Multivariate Searchlight Classification of Structural Magnetic Resonance Imaging in Children and Adolescents with Autism

Supplemental Information

Methods

Voxel-Based Morphometry (VBM) Analysis

Structural images were first resliced with tri-linear interpolation to isotropic 1 x 1 x 1 voxels and manually aligned to conventional AC-PC space using the anterior commissure and posterior commissure as landmarks. Images were spatially normalized to the Montreal Neurological Institute (MNI) common stereotactic space, then segmented into gray matter (GM), white matter (WM), and cerebrospinal fluid using a modified mixture model cluster analysis technique with the following parameters: bias regularization = 0.0001, bias full width at half maximum cutoff = 70 mm, sampling distance = 3, hidden Markov random field weighting = 0.3. As recommended by Gaser for children or elderly populations (http://dbm.neuro.uni-jena.de/vbm/vbm5-for-spm5/use-of-tissue-priors-experimental), we used no tissue priors for segmentation. Voxel values were modulated by the Jacobian determinants derived from the spatial normalization such that areas that were expanded during warping were proportionally reduced in intensity. We used modulation for nonlinear effects only. When using modulated images for performing subsequent group comparisons, the inference is made on measures of volume rather than tissue concentration (density). The use of modulation for nonlinear but not affine effects ensures that further statistical comparisons are made on relative (controlling for overall brain size) rather than absolute measures of volume. The segmented modulated images for WM and GM were smoothed with an isotropic Gaussian kernel (10 mm full width at half maximum). The size of the kernel for smoothing was chosen as recommended by Gaser for modulated images, since modulation introduces additional smoothing.

Multivariate Pattern Analysis (MPA)

The MPA technique provides greater sensitivity than the univariate VBM approach as it evaluates spatial patterns in multiple voxels at a time. This can best be illustrated by the following example. If, as in the diagram below, there is a population of subjects (x = autism spectrum disorders, o = typically developing) with voxel values (v_1 and v_2, for example), then

evaluation of one voxel at a time (that is v_1 and v_2 separately, as with univariate VBM) would not differentiate the two groups because there is a substantial amount of overlap between the two groups on each dimension (as shown by the dashed red and blue lines). Thus a univariate analysis that incorporates data from one voxel at a time (e.g. either v_1 alone v_2) would not be able to detect group differences in such a scenario. However, if v_1 and v_2 are considered together, a plane separating the two groups can be constructed, thereby identifying a neighborhood where the two groups differ in spatial patterns of the anatomical measures of interest. In the more general case (e.g. a 3 x 3 x 3 neighborhood around each voxel, as used in our study), a separation may potentially be more readily achieved via support vector machine. A multivariate analysis that takes into account spatial patterns in the data would detect differences here, while the univariate would fail. Thus the improved sensitivity is due to the consideration of spatial patterns of group differences, above and beyond those detectable at the individual voxel level.

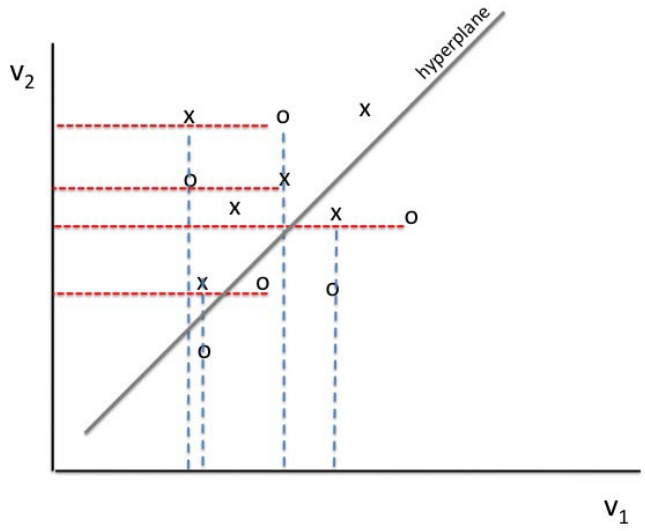

Figure S1. Heightened sensitivity of multivariate analyses to group differences.

Results

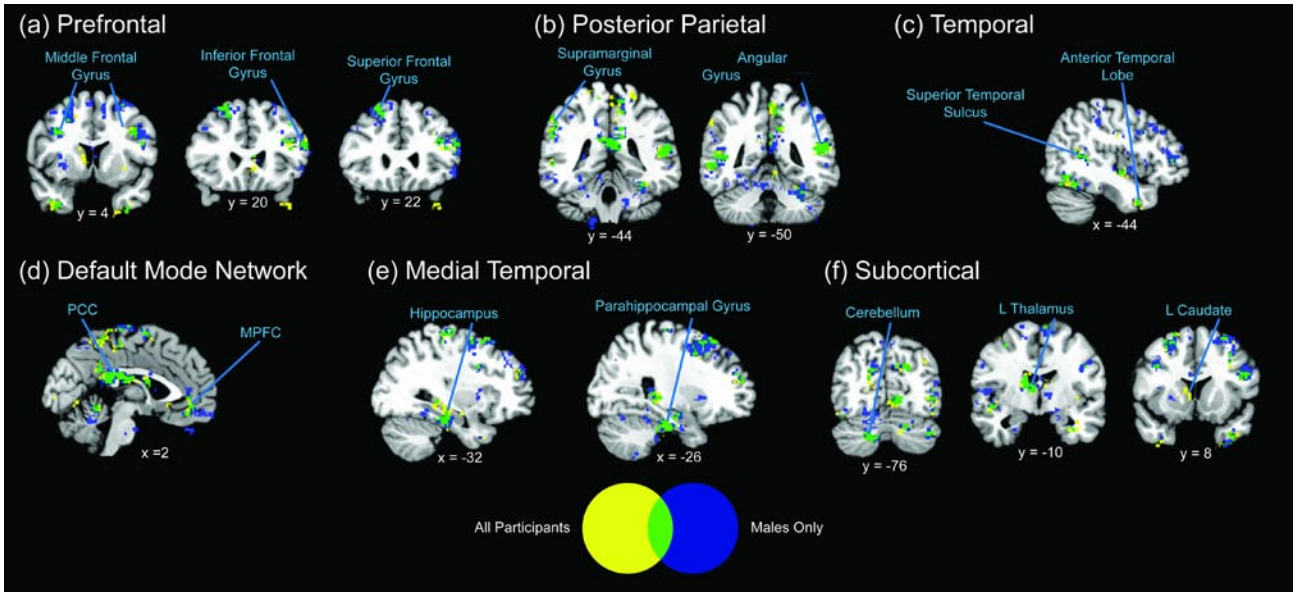

Figure S2. Results from searchlight classification of gray matter showing effects of excluding female participants. L, left; MPFC, medial prefrontal cortex; PCC, posterior cingulate cortex.