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Review Article

Neuropathogenesis of HIV-1-associated neurocognitive disorders: a possible involvement of D-serine

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Abstract: A unique feature of N-methyl-D-aspartate receptors (NMDARs) that distinguishes them from other ionic receptors is that their activation requires more than one agonist to bind simultaneously to distinct binding sites on the receptor. D-serine, a co-agonist binding to the glycine site of NMDARs, has been implicated in several NMDAR-dependent physiological processes, and altered D-serine levels under certain pathophysiological conditions contribute to neural dysfunction via NMDARs in the central nervous system. Entry of HIV-1 in the brain causes neuronal injury leading to cognitive, behavioral and motor impairments known as HIV-associated neurocognitive disorders (HAND). As HIV-1 does not infect neurons, neuronal injury is believed to be primarily mediated by an indirect mechanism, that is, HIV-1-infected and/or immune-activated macrophages and microglial cells release soluble molecules leading to neuronal injury or death. Among the soluble factors is D-serine. In this article we try to address recent progresses on the role D-serine might play in the pathogenesis of neurodegenerative disorders with a particular emphasis of the involvement of D-serine in HIV-1-associated neurotoxicity. (IJPPP1305001).

Keywords: D-serine, D-amino acids, NMDA receptors, glycine site, neurodegeneration, central nervous system

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