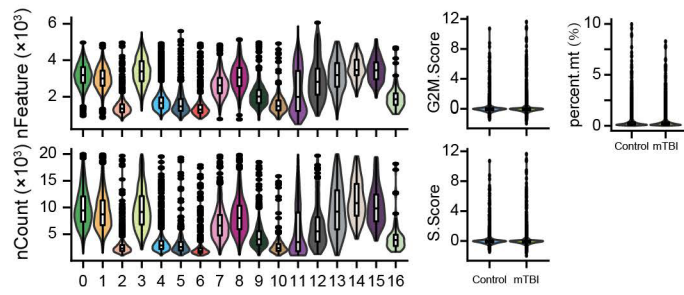
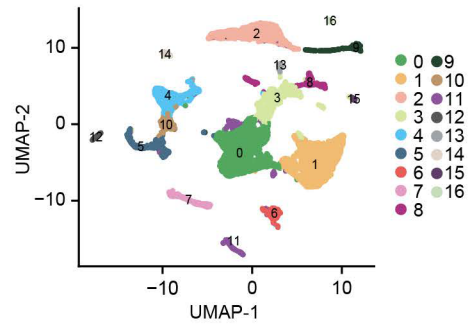
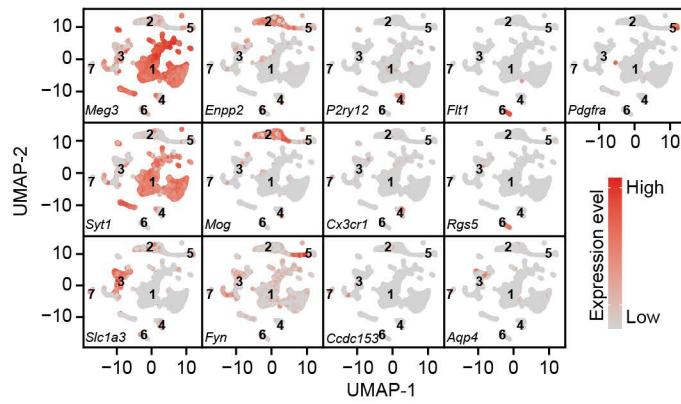
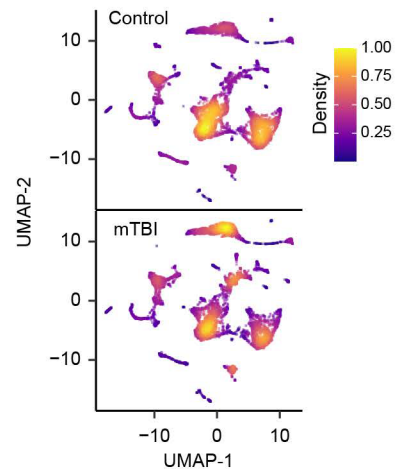


A**B****C****D**

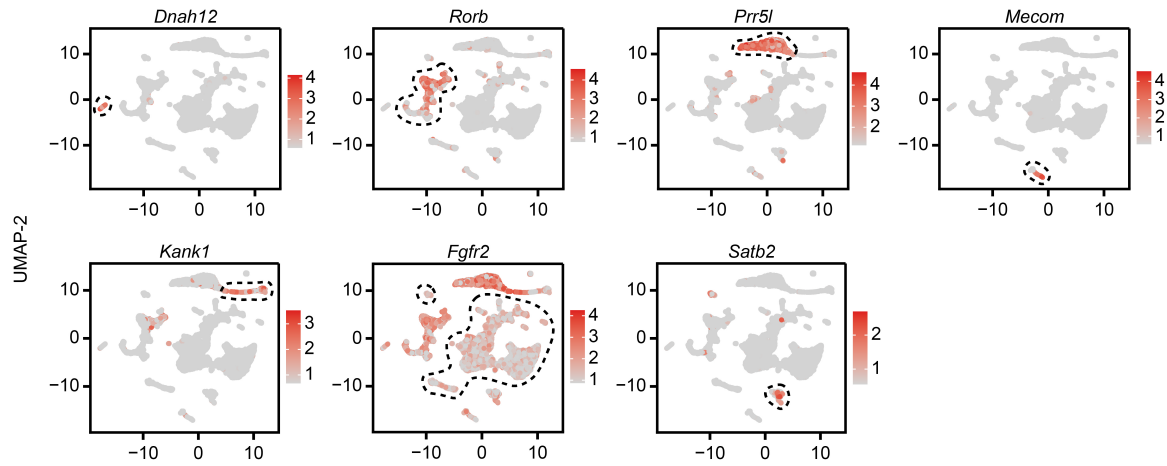
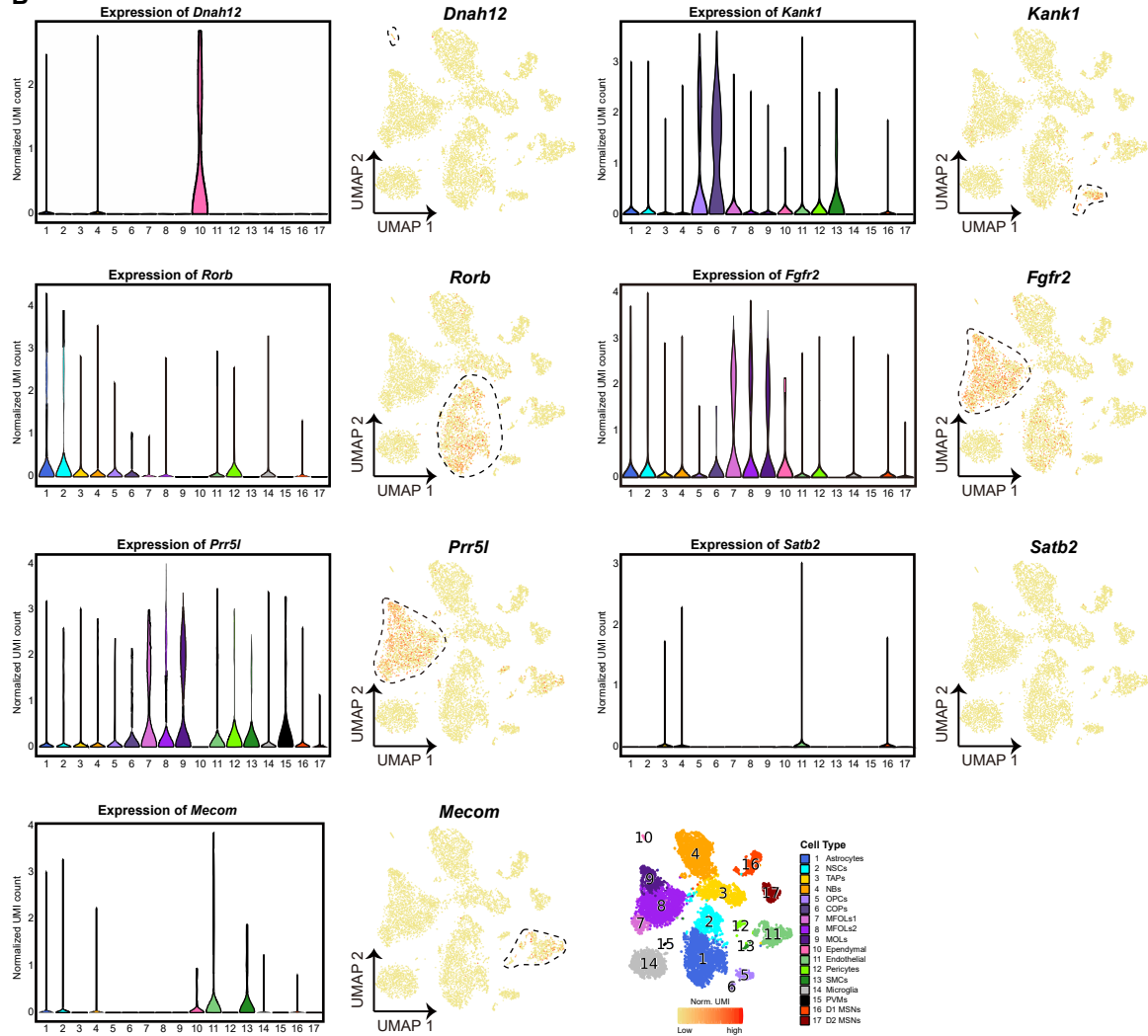
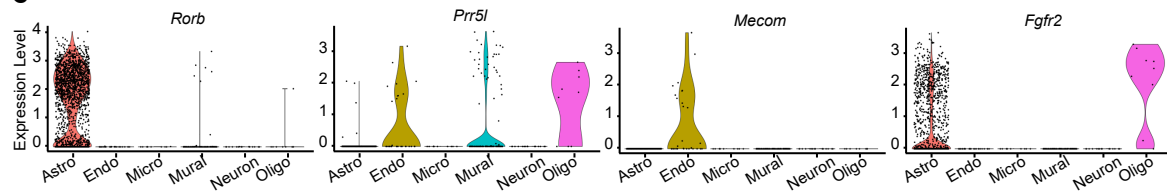
Supplemental_Fig_S1. Quality control of the snRNA-seq. Related to Figure 1.

A. Left: total gene and UMI counts for individual cells grouped by cell cluster in the control and the mTBI SVZ. Right: the proportion of G2M phase, S phase cell and mitochondrial RNA in the control and the mTBI SVZ.

B. UMAP plot of 16 clusters in the SVZ niche. Cells are coloured according to their cell clusters.

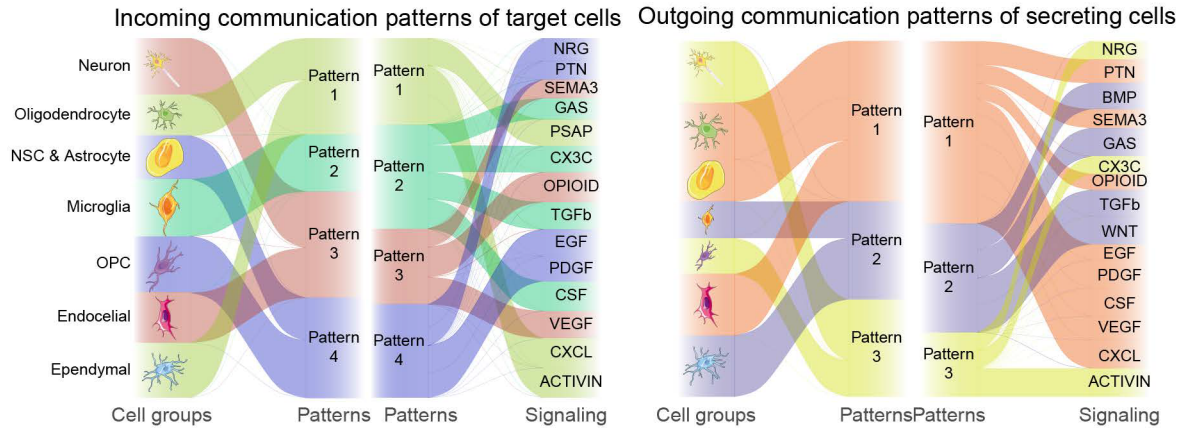
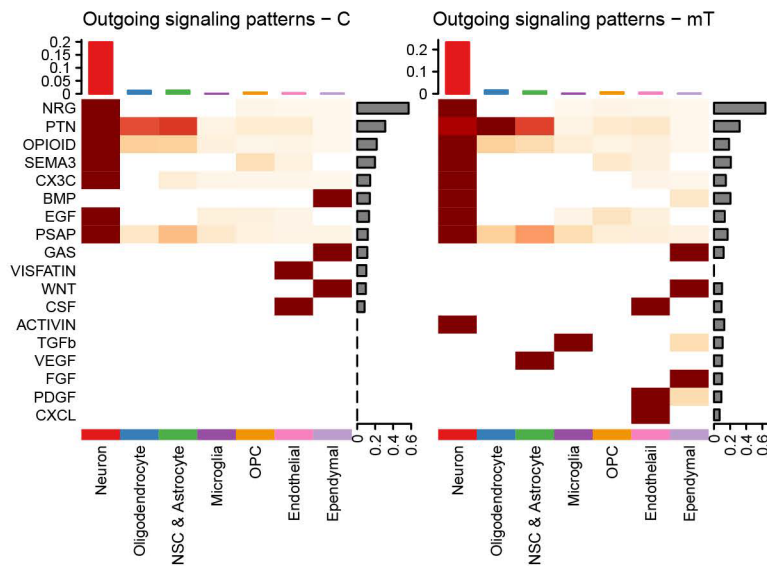
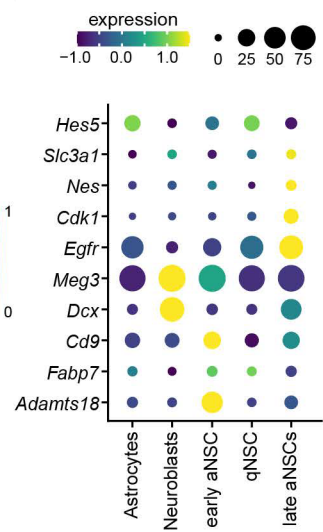
C. Distribution of known markers in the UMAP: *Meg3*, *Syt1* (Neuron); *Enpp2*, *Mog* (Oligodendrocyte); *Slc1a3* (Endothelial); *Cx3cr1*, *P2ry12* (OPC); *Fyn*, *Pdgfra* (Microglia); *Rgs5*, *Fit1* (Astrocyte & NSC); *Ccdc153*, *Aqp4* (Ependymal).

D. UMAP plot of single cells in the control and mTBI group. A gradient of purple to yellow indicates low to high density in the plot.

A**B****C**

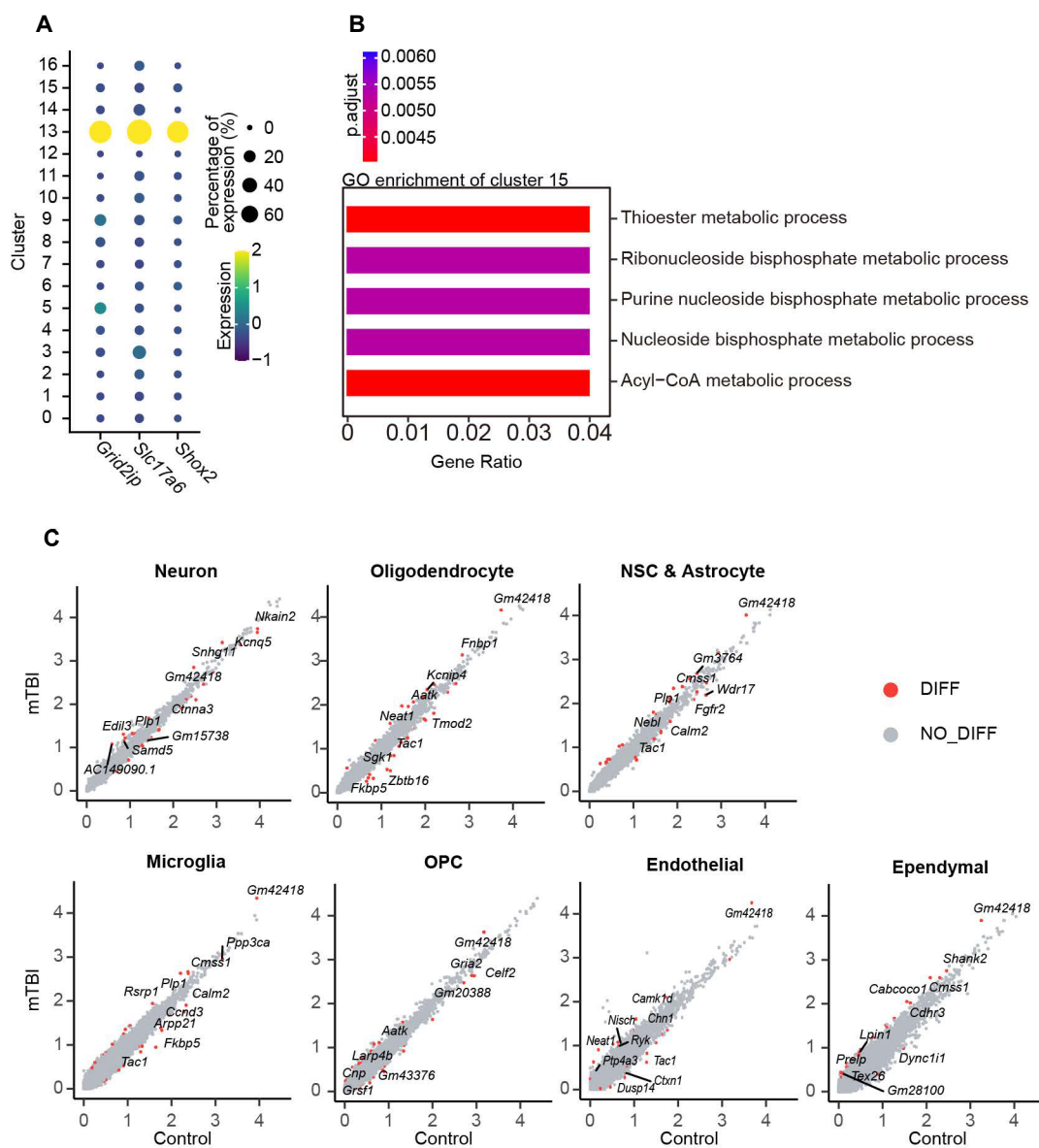
Supplemental_Fig_S2. Novel markers of each cell type. Related to Figure 1.

- A.** Distribution of novel markers on the UMAP in each cell type.
- B.** Expression profiles of novel cell type-specific markers in other SVZ single-cell dataset. Violin plots depict the expression levels of novel cell type-specific markers in each cell population, while UMAP visualizes the relative expression of each novel cell type-specific marker.
- C.** Expression profiles of novel cell type-specific markers in the other cortex and hippocampus single-cell dataset. Violin plots depict the expression levels of novel cell type-specific markers in each cell population.

A**B****C**

Supplemental_Fig_S3. Transcriptional heterogeneity of certain cell types in response to the mTBI. Related to Figure 2.

- A.** Dot plot showing the specific gene expression in cluster 13.
- B.** GO analysis exhibiting enriched terms in cluster 15.
- C.** Volcano plot displaying highly variable genes in each cell type.

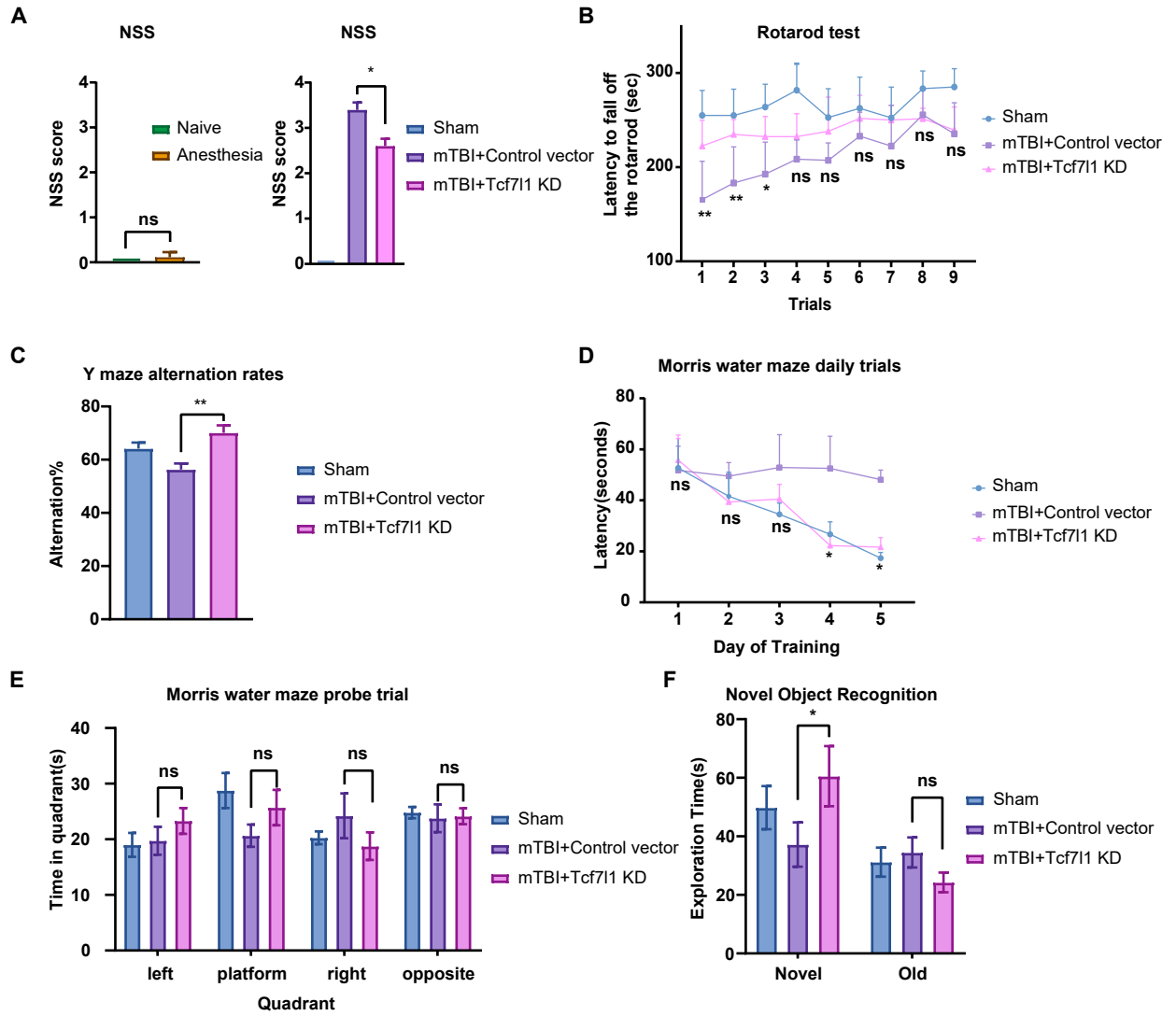


Supplemental_Fig_S4. Additional information for the cell-cell interactions changed in the SVZ after mTBI, and markers for each NSC & astrocyte subtype. Related to Figure 3 & 6.

A. Incoming and outgoing communication patterns of target cells in each cell type.

B. Heatmap of the CellChat signaling in each cell type. Left panel: the outgoing signaling patterns in the control (expression weight value of signaling molecules), right panel: the outgoing signaling patterns in the mTBI (expression weight value of signaling receptors). A gradient of white to crimson indicates low to high expression weight value in the heatmap.

C. Dot plot of the representative markers for each NSC & astrocyte subtype.



Supplemental_Fig_S5. The impact of Tcf7l1-KD on NSS score and long-term behavioral outcomes in mice.

A. Left: NSS score of naive and anesthesia-only mice. Right: NSS score of mTBI+Tcf7l1-KD, mTBI+Control vector and Sham mice. NSS assessment was conducted on mice 1 hour after injury.

B. Rotarod test. The latency time of each mouse falling off the rod was recorded. The speed ranged from 4rpm to 40rpm, with a total duration of 300 seconds. Each mouse was tested 3 times/day, with a minimum interval of 10 minutes between tests, for a total of 9 tests over 3 days.

C. Y-maze test. Alternation rate = (Number of alternations / Total number of arm entries - 2) \times 100%.

D. Morris water maze (MWM) daily trials for spatial localization and navigation. Animals need to find a hidden platform in a circular pool in the 1st stage (1-5 days), and the time from entering the water to finding the platform is recorded as latency.

E. MWM probe trial. The time spent by mice moving in different quadrants was recorded.

F. Novel object recognition test. The time each mouse spends exploring the novel and old objects was recorded.

Statistical significance was determined by Student's *t*-test or two-way ANOVA(**p* < 0.05, ***p* < 0.01).