

HIV GP120 protein increases the function of connexin 43 hemichannels and pannexin-1 channels in astrocytes: Repercussions on astroglial function

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At least half of human immunodeficiency virus (HIV)-infected individuals suffer from a wide range of cognitive, behavioral and motor deficits, collectively known as HIV-associated neurocognitive disorders (HAND). The molecular mechanisms that amplify damage within the brain of HIV-infected individuals are unknown. Recently, we described that HIV augments the opening of connexin-43 (Cx43) hemichannels in cultured human astrocytes, which result in the collapse of neuronal processes. Whether HIV soluble viral proteins such as gp120, can regulate hemichannel opening in astrocytes is still ignored. These channels communicate the cytosol with the extracellular space during pathological conditions. We found that gp120 enhances the function of both Cx43 hemichannels and pannexin-1 channels in mouse cortical astrocytes. These effects depended on the activation of IL-1 β /TNF- α , p38 MAP kinase, iNOS, cytoplasmic Ca²⁺ and purinergic signaling. The gp120-induced channel opening resulted in alterations in Ca²⁺ dynamics, nitric oxide production and ATP release. Although the channel opening evoked by gp120 in astrocytes was reproduced in ex vivo brain preparations, these responses were heterogeneous depending on the CA1 region analyzed. We speculate that soluble gp120-induced activation of astroglial Cx43 hemichannels and pannexin-1 channels could be crucial for the pathogenesis of HAND. © 2020 by the authors. Licensee MDPI, Basel, Switzerland.

Astrocyte

Connexins

Cx43 hemichannels

Glia

Gp120

HIV

cation channel

connexin 43

glycoprotein gp 120

interleukin 1beta

mitogen activated protein kinase

mitogen activated protein kinase p38

nitric oxide

pannexin 1 channel

probenecid

tumor necrosis factor

unclassified drug

animal cell

animal experiment

animal model

Article

astrocyte

cell body

cell culture

confocal microscopy

controlled study

hippocampus

HIV associated dementia

human

human cell

Human immunodeficiency virus infection

immunofluorescence test

incidence

macroglia

male

mouse

nerve function

neuropathology

nonhuman

protein expression

time lapse imaging