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OBJECTIVES

Disruptions in functional connectivity have been associated with Parkinson disease (PD) in comparison to healthy controls. However, it remains unclear if network alterations are reflective of asymmetric motor features or cognitive aspects of variable disease presentation. To investigate the differential networks affected based on extent of motor versus cognitive features of PD, we evaluated PD patients stratified on extent of cognitive impairment and displaying right or left motor onset disease (LMO, RMO). Patients were compared in resting-state functional connectivity MRI (rs-fcMRI) based on classifications of normal cognition (PD-NC) or mild cognitive impairment (PD-MCI) with involvement in single or multiple domains.

METHODS

SUBJECTS

- PD patients (n = 50) ages 57 – 77 years of age
- UPDRS III motor scale and Hoehn & Yahr Ratings <3. Patients were classified based on side of motor onset (n_{LMO} = 25; n_{RMO} = 25).
- Neuropsychological Assessment classified cognitive profiles.

PD Normal Cognition (PD-NC, n = 15)
PD MCI single domain (PD-MCIs, n = 17)
PD MCI multiple domains (PD-MCIm, n = 18)

FUNCTIONAL CONNECTIVITY

- **Resting state fMRI data** were acquired in a Siemens MRI Prisma 3T Scanner.
- **Standard procedures for rs-fcMRI** data were processed with **Conn Tool box (v18)**- slice timing, realignment, segmentation, normalization, smoothing, band-pass filtering and denoising.
- **Group comparisons with the GLM** were conducted with significance levels set at a voxel threshold of p-value of 0.008 (uncorrected) and cluster threshold of FDR p-value of 0.05 (corr).

CONCLUSIONS

Seed-based connectivity analyses from bilateral insula revealed bilateral and widespread increased (PD-MCIs > PD-NC) and decreased (PD-MCIs < PD-NC) connectivity in attention and executive networks bilaterally for patients with cognitive decline in a single domain. Patients at higher risk for conversion to dementia displayed bilateral hippocampal-medial temporal lobe network increased connectivity reflective of compensation for abnormal memory function (PD-MCIm > PD-NC). These findings support differential network connectivity changes reflective of clinical features of the disease, and suggest that network changes have potential to predict variable patterns of disease progression and risk of conversion to dementia.

ROIs with SIGNIFICANCE

PreCG	PreCentral Gyrus	STG	Superior Temporal Gyrus	CB	Cerebellum
PostCG	PostCentral Gyrus	MTG	Middle Temporal Gyrus	FU	Fusiform
FP	Frontal Pole	ITG	Inferior Temporal Gyrus	IC	Insular Cortex
SFG	Superior Frontal Gyrus	TP	Temporal Pole	AMG	Amygdala
AG	Angular Gyrus	LOC	Lateral Occipital Cortex	I / s	Inferior / Superior
SMG	Supramarginal Gyrus	PH	Parahippocampus	R / L	Right / Left
SPL	Superior Parietal Lobule	HI	Hippocampus	a / p	Anterior / Posterior

RESULTS

Rs-fcMRI from the left insular cortex

PD-MCI vs PD-NC : increased FC in ipsilateral PreCG, PostCG, SPL, sLOC, aSMG, TP, pSTG, aMTG, pMTG, pITG, HI; decreased in the contralateral FP.

PD-MCIs vs PD-NC : increased FC in ipsilateral PostCG, SPL, aSMG, sLOC, AG, iLOC, toMTG, and decreased FC in ipsilateral CB crust 1, 2, 6 and vermis 6, 7.

PD-MCIm vs PD-NC : increased FC in ipsilateral PostCG, PreCG, aSMG, pMTG, pITG, aMTG, HI; decreased FC in contralateral FP.

Rs-fcMRI from the right insular cortex

PD-MCI vs PD-NC : increased FC in the right PostCG, PreCG, SPL, aSMG, aMTG, pMTG, TP and left FP, SFG; decreased in CB 1, 2, 6, 7, 8 and vermis 7, and ipsilateral FP.

PD-MCIs vs PD-NC : increased FC in ipsilateral PreCG, bilateral PostCG, SPL, SMG, and right PH, HI, amygdala; decreased in contralateral CB 1,2, 6, 7, 8 and vermis 7, and right CB 1, 2, 6. **PD-MCIm vs PD-NC** : increased FC in ipsilateral PH gyrus, HI, and posterior temporal FU.

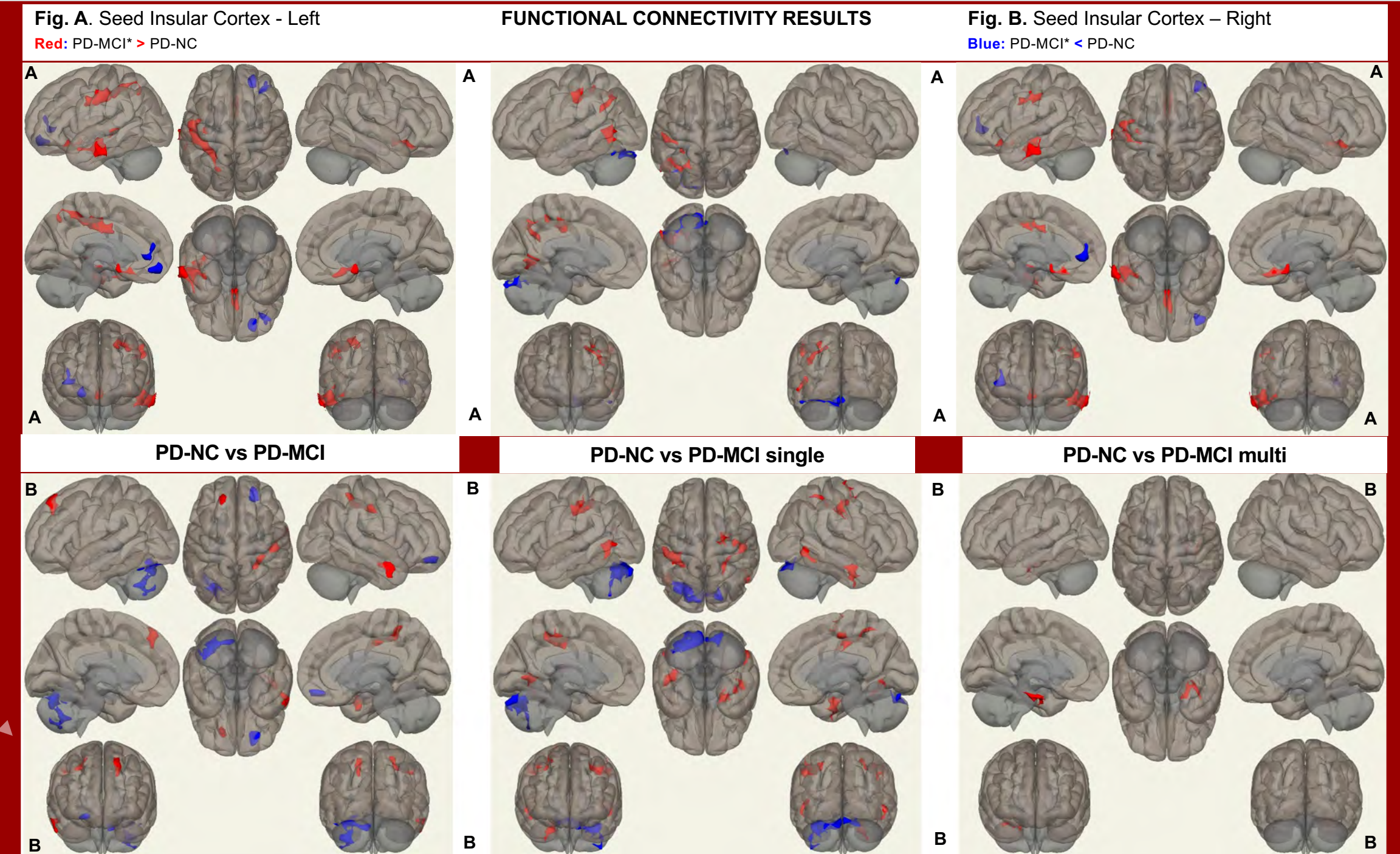


Table 1.	(x, y, z)	Voxel Size	p FDR	PreCG	PostCG	FP	SFG	AG	SMG	SPL	STG	MTG	ITG	TP	LOC	PH	HI	CB	FU	AMG
Left Insular Seed																				
PD-NC vs PD-MCI	increase (-30, -40, +48)	1161	< 0.0001	221 (L)	422 (L)				46 (L)	126 (L)					100 (L)					
	decrease (-52, -14, 22)	1019	< 0.0001				236 (R)				20 (L)	367 (L)	176 (L)	33 (L)			20 (L)			17 (L)
	increase (+26, +50, -14)	270	0.037				148 (R)													
	decrease (+38, +36, -02)	250	0.041																	
PD-NC vs PD-MCIs	increase (-46, -28, +44)	407	0.0097		229 (L)			52 (L)	44 (L)	45 (L)										
	decrease (-38, -54, +32)	333	0.0097																	
	increase (-46, -62, +02)	285	0.0169									29 (L)	25 (L)							143 (L)
	decrease (-04, -76, -24)	463	0.0036																	370 (L)
PD-NC vs PD-MCIm	increase (-04, -76, -24)	463	0.00356																	
	decrease (-46, -28, +44)	407	0.00428	167(L)	192(L)				13 (L)			312(L)	169(L)				12 (L)			14 (L)
	increase (-46, -62, +02)	285	0.0169																	
PD-NC vs PD-MCIs	increase (-46, -28, +44)	407	0.0097		229 (L)				44 (L)	45 (L)										
	decrease (-38, -54, +32)	333	0.0097					52 (L)												143 (L)
Right Insular Seed																				
PD-NC vs PD-MCI	increase (46, -20, +40)	467	0.0029		233 (R)				15 (R)	111 (R)										
	decrease (-18, +42, +52)	261	0.035				108 (L)	87 (L)				48 (R)								
	increase (64, +04, -24)	231	0.049									146 (R)								
	decrease (-38, -64, -42)	986	< 0.0001																867 (L)	80 (L)
	increase (+22, +50, -16)	285	0.036				232 (R)													
PD-NC vs PD-MCIs	increase (-30, -42, +48)	694	< 0.0001			359(L)			92(L)	89(L)										
	decrease (+30, -34, +46)	678	< 0.0001	191 (R)	272 (R)				18 (R)	81 (R)										
	increase (+20, -02, -24)	368	0.00495																	
	decrease (-06, -76, -26)	1461	< 0.0001																	
PD-NC vs PD-MCIm	increase (+20, -10, -26)	335	0.0396																	