Computational and experimental approaches reveal convergences and differences between mice LPS-MCAO astrogliosis and PBMC from Parkinson's disease patients

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Abstract: Neuroinflammation and dysmetabolism appear relevant pathogenetic mechanisms for neurological and neurodegenerative disorders, such Parkinson’s disease (PD), stroke, etc. Moreover, a better understanding of these pathologies should take into account the recent concept of a peripheral origin of brain diseases, i.e. the relevance of systemic inflammation and/or metabolic alterations, which are hallmarks of aging. On the other hand, this hypothesis inspires the urge of identifying peripheral biomarkers of brain disorders for early diagnosis, which would be fundamental for effective therapeutic interventions. We applied a gene set enrichment analysis method (GSEA) to compare transcriptomic datasets of astrocytes from mice treated with LPS or MCAO (GSE35338) and a dataset of PBMC from PD patients (GSE100054). We found that immune response and hemostasis are up-regulated both in LPS-MCAO models and in PD-PBMCs. Remarkably, GSEA revealed a convergence between LPS, MCAO and PBMC in terms of inflammatory components, such as upregulation of the inflammasome and cytokines receptors/signaling. This is a remarkable finding from a translational perspective, as we found an increase in Interleukin-6 receptor subunit beta Precursor (IL6ST) expression in our PD-PBMC samples, as compared to healthy subjects. Downregulation of TCA cycle and electron transport chain was instead peculiar of MCAO. However, similar changes might well be a consequence of the downregulated mitochondrial protein translation machinery found in the PD-PBMC dataset. In conclusion, the integration of computational analysis of pre-existing datasets by applying new computational tools, together with de novo experimental data, can be helpful in unraveling complex biological processes underlying multifactorial disorders. This is an example of how this strategy can be useful to solve a variety of biomedical problems and specifically find new possible pathogenetic aspects of neurodegenerative diseases and biomarkers of pathology.