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Native-Space Cortical Thickness Measurement And The Absence of Correlation to Cerebral Volume

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Objective: To assess the necessity of spatial normalization of cortical thickness when inter-subject vertex correspondence is assured, and evaluate the likelihood of reducing signal-to-noise ratio by measuring cortical thickness in Talairach space.
Methods: Structural MRI scans of 150 subjects from the ICBM database (mean age: 25.9 yr (SD 5.96); 84 men, 66 women) were entered into the CIVET pipeline: Native images were linearly registered to standardized MNI-Talairach space[1]; corrected for intensity non-uniformity artifacts[2]; tissue-classified into white matter (WM), gray matter (GM), cerebrospinal fluid (CSF) and background using an advanced neural net classifier (INSECT)[3]; and fitted with a deformable mesh model to extract inner and outer cortical surfaces using the CLASP algorithm[4]. Both cortical surfaces then underwent inter-subject non-linear surface registration to establish correspondence of vertices across subjects[5]. A reverse transformation of volume is then applied on the data to allow thickness measurement in native-space, and thickness at each vertex is calculated using the *link* metric[6].. Each subject's cortical thickness map was blurred using a 20-millimeter full-width half-maximum (FWHM) surface-based diffusion smoothing kernel[7]. Native-space cortical thickness was linearly regressed against subject's total cerebral volume at each vertex after accounting for the effects of gender and age.
Results & Discussion: No main effects for cerebral volume (p=0.12), age (p=0.65), or gender (p=0.88) were detected. Plotting native-space cortical thickness against cerebral volume in a vertex-based fashion also failed to demonstrate any consistent correlations. When this method of producing native-space cortical thickness was used in vertex-based analysis of group differences in other data-sets and compared with Talairach-space cortical thickness maps, group differences tended to be minimized in Talairach-space thickness maps. In addition, native-space thickness maps were superior in demonstrating age-related developmental changes in pediatric samples. These comparisons suggested that spatial normalization introduced substantial noise and confounded the analysis of the impact biological variables of interest on cortical thickness. The complex and highly variable structure of the cerebral cortex probably predisposes linear transformation protocols to introducing substantial distortions because of the non-uniformity of the registration parameters. In addition, the biological dissociation between the development of the cerebral cortex and the cerebral volume, the former becoming thinner with age while the latter increases before it plateaus then declines, suggests that volumetric normalization could be especially problematic in developmental data-sets.
Conclusions: It is unnecessary to measure cortical thickness in Talairach space due to the lack of correlation with cerebral volume. It may also introduce additional confounders and noise that reduces the likelihood of detecting meaningful or statistically significant results.
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