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Titolo Cytokines as players of neuronal plasticity and sensitivity to

environment in healthy and pathological brain / / Silvia Alboni and

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Sommario/riassunto It is now accepted that immune molecules are not only present within

the brain during pathology but they exert physiological functions in the "healthy" brain as well. Increasing evidence points to a neuromodulatory role of cytokines and chemokines (CHEMOtactic cytoKINES) in basal transmission and plasticity processes where signaling between peri-synaptic astrocytes, microglia and neurons plays an important role. Nevertheless, the exact mechanisms as to how cytokines, and in particular chemokines, participate in the molecular and cellular processes thought to subserve memory formation, plasticity processes and responsiveness to environmental stimuli remain to be clarified. Interestingly, in in vitro preparations, molecules like TNF-a, interleukin (IL)-1ß, IL-6, CX3CL1, CXCL12, CCL2 and CCL3 are implicated in synaptic formation and scaling, in modulation of glutamatergic transmission, in plasticity and neurogenesis, in particular in the hippocampus. The hippocampus is an extremely plastic structure, one of the main neurogenic niches in the adult brain, that exhibits a marked sensibility to environmental stimuli. Indeed exposure of mice to environmental enrichment (EE) modifies learning and memory

abilities increasing neurogenesis and neuronal plasticity whether exposure to severe stressful experiences diminishes neurotrophic

support, impairs neurogenesis, plasticity and cognition. In the hippocampus cytokines play a key role in mediating both positive as well as negative effects of the environment affecting neuronal plasticity also in stress related pathologies, such as depression. It has been reported that mice lacking type 1 receptor for IL-1 display impaired hippocampal memory and LTP that are restored by EE; moreover negative effects on neuronal plasticity (and thus behavior) induced by stress exposure can be prevented by blocking IL-1 activity. In addition, mice lacking IL-6 have improved cognitive functions whereas the absence of microglia-driven CX3CR1 signaling increases hippocampal plasticity and spatial memory occluding the potentiating effects of EE. However, the factors mediating the effect of environmental stimuli on behavior and plasticity has been only partially identified. Interestingly, it has been suggested that chemokines can play a key role in the flexibility of hippocampal structure and may modulate neuronal signaling during behavior. The question is how cytokines may translate environmental stimuli in plasticity and behavioral changes. This research topic is proposed to explore the role of cytokines, and more in particular chemokines, in the modulation of neuronal activity as a fundamental step for the correct brain wiring, function and susceptibility to environment. We encourage the submission of original research reports, review articles, commentaries, perspectives or short communications, in the following (but not limited to) topics: - Role of cytokines and chemokines in neuronal plasticity - Immune molecules and responsiveness to environment - Role of chemokine in the flexibility of hippocampal structure