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HIV: Current Research

Commentary

Neurocognitive Decline in HIV Positive Individuals through Pathophysiology and Prevention

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DESCRIPTION

HIV infection, once primarily regarded as an immunological disease, is now recognized for its broader systemic impact, particularly its effects on the Central Nervous System (CNS). Despite advancements in antiretroviral therapy (ART), neurocognitive decline remains a significant concern among HIV-positive individuals, affecting quality of life and functional capacity. HIV-associated neurocognitive disorders (HAND) range in severity from asymptomatic neurocognitive impairment (ANI) to HIV-associated dementia (HAD), and continue to affect nearly 30%–50% of people living with HIV (PLWH), even in the ART era. Understanding the underlying pathophysiology and exploring avenues for prevention is crucial for comprehensive HIV care.

The pathophysiology of HIV-related neurocognitive decline is multifaceted. HIV does not directly infect neurons but invades the CNS early after infection by crossing the Blood-Brain Barrier (BBB) via infected monocytes often referred to as the "Trojan horse" mechanism. Once inside the CNS, the virus targets microglia and macrophages, leading to persistent inflammation, release of neurotoxic viral proteins (such as gp120 and Tat), and neuronal injury. Chronic immune activation and inflammation are central to the neurodegenerative processes observed in HAND. Furthermore, the persistence of viral reservoirs in the brain, despite systemic viral suppression with ART, contributes to ongoing CNS damage.

Another contributing factor is the role of comorbidities and aging. As HIV-positive individuals live longer due to effective ART, age-related neurodegenerative processes may intersect with HIV-related neuronal stress, amplifying cognitive decline. Conditions such as cardiovascular disease, diabetes, depression, and substance use disorders further exacerbate this vulnerability. Additionally, certain ART drugs themselves may have neurotoxic effects or limited CNS penetration effectiveness (CPE), which affects their capacity to suppress viral replication within the brain.

Neuroimaging studies and cerebrospinal fluid (CSF) biomarkers have enhanced our understanding of HIV-related brain changes. Structural imaging often reveals cortical thinning, white matter abnormalities, and reduced subcortical volumes in affected individuals. Functional imaging studies show altered connectivity patterns in key cognitive networks. Biomarkers such as neurofilament light chain (NfL), beta-2 microglobulin, and neopterin levels in CSF provide insights into ongoing neuroinflammation and axonal damage, serving as potential tools for early diagnosis and monitoring of HAND.

Preventive strategies must address both virological and non-virological components of neurocognitive decline. Optimal ART initiation remains the cornerstone of prevention, with evidence supporting the benefits of early treatment in reducing CNS viral load and inflammation. ART regimens with high CPE scores should be considered in patients with or at risk for HAND, ensuring better penetration and suppression of HIV in the CNS. However, the choice of ART must be balanced against potential neurotoxicity, necessitating individualized treatment planning.

In addition to virological control, adjunctive therapies targeting inflammation, oxidative stress, and neuroprotection are under investigation. Agents such as minocycline, statins, and anti-inflammatory cytokines have shown promise in preclinical models, though results from clinical trials have been mixed. Cognitive rehabilitation and lifestyle interventions such as regular physical activity, cognitive training, dietary modifications, and psychosocial support have also demonstrated efficacy in mitigating cognitive impairment and improving mental well-being in HIV-positive populations.

Regular neurocognitive screening is essential for early detection and management of HAND. Tools such as the International HIV Dementia Scale (IHDS), Montreal Cognitive Assessment (MoCA), and computerized cognitive testing platforms allow for routine monitoring in clinical settings. Integrating mental health services and neurologic assessments into HIV care frameworks, particularly in resource-limited settings, is vital for holistic management. Multidisciplinary care models involving infectious disease specialists, neurologists, psychologists, and social workers offer the best outcomes in managing HAND.

In the Finnish healthcare system, known for its integration and accessibility, addressing the neurocognitive effects of HIV has

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gained increasing attention. National guidelines now recommend routine cognitive screening for all individuals diagnosed with HIV and advocate for early ART initiation regardless of CD4 count. Research efforts in Finland are also focusing on the neurobiology of HAND, aiming to identify population-specific risk factors and therapeutic targets.

In conclusion, neurocognitive decline in HIV-positive individuals remains a pressing challenge despite virological control achieved through ART. The pathophysiology involves complex interactions between viral persistence, inflammation, and host factors, necessitating a multifactorial approach to prevention and treatment. Early ART initiation, tailored therapy with CNS-penetrant drugs, lifestyle modifications, and cognitive support interventions are crucial elements in managing HAND. As global HIV populations continue to age, understanding and addressing neurocognitive outcomes will be critical to improving long-term quality of life and ensuring that the neurological burden of HIV does not undermine the remarkable gains achieved in its systemic management.