ABSTRACT

Charles University

Faculty of Pharmacy in Hradec Králové

Department of Pharmacology and Toxicology

Student: Anna Orbisová

Supervisor: Prof. PharmDr. František Štaud, Ph.D.

Consultant: Dr. Cilia Abad, Ph.D.

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Maternal inflammation throughout pregnancy has been firmly linked to the development of neuropsychiatric disorders in the offspring. Furthermore, intrauterine infections, whether viral or bacterial, are widely recognized as significant risk factors for conditions like autism and schizophrenia. Tryptophan metabolism has been suggested as a plausible pathway through which maternal inflammation during gestation can hinder fetal brain development and programming. This occurs as tryptophan is metabolized through the serotonin (5-HT) pathway, producing metabolites that exert direct effects on the development of the fetal brain. In this work, using an *ex vivo* model, we assess the impact of bacterial (LPS) and viral (poly I:C) placental infection on the 5-HT pathway. Human term placenta explants were treated with LPS or Poly I:C for different times (4 or 18 hours). Subsequently, the impact on gene and protein expressions of the key enzymes within the 5-HT pathway, along with their functional enzymatic activities, was assessed. Our results confirm that the expression and function of the main enzymes of the 5-HT pathway are affected by inflammation. Tryptophan hydroxylase (TPH), the first and rate-limiting enzyme for the 5-HT pathway, declined significantly at gene, protein as well as at functional levels in explants treated with LPS. Conversely, the gene expression of the 5-HT-metabolizing enzyme, monoamine oxidase A (MAO-A), was upregulated by inflammation. We conclude that placental inflammation impairs 5-HT homeostasis in the placenta and thus may affect the neurodevelopmental programming of the fetus.