HALLMARKS OF CORTICOGENESIS AFTER ISCHEMIC STROKE IN MICE

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Background

Stroke represents the most common acute neurological condition leading to permanent disability, and as such a significant burden of disease in a modern aging society. Animal models of ischemic stroke mirror the postischemic changes at the molecular and cellular level, enabling the study of recovery mechanisms, that are presumably based on revoking the process of corticogenesis. The goal of this study was to identify the role of prominent markers of corticogenesis, SatB2 and Ctip2, in postischemic recovery.

Material & Methods

ANIMALS:

- male adult C57Bl6 mice (n = 14)

PROCEDURE:

- Transient middle cerebral artery occlusion (tMCAo, 9) vs sham surgery (5)
- Neurological Score (NS), day 3, 7
- 5 dosages of 5-bromo-2'-deoxyuridine (BrdU) after day 3
- 7T BioSpec MRI system brain MRI
- Immunofluorescence for SatB2, Ctip2, NeuN, cCASP3, DCX and BrdU
- Imaged cortex, hippocampus and striatum

Results

- The lesion was the largest on the Day 3 after tMCAo, and this was in positive correlation with the ND.
- IF signal of SatB2 and Ctip2 was significantly different between the IL and CL hemispheres of the tMCAo mice, and in comparison to the sham operated group.
- Amount of cells co-expressing both markers (S+C) increased after tMCAo, as well as the number of **BrdU** positive cells.
- GFAP has shown an astrocytic reaction, while the total number of neurons (NeuN) was impaired in IL hemisphere after tMCAO.

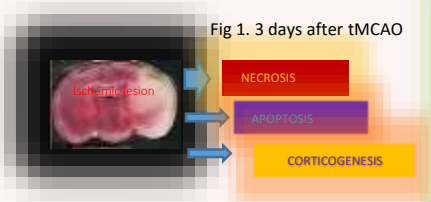


Fig 1. 3 days after tMCAO

Fig. 2. MRI after tMCAO

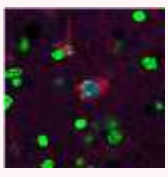
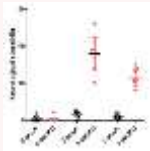


Fig. 3. IF 7 days after tMCAO, DCX in red, Ctip2 – Blue, DAPI-green

Fig. 4. NS 3 and 7 days after tMCAO (red), and sham surgery (black)



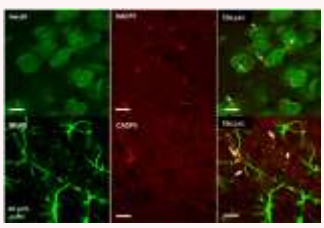


Fig. 5. NeuN, Casp3, and GFAP 4 days after stroke showing astrocytic reaction

Conclusion

- Subacute stage of ischemic stroke in mice includes increased proliferation of cells
- Changes in the neuronal cortical profiling (SatB2, Ctip2) resemble immature patters during corticogenesis.
- Modulation of those events could not only prevent the postischemic epileptogenic conversion, but also enhance the speed and quality of rehabilitation in affected patients.