Subcortical volume and morphology in Alzheimer's disease and mild cognitive impairment

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Introduction

The neurodegenerative processes in Alzheimer's disease have been well-characterized at the level of the neocortex and the hippocampus. Surprisingly, subcortical structures such as striatum, thalamus, and pallidum have received little attention. This is despite the fact that we know the thalamus and striatum are sites of accumulation for neurofibrillary tangles and neuropil threads [1]. The goal of this work is to investigate the morphological changes of the subcortical structures with subject diagnosis.

Methods

3186 T1-weighted images from ADNI2/GO (2829/357) acquired at 3T were preprocessed with minc-bpipe-library then processed using MAGeT brain [2,3], which outputs volume, vertex displacement (DP), and vertex surface area (SA) on a per structure basis. The Colin-27 Subcortical Atlas was used as a single input atlas [4]. 2488 passed a manual quality control. Effects of diagnosis were examined using a linear mixed effects model, accounting for age, and sex. Modelling of volume changes was done with and without covarying for ICV. For volume, DP and SA, each of EMCI, LMCI and AD was compared to the reference CN group. DP and SA were corrected for multiple comparisons with FDR.

Diagnosis	CN		EMCI		LMCI		AD		Test Statistic
Gender	Female	Male	Female	Male	Female	Male	Female	Male	
Baseline N	93	88	133	168	74	81	59	82	$X^2(df=1) = 4.627$ (p=0.03)
Age	72.1 ± 5.6	74.6 ± 6.7	70.4 ± 7.7	71.9 ± 7.0	71.2 ± 7.6	72.9 ± 7.7	72.5 ± 8.1	75.5 ± 7.9	CN-EMCI: t =7.734 (p<0.001) CN-LMCI: t =4.127 (p<0.001) CN-AD: t =-2.87 (p=0.004) EMCI-LMCI: t =-2.13 (p=0.03) EMCI-AD: t = -8.3947 (p<0.001) LMCI-AD: t =-5.8138 (p<0.001)
ADAS11	4.77 ± 2.48	6.19 ± 3.29	7.25 ± 4.07	8.32 ± 4.28	11.60 ± 5.91	13.12 ± 6.05	23.69 ± 9.42	21.85 ± 8.07	CN-EMCI: t =-13.15 (p<0.001) CN-LMCI: t =-23.76 (p<0.001) CN-AD: t =-35.41 (p<0.001) EMCI-LMCI: t =-15.23 (p<0.001) EMCI-AD: t = -30.24 (p<0.001) LMCI-AD: t =-18.99 (p<0.001)

Table 1: Demographics breakdown of the baseline ADNI2/GO T1 images analyzed, showing distribution over the diagnoses of normal control (CN), early mild cognitive impairment (EMCI), late mild cognitive impairment (LMCI) and Alzheimer's Disease (AD)

Results

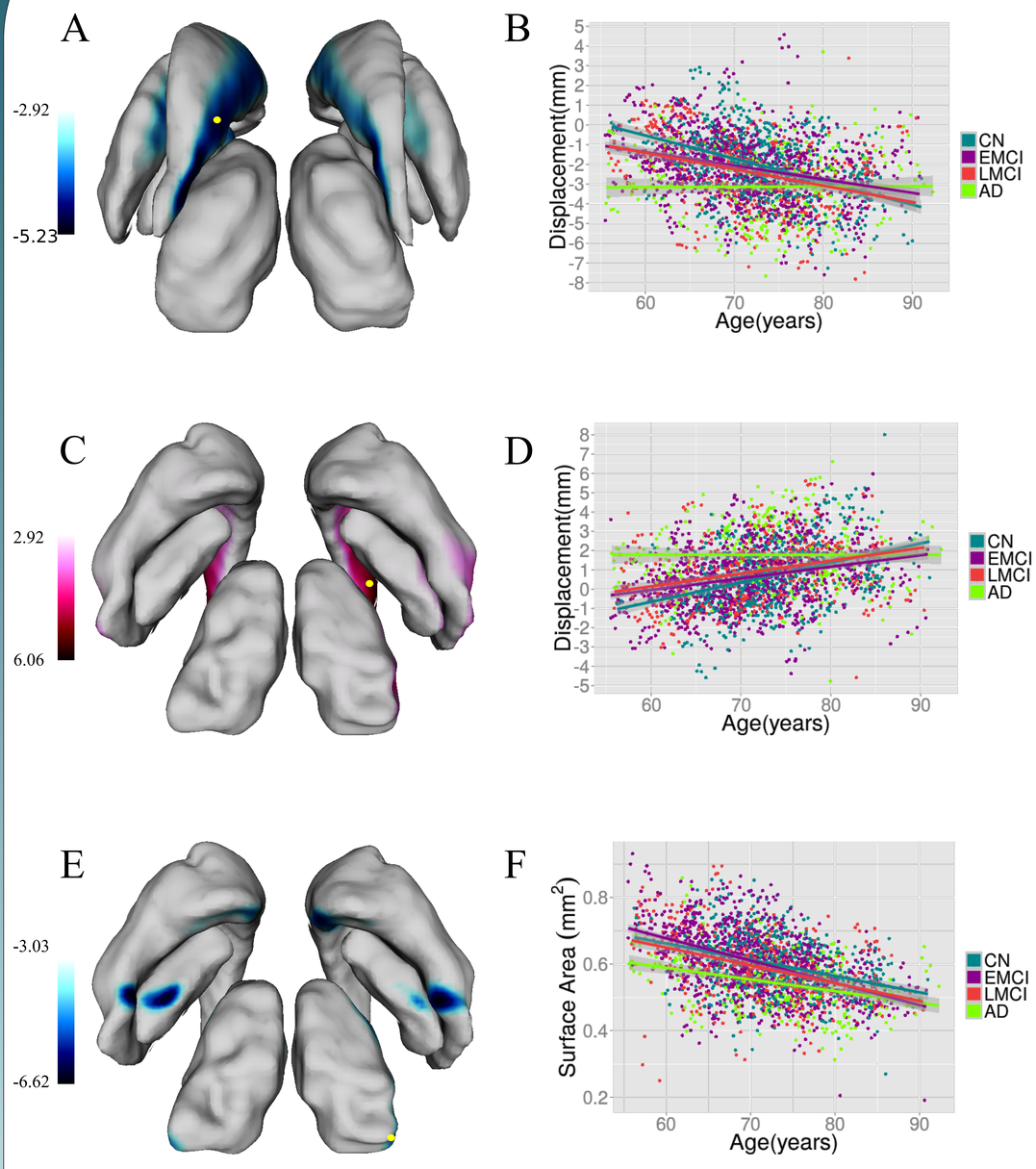

Figure 1: Vertex wise linear mixed effects modelling for displacement (A-D) and surface area (E,F). T statistics mapped on to subcortical regions (corrected to 1% FDR) show outward displacement in the postcommisural caudate (C), and inward displacement in the precommisural caudate (A) of the AD group compared to CN. In (E), we see decreased surface area in the ventral posterior, ventral anterior, and ventral lateral nuclei of the thalamus in AD compared to CN. Plots of DP at the location of a peak t statistic attribute effects to longitudinal trajectories (B,D), while plots of SA attribute affects to cross-sectional anatomical differences more than longitudinal trajectories (F). The location of the plotted vertex is denoted with a yellow dot. Linear mixed effects modelling shows left (G) and right (H) thalamus volumes of AD patients (left, t=-3.3; right, t=-3.5) being lower than volumes of normal controls.

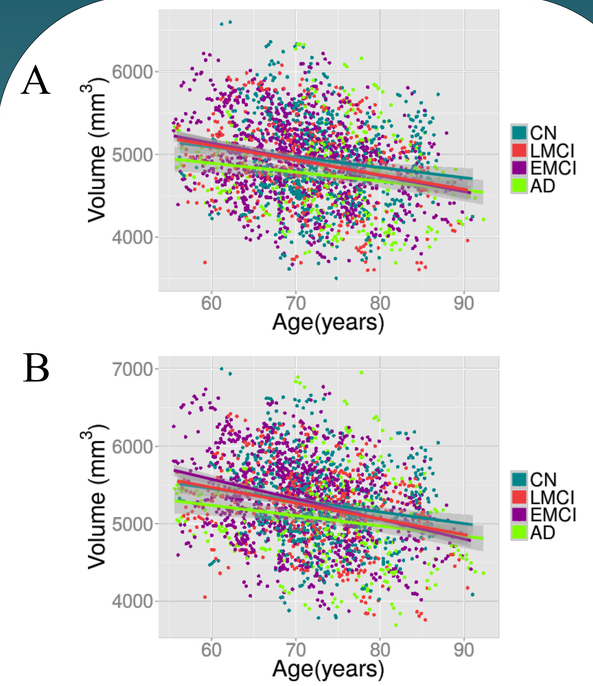

Figure 2: Linear mixed effects modelling shows left (A) and right (B) thalamus volumes of AD patients (left, p=0.004 t=-2.88; right, p=0.002 t=--3.02) being lower in comparison to thalamic volumes in CN subjects.

Conclusion

We found that the thalamus shows pronounced degeneration in AD patients. We saw that AD caudate show a posterior bulging out DP, suggesting an accompanying thinning of the nearby internal capsule. Finally, we found that subcortical structures do not appear to be major factors in distinguishing AD from MCI patients. Volumetric and SA analysis shows degeneration in AD patients already apparent in the early aging process, as opposed to an increased rate of degeneration over the ages 60-80, suggesting these measures may be involved in the onset of the prodromal of Alzheimer's disease.

References & Acknowledgement

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