Influence of β-Amyloid Accumulation in Subcortical Morphology

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Introduction

An essential hallmark of Alzheimer's Disease (AD) is β-amyloid (Aβ) plaque formation[1]. However, a strong association between Aβ accumulation and structural atrophy is less clear. Thus, we sought to investigate the influence of Aβ deposition in subcortical volume and morphology.

Methods

3T t1-weighted images of participants enrolled in the Alzheimer's Disease Imaging Neuroinitiative (ADNI) phase 2 were first pre-processed with minc-bpipe library, then processed with MAGeTBrain[2,3] to obtain outputs of volume, and surface area per structure, with the Colin27 atlas as a single input[4]. Out of 2397 images, 2108 of them passed manual quality control. Florbetapir Standardized Value Uptake Ratio (SUVR, calculated with cerebellum as reference) of 1.11 is used to define Aβ positivity. Linear mixed effects model is applied to examine the influence of Aβ positivity on subcortical (striatum, thalamus, and pallidum) volume and morphology, accounting for age, sex, diagnosis, ApoE4 status; and corrected for multiple with FDR.

Aβ Class	Negative		Positive	
Diagnosis	Cog. Normal	MCI	Cog. Normal	MCI
Female	35	53	23	55
Male	36	73	14	85
Age	73 ± 6	71.1 ± 7.9	75 ± 5.9	72.1 ± 7.5
ADAS11	5.9 ± 2.9	10.8 ± 4.7	6 ± 3.1	11.2 ± 4.6
ADAS13	9.2 ± 4	17.6 ± 7.1	9.5 ± 5	18. ± 6.8
MMSE	29 ± 1.3	27.7 ± 1.9	29.2 ± 1	27.4 ± 1.9
Apoε4 carrier	20	69	15	90

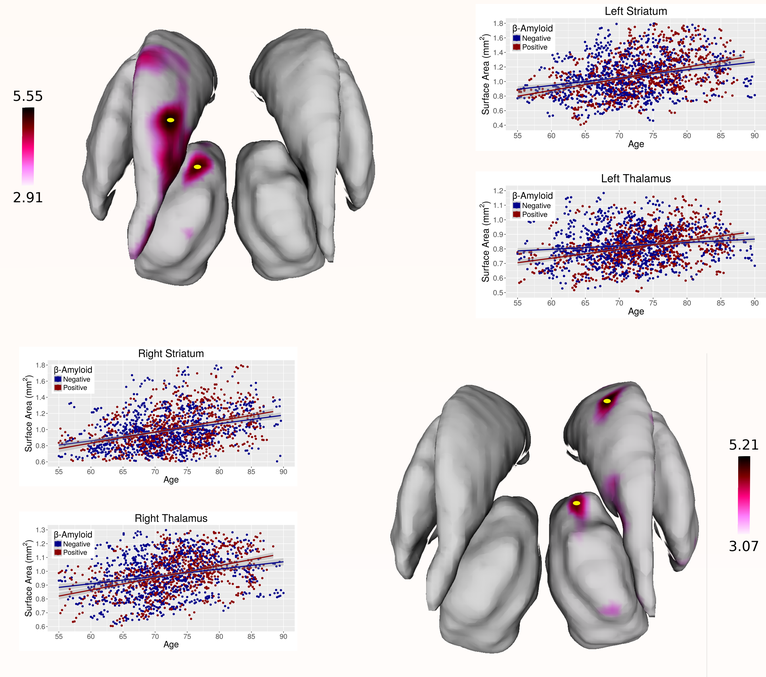

Figure 1. Vertex-wise linear mixed effects modelling for surface area in Aβ negative and positive individuals. T-statistics mapped onto striatal and thalamic surfaces (corrected to 5% FDR) show increasing surface area along the tail of caudate for the left hemisphere, while similar increase occur along the body caudate for the right hemisphere over time, in Aβ positive versus Aβ negative individuals. For thalamus, surface area changes over time occur bilaterally along the mediodorsal nuclei, with decrease in the left, and increase in the right hemisphere in Aβ positive compared to Aβ negative individuals. For each strcuture, the location of the plotted vertex of a peak t-statistic is denoted with a yellow dot.

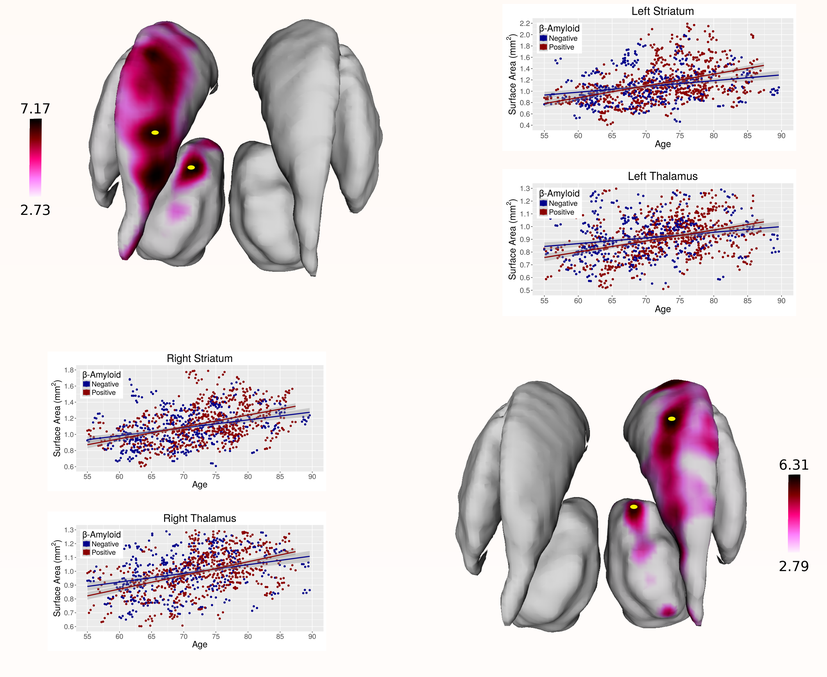

Figure 2. Vertex-wise linear mixed effects modelling for surface area in individuals diagnosed with mild cognitive impairment (MCI) and categorized as Aβ negative or positive. T-statistics mapped onto striatal and thalamic surfaces (corrected to 5% FDR) show increasing surface area over time along the caudate of both left and right hemispheres of Aβ positive MCI compared to Aβ negative MCI individuals. Thalamus of Aβ positive MCI individuals show increasing surface area changes over time occur bilaterally along the mediodorsal nuclei, compared to Aβ negative MCI individuals. For each strcuture, the location of the plotted vertex of a peak t-statistic is denoted with a yellow dot.

Summary

Individuals diagnosed with AD were not included in the analysis because of low number of Aβ negative individuals.
When all participants irrespective of diagnosis is considered, Aβ positive individuals show bilaterally reduced surface area in the early aging process with a slighlty increased rate of surface area changes between ages 60-80, in the mediodorsal thalamic nuclei and caudate, whereas with no changes in the globus pallidus.
These found differences between Aβ positive and negative individuals become more pronounced within participants diagnosed with early or late MCI. Finally, Aβ positivity did not effect surface area in any of these structures in cognitively healthy individuals.
Overall, these results suggest an overall effect of Aβ accumulation on striatal and thalamic morphology, with no effect on subcortical volume.

References

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