Les chimiokines dans le cerveau: des Janus moléculaires contrôlant l'activité neuronale ? The brain chemokines: molecular Janus controling neuronal activity ?

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Following inflammation, cytokines are released in the blood. Besides their effect on the immune system, cytokines can also act on the brain to modulate our behaviors, inducing either obesity (under low-grade inflammation) or anorexia (under high grade inflammation). I will present our current knowledge on how cytokines can influence the brain and feeding behavior through several possible pathways: modulating peripheral neurons which project to the brain through the vagal nerve, modulating the levels of hormones such as leptin which can act to the brain through the humoral pathway and possibly acting directly in the brain, through the local production of cytokines/chemokines. In particular, the chemokines CXCL12/SDF-1α, CCL2/MCP1 and CCL5/RANTES and their cognate receptor are co-expressed in many neuronal populations. We have investigated the actions of these chemokines on neuronal excitability in a neuronal population linked to feeding behavior/energy homeostasis control, i.e. the melanin concentrating hormone (MCH) neurons of the lateral hypothalamus. These chemokines can modulate the activity of the MCH neurons by multiple regulatory pathways including and often combining: i) modulation of voltage-dependent channels (sodium, potassium and calcium), ii) activation of the G-protein activated inward rectifier potassium (GIRK) current, iii) increase in neurotransmitter release (GABA, glutamate, dopamine), often via calcium-dependent mechanisms. The possible mechanisms underlying these effects and their consequences in terms of physiopathology of neuroendocrine systems involved in feeding behavior and body weight regulation will be discussed.

Financial supports from the CNRS, ARC, FRM and Société Française de Nutrition.