Redistribution of oligodendrocyte phenotypes in the medial vestibular nuclei after unilateral labyrinthectomy

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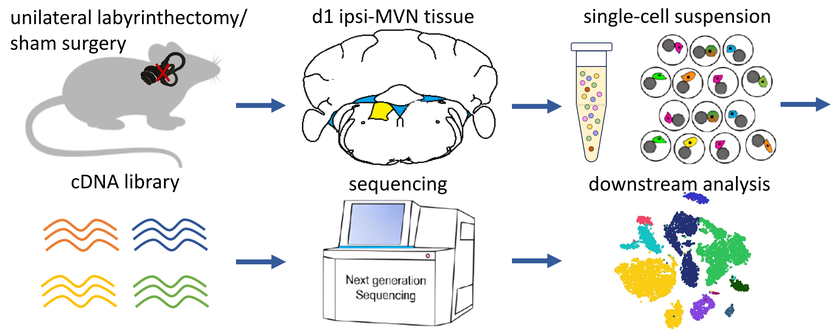
Introduction

- Earlier findings revealed a reactive gliogenesis in the medial vestibular nuclei (MVN) after vestibular leisions.
- Oligodendrocytes are highly heterogeneous and commonly involved in the regulation of neural circuit function.
- How oligodendrocytes in the deafferented vestibular nuclei reacts to the acute unilateral vestibular dysfunction remains unclear.

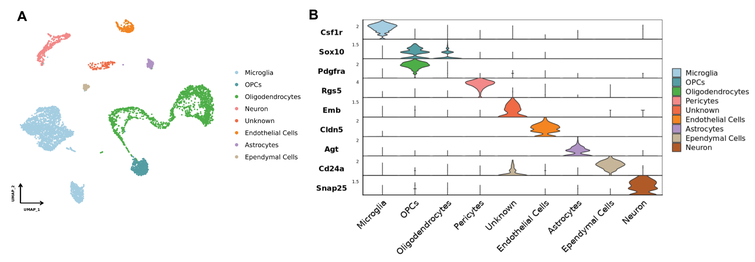
Purpose: to investigate the response status of oligodendrocytes in the MVN after unilateral vestibular loss.

Methods



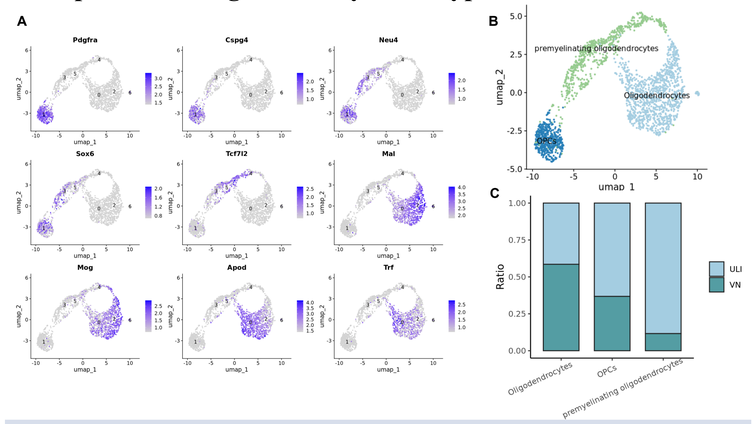
Results

1. Identification of cell types in the ipsilateral MVN



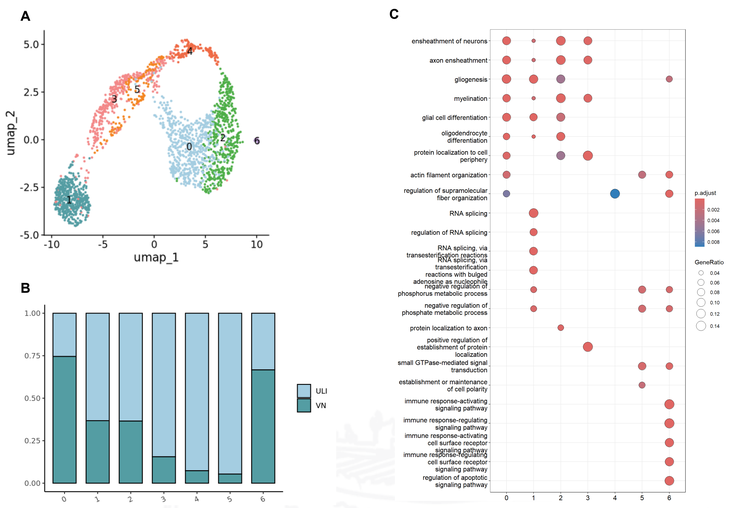
We identified 8 cell types based on the expression of the marker genes *Csf1r*, *Sox10*, *Pdgfra*, *Rgs5*, *Cldn5*, *Agt*, *Cd24a* and *Snap25*. (A) UMAP plots of the major cell types in MVN from UL and control group. (B) The violin plots of known cell marker genes in each cell cluster.

2. Proportion of oligodendrocytic subtypes



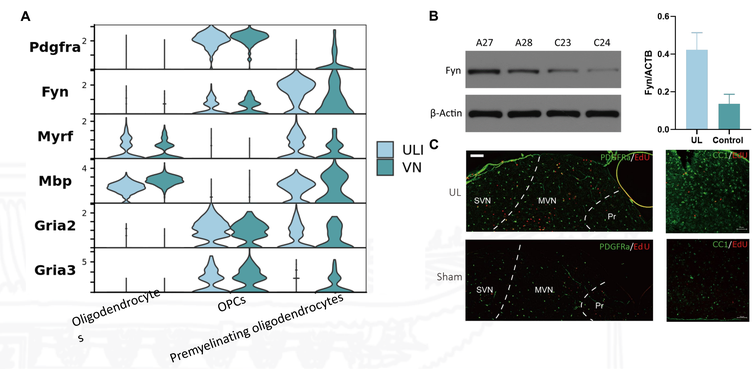
Oligodendrocytes were identified as three subtypes based on the distinct expression patterns. Compared to the control group, proportions of oligodendrocyte progenitor cells (OPCs) and premyelinating oligodendrocytes are higher in the UL group.(A) UMAP plots of marker genes. (B) UMAP plots of oligodendrocyte subtypes. (C) Proportion of each oligodendrocyte subtype in the UL and control group. ULI: ipsilateral MVN of mice after unilateral labyrinthectomy; VN: ipsilateral MVN of mice after sham surgery.

3. Oligodendrocyte sub-clusters and functional analysis



Oligodendrocytes were reclustered into 7 subpopulations with different transcriptional features. Cluster 1-5, associated with cell proliferation, differentiation, and myelination, increased in the UL group. (A) UMAP plots of oligodendrocyte sub-clusters. (B) Proportion of each sub-cluster in the UL and control group. (C) Gene Ontology terms (GO) analysis of differentially expressed genes among sub-clusters.

4. OPCs proliferation in the MVN of UL mice



We observed an elevated expression level of Fyn in the UL group on the first day after surgery. The number of EDU-labeled Pdgfra (+) OPCs and CC1 (+) matured oligodendrocytes increased in the UL group seven days post-surgery, indicating that OPCs proliferation and differentiation were promoted. (A) The violin plots of gene expression level in three oligodendrocytic subtypes on the first day after surgery. (B) Western blot of Fyn levels in the ipsilateral MVN on the first day after surgery. (C) Confocal analysis of newly generated oligodendrocytes in the ipsilateral MVN seven days post-surgery.

Conclusion

Our findings reveal the adaptive changes of oligodendrocyte subtypes in the early vestibular compensation following peripheral vestibular damage, implicating the potential roles of oligodendrocytes in remodeling neural circuits to reverse behavioral deficits.

Reference

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