59. A role for high mobility group box-1 protein as an endogenous inflammatory mediator in the rat brain

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Recently, a role for the alarmin high mobility group box-1 protein (HMGB-1) has been proposed as a late mediator of experimental sepsis. Here, we aimed to further elucidate its role as an endogenous inflammatory mediator in the brain. Rats received an intraperitoneal injection of a septic-like dose of lipopolysaccharide (LPS, 10 mg/kg) and HMGB-1-mRNA-expression and -release was measured in the brain and periphery by RT-PCR, immunohistochemistry and ELISA. Moreover, we investigated the inflammatory potential and the direct action of HMGB-1 on brain cells in primary neuroglial cell cultures of the area postrema and the hypothalamic paraventricular nucleus, brain structures known to be involved in inflammatory signal-processing. We observed an increase of HMGB-1 in serum samples 8 and 24 h after injection with LPS, compared to PBS-injected controls. In hypothalamic tissue, we found HMGB-1-mRNA levels to be basal after LPS injection but immunohistochemical analyses revealed that nuclear hypothalamic HMGB-1-signals decreased and cytoplasmatic signals occurred (24 h), suggesting its local release. *In vitro*, neuroglial-cells were directly activated by recombinant (r) HMGB-1, as shown by increases of intracellular Ca2+-concentration (calcium-imaging), nuclear factor kappaB translocation and induction of cytokines. Overall, our results substantiate the hypothesis that HMGB-1, released locally within the brain or derived from the circulation, is involved in signaling processes in the brain during LPS-induced inflammation via direct action on brain cells and induction of inflammatory mediators including cytokines.

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60. Nuclear factor interleukin 6 deficient mice show alterations in the stress-axis and the serotonin metabolism

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The transcription factor nuclear factor interleukin-6 (NF-IL6) has previously been proposed to be involved in stress-responses. Stress is also known to influence the serotonin system, which is important for the development of depressive disorders. Here, we aimed to further investigate the role of NF-IL6 on the stress-axis and the melatonin system using NF-IL6 deficient mice (NF-IL6KO). NF-IL6KO and wildtype mice (WT) were psychologically stressed with a novel environment followed by immunological stress (2.5 mg/kg Lipopolysaccharide, LPS) a few days later. Motor activity was measured by a telemetric system; 8 or 24 h later animals were sacrificed, brains and blood samples collected and analyzed using RT-PCR and ELISA. NF-IL6KO showed dramatically reduced activity under basal or LPS-stimulated conditions but enhanced activity in response to psychological stress compared to WT. These findings were accompanied by reduced proopiomelanocortin expression 8 h after LPS-stimulation and an abolished day-night-rhythm in corticosterone plasma levels in NF-IL6KO. In addition, NF-IL6KO showed reduced expression of the indolamine-2,3-dioxygenase 8 h after LPS-stimulation, while tryptophan hydroxylase 2 was enhanced; both known as major enzymes for serotonin metabolism. Moreover, expression of the serotonin transporter was enhanced basally and after LPS-stimulation. Overall, we strengthened the implication of NF-IL6 in stress-responses and showed, for the first time, that NF-IL6 seems to be involved in serotonin metabolism. Thus, modulation of NF-IL6-activity might have therapeutic potential for stress- or depressive disorders.

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61. *Toxoplasma gondii* seropositivity is positively associated with anxiety and burnout-syndrome

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Toxoplasma gondii (TOX) is a common parasite affecting approximately one-third of the human population, primarily targeting neurons and causing neuroinflammation. An increasing number of studies are providing evidence that the disease is associated with behavioural changes and psychiatric disease. The objective of this study is to examine TOX seropositivity in a large human population in relation to psychiatric symptoms. A population of 548 participants was initially included and the participants went through a semi-structured diagnostic interview (SCAN interview) followed by blood sampling. From this population, a control group ($n = 158$) with no diagnosis of psychiatric disorders was extracted as well as a group consisting of subjects showing symptoms of anxiety ($n = 106$) and burnout syndrome ($n = 51$). Blood serum was examined for IgG antibodies to TOX using ELISA assays. Data were analysed using logistic regression models and show that seropositivity of TOX is positively associated with anxiety (adjusted odds ratio [OR]=2.05; 95% CI, 1.14–3.70; $p = 0.016$). In addition, we find an association between seropositivity and burnout syndrome (OR = 3.43; 95% CI, 1.67–7.05; $p < 0.001$). These data supports the notion that TOX is associated with psychiatric disorders. Our results are consistent with previous reports on an association between TOX and anxiety. Furthermore, we show a positive association between TOX seropositivity and the stress related syndrome, burnout syndrome.

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62. Chronic LPS administration induces prolonged sickness behavior in rats

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Background: Acute inflammation produces an adaptive motivational state termed sickness behavior, to cope with inflammatory mediators and the subsequent negative energy balance. This response is short acting, whereas prolonged sickness behavior