

Neuronal ferritin heavy chain and opiate abuse affect HIV-associated cognitive dysfunction



The chemokine CXCL12 and its cognate receptor CXCR4 perform multiple functions essential for CNS development and function. The importance of these functions are further highlighted within the context of neuroinflammatory disease, as the CXCL12/CXCR4 signaling axis aids recovery. Among the numerous causes of neuroinflammatory disease, CXCR4 dysfunction may be particularly relevant in the context of HIV-associated neurocognitive disorders (HAND). Due to its role as an HIV coreceptor and its expression in both neuronal and non-neuronal cells. The neuropathology of HAND is complex, and is associated with elevation of inflammatory cytokines, neuronal loss and decreased synaptic density. Furthermore HAND is both accelerated and complicated by the frequent comorbidity of illicit drug abuse, primarily intravenous opiate abuse. Clinical studies have found that compared with non-drug-abusing HIV patients, drug-abusing HIV patients exhibited complications including increased HIV encephalitis frequency and increased blood-brain barrier disruption. u-Opioid

agonists have been shown to specifically elevate neuronal levels of the protein ferritin heavy chain (FHC), which negatively regulates CXCR4 signaling and affects the neuroprotective function of the CXCL12/CXCR4 axis. This study determined that CXCL12/CXCR4 activity increased dendritic spine density, and also examined FHC expression and CXCR4 status in opiate abusers and patients with HAND. They found that drug abusers and HIV patients with HAND had increased levels of FHC, which correlated with reduced CXCR4 activation, and deregulated CXCR4 signaling. Furthermore, they found that FHC contributed to morphine-induced dendritic spine loss. Thus implicating FHC-dependent deregulation of CXCL12/CXCR4 as a contributing factor to cognitive dysfunction in neuroAIDS and disclosing a novel mechanism in the neuropathogenesis and neurocognitive impairment seen in drug-abusing HIV patients.

[Pitcher, J. et al. 2014. Neuronal ferritin heavy chain and drug abuse affect HIV-associated cognitive dysfunction. *The Journal of Clinical Investigation*.](#)