Subcortical matter in the α-synucleinopathies spectrum: an MRI pilot study.

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INTRODUCTION

α-synucleinopathies, such as Parkinson's Disease (PD) and Dementia with Lewy Bodies (DLB), are characterized by an ascending accumulation of α-synuclein extending from brainstem structures to the neocortex1.

Clinically, PD and DLB are clearly distinguished, while discrimination between Parkinson dementia (PDD) and DLB can be subtle and actually based on temporal relationship between motor and cognitive symptoms2.

The study of subcortical structures, early and similarly involved in these conditions, is of interest: identification of abnormal MRI measures in such areas could be of help in the differential diagnosis and in the prediction of cognitive impairment.

OBJECTIVE

To explore the patterns of global (volume analysis) and regional (shape analysis) atrophy of subcortical structures, obtained by means of automated segmentation of T1 scans.

In particular, we were interested in the markers of evolution from PD to PDD and in the discrimination between DLB and PDD.

METHODS

16 PD, 11 PDD and 16 DLB patients were recruited and underwent 1.5T MPRAGE MRI scanning. Segmentation of subcortical structures was performed with the fully-automated FMRIB's Integrated Registration and Segmentation Tool (FIRST) implemented in FSL. Then, volume and shape of each structure were compared between groups.

RESULTS

PD patients showed significant higher mean volumes of total brain, caudati, pallidi, accumbens nuclei, thalami and hippocampi compared to both PDD and DLB subjects (**Table 1**).

When considering the differences between PD and PDD, hippocampal atrophy was found to be the best predictor of dementia ($p < 0.001$).

When comparing PDD and DLB, the only significant difference was found in the pallidi, more impaired in DLB. Box plots of mean hippocampal and pallidal volumes are reported in **Figure 1.**

Shape analysis revealed specific shape differences of the dorsolateral and ventrolateral hippocampal surface (**Figure 2, panel A**) and of the dorsal and ventral pallidal surface (**Figure 2, panel B**).

CONCLUSIONS

Our results expand previous findings obtained with manual and automated segmentation of subcortical structures in PD, showing a widespread subcortical atrophy when dementia is overt3-4.

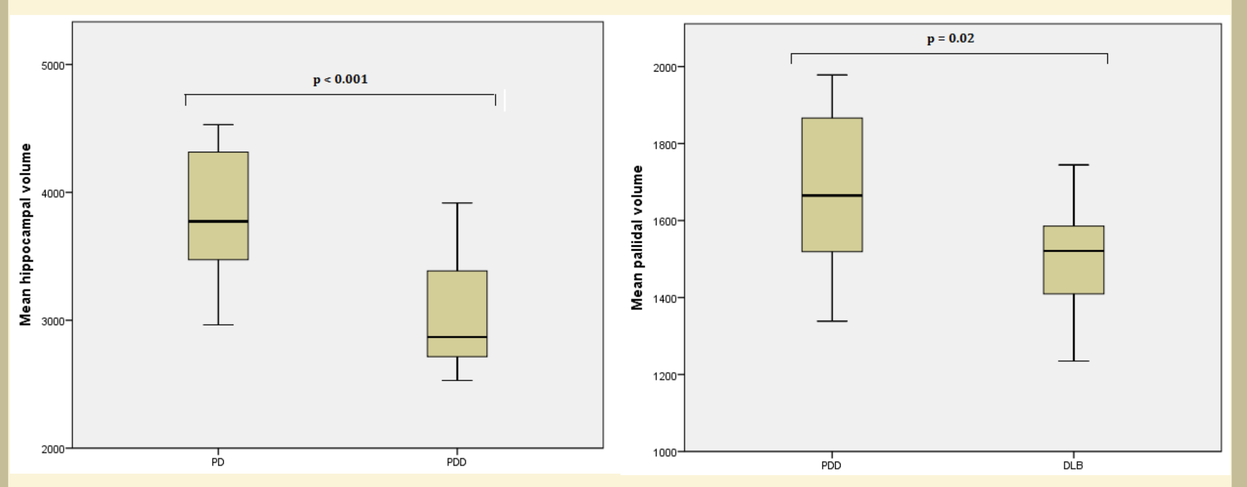
Subcortical structures are crucial in α-synucleinopathies, representing potential targets for automated time-sparing shape analyses, which could be of help in predicting the course of pathology and in discriminating PDD from DLB.

TABLE 1

	PD	PDD	DLB	p	p^	p†
TBV	$1094x10^3±53x10^3$	$1006x10^3±61x10^3$	$976x10^3±69x10^3$	<0.001	0.001	-
Caudate, L	3153±264	2781±278	2904±380	0.008	0.002	-
Caudate, R	3198±278	3015±331	2876±332	-	-	-
Caudate, mean	3176±260	2899±215	2891±330	0.031	0.013	-
Putamen, L	4349±502	4049±366	4058±412	-	-	-
Putamen, R	4264±498	4105±413	4003±416	-	-	-
Putamen, mean	4307±477	4078±341	4031±366	-	-	-
Pallidum, L	1647±178	1709±294	1519±153	-	-	-
Pallidum, R	1665±145	1631±203	1444±211	0.014	-	0.014
Pallidum, mean	1657±145	1670±235	1482±173	0.049	-	0.02
Accumbens, L	427±135	327±88	304±130	-	0.036	-
Accumbens, R	351±112	238±91	201±107	0.001	0.02	-
Accumbens, mean	389±107	283±67	253±109	0.005	0.011	-
Thalamus, L	7203±511	6688±578	6717±474	0.04	0.017	-
Thalamus, R	7052±445	6599±481	6514±428	0.019	0.018	-
Thalamus, mean	7128±460	6644±517	6615±407	0.02	0.012	-
Hippocampus, L	3759±602	2825±520	3193±371	<0.001	<0.001	0.03
Hippocampus, R	3855±632	3281±460	3213±471	0.028	0.02	-
Hippocampus, mean	3808±505	3053±452	3204±351	<0.001	<0.001	-
Amygdala, L	1438±228	1334±217	1364±147	-	-	-
Amygdala, R	1486±200	1454±256	1274±262	-	-	-
Amygdala, mean	1462±192	1395±209	1319±190	-	-	-

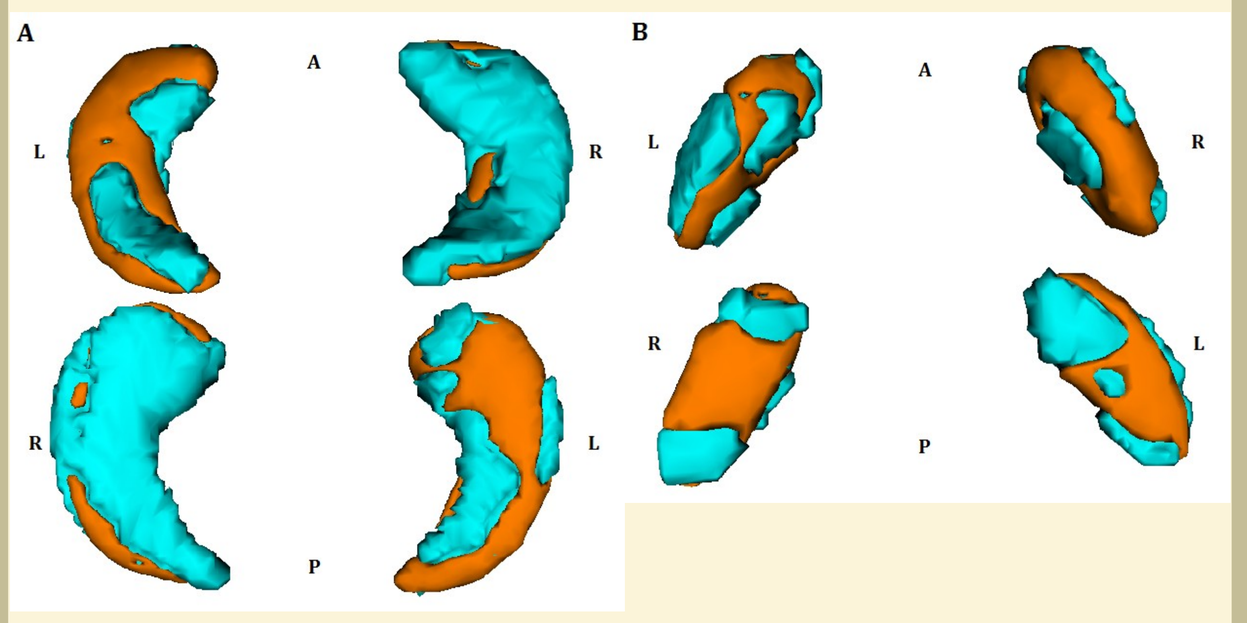
Cortical and subcortical volumes of the cohort.
Multivariate analysis, considering age, gender and disease duration as nuisance variables. Volumes are expressed as mean ± standard deviation (mm3).
p^ and p† refer to post-hoc comparison (LSD). p^ = PD vs PDD; p† = PDD vs DLB.
L: Left. R: Right. TBV: total brain volume.

FIGURE 1



Box plots of hippocampal and pallidal volumes.
Box: mean volume of the structure in mm3
Plot: standard deviation in mm3

FIGURE 2



Shape analysis of structures affected by atrophy.
Panel A: dorsal and ventral view of left and right hippocampus in the PDD < PD contrast.
Panel B: dorsal and ventral view of left and right globus pallidus in the DLB < PDD contrast.
Light blue: structure shape; orange: shape difference. $P < 0.05$ FDR corrected.
A: anterior. P: posterior. L: left. R: right.

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