Neuroimaging – Movement disorders

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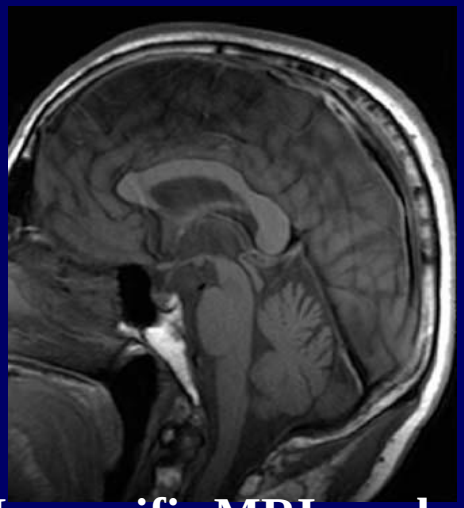
PD AND PARKINSONISMS

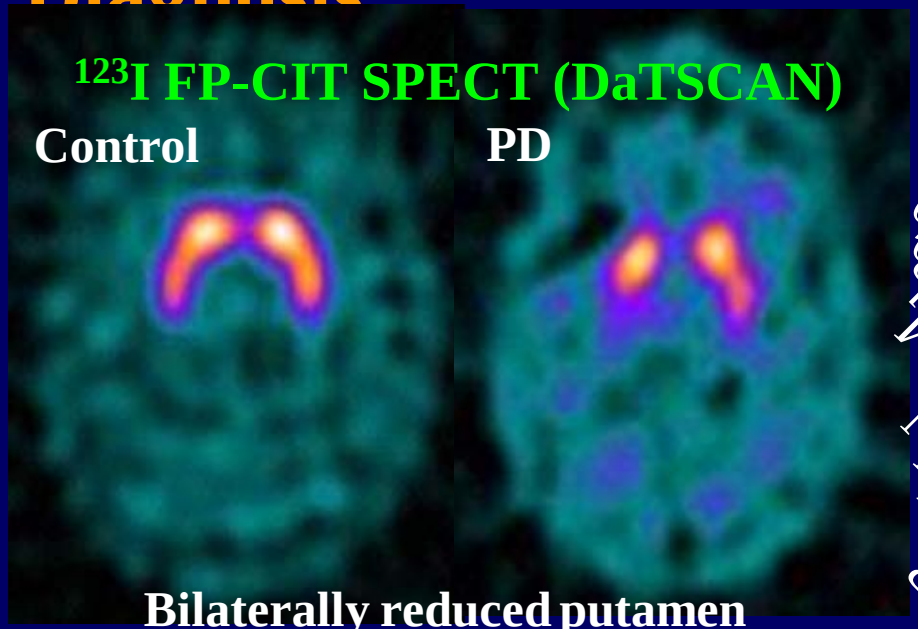
PD / Diagnosis

Conventional MRI



No specific MRI marker

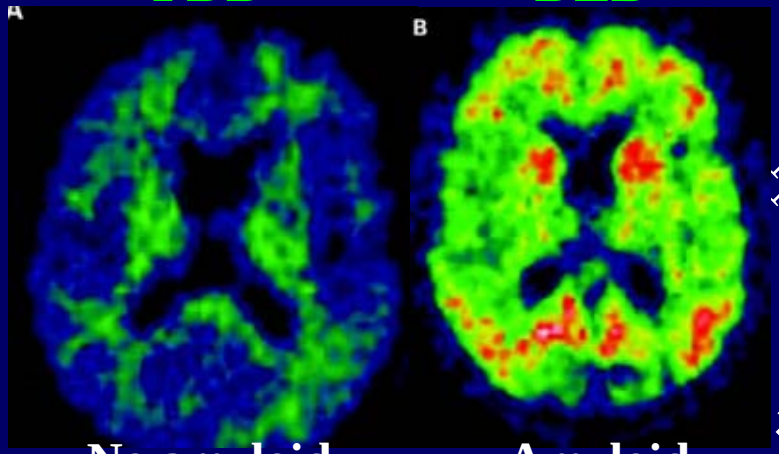
^{123}I FP-CIT SPECT (DaTSCAN)



Bilaterally reduced putamen dopaminergic terminal function

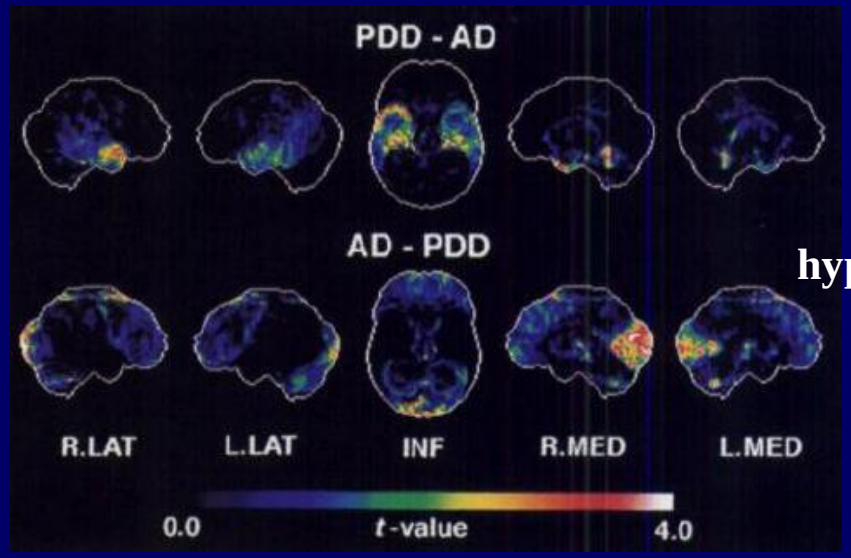
Booij and van Royen, 2005

PIB PET



No amyloid Amyloid

Edison et al., 2008



PDD *vs* AD: occipital hypometabolism

Vander-Borght et al., J Nucl Med 1997

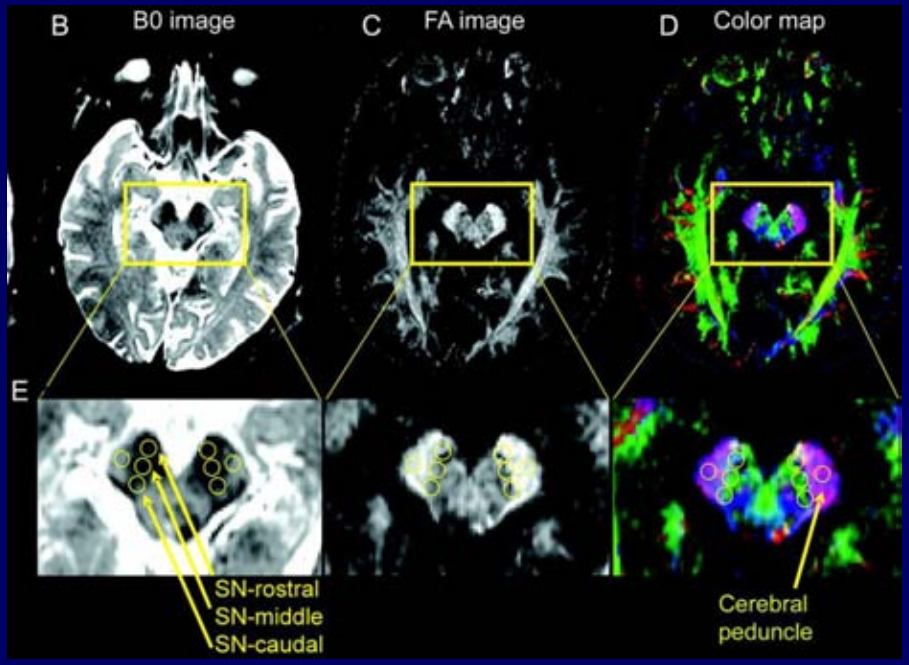
PD AND PARKINSONISMS

PD / The future landscape of imaging biomarkers of PD

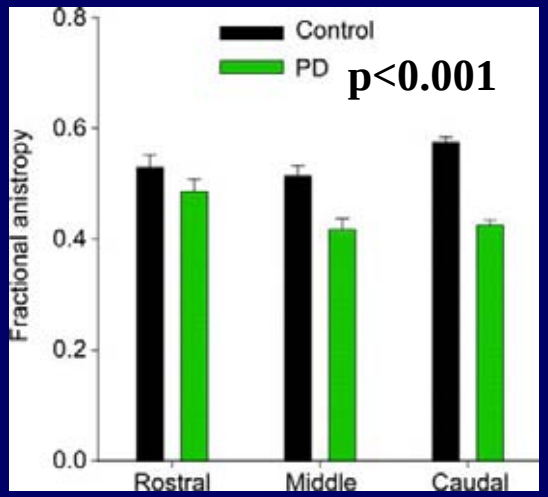
- **SN damage**
- **Progression of GM damage**
- **WM microstructural damage**
- **Cortical reorganization**
- **Imaging premotor stages of PD**

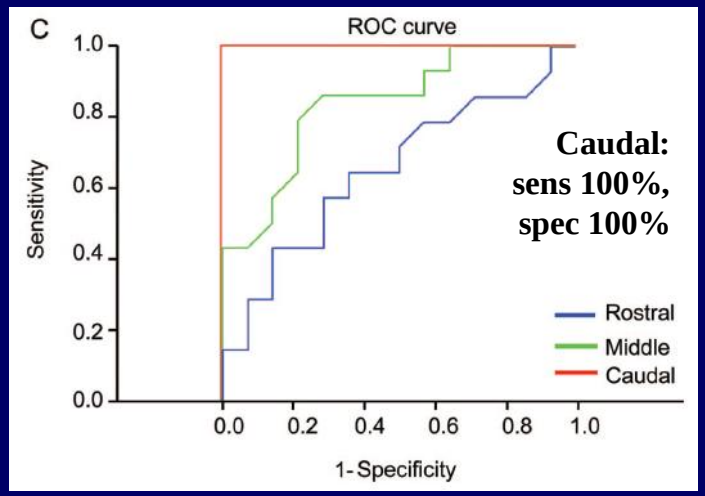
PD AND PARKINSONISMS

PD / SN damage



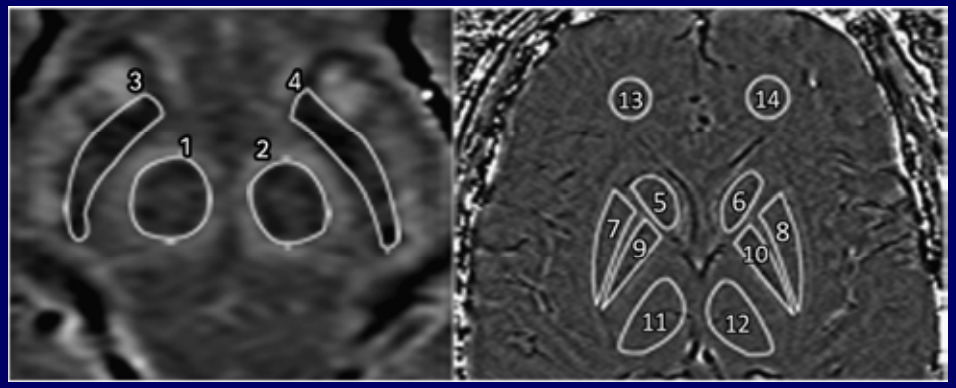
DT MRI





Vaillancourt et al., Neurology 2009

Susceptibility-weighted imaging



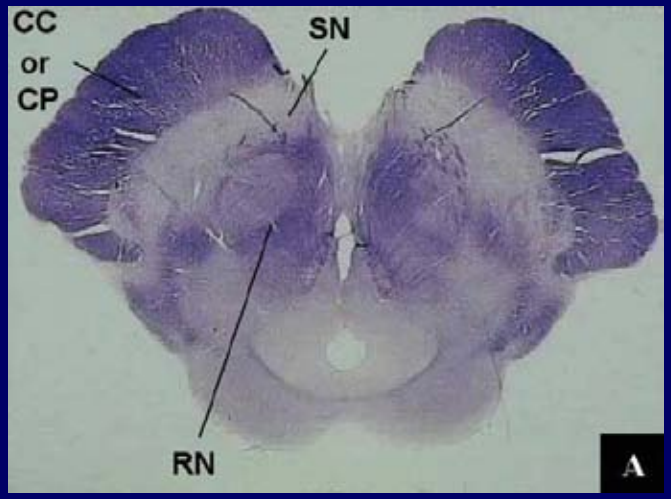
ROI	Most affected side	Healthy controls	t value	P value
RN	0.07386±0.02918	0.08011±0.02498	1.105	0.272
SN	0.15669±0.05371	0.12207±0.04155	−3.488	0.001
CA	0.03756±0.01354	0.03983±0.01240	0.836	0.405
GP	0.09088±0.05250	0.08845±0.05966	−0.204	0.839
PU	0.03538±0.02494	0.03739±0.03379	0.315	0.753
TH	0.01265±0.00476	0.01451±0.00701	1.440	0.153
FWM	0.00299±0.00647	0.00215±0.00486	0.616	0.540

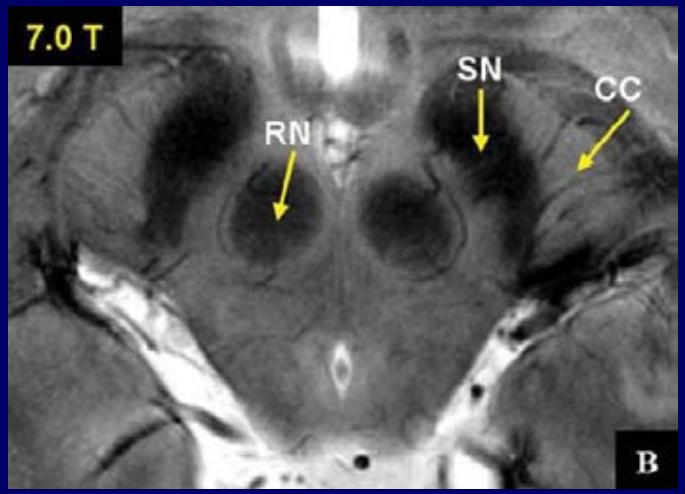
Vaillancourt et al., Neurology 2009

PD AND PARKINSONISMS

PD / SN damage – Ultra-high field MRI

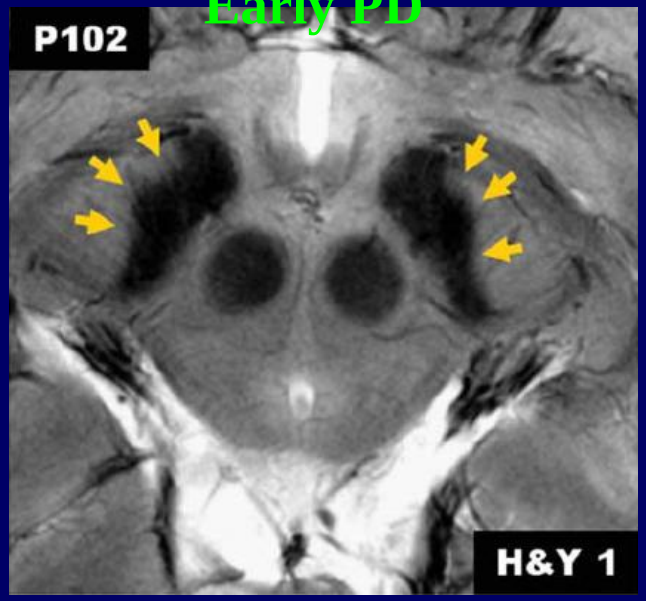
7.0 T



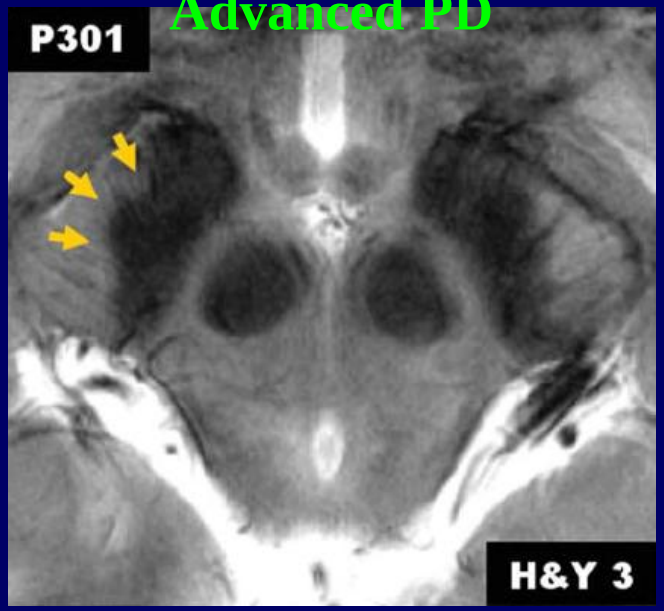


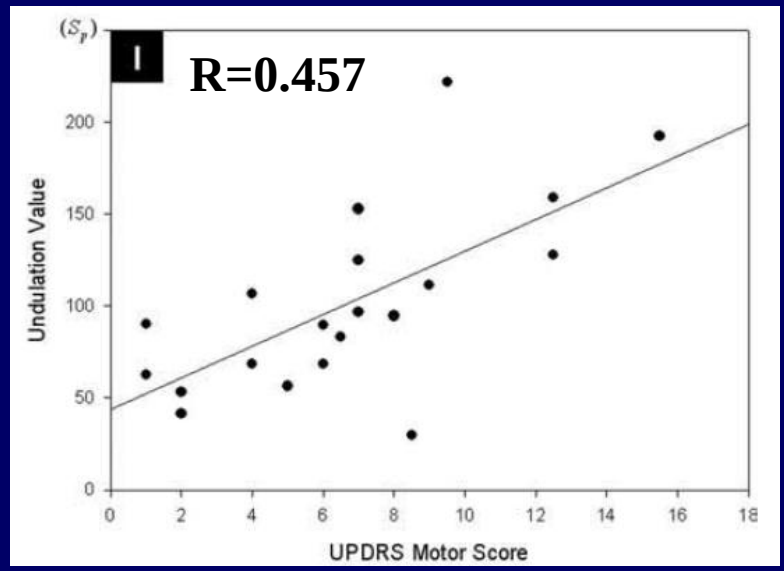
SN: substantia nigra
RN: red nucleus
CC: crus cerebri

Early PD



Advanced PD





Sensitivity 90%, specificity 100%

Cho et al., Mov Disord 2011

PD AND PARKINSONISMS

PD / The future landscape of imaging biomarkers of PD

- SN damage
- Progression of GM damage
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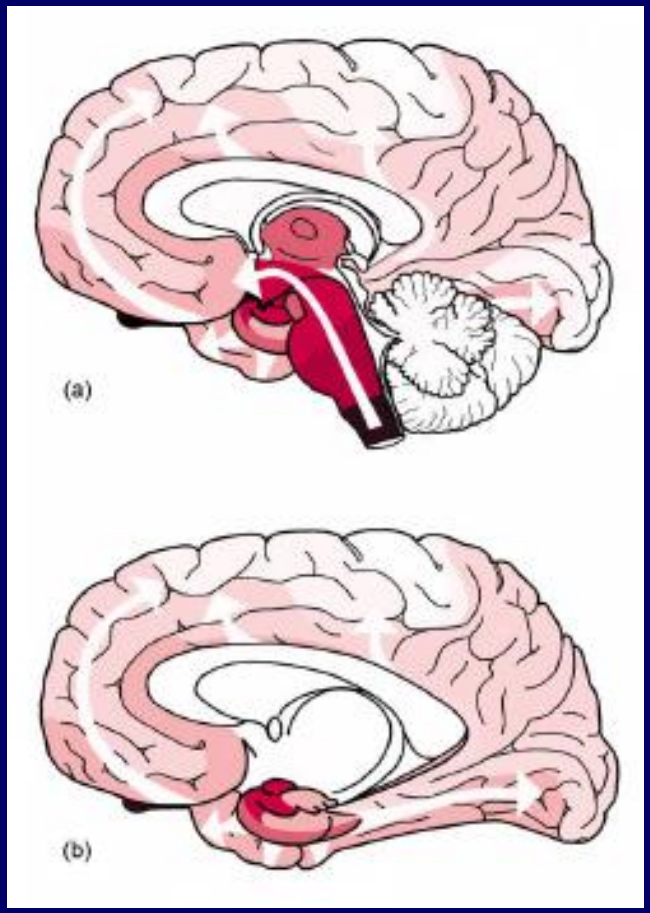
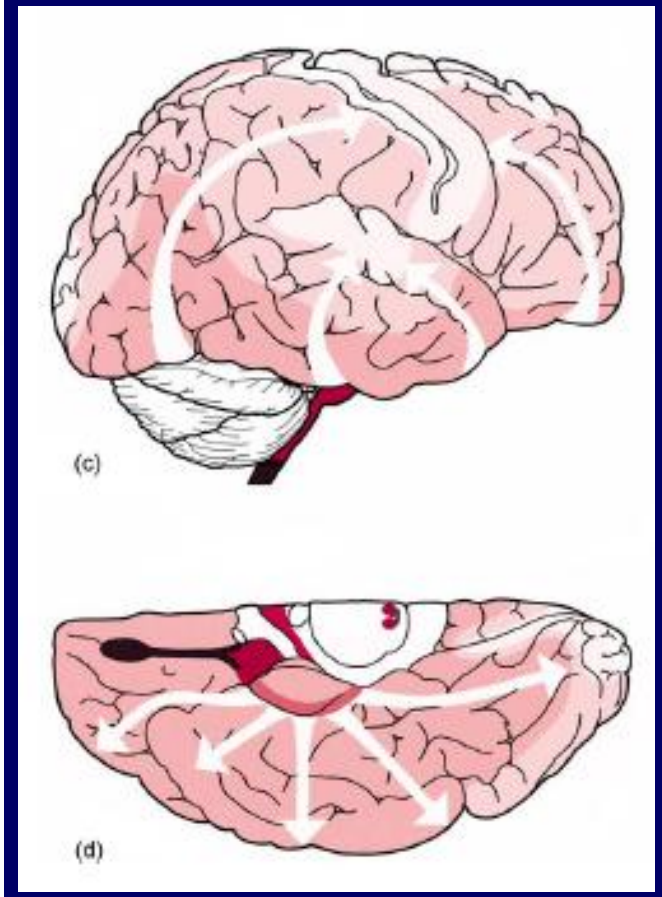
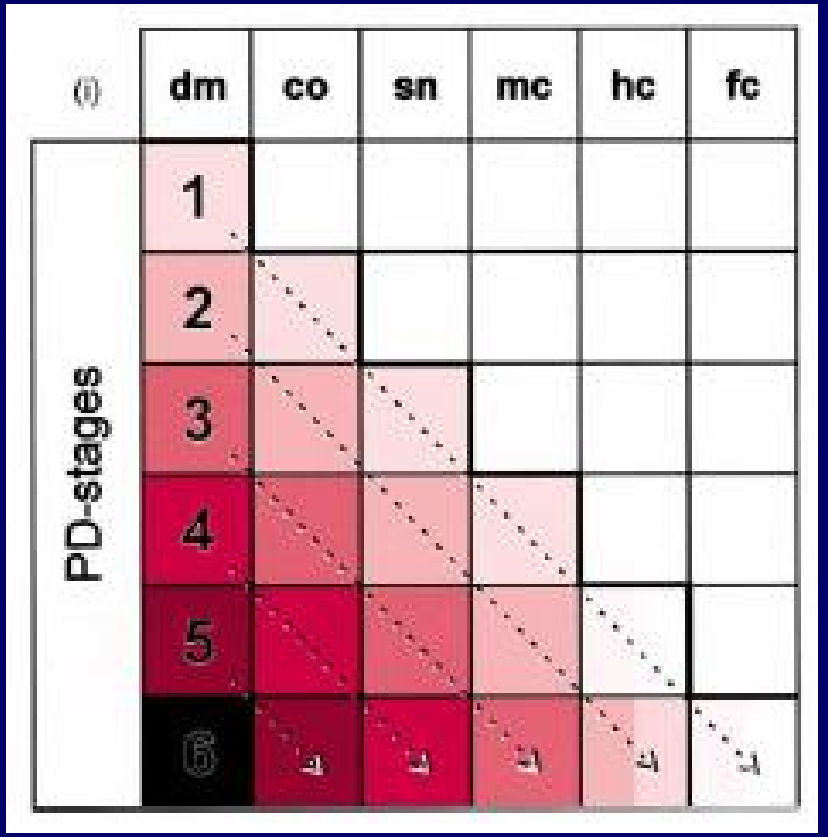
- Imaging premotor stages of PD

PD AND PARKINSONISMS

PD / Progression of intraneuronal pathology





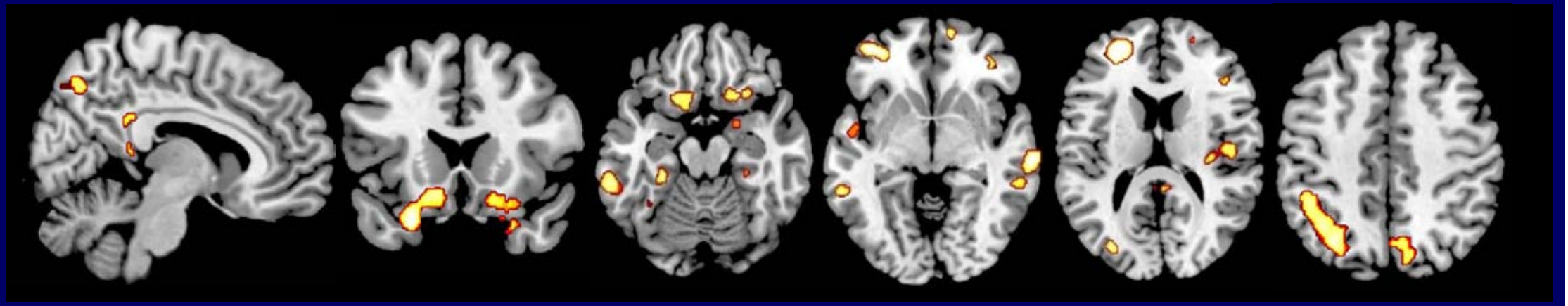


Braak et al., Neurobiol Aging 2003

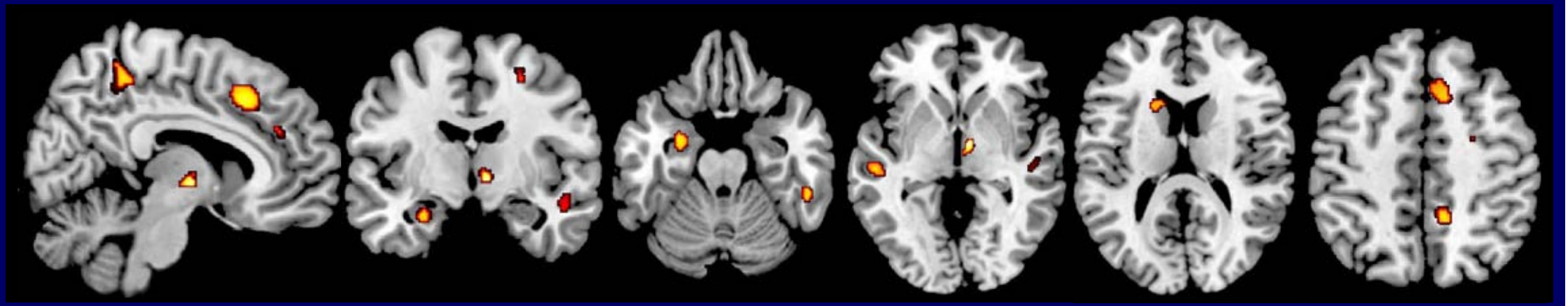
PD AND PARKINSONISMS

PD / GM atrophy

Early PD *vs.* controls



Moderate *vs.* mild PD



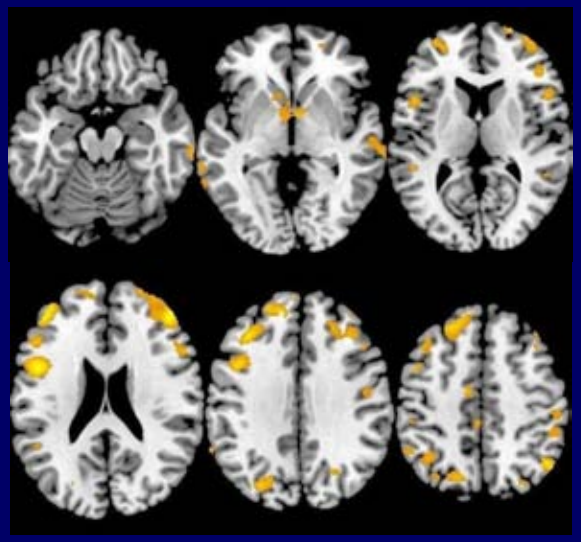
Medial and lateral temporal, orbitofrontal, prefrontal, parietal and occipital regions

Agosta, …Filippi. Hum Brain Mapp 2012

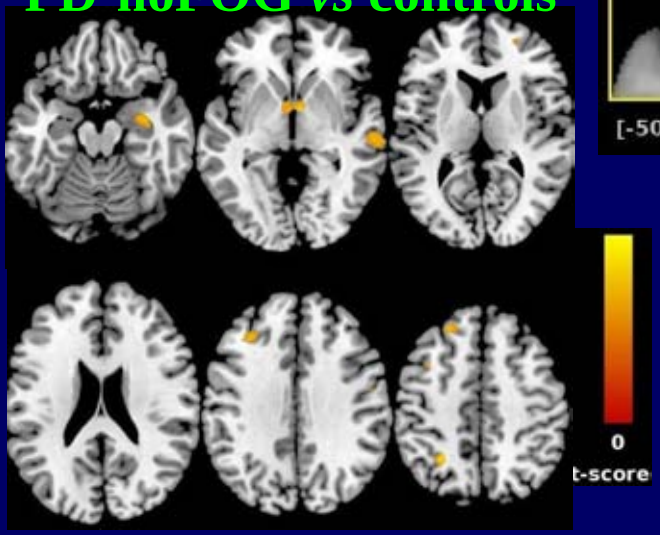
PD AND PARKINSONISMS

PD / GM atrophy *vs* FOG

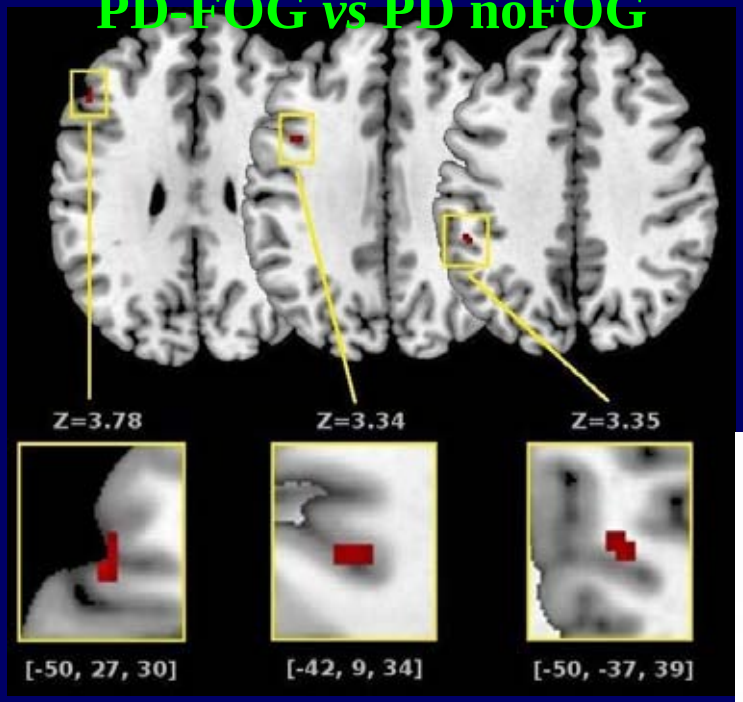
PD-FOG *vs* controls



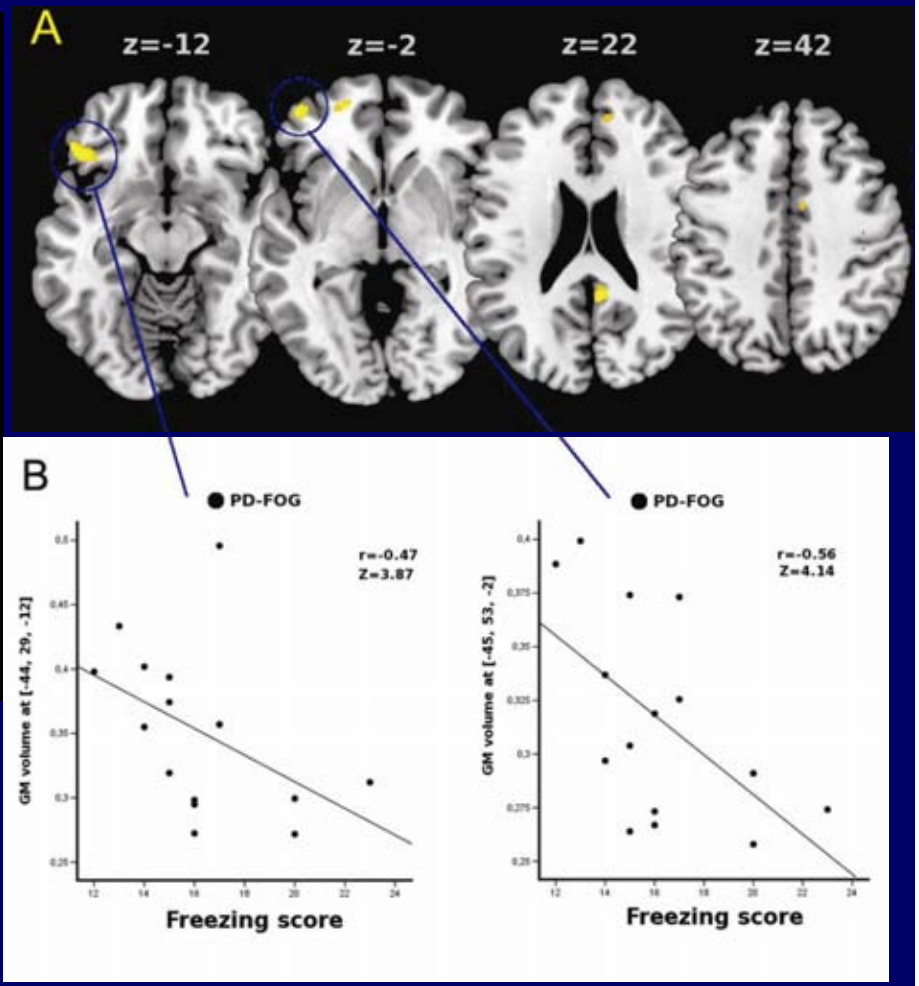
PD-noFOG *vs* controls



PD-FOG *vs* PD noFOG



GM atrophy *vs* FOG

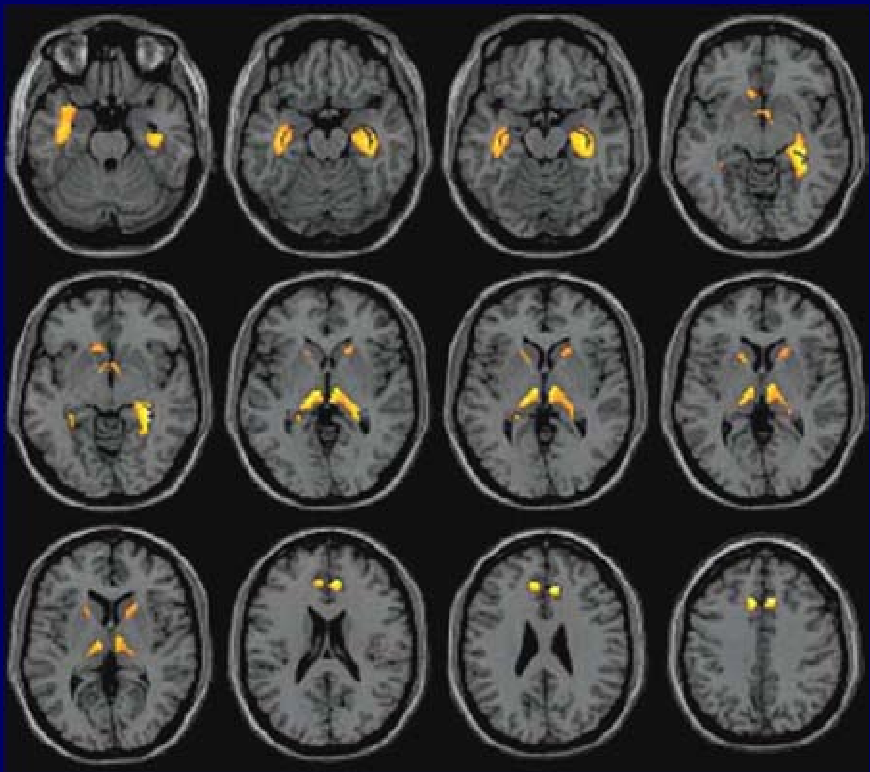


Kostic,… Filippi. Neurology 2011

PD AND PARKINSONISMS

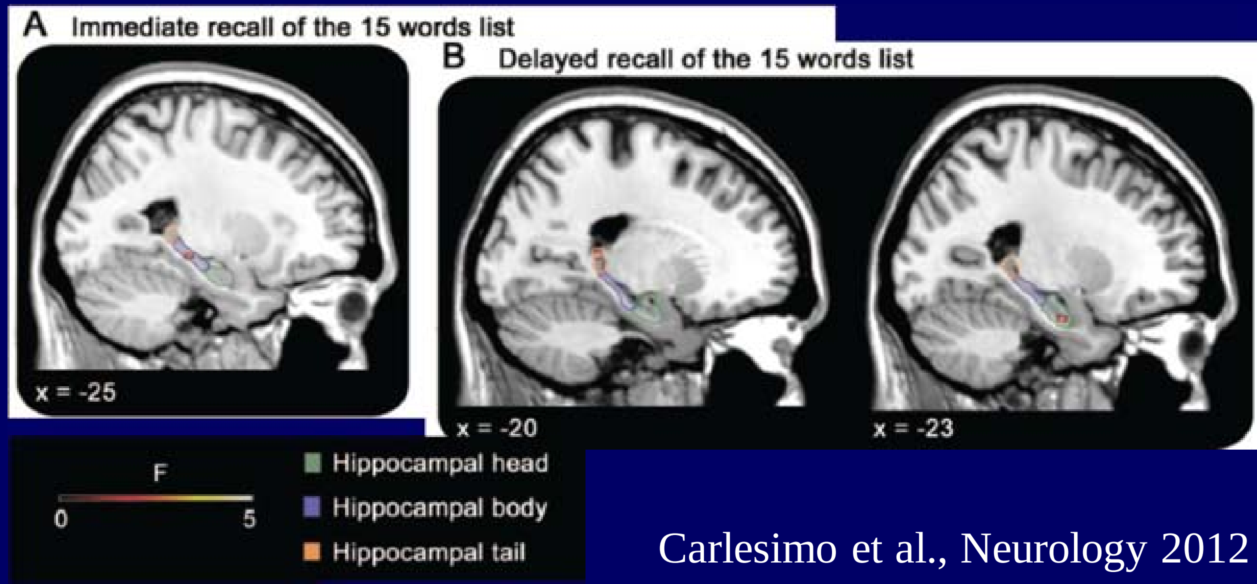
PD / GM atrophy *vs* dementia

PD-dementia patients



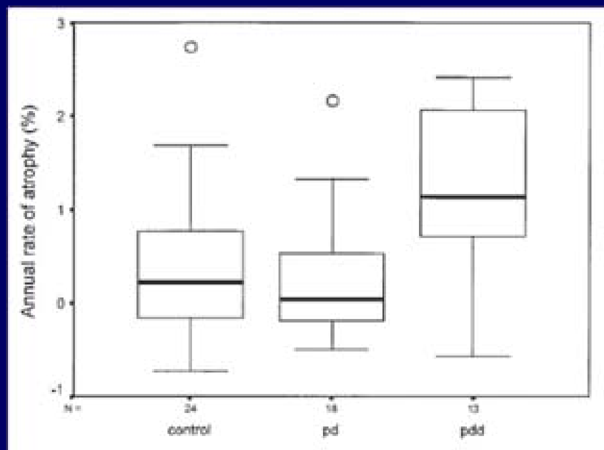
Summerfield et al., Arch Neurol 2005

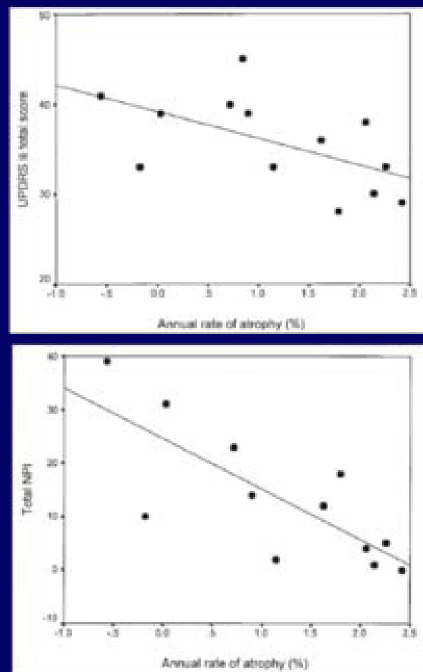
Hippocampal volume *vs* memory deficits



Carlesimo et al., Neurology 2012

Annual rate of atrophy %





Burton et al., Mov Disord 2005

PD AND PARKINSONISMS

PD / The future landscape of imaging biomarkers of PD

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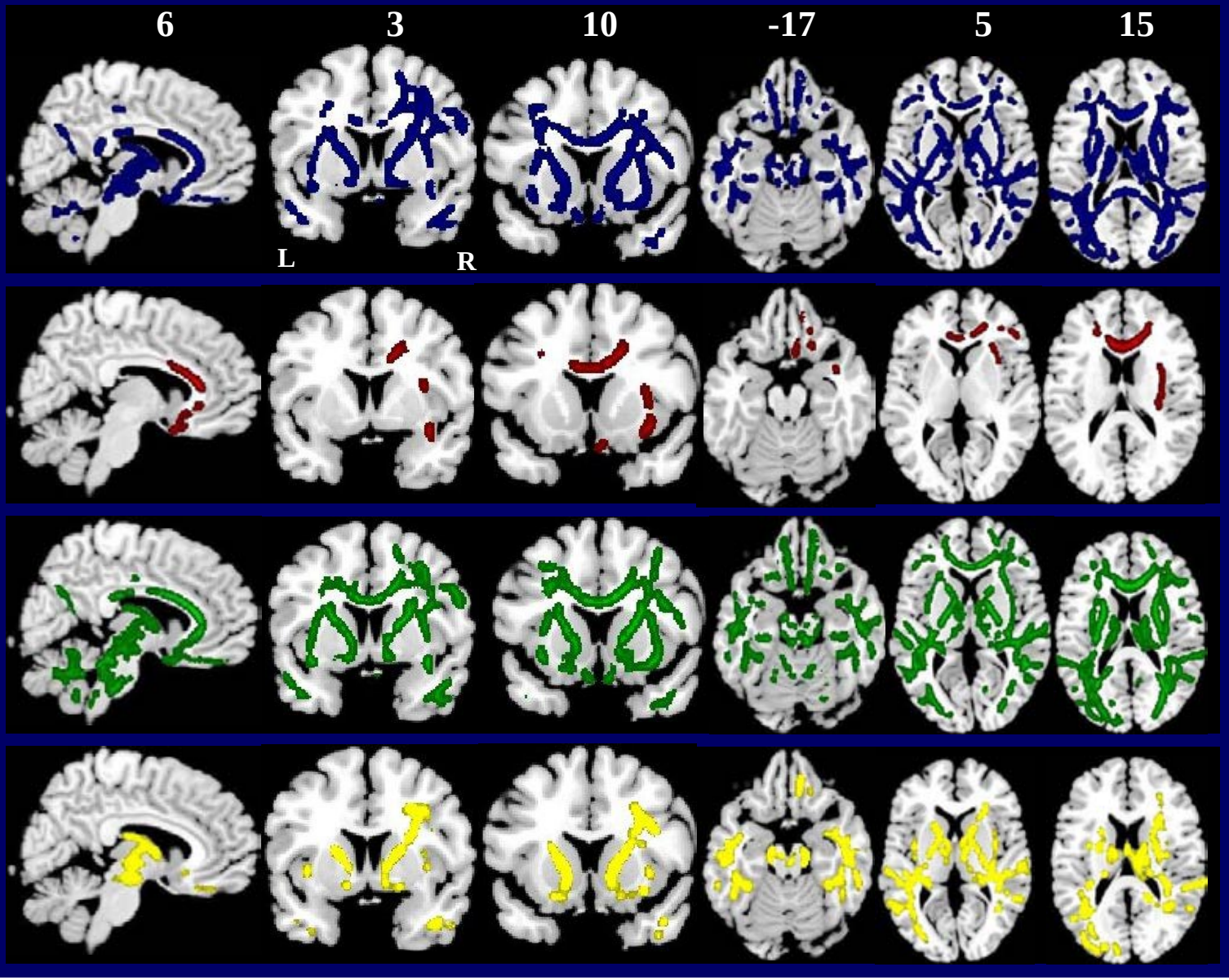
PD AND PARKINSONISMS

PD / WM damage *vs* disease severity

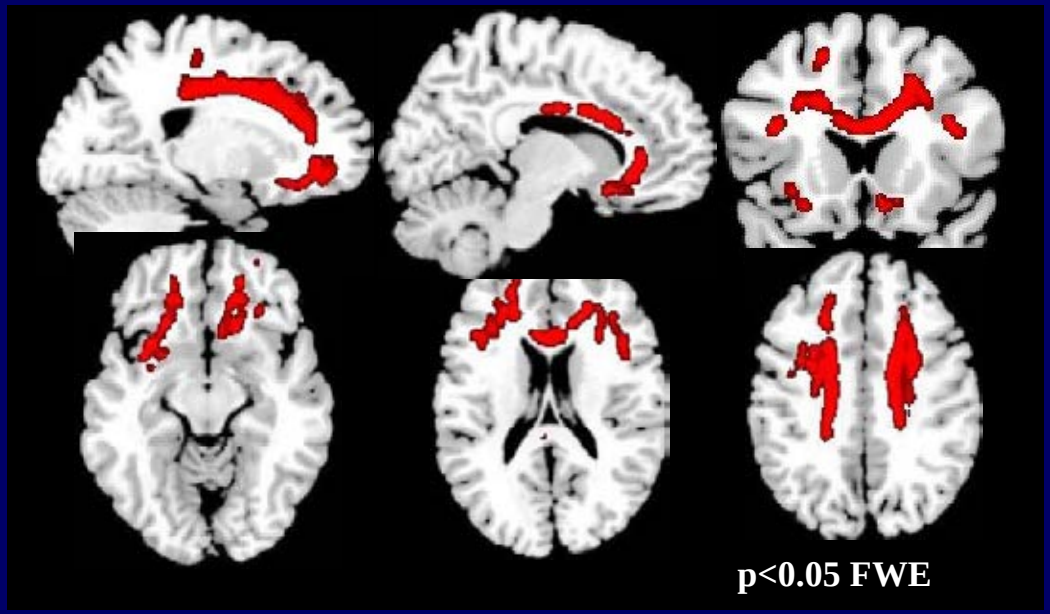
Moderate + Severe PD *vs*. Early + Mild PD



PD AND PARKINSONISMS

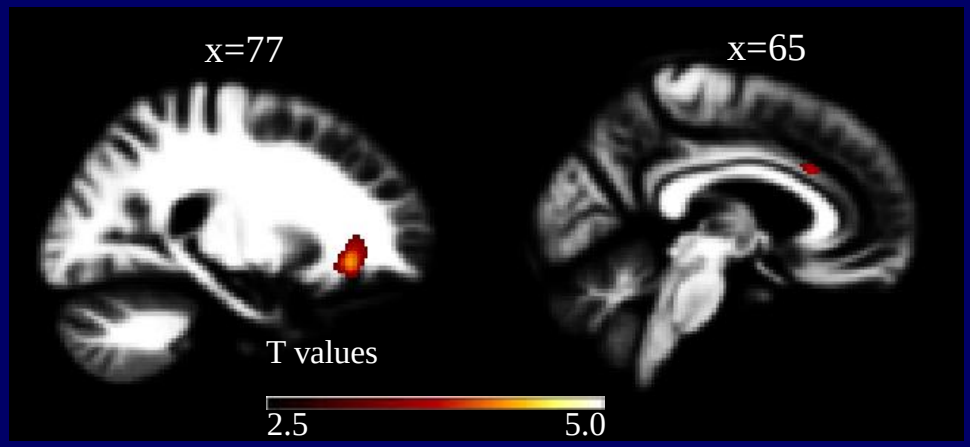
PD / WM damage *vs* cognition and behaviour

PD-MCI *vs.* PD-Cu patients



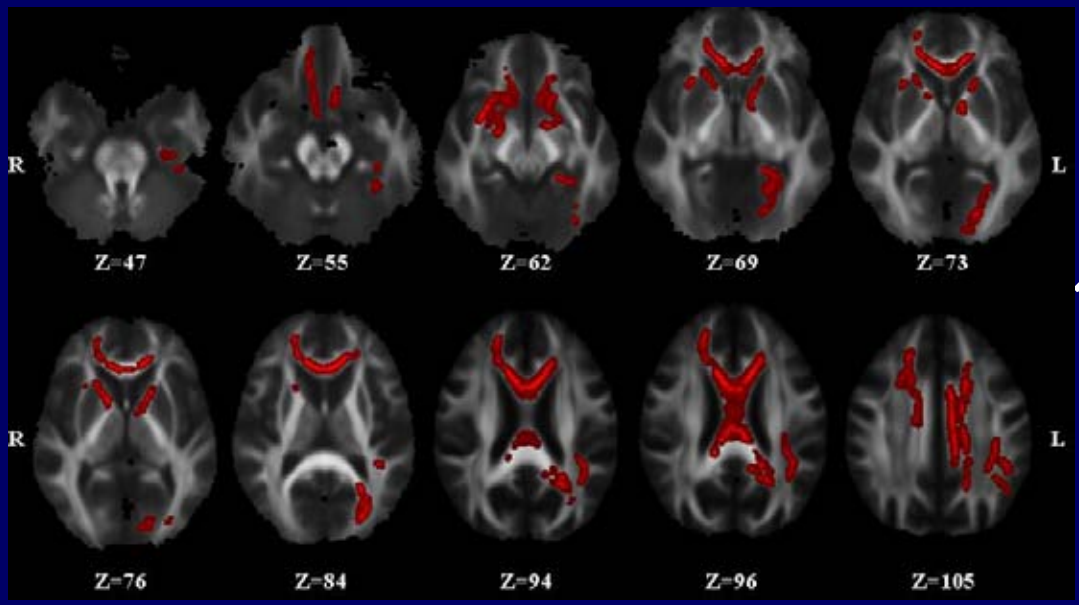
Agosta, … Filippi. Hum Brain Mapp 2013

WM volume: PD with depression < PD without depression



Kostic, … Filippi. Neurology 2010

FA decrease in GBA-PD



Filippi, … Neurology 2013

PD AND PARKINSONISMS

PD / The future landscape of imaging biomarkers of PD

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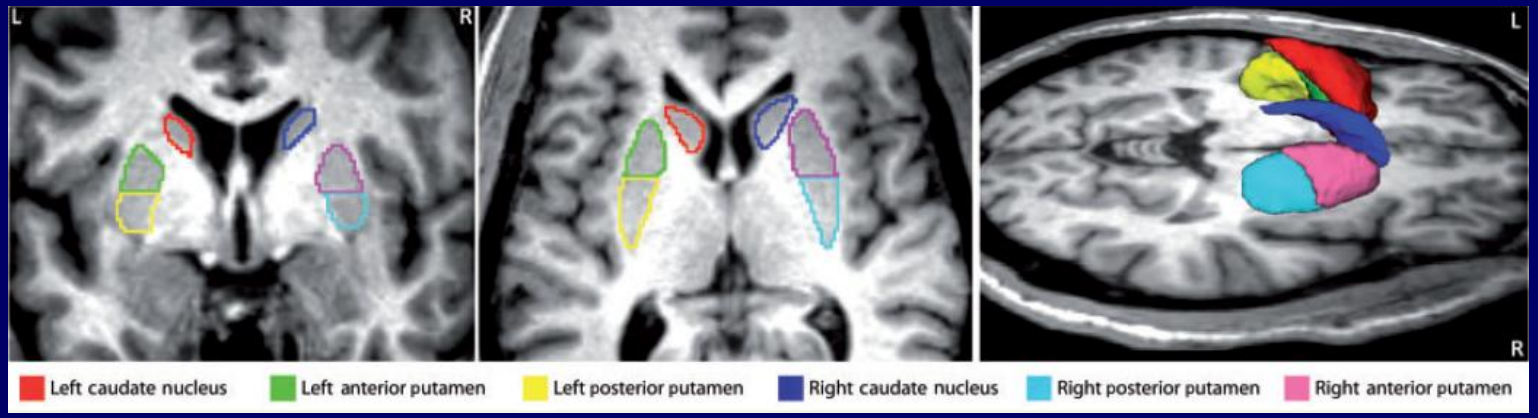
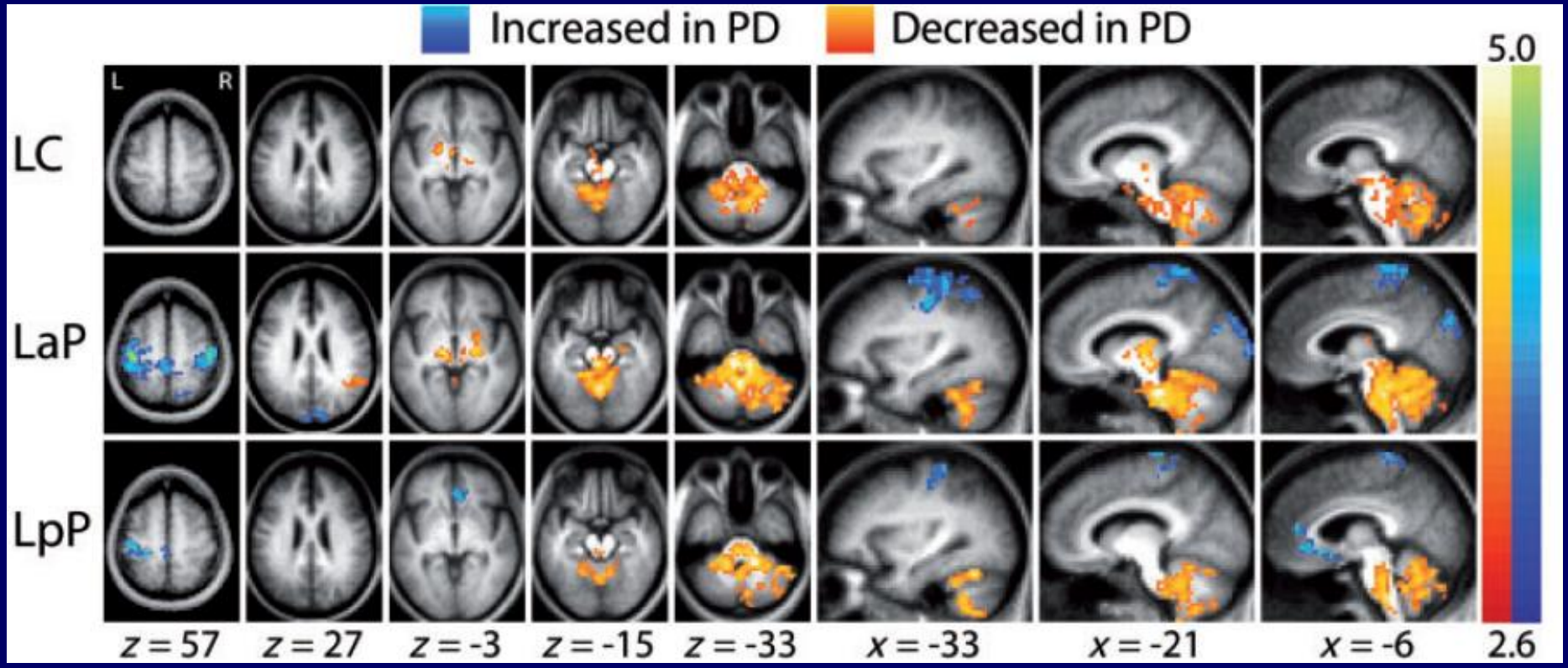
PD AND PARKINSONISMS

PD / Resting state fMRI





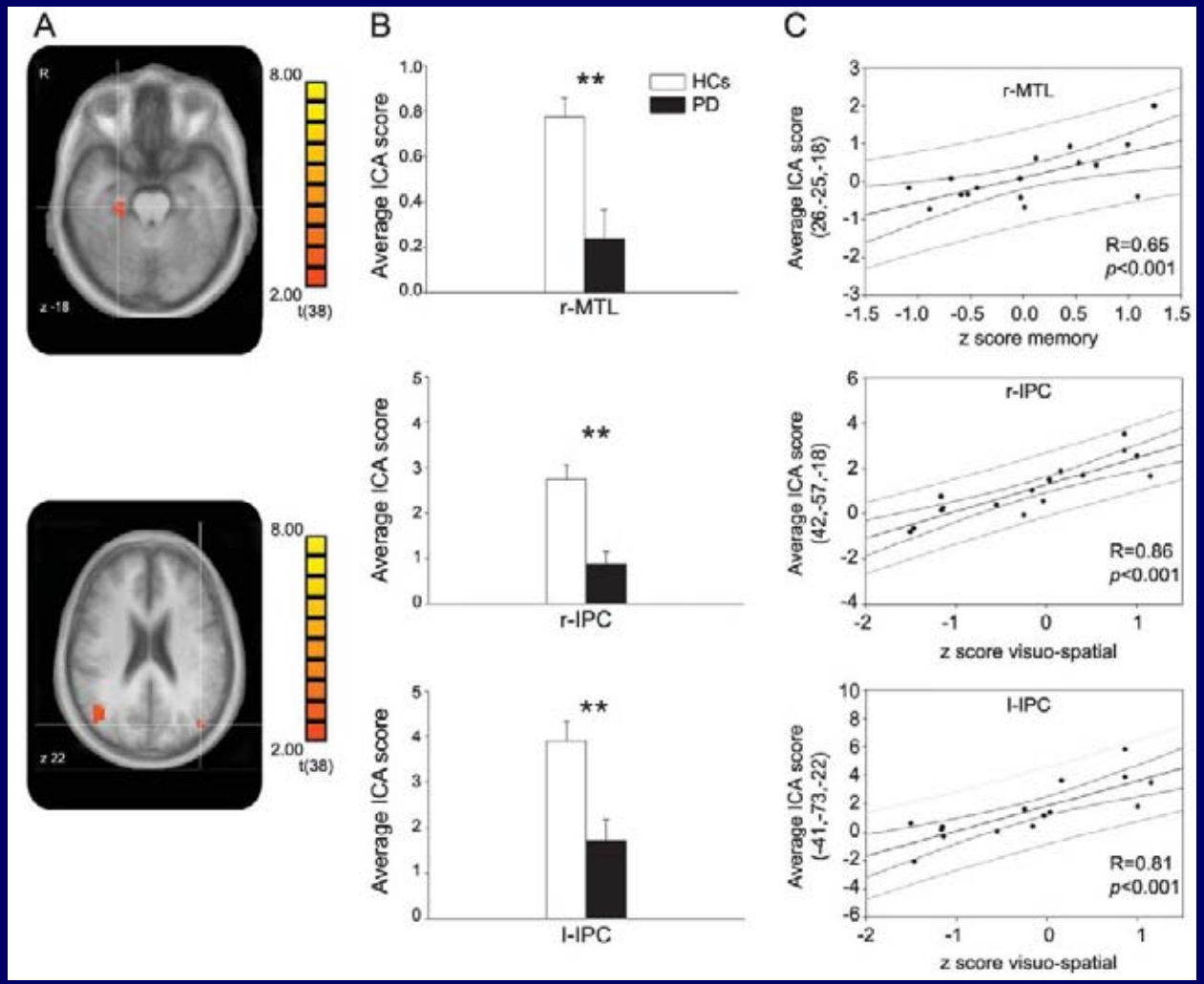
Hoffstetter, Parkinsonism

PD AND PARKINSONISMS

PD / Resting state fMRI *vs* cognition

16 cognitively unimpaired PD

Decreased DMN activity



Tessitore et al., Neurology 2012

PD AND PARKINSONISMS

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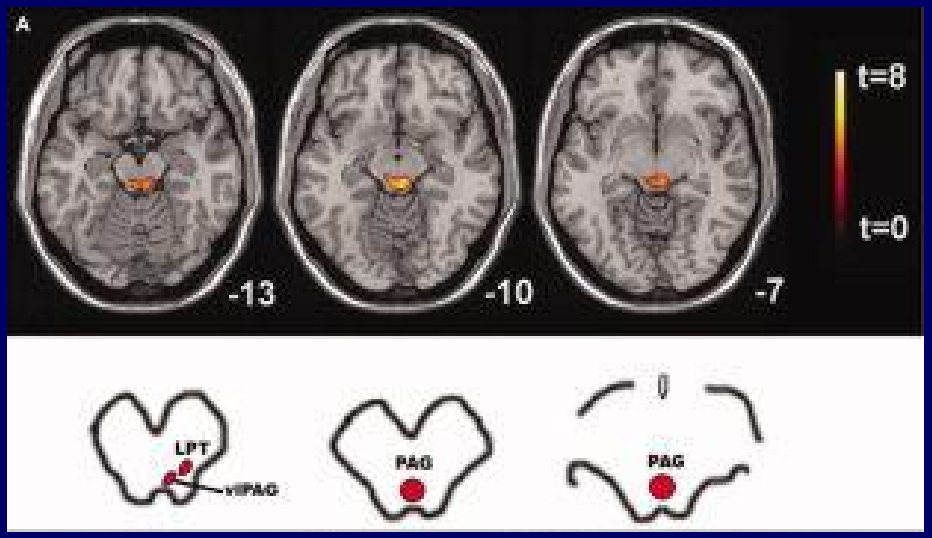
PD AND PARKINSONISMS

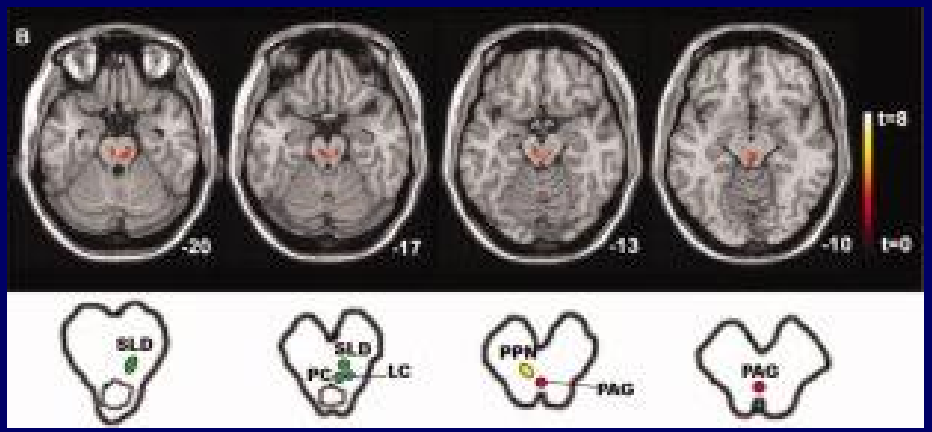
PD / Pre-motor stages

Rapid eye movement sleep behavior disorder

Decreased FA



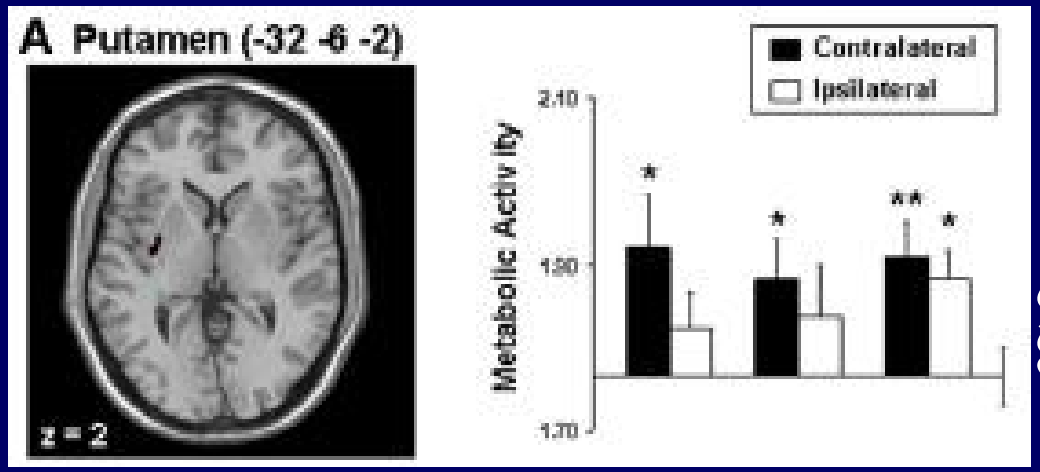
Increased MD



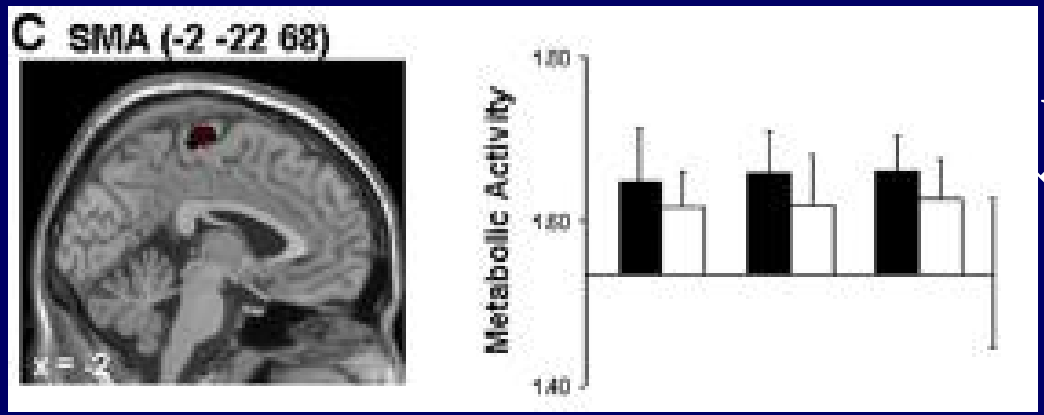
Scherfler et al., Brain 2007

Metabolic changes in hemiparkinsonism

Baseline



Year 2

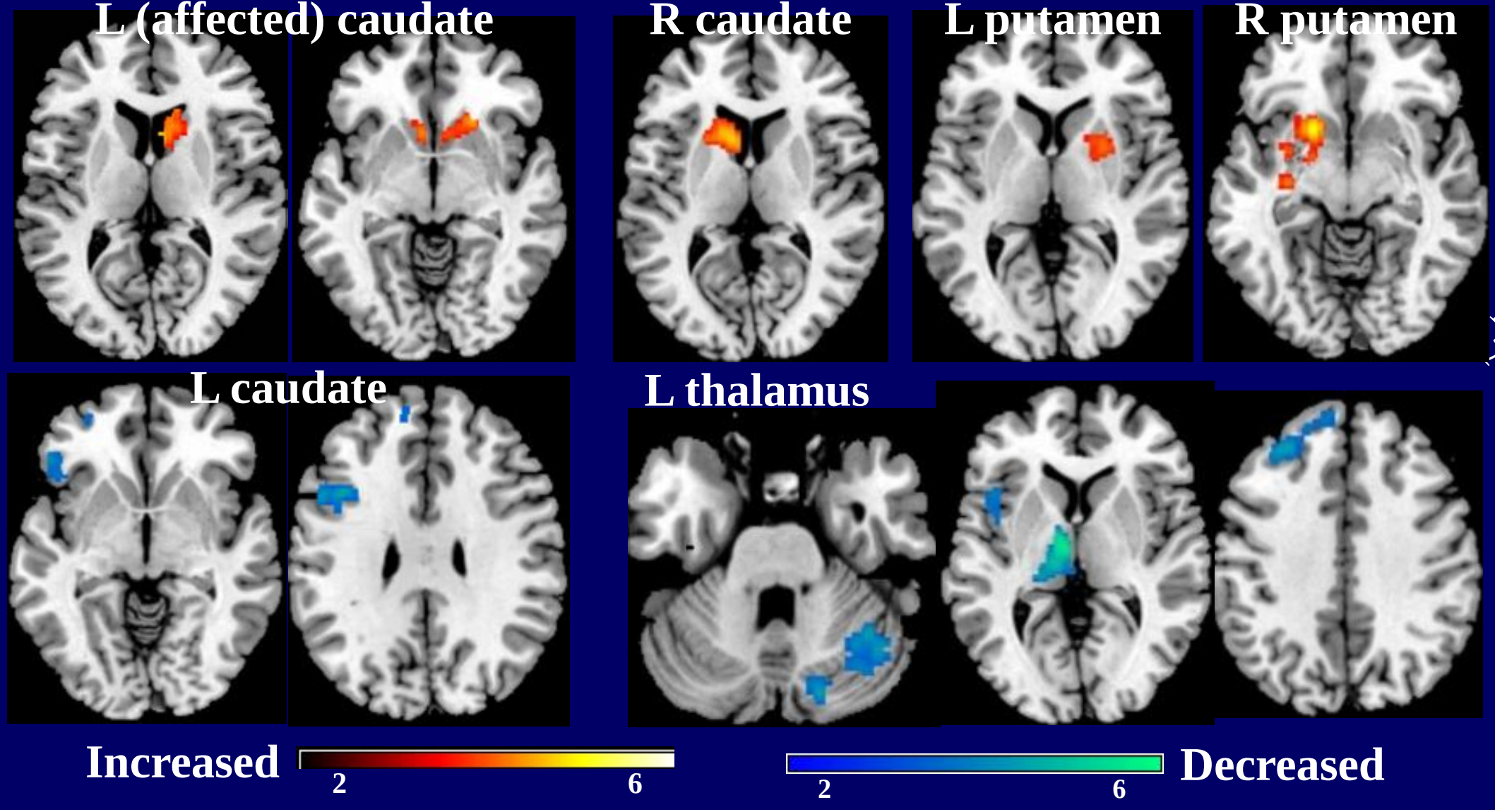


Tang et al., Neurology 2010

PD AND PARKINSONISMS

PD / Pre-motor stages

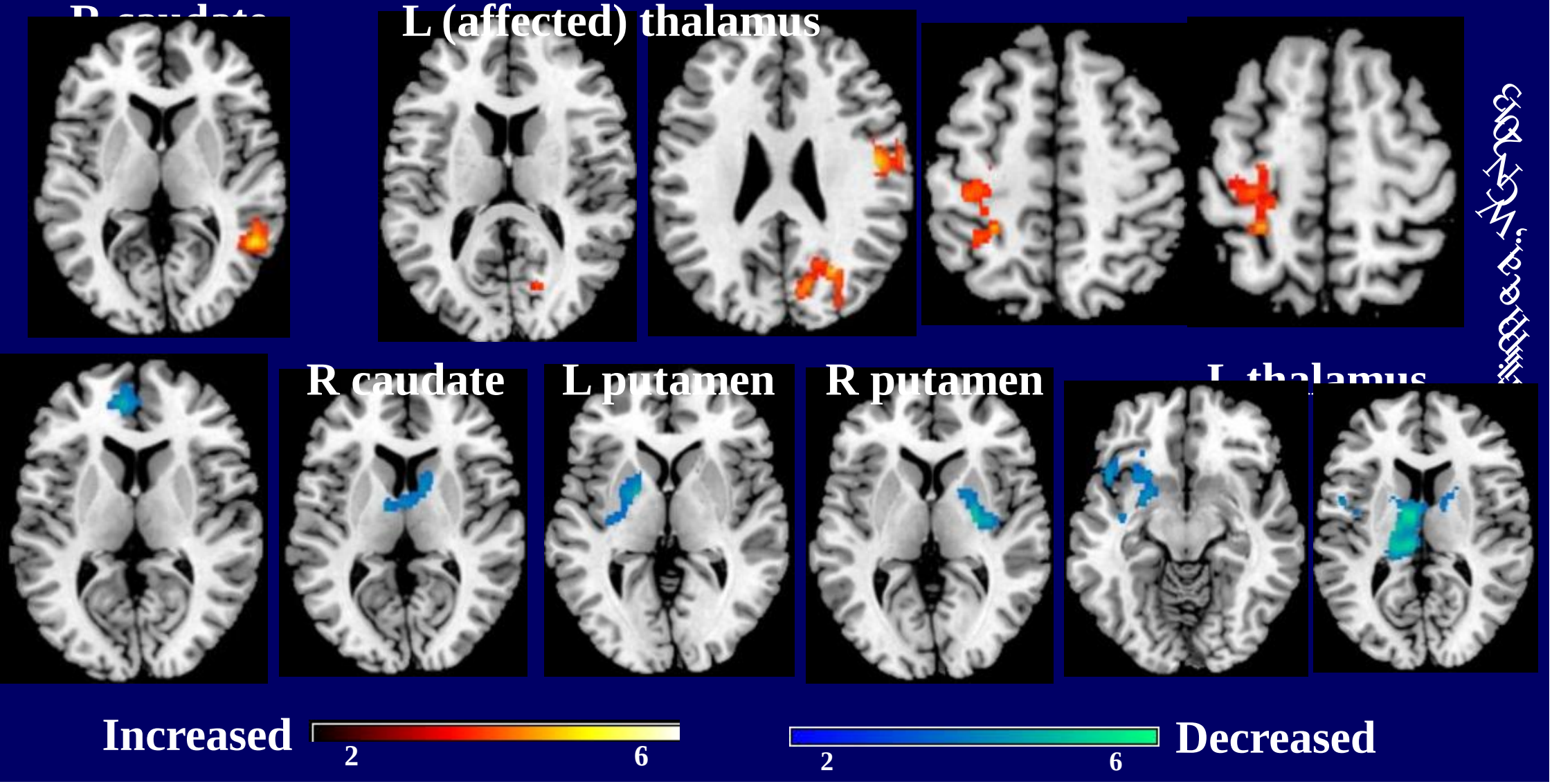
Drug-naïve hemiparkinsonism



PD AND PARKINSONISMS

PD / Pre-motor stages

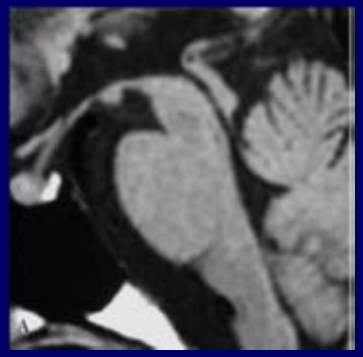
L-dopa treated hemiparkinsonism



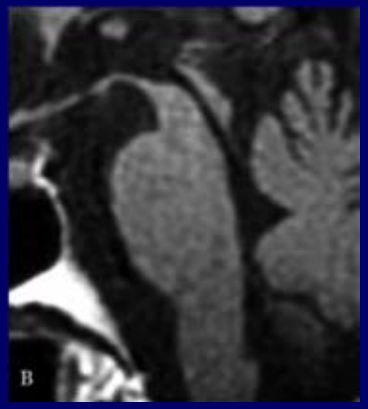
PD AND PARKINSONISMS

Atypical parkinsonisms / Conventional MRI

PD



PSP



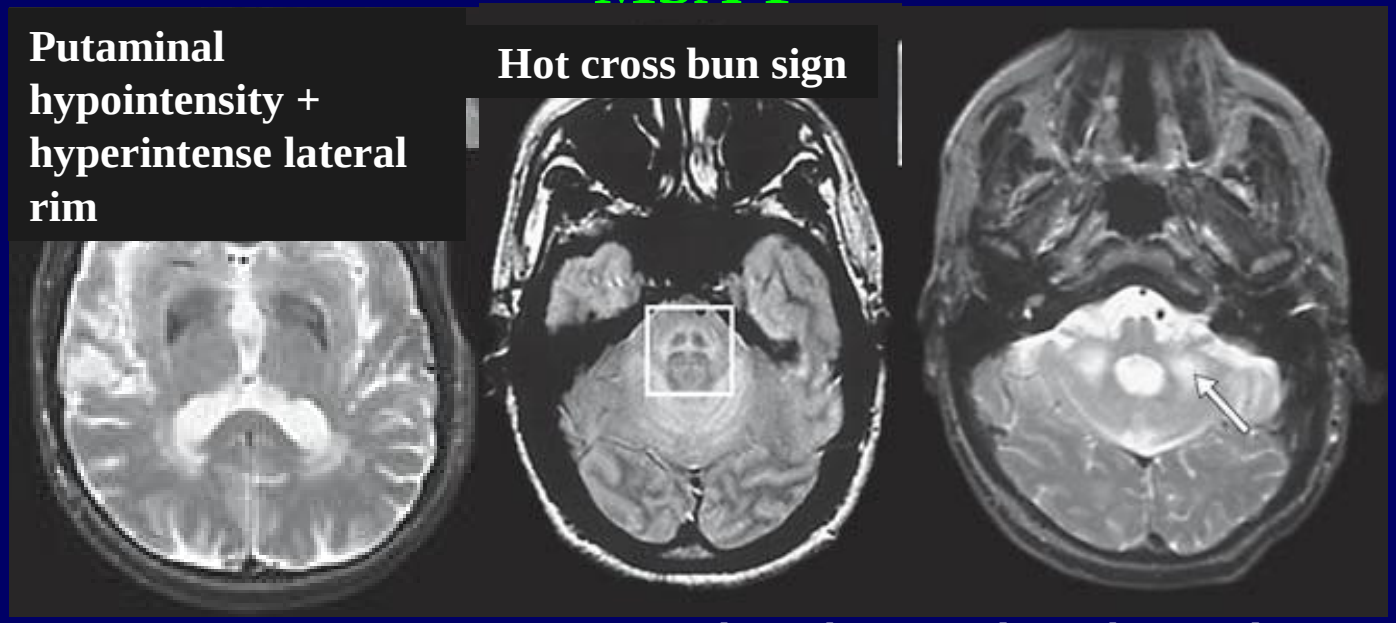
MSA-P

Oba et al., Neurology 2006

MSA-P

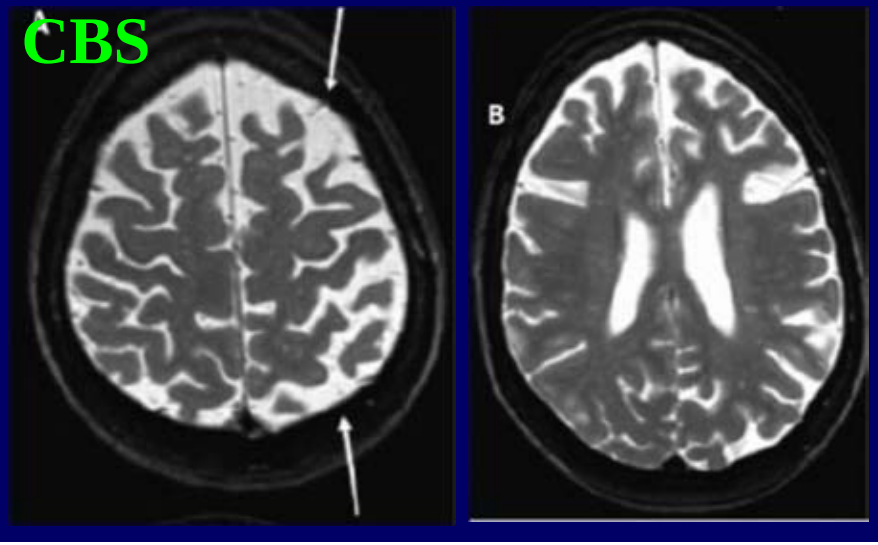
Putaminal hypointensity + hyperintense lateral rim

Hot cross bun sign



Bhattacharya et al., Arch Neurol 2002

CBS



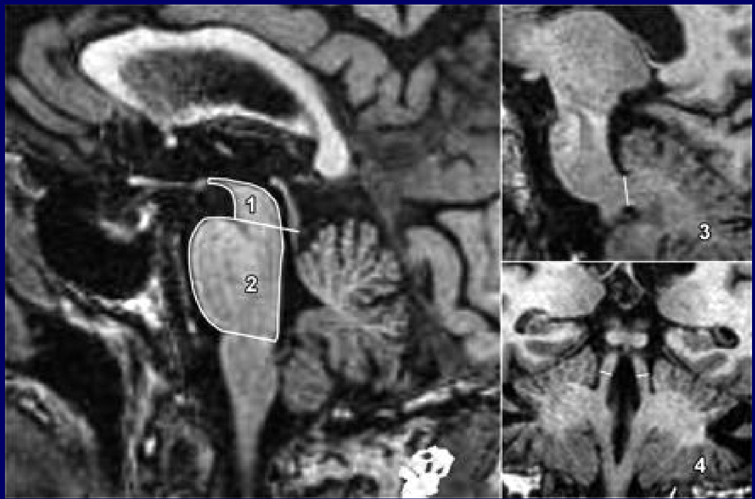
Asimmetric frontal and parietal atrophy

Vitali et al., Sem Neurol 2009

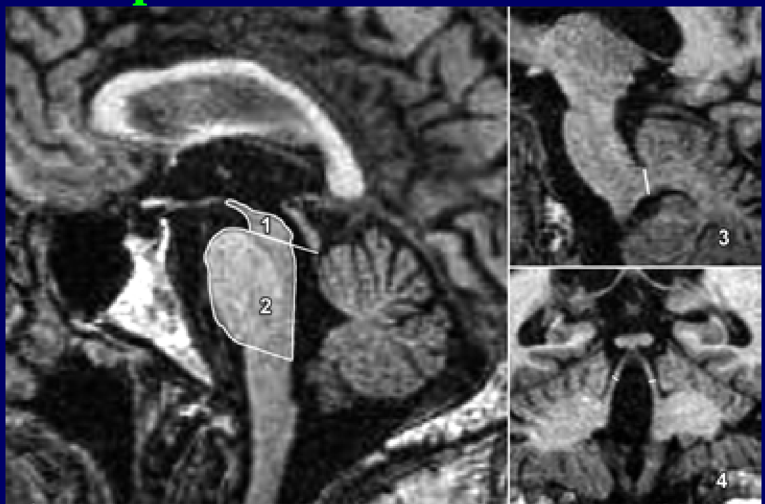
PD AND PARKINSONISMS

PSP *vs* PD / MRI brainstem measurements

Healthy control



PSP patient



Index: [(P/M) * (MCP/SCP)]

Cutoff and Statistical Values	MR Parkinsonism Index Value	MCP/SCP Value	P/M Value
PSP patients vs PD patients			
Cutoff value	≥13.55	≥2.69	≥4.88
Sensitivity (%)	100	78.8	90.9
Specificity (%)	100	88.9	93.5
PPV (%)	100	68.4	81.1
PSP patients vs MSA-P patients			
Cutoff value	≥12.85	≥2.43	≥4.62
Sensitivity (%)	100	93.9	97.0
Specificity (%)	100	89.5	94.7
PPV (%)	100	93.9	97.0
PSP patients vs control participants			
Cutoff value	≥13.58	≥2.69	≥4.65
Sensitivity (%)	100	78.8	97.0
Specificity (%)	100	88.0	94.0
PPV (%)	100	81.2	91.4

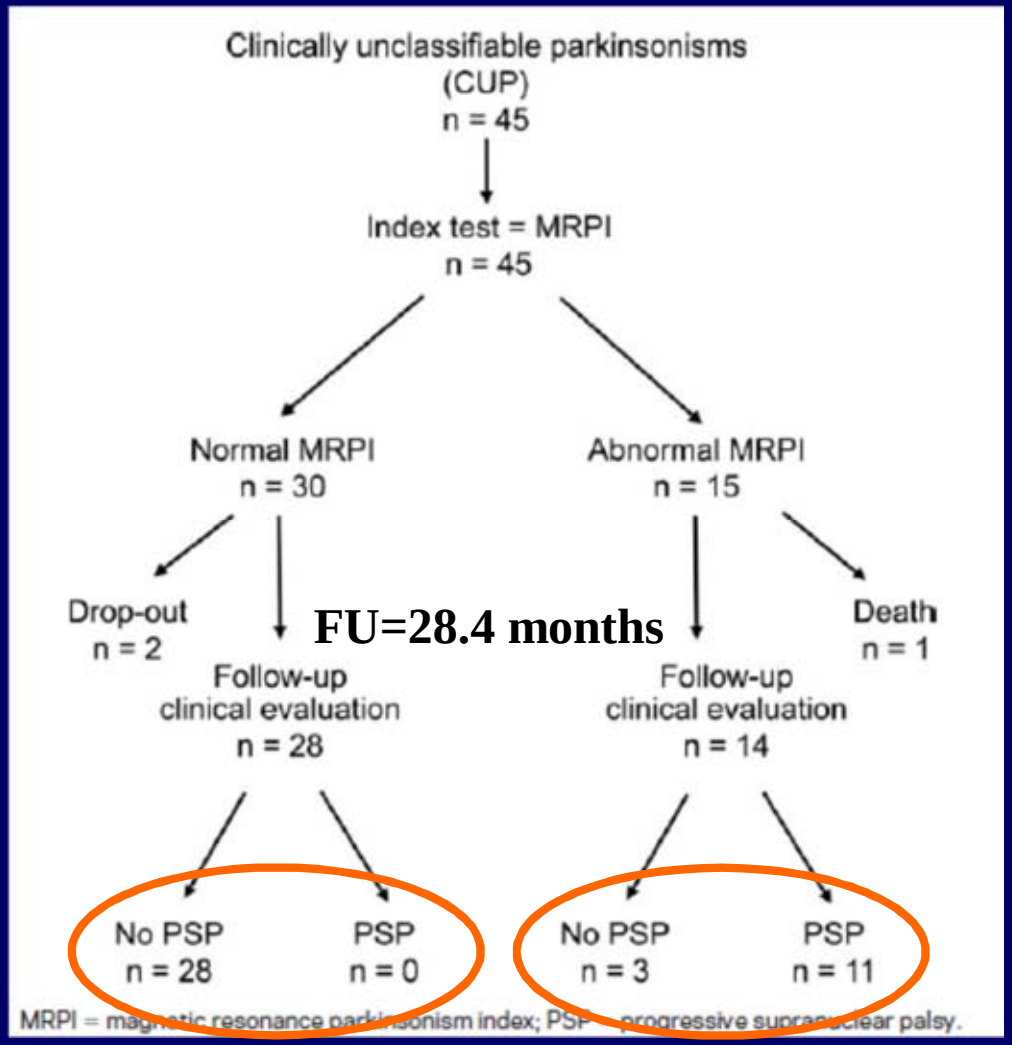
Quattrone et al. Radiology 2008

	Cut-off values	Sensitivity (%)	Specificity (%)	Accuracy (%)
Pons/midbrain ratio				
PSP-RS vs. controls	≥5.00	100	87.5	91
PSP-P vs. controls	≥4.52	80	67	47
PSP-RS vs. PD	≥6.01	90	96	94
PSP-P vs. PD	≥6.02	60	96	86
PSP-P vs. PSP-RS	<7.32	90	70	80
MR parkinsonism index				
PSP-RS vs. controls	≥13.44	100	92	94
PSP-P vs. controls	≥15.40	60	100	88
PSP-RS vs. PD	≥13.57	100	92	97
PSP-P vs. PD	≥ 11.07	70	68	40
PSP-P vs. PSP-RS	<17.50	80	70	75

Longoni et al.

PD AND PARKINSONISMS

PSP / MRI brainstem measurements



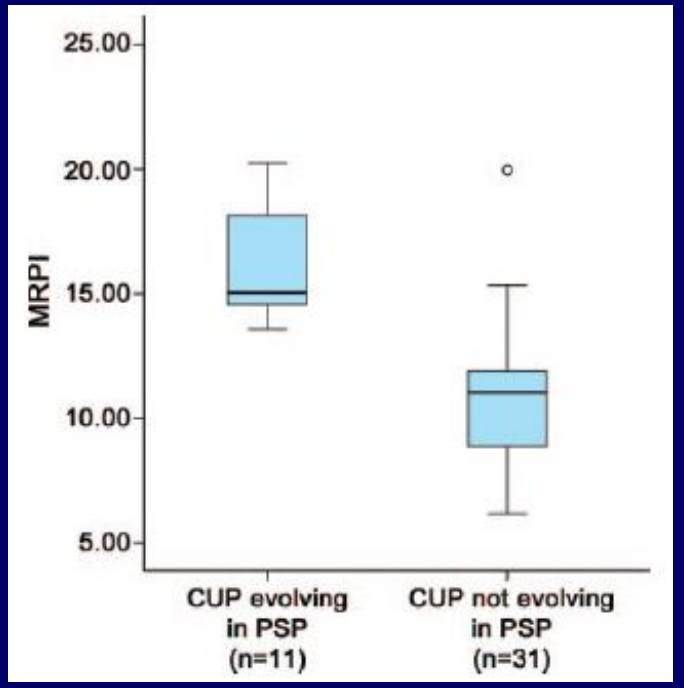


Table 2 Validity of clinical features and MRPI for PSP in patients with CUP

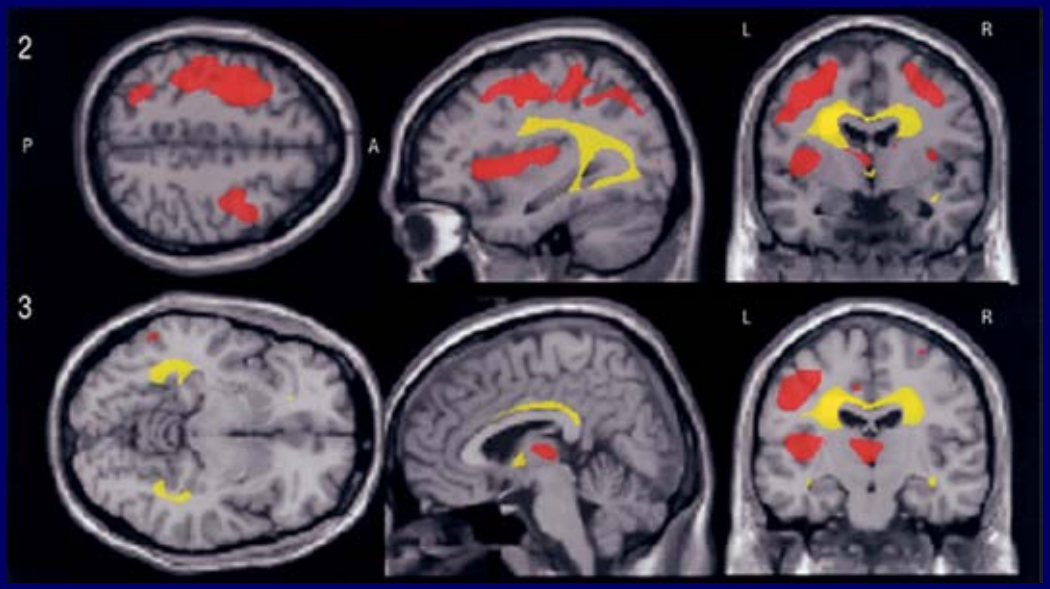
Baseline evaluation	Sensitivity, %	Specificity, %	PPV, %	NPV, %	Accuracy, %
Clinical features					
Isolated postural instability with falls in the first year of disease	45.4	83.9	50	81.2	73.8
Slowness of vertical saccades	18.2	77.4	22.2	72.7	61.9
Postural instability with falls after the first year of the disease and slowness of vertical saccades	27.3	93.5	60	78.4	76.2
Freezing in the first 3 years of disease	9.1	58.1	7.1	64.3	45.2
MRI features					
MRPI value ≥13.55	100	90.3	78.6	100	92.9

Morelli et al., Neurology 2011

PD AND PARKINSONISMS

PSP and CBS / GM and WM atrophy

PSP and CBS *vs* controls

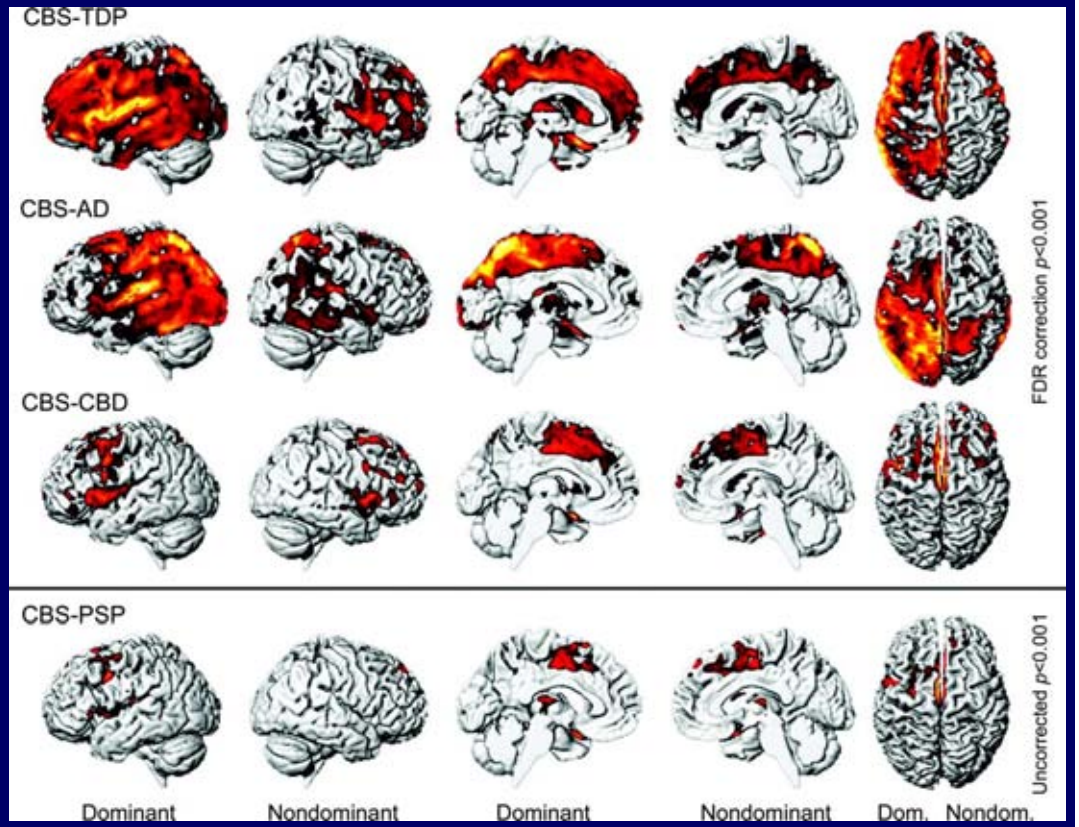


■ GM loss ■ WM loss

Bilateral premotor cortex, superior parietal lobules, striatum, frontal subcortical WM (L>R)

Boxer et al., Arch Neurol 2006

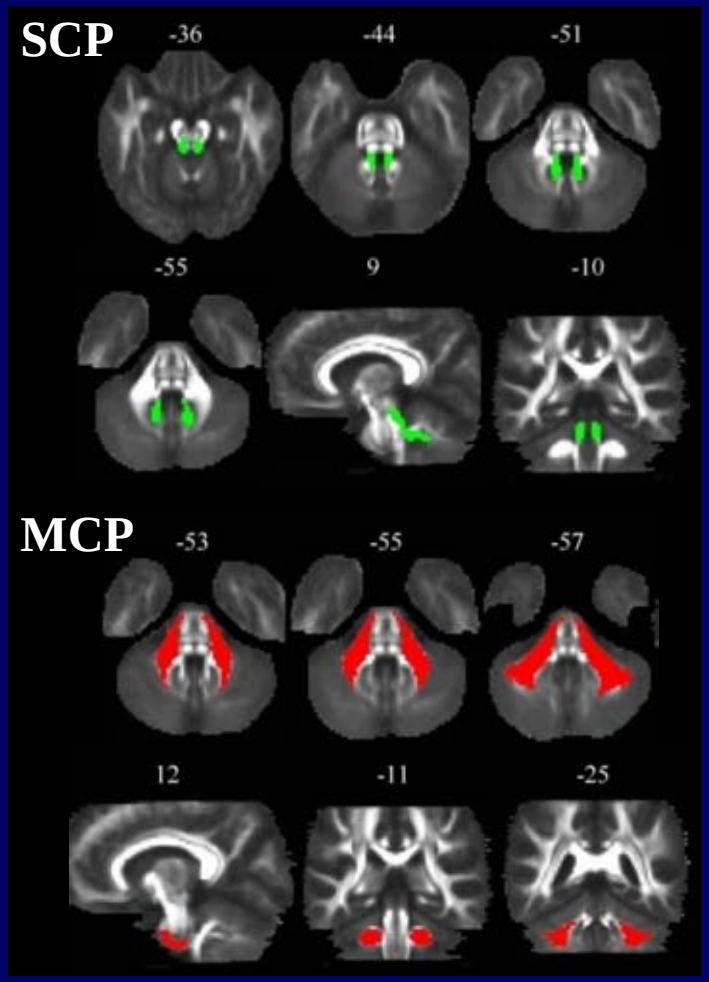
CBS: GM atrophy *vs.* pathology



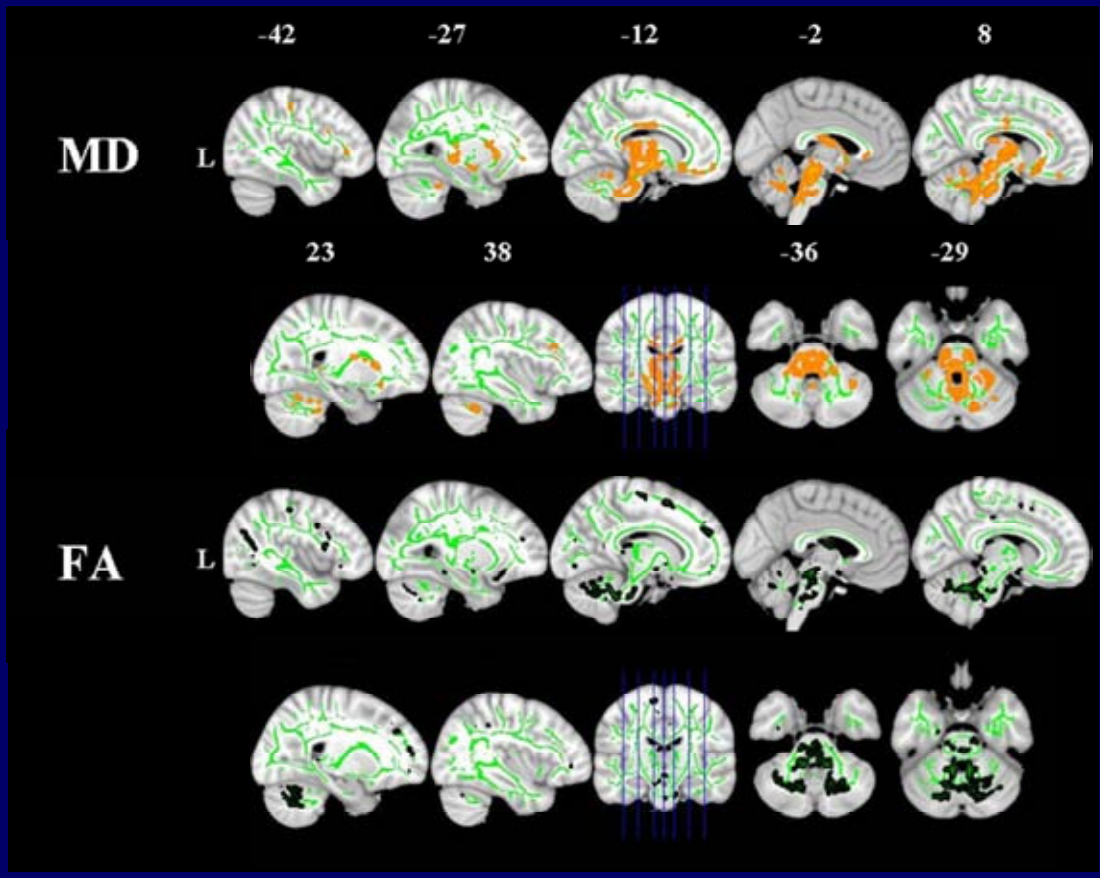
Whitwell et al., Neurology 2010

PD AND PARKINSONISMS

PSP / WM damage



PSP-RS *vs.* PSP-P



↑ MD: SCPs and CC

↓FA: SCPs, CC, and cingulum bilaterally

↑radD: SCPs, CC, and R cingulum

↓axD: SCPs, cingulum bilaterally, and L MCP

No change in: uncinate, SLF, ILF and IFO

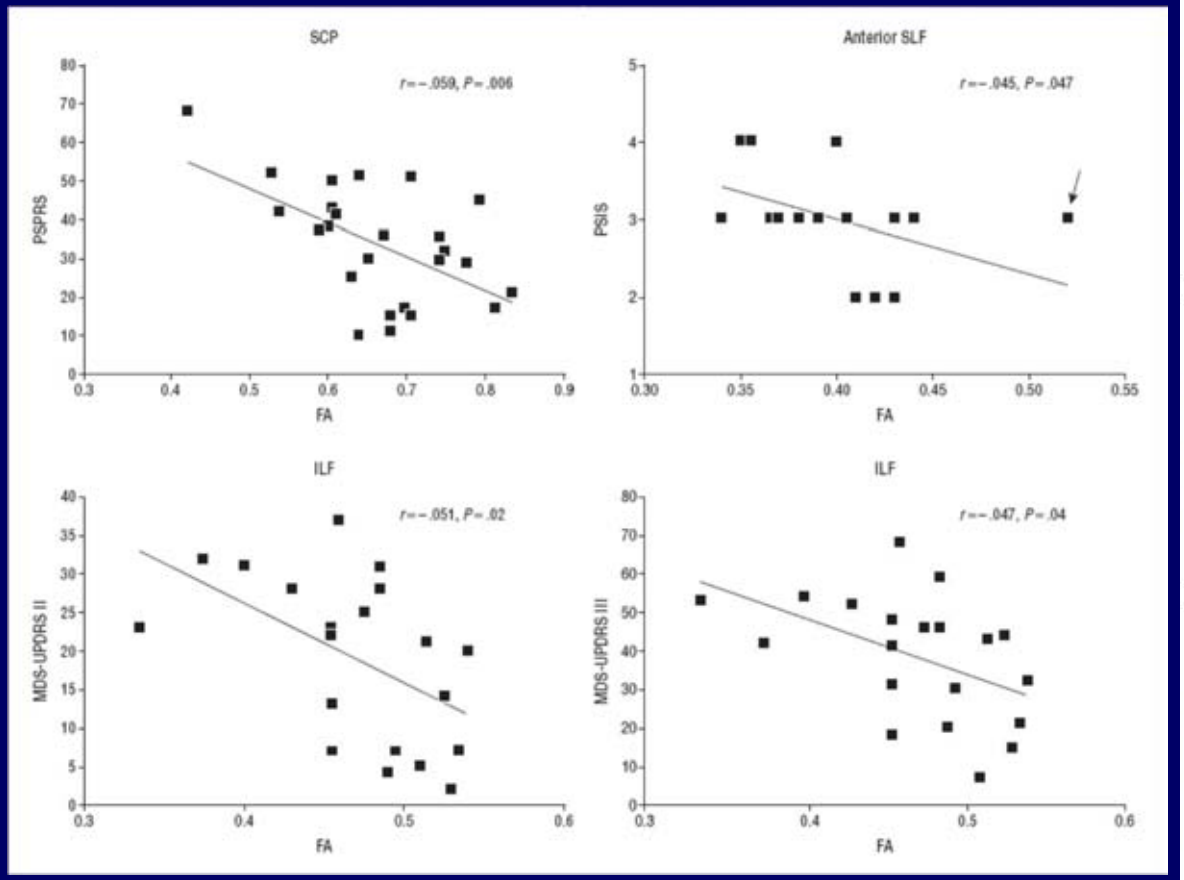
	MRPI	MRPI and DT MRI measures	
	C-index (95% CI)	C-index (95% CI)	Relative IDI (%)
PSP-RS versus healthy controls	0.92 (0.85–0.99)	0.98 (0.94–1.00)	38
PSP-P versus healthy controls	0.70 (0.54–0.86)	0.82 (0.67–0.97)	141
PSP-RS versus PSP-P	0.77 (0.61–0.93)	0.84 (0.73–0.99)	96

Canu, … Filippi. Mov Disord 2011

PD AND PARKINSONISMS

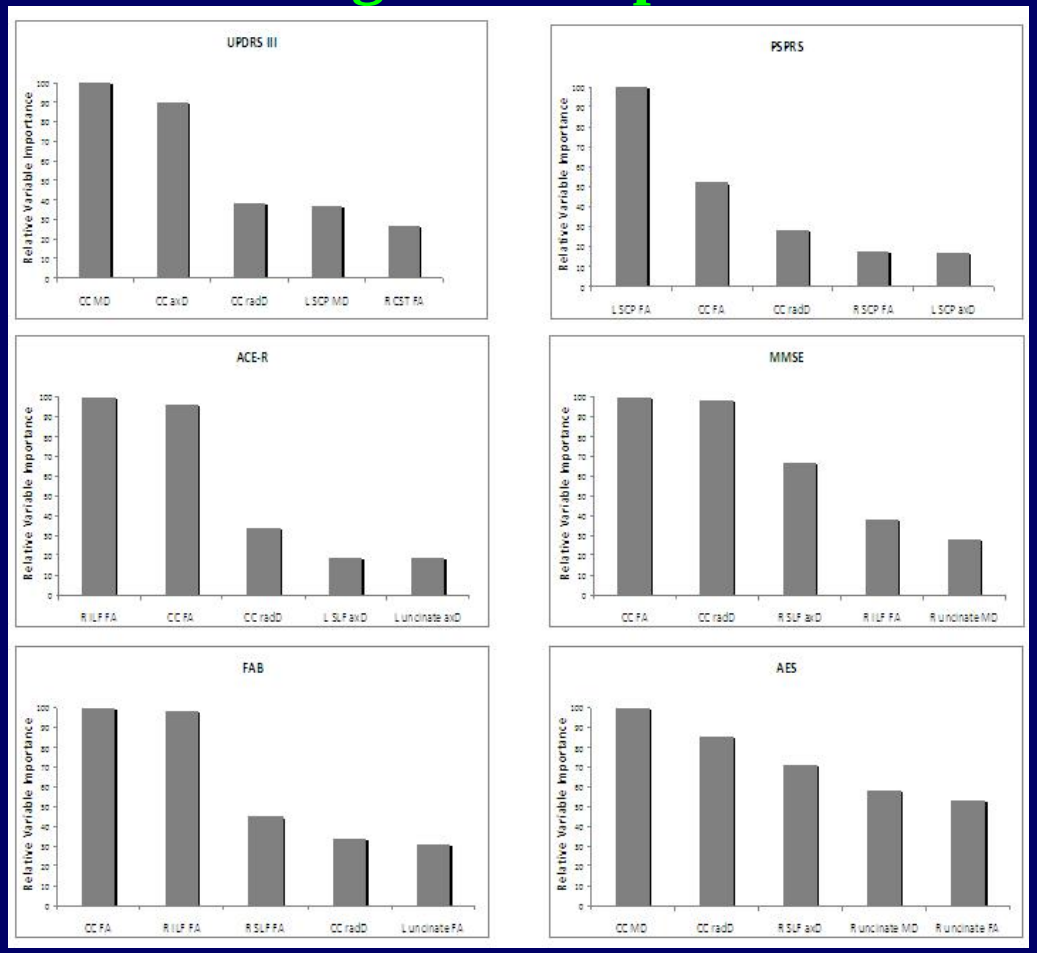
PSP / WM damage

WM damage *vs* motor disability



Whitwell et al., Arch Neurol 2011

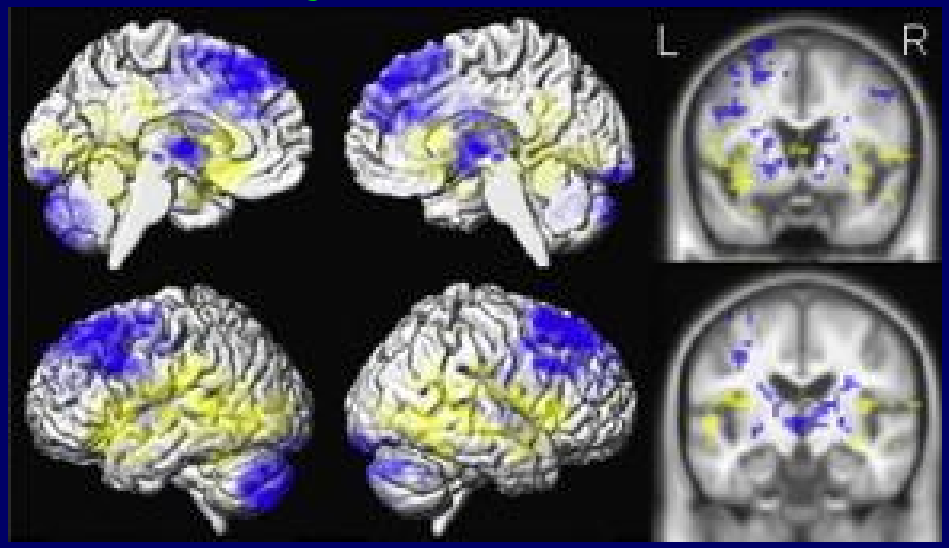
WM damage *vs* motor disability and cognitive impairment



Agosta, … Filippi. Submitted

PD AND PARKINSONISMS
PSP / Cortical reorganization

Seed-analysis thalamus

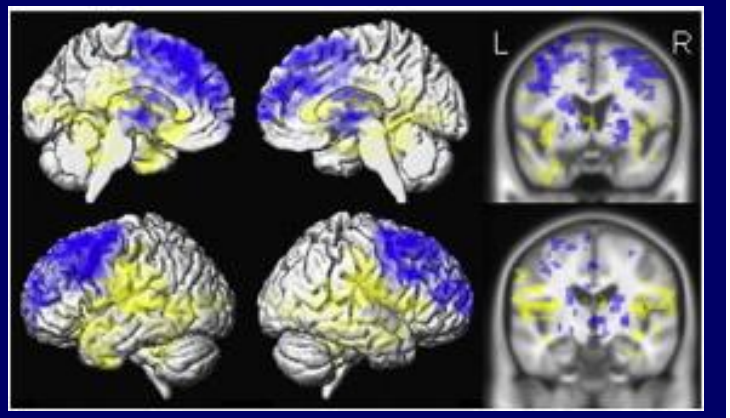


- Increased connectivity
- Decreased connectivity

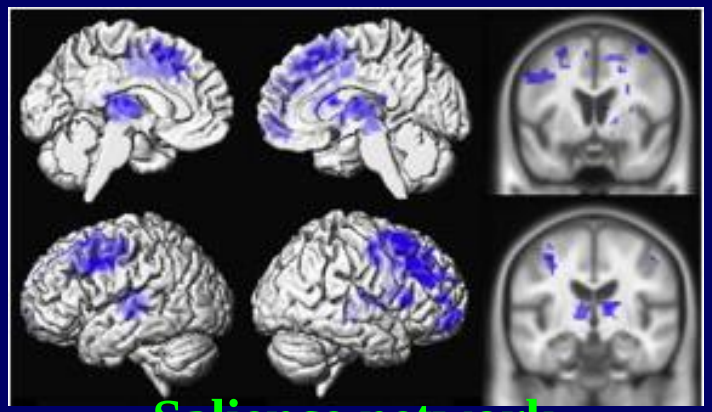
Mean FA of the SCP was correlated with functional connectivity changes in the thalamus

Whitwell et al., Parkinsonism & Relat Disord 2011

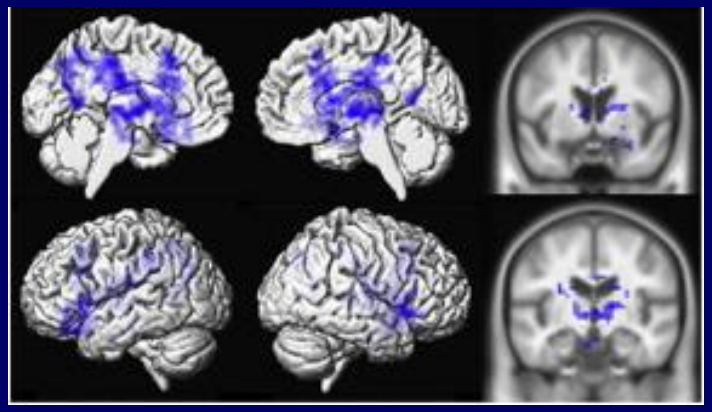
Basal ganglia network



DMN



Salience network



PD AND PARKINSONISMS
Atypical aprkinsonisms / Conclusions

Table 2
Brain MR features in neurodegenerative parkinsonism

Brain MR Feature	PD	MSA-P	PSP	Refs.
cMR imaging				
Normal (in the age range)	++	–	–	32,64,67,68,70,72,78a
Putaminal atrophy	–	++	++	64,68,70,72,83a
Putaminal hyperintense rim at 1.5 T	+	++	+	64,67–70,72,75,83a
Putaminal hypointensity at 1.5 T	–	++	–	32,64,67,68,70,72,83a
Pontine and cerebellar vermian atrophy	–	++	+	64,72,75,83a
Signal changes in the pons or MCP including "hot-cross bun" sign at 1.5 T	–	++	–	64,66,75,83a
Midbrain atrophy including indirect signs of midbrain atrophy	–	–	++	59,72,78,80,83,87a
MR planimetry				
Reduced AP midbrain diameter	–	+	++	78,83,87,88
Reduced ratio between midbrain and pontine areas	–	–	+++	79,95,96
DW/DT imaging				
Increased putaminal diffusivity at 1.5 T	–	+++	++	43,70,116–118,126–129
Increased SCP diffusivity at 1.5 T	–		+++	114,116,128

Seppi and Poewe, Neuroimaging Clin N Am 2010

PD AND PARKINSONISMS

Conclusions

- In the diagnostic work up of patients with parkinsonian syndromes, the main role of conventional MRI is still to exclude alternative conditions.
- The development of new markers from conventional MRI and modern MR techniques has undoubtedly improved our ability to differentiate neurodegenerative parkinsonisms.
- Modern nuclear medicine and MR techniques are useful to gain insight into the pathophysiology of parkinsonisms.
- To define which neuroimaging techniques will emerge as standard investigations in the work up of patients with parkinsonisms requires longitudinal studies to be conducted, which should start as close as possible to the clinical onset when diagnosis is uncertain.

DIVISION OF NEUROSCIENCE

BRAINMAP

Human BRAin IN-vivo MAPping with neuroimaging

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