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Learning deficit and altered *MMP9* and *TIMP1* gene expression in adult rats exposed to bacterial endotoxin during early postnatal development

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Perinatal brain pathologies are known to impair the development of CNS functioning and are involved in the etiology of chronic cognitive dysfunction. These pathological conditions are associated with high production of pro-inflammatory cytokines by the cells of the immune and nervous systems. It is well established that neurons express receptors for pro-inflammatory cytokines, which provides evidence for the functioning of cytokines as neuromodulators. However, the exact molecular and cellular mechanisms of cytokines in the impairment of brain development have not yet been fully elucidated. To address this question, we studied the expression of neuroplasticity-regulating genes matrix metalloproteinase-9 (*MMP9*) and tissue inhibitor of metalloproteinases-1 (*TIMP1*) in the medial prefrontal cortex and dorsal and ventral hippocampus. Wistar rat pups were treated with lipopolysaccharide (LPS; 25 μg/kg), an inducer of pro-inflammatory cytokine synthesis, during the 3rd week of postnatal life. Adolescent and adult LPS-treated animals demonstrated increased anxiety-like behavior and decreased exploratory behavior in the open field arena. Impaired learning in the active avoidance task and Morris water maze was also observed. Gene expression of *MMP9* and *TIMP1* was differentially altered in the cortex and hippocampus of pups vs. adult untrained rats and remained unchanged in rats trained in either learning task, revealing that prolonged pro-inflammatory challenge during early postnatal development negatively affects the plasticity factors involved in memory acquisition in adulthood. These results suggest that an increase in cognitive stimulation might be an effective approach to reduce the negative effects of neonatal immune challenges on brain functioning.

Biography

Alexander Nikolaevich Trofimov is a Research Fellow and pursuing his PhD at the Institute of Experimental Medicine, Saint Petersburg, Russia. He has completed his BSc and MSc degrees in 2009 and 2011, respectively from Saint Petersburg State University, Russia. His work focuses on the investigation of molecular and cellular mechanisms in the context of immune activation in CNS functioning and in impaired brain development.

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