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Neonatal immune challenges affect behaviour, cytokine profiles and brain morphology parameters in adult rats

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Perinatal immune challenge can induce neurodevelopmental dysfunction, permanent immune dysregulation and abnormal behaviour which have been documented in clinic findings of human neuropsychiatric disorders. The aim of this study was to evaluate the response to an inflammatory stimulus in rats exposed to lipopolysacccharide (LPS) as a model of neonatal subchronic infectional stimulus (realized at postnatal days 5-9) on immune, neurodegerative and behavioural parameters, which may be relevant to human neurobiology. The series of molecules of interest leukotriene B_4 (LTB4), interleukine 4 (IL-4), interleukine 10 (IL-10) and tumor necrosis factor α (TNF $_{\alpha}$) were determined by metabolomic and proteomic techniques. An analytical method combining immunomagnetic separation with MALDI-TOF MS determination was used for the determination of protein biomarkers. The analysis of small molecule biomarkers (leukotriene B_4) was realized by LC-ESI-MS/MS. Our results showed that early immune stimulation evaluated in adult animals alters the levels of leucotrienes ((LTB4), IL4 and leads to neurodegenerative processes and behavioural deviations which are amplified by acute dopaminergic or glutamatergic stimulation. Leucotrienes (LTSB4) and cytokine IL4 were elevated in LPS rats acute exposed to MK-801 or to GBR 12909. Moreover, the behavioral observations documented hyperlocomotion, impairment of prepulse inhibition and cognitive deficit in LPS rats injected with acute NMDA antagonist (i.e., MK-801) or dopamine releaser (GBR 12909). These findings support the crucial pathophysiological role of early immune stimulation in many neuropsychiatric disorders (e.g., schizophrenia, autism).

Biography

Hana Tejkalová completed her PhD from Faculty of Science, Charles University in Prague. She is a Senior Researcher at National Institute of Mental Health (NIMH). She has published nearly 50 papers in reputed journals (total citations 166). Her research activities involve "The use of behaviour in the animal modelling of psychiatric disorders, especially schizophrenia". She also acted as the Czech representative in FELASA from 2010 until 2014".

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