METABOLOMICS REVEAL POTENTIAL BIOLOGICAL PATHWAYS INVOLVED IN STRESS-RELATED DISORDERS

Giovana Mezzomo[1,2], Tainá Schons[1,2], Pedro Henrique da Rosa[1,2], Gabriel Rocha[2], Paola Rampelotto Ziani[2], Rianne Remus Pucinelli[1,2], Laura Hoefel[2], Adriane Ribeiro Rosa[1,2,3]

[1.] UFRGS, Universidade Federal do Rio Grande do Sul, Porto Alegre - RS, 90035-003;
[2.] HCPA, Hospital de Clínicas de Porto Alegre, Porto Alegre - RS, 90035-903;
[3.] ICBS, Instituto de Ciências Básicas da Saúde, Porto Alegre - RS, 90035-003;

Stressful life experiences trigger biological and behavioral responses that increase the risk of developing stress-related disorders (SRDs), including major depressive disorder (MDD), bipolar disorder (BD), and post-traumatic stress disorder (PTSD). It is still unknown the underlying biological mechanisms of these disorders and identify new biomarkers may improve the diagnosis and the development of drugs tailored to specific biomarkers. The metabolome reflects the end products of genetic expression and serves as a direct signature of biochemical activity. With advancements in emerging mass spectrometry technologies, it is now possible to quantitatively measure thousands of metabolites from minimal amounts of biological material. This progress has enabled analyses at the systems biology level and holds the potential to significantly enhance the practice of precision medicine. Through the application of bioinformatics tools, we aim to explore metabolic pathways and biomarkers linked to MDD, BD, and PTSD, with the goal of gaining promising insights into the underlying pathophysiology. Metabolomics data from SRD patients blood, obtained using MS, were collected through systematic literature review. Metabolic pathway enrichment analysis and pathway topology analysis were performed using the MetaboAnalyst 6.0 computational platform ($p < 0.05$). Our analysis of differential metabolite enrichment revealed several differentially enriched pathways, including tryptophan metabolism, phenylalanine and tyrosine metabolism, malate-aspartate shuttle, catecholamine biosynthesis, citric acid cycle, glucose-alanine cycle, cysteine metabolism, Warburg effect, alanine metabolism, and glutamate metabolism. Pathway analysis highlighted phenylalanine, tyrosine, and tryptophan biosynthesis, citric acid cycle (TCA cycle), butanoate metabolism, alanine, aspartate, and glutamate metabolism, as well as glycolate and dicarboxylate metabolism as the main metabolic processes influenced by the identified metabolites. We identified significant associations with energy production, neurotransmission, and cellular function. Our results suggest that these pathways are involved in energy availability in nerve cells, impacting brain function and emotional balance. For a more comprehensive understanding, future studies should investigate these pathways as dynamic systems, rather than focusing solely on specific metabolites, in order to validate potential targets identified in SRDs.

Agradecimentos: