

Online figures DS1-DS5

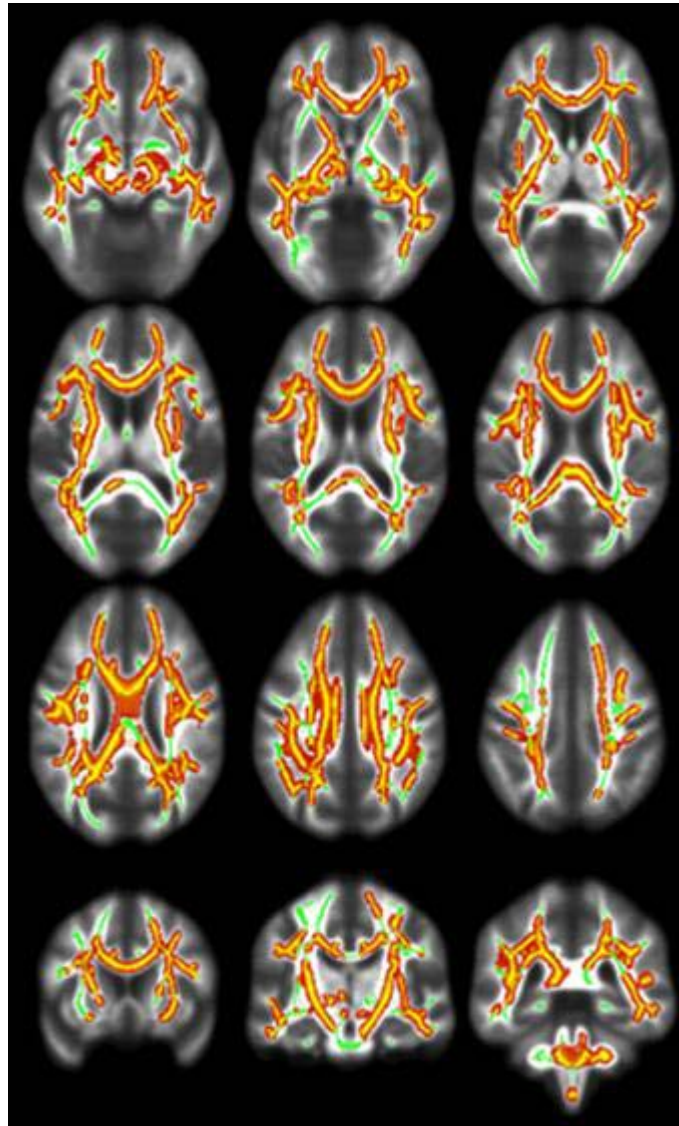


Fig. DS1 Fractional anisotropy (FA) reductions in patients with major depressive disorder compared with controls.

Patients had significantly reduced FA measures in widespread white matter regions compared with controls (family-wise error corrected $P < 0.05$). Regions of yellow (bounded by red to aid visualisation) indicate significant voxels overlaid on the mean FA template and FA skeleton (in green).

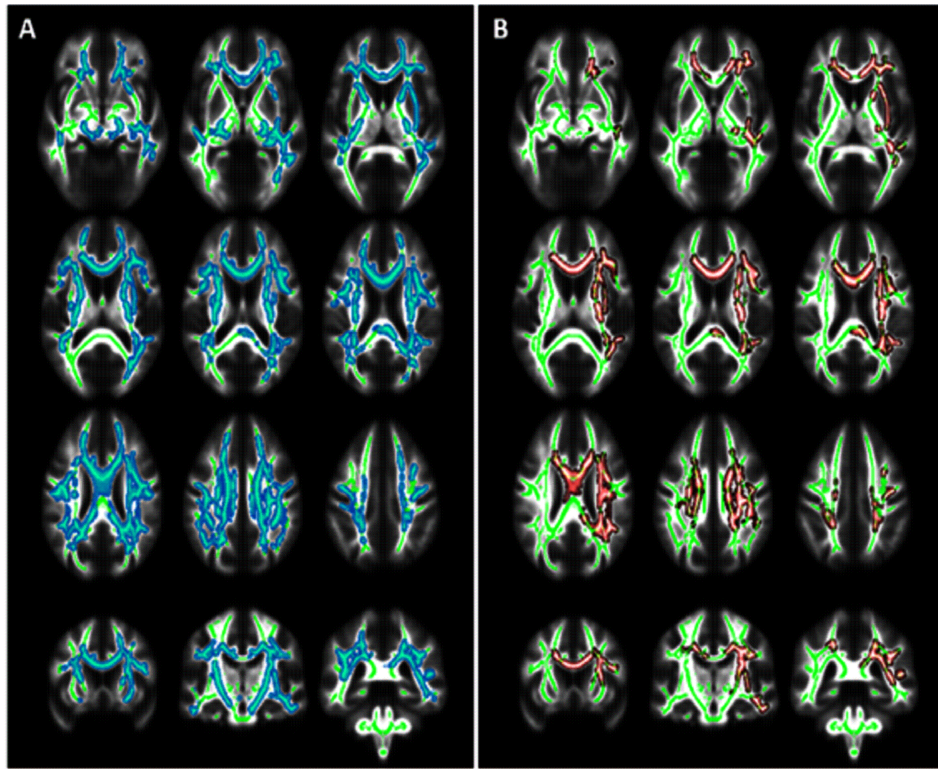


Fig. DS2 Radial and mean diffusivity increases in patients with major depressive disorder compared with controls.

(A) Regions (in blue) in which mean diffusivity was significantly increased in patients compared with controls (family-wise error (FWE) corrected $P < 0.05$). (B) Regions (in white bounded by red) in which radial diffusivity was significantly increased in patients compared with controls (FWE-corrected $P < 0.05$). This indicates that average voxelwise diffusivity was increased in patients, driven largely by increases in diffusivity perpendicular to the main axonal orientation, thought to reflect microstructural alterations in myelination.

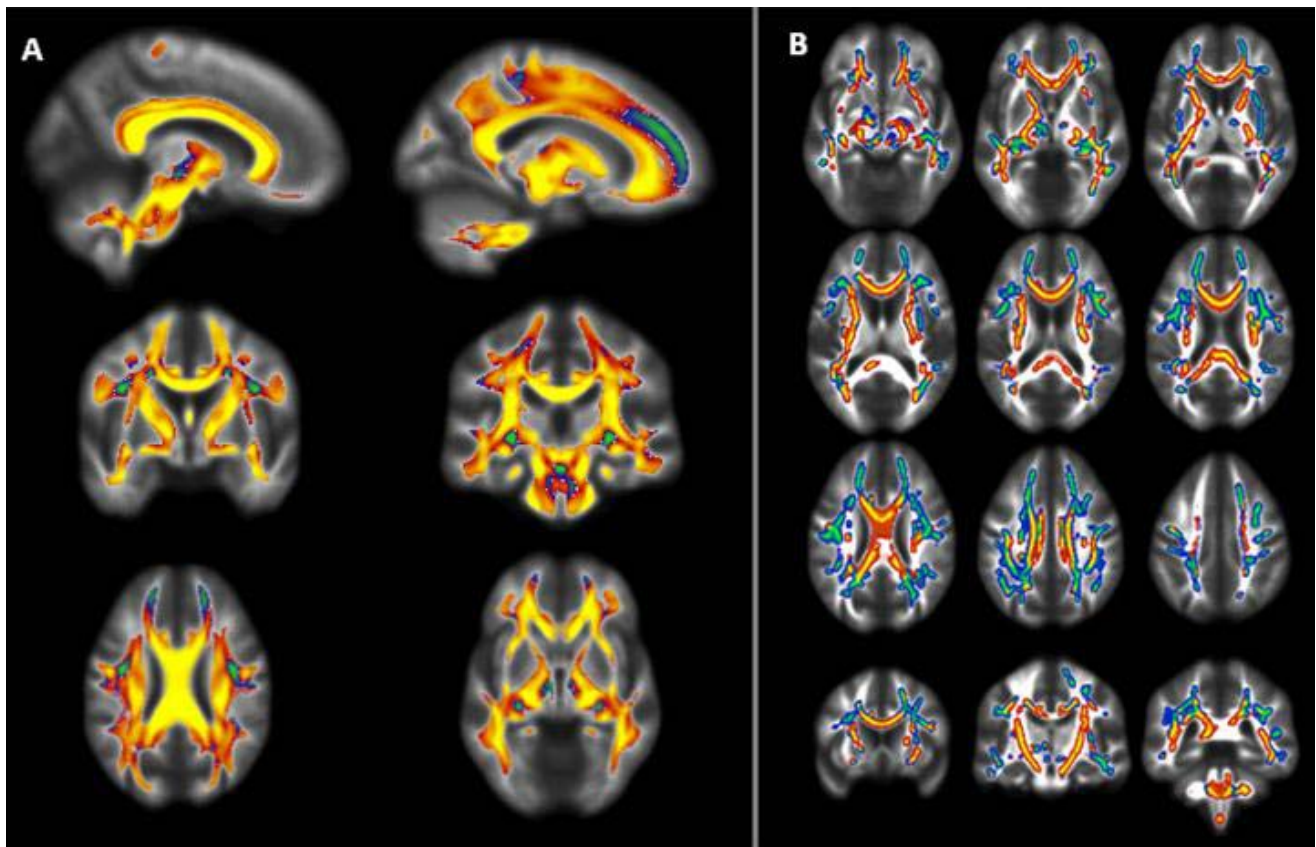


Fig. DS3 Deficits in white matter integrity in major depressive disorder.

(A) Mean fractional anisotropy (FA) template, overlaid with the mode of anisotropy (MO) mask. MO scale runs from -1 (highly planar anisotropy) to 1 (highly linear anisotropy). Colours blue-green indicate increasing negative (planar) MO. Colours red-yellow indicate increasing positive (linear) anisotropy. (B) Regions in which in patients with major depressive disorder had reduced FA compared with controls, after the application of the MO mask. Regions highlighted in yellow (bounded by red) denoting high MO (>0.5), which gives greater confidence that the FA reductions in these areas are due to pathological changes in white matter microstructure and not contaminated by increased crossing fibres. Regions in green (bounded by blue) indicate low or negative MO (<0.5), which may contain increased crossing fibres.

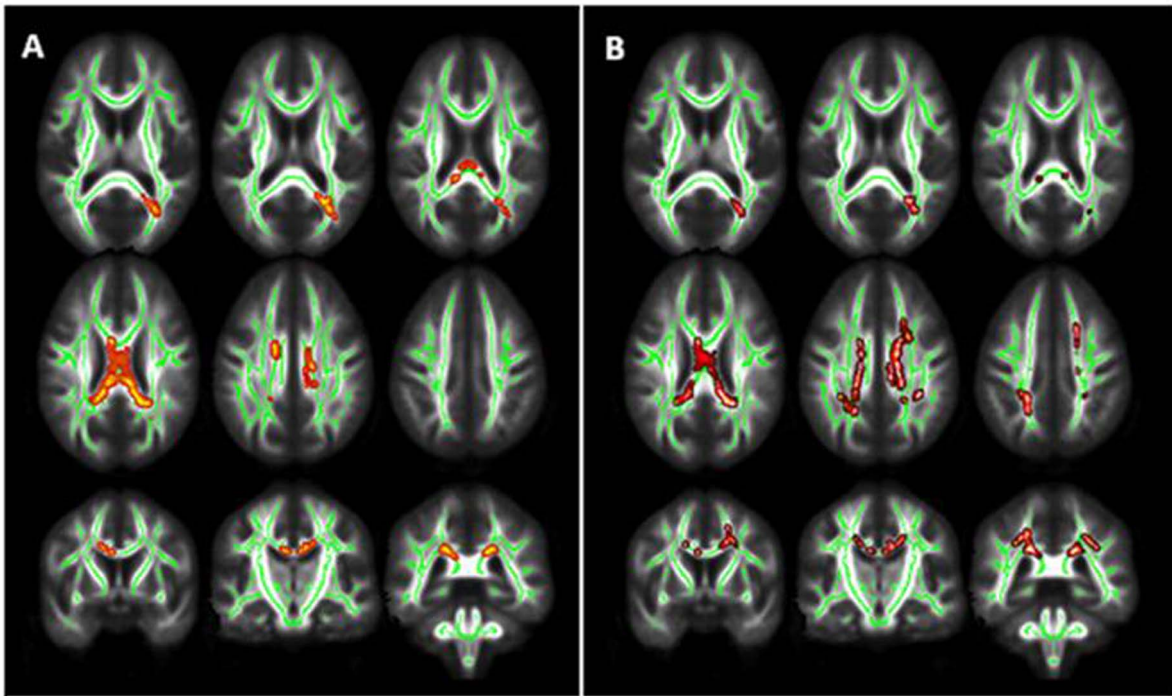


Fig. DS4 Association of white matter disruptions with severity of depression.

(A) Areas that show a significant negative correlation between fractional anisotropy and depression severity as measured by Beck Depression Inventory (BDI) score in patients with major depressive disorder (yellow bounded by red). (B) Corresponding positive correlation between radial diffusivity and BDI score (white bounded by red), indicating that myelin in the corpus callosum is increasingly disrupted in patients with greater illness severity. All maps family-wise error corrected $P < 0.05$.

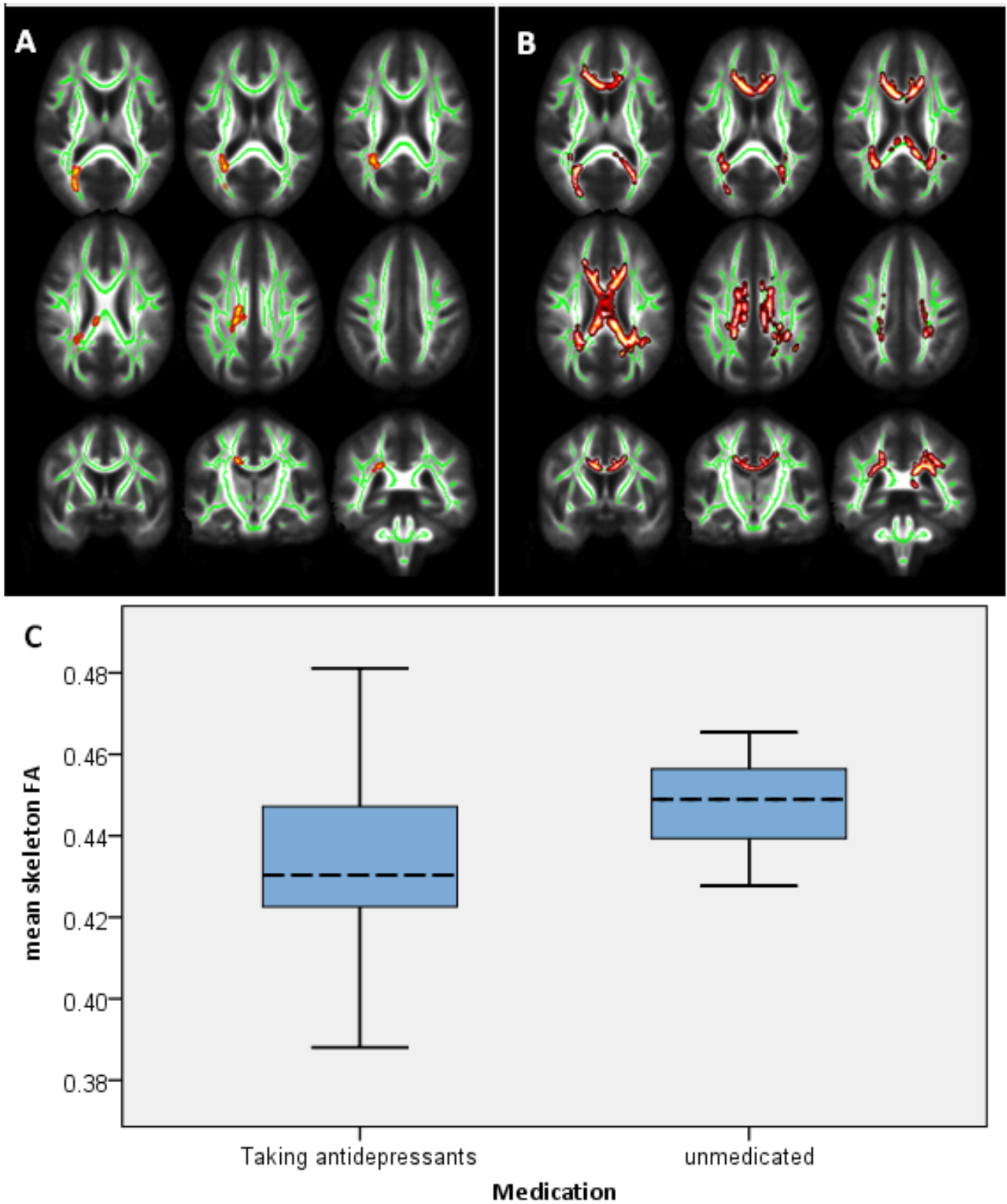


Fig. DS5 Fractional anisotropy (FA) and radial diffusivity (RD) maps for antidepressant use in patients with major depressive disorder.

(A) Regions where currently medicated patients had significantly reduced FA, compared with patients not taking antidepressants (yellow, bounded by red). (B) Corresponding increases in RD (white bounded by red) in medicated patients. All maps family-wise error corrected $P < 0.05$. (C) Box plots of mean skeleton FA for the medicated and unmedicated groups, demonstrating the differing variance between groups, with the dashed lines representing each group mean.