

# **Influence of processing pipeline on cortical thickness measurement and its heritability estimates**

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## **Introduction**

Cortical thickness (CT) is one aspect of the brain structure that is studied in the context of development, aging and inter-individual variability of behaviour. Also, local variations of CT has frequently been used as an intermediate phenotype in imaging genetics studies. While no gold standard assessment of CT exists, a wealth of analysis tools has been created to estimate CT from the in-vivo T1w MRIs with three of these (FreeSurfer (FS), CAT and CIVET) enjoying high popularity.

The current study compares global (gb-) and regional CT estimation from three different pipelines and assesses whether variation of tools also affect estimation of CT heritability.

## **Methods**

A sample composed of 977 related-adults (age:  $28.8 \pm 3.7$ ) was provided through the Human Connectome Project (HCP; <http://www.hcp.org>), WU-Minn Consortium [Van Essen, 2012]. CT-estimation were performed using two surface-based pipelines (FS v5.3 and CIVET v2.1.0) and a volume-based one (CAT v12.5). FS-preprocessed surfaces (modified FS-pipeline for high resolution data and using T2w-images to improve surface estimations) were downloaded from the HCP website, while we assessed CT in CIVET and CAT using standard pipelines (on distortion and bias-field corrected T1w-images, identical to T1w-input of the FS-routine but

without T2w-images) and resampled the CT-estimations to faverage (Lewis, 2019; Yotter, 2011).

Comparisons are performed on mean gb- as well as regional mean CT-estimations on 400 functionally defined parcels [Schaefer, 2017]. Univariate analysis of heritability ( $h^2$ ) was performed using Solar Eclipse 8.4.0 (<http://solar-eclipse-genetics.org>).

## **Results**

While CT-estimations from FS-pipeline were generally lower than the other pipelines (FS:  $2.6 \pm .08$  mm, CIVET  $2.7 \pm .07$  mm, CAT  $2.8 \pm .09$  mm), the global and regional CT correlated highly between three routines (Fig1).

Gb-CT from all three pipelines showed high  $h^2$  (FS: .86, CIVET: .78 and CAT: .88), when controlling for linear and quadratic effect of age, sex and their interaction. Nevertheless, examination of parcel-wise CT estimates revealed that, despite comparably higher  $h^2$  of CT within the sensorimotor, superior temporal, entorhinal cortex and dorsal medial frontal cortex in all three methods, differences as large as 20% between estimated regional  $h^2$  were evidenced in the precentral gyrus, subgenual-cingulate cortex, medial and lateral frontal and parietal lobes (see Fig2 A-C).

## **Conclusion**

Examining the replicability of gb- and regional CT across three CT-estimation pipelines confirmed thinner FS-CT-estimates and thicker CAT's CT-estimates, as previously reported [Seiger et al., 2018; Walhovd et al., 2017]. In interpreting our results three issues should be taken into account: 1) Our FS-based CT-estimations are assessed using modified FS-pipeline that uses the high resolution T1w-MRI and additionally use T2w-MRI to refine surface estimation. For the other two routines we used standard pipelines without T2w. Yet, it is possible to improve surface estimations by incorporating T2w-MRI as well as automatic blood-vessels masking in CIVET to improve gray and white surface estimations. 2) While FS and

CAT CTs are resampled only once from subject-space to fsaverage space, CT-estimations in CIVET are resampled twice, namely from subject space to ICBM surface and then resampled to fsaverage space to extract the mean regional CT.

3) FS-surfaces are extensively visually quality controlled, yet CAT and CIVET QC consisted of only excluding subjects with gross failed surface estimations. Despite these differences, our results suggest acceptable similarity of CT estimation using these three pipelines [Dickie, 2017], with few regions showing poor correspondence between pipelines. Also, we show that while all the three pipelines depicted qualitatively comparable spatial distribution of  $h^2$ , one could not directly compare  $h^2$  values of CT-estimations from different softwares.

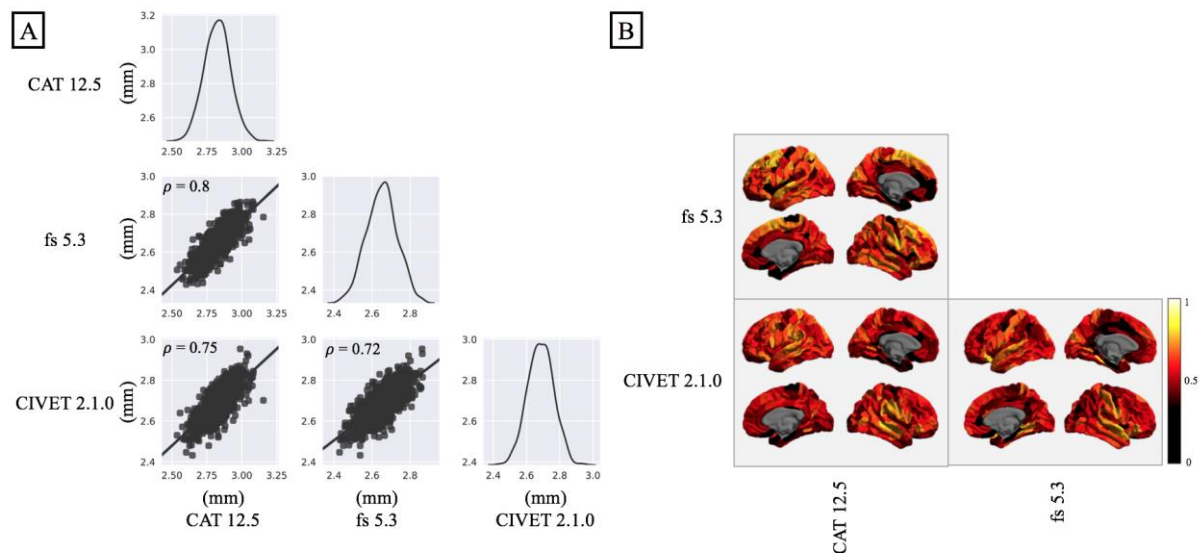


Fig 1. global cortical thickness: histograms and scatter plots (with Spearman rank correlation coefficient) of global thickness estimations between pairs of pipelines (A). Spatial maps of bivariate Spearman correlation coefficient of regional mean cortical thickness within every of the 400 parcels, between each two pairs of thickness estimation pipelines (B).

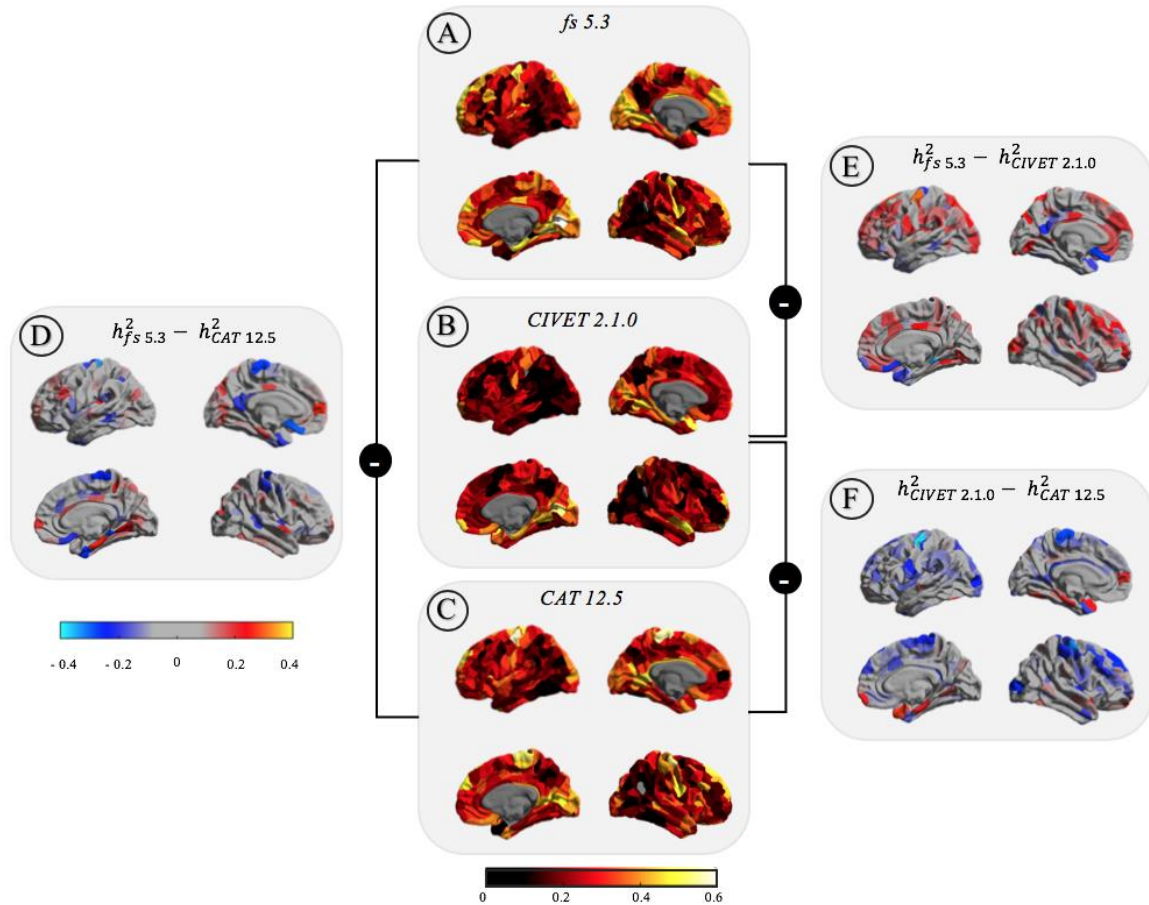


Fig 2. Regional estimates of heritability of cortical thickness (from three algorithms), controlled for age, sex, age<sup>2</sup>, interaction of age and sex, as well as global cortical thickness (A-C); Difference between regional heritability estimates from different algorithms (D-F);

### References:

- Dickie et al., (2017): Tools Matter: Comparison of Two Surface Analysis Tools Applied to the ABIDE Dataset. Res Ideas Outcomes 3:e13726.
- Lewis, L.B. (2019) An extended MSM surface registration pipeline to bridge atlases across the MNI and the FS/HCP worlds. OHBM 2019 (submitted), Rome.
- Schaefer et al., (2017): Local-Global Parcellation of the Human Cerebral Cortex from Intrinsic Functional Connectivity MRI. Cereb Cortex.
- Seiger et al., (2018): Cortical Thickness Estimations of FreeSurfer and the CAT12 Toolbox in Patients with Alzheimer's Disease and Healthy Controls. Journal of Neuroimaging.
- Van Essen et al., (2013): The WU-Minn Human Connectome Project: An overview. Neuroimage.
- Walhovd et al., (2017): Through Thick and Thin: a Need to Reconcile Contradictory Results on Trajectories in Human Cortical Development. Cereb Cortex.

Yotter et al. (2011): Algorithms to Improve the Reparameterization of Spherical Mappings of Brain Surface Meshes. J Neuroimaging.

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