#609 Heritability of Subcortical Structures Using a Twin and Non-Twin Sibling Design

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INTRODUCTION

In imaging-genetics, the **heritability** of the quantitative phenotype under study is often considered a prerequisite for future studies, such as genome-wide association studies (GWAS)[1]. The current work extends previous work from our group[5,6] to examine the heritability of the volume and shape of the striatum, thalamus and globus pallidus. It is the first study to examine the **shared heritability** and **genetic correlation** between subcortical structure morphometry (vertex-wise surface area (SA) and displacement) and aggregate measures (total brain volume (TBV), subcortical structure volume and total SA) as a means of providing a nuanced description of subtle variation in neuroanatomy.

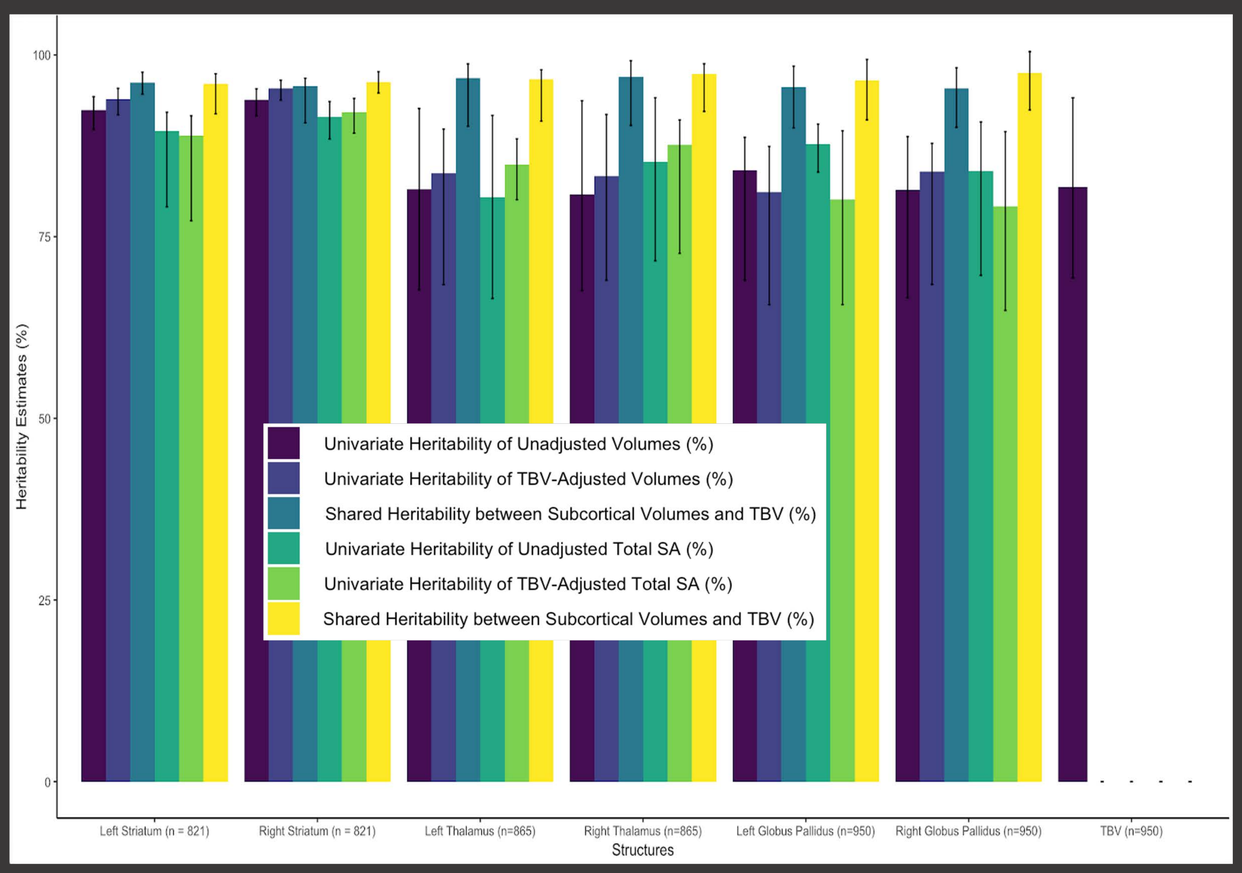

Figure 1. Univariate and bivariate heritability (h^2) estimates of subcortical structure volumes and total SA

GLOSSARY

[Univariate] heritability (h^2): proportion of variance of a phenotype attributable to additive genetic (*as opposed to environmental*) effects
[Bivariate] shared heritability (h^2): proportion of covariance between two phenotypes attributable to additive genetic (*as opposed to environmental*) effects
[Bivariate] genetic correlation (r_g): Proportion of the genetic factors that explain the variance of phenotype 1 which also explain the variance of phenotype 2.

METHODS

Data Acquisition: The WU-Minn Human Connectome Project[2]. S1200 Release of structural MRI data on healthy young adult twin and non-twin siblings (N = 1086).

Image Processing: minc-bpipe library and MAGeTbrain[3, 4]

Heritability Estimates.

- The OpenMx package (version 2.12.2) in R (version 3.5.1) was used to compute heritability estimates[5].
- Univariate model: heritability of one phenotype (structure volume, structure total SA, vertex-wise SA, vertex-wise displacement) at a time
- Bivariate model: shared heritability and genetic correlation between two phenotypes at a time: TBV and more local measures (structure volume, vertex-wise SA, vertex-wise displacement)

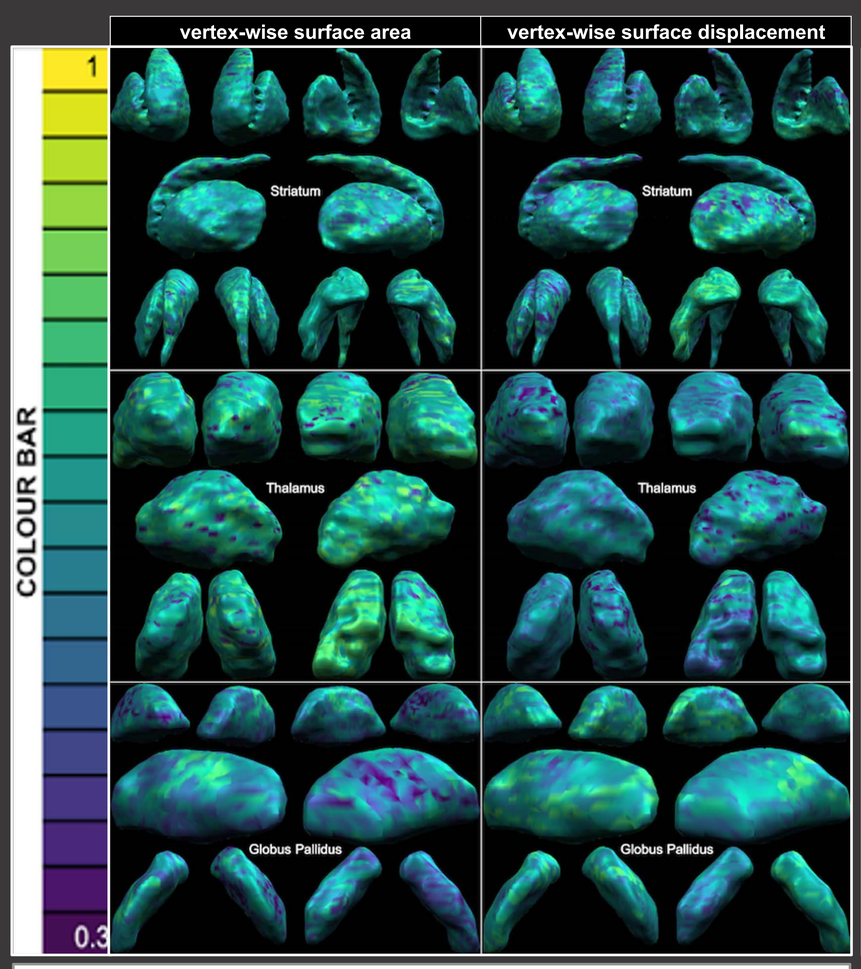

Figure 2. Vertex-wise **univariate heritability**

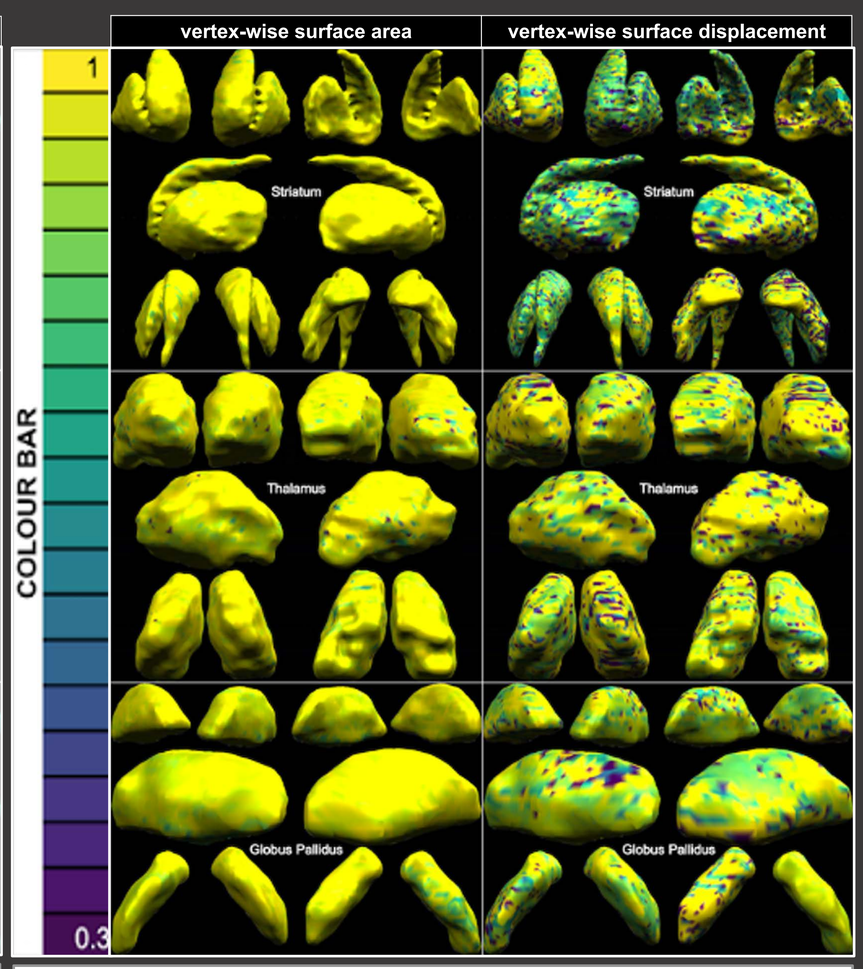

Figure 3. **Shared heritability** between TBV and vertex-wise measures

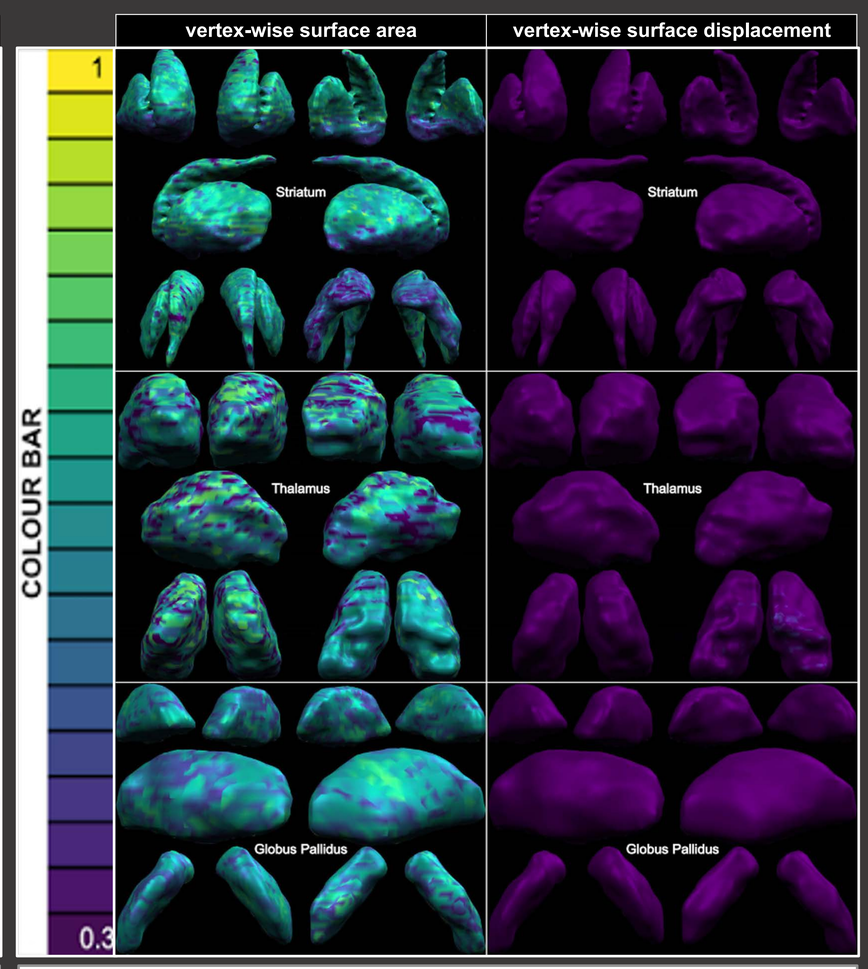

Figure 4. **Genetic correlation** between TBV and vertex-wise measures

MAIN FINDINGS

- Subcortical structure **volumes are highly heritable**. A huge portion of their covariance with TBV is explained by additive genetic effects
- Indirect evidence for the existence of **genetic factors with highly localized effects** on subcortical structures
  → vertex-wise heritability estimates are highly heritable yet only moderately genetically correlated with TBV
- The **ventral striatum** (associated with habit formation and addition) is a lot less correlated with TBV than the dorsal striatum (associated with motor control).
- Supplementary results

FUTURE DIRECTIONS

- Intuitively, one would assume an inverse relationship between heritability and brain plasticity. Our current work therefore seeks to understand the relationship between heritability and evolutionary expansion of subcortical structures across non-human primates.

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