TÍTULO

THE HIV-1 GP120 NEUROTOXICITY ASSOCIATED TO AFFECTIVE DISORDERS

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RESUMO

The current work emphasizes the revision of the role of gp120 in brain neurotoxicity and the mechanisms to neurological disorders development. Envelope proteins gp120 and gp41 play critical roles in the infection and entry processes of HIV. The first step in the HIV entry process is initiated by the binding of HIV gp120 to CD4 on the target cell surface. HIV-1 infects T cells through CD4 receptor, then virus membrane glycoprotein gp120 and CD4 binding triggers conformational changes in gp120 that enable it to interact with chemokine co-receptors CXCR4 (X4) or CCR5 (R5) and in some cases, both of them, resulting in membrane fusion and viral entry. After entry process of HIV, two proteins associated with the AIDS virus, gp120 and Tat are responsible for triggering neurotoxic effects. Gp120 has been correlated with neurotoxin production by mononuclear cells like macrophages and microglia, as well as in the pathogenesis of HIV-1–associated neurocognitive disorders (HAND) that appears due to the neurotoxicity and inflammatory disorders such as encephalitis. Interaction of glycoprotein gp120 with CXCR4 chemokine receptor causes caspase-3-dependent apoptosis and ceramide release, activating apoptotic proteins p53 and retinoblastoma. In brain-derived cells, gp120 is responsible for initiate signaling cascade that involves p38 mitogen-activated protein kinase and leads to neuronal cell death. On the other hand, Tat produces dendritic loss by interacting with the low-density lipoprotein receptor (LRP) and also overstimulates N-methyl D-aspartate receptors. Finally, central nervous system affected by HIV infection results in HIV associated HAND that is characterized by depression, behavioral and motor dysfunctions. In conclusion, studies are needed to understand the potential effects of cure strategies on the nervous system and so the affective disorders associated to HIV-1 neurotoxicity.