Heritability of subcortical volume asymmetries in twins from the Mexican Twin Registry, TwinsMX

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Introduction. Multiple regions of the brain show morphological differences with their homologous region in the contralateral hemisphere. Some of these asymmetries might be functionally and developmentally relevant, as they have been associated with performance in different behavioral tasks and aging. It is less known the weight of genetic and environmental factors influencing such asymmetries. Heritability, the proportion of the variance of a phenotype explained by genetic factors, can be estimated through a twin study. Most studies on the heritability of brain asymmetry have been focused on the cortex, and have been done in populations of European ancestry.

Objective. The goal of this study is to characterize the heritability of subcortical volume asymmetry in a Mexican sample of twins from the Mexican Twin Registry: TwinsMX.

Methods. A total of 188 adults (30.3 ± 9.36 years of age) twins (58 DZ, 130 MZ) of both sexes (152 females) were invited to participate in an MRI study as part of TwinsMX, which included the acquisition of high resolution (1x1x1 mm^3) and high contrast T1 weighted images covering the whole brain and cerebellum. These were preprocessed through FreeSurfer's (v. 7.1.1) recon-all pipeline, which includes a segmentation of subcortical structures (Thalamus, Amygdala, Hippocampus, Caudate, Putamen, and Pallidum), and a calculation of their volume. We calculated volume asymmetry as the difference between both homologous regions (Right $_{region}$ - Left $_{region}$) / (Right $_{region}$ + Left $_{region}$). We then estimated the heritability of volume asymmetry for each subcortical region with an ACE model using R's (v. 4.2.1) umx and OpenMX packages, and the mean asymmetry of each region through a linear mixed model using the lme4 and lmerTest packages, controlling for age, sex, and family. Results were corrected for multiple comparisons (Bonferroni).

Results. The hippocampus ($p < 0.05$) and amygdala ($p < 0.001$) showed significant asymmetry favoring the right hemisphere, while the thalamus showed left-favoring asymmetry ($p < 0.01$), but none of the structures of the striatum showed significant volume asymmetry (figure 1). None of these structures showed significant heritability estimates (figure 2).

Conclusion. We found a similar pattern of subcortical volume asymmetry to that reported in the ENIGMA study, with the exception that we didn't detect significant asymmetries in the

striatum. Although subcortical structures, such as the amygdala, hippocampus, and thalamus, show volume asymmetry, genetic factors seem to have a weak influence on the variability of this morphological trait.

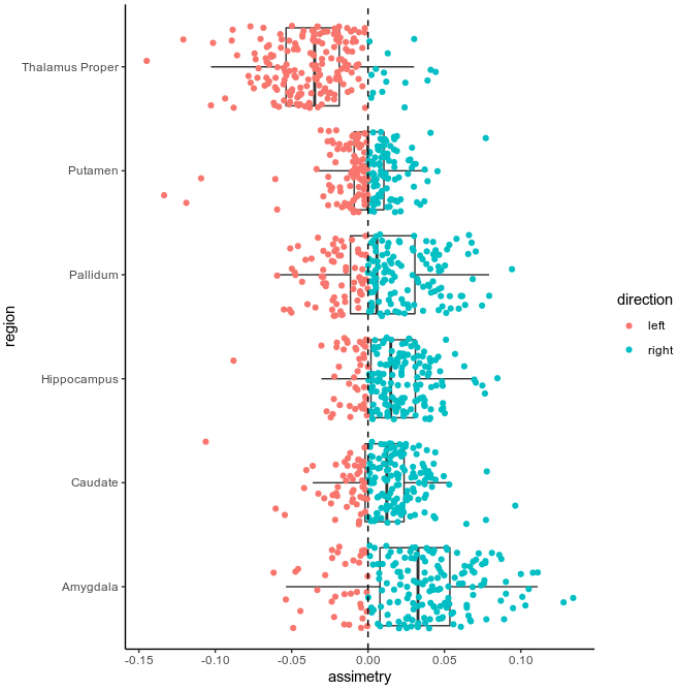

Figure 1. Distribution of volume asymmetry for each subcortical region.

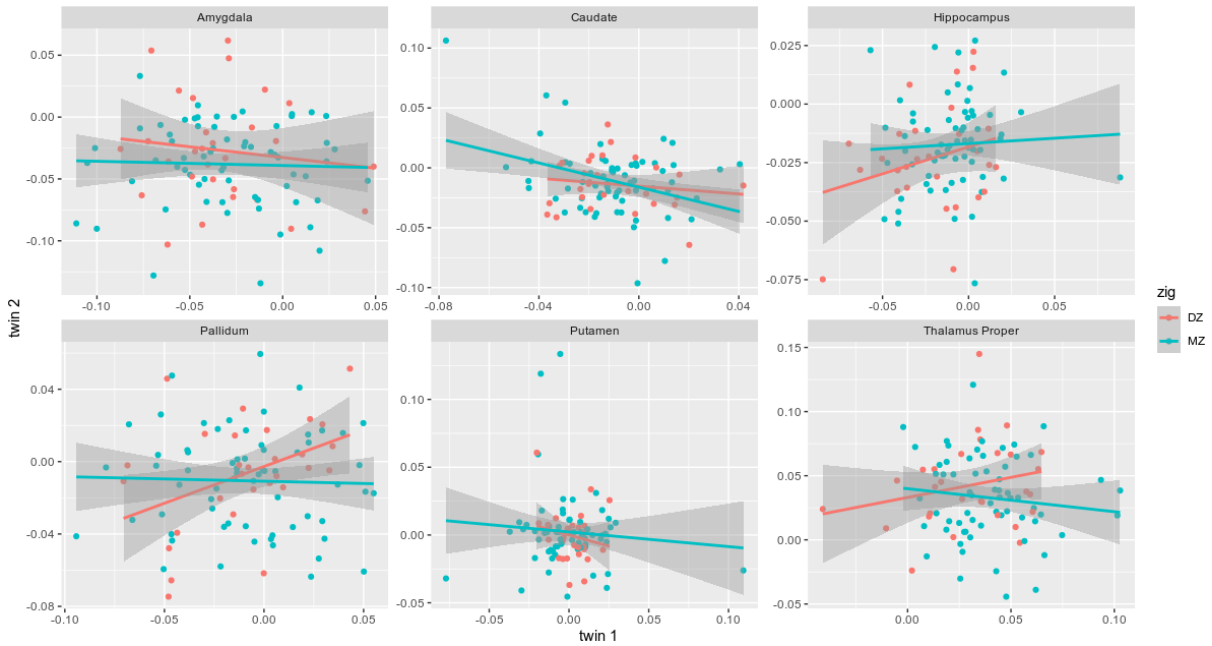

Figure 2. Subcortical volume correlations in sets of MZ and DZ twins.

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