Supplementary Information (SI)

Abbreviation	Name
L_OLF	L_Olfactory areas
R_OLF	R_Olfactory areas
L_Isocortex	L_Isocortex
R_Isocortex	R_Isocortex
L_HPF	L_Hippocampal formation
R_HPF	R_Hippocampal formation
L_AMY	L_Amygdala
R_AMY	R_Amygdala
L_STR	L_Striatum
R_STR	R_Striatum
L_PAL	L_Pallidum
R_PAL	R_Pallidum
L_TH	L_Thalamus
R_TH	R_Thalamus
L_HY	L_Hypothalamus
R_HY	R_Hypothalamus
L_MB	L_Midbrain
R_MB	R_Midbrain
L_HB	L_Hindbrain
R_HB	R_Hindbrain
L_CB	L_Cerebellum
R_CB	R_Cerebellum

SI, Table S1. List of ROIs used in the regions analysis.

Abbreviation	Name
L_OLF	L_Olfactory areas
R_OLF	R_Olfactory areas
L_GU	L_Gustatory areas
R_GU	R_Gustatory areas
L_FRP	L_Frontal pole, cerebral cortex
R_FRP	R_Frontal pole, cerebral cortex
L_ECT	L_Ectorhinal area
R_ECT	R_Ectorhinal area

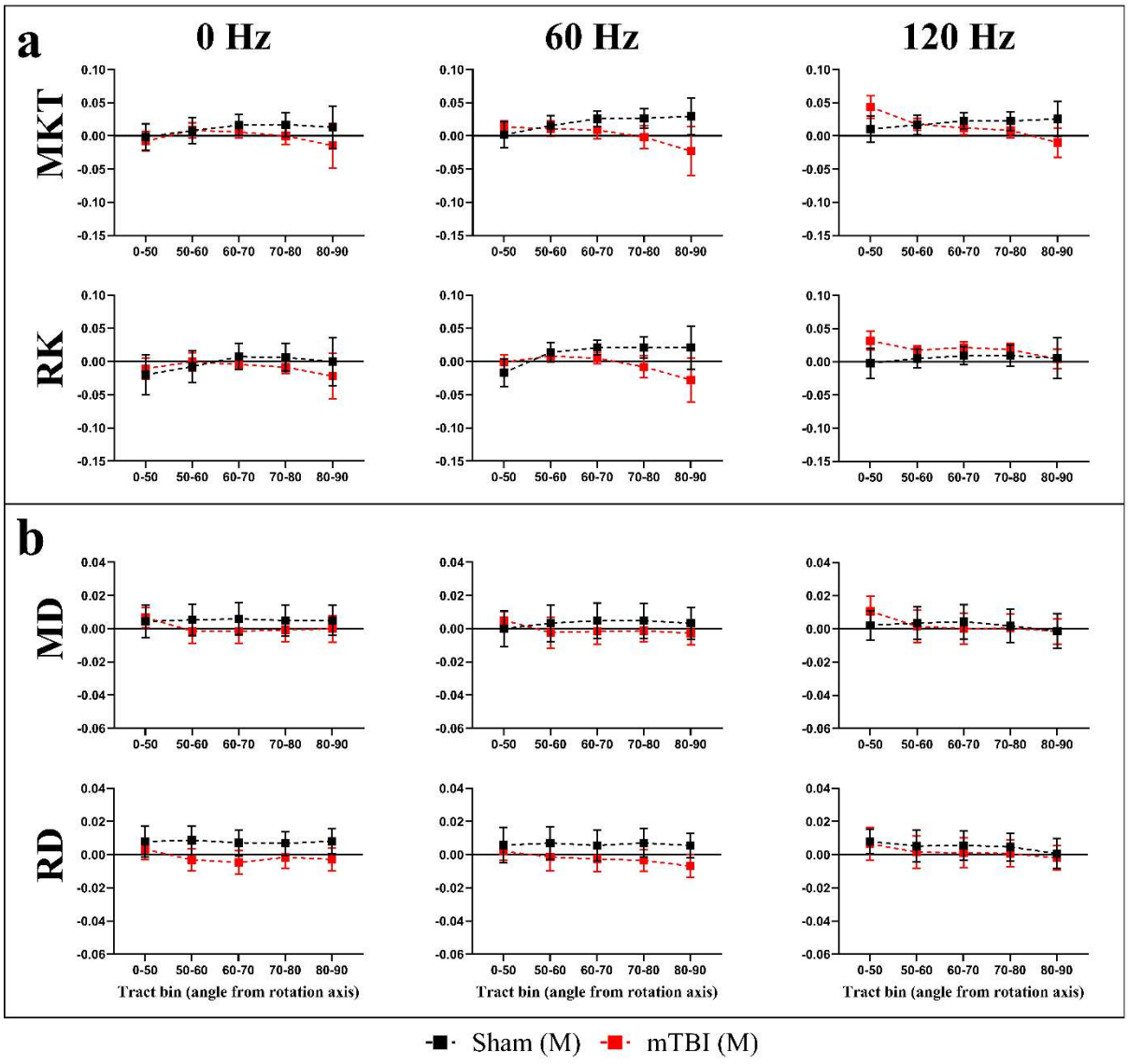
L_RSP	L_Retrosplenial area
R_RSP	R_Retrosplenial area
L_SS	L_Somatosensory areas
R_SS	R_Somatosensory areas
L_ILA	L_Infralimbic area
R_ILA	R_Infralimbic area
L_ACA	L_Anterior cingulate area
R_ACA	R_Anterior cingulate area
L_MO	L_Somatomotor areas
R_MO	R_Somatomotor areas
L_AI	L_Agranular insular area
R_AI	R_Agranular insular area
L_ORB	L_Orbital area
R_ORB	R_Orbital area
L_AUD	L_Auditory areas
R_AUD	R_Auditory areas
L_VISC	L_Visceral area
R_VISC	R_Visceral area
L_PERI	L_Perirhinal area
R_PERI	R_Perirhinal area
L_TEa	L_Temporal association areas
R_TEa	R_Temporal association areas
L_PTLp	L_Posterior parietal association areas
R_PTLp	R_Posterior parietal association areas
L_PL	L_Prelimbic area
R_PL	R_Prelimbic area
L_VIS	L_Visual areas
R_VIS	R_Visual areas
L_DG	L_Dentate gyrus
R_DG	R_Dentate gyrus
L_CA	L_Ammon's horn
R_CA	R_Ammon's horn
L_PAR	L_Parasubiculum
R_PAR	R_Parasubiculum
L_PRE	L_Presubiculum
R_PRE	R_Presubiculum
L_POST	L_Postsubiculum
R_POST	R_Postsubiculum
L_ProS	L_Prosubiculum
R_ProS	R_Prosubiculum
L_SUB	L_Subiculum

R_SUB	R_Subiculum
L_ENT	L_Entorhinal area
R_ENT	R_Entorhinal area
L_AMY	L_Amygdala
R_AMY	R_Amygdala
L_STRv	L_Striatum ventral region
R_STRv	R_Striatum ventral region
L_STRd	L_Striatum dorsal region
R_STRd	R_Striatum dorsal region
L_LSX	L_Lateral septal complex
R_LSX	R_Lateral septal complex
L_PAL	L_Pallidum
R_PAL	R_Pallidum
L_DORpm	L_Thalamus, polymodal association cortex related
R_DORpm	R_Thalamus, polymodal association cortex related
L_DORsm	L_Thalamus, sensory-motor cortex related
R_DORsm	R_Thalamus, sensory-motor cortex related
L_HY	L_Hypothalamus
R_HY	R_Hypothalamus
L_MBsen	L_Midbrain, sensory related
R_MBsen	R_Midbrain, sensory related
L_MBsta	L_Midbrain, behavioral state related
R_MBsta	R_Midbrain, behavioral state related
L_MBmot	L_Midbrain, motor related
R_MBmot	R_Midbrain, motor related
L_HB	L_Hindbrain
R_HB	R_Hindbrain
L_HEM	L_Hemispheric regions
R_HEM	R_Hemispheric regions
L_CBN	L_Cerebellar nuclei
R_CBN	R_Cerebellar nuclei
L_VERM	L_Vermal regions
R_VERM	R_Vermal regions

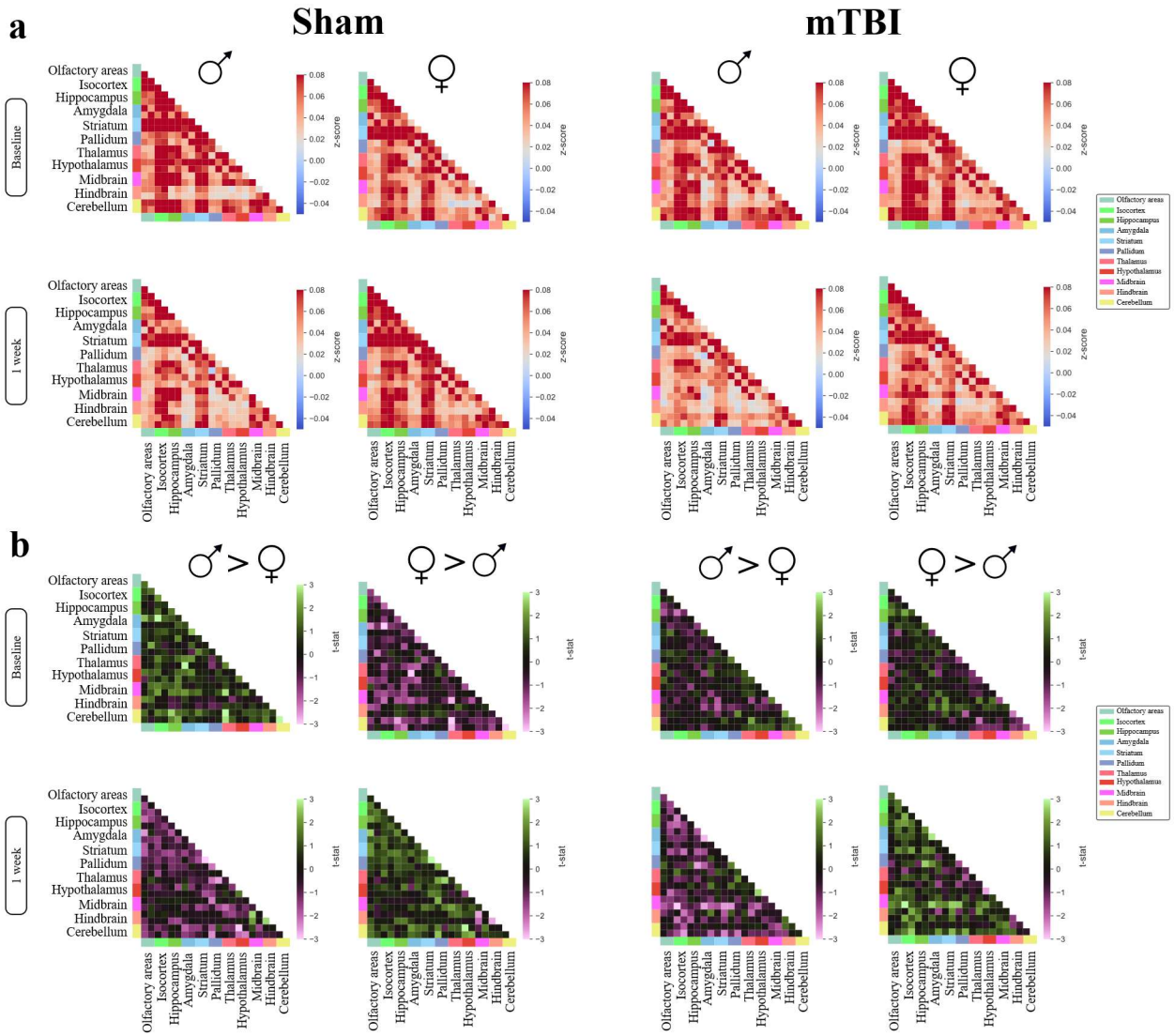
SI, Table S2. List of ROIs used in the subregions analysis.

Experiment ID	Tracts	Primary injection site	Direction	Source	Target
298718072	Genu of corpus callosum (ccg)	Secondary motor area	parallel	motor area	motor area (contralateral)
175739085	Stria teminalis (st)	Bed nuclei of the stria terminalis	parallel	Pallidum	Central and Medial amygdalar nucleui (ipsilater
119848249	Arbor vitae/cerebellar commissure (arb/cbc)	Lobule II	parallel	Central Lobule	Central Lobule (contralateral)
287600392	Cingulum bundle (cing)	Anterior cingulate area, ventral part	orthogonal	Anterior cingulate area	Retrosplenial area (ipsilateral)
180720175	Corticospinal tract (cst)	Primary motor area	orthogonal	Motor area	Pons (ipsilateral)
306957248	Optic tract (opt)	Retina, Dorsal part of the lateral geniculate complex	orthogonal	Dorsal part of the lateral geniculate complex	Superior colliculus (ipsilateral)
543881679	Cerebellar peduncles/rubrospinal tracts (cbp/rust)	Red nucleus	orthogonal	Red nucleus	Intermediate reticular nucleus (contralateral)

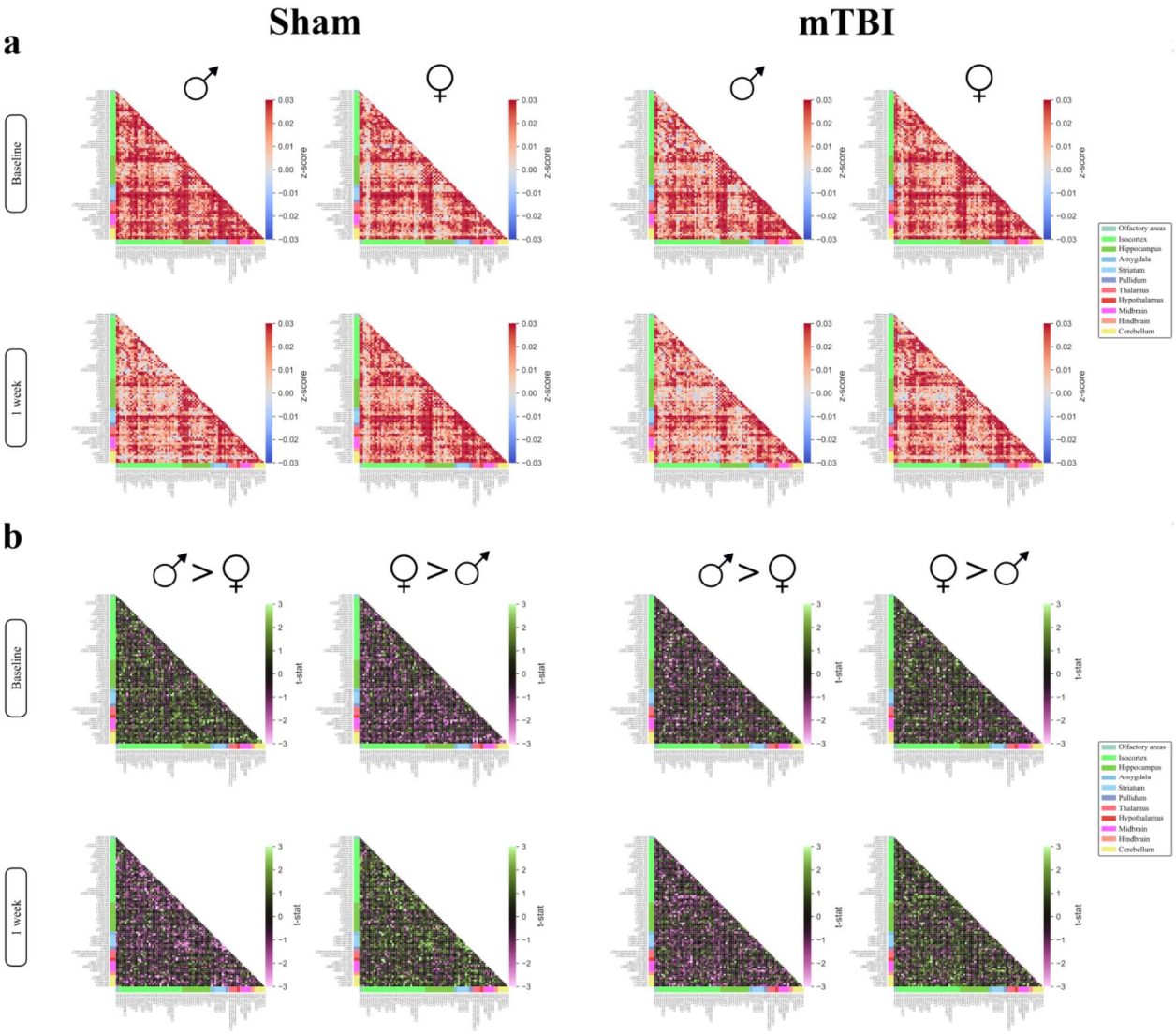
SI, Table S3. Viral tracing experiments used to extract white matter tracts.



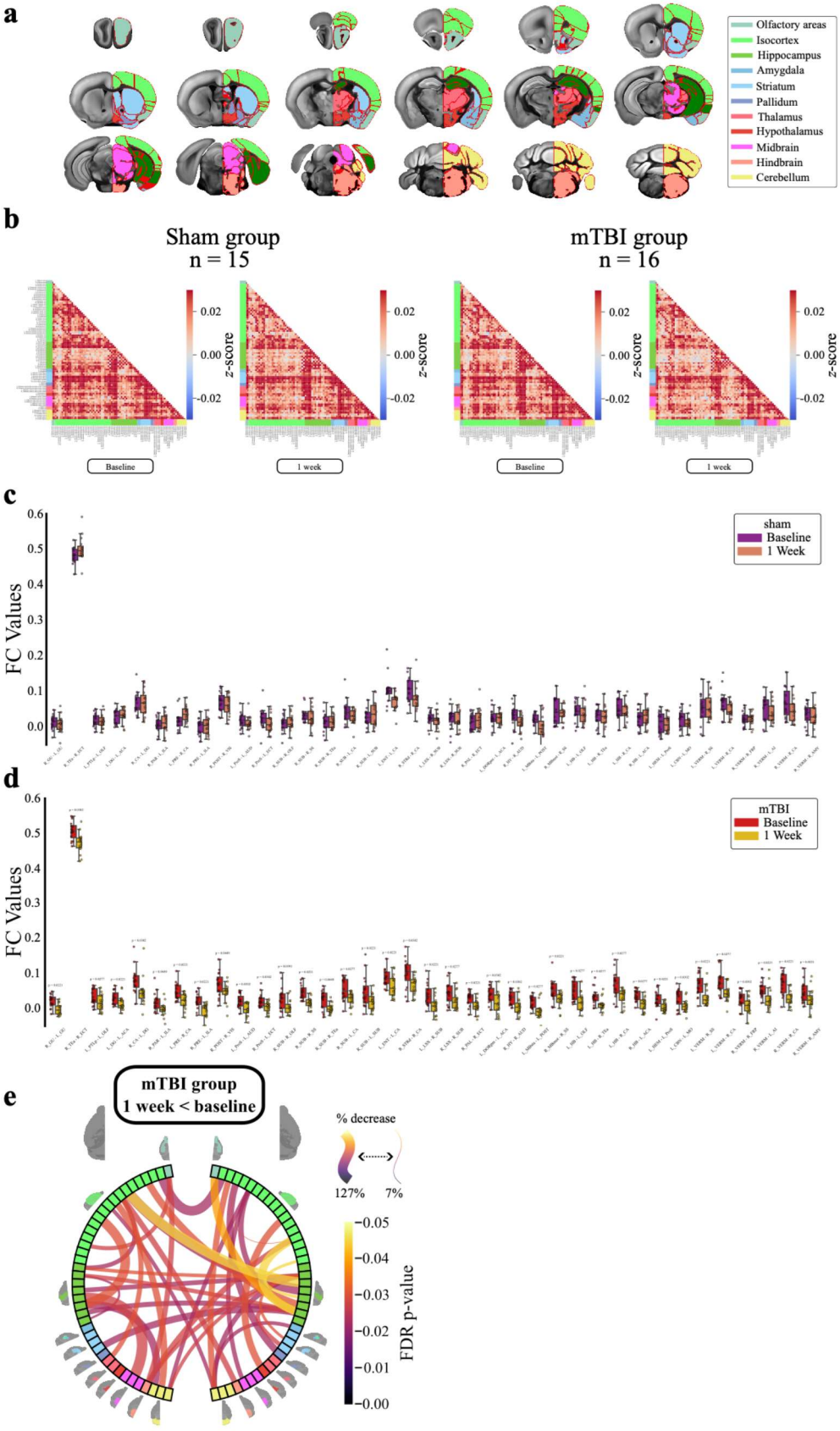
SI, Fig S1. dMRI metric changes in sham and mTBI male mice across tract orientation bins. **a)** shows group differences in MKT and RK across acquisition frequencies. **b)** shows group differences in MD and RD across acquisition frequencies. The data is shown as change in each cohort post-injury relative to baseline, mean +/- SEM. **Abbreviations:** MD, mean diffusivity; MKT, mean kurtosis tensor; RD, radial diffusivity; RK, radial kurtosis; SEM, standard error of the mean



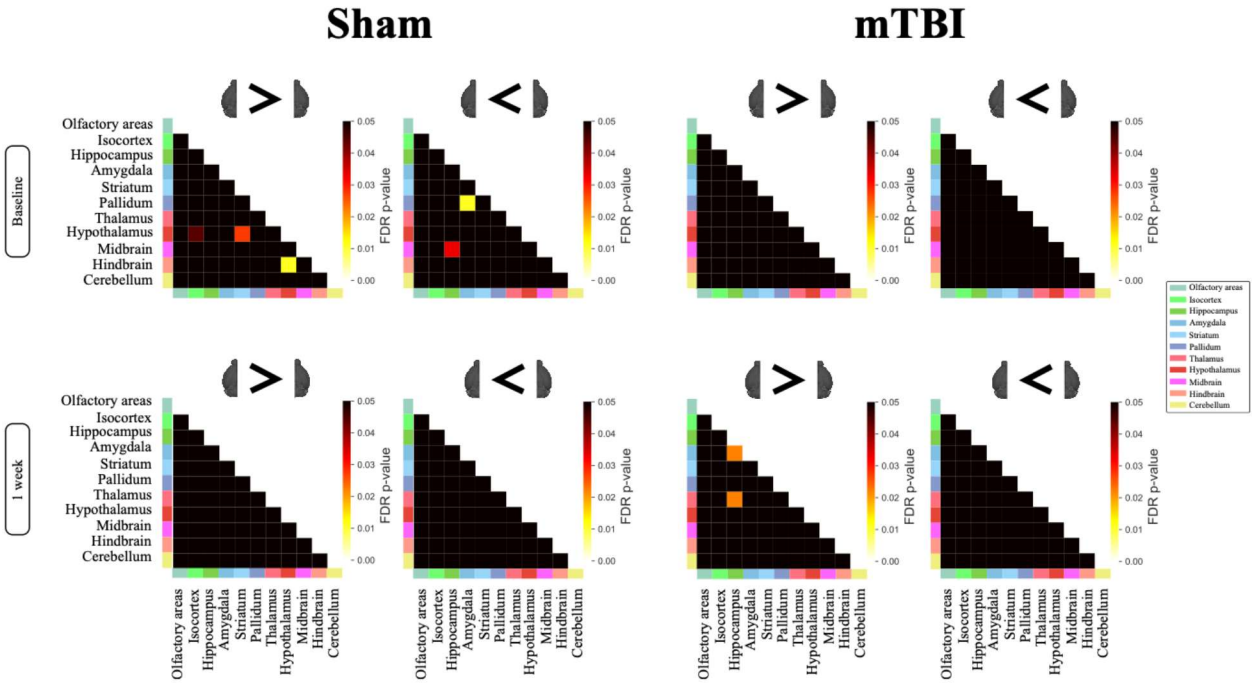
SI, Fig S2: No observable sex change before and 1 week after injury or sham procedure using 22 ROI atlas. **A)** Average connectivity matrices males and females in the sham on the left and in the mTBI group on the right at baseline (top) and after 1 week (bottom). **B)** t-statistics of hypothesis testing between males and females within sham (left) and mTBI (right) at baseline (top) and after 1 week (bottom). Connectivity strength was calculated as Pearson's correlation coefficient and converted to *z*-score using Fisher's transformation. Hypothesis testing was done using permutation testing with 10,000 permutations and corrected for multiple comparisons using false-discovery rate. Anatomical structures in each matrix are color-coded and the legends are on the right. **Abbreviations:** mTBI, mild traumatic brain injury; ROI, region of interest; ♀, female; ♂, male.



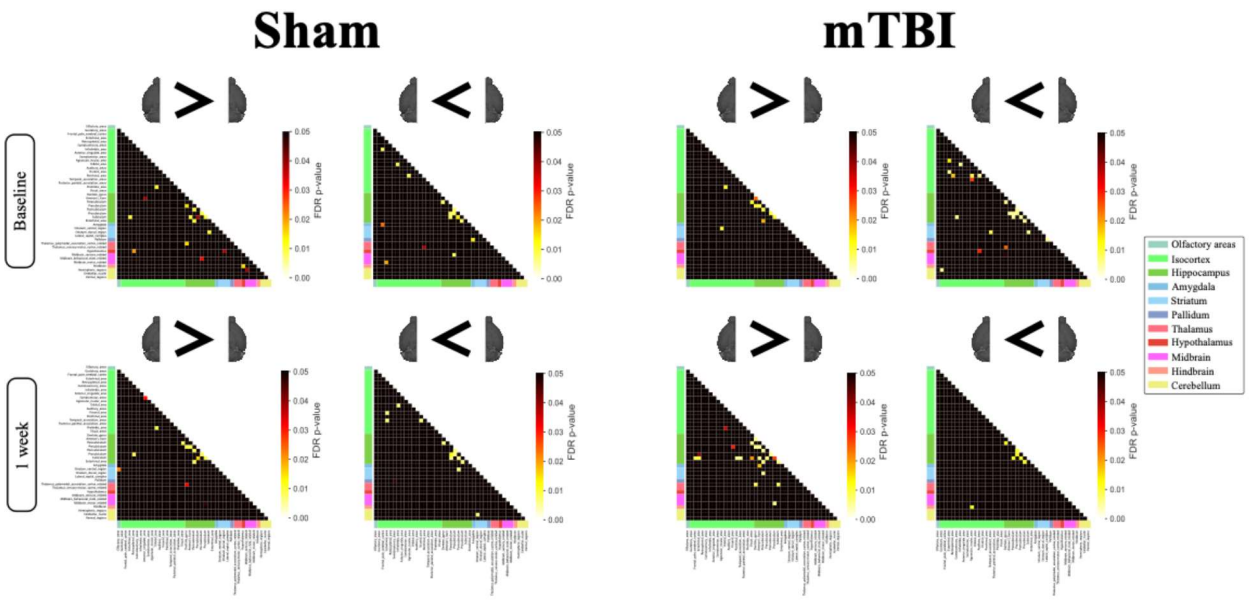
SI, Fig S3: No observable sex change before and 1 week after injury or sham procedure using 82 ROI atlas. **A)** Average connectivity matrices males and females in the sham on the left and in the mTBI group on the right at baseline (top) and after 1 week (bottom). **B)** t-statistics of hypothesis testing between males and females within sham (left) and mTBI (right) at baseline (top) and after 1 week (bottom). Connectivity strength was calculated as Pearson's correlation coefficient and converted to *z*-score using Fisher's transformation. Hypothesis testing was done using permutation testing with 10,000 permutations and corrected for multiple comparisons using false-discovery rate. Anatomical structures in each matrix are color-coded and the legends are on the right. **Abbreviations:** mTBI, mild traumatic brain injury; ROI, region of interest; ♀, female; ♂, male.


a
Olfactory areas
Isocortex
Hippocampus
Amygdala
Striatum
Pallidum
Thalamus
Hypothalamus
Midbrain
Hindbrain
Cerebellum
b
Sham group
n = 15
mTBI group
n = 16
z-score
0.02
0.00
-0.02
Baseline
1 week
c
FC Values
sham
Baseline
1 Week
d
mTBI
Baseline
1 Week
e
mTBI group
1 week < baseline
% decrease
127%
7%
FDR p-value
−0.05
−0.04
−0.03
−0.02
−0.01
−0.00

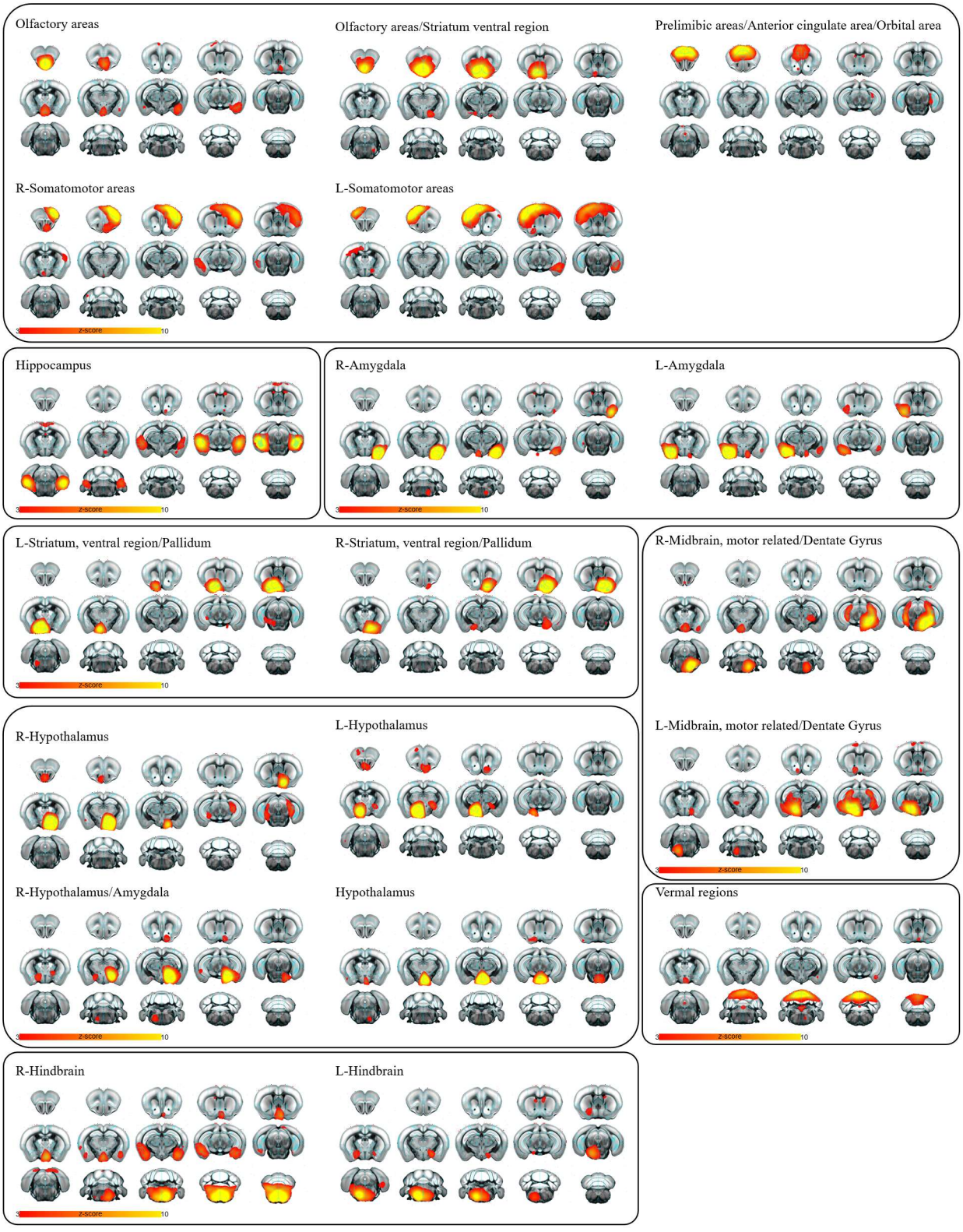
SI, Fig S4. mTBI induces loss of connectivity one week after injury. Hypothesis testing within each group before and after sham procedure or injury was done using permutation testing with 10,000 permutations and corrected for multiple comparisons using FDR. **A)** Atlas used to segment the brain. The subregions atlas was adapted from ABA CCFv3 and consists of 41 ROI per hemisphere. Structures on the right hemisphere are color-coded and show boundaries between different regions. The anatomical atlas is shown on the left hemisphere. **B)** Average connectivity matrix of the sham group (left) and mTBI group (right), at baseline (top) and after 1 week of the sham procedure of head injury (bottom). Correlation strengths were calculated as Pearson's correlation coefficient between each pair of nodes and converted to *z*-score using Fisher's transformation. **D&E)** Boxplots of regions that showed significant decrease after the sham procedure **(C)** and after mTBI **(D)** for comparison. **E)** Circular plot showing edges with significant decrease from baseline, 1 week after injury. The thickness of the lines reflects the percentage of decrease with the thickest line represent biggest decrease from baseline correlation (127% decrease) and the thinnest line shows smallest decrease from baseline (7%). **C) Abbreviations:** ABA, Allen Brain Atlas; ACA, anterior cingulate area; AI, agranular insular area; AMY, amygdala; AUD, auditory areas; CA, ammon's horn; CBN, cerebellar nuclei; CCFv3, common coordinate framework version 3; DG, dentate gyrus; DORpm, thalamus, polymodal association cortex related; ECT, ectorhinal area; ENT, entorhinal area; FC, functional connectivity; FDR, false-discovery rat; FRP, frontal pole, cerebral cortex; GU, gustatory areas; HEM, hemispheric regions; HY, hypothalamus; ILA, infralimbic area; L, left; LSX, lateral septal complex; MBsta, midbrain, behavioral state related; MO, somatomotor areas; mTBI, mild traumatic brain injury; OLF, olfactory areas; PAL, pallidum; PAR, parasubiculum; POST, postsubiculum; PRE, presubiculum; ProS, prosubiculum; PTLp, posterior parietal association areas; R, right; SS, somatosensory areas; STRd, striatum dorsal region; SUB, subiculum; TEa, temporal association areas; VERM, vermal regions; VIS, visual areas.



SI, Fig S5. Right hemisphere vs left hemisphere functional connectivity statistical comparisons in each group and in each condition using 22 ROI atlas. Paired hypothesis testing was done between left and right hemisphere functional connectivity using permutation testing with 10,000 permutations and false-discovery rate for multiple comparisons correction. Each matrix represents one contrast, black squares are edges with no significant change and colored ones reflect statistically significant changes (*P* value < 0.05) between hemispheres in sham group (left) or mTBI group (right) at baseline (top) or 1 week after intervention (bottom). Anatomical structures in each matrix are color-coded and the legends are on the right. **Abbreviations:** mTBI, mild traumatic brain injury; ROI, region of interest.



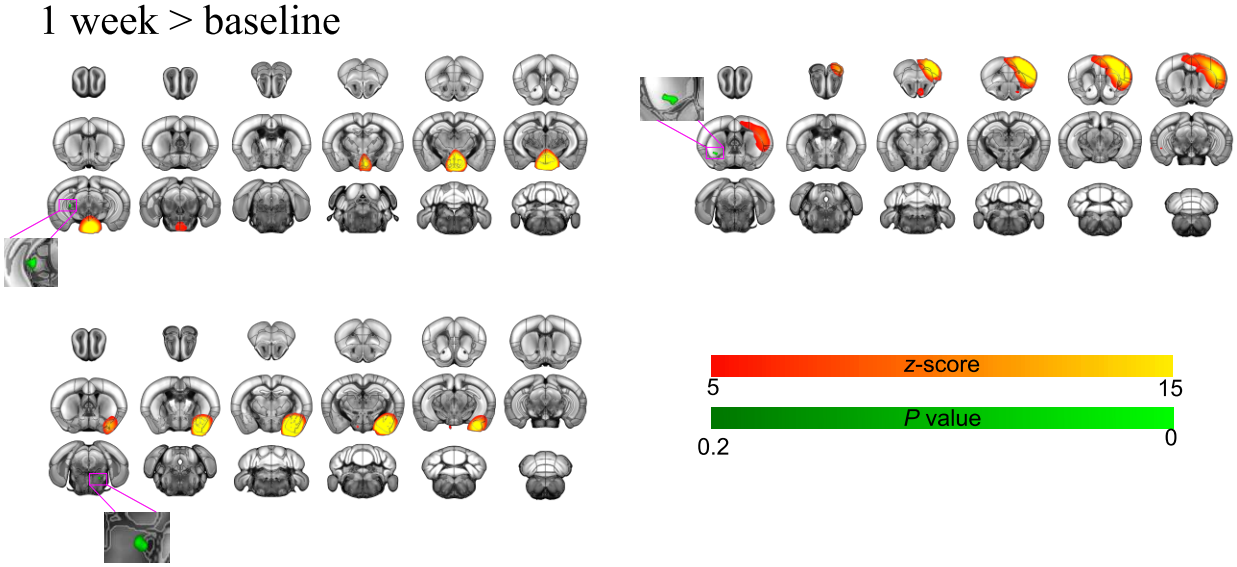
SI, Fig S6. Right hemisphere vs left hemisphere functional connectivity statistical comparisons in each group and in each condition using 82 ROI atlas. Paired hypothesis testing was done between left and right hemisphere functional connectivity using permutation testing with 10,000 permutations and false-discovery rate for multiple comparisons correction. Each matrix represents one contrast, black squares are edges with no significant change and colored ones reflect statistically significant changes (*P* value < 0.05) between hemispheres in sham group (left) or mTBI group (right) at baseline (top) or 1 week after intervention (bottom). Anatomical structures in each matrix are color-coded and the legends are on the right. **Abbreviations:** mTBI, mild traumatic brain injury; ROI, region of interest.



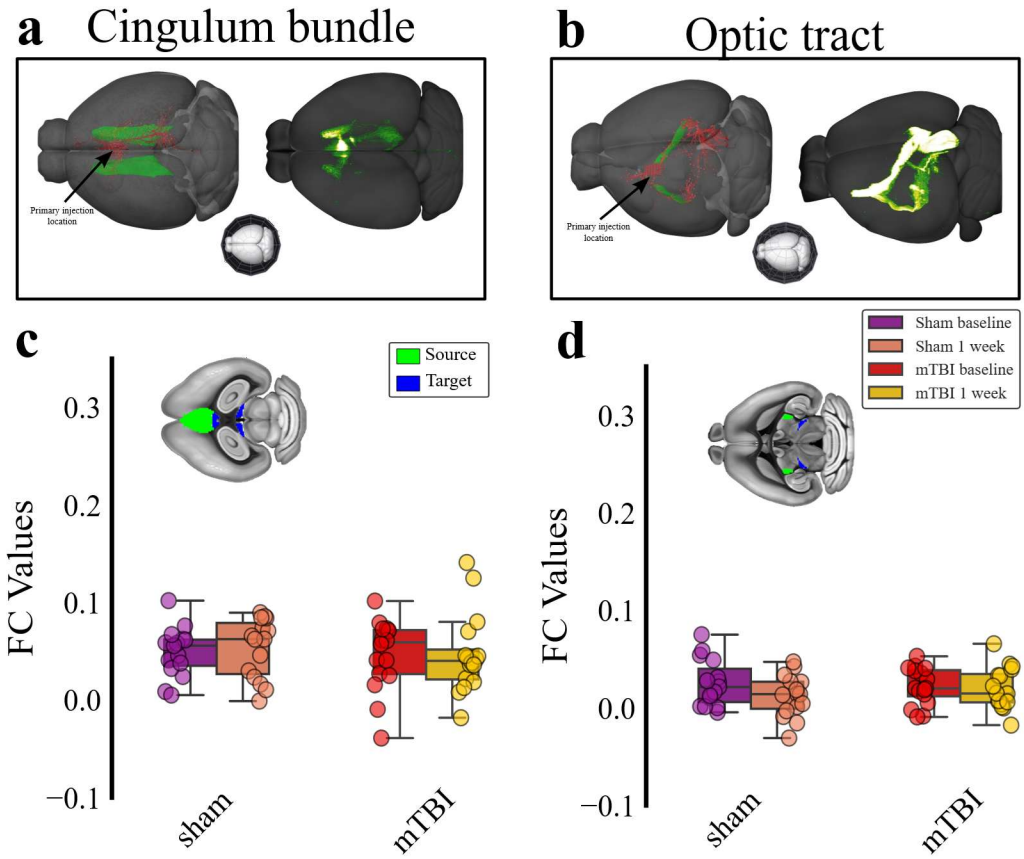
SI, Fig S7. **RSNs identified by ICA.** We used probabilistic ICA on the concatenated prefiltered group data from all subjects in both sessions (before and after) to identify different RSNs. We

identified networks in the cerebral cortex, the thalamus, the hippocampus, the amygdala, the striatum, and the cerebellum. All components showed significant overlap with known anatomical structures and were labeled based on ABA CCFv3. The images are shown in anatomical view overlaid on ABA CCFv3 anatomical atlas and the networks are scaled in pseudo-*z*-scores. Abbreviations: ABA, Allen Brain Atlas; CCFv3, common coordinate framework version 3; ICA, independent component analysis; RSNs, resting-state networks.

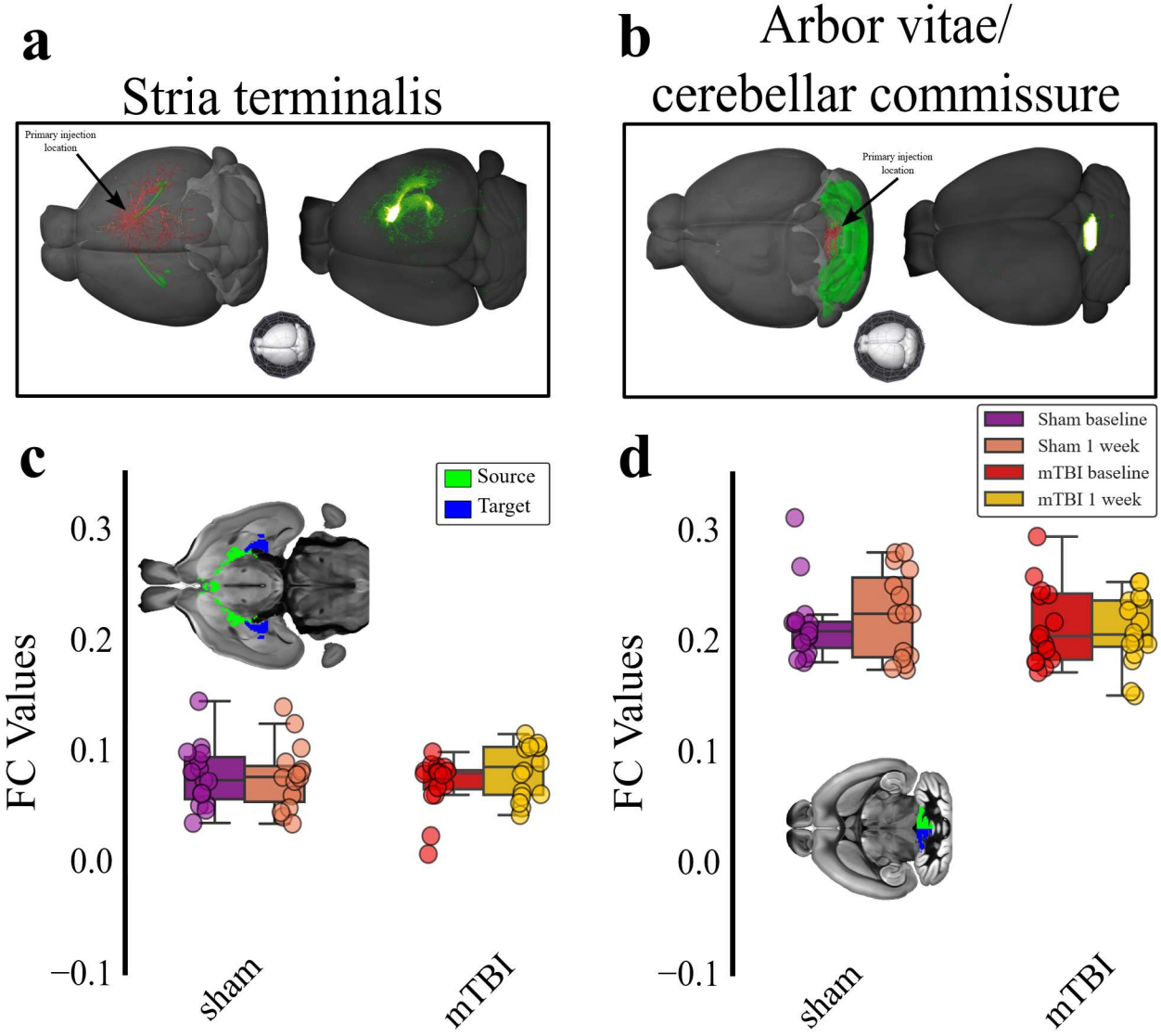
Sham



SI, Fig S8. Dual regression analysis shows upregulation of connectivity strength in sham group after sham procedure. voxel-wise analysis shows increase in functional connectivity between a number of ICA networks and various clusters across the brain in the sham group 1 week after the procedure. Permutation testing with 10,000 permutations was used for hypothesis testing. All the results are corrected across voxels, networks, and contrasts using family-wise error. ICA networks are showed overlaid on an ABA CCFv3 anatomical atlas. **Abbreviations:** ABA, Allen Brain Atlas; CCFv3, common coordinate framework version 3; ICA, independent component analysis.


a
Cingulum bundle
Primary injection location
b
Optic tract
Primary injection location
c
Source
Target
FC Values
0.3
0.2
0.1
0.0
−0.1
sham
mTBI
d
Sham baseline
Sham 1 week
mTBI baseline
mTBI 1 week
FC Values
0.3
0.2
0.1
0.0
−0.1
sham
mTBI
e
Cerebellar peduncle
Primary injection location
f
FC Values
0.3
0.2
0.1
0.0
−0.1
sham
mTBI

SI, Fig S9. Tractography-based functional connectivity across fibers orthogonal to plane of rotation. Cingulum bundle **(A)**, optic tract **(B)**, and cerebellar peduncle **(E)** fiber tracts was isolated using viral tracers injected in various location. The left shows primary injection location in red and the fibers 3D rendering based on ABA CCFv3, the right shows signal density, and an orientation compass is in the middle. **C, D, &F)** Box plots of connectivity strength between regions connected through cingulum bundle **(C)**, optic tract **(D)**, and cerebellar peduncle **(F)**. Paired Student's t-test was performed within each group. The top view shows masks of the source and the target used to calculate FC overlaid on an ABA CCFv3 anatomical atlas. **Abbreviations:** ABA, Allen Brain Atlas; CCFv3, common coordinate framework version 3; FC, functional connectivity.



SI, Fig S10. Tractography-based functional connectivity across fibers parallel to plane of rotation. Stria terminalis **(A)** and arbor vitae **(B)** fiber tracts was isolated using viral tracers injected in various location. The left shows primary injection location in red and the fibers 3D rendering based on ABA CCFv3, the right shows signal density, and an orientation compass is in the middle. **C&D)** Box plots of connectivity strength between regions connected through stria terminalis **(C)** and arbor vitae **(D)**. Paired Student's t-test was performed within each group. The top view shows masks of the source and the target used to calculate FC overlaid on an ABA CCFv3 anatomical atlas. **Abbreviations:** ABA, Allen Brain Atlas; CCFv3, common coordinate framework version 3; FC, functional connectivity.