MR-based age- and sex-related effects on the striatum, globus pallidus and thalamus in healthy individuals across the adult lifespan

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Introduction

While age-related changes are major risk factors in neurodegenerative diseases, there are limited studies investigating changes in subcortical morphology associated with healthy aging. Furthermore, since prevalence, onset age and symptomatology of many neuropsychiatric disorders differ between males and females, we examined the effect of age and sex on the volume, shape, and myelin of the striatum, globus pallidus and thalamus.

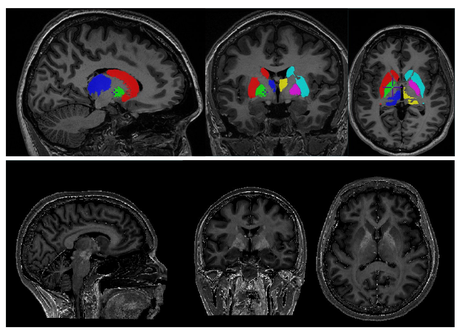
Methods

90 healthy subjects (aged 18 to 80) were imaged on a Siemens 3T Trio machine using an 8-channel head coil. T1-weighted structural scans were acquired at 1mm^3 isotropic using the ADNI MPRAGE protocol (TE/TR=2.98 ms/2300 ms, TI=900 ms, α=9°, FOV= 256 mm, slice thickness=1.00 mm, and 1.00 mm^3 isotropic voxel dimensions). T2-weighted MR images were acquired at 0.64 mm^3 isotropic using a turbo spin echo sequence (TE/TR=198 ms/2500 ms, FOV=206 x 206 x 204 mm3, partial Fourier 6/8, GRAPPA of 2, 10 min).

Volumes and surface area were obtained using MAGeTbrain (Chakravarty et al. 2013; Pipitone et al., 2014) to examine the relationship with age. To better understand how morphological alterations may be related to microstructural alterations at the level of myelination, the ratio of signal intensity in T1w and T2w MRIs (a proposed measure of myelin (Glasser & van Essen, 2011)) was examined at a voxel-wise basis. Statistical analyses used age and sex as covariates in a general linear model. Total brain volume (Eskildsen et al., 2012) was used as a nuisance variable. False discovery rate was used to correct for multiple comparisons.

A) Labels of the striatum, globus pallidus and thalamus

B) T1/T2 image



Morphological Analyses

Volume and Age relationship:

Surface Area and Age relationship:

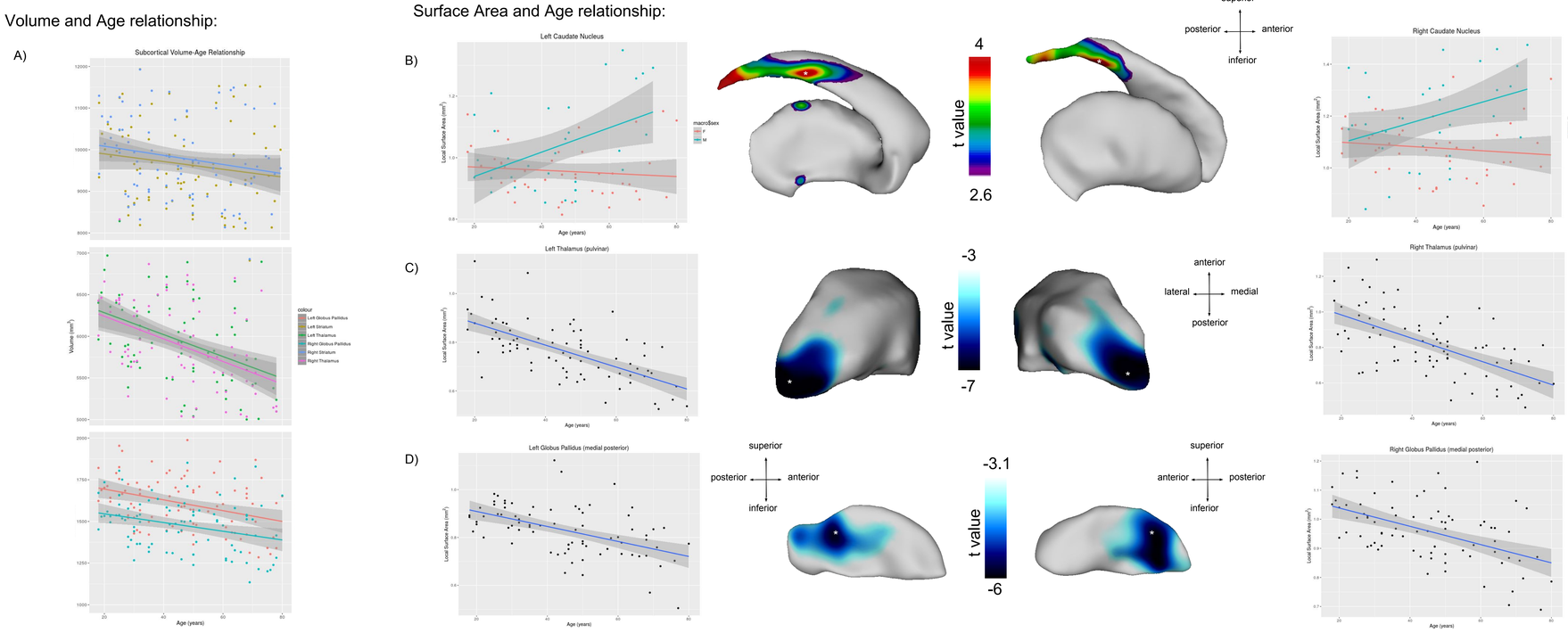


Figure 1: Age-related changes in volume and shape. A) Volumetric age-related decline was observed in left and right striatum, globus pallidus and thalamus (left and right striatum: p<0.0001; left and right globus pallidus: p=0.005; left and right thalamus: p<0.0001). B) Age by sex interaction observed in the left and right posterior caudate nucleus of the striatum at FDR 5%, denoting a steeper rate of surface area expansion in males compared to females. C) Age-related decline in surface area of the bilateral thalami, particularly the pulvinar nucleus (located at the posterior end of the thalamus) was observed at FDR 1%. D) Decreased surface area with age observed in the medial posterior part of the left and right globus pallidus at FDR 1%.

Microstructural Analyses

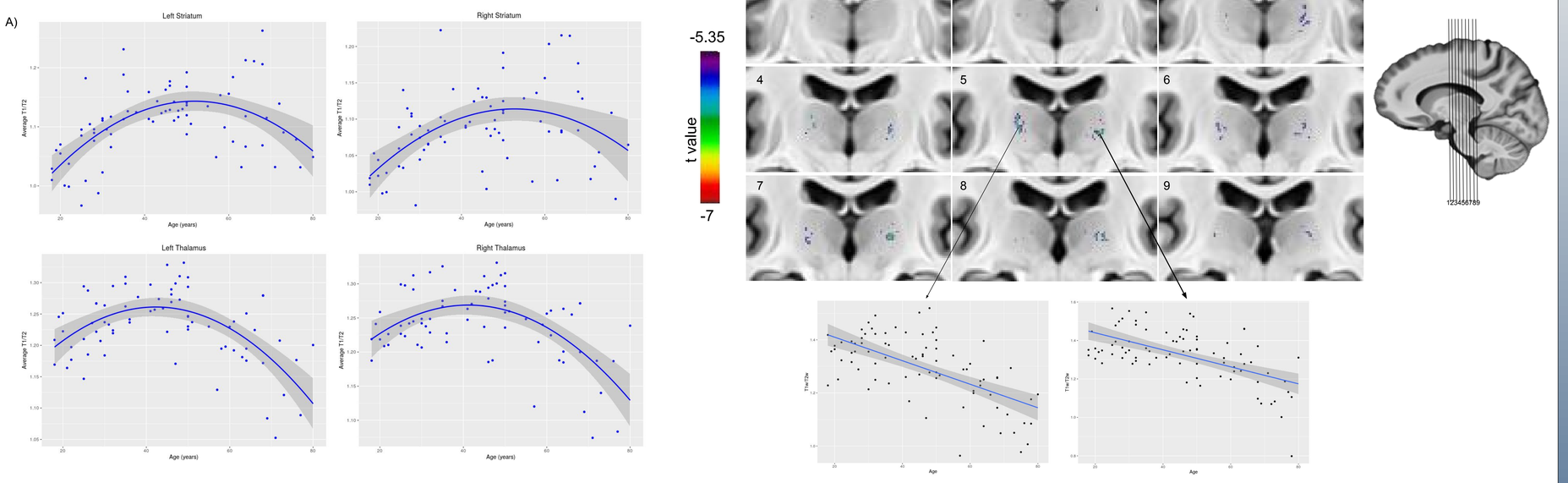


Figure 2: Age-related changes in myelin (T1w/T2w ratio used as a proxy for myelin measures). A) Average T1w/T2w values computed across all voxels within the three structures of interest bilaterally. Quadratic age-related decline observed in the striatum and thalamus bilaterally (left striatum: p<0.0001; right striatum: p=0.012; left thalamus: p=0.0002; right thalamus: p=0.002). B) Voxel-wise analysis of T1w/T2w with age across the striatum, globus pallidus and thalamus bilaterally. Significant age-related decline in T1w/T2w values observed in the lateral thalami at FDR 5%. Results of voxel-wise T1w/T2w-age analysis shown for peak voxel in the left and right thalamus respectively.

Summary

1. Bilateral age-related volumetric decreases were observed in all three structures of interest (p<0.005 for all three structures of interest bilaterally) (Figure 1A).
2. Sex-specific age-related increase in surface area of bilateral posterior caudate nucleus was observed, with a marked expansion observed in males across the adult lifespan (Figure 1B) at FDR 5%.
3. Decreased surface area with age was observed in bilateral pulvinar nuclei (Figure 1D) at FDR 1%; an important relay to the parietal and temporal cortex which is affected in neurodegenerative diseases, particularly dementia.
4. Decreased surface area with age was observed in bilateral medial posterior part of the globus pallidus (Figure 1C) at FDR 1%.
5. Quadratic age-related decline of myelin (average T1w/T2w value per structure) was observed bilaterally in the striatum and thalamus (p<0.01) (Figure 2A).
6. Age-related decline of myelin (voxel-wise T1w/T2w) was observed bilaterally in the thalamus at FDR 5% (Figure 2B).

References

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