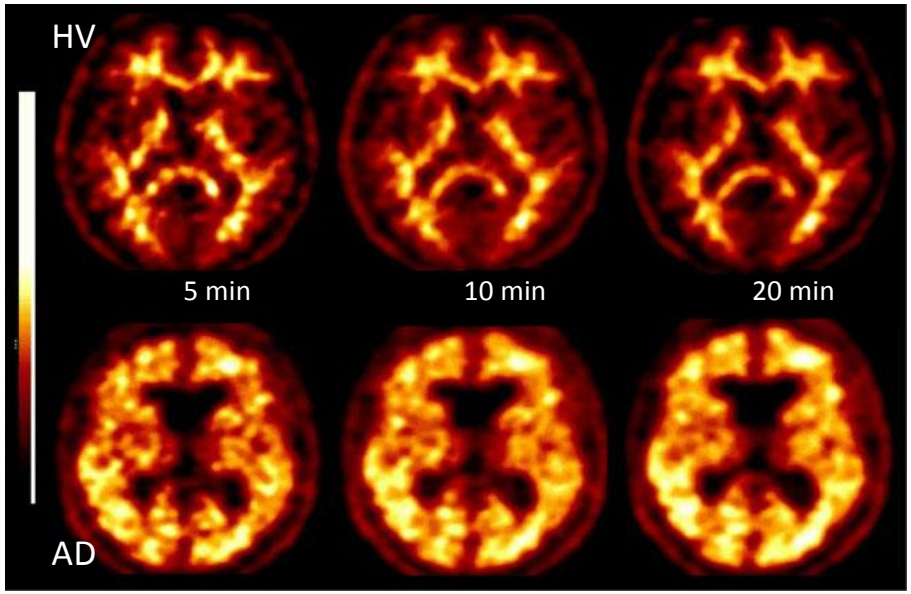
The influence of biological and technical factors on quantitative analysis of amyloid PET: Points to consider and recommendations for controlling variability in longitudinal data

Mark E. Schmidt[a,*], Ping Chiao[b], Gregory Klein[c], Dawn Matthews[d], Lennart Thurfjell[e], Patricia E. Cole[f], Richard Margolin[g], Susan Landau[h], Norman L. Foster[i], N. Scott Mason[j], Susan De Santi[k], Joyce Suhy[c], Robert A. Koeppe[l], William Jagust[h], for the Alzheimer's Disease Neuroimaging Initiative

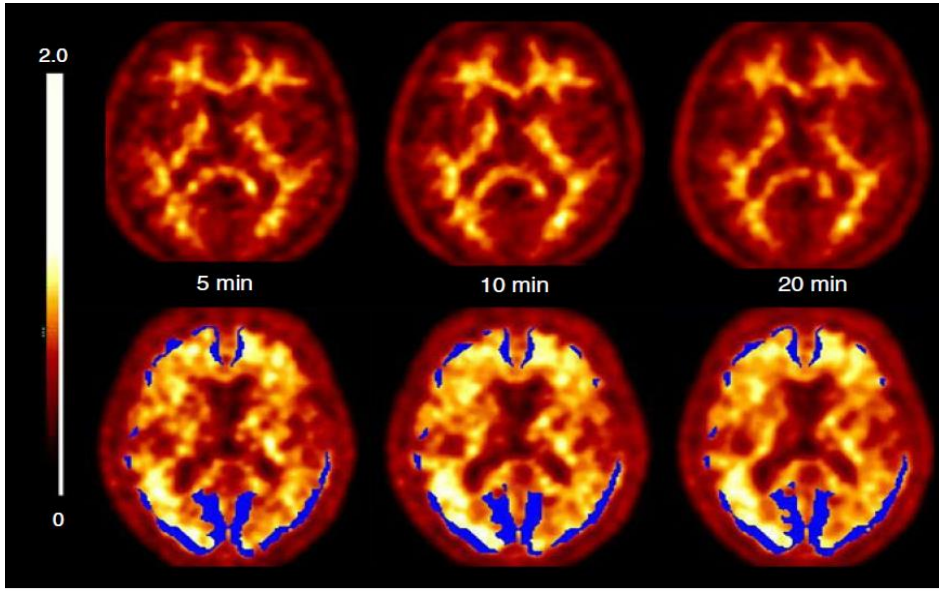
→ Measurement of subtle changes in amyloid burden requires quantitative analysis of image data.

→ Reliable quantitative analysis of amyloid PET scans acquired at multiple sites and over time requires rigorous standardization of

- acquisition protocols
- subject management
- tracer administration
- image quality control
- image processing and analysis methods



Scan duration 90 min after injection



Blue clusters represent brain regions with z-scores >2.5

PET amyloid tracers: visual assessment

Visual assessment of florbetaben PET images by three blinded readers in the whole-brain analysis group (n = 74)

	Estimate	95% Lower CI	95% Upper CI
Sensitivity (%)			
Majority read	97.9	93.8	100.0
Reader 1	97.9	93.8	100.0
Reader 2	100.0	92.5	100.0
Reader 3	97.9	93.8	100.0
Specificity (%)			
Majority read	88.9	77.0	100.0
Reader 1	88.9	77.0	100.0
Reader 2	85.2	71.8	98.6
Reader 3	85.2	71.8	98.6

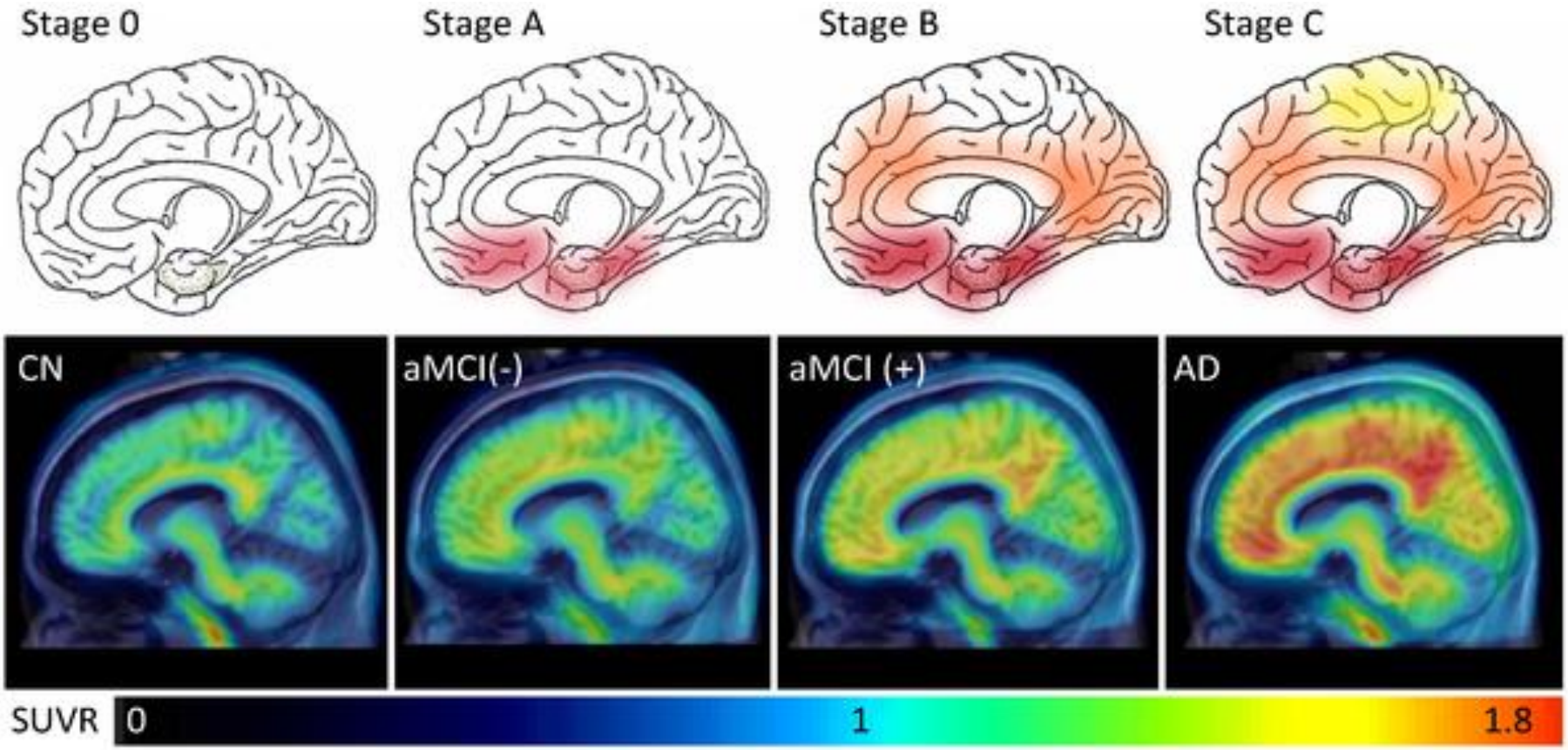
Alzheimer's & Dementia 11 (2015)

Inter-reader agreement in visual assessment of 18F-FBB images (n = 86)

	Amy+	Amy-	Severity Score 3	Severity Score 2
Major Reader	59	27	48	11
Reader 1	59	27	47	12
Reader 2	57	29	45	12

AOU-PR
AIFA certified training

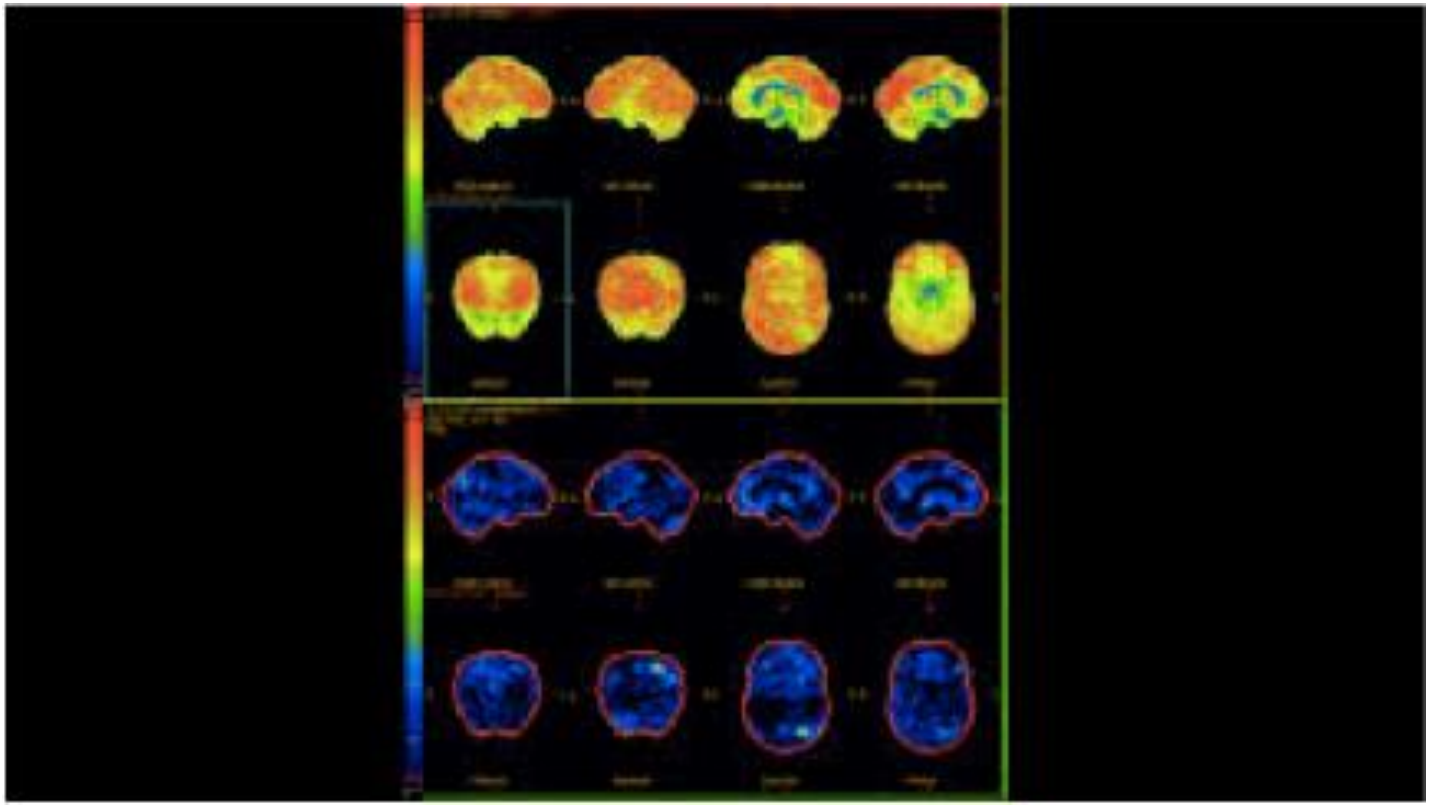
Cerebral amyloid burden in Amnestic Mild Cognitive Impairment and Alzheimer's Disease



QUANTITATIVE ANALYSIS

Method: Cortex ID Suite (GE Healthcare)

Normal database for 18F-Flutemetamol



Quantitative maps with comparison to age-matched normals

QUANTITATIVE ANALYSIS (Normal)

Method: Cortex ID Suite (GE Healthcare)

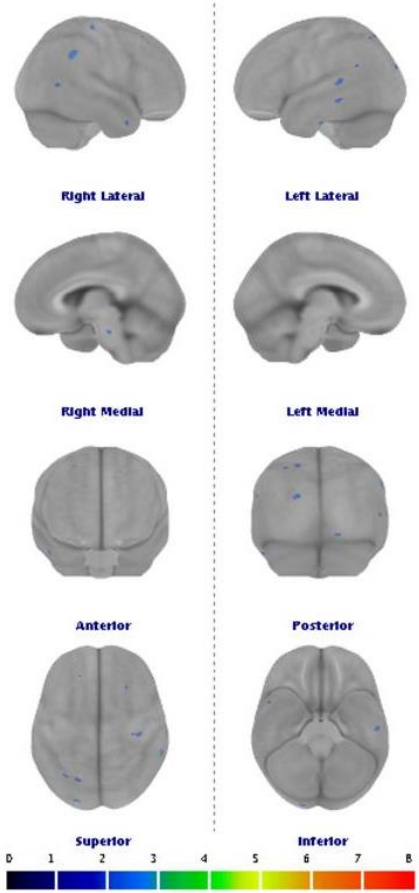
PET Flutemetamol Test Results

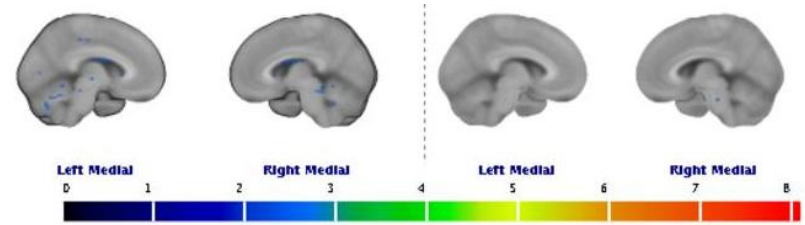
Ordering Provider : Not Available
Reading Physician : VP 20 min
Inj.Dose : 176.59 MBq/ml Flutemetamol

Age : 79
Test Date : 09 May 2016
Birth Date : 24 Aug 1936
Exam : PET BRAIN VIZAMYL LATE
Scanner : GE MEDICAL SYSTEMS Discovery IQ

Region	Uptake Ratio	Z-Score
Composite	0.48	-0.53
Prefrontal R	0.43	-1.02
Prefrontal L	0.42	-1.10
Anterior Cingulate R	0.46	-0.55
Anterior Cingulate L	0.51	-0.22
Precuneus PostCing R	0.45	-0.83
Precuneus PostCing L	0.47	-1.11
Parietal R	0.51	0.12
Parietal L	0.50	0.28
Temporal Lateral R	0.54	0.28
Temporal Lateral L	0.54	0.40
Occipital R	0.53	-0.16
Occipital L	0.51	-0.74
Sensorimotor R	0.48	-0.57
Sensorimotor L	0.46	-0.59
Temporal Mesial R	0.47	-1.39
Temporal Mesial L	0.48	-1.03
Cerebellum Grey	0.36	-1.45
Cerebellum Whole	0.44	-1.17
Pons	1.00	0.00
Reference Region: Pons		

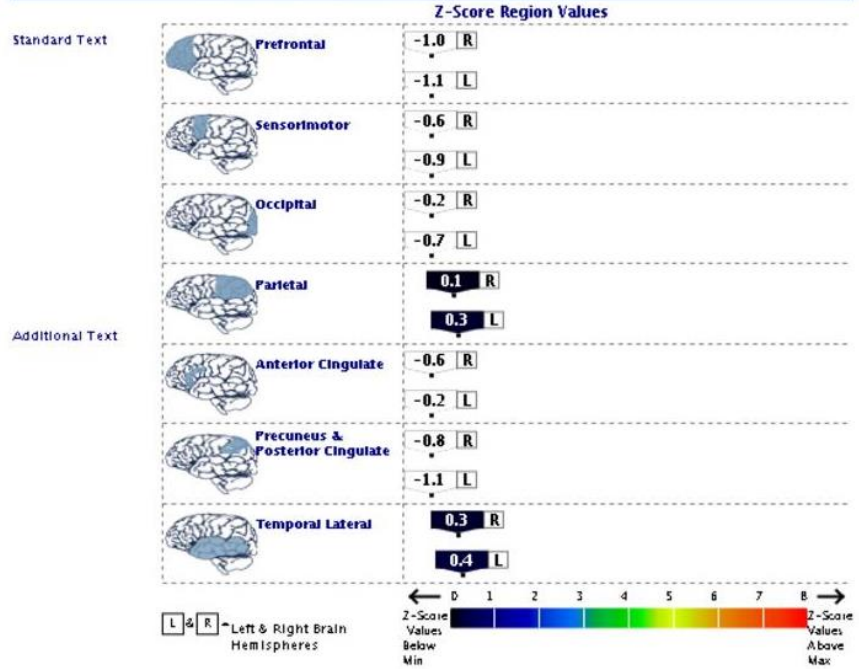
Z-Score Images





*Representative normal images have Z-scores for most brain areas less than 2 SD.
Images shown have a 2 SD threshold applied

Z-Score Region Values



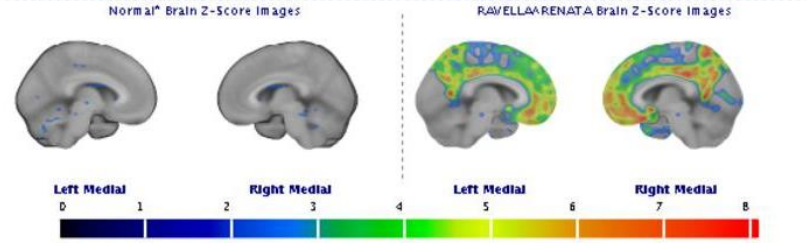
QUANTITATIVE ANALYSIS (AD)

Method: Cortex ID Suite (GE Healthcare)

PET Flutemetamol Test Results

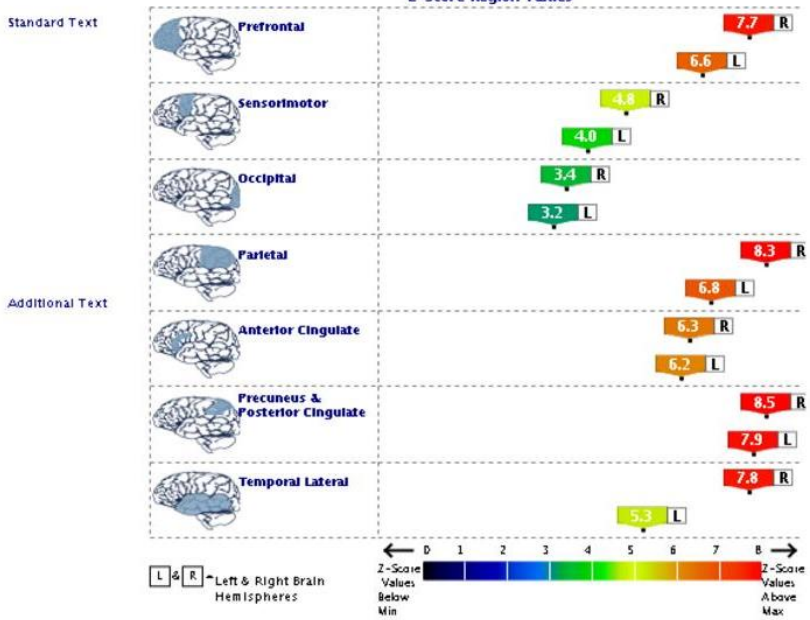
Patient Id : ASLTRAS000230275
Ordering Provider : Not Available
Reading Physician : VP 20 min
Inj.Dose : 194 MBq/ml Flutemetamol

Age : 83
Test Date : 30 May 2016
Birth Date : 17 Jan 1933
Exam : PET VIZAMYL LATE
Scanner : GE MEDICAL SYSTEMS Discovery IQ



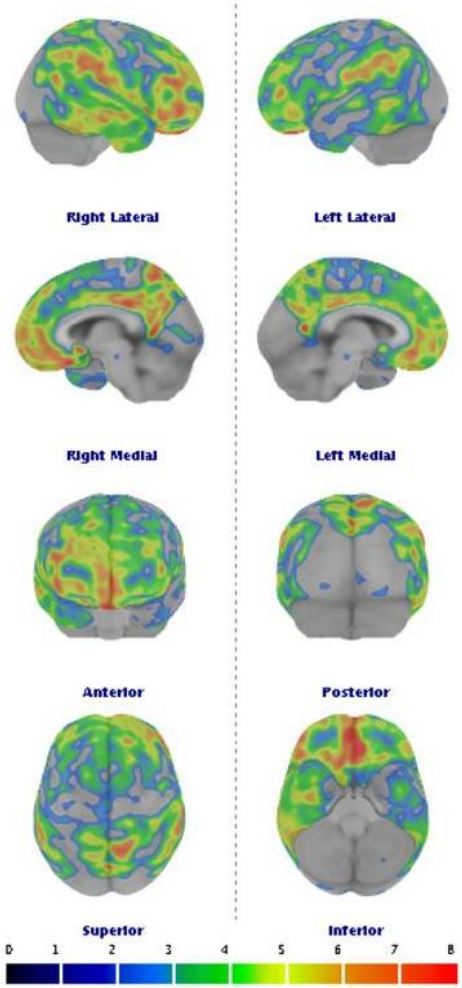
*Representative normal images have Z-scores for most brain areas less than 2 SD.
Images shown have a 2 SD threshold applied

Z-Score Region Values

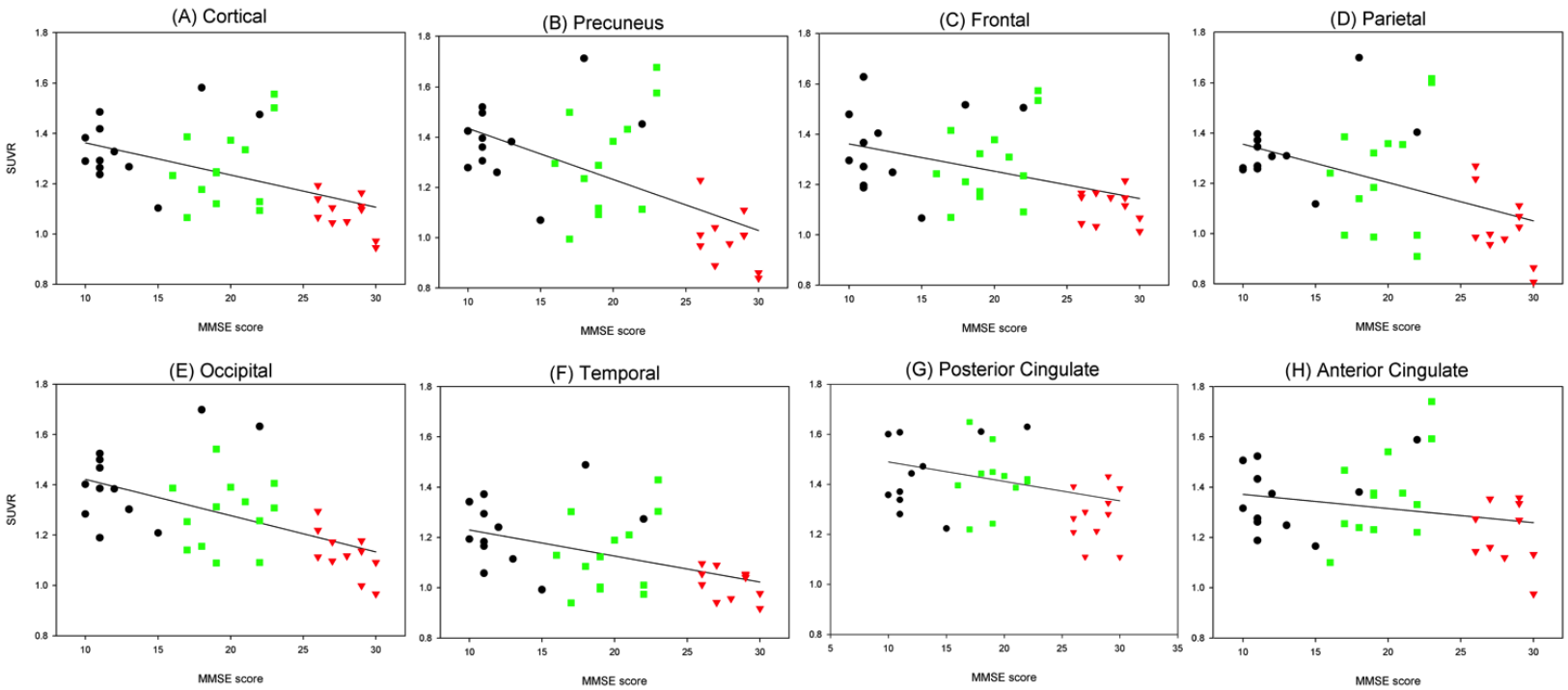


Region	Uptake Ratio	Z-Score
Composite	0.85	7.92
Prefrontal R	0.88	7.73
Prefrontal L	0.83	6.61
Anterior Cingulate R	0.88	6.34
Anterior Cingulate L	0.93	6.19
Precuneus PostCing R	0.94	8.54
Precuneus PostCing L	0.93	7.89
Parietal R	0.90	8.27
Parietal L	0.83	6.82
Temporal Lateral R	0.85	7.76
Temporal Lateral L	0.74	5.26
Occipital R	0.69	3.42
Occipital L	0.68	3.15
Sensorimotor R	0.76	4.84
Sensorimotor L	0.72	4.00
Temporal Mesial R	0.57	1.58
Temporal Mesial L	0.54	0.56
Cerebellum Grey	0.39	-0.32
Cerebellum Whole	0.50	0.71
Pons	1.00	0.00
Reference Region: Pons		

Z-Score Images



Correlations between amyloid deposition and Cognitive Function



Negative correlation of MMSE scores with
SUVRs after adjustment for age and education

Multiple modality biomarker prediction of cognitive impairment in prospectively followed de novo Parkinson disease

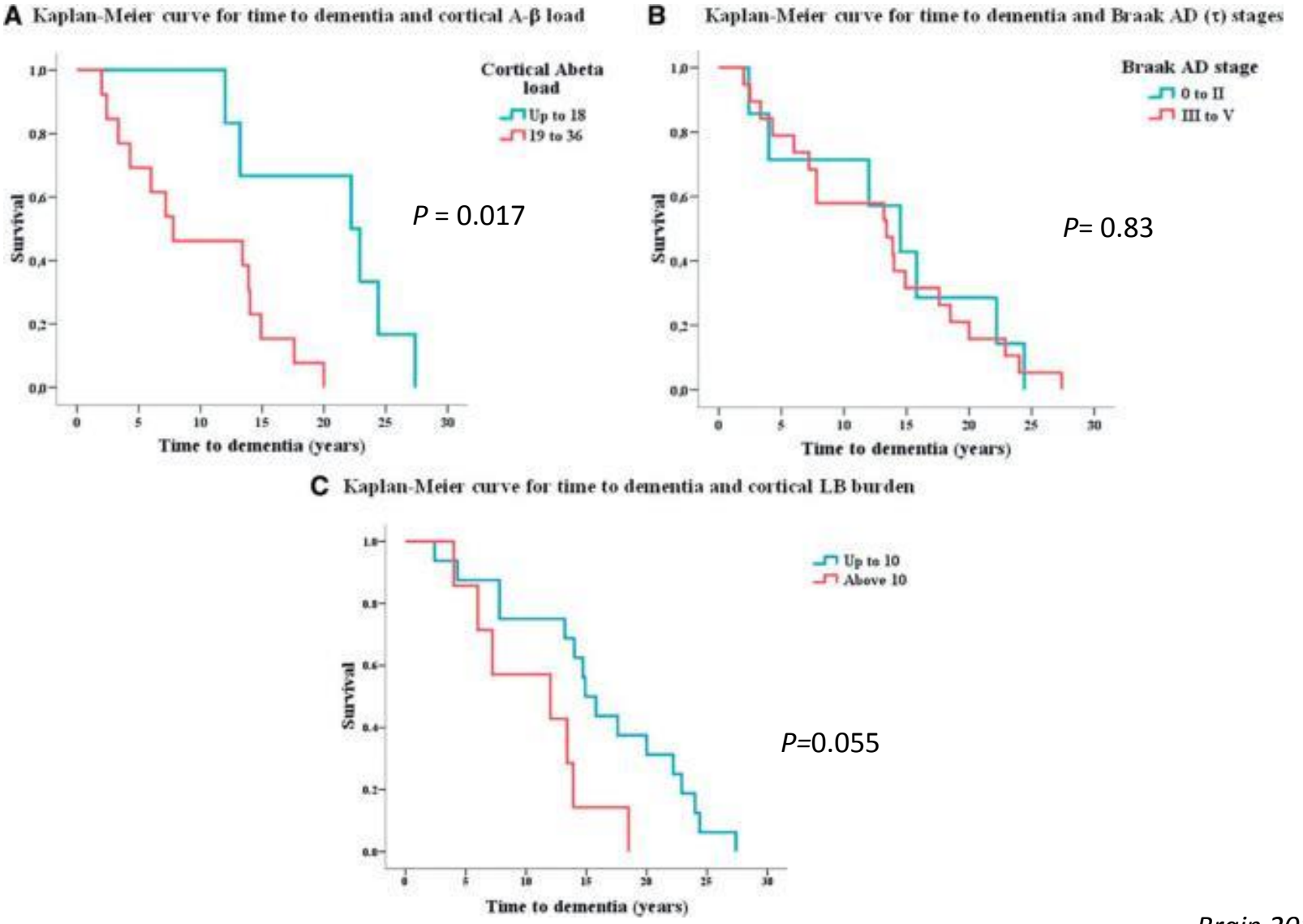
- **Cognitive impairment in PD increases in frequency 50–200%** in the first several years of disease, and is independently predicted by biomarker changes related to nigrostriatal or cortical dopaminergic deficits, global atrophy due to possible widespread effects of neurodegenerative disease, co-morbid Alzheimer's disease plaque pathology, and genetic factors.
- In Parkinson disease (PD) cognitive impairment can occur in a range of cognitive domains:
  - dementia (PDD) affects up to 80% of patients long-term
  - mild cognitive impairment (PD-MCI) occurs in 25–30% of non-demented patients and is a risk factor for dementia, and
  - cognitive deficits are present in some patients at the time of diagnosis.
- A range of demographic and clinical correlates or potential risk factors for cognitive decline have been identified, **increasing age and duration of PD**, **male sex**, **specific motor features** (postural instability gait disorder [PIGD] subtype), and a range of **non-motor symptoms** (e.g., visual hallucinations, apathy, depression, and rapid eye movement (REM) sleep behaviour disorder).
- Cortical Lewy body disease (LBD) pathology appears to be the major contributing pathology to cognitive decline in PD, but Alzheimer disease (AD)-related changes are also present in a significant percentage of patients.

Parkinson's Progression Markers Initiative (PPMI) http://www.ppmi-info.org

- ongoing, prospective, longitudinal, biomarker-rich observational study of disease progression in early PD
- up to 3 years, 423 newly diagnosed patients with idiopathic PD, untreated at baseline, from 33 international movement disorder centers

PLoS One 2017 May 17;12(5)

Aβ-amyloid load and survival analysis of time to dementia in patients with PD



Brain 2011

Cerebral Amyloid Deposition Is Associated with Gait Parameters in the Mayo Clinic Study of Aging

Amy-PET SUVR, independent of general measures of AD-associated neurodegeneration, is associated with poorer performance on multiple gait parameters (speed, cadence, stride length, double support time, and intra-individual stance time variability) among cognitively normal women, aged 50 to 69 years.

Table 5. Cross-Sectional Association Between PiB-PET SUVR and Gait Parameters in Women After Adjusting for AD-Associated Neurodegeneration

	B (95% CI)				
ROIs	Gait Speed (N = 285)	Cadence (N = 285)	Stride Length (N = 285)	Double Support Time (N = 285)	Stance Time CoV (N = 284)
Prefrontal	−0.34 (−0.61, −0.07)*	−0.52 (−0.84, −0.21)**	−0.11 (−0.33, 0.12)	0.47 (0.14, 0.79)**	0.19 (0.05, 0.34)**
Orbitofrontal	−0.64 (−1.17, −0.11)*	−0.96 (−1.57, −0.35)**	−0.22 (−0.65, 0.21)	0.89 (0.27, 1.5)**	0.40 (0.12, 0.69)**
Parietal	−0.33 (−0.61, −0.04)*	−0.50 (−0.83, −0.17)**	−0.11 (−0.34, 0.13)	0.47 (0.14, 0.81)**	0.21 (0.06, 0.36)**
Temporal	−1.06 (−1.83, −0.28)**	−1.45 (−2.34, −0.55)**	−0.45 (−1.08, 0.17)	1.33 (0.42, 2.23)**	0.59 (0.17, 1.01)**
Anterior cingulate	−0.77 (−1.35, −0.19)**	−1.16 (−1.82, −0.49)**	−0.28 (−0.75, 0.19)	1.08 (0.41, 1.75)**	0.43 (0.12, 0.75)**
Posterior cingulate/ precuneus	−0.65 (−1.19, −0.12)*	−0.96 (−1.57, −0.35)**	−0.25 (−0.68, 0.18)	0.95 (0.33, 1.57)**	0.42 (0.14, 0.71)**
Motor ROI	−0.13 (−0.25, −0.02)*	−0.20 (−0.34, −0.07)**	−0.05 (−0.14, 0.05)	0.18 (0.05, 0.32)**	0.07 (0.008, 0.13)*
	slower gait speed (m/sec)	lower cadence (steps/min)		longer double support time (sec)	greater stance time variability

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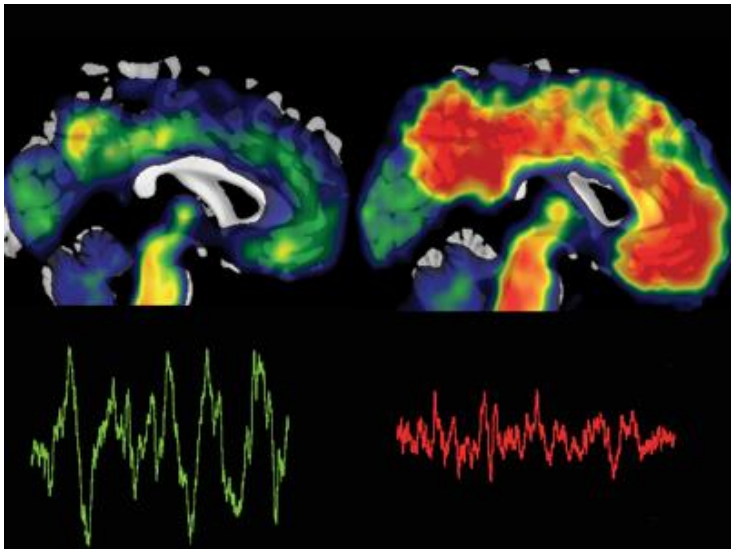
J Am Geriatr Soc 65:792–799, 2017

β-amyloid pathology relationship with both non-rapid eye movement (NREM) sleep disruption and memory impairment in older adults

Amy-PET



Normal Sleep

Amyloid deposition in poor sleep

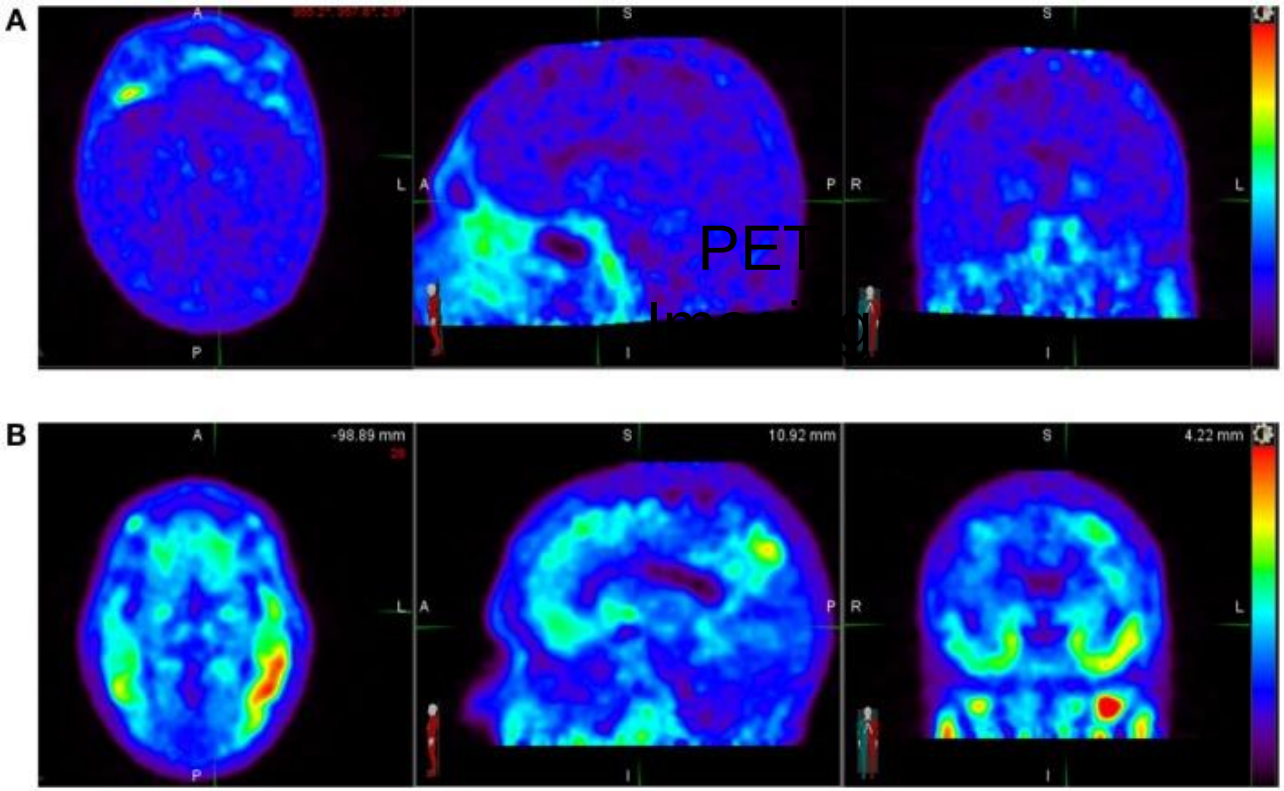
- β-amyloid burden in medial prefrontal cortex (mPFC) correlates significantly with the severity of impairment in NREM slow waves generation.
- By linking β-amyloid pathology with impaired NREM SWA, these data implicate sleep disruption as a mechanistic pathway through which β-amyloid pathology may contribute to hippocampus-dependent cognitive decline in the elderly.

NATURE NEUROSCIENCE 2015

Arriving.....

PET Imaging of Tau Pathology in Alzheimer's Disease and Tauopathies

18F-AV-1451



Normal

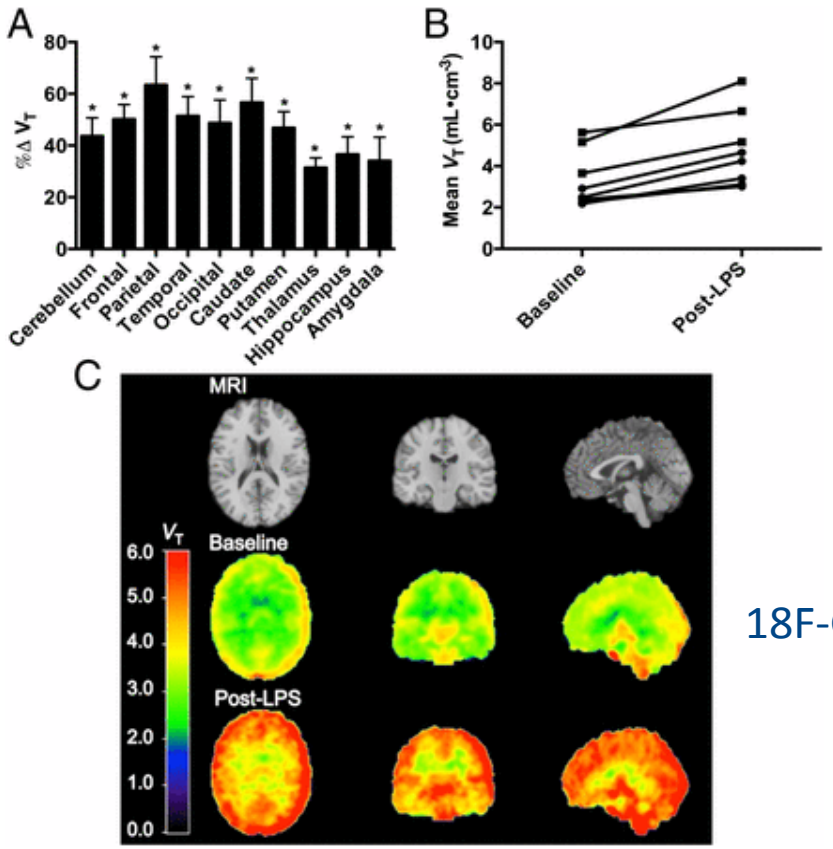
AD
(MMSE score 22)

Very low non-specific binding in white matter as well as cortical gray matter of healthy subjects

Frontiers in Neurology 2015

Arriving.....

Neuroinflammation imaging



18F-GE180

Activation of microglia after administration of a potent immune activator (LPS)

PNAS 2015