## ON-LINE APPENDIX

### *Automated Processing Steps within BrainSuite*

For each scan included in this study, the T1-weighed MPRAGE images were converted into NIfTI-1 format and underwent a series of automated processing steps within BrainSuite:

1) The skull is stripped by using the Brain Surface Extractor tool,[1] which uses a combination of anisotropic diffusion filtering, edge detection, and mathematic morphology to extract the brain from the surrounding skull and scalp tissues.

2) Spatial variations in signal gain are corrected by using the Bias Field Corrector tool.[1]

3) Tissue classification is performed by using the Partial Volume Classifier,[1] which assigns an integer label to each voxel in the image. The label represents the types of tissue present in the voxel and is modeled to include CSF, WM, GM, and pair-wise combinations of these. The Partial Volume Classifier also estimates a fractional content for each voxel, indicating what proportion of each type of tissue is present.

4) A labeled reference atlas[2] is aligned by using volumetric registration[3] to map a set of labeled regions (cerebrum, cerebellum, brain stem, subcortical regions, left/right hemispheres) to the subject brain. These labels are then used (together with the Partial Volume Classifier tissue classification result) to automatically produce a binary mask identifying the cerebral white matter.

5) The initial cerebral white matter mask is then processed by using a series of filters to enhance the boundary of the object and ensure that a topologically spheric surface can be produced from the mask. These steps consist of filling small pits in the boundary of the binary mask, applying the Topological Correction Algorithm[4] to remove topologic holes and handles in the binary object and removing small strands of voxels that remain attached to the cerebral white matter mask.

6) An inner cortical surface model is generated from the cerebral white matter mask by using the Marching Cubes Algorithm.[5] A pial surface model is produced by expanding the inner cortical surface outward through the brain volume until it reaches the GM/CSF boundary. The surface models are split into left and right hemispheres on the basis of the volumetric labeling produced in step 4.

7) Automated Spatial Alignment and Labeling is performed by the SVReg tool. It uses anatomic information from both the surface models and volume of the brain images for accurate automated coregistration between the subject and an atlas. This mapping allows consistent surface and volume labeling.[6,7] The atlas is a stereotaxic average of 27 scans of an individual. The inner, middle, and pial cortical surfaces were carefully extracted for the atlas brain scan. The surfaces and volumes of the atlas were hand-labeled by an expert neuroanatomist. The final parcellation by SVReg computes volumes of 140 brain regions (70 for each hemisphere). WM, GM, and CSF volumes are reported separately by SVReg for each of these regions. For each patient, this process takes approximately 2 hours on a regular PC.

## REFERENCES


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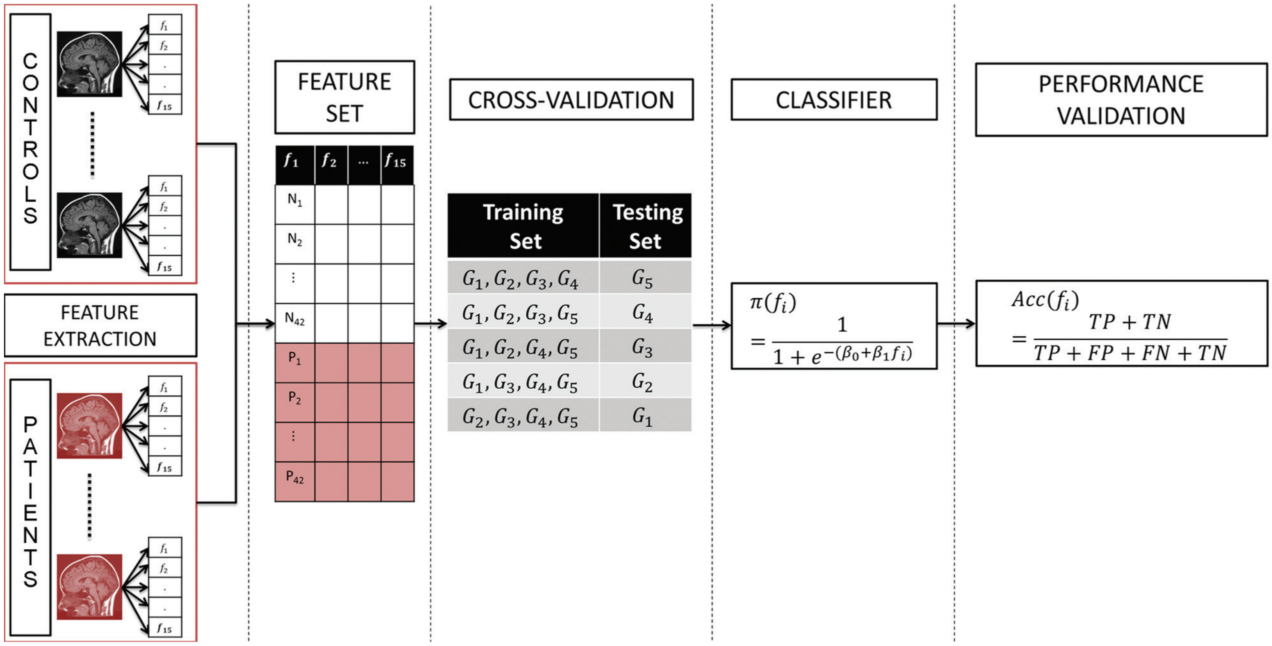


**ON-LINE FIG 1.** Statistical workflow. Volumetric ratio measures (15 in total) from 42 controls and 42 patient scans were used to train a logistic regression classifier. The performance of the classifier was assessed via 5-fold cross-validation. The mean values of accuracy across the 5 trials were used to quantify the performance of the classifier.