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Role of the cingulate cortex in dyskinesias-reduced-self-awareness: a piloting fMRI study on a couple of Parkinson's disease patients

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OBJECTIVES

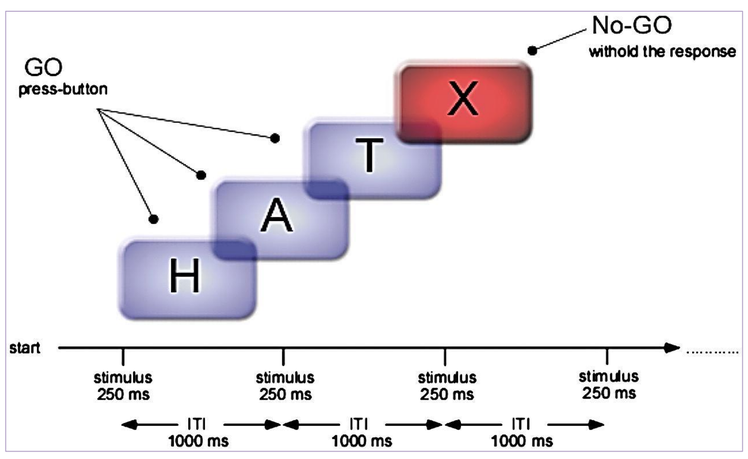
The presence of dyskinesias-reduced-self-awareness [DRSA] in patients suffering from Parkinson's disease [PD] was previously related to executive-metacognitive deficits due to dopaminergic overstimulation of mesocorticolimbic circuits (Amanzio et al., 2014). Response-inhibition dysfunction is often assessed in PD. Besides being involved in response-inhibition tasks, the anterior cingulate cortex [ACC] is part of a functional system based on self-awareness that is engaged across cognitive, affective, and behavioral contexts (Medford & Critchley, 2010). The aim of this piloting study was to approach the relationship between response-inhibition disabilities and DRSA using fMRI and an event-related specific executive task.

MATERIAL AND METHODS

Two cognitively non-impaired PD patients presenting motor fluctuations and dyskinesias were studied. Subjects were assessed to measure awareness of dyskinesias. They underwent a neurological evaluation, a neuropsychological assessment and questionnaires on behavioral mood changes.

Cingulate functionality was assessed with fMRI, while patients performed an ACC sensitive go/no-go task. Neuroimaging data acquisition was performed on a 3T Philips Ingenia scanner. Subjects had to respond to 'go' stimuli inhibiting the response to infrequent 'no-go' stimuli (Braver et al., 2001). Image preprocessing was performed using SPM8. All functional images were spatially realigned to the first volume and anatomical images were co-registered to the mean of them. The functional images were normalized to the MNI space and smoothed. After preprocessing, for both patients in order to investigate their response inhibition disabilities, we applied a General Linear Model to convolve the 'no-go' and 'go' stimuli with canonical hemodynamic response function. A difference between unaware and aware subjects was performed to compare functional activations.

BEHAVIOURAL TASK PRESENTED TO THE PATIENTS, ADAPTED FROM BRAVER ET AL. (2001).



SUBJECTS HAD TO RESPOND TO 'GO' STIMULI (THE LETTERS 'NOT-X' WITH A FREQUENCY OF 83%) INHIBITING THE RESPONSE TO INFREQUENT 'NO-GO' STIMULI (THE LETTER 'X' WITH A FREQUENCY OF 17%). EVERY STIMULUS WAS SHOWN FOR 250 MS WITH A 1000 MS INTER-STIMULUS INTERVAL (ITI).

RESULTS [1]

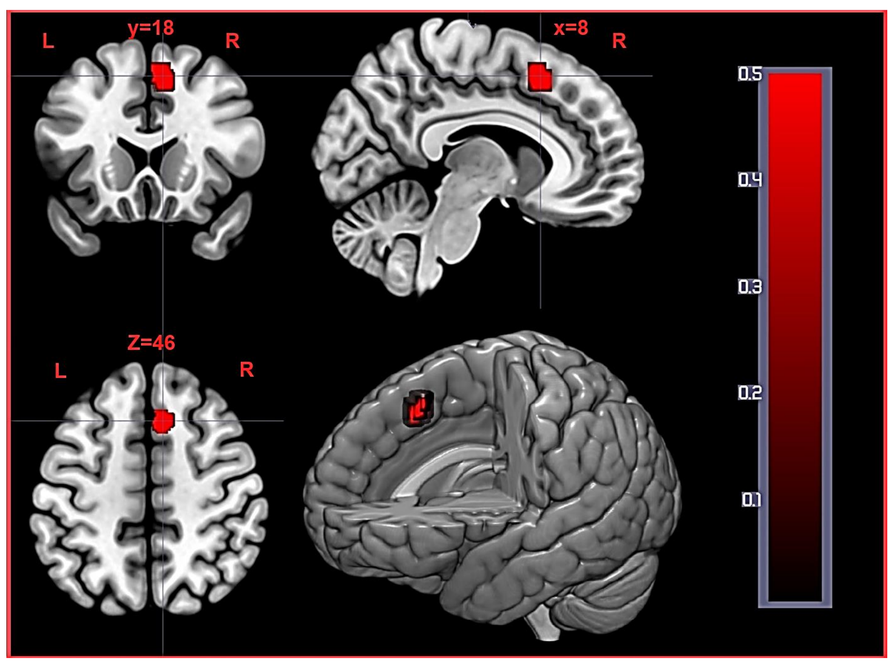
The unaware PD patient showed worse response-inhibition as measured by the three runs of the go/no-go task. Moreover, MRI analysis revealed significant different brain activations in ACC-ROI (MNI x=4, y=21, z=38) for the contrast 'no-go' vs 'go'.

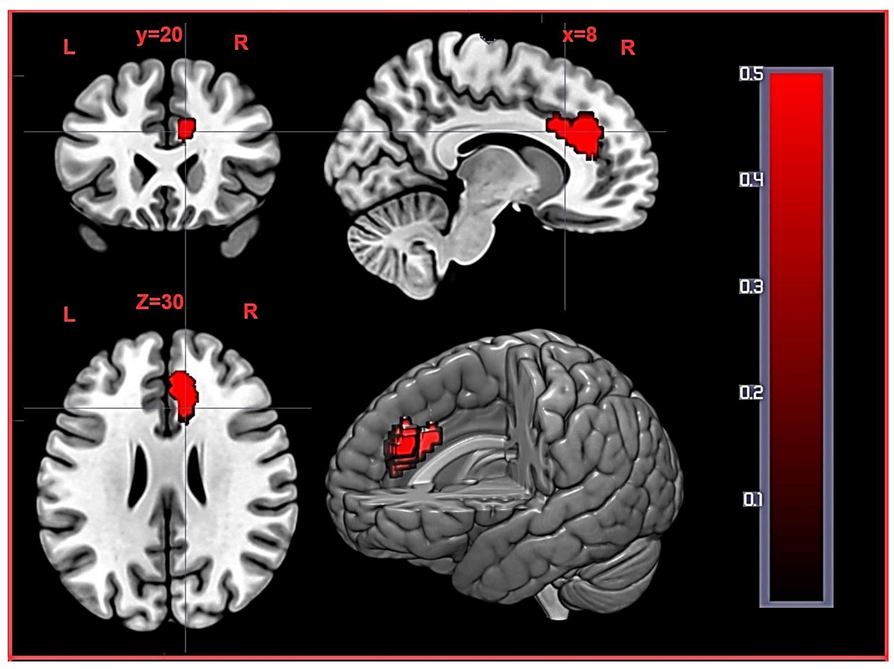
	AWARE PD PATIENT			UNAWARE PD PATIENT		
RUN1	Correct answers	Errors	ReactionTime (msec)	Correct answers	Errors	ReactionTime (msec)
GO	190 (99,00 %)	2 (1,00 %)	310,847	167 (86,98 %)	25 (13,02 %)	348,928
NOGO	21 (52,50 %)	19 (47,50 %)	307,21	13 (32,50 %)	17 (42,50 %)	255,588
RUN2						
GO	189 (98,44 %)	3 (1,60 %)	296,989	165 (85,94 %)	27 (14,06 %)	411,212
NOGO	33 (82,50 %)	7 (7,50 %)	271,181	12 (30,00 %)	18 (70,00 %)	291,555
RUN3						
GO	187 (97,40 %)	5 (2,60 %)	314,438	151 (78,65 %)	41 (21,35 %)	387,788
NOGO	33 (82, 50 %)	7 (17,50 %)	274,848	14 (35,00 %)	26 (65,00 %)	287,562

	cluster p(FWE-corr)	**cluster** p(FDR-corr)	**cluster** equivk	**cluster** p(unc)	**peak** **p(FWE-corr)**	x,y,z {mm}	x,y,z {mm}	x,y,z {mm}
AWARE	0.074554	0.500417	16	0.500417	**0.00384481**	8.700001	18.35	46
UNAWARE	0.002892	0.01067	123	0.01067	**0.007419892**	3.750001	23.3	46
					0.009557225	8.700001	20	30
					0.061749525	5.400001	28.25	42
					0.077903478	3.750001	29.9	34

RESULTS [2]

FMRI results for the contrast " no-go " vs " go " conditions, for the aware (on the left) and the unaware (on the right) PD patients. Maps were thresholded at $p < 0.05$ cluster-level corrected using a small volume correction [SVC] with a sphere of 10 mm radius centered on ACC according to the coordinates reported in Braver et al (2001). Before using SVC, we transformed coordinates given by Braver et al (2001) from Talairach space to MNI space using *"Seed-based d Mapping"* web utilities (http://www.sdmproject.com). Maps are projected on a 2D brain surface with MRIcroGL software. The ROI activation cluster is also projected on a 3D brain surface.





DISCUSSION AND CONCLUSIONS

These preliminary findings may have implications in considering executive functions and the related ACC functionality as a clinically important imaging biomarker for DRSA, even though the neuropsychological assessment appeared to be normal. Future study on DRSA, its neuropsychological correlates and neuronal substrates will have important clinical implications as this phenomenon can involve diagnostic, nosological and prognostic factors. We believe that theoretical models of DRSA will have greater clinical utility and be more effective if they integrate functional MRI and neuropsychological data, given the relevance of detecting possible psycho-biological markers of this phenomenon in PD patients.

REFERENCES

1. Amanzio M, Palermo S, Zibetti M, Leotta D, Rosato R, Geminiani G, Lopiano L. Self-unawareness of levodopa induced dyskinesias in patients with Parkinson's disease. Brain Cogn. 2014; 90:135-41.
2. Medford N, Critchley HD. Conjoint activity of anterior insular and anterior cingulate cortex: awareness and response. Brain Struct Funct. 2010; 214(5-6):535-49.
3. Braver TS, Barch DM, Gray JR, Molfese DL, Snyder A. Anterior cingulate cortex and response conflict: effects of frequency, inhibition and errors. Cereb Cortex 2001; 11(9):825-36.