

Introduction

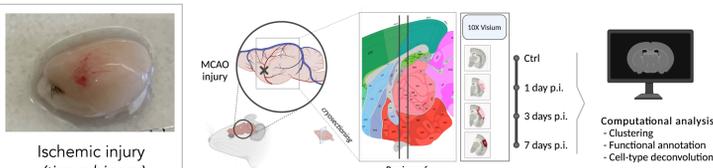
Ischemic stroke is a manifestation of reduced nutrition delivery to the brain due to impairment of the cerebral blood flow. It is a life-threatening neurological disease, with its risks underlying in the lack of efficient medication procedures and mechanistic understanding of the processes following the injury. In this study, we inspect the time-course of up to 7 days after the ischemic stroke in the mouse model of permanent middle-cerebral artery occlusion (pMCAO), mimicking the permanent clogging of major cerebral artery. The information from whole-transcriptome combined with the spatial component provides valuable insights into the anatomy of the ischemic injury, functional annotation of its processes and cell-type composition. With a follow up single-cell transcriptomic experiment, we identified key reactive glial subpopulations, which operate at the lesion border.

Impact

Goal of this study is to:

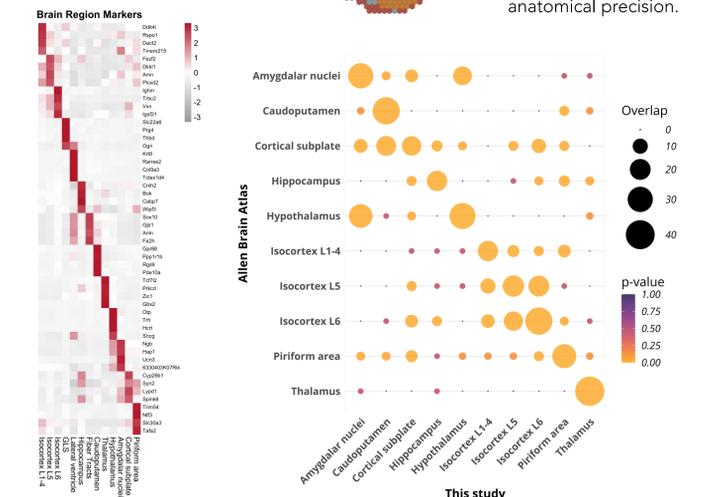
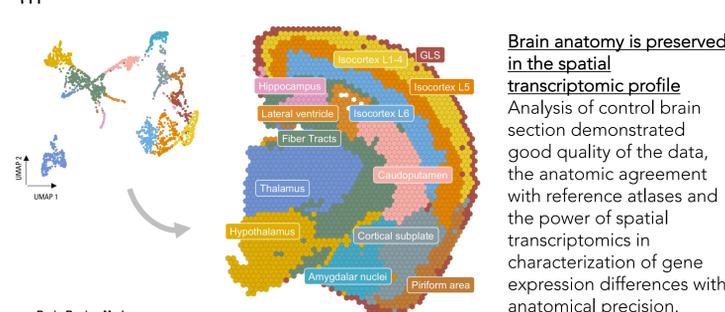
- Describe the change in gene expression landscape after the ischemic stroke, by transcriptome-wide analysis in tissue sections.
- Display similarities in glial response between acute brain injury and neurodegenerative disease through the lens of transcriptome response.
- Provide the scientific community with a high-quality resource revealing genome-wide transcriptomic changes during acute phase of ischemic brain injury.

Experimental design

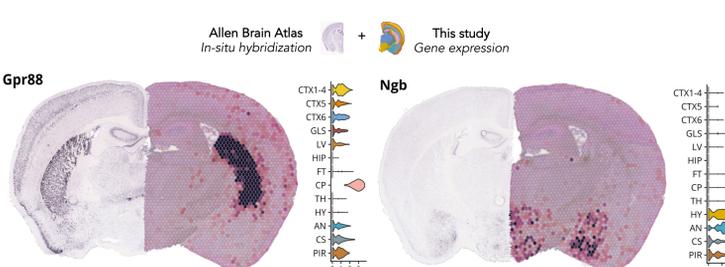


Mouse cerebra were collected in a timeseries of no injury (Ctrl), 1 day (D1), 3 days (D3) and 7 days (D7) after permanent middle cerebral artery occlusion (pMCAO) brain injury. Fresh frozen tissues were later cryo-sectioned to 10 μm thickness and processed on a 10X Visium platform. Similarly, mouse cerebra were collected and processed for single-cell RNA-Seq in a follow-up experiment. Data were processed using R package Seurat v4 (Hao et al., 2021). Brain regions were annotated with the help of Allen Brain Atlas – Mouse, P56.

Control mouse brain section

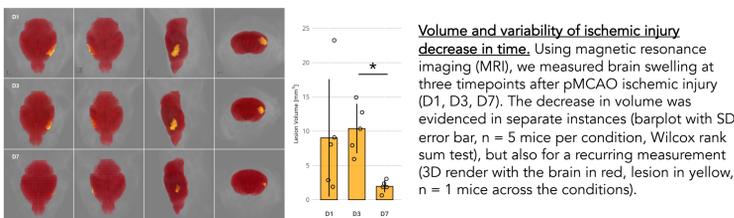


Allen Brain Atlas *In-situ* hybridization + This study Gene expression

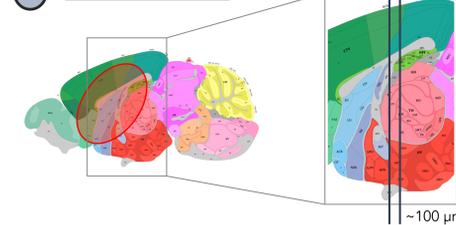


Ischemic stroke

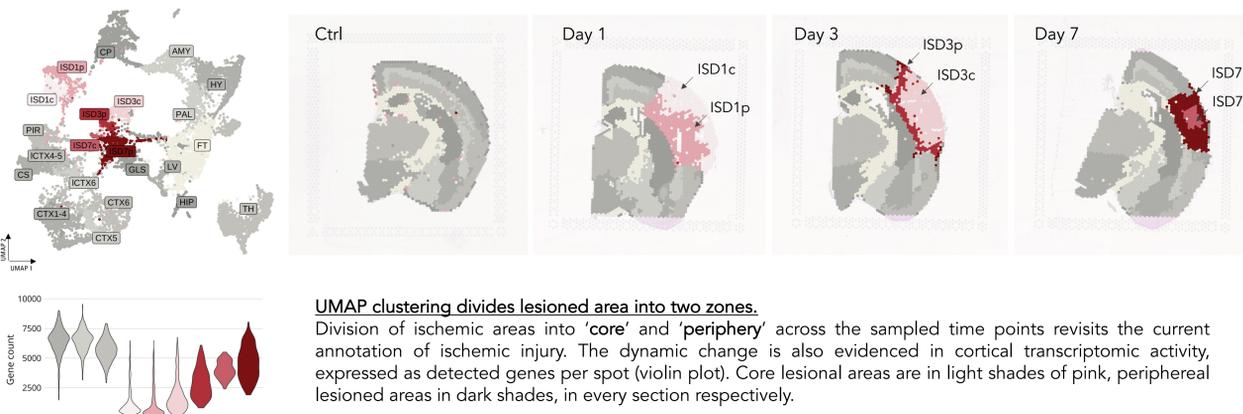
1 Assessing the variability of lesioned area volume



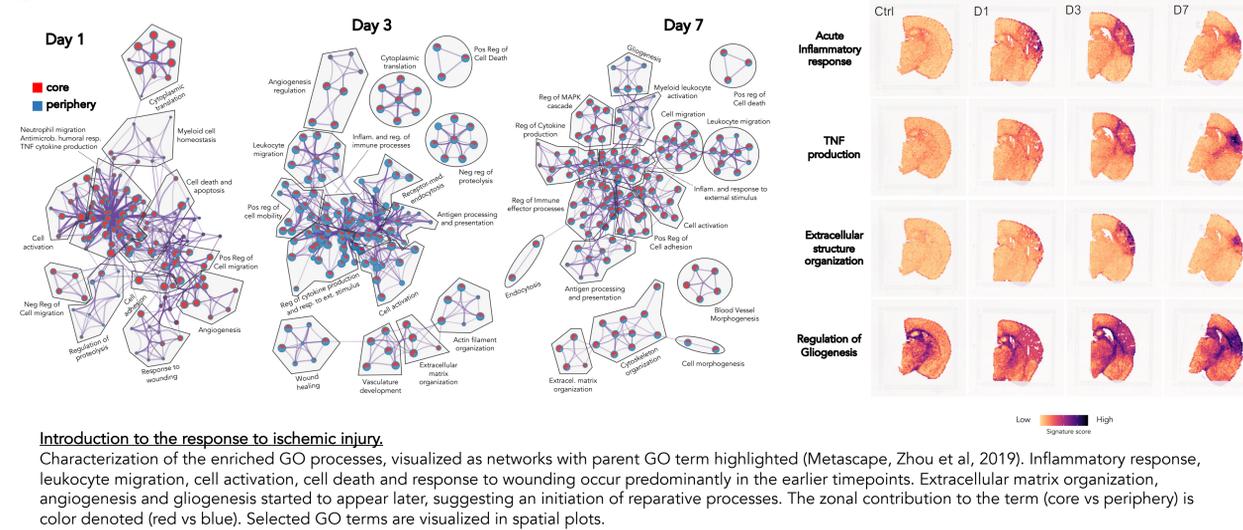
2 Section localization



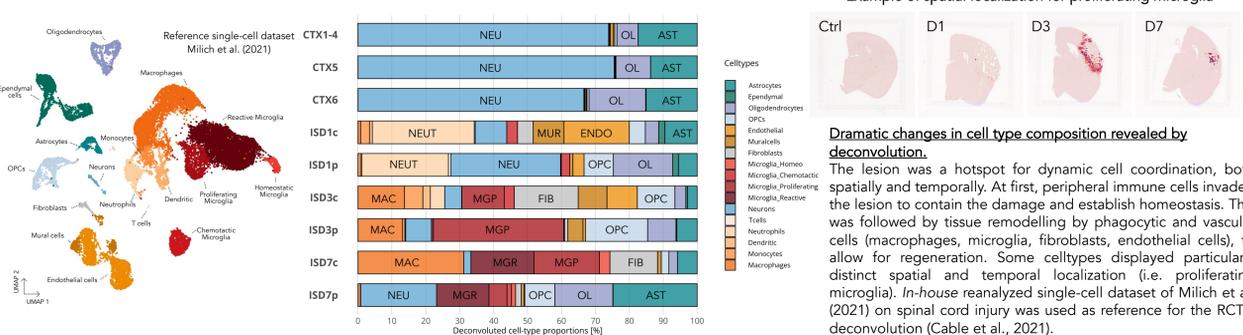
3 Disruption of the cortical gene expression landscape



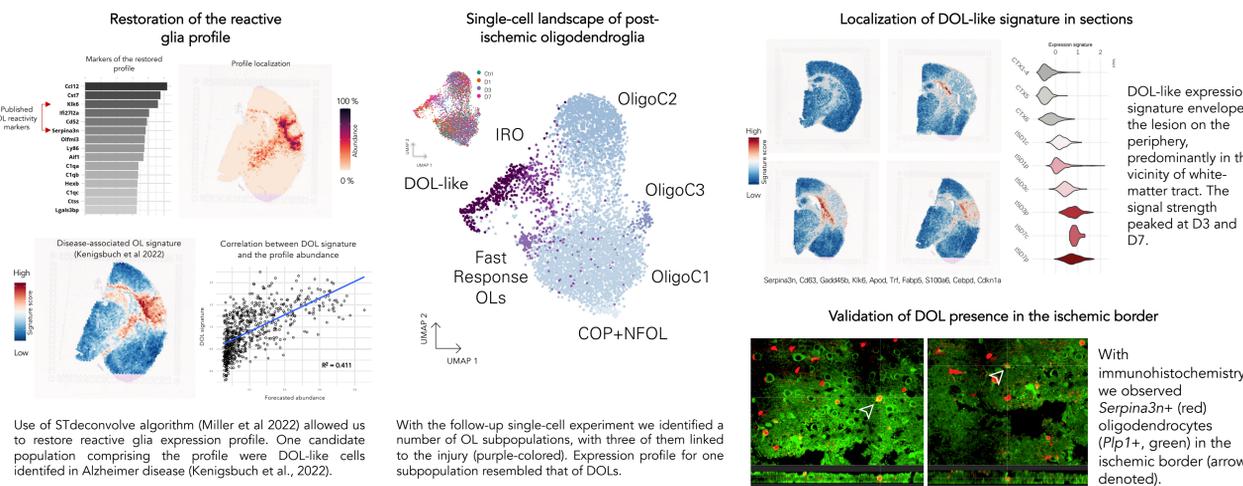
4 The networks of transcriptomic response



5 Deciphering of celltype response to injury



6 Characterization of reactive glia after the injury – demonstrated on oligodendrocytes (OLs)



References

Allen Brain Atlas, portal.brain-map.org
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