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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, as well as motor performance on the volume and shape of the striatum, globus pallidus and thalamus, and examined the interaction between subcortical morphology and myelin in healthy individuals.

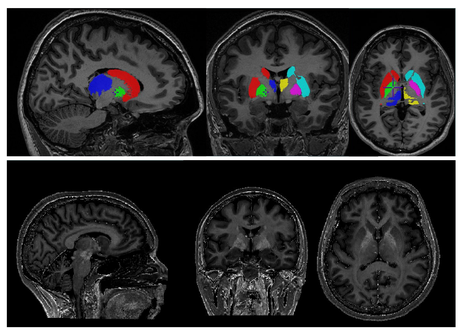
Methods

90 healthy subjects (aged 18 to 80) were scanned 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 mm3 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 mm^3, partial Fourier 6/8, GRAPPA of 2, 10 min).

Volumes and surface area were obtained using MAGeTbrain (Chakravarty et al. 2013) 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 & 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 was used as a nuisance variable. False discovery rate was used to correct for multiple comparisons. A secondary analysis included performance on the grooved pegboard task in the model.

A) Labels of the striatum, globus pallidus and thalamus

B) T1/T2 image



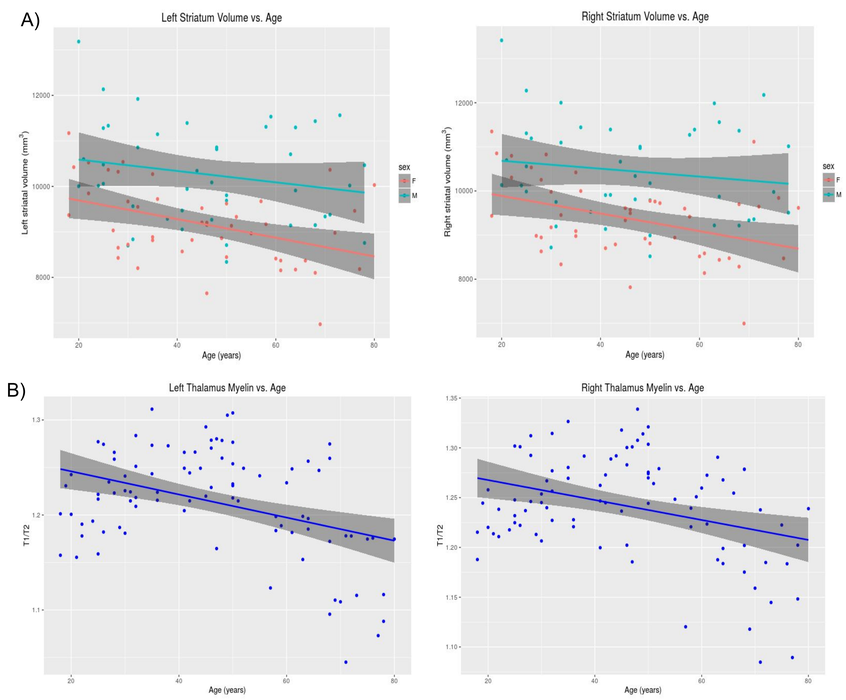


Figure 1: Age related changes. A) Sex-specific rates of bilateral striatal volumetric decline were observed, with a steeper rate in females (left p=0.03; right p=0.05). B) Age-related decline in myelin was observed in bilateral thalami (left p=0.032; right p=0.026). C) Decreased surface area with age was observed in bilateral pulvinar nuclei (FDR 1%). D) A relationship between volume and myelin across age was observed in bilateral thalamus, such that subjects of younger age had larger volumes and more myelin (higher T1w/T2w values) (left p=0.043; right p=0.031).

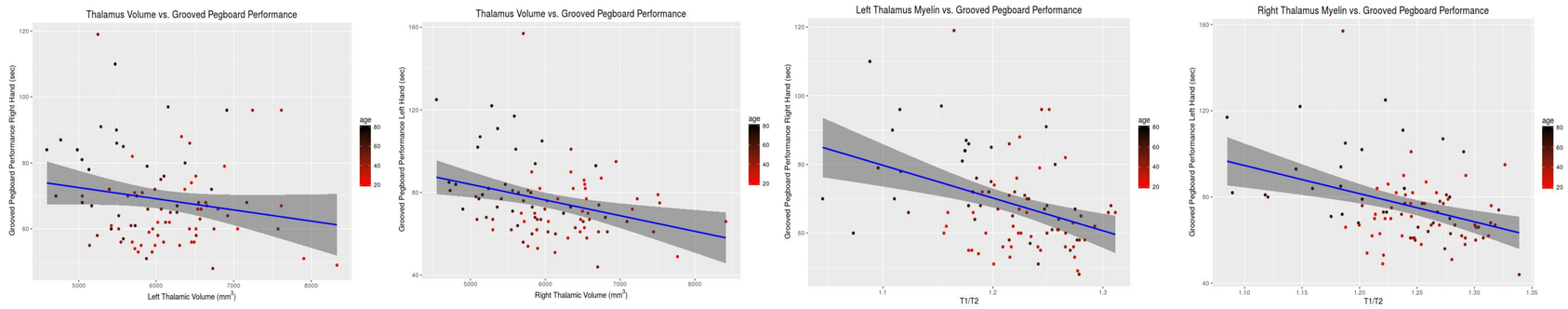


Figure 2: Relationship between volume and myelin with motor performance. Increased contralateral thalamic volume and myelin predicted faster performance on the grooved pegboard task (volume: left p=0.05, right p=0.04; myelin: left p=0.03, right p=0.005).

Summary

Bilateral age-related volumetric decreases were observed in all three structures of interest (striatum: left: t=-3.32, p=0.0007, right: t=-3.8, p=0.0002; globus pallidus: left: t=-3.1, p = 0.003, right: t=-2.5, p=0.01; thalamus: left : t=-4.8, p=7.8*10-6, right: t=-5.5, p=3.7*10-7). Sex-specific rates of striatal volumetric decline were observed bilaterally, denoting a steeper rate of decline in females compared to males (age*sex for left: t=2.2, p=0.03; and right striatum: t=1.9, p=0.05). Age-related decline in myelin was observed in bilateral thalami (p=0.03). Moreover, decreased surface area with age was observed in bilateral pulvinar nuclei, which is an important relay to the parietal and temporal cortex which are affected in neurodegenerative diseases, particularly dementia. Moreover, bridging structure and function, contralateral thalamic volume and myelination predicts grooved pegboard motor performance.

These results support and expand upon the framework of age-related changes of the normal aging brain, suggesting a substantial modulation of sex on the rate of volumetric decline. A clearer understanding of adult lifespan trajectories of subcortical structures can provide a normative baseline for neuropsychiatric disorders in which these subcortical structures are heavily implicated (e.g. Parkinson's disease, schizophrenia and geriatric depression).

Bibliography

1. Bohnen, N. I., Kuwabara, H., Constantine, G. M., Mathis, C. A., & Moore, R. Y. (2007). Grooved pegboard test as a biomarker of nigrostriatal denervation in Parkinson's disease. Neuroscience Letters, 424(3), 185-189. doi:10.1016/j.neulet.2007.07.035
2. Chakravarty, M. M., Steadman, P., Eede, M. C., Calcott, R. D., Gu, V., Shaw, P., . . . Lerch, J. P. (2013). Performing label-fusion-based segmentation using multiple automatically generated templates. Human Brain Mapping, 34(10), 2635-2654. doi:10.1002/hbm.22092
3. Eskildsen, S.F., Coupé, P., Fonov, V., Manjón, J.V., Leung, K.K., Guizard, N., Wassef, S.N., Østergaard, L.R., Collins, D.L.; Alzheimer's Disease Neuroimaging Initiative. (2012). BEaST: Brain extraction based on nonlocal segmentation technique. NeuroImage, 59(3), 2362-73. doi:10.1016/j.neuroimage.2011.09.012
4. Glasser, M. F., & Essen, D. C. (2011). Mapping Human Cortical Areas In Vivo Based on Myelin Content as Revealed by T1- and T2-Weighted MRI. Journal of Neuroscience, 31(32), 11597-11616. doi:10.1523/jneurosci.2180-11.2011