Regional shape changes of the striatum and thalamus in Alzheimer's disease; a morphometrical MRI study

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Introduction

Atrophy is regarded as a sensitive marker for neurodegenerative pathology in Alzheimer's disease (AD). Besides neuronal loss in the neocortex, especially in the medial temporal lobe, atrophy also occurs in the deep grey matter. Within the subcortical region, the thalamus and putamen show the strongest reduction in size in AD, with a strong correlation between smaller left volumes and poorer cognitive test results, regardless of neocortical grey matter volume [1]. This morphometrical study investigates more specifically which regions on the surface of the deep grey matter structures are most prone to atrophic changes in AD.

Material and Method

For this study, subjects were recruited who attended the memory clinic of the Leiden University Medical Center between January 2006 and May 2008. Thirty-five subjects diagnosed with probable AD (according to the NINHDRS criteria [2]) were compared to 35 subjects without cognitive deficits who matched in age, gender and years of education. Clinical T1 MR images were acquired on a 3.0 Tesla whole body MRI scanner (Philips, Clinical systems, Best, The Netherlands), with acquisition parameters as follows: TR = 9.8 msec; TE = 4.6 msec; flip angle = 8°; section thickness = 1.2 mm; number of sections = 120; no section gap; whole brain coverage; FOV = 224 mm; matrix = 192, reconstruction matrix = 256. Automatic segmentation of the deep grey matter structures was performed using *FIRST* from FSL [3]. Shape modeling and analysis for the caudate nucleus, putamen, pallidum and caudate nucleus were performed as presented in [4], in order to highlight significant local shape changes between the groups. For each location on the surface, we also evaluated the displacement vectors needed to locally deform the average shape of the control group to the average shape of the AD group.

Results

Table 1 displays the volume differences of the deep grey matter structures and their estimated differences when corrected for head size. A reduction in size is seen for all subcortical structures, but strongest for the putamen, thalamus and right caudate nucleus. Figure 1 summarizes the results of the shape analysis, showing the regions on the surface of the deep grey matter structures, which were found significantly different between AD-patients and the control group. Except for a small area on the posterior end of the right putamen, all vector displacements between the groups were found inward, supporting the previous findings on volume reduction in AD. Inward shape differences in AD subjects appear to be localized bilaterally in the medial side of the caudate nucleus, antero-medial thalamus and ventral putamen. The pallidum also showed significant differences but these were found more globally distributed on the whole surface of the structure.

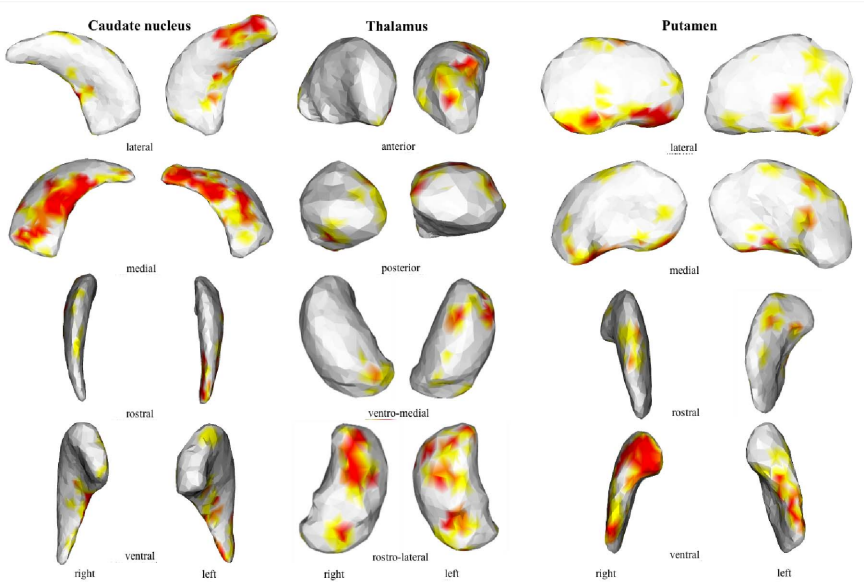

Figure 1 Mean shapes of the caudate nucleus, thalamus and putamen with the results of the permutation tests depicted in color on their surfaces. The yellow regions correspond to a *p*-value of 0.1, red to a *p*-value of 0.05.

Interpretation

AD subjects suffer local atrophic changes in the striatum and thalamus compared to controls without cognitive deficits. The regions highlighted in our study as affected by AD are projecting on the medio temporal lobe (i.e. antero medial nuclei of the thalamus [5]), the medial prefrontal and orbitofrontal lobe (i.e. antero-medial thalamus, ventral putamen [6]), the dorsolateral prefrontal lobe (i.e. medial caudate nucleus [6]), or involved in known dopaminergic circuits (i.e. ventral putamen, [7]). Thus, our findings shed more light on the disruption of limbic-mediotemporal circuits, and on possible causes of mood symptoms related to AD [8]. To the best of our knowledge, this is the first study detecting such changes in *in-vivo* clinical MR images.

	Memory Complainers (n=35)	**Probable AD (n=35)**	B (*p*-value)
CN L	6163 (927)	6013 (1173)	150 (.556)
CN R	6770 (995)	6320 (1024)	450 (.066)
PUT L	7019 (773)	6376 (1024)	643 (.004)
PUT R	7526 (782)	7214 (1035)	311 (.140)
GP L	2851 (1091)	2655 (575)	196 (.351)
GP R	2808 (1184)	2495 (630)	313 (.171)
TH L	9383 (1231)	8791 (1366)	789 (.061)
TH R	9465 (1216)	8667 (1285)	196 (.010)

Table 1 Volumetric differences of the deep grey matter structures between probable AD patients and controls

References

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