Is posterior cerebral hypometabolism always predicitve of dementia in Parkinson's disease?

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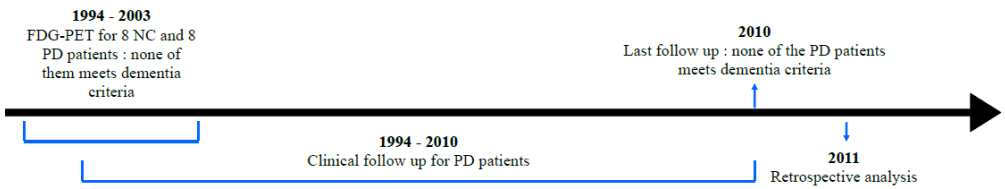
I. INTRODUCTION

In Parkinson's disease (PD) patients with dementia, 18F-fluodeoxyglocose (FDG) positron emission tomography (PET) has demonstrated a characteristic pattern of reduced resting-state regional cerebral glucose metabolism in posterior cingulate, parietal, and temporal associative regions, with lesser involvement of the prefrontal cortex.

This pattern has also been observed in PD patients without demonstratable dementia, and in patients with multidomain mild cognitive impairment (MCI), who are at high risk of dementia. However, in the study of Hu et al. (2000), the bilateral temporo-parietal reductions in gray matter glucose metabolism failed to correlate with individual performance on neuropsychological testing. Moreover, in our labs, we observed hypometabolism in posterior brain areas in PD patients with activated deep brain stimulations (Garraux et al., 2011). Furthermore, in the absence of longitudinal clinical follow up, it remains to be determined if this hypometabolic pattern is reliable marker of a progression toward dementia in PD.

We addressed this issue by comparing FDG-PET scans acquired in 8 healthy controls (HC) age- and gender-matched with 8 PD patients who did not meet dementia criteria at the time of PET according to MDS consensus criteria (Dubois et al., 2007). In this retrospective analysis, clinical follow up was available for PD patients on average 10,37 years after PET. None of them meets dementia criteria at last follow up.

II. METHODS



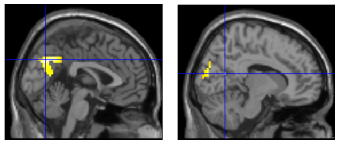
Voxel-based image analyses were conducted in a framework of the General Linear Model. Prior to their analysis, PET images were scaled to the activity in regions where FDG uptake was mostly preserved in the patients compared with controls. This region was identified using the cluster reference approach proposed by Yakushev et al. (2009) and encompassed right insula. Mean individual metabolic values in this cluster were extracted on a scan-by-scan basis in both HC and PD groups.

Regional differences in FDG uptake between HC and PD groups were statistically assessed using a two sample t-test (HC minus PD). ROI has been described using inclusive mask based on study of Garraux et al. (2011) ans encompassed posterior brain areas, basal ganglia and anterior frontal cortex.

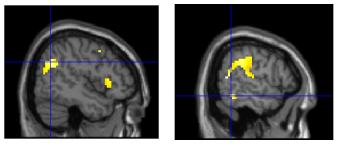
III. RESULTS

PD patient showed decreased FDG uptake mostly localised in right hemisphere (for the display purposes, significance level was set at $p < 0{,}005$):

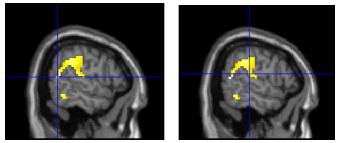
Precuneus (BA 7, 31)



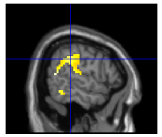
Right middle temporal (BA 37, 38)



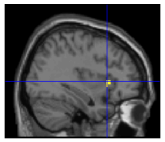
Superior temporal (BA 22, 42)



Right inferior parietal (BA 40)



Right insula (BA 13)



Region	BA	NNI coordinate x	y	z	Z score	Cluster size (voxel)	Peak P value (uncorrected)
Precuneus	7	0	-70	34	3,78	65	0,000
Rt superior temporal	22	60	-55	10	3,59	3	0,000
Rt precuneus	31	12	-61	16	3,56	2	0,000
Rt middle temporal	39	48	-61	32	3,51	23	0,000
Rt inferior parietal	40	60	-34	31	3,31	10	0,000
Rt middle temporal	37	60	-49	-14	3,23	1	0,001
Rt insula	13	36	17	4	3,16	2	0,001
Rt superior temporal	42	60	-28	16	3,83	1	0,001

IV. DISCUSSION

This is the first FDG-PET study performed in non-demented PD patients with about 10 years of clinical follow up after PET, testing if decreased resting-state FDG uptake in posterior associative cerebral cortices is a reliable imaging marker of dementia as defined by the MDS consensus criteria (Dubois et al., 2007).

Our results showed that this pattern has been described in PD patients who were not demented at the time of PET, and in PD patients who did not meet dementia criteria on average 10,37 years after PET. Altogether, these results allow us to doubt that reduced resting-state FDG uptake in posterior associative cortices is a reliable imaging marker of a progression toward dementia in PD. Other risk factors for dementia have been identified, and the reason for this cortical hypometabolism in non-demented PD patients requires further investigation.

The present work has some limitations:

- the number of patients with clinical follow up is low;
- regarding brain imaging, PET sampling in the axial direction was suboptimal and the vertex and bottom of cerebellum could not be imaged in all patients;
- brain MRI was not available and no attempt could be made to correct PET data for partial volume effects that may occur as a result of larger regional brain atrophy in PD patients as compared with controls.

However, non of these limitations should invalidate the main finding of the present study suggesting that decreased resting-state cerebral activity in posterior associative cortices in PD patients without dementia is not always reliable predictive marker of dementia.

References:

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