Supplementary Material: e-Methods

e-Methods: Whole-brain FBA in BOSD without aligning lesion side

In addition to the primary whole-brain fixel-based analyses in this study, in which we aligned lesion hemisphere across all patients, we also performed whole-brain FBA comparing BOSD patients to controls without aligning lesion side. For these analyses, unflipped FOD images from patients and controls were registered to the same symmetric population template. Whole-brain fixel-based analysis was performed at each white matter fixel to compare FD, FC, and FDC between BOSD patients and controls using a General Linear Model, with age, intracranial volume, and scanner included as nuisance covariates. As with the primary analyses, connectivity-based smoothing and statistical inference were performed with CFE, and family-wise error corrected *p*-values were assigned to each fixel using non-parametric permutation testing over 5000 permutations.

e-Methods: Whole-brain FBA in frontal and parietal BOSD

To explore any potential differences between those with frontal and parietal BOSD lesions, we additionally performed an exploratory secondary whole-brain fixel-based analysis. Here, we included patients with a frontal BOSD (n=12), patients with a parietal BOSD (n=6), and matched control participants (n=36). Those with left-sided lesions had their FOD images flipped left-to-right to align lesion hemisphere across all patients, and FOD images from the matched controls were also flipped left-to-right. Whole-brain fixel-based analysis was performed at each white matter fixel to compare FD, FC, and FDC between BOSD patients and controls using a General Linear Model, with age, intracranial volume, and scanner included as nuisance covariates. Given the significantly higher seizure frequency and disease duration in frontal BOSD patients when compared to parietal BOSD patients, we additionally included seizure frequency and disease duration as nuisance covariates, when comparing the frontal and parietal BOSD patient groups to one another. As with the primary analyses, connectivity-based smoothing and statistical inference were performed with CFE, and family-wise error corrected *p*-values were assigned to each fixel using non-parametric permutation testing over 5000 permutations.

Supplementary Material: e-Results

e-Results: Whole-brain FBA in BOSD without aligning lesion side

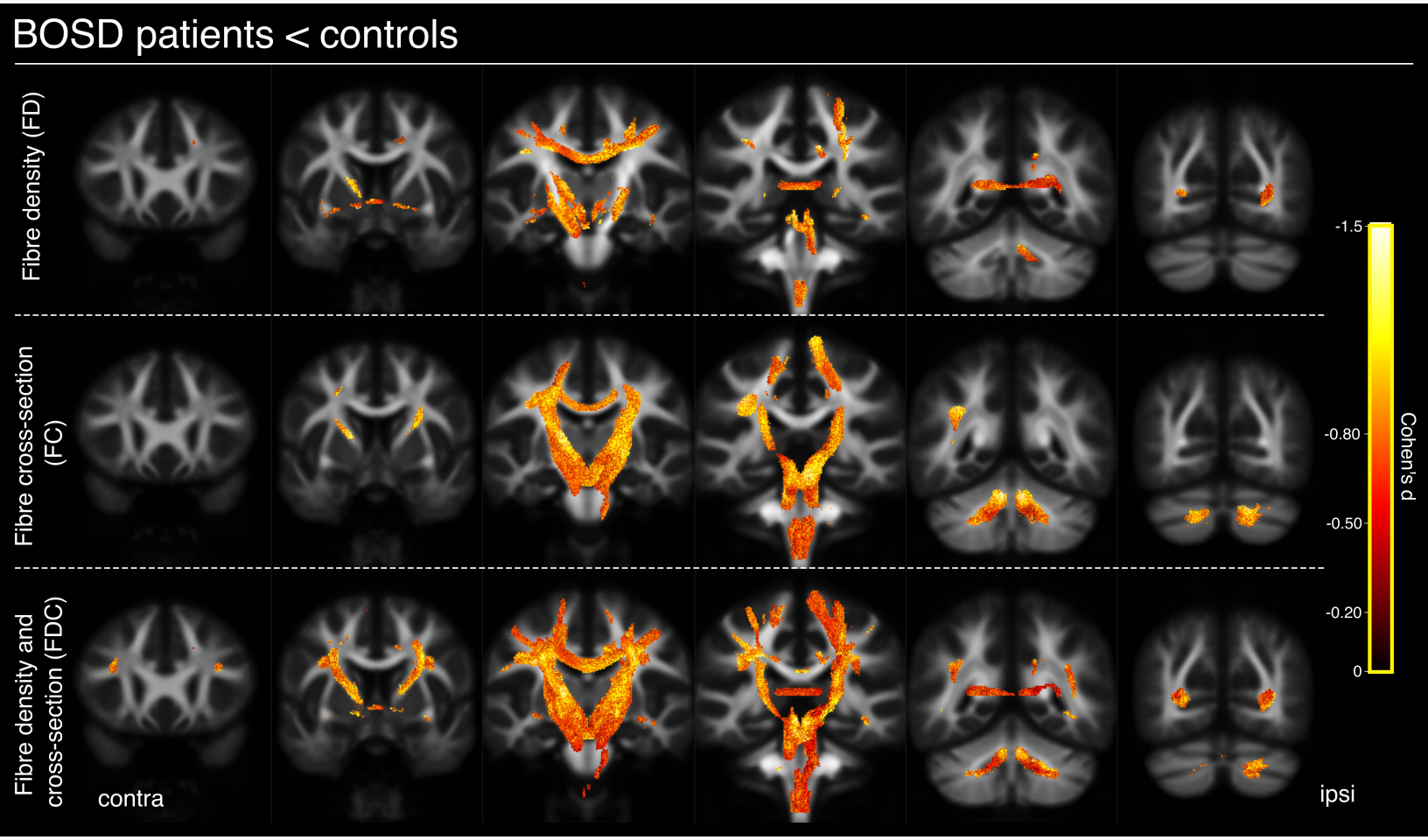
Whole-brain FBA revealed significant decreases (FWE-corrected p-value < 0.05) in BOSD patients when compared to controls for all three fixel-based metrics (Supplementary Figure e-2). These fixel-based differences were evident bilaterally, although fibre tract-specific differences tended to be greater in extent in the right than left hemisphere.

e-Results: Whole-brain FBA in frontal and parietal BOSD

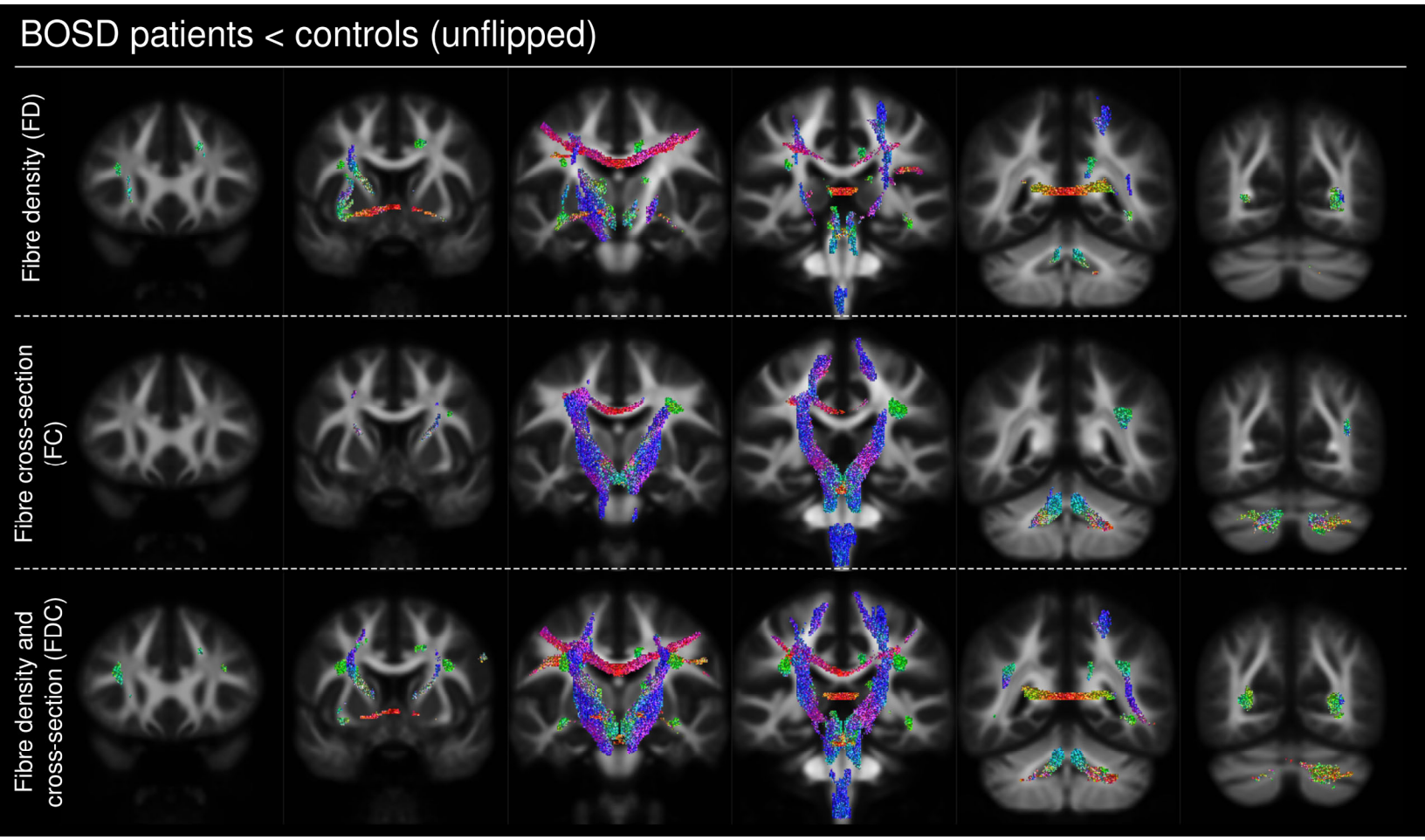
Whole-brain FBA revealed significant decreases (FWE-corrected p-value < 0.05) in frontal BOSD patients when compared to controls for all three fixel-based metrics (Supplementary Figure e-3). No significant differences were observed for any of the fixel-based metrics for the parietal BOSD group. Select fibre-tract regions exhibited significantly lower fibre cross-section (FC) in the frontal BOSD group when compared to the parietal BOSD group (data not shown).

We should caution against conclusive interpretation of these findings in frontal and parietal BOSD participants, given the small sample size of our cohort, and of these subgroups.

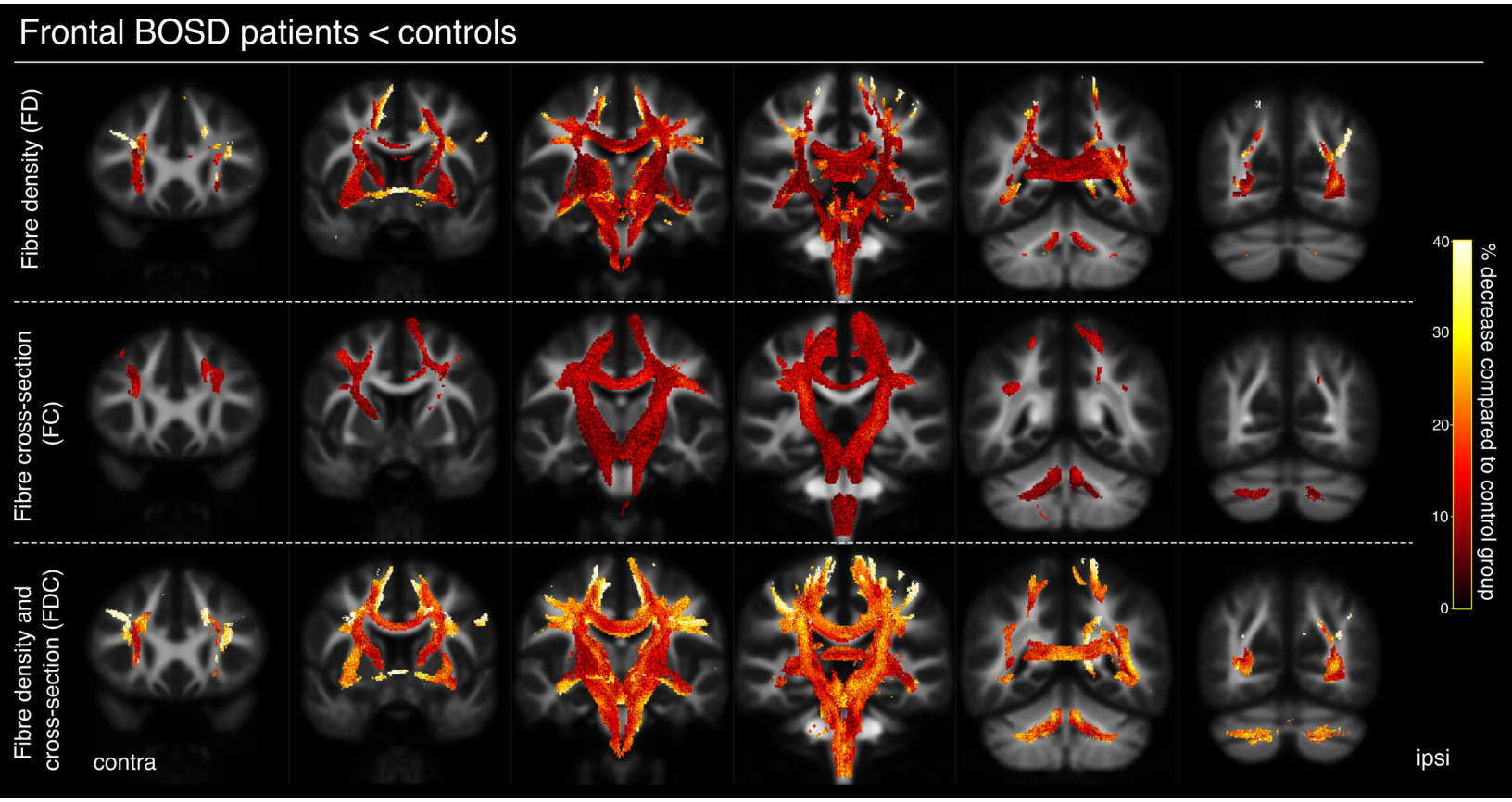
eFigure 1


BOSD patients < controls
Fibre density (FD)
Fibre cross-section (FC)
Fibre density and cross-section (FDC)
contra
ipsi
-1.5
-0.80
-0.50
-0.20
0
Cohen's d

eFigure 2


BOSD patients < controls (unflipped)
Fibre density (FD)
Fibre cross-section (FC)
Fibre density and cross-section (FDC)

eFigure 3


Frontal BOSD patients < controls
Fibre density (FD)
Fibre cross-section (FC)
Fibre density and cross-section (FDC)
contra
ipsi
40
30
20
10
0
% decrease compared to control group