Scuola Superiore di Neurologia Sin

V CORSO

Neuroimmagini nella Malattia di Parkinson e Parkinsonismi

Genova, 21-22 febbraio 2017

Accademia Nazionale di Medicina - Via M. Piaggio 17/6 - Genova

NUOVE TECNICHE DI NEUROIMAGING

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MRI IN PD & PARKINSONISMS

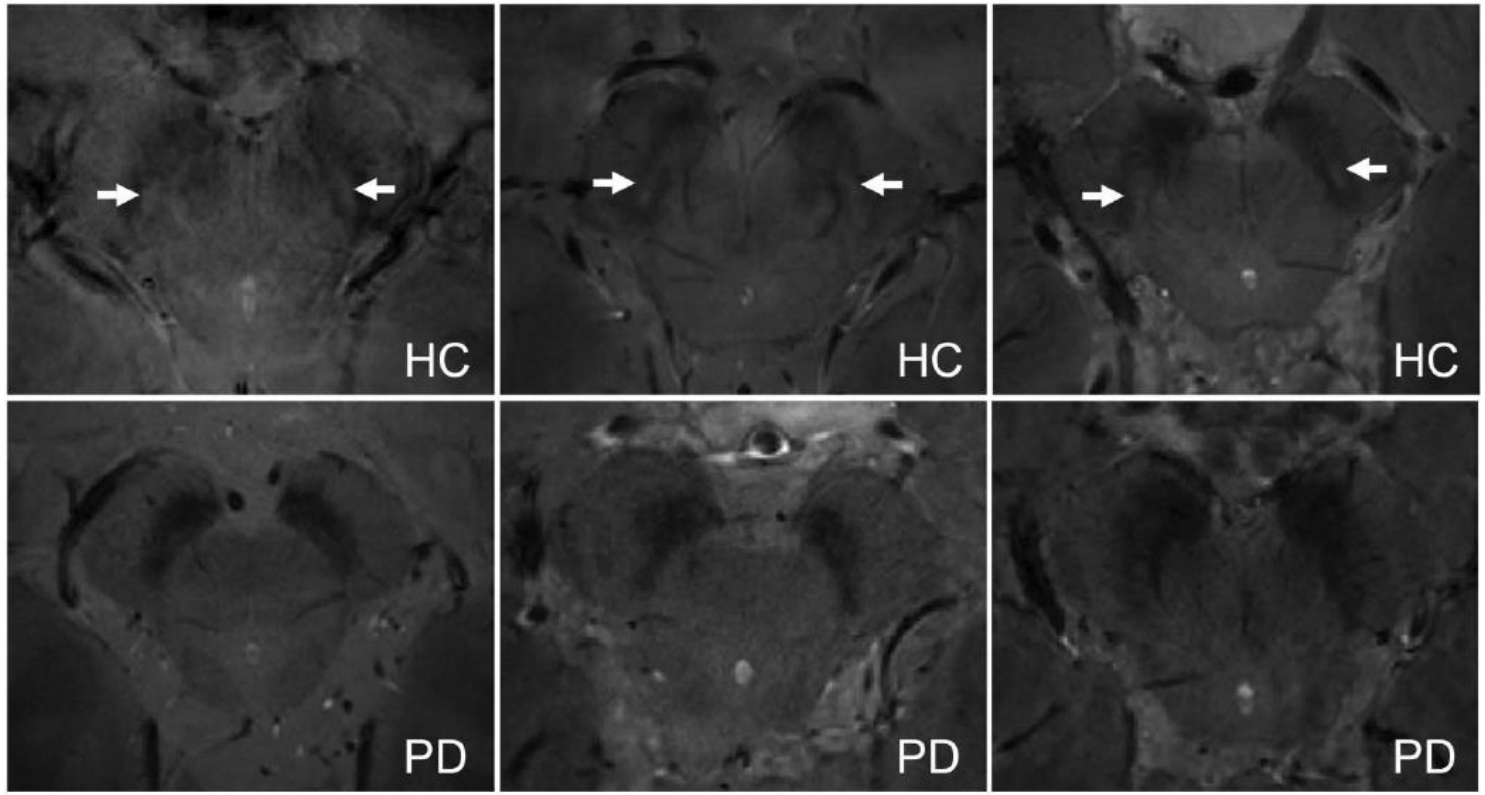
Outline of the presentation

- ✓ **Diagnosis**
- ✓ Structural and functional correlates of motor and non-motor features
- ✓ Monitoring disease progression

MRI IN PD & PARKINSONISMS

Diagnosis / Substantia nigra

7.0 T



Blazejewska et al., Neurology 2013

Bilateral absence of Nigrosome 1 in PD

7.0 T **Sensitivity 93%, specificity 100%, accuracy 96%**

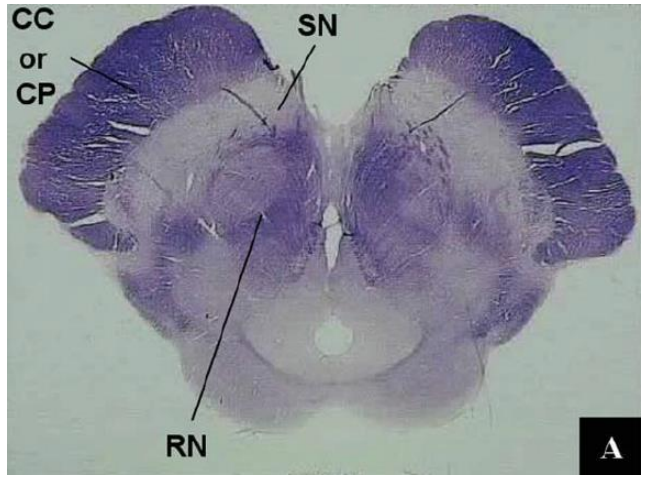
3.0 T **Sensitivity 79%, specificity 94%, accuracy 86%**

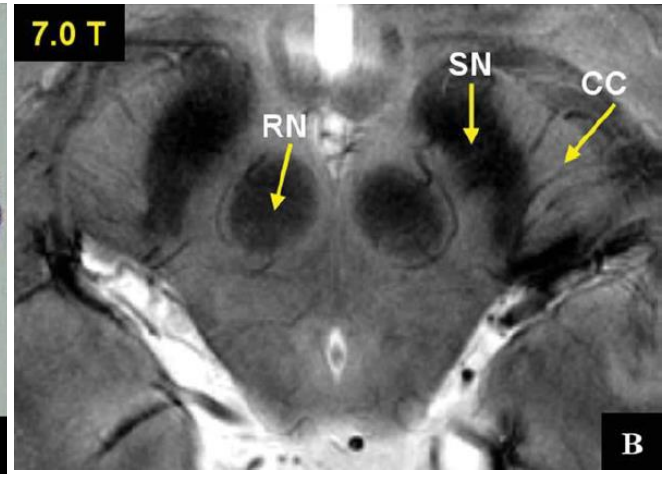
Cosottini et al., Radiology 2014; AJNR 2015

MRI IN PD & PARKINSONISMS

Diagnosis / Substantia nigra

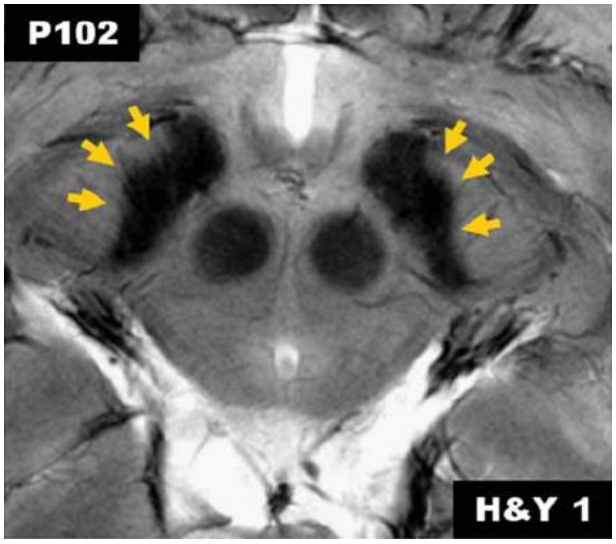
7.0 T



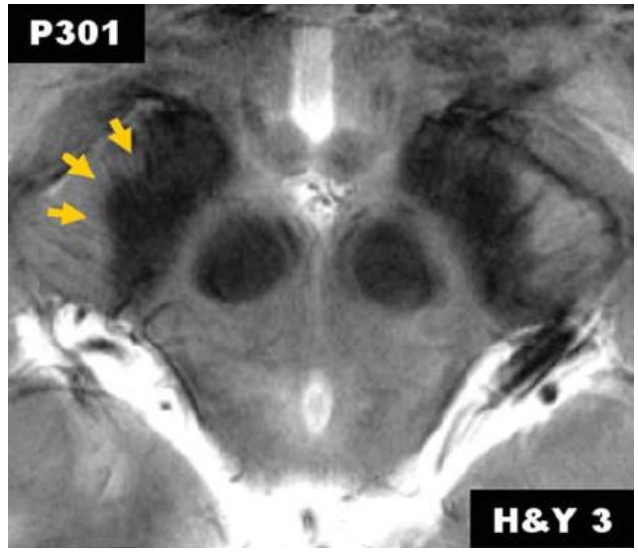


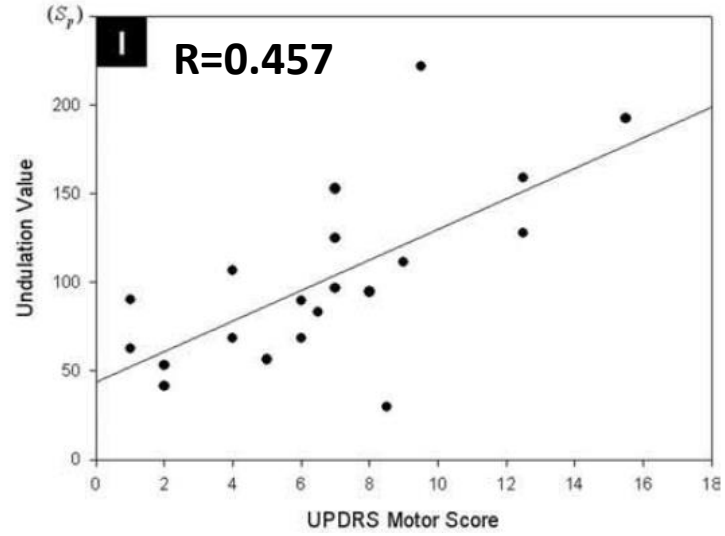
SN: substantia nigra
RN: red nucleus
CC: crus cerebri

Early PD



Advanced PD





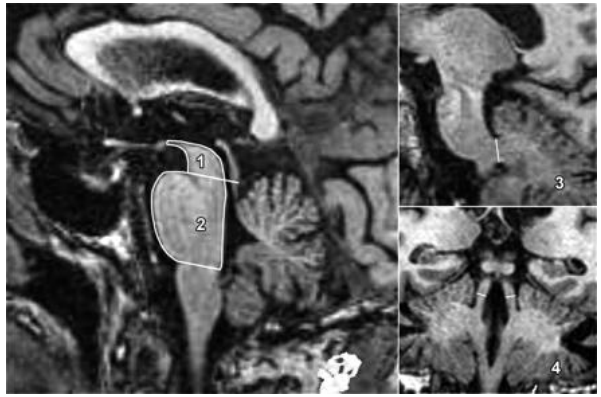
Sensitivity 90%, specificity 100%

Cho et al., Mov Disord 2011; Ann Neurol 2012

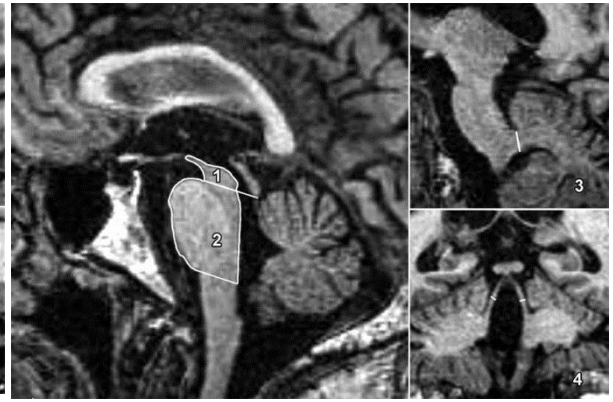
MRI IN PD & PARKINSONISMS

Diagnosis / Brainstem structures

Healthy control



PSPs patient

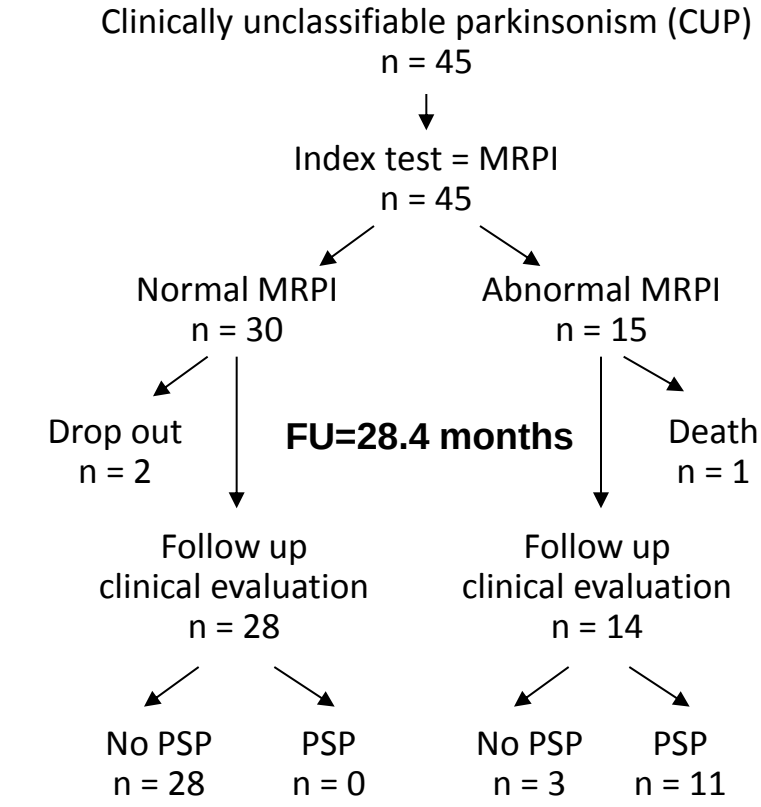


Index: [(P/M) * (MCP/SCP)]

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

Predicting PSP in unclassifiable parkinsonisms



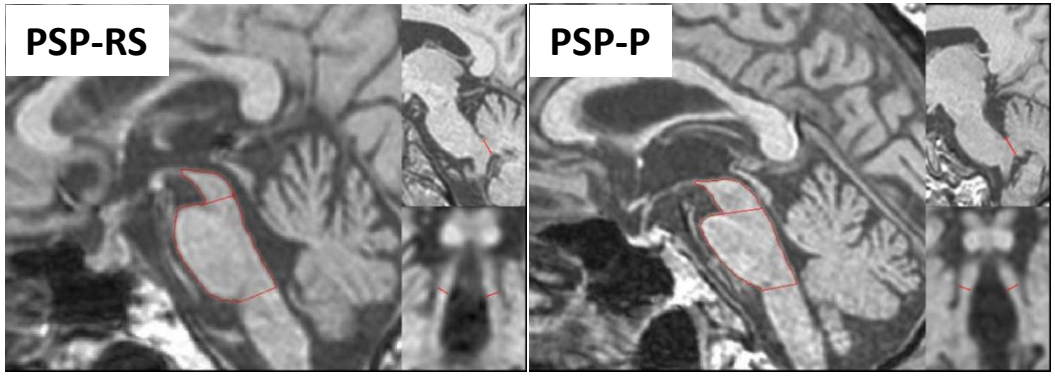
MRPI: accuracy= 92.9%
Vertical ocular slowness: accuracy= 61.9%
First-year falls: accuracy= 73.8%

Morelli et al., Neurology 2011

MRI IN PD & PARKINSONISMS

Diagnosis / Brainstem structures

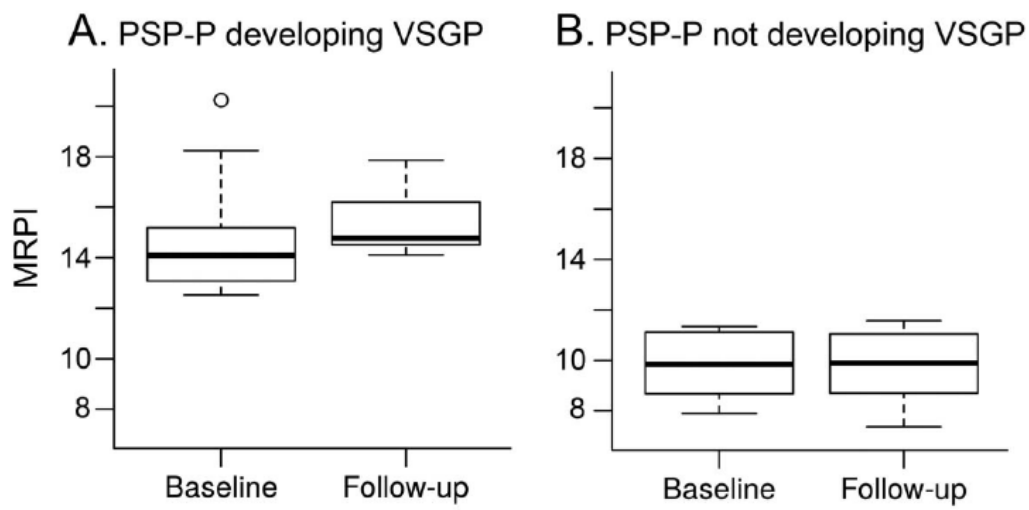
PS-RS *vs* PSP-P



	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., Mov Disord 2011

Predicting vertical supranuclear gaze palsy in PSP-P



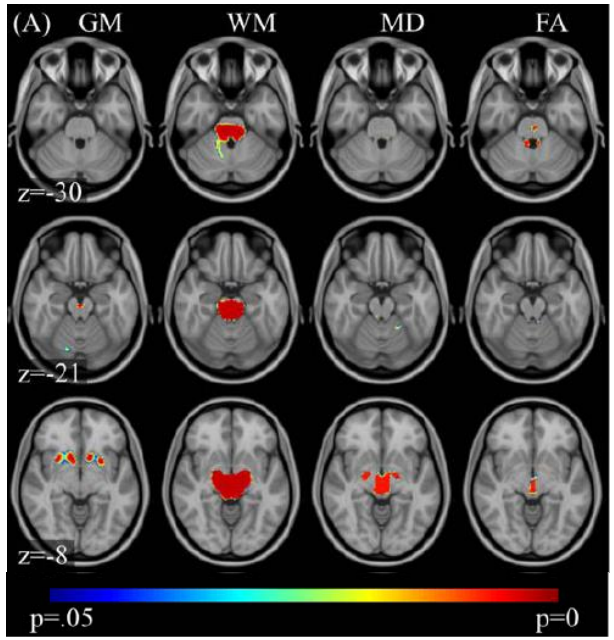
	Sensitivity, %	Specificity, %	PPV, %	NPV, %	Accuracy, %
Clinical features					
Isolated postural instability with backward falls after 2 y of disease onset	0	90	0	45	42.9
Slowness of vertical saccades after 2 y of disease onset	45.5	20.0	38.5	25.0	33.3
Postural instability with backward falls and slowness of vertical saccades after 2 y of disease onset	54.6	90.0	85.7	64.3	71.4
MRI measurements					
Midbrain area (cutoff value ≤95.0)[a]	81.8	90	90	81.8	85.7
SCP width (cutoff value ≤3.41)[a]	63.6	100	100	71.4	81.0
MRPI (cutoff value ≥12.52)[a]	100	100	100	100	100

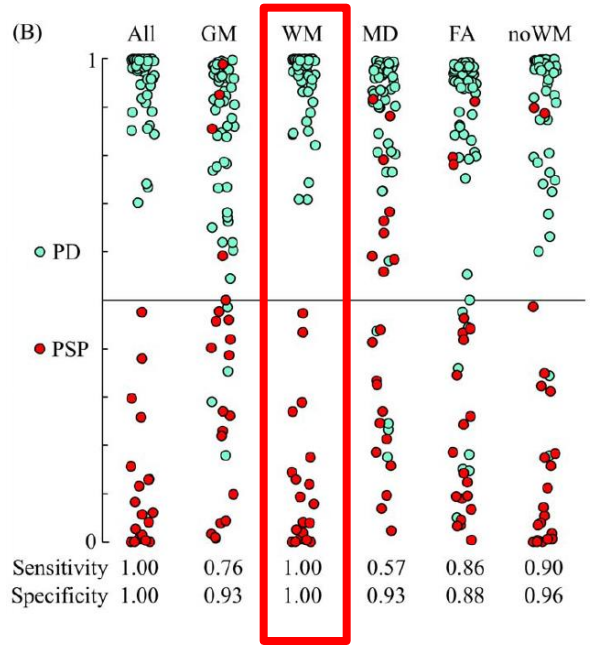
Quattrone et al., Neurology 2016

MRI IN PD & PARKINSONISMS

Diagnosis / Whole brain

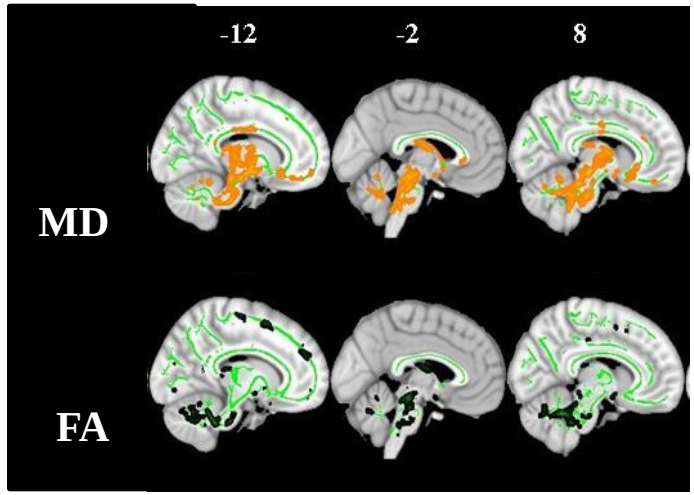
PD *vs* PSP-RS





Cherubini et al., Mov Disord 2014

PSP-RS *vs* PSP-P



	MRPI	Composite MRI score (MRPI + DT MRI)	
	C-index (95% CI)	C-index (95% CI)	Relative IDI (%)
PSP-RS *vs* HC	0.92 (0.85-0.99)	0.98 (0.94-1.00)	38
PSP-P *vs* HC	0.70 (0.54-0.86)	0.82 (0.67-0.97)	141
PSP-RS *vs* PSP-P	0.77 (0.61-0.93)	0.84 (0.73-0.99)	96

Agosta et al., Neurobiol Aging 2012

MRI IN PD & PARKINSONISMS

Outline of the presentation

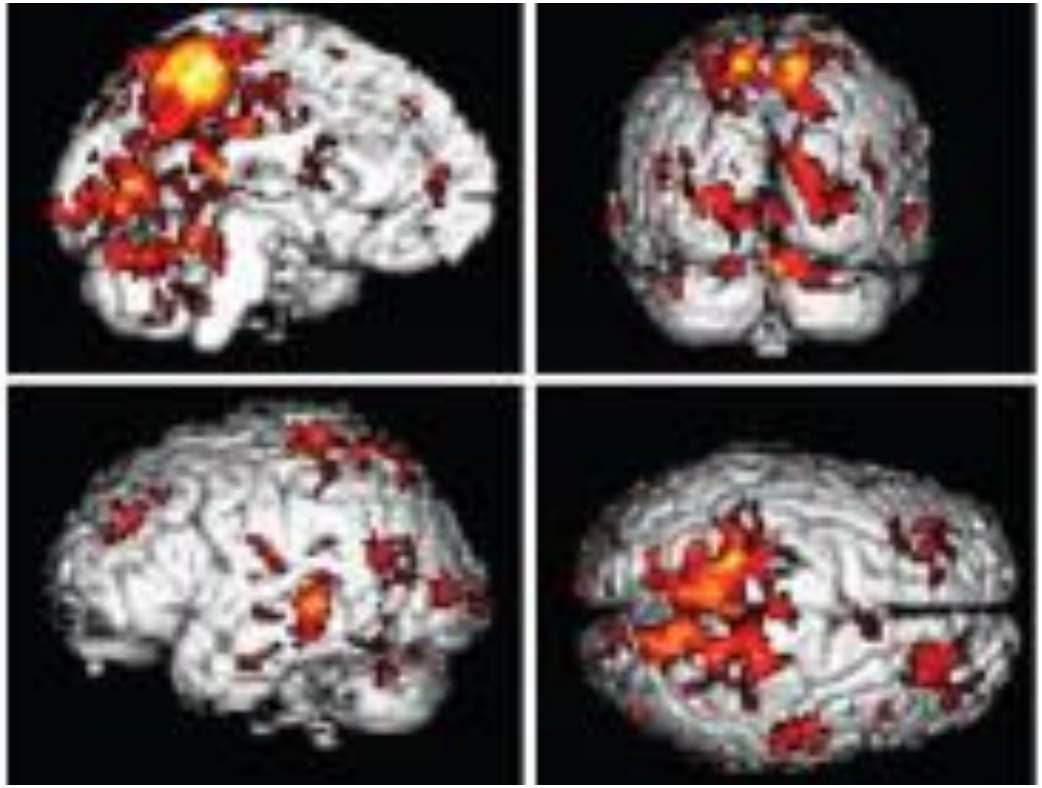
- ✓ Diagnosis
- ✓ **Structural and functional correlates of motor and non-motor features**
- ✓ Monitoring disease progression

MRI IN PD & PARKINSONISMS

Bradykinesia / Brain functional changes

Dual tasking

Right hand finger movement + counting letters
PD > controls

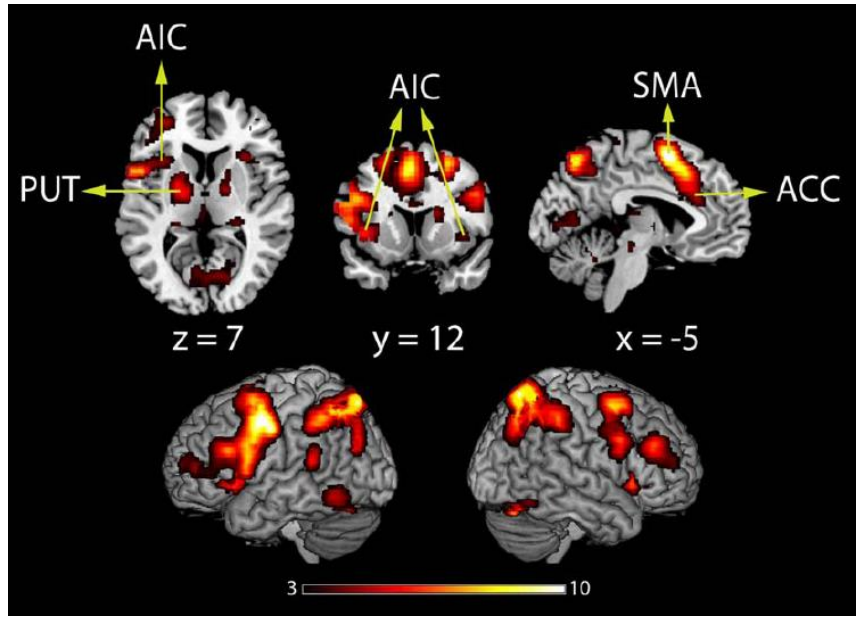


Increased brain activity at comparable performance

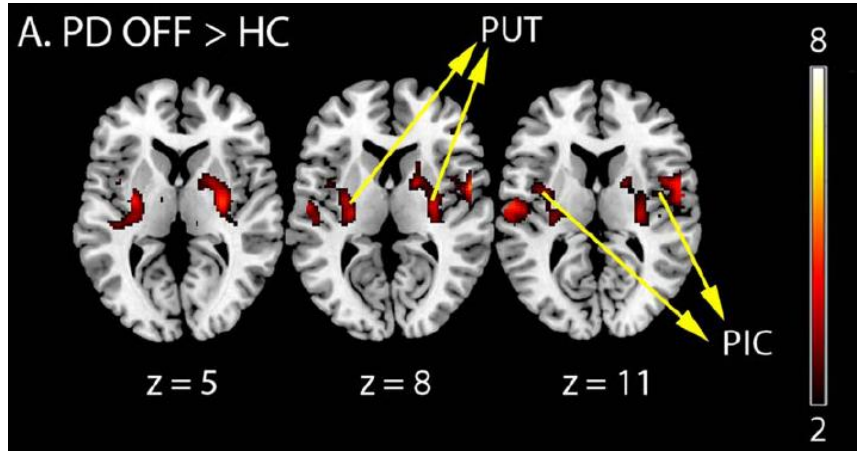
Wu & Hallett, JNNP 2008

Load-dependent activation

(high-load minus low-load) in controls and PD



Load-dependent activation: PD > controls

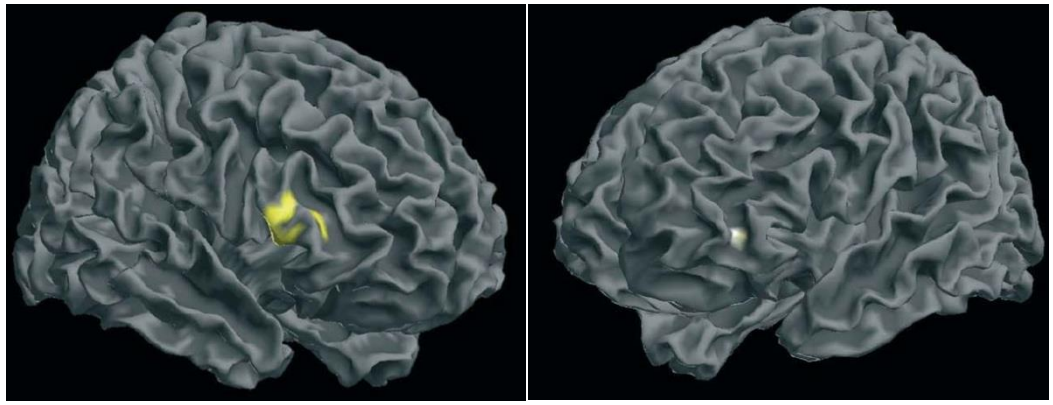


Poston et al., Ann Neurol 2016

MRI IN PD & PARKINSONISMS

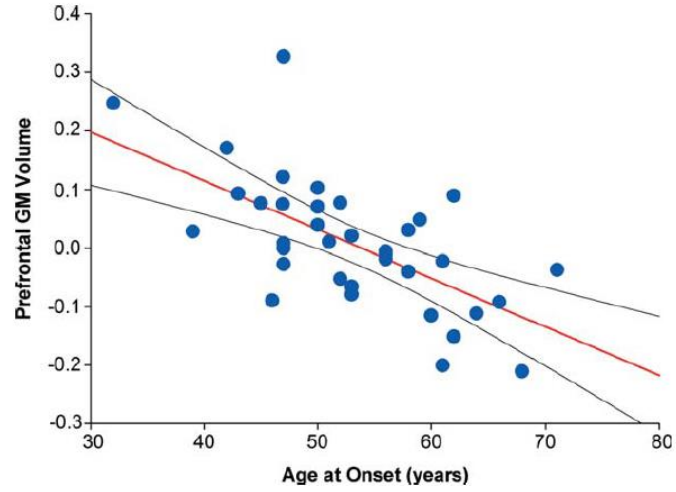
Dyskinesia / Brain functional and structural changes

Dyskinetic > nondyskinetic PD (thickness)



Bilateral inferior frontal gyrus

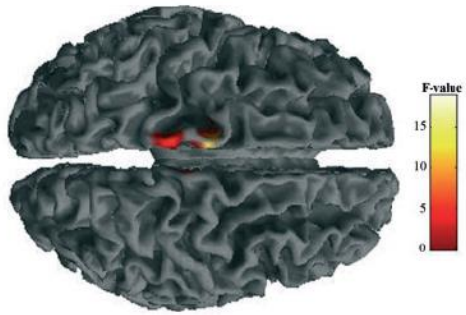
Right frontal GM *vs* age at onset in dyskinetic PD



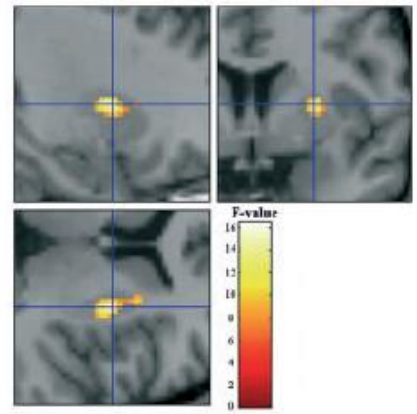
Cerasa et al., Mov Disord 2011

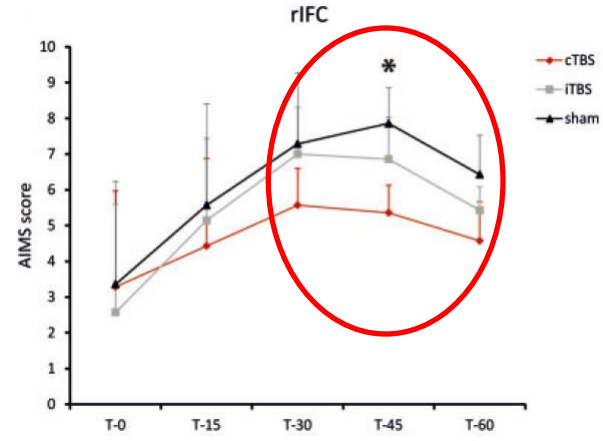
fMRI

Dyskinetic < nondyskinetic



Dyskinetic > nondyskinetic

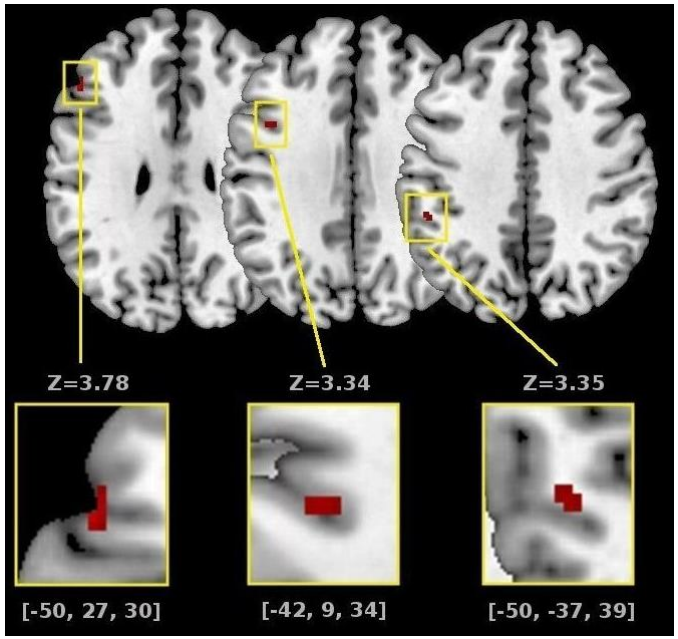




Cerasa et al., Brain 2015

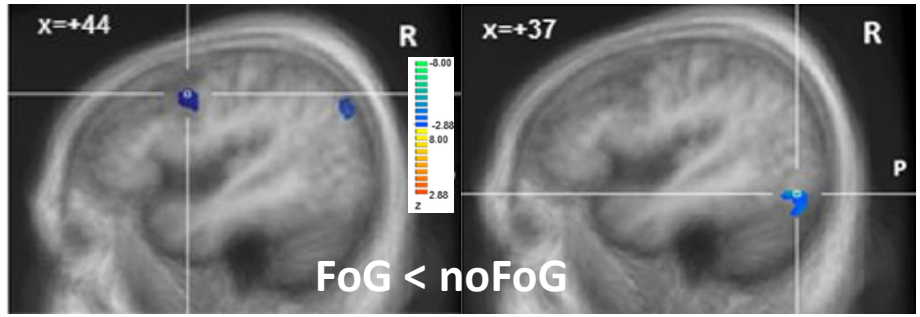
MRI IN PD & PARKINSONISMS

Freezing of gait / Brain functional and structural changes



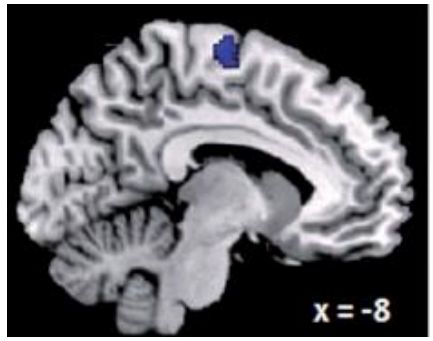
Kostic et al., Neurology 2012

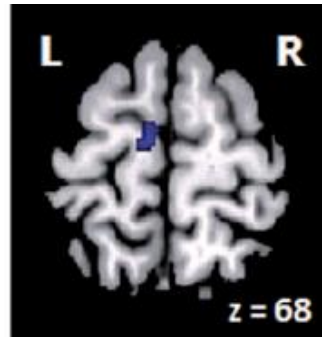
RS fMRI: PD-FoG *vs* PD noFoG

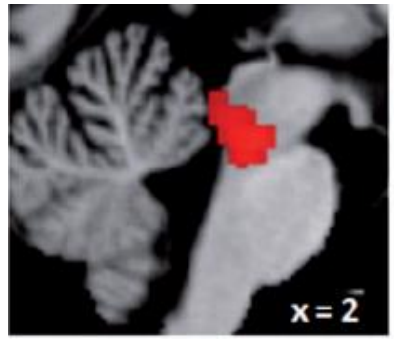


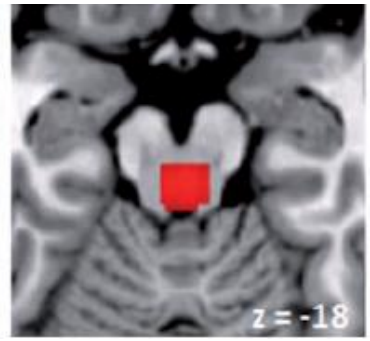
Tessitore et al., Parkinsonism Relat Dis 2012

fMRI of imagined forward walking: PD-FoG *vs* PD-noFoG







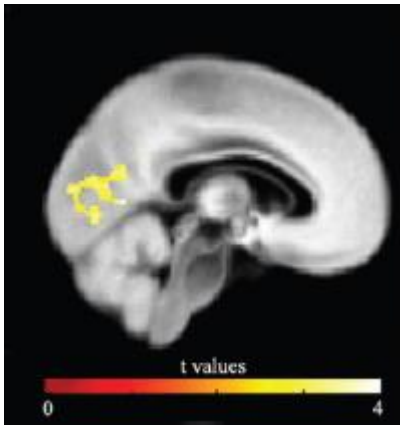


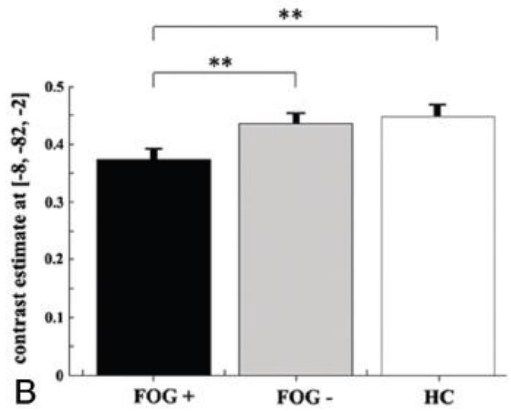
PD-FoG < PD-noFoG

PD-FoG > PD-noFoG

Snijders et al., Brain 2011

PD-FoG *vs* PD noFoG



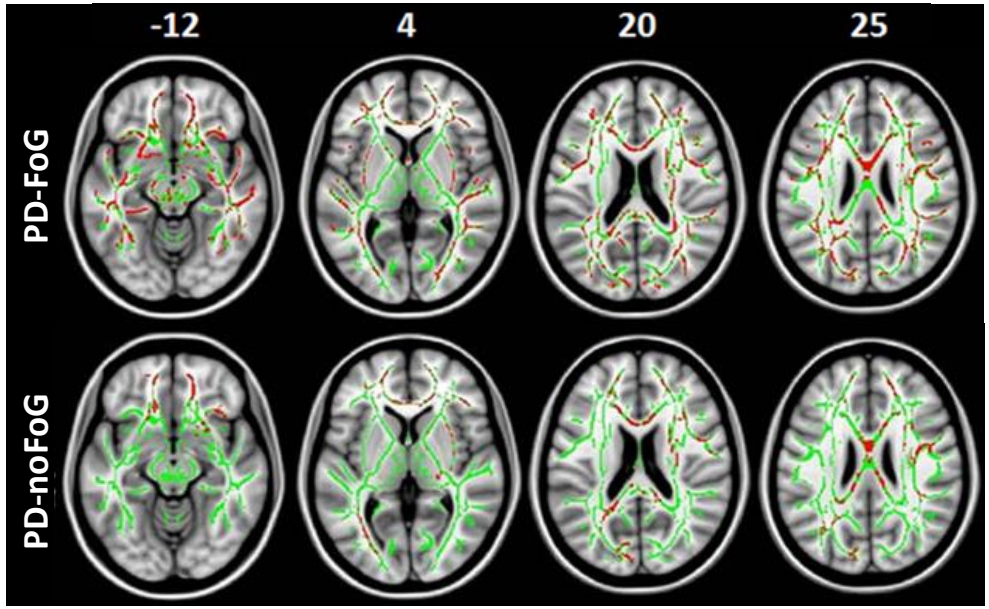


Tessitore et al., AJNR 2012

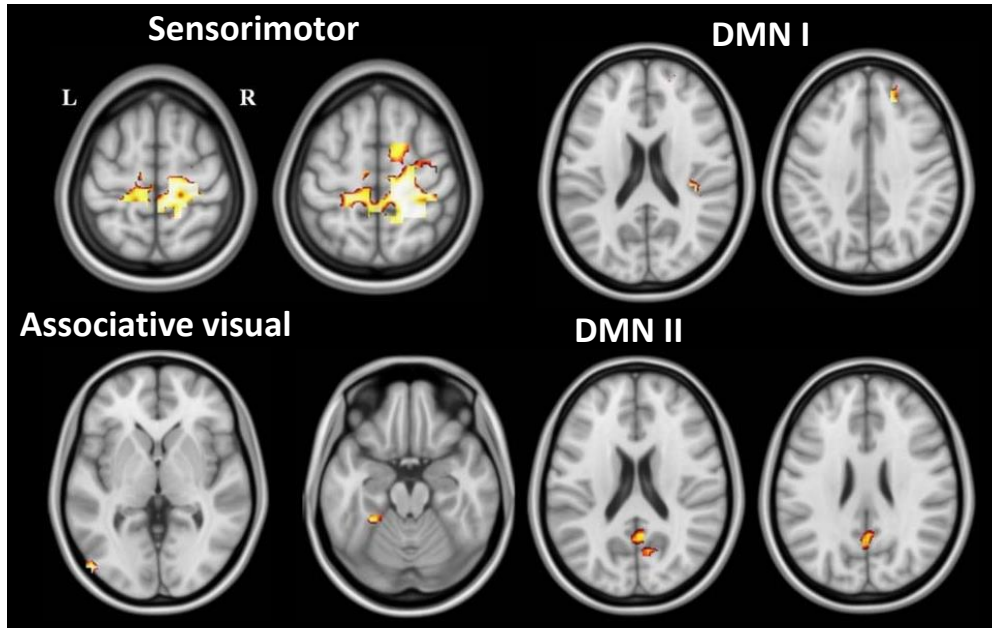
MRI IN PD & PARKINSONISMS

Freezing of gait / Brain functional and structural changes

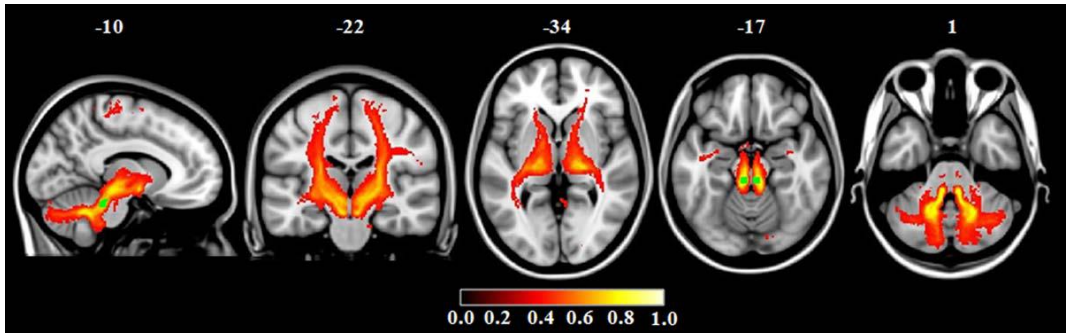
Decreased FA in PD-FoG and PD-noFoG



↓ RS functional connectivity in PD-FoG *vs* HC

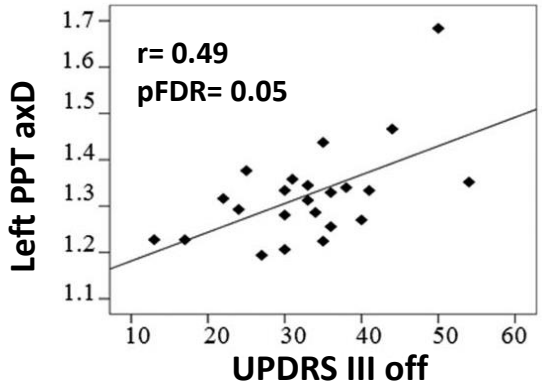


Increased axD of L pedunculopontine tract in PD-FoG *vs* HC



Probability map of PPT in PD-FoG

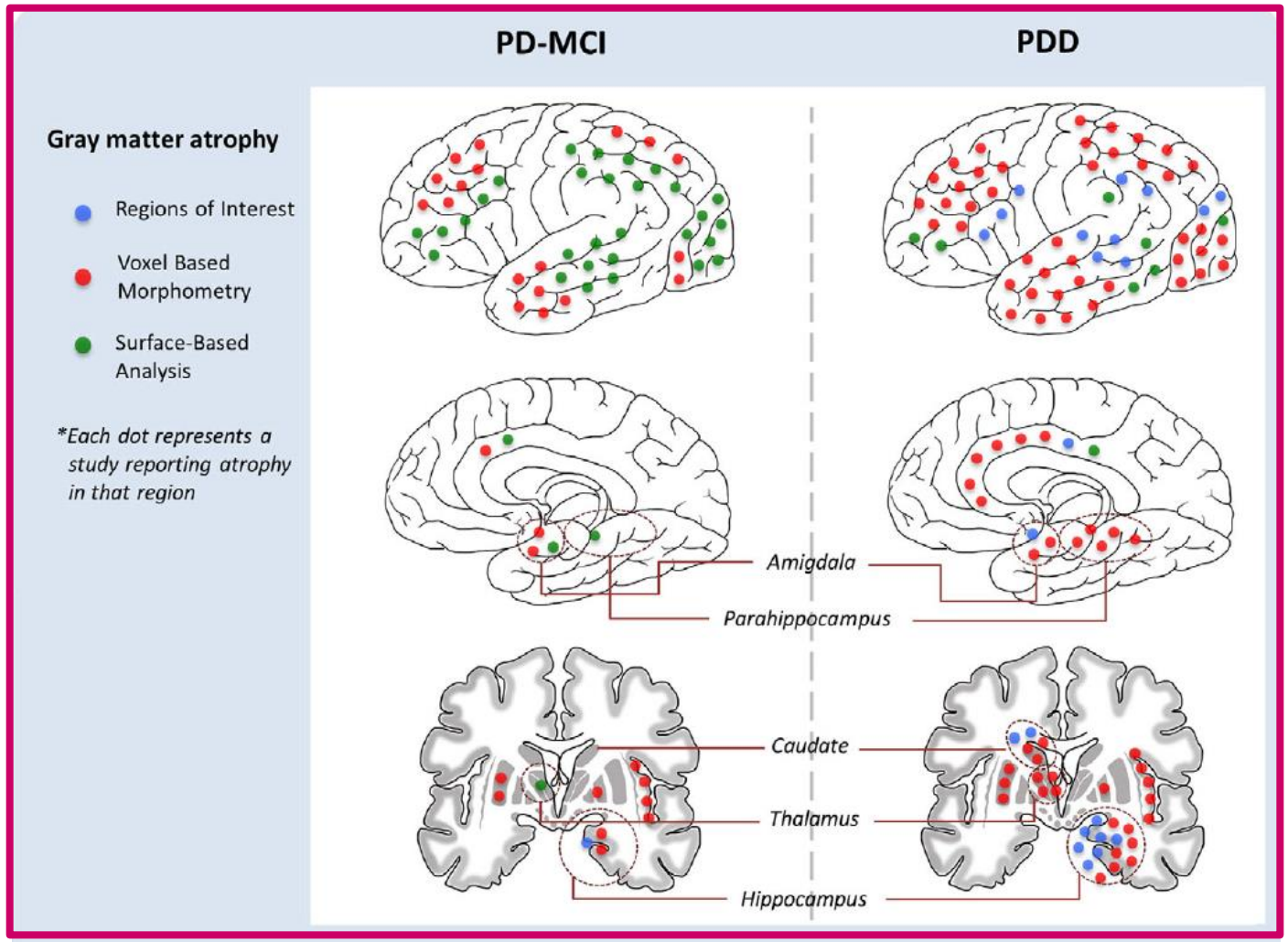
Left PPT axD *vs* UPDRS III



Canu et al., Hum Brain Mapp 2015

MRI IN PD & PARKINSONISMS

Cognitive impairment / Brain structural changes



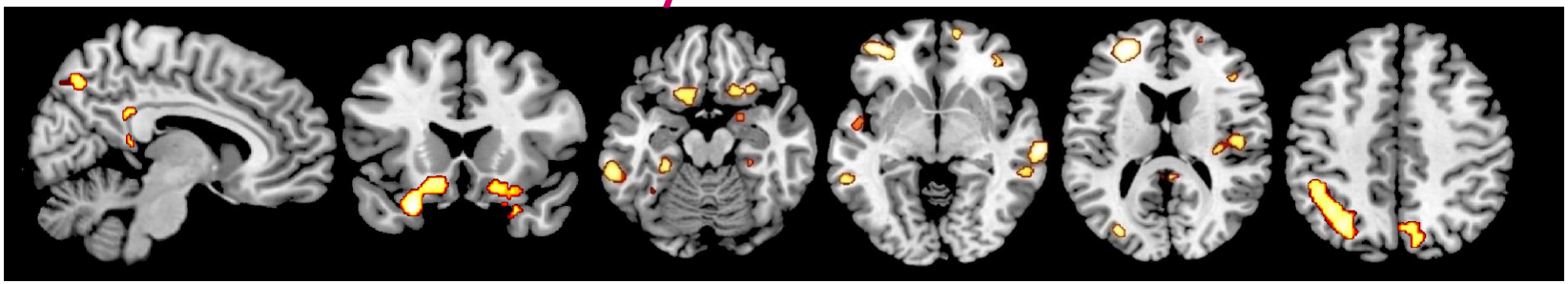
DTI: Tract damage	Superior longitudinal, inferior fronto-occipital and uncinate fasciculi, cingulum, corpus callosum, corona radiata	Widespread WM, superior and inferior longitudinal, inferior fronto-occipital and uncinate fasciculi, cingulum, internal capsule, substantia nigra, hippocampus

Delgado-Alvarado et al., Mov Disord 2016

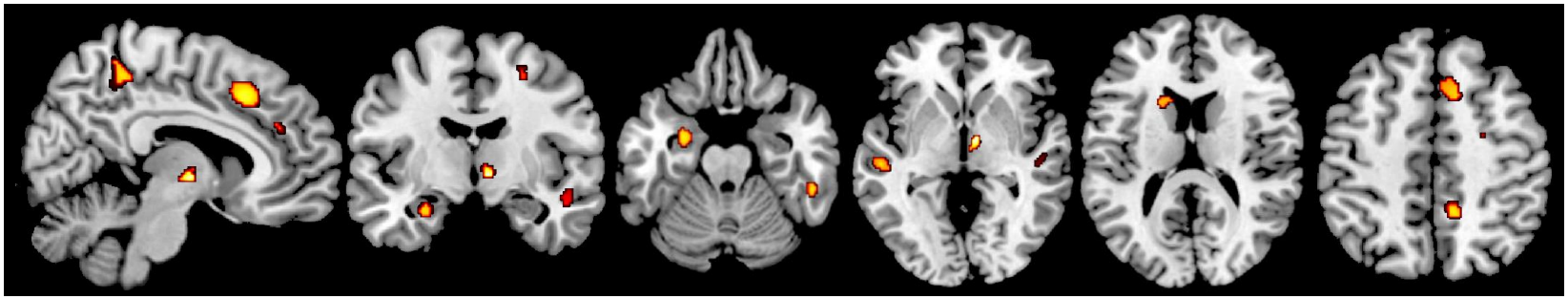
MRI IN PD & PARKINSONISMS

Cognitive impairment / Brain structural changes

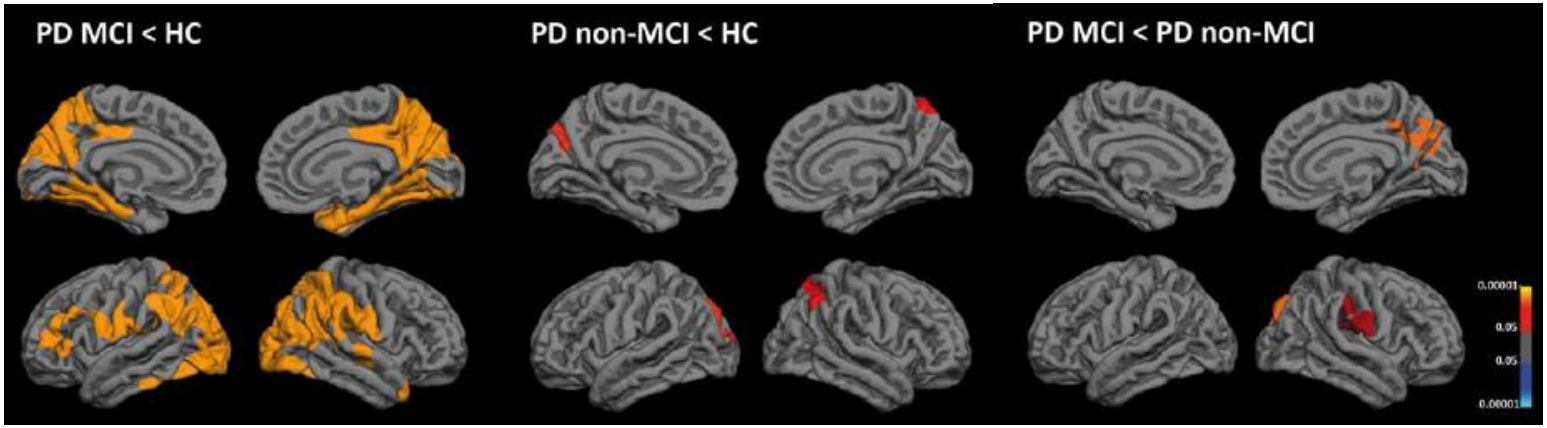
Early PD *vs* controls



Moderate *vs* mild PD



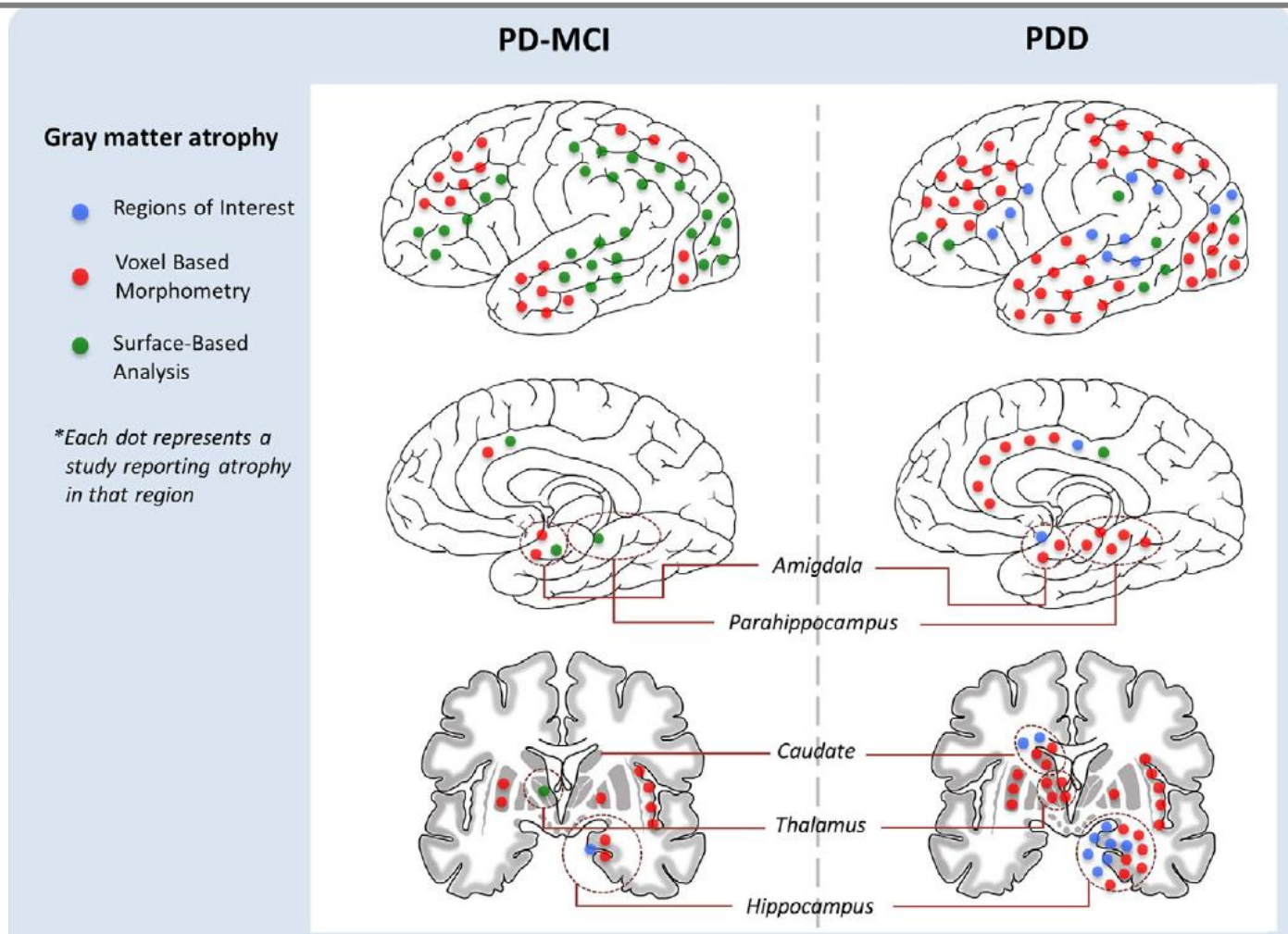
Agosta et al., Hum Brain Mapp 2012



Segura et al., Mov Disord 2014

MRI IN PD & PARKINSONISMS

Cognitive impairment / Brain structural changes



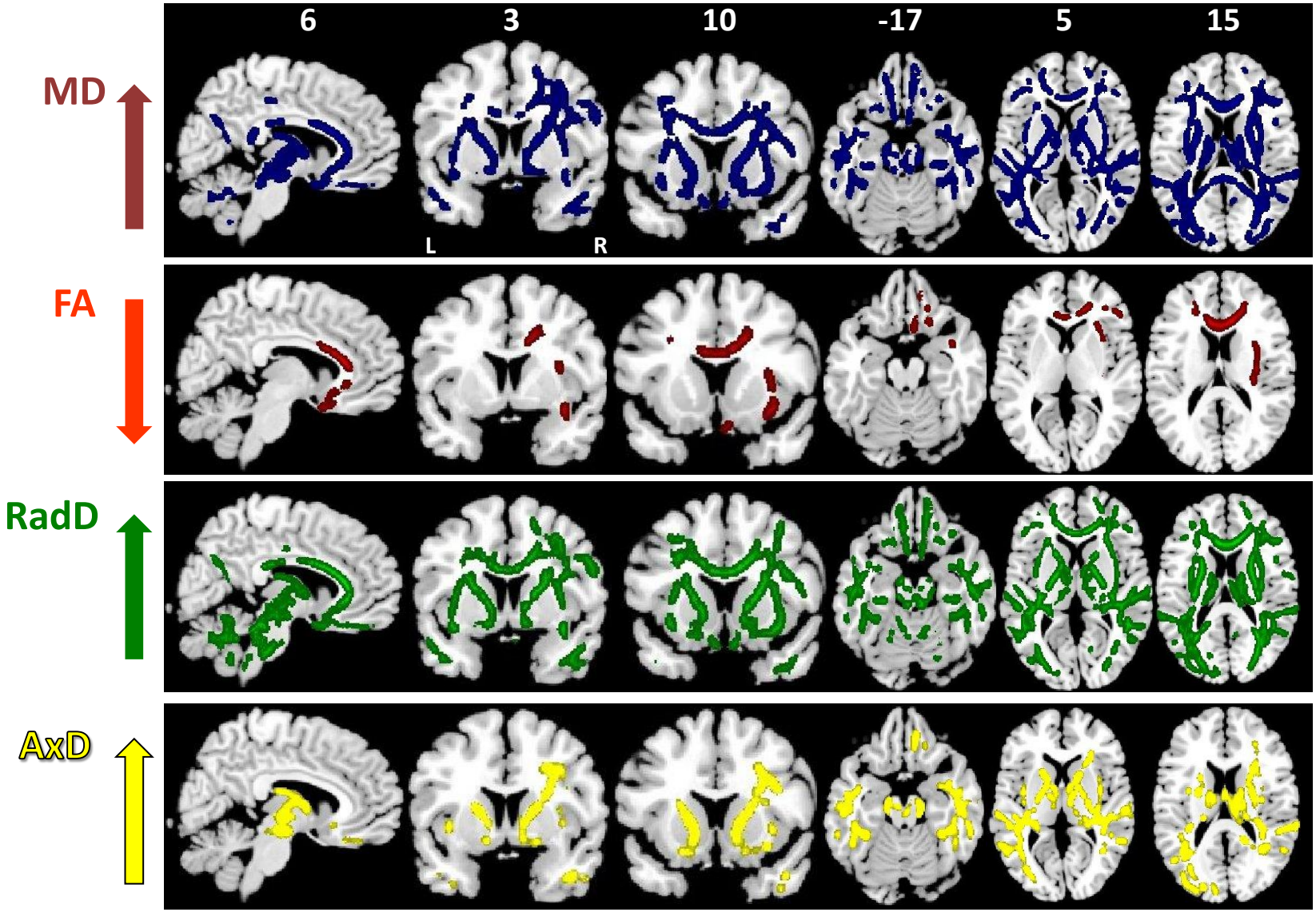
DTI: Tract damage	Superior longitudinal, inferior fronto-occipital and uncinate fasciculi, cingulum, corpus callosum, corona radiata	Widespread WM, superior and inferior longitudinal, inferior fronto-occipital and uncinate fasciculi, cingulum, internal capsule, substantia nigra, hippocampus

Delgado-Alvarado et al., Mov Disord 2016

MRI IN PD & PARKINSONISMS

Cognitive impairment / Brain structural changes

Moderate + Severe PD *vs* Early + Mild PD

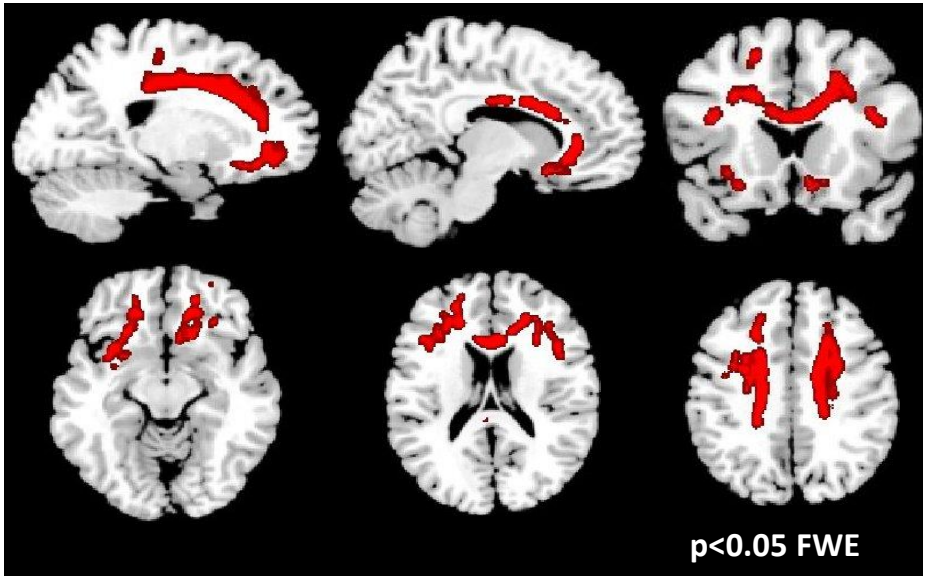


Agosta et al., Hum Brain Mapp 2013

MRI IN PD & PARKINSONISMS

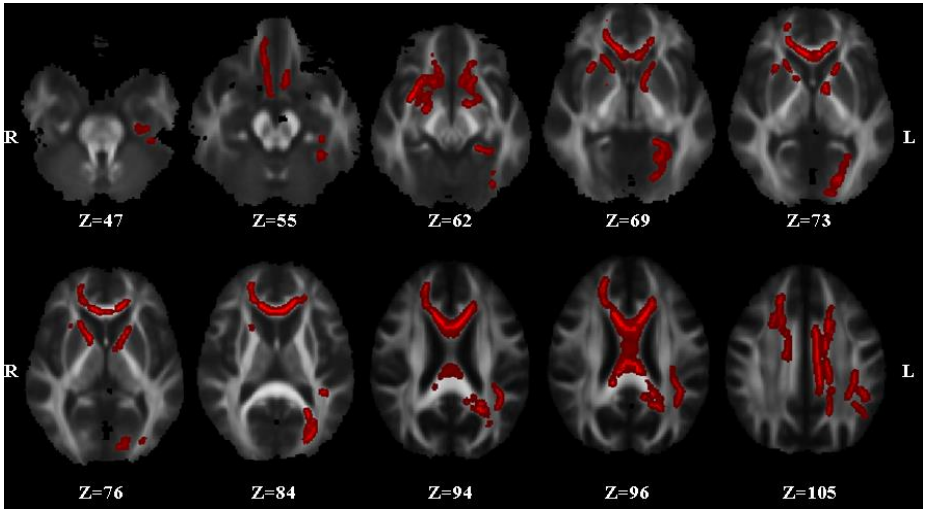
Cognitive impairment / Brain structural changes

PD-MCI *vs* PD-NC patients



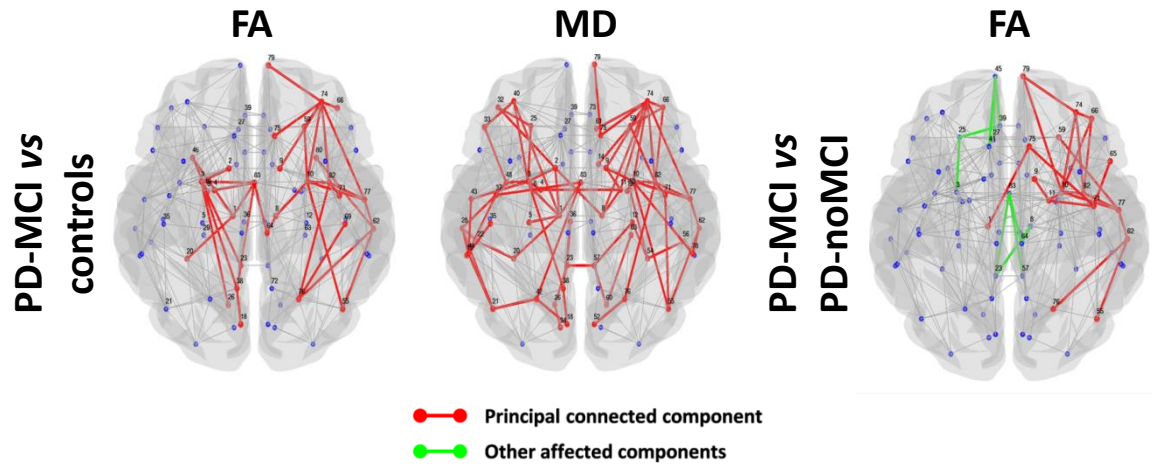
Agosta et al., Hum Brain Mapp 2014

FA decrease in GBA-PD

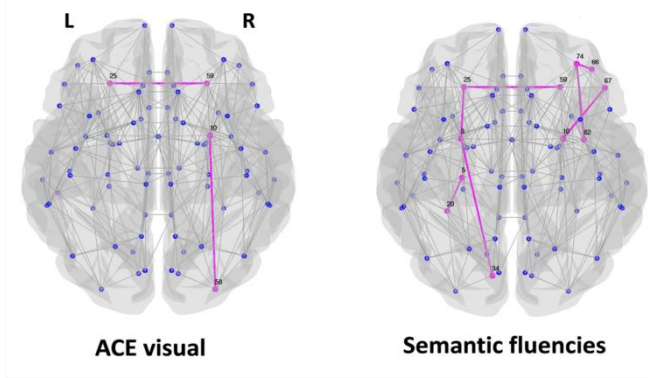


Agosta et al., Mov Disord 2013

Altered structural connections



Decreased FA *vs* cognitive deficits

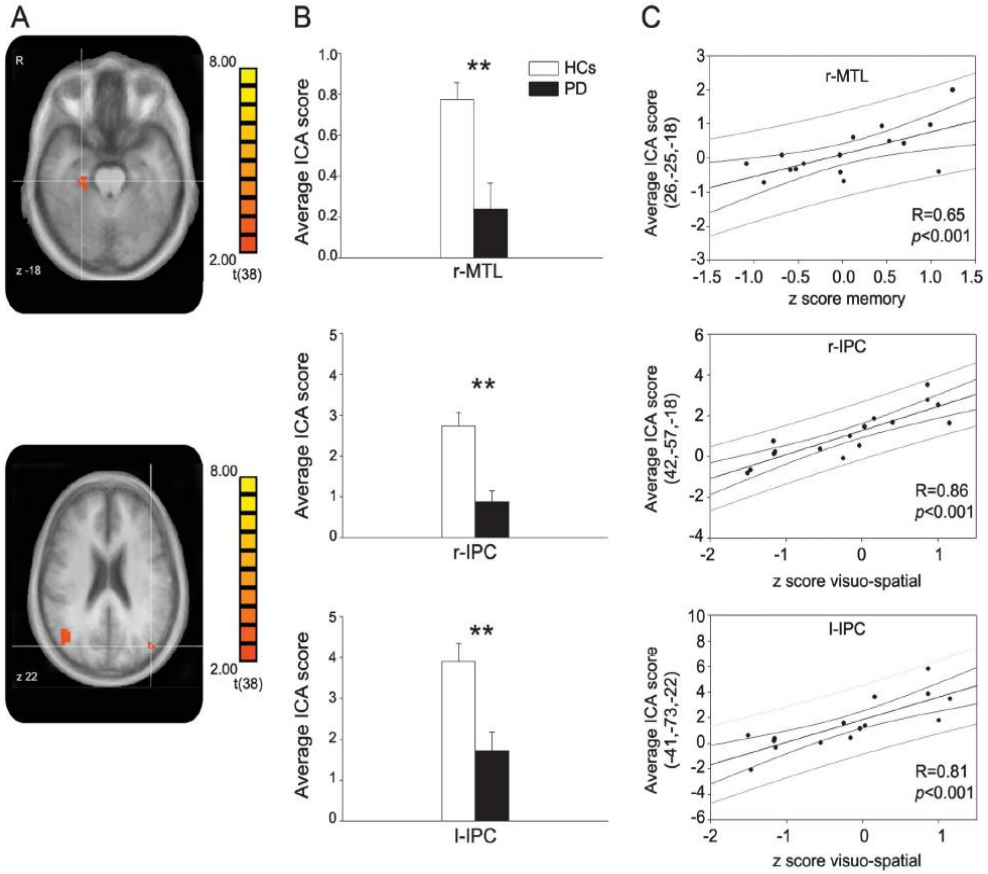


Galantucci et al., Radiology 2017

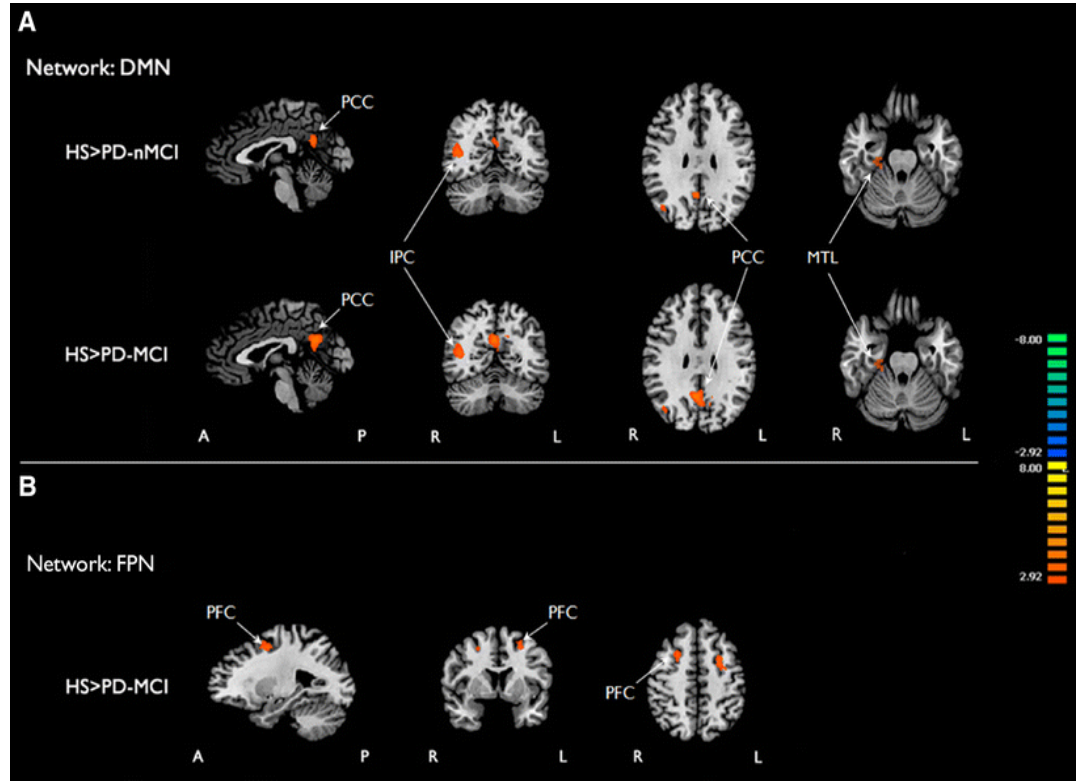
MRI IN PD & PARKINSONISMS

Cognitive impairment / Brain functional changes

Cognitively unimpaired PD



PD-MCI *vs* PD-nMCI



Decreased DMN activity

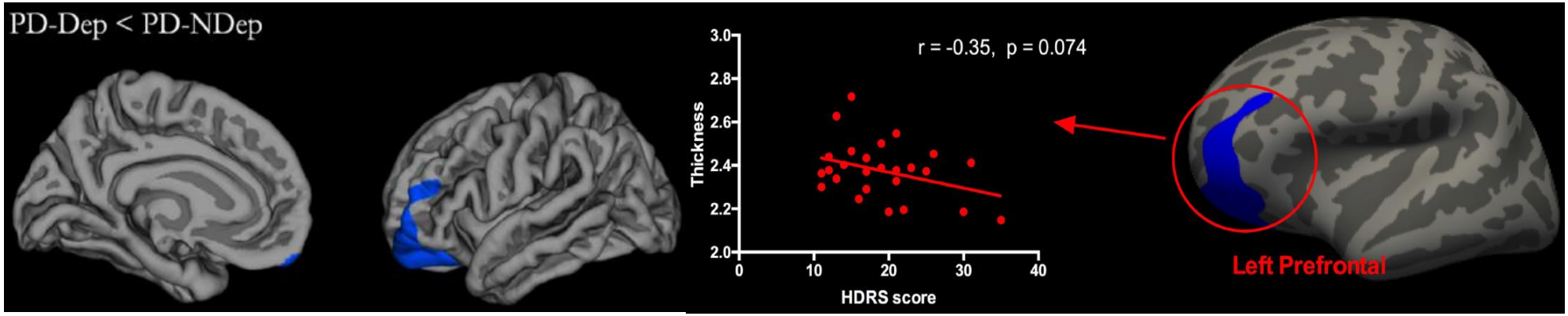
Tessitore et al., Neurology 2012

Amboni et al., J Neurol 2015

MRI IN PD & PARKINSONISMS

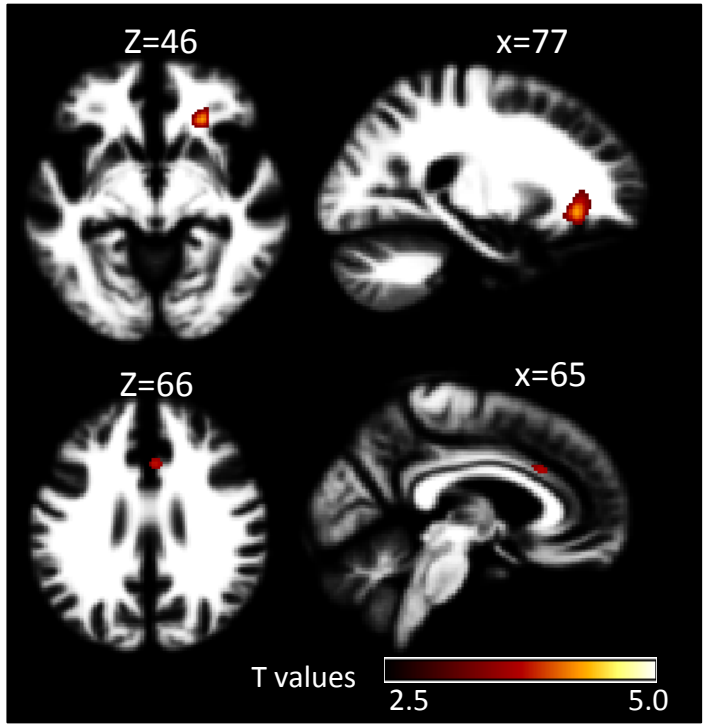
Depression / Brain structural changes

Cortical thickness: PD-dep < PD-NDep

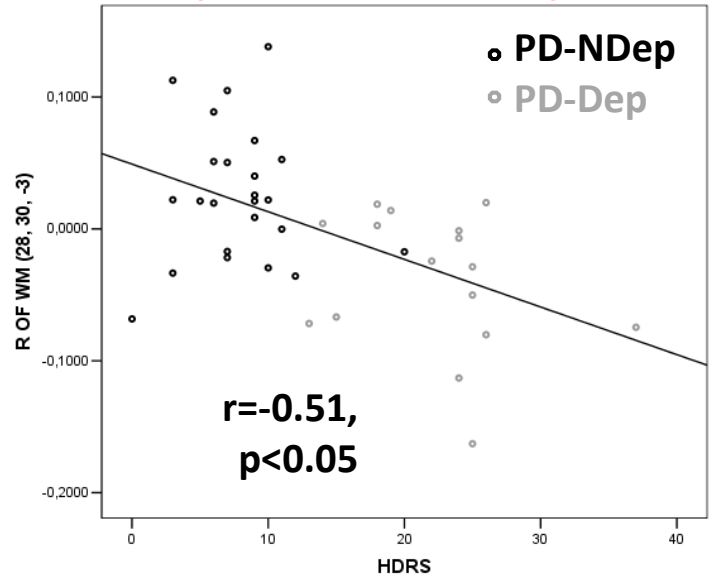


Luo et al., J Neurol 2016

WM volume: PD-dep < PD-NDep



R orbitofrontal WM atrophy *vs* depression severity scale

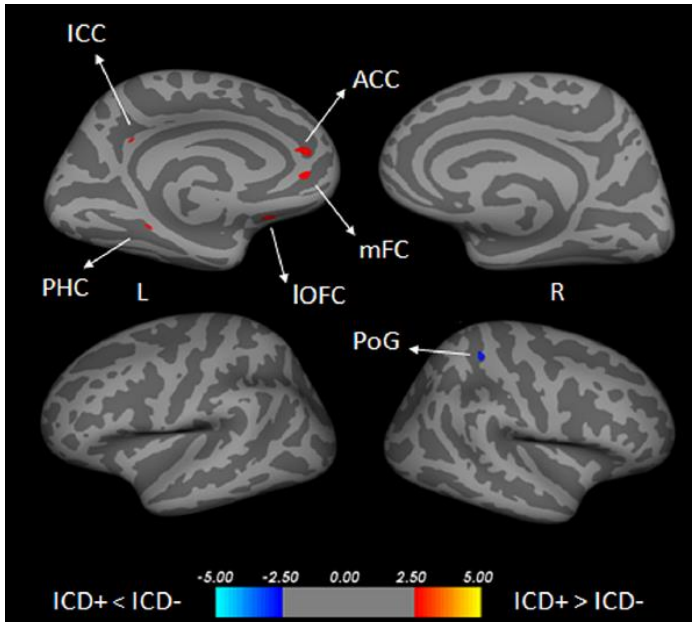


Kostic et al., Neurology 2010

MRI IN PD & PARKINSONISMS

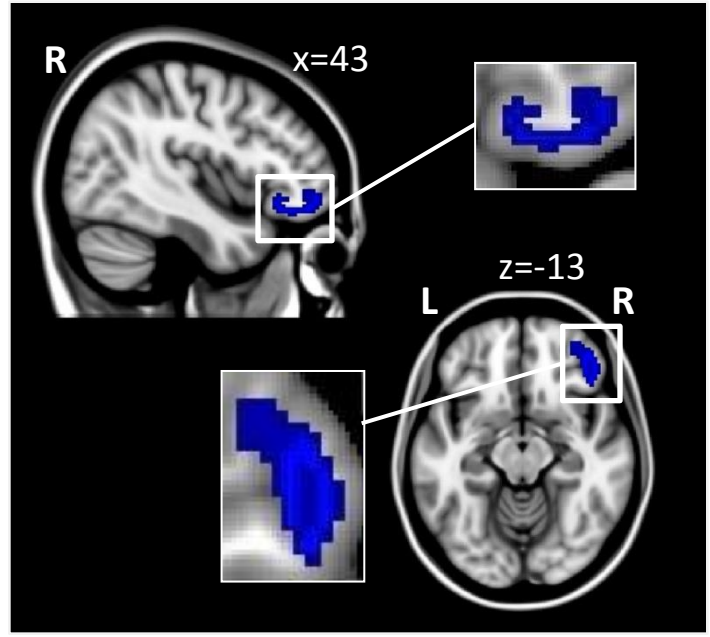
Impulsive-compulsive behaviours / Brain structural changes

PD-ICB *vs* PD no-ICB



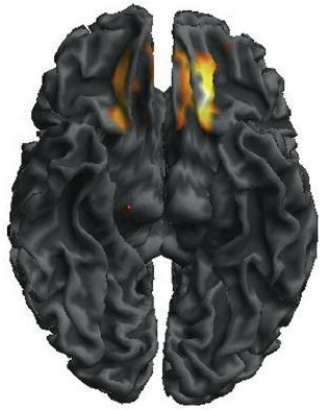
Tessitore et al., Parkinsonism Relat Disord 2016

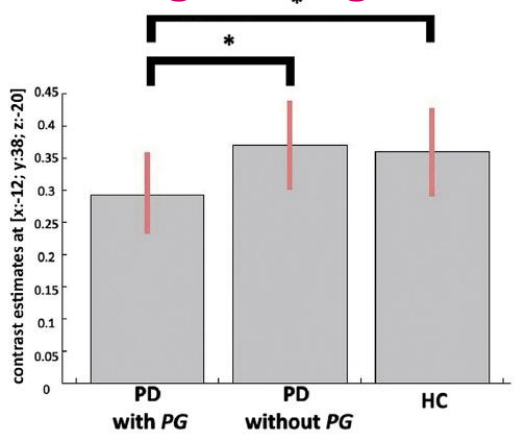
PD-punding *vs* PD no-ICB

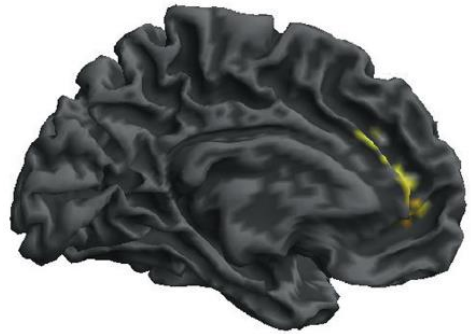


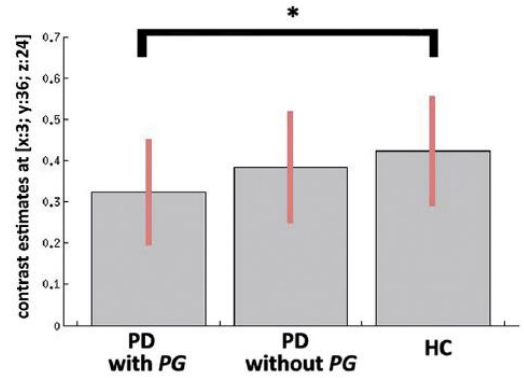
Agosta et al., Neurology 2017

PD-gambling *vs* PD no gambling







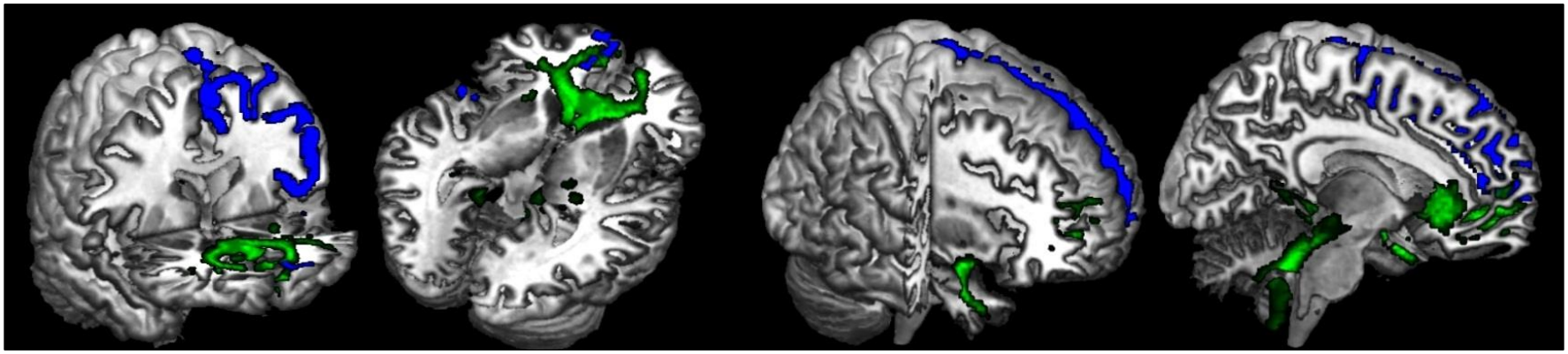


Cerasa et al., Parkinsonism Relat Disord 2014

MRI IN PD & PARKINSONISMS

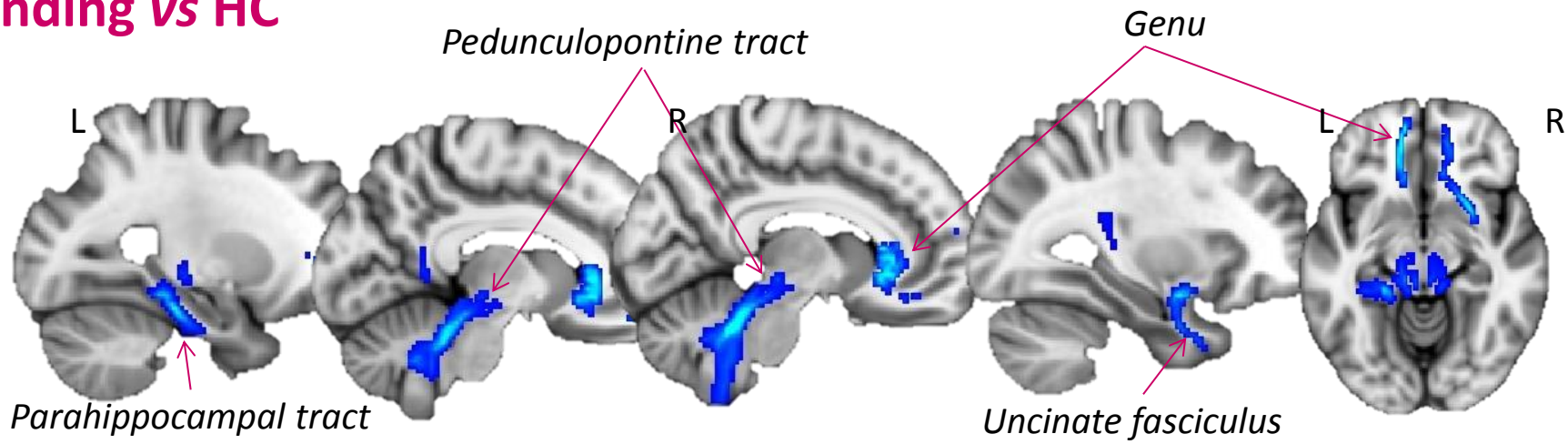
Impulsive-compulsive behaviours / Brain structural changes

PD-ICB *vs* PD no-ICB



Imperiale et al., Mol Psychiatry 2017

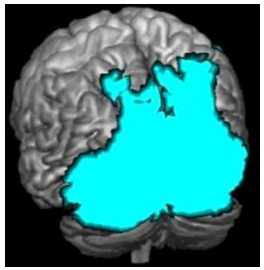
PD-punding *vs* HC



M. Filippi et al., unpublished data

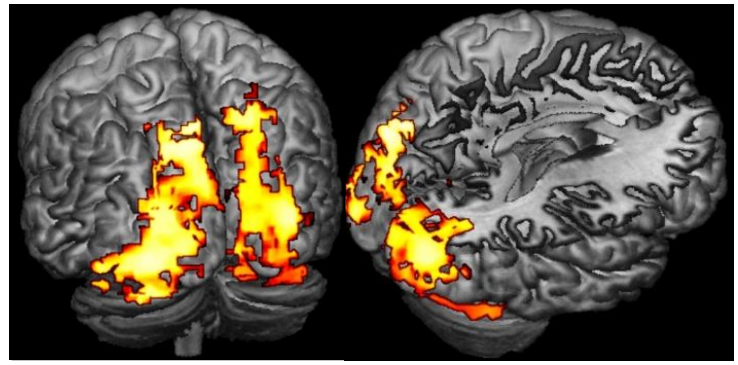
MRI IN PD & PARKINSONISMS

Impulsive-compulsive behaviours / Brain functional changes

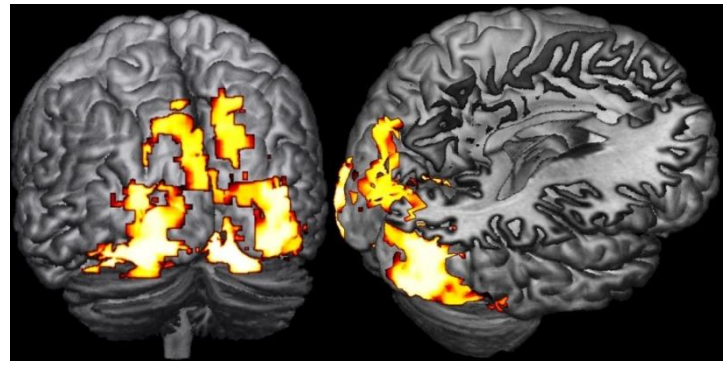


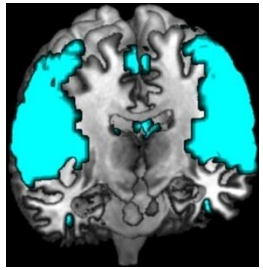
Visual

PD no-ICB *vs* HC



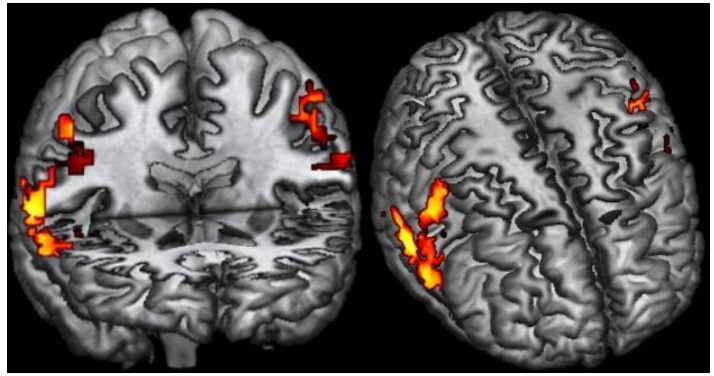
PD-ICB *vs* HC



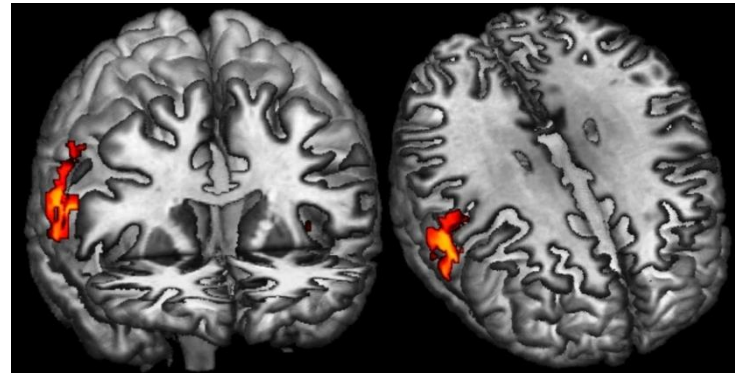


Sensorimotor

PD no-ICB *vs* HC



PD no-ICB *vs* PD-ICB

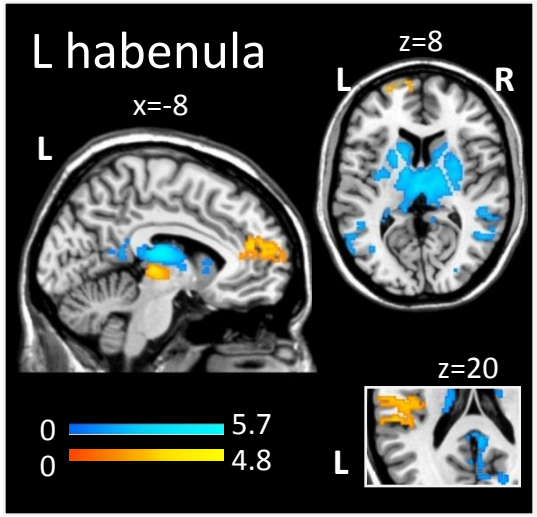


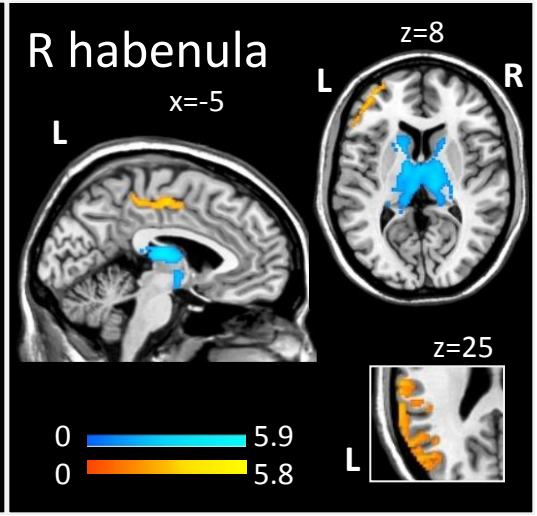
Imperiale et al., Mol Psychiatry 2017

MRI IN PD & PARKINSONISMS

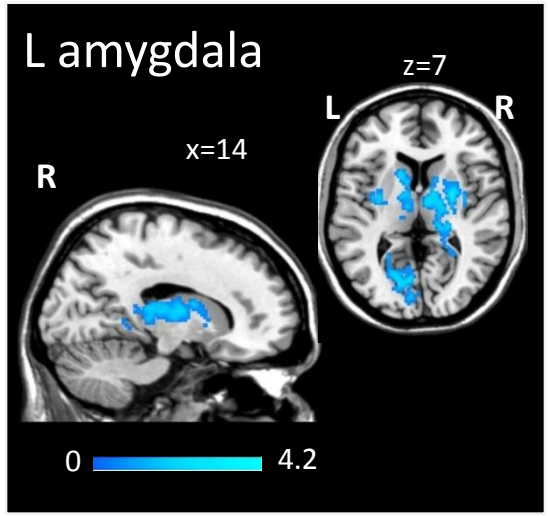
Impulsive-compulsive behaviours / Brain functional changes

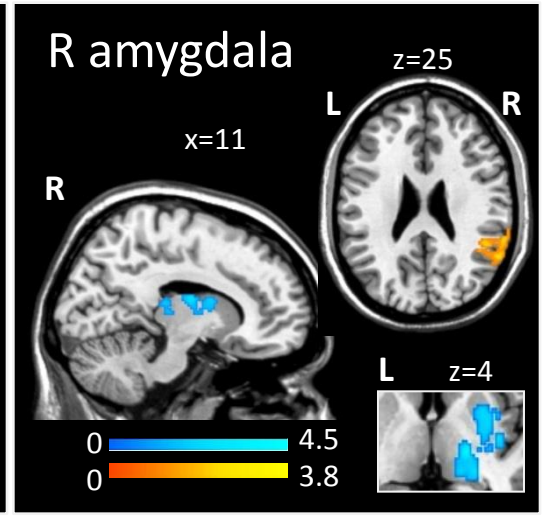
PD-punding *vs* healthy controls



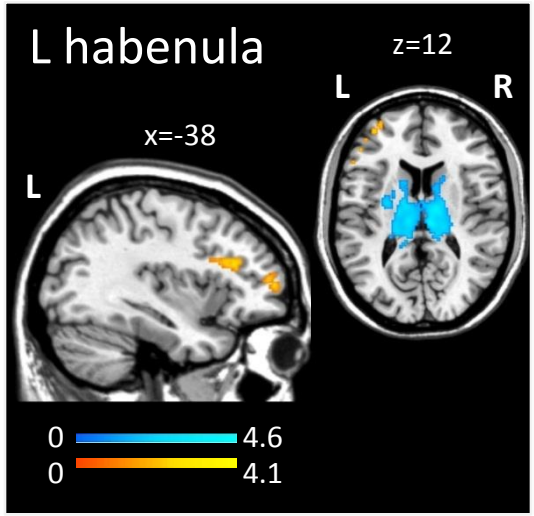


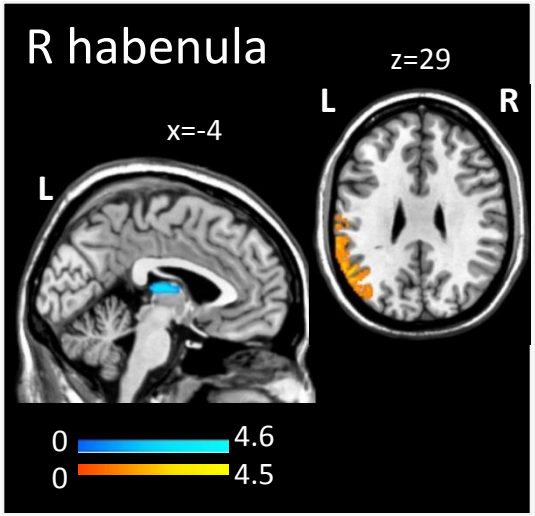
PD-punding *vs* healthy controls



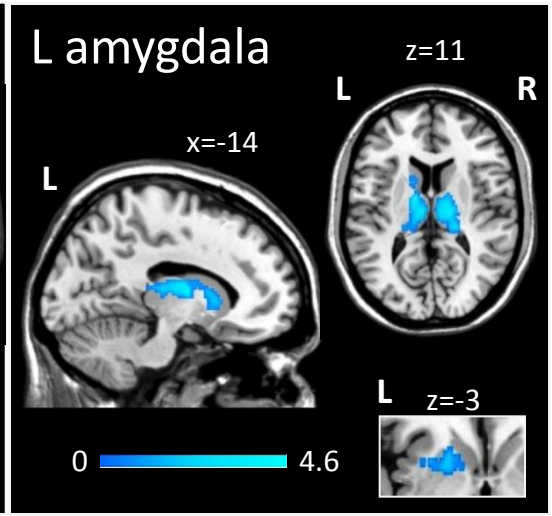


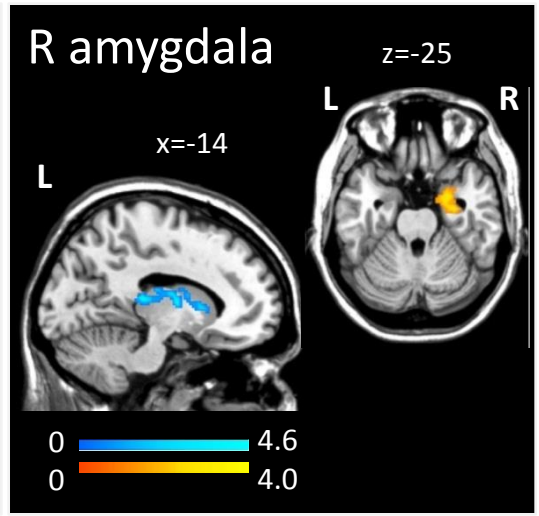
PD-punding *vs* PD no-ICB





PD-punding *vs* PD no-ICB





Agosta et al., Neurology 2017

MRI IN PD & PARKINSONISMS

Outline of the presentation

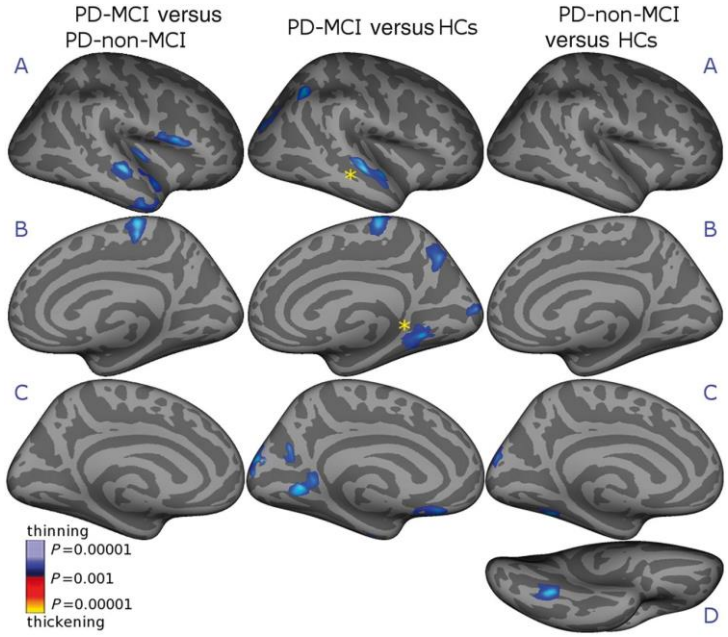
- ✓ Diagnosis
- ✓ Structural and functional correlates of motor and non-motor features
- ✓ **Monitoring disease progression**

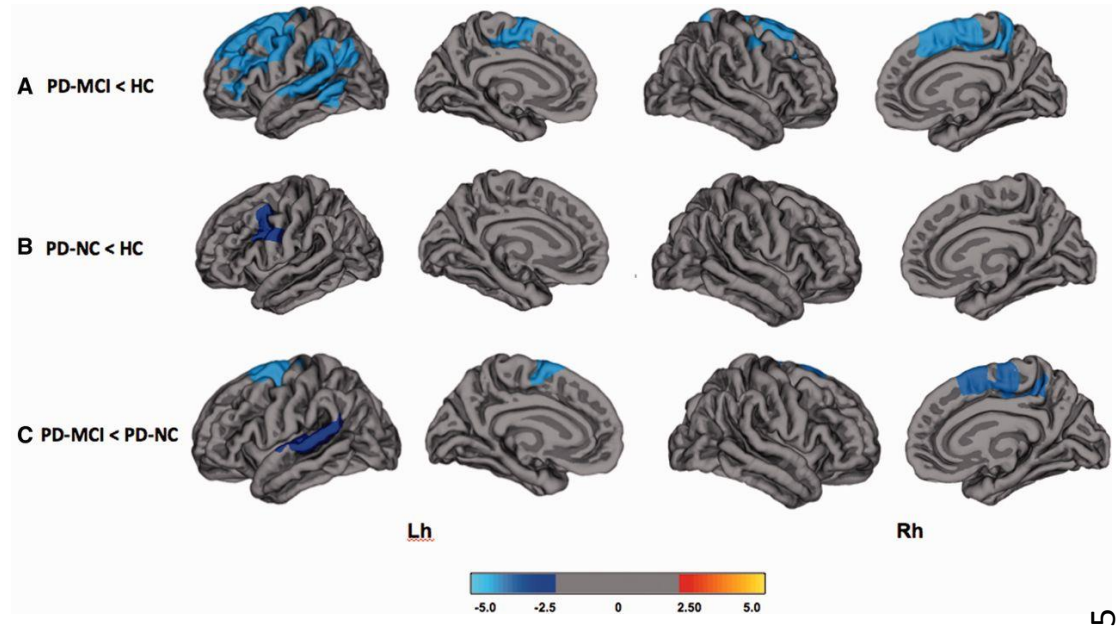
MRI IN PD & PARKINSONISMS

Monitoring disease progression in PD

Rate of change of cortical thickness *vs* cognitive decline

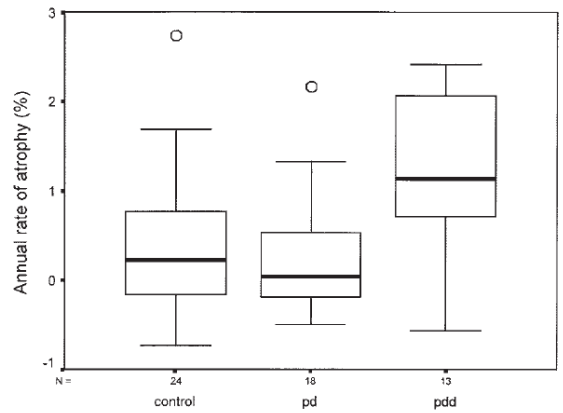
Hanganu et al., Brain 2014

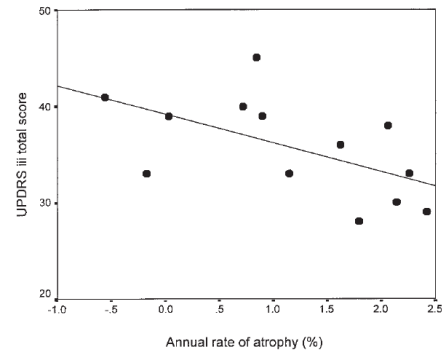


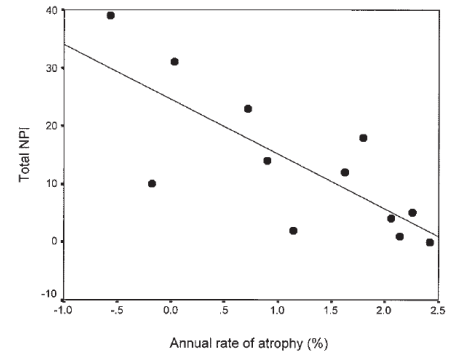


Mak et al., Brain 2015

Annual rate of atrophy %





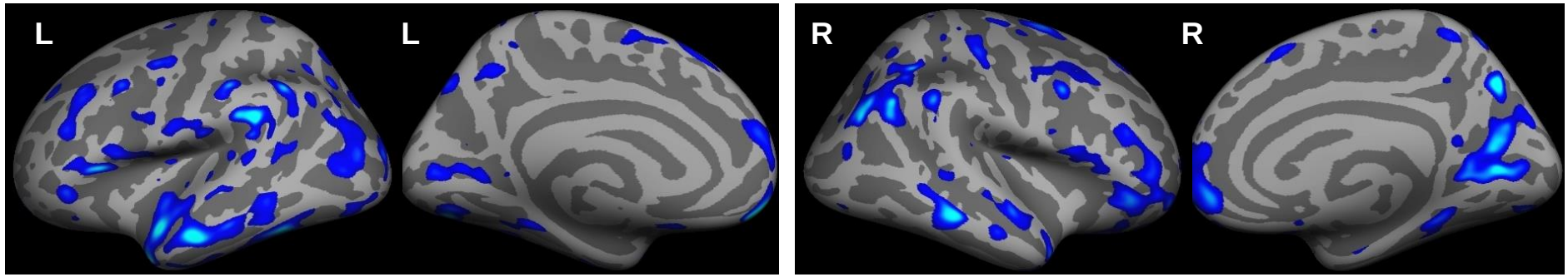


Burton et al., Mov Disord 2005

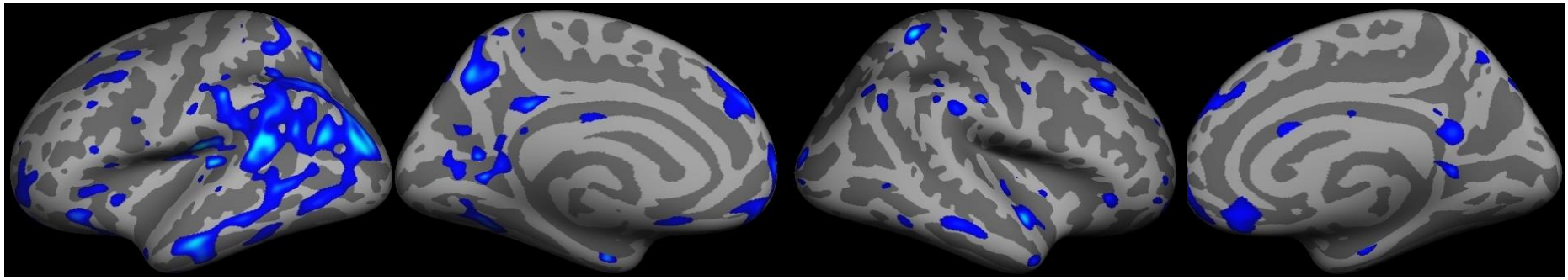
MRI IN PD & PARKINSONISMS

Monitoring disease progression in PD

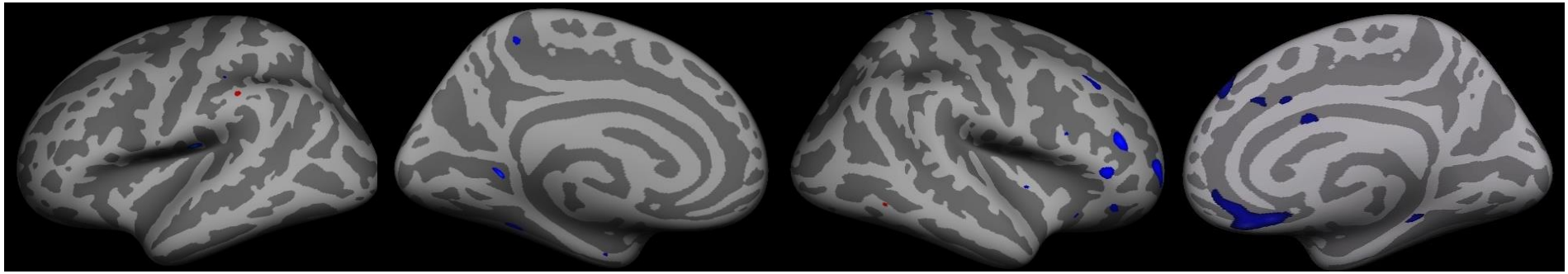
35 ICB-negative patients



20 ICB-positive patients (at least 1 ICB)



ICB-positive > ICB-negative, 4 years

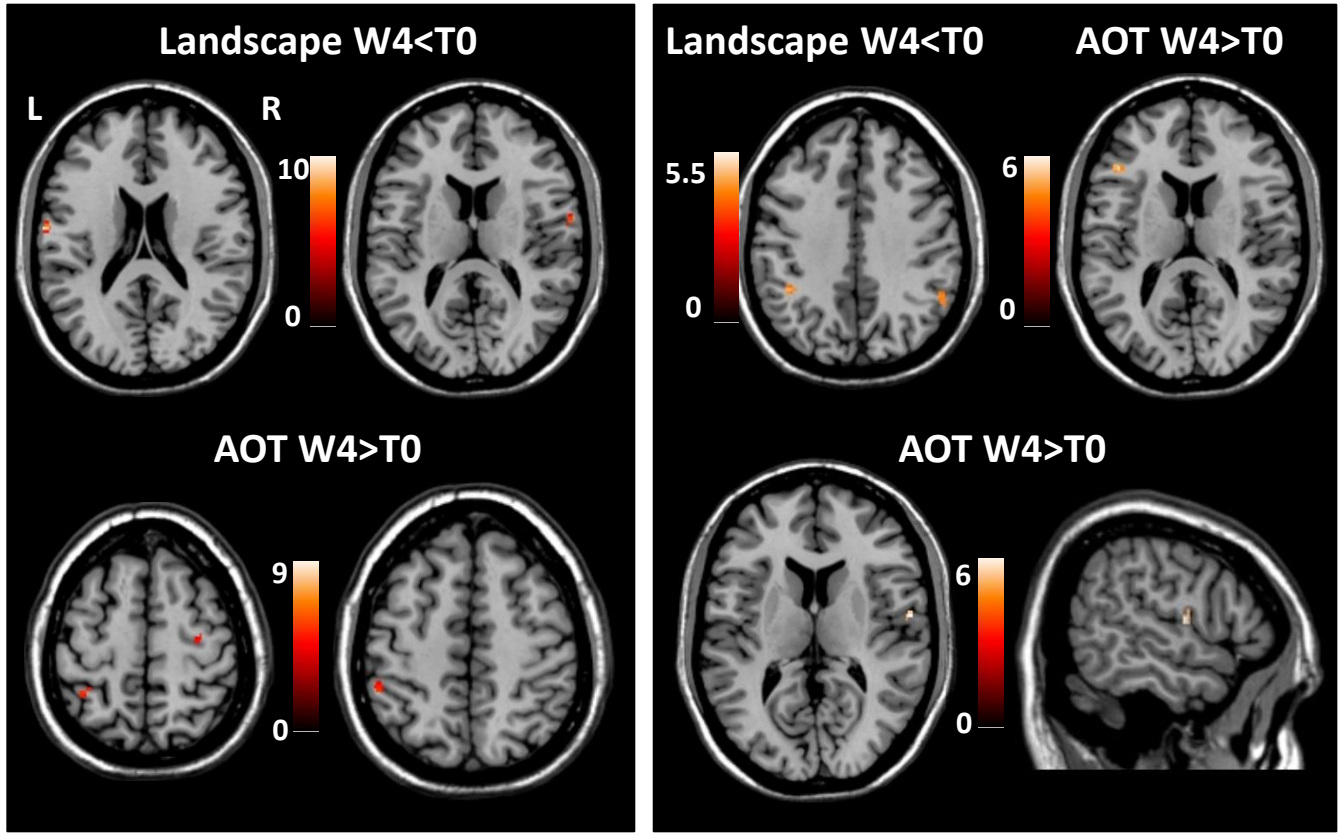


M. Filippi et al., unpublished data

MRI IN PD & PARKINSONISMS

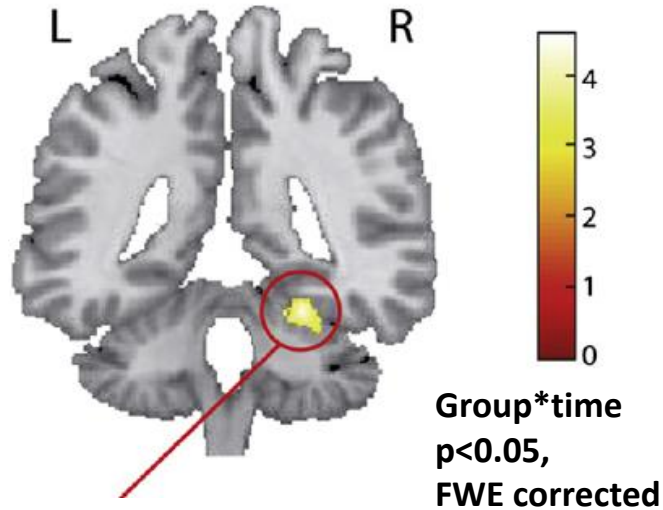
Monitoring disease progression in PD

Freezing of gait / Action observation training & fMRI



Agosta et al., J Neurol 2017

Learning balance tasks (6 w): structural changes

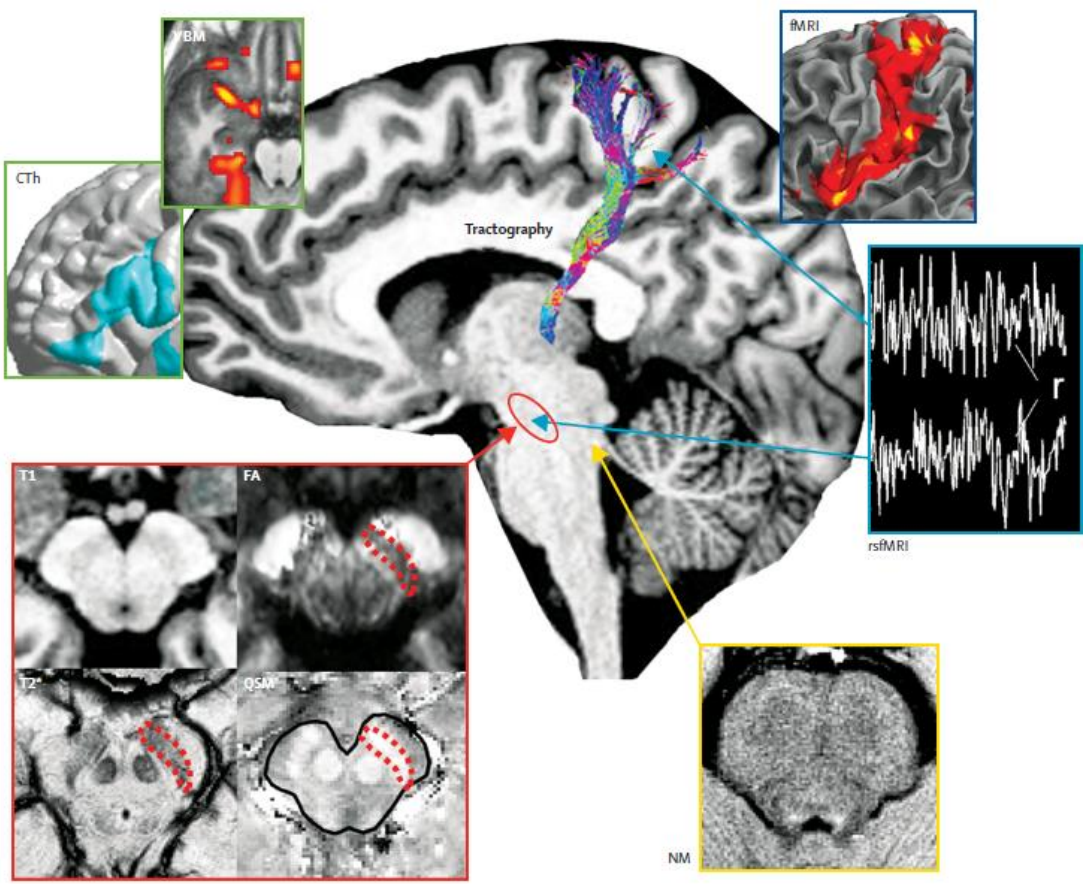


Group*time
p<0.05,
FWE corrected

Right cerebellum
(lobule V-VI)

Sehm et al, Neurobiol Aging 2014

From a basal ganglia network alteration…



..to a whole-brain dysfunction

Stoessl et al., Lancet 2014

OSR

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