ABSTRACT

Charles University in Prague, Faculty of Pharmacy in Hradec Králové
Department of Biochemical Sciences

University of Seville, Faculty of Pharmacy
Department of Biochemistry and Molecular Biology

Candidate: Karolína Veselá
Supervisors: Prof. Dr. José Luis Venero Recio, Prof. Ing. Vladimír Wsól, Ph.D
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Parkinson's disease (PD) is the second most common ageing-related neurodegenerative disorder after Alzheimer's disease and the prevalence in population is increasing. The characteristic movement disorder is caused by selective dopaminergic neurons loss, while the mechanism of this neurodegeneration is not well understood. Increasing evidence points out the key role of vicious cycle of microglial overactivation and oxidative stress, while the questions "where it begins" and „how to stop it" remain without clear answers. This thesis investigates implication of peripheral inflammation as a deteriorating circumstance and possible inductor of brain inflammation and progressive dopaminergic neurodegeneration. We use mice model of Parkinson's disease employing single intraperitoneal injection of toxin *N*-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) that induces specific degeneration of DA neurons and in contrast to other animal models, does not alter the integrity of blood-brain barrier (BBB) that is important in transmission of the peripheral inflammation to brain. Systemic inflammation is induced by intraperitoneal injection of lipopolysaccharide (LPS).

Our results show that peripheral inflammation triggers inflammation in brain, increases the activation of microglia and accelerate its onset, and exacerbates the dopaminergic neurodegeneration in substantia nigra caused by MPTP; all in absence of other BBB deleterious insult. Microglial activation appears earlier than loss of dopaminergic neurons, showing that overactivation of microglia is rather the cause than a consequence of neuronal death.