**Estimation of Cortical Thickness**

Cortical thickness was estimated in two ways, with each method undertaking dissimilar approaches to image processing of T1-weighted MRI.

Advanced Normalisation Tools (ANTS) used an automated volume based cortical thickness estimation workflow according to the following steps: 1) initial N4 bias correction on input anatomical MRI; 2) brain extraction using a hybrid segmentation/template-based strategy; 3) alternating between prior-based segmentation and white matter posterior probability weighted bias correction; 4) DiReCT-based cortical thickness estimation; and 5) normalization to a group specific template

(Avants, Tustison and Johnson, n.d.; Tustison, Avants and Cook, 2013; Das, Avants, Grossman and Gee, 2009).

Cortical reconstruction and thickness estimation was performed with the FreeSurfer image analysis suite (http://surfer.nmr.mgh.harvard.edu/). Briefly, processing included: 1) motion correction and averaging of multiple volumetric T1 weighted images (when more than one was available) (Reuter, Rosas and Fischl, 2010); 2) removal of non-brain tissue using a hybrid watershed/surface deformation procedure (Ségonne et al., 2004); 3) automated Talairach transformation, segmentation of the subcortical white matter and deep gray matter volumetric structures (including hippocampus, amygdala, caudate, putamen, ventricles) (Fischl et al., 2002; 2004); 4) intensity normalization (Sled, Zijdenbos and Evans, 1998); 5) tessellation of the gray matter white matter boundary, automated topology correction (Fischl, Liu and Dale, 2001; Ségonne, Pacheco and Fischl, 2007); and 5) surface deformation following intensity gradients to optimally place the gray/white and gray/cerebrospinal fluid borders at the location where the greatest shift in intensity defines the transition to the other tissue class (Dale, Fischl and Sereno, 1999; Dale and Sereno, 1993; Fischl and Dale, 2000).

**Voxel Based Morphometry**

Estimates of grey and white matter volumes at each intracerebral location were from T1-weighted MRI with FSL-VBM (<http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSLVBM> (Douaud et al., 2007) an optimized VBM protocol (Good et al., 2001) carried out with FSL tools (Smith et al., 2004). First, structural images were brain-extracted and grey matter-segmented before being registered to the MNI 152 standard space using non-linear registration

(Andersson, Jenkinson and Smith, n.d.). The resulting images were averaged and flipped along the x-axis to create a left-right symmetric, study-specific grey matter template. Second, all native grey matter images were non-linearly registered to this study-specific template and "modulated" to correct for local expansion (or contraction) due to the non-linear component of the spatial transformation. The modulated grey matter images were then smoothed with an isotropic Gaussian kernel with a sigma of 2 mm.

**Tract Based Spatial Statistics (TBSS)**

Pre-statistical processing of diffusion images included eddy current correction, motion correction, and averaging of the three sets of 63 diffusion directions using software from FMRIB’s Diffusion Toolbox, FDT (Smith et al., 2004). A brain mask produced using the Brain Extraction Tool (Smith, 2002) (BET) along with the diffusion data, was used by DTIFit(Smith et al., 2004) to calculate the 3x3 diffusion tensor for each brain voxel, and subsequently compute fractional anisotropy (FA) and mean diffusivity (MD) from the tensor’s three eigenvalues.

Voxelwise statistical analysis of the FA and MD data was carried out using TBSS (Smith et al., 2006), part of FSL (Smith et al., 2004). All participant’s FA images were aligned into the standard anatomical space of the Montreal Neurological Institute (MNI) using the non-linear registration tool FNIRT

(Andersson, Jenkinson and Smith, n.d.; n.d.), which used a b-spline representation of the registration warp field (Rueckert et al., 1999). This same transform was subsequently applied to the MD images. Next, the mean FA image was created and thinned to create a mean FA skeleton that represented the centres of all tracts common to the group. The mean WM skeleton was then thresholded to include only those voxels with FA > 0.3, which excludes regions of high between-subject variability. Each participant’s aligned FA image was then projected onto this skeleton, with an identical procedure for the MD images.

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