Convergent Microstructural Brain Changes Across Genetic Models of Autism Spectrum Disorder – A Pilot Study

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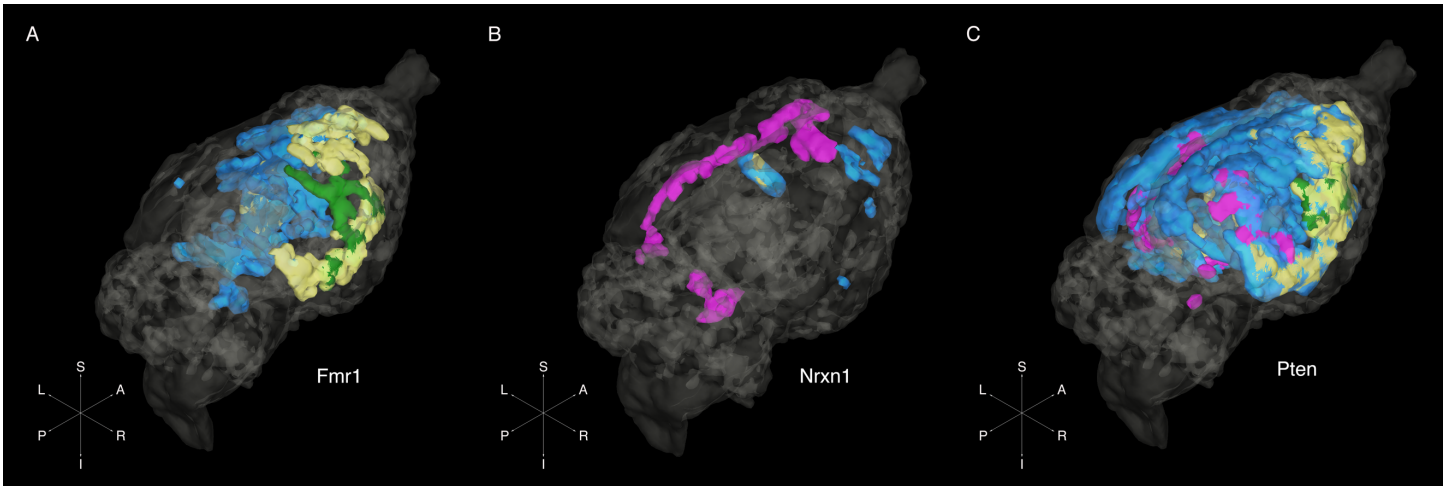
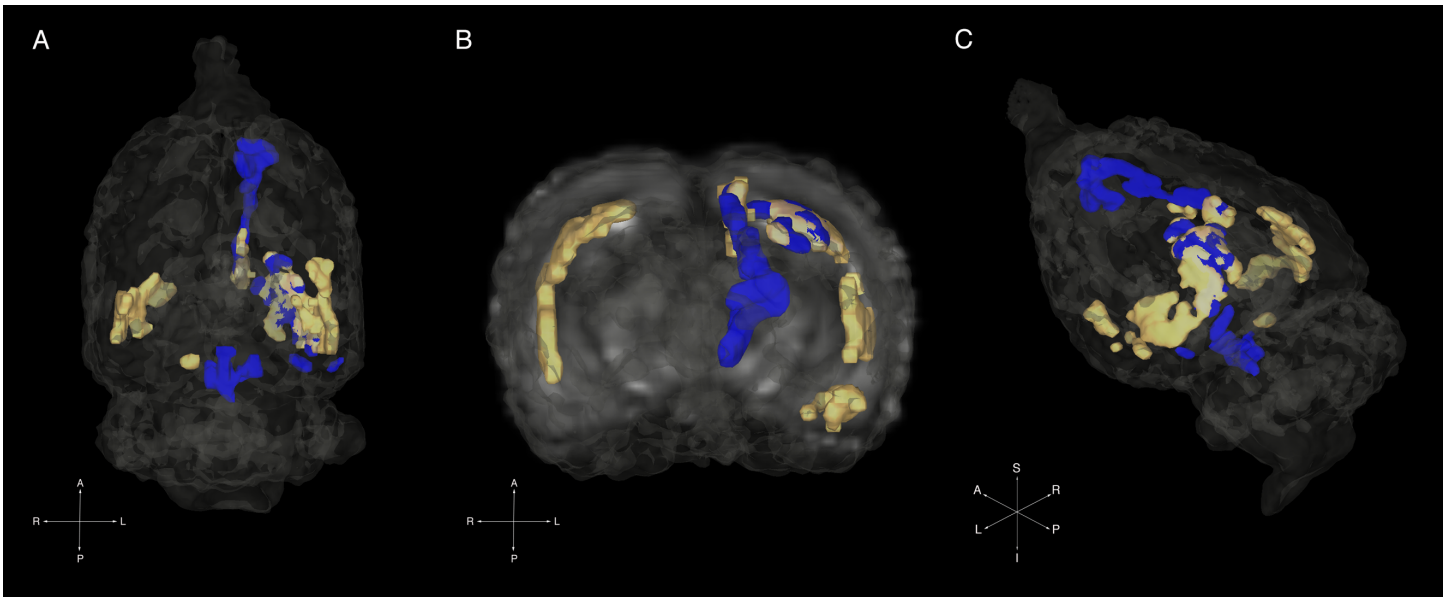
Supplemental Data



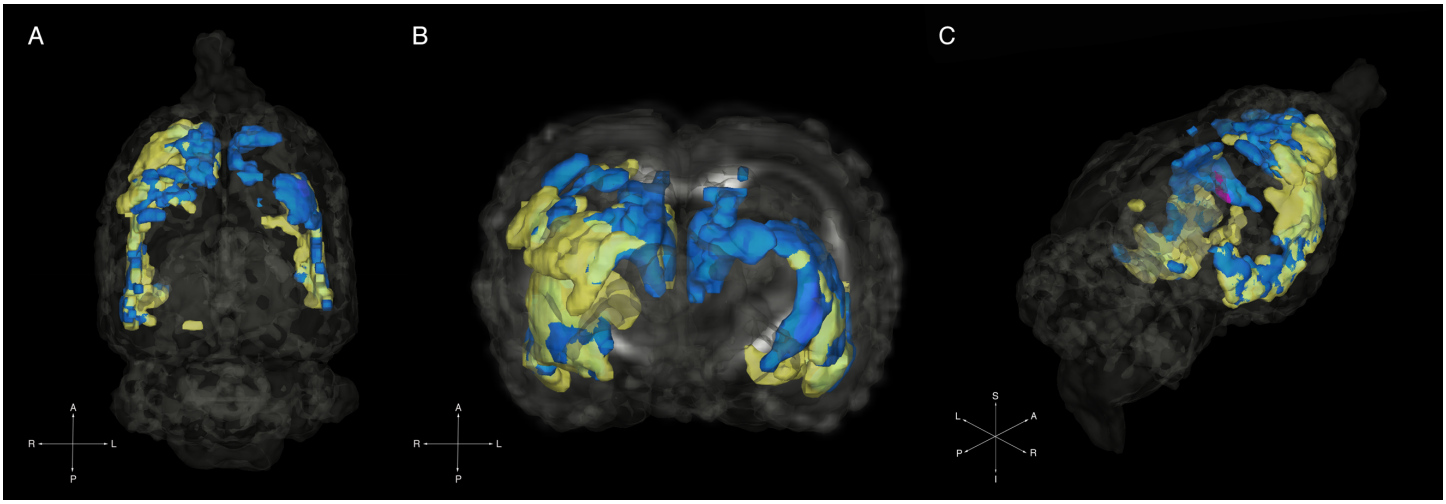
Supplemental Figure 1. Tract-based Spatial Statistics: 3-D rendering of significant DTI changes in genetic models of ASD

Ex-vivo diffusion tensor imaging (DTI) was performed on post natal day 45 (P45) male rat *Fmr1*, *Nrxn1*, and *Pten* genetic models of autism spectrum disorder (ASD) (*n*=4 for each genetic model) to measure gene-dependent changes in the diffusion tensor when referenced to control animals. Following tract-based spatial statistics (TBSS) analysis, areas of differing change in fractional anisotropy (FA) and mean (MD), axial (AD), and radial diffusivity (RD) for *Fmr1* (**A**), *Nrxn1* (**B**), and *Pten* (**C**) (as compared to control animals) were identified and are displayed over oblique fractional anisotropy maps. Magenta=FA; yellow=MD; green=AD; blue=RD. N.B.: Areas rendered were identified after thresholding statistical output images to exclusively capture areas of statistical significance (FWE-corrected $p<0.05$).



Supplemental Figure 2. TBSS: 3D rendering of areas of FA significance

Whole-brain voxel-wise TBSS reveals regions of statistically significant FA change (FWE-corrected $p<0.05$) for Pten (yellow) and Nrxn1 (blue) genetic models of ASD in the axial (A), coronal (B) and oblique sagittal (C) planes. Changes in fractional anisotropy in our *Fmr1* model were not statistically different from control animal FA values. In both the *Pten* and *Nrxn1* models of ASD, we observed overlapping changes in FA concentrated in the left external capsule. However, *Nrxn1* demonstrates additional unique areas of FA increase anteriorly in the left neocortex and posteriorly in the brain stem. Similarly, *Pten* shows distinct areas of FA increase in the left and right external capsule. The overlay of significant FA changes encountered in both *Pten* and *Nrxn1* uncover both similar areas of structural change but also areas unique to each genetic variant thus suggesting potential opportunities to validate gene-specific neuroimaging biomarkers.



Supplemental Figure 3. TBSS: 3D rendering of areas of TR significance

Whole-brain voxel-wise TBSS analysis reveals regions of statistically significant (FWE-corrected $p<0.05$) TR decreases in the *Pten* (yellow), *Nrxn1* (blue), and *Fmr1* (magenta). The spatial distribution of these effects is presented in the axial (A), coronal (B) and oblique sagittal (C) planes over volumetric FA maps (as a spatial reference). Consistent with the spatial distribution of increased FA in TBSS results for the *Pten* model, there are confluent areas of decreased TR in the *Pten* model with most changes concentrated in the right forebrain and neocortex (**A**). The spatial distribution of decreased TR in the *Nrxn1* model is encompasses most areas of decreased TR in the *Pten* model (**B**); however, the distribution of decreases in TR appear more symmetrical with most changes occurring in the external capsule. While no significant differences in FA were observed in the TBSS results for *Fmr1* model, there are confluent areas of decreased TR in Fmr1 (**C**).