INTERACTIONS BETWEEN HIV-1 VIRAL PROTEINS AND GLUTAMATE RECEPTORS: ROLE IN NEUROAIDS

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Neurological manifestations and decline in neuropsychological performances are threatening complications of HIV-1 infections. Although their incidence has decreased among people who have access to antiretroviral treatments, the cumulative prevalence has actually risen because of the improved survival in AIDS. Unfortunately, the molecular events involved in the onset of central deficits have not been so far identified. HIV-1 virus can enter Central Nervous System (CNS) and affects physiological neuronal functions either *directly*, by altering the normal neuronal network or *indirectly*, by causing immunodeficiency, with resultant susceptibility to opportunistic infections. As to the *direct* effect, the finding that the virus cannot infect neurones seems to imply that molecular events other than the infectious ones are possibly involved in central effects. It is widely accepted that proteins shed by the virus, such as the envelope glycoprotein gp120 and the non-structural viral protein Tat, may themselves cause alterations to CNS. By one side, viral proteins are toxic to neurones, because of their ability i) to act as excitotoxins and ii) to evoke the release of endogenous neurotoxins and/or pro-inflammatory cytokines. By the other side, evidences are emerging that viral components can alter neuronal functions, either by modifying the release of neurotransmitters or by influencing the functions of classical receptors controlling central neurotransmission. We will summarize results concerning the effect of viral proteins and pro-inflammatory chemokines on central neurotransmission. In particular we will discuss recent results concerning the role of glutamate receptors in mediating the effects of the viral proteins gp120 and Tat on the release of neurotransmitters from human and rodent isolated nerve terminals. Granted by MIUR and ISS