New evidence of a different activation of astrocytes in LPS and MCAO gliosis mice model: a computational trascriptome analysis

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Abstract:

Reactive astrogliosis is a response of astrocytes to brain disease and injuries as ischemia, neurodegeneration and infection. Studies suggest a possible polarization of astrocytes induced by different stimuli. A classification in two phenotype was proposed: A1 after LPS stimuli with a detrimental phenotype and A2 after ischemia with neuroprotective effects. However, this simple classification does not summarize the heterogeneity of astrocytic responses. To better understand the divergence between LPS and ischemic stimuli, we analyzed gene expression data (from GEO database, GSE35338) of astrocytes taken from LPS-treated mice and mice with focal ischemic stroke produced by transient middle cerebral artery occlusion (MCAO) [Zamanian et al., 2012]. The authors of this study conducted a transcriptome analysis which led to the identification of a list of induced genes. We conducted a different analysis using a gene set analysis method (GSEA), which allowed us to identify pathway alterations capable of adding new information on phenotypic differences in the two gliosis status. Data suggest a different upregulation of nucleotide metabolism pathways, i.e., pathways concerning nucleotide catabolism and biosynthesis are respectively upregulated in the LPS and MCAO groups. Instead, TCA cycle and respiratory electron transport chain pathways are significantly downregulated at day-1 after MCAO, in contrast to what occurs in the LPS astrocytes groups and MCAO at day-3. Moreover, upregulation of biosynthesis of specialized pro-resolving mediators [Tiberi, 2021] in MCAO groups suggest that reactive astrocytes in ischemia exhibit a protective phenotype. Finally, analysis suggests that specific DNA repair (base excision repair and DNA double-strand break repair) and cell cycle pathways are upregulated predominantly after MCAO at day-3. In conclusion, this study highlights how different computational approaches may be helpful in refining and detailing experimental data.

References

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