# Supplementary Materials

Segmentation of regions-of-interest

Anatomical regions-of-interest were identified using the John Hopkins University Probabilistic Tractography Altlas and John Hopkins University White Matter Labels Atlas, both integrated in FSL. Masks derived from the tractography atlas, thresholded at probabilities >25%, were used for the uncinate fasculi and callosal regions. These masks were smoothed at 1.05 mm FWHM and binarized (>0). Masks derived from the white matter labels atlas were used to segment all other regions. These masks were smoothed with a kernel of 1.1 mm FWHM, thresholded at >0.2 and binarized. Accurate overlap with the TBSS skeleton was visually verified (**Supplementary Figure S1**). Each mask was multiplied by the TBSS skeleton mask to obtain a parcellation of the center of each region-of-interest and mean FA values within each region was extracted for each subject.

Figure S1. Regions of interest as determined by the John Hopkins University probabilistic tractography and white matter labels atlases.
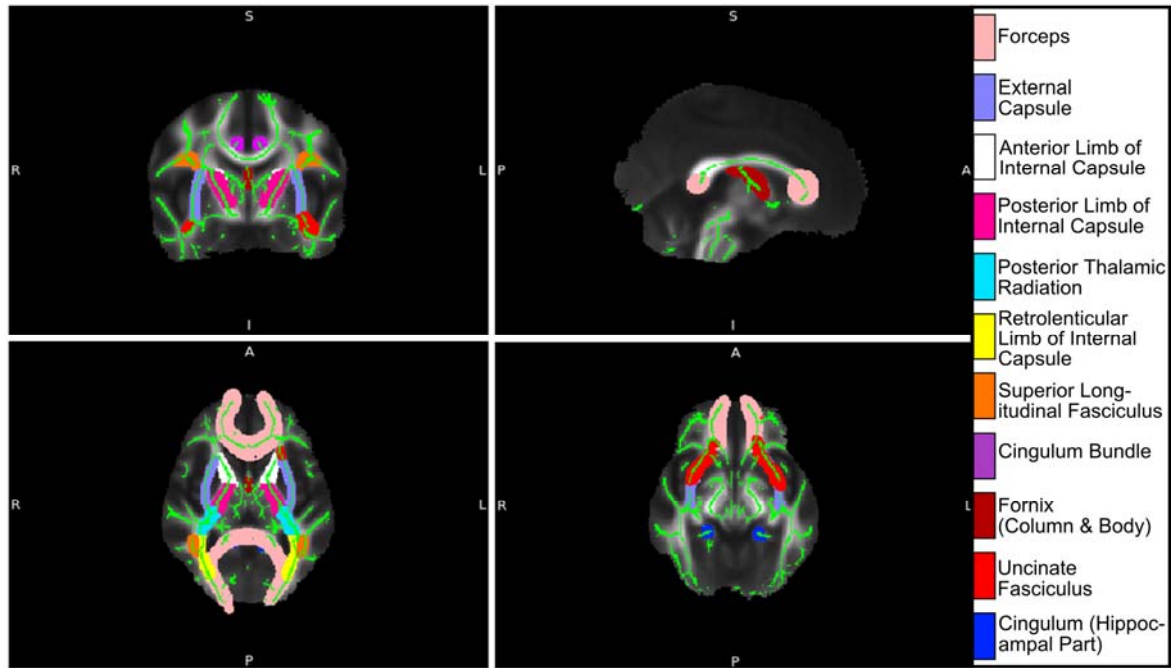
Figure S2. Reduced FA in patients compared to controls, according to "cluster-extent" significance, corrected at $p_{FWE} < 0.05$.
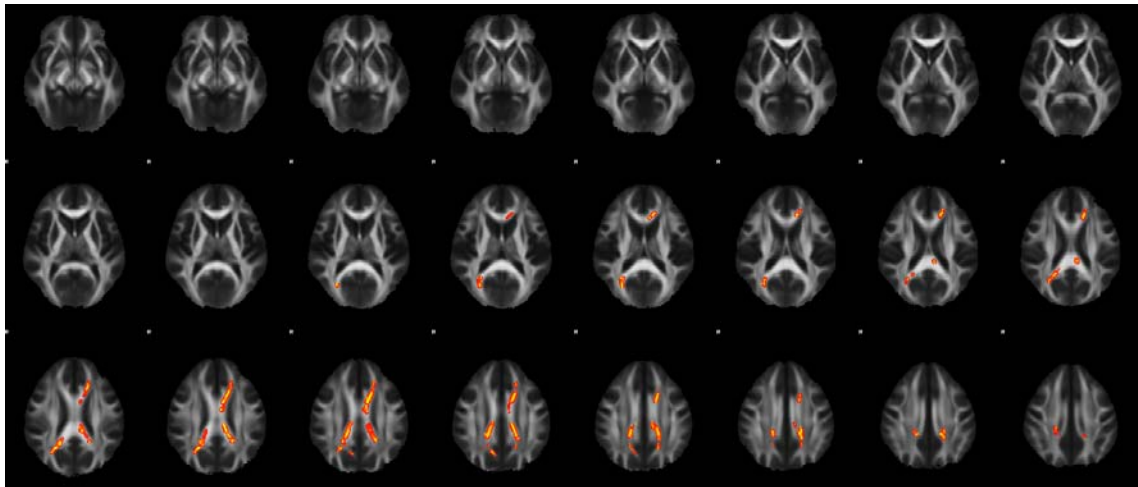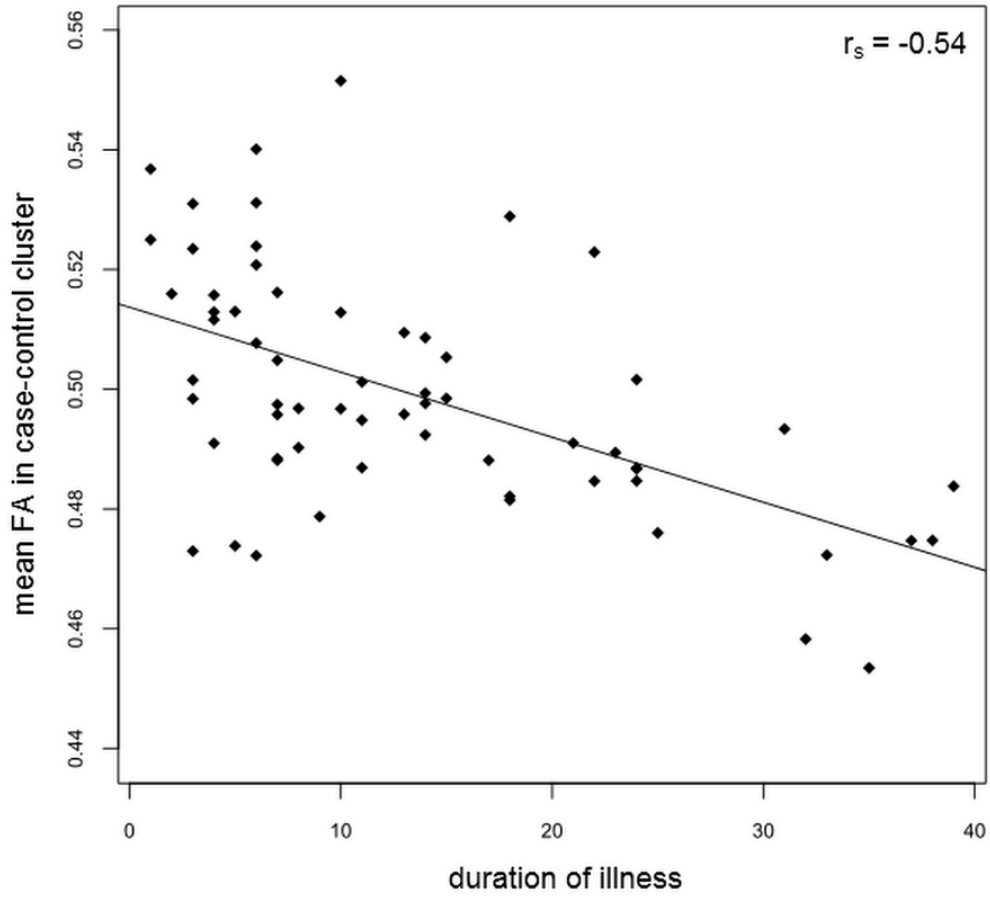
Figure S3. Plot showing the correlation between mean FA in the case-control cluster and duration of illness since the first episode of mania.

Supplementary Table S1. Locations of significant TBSS voxels of the case-control contrast ($P_{FWE} < 0.05$).

#voxels	Max TFCE MNI coordinates	Atlas anatomical structures
46,935	-16, -30, 30	All of the 20 tracts from the Probabilistic Tractography Atlas and 45 out of 48 regions from the White Matter Labels Atlas (not the left tapetum and bilateral hippocampal parts of the cingulum).
242	19, 50, 14	Unclassified
190	8, 52, -18	Unclassified
126	13, 33, 42	Unclassified
72	9, -41, 63	Unclassified
22	32, 41, 23	Unclassified
13	32, 34, 20	Unclassified

Note that TFCE modifies the values of each voxel to reflect not only its own t-statistic but also those of other voxels within the same consecutive TFCE-specific "cluster". While in TFCE the peak statistic reflects a maximum of a function of both of spatial extent and local effect size, the traditional peak-voxel of t-static reflects the maximum local effects size only. Thus, these statistics do not necessarily point to the same peak voxel. Please refer to Smith & Nichols (2009) for a complete explanation of TFCE.

Supplementary Table S2. Locations of significant TBSS voxels of the sibling-control contrast ($P_{FWE} < 0.05$).

#voxels	Max TFCE MNI coordinates	Atlas anatomical structures (> 10% probability)
1,552	-1, 0-35, 20	Splenium and body of corpus callosum,
401	-27, -64, 12	Posterior thalamic radiation
127	25, -53, 25	Splenium, posterior corona radiata
83	-34, -18, 35	Superior longitudinal fasciculus
69	-38, -48, 19	Superior longitudinal fasciculus
26	-16, -30, 31	Body and splenium of corpus callosum