

**Comment:****Getting a handle on HAND in the era of cART**

Despite the effectiveness of combined antiretroviral therapy (cART) in suppressing HIV viral load and reducing cognitive impairment,<sup>1</sup> for many chronically HIV-infected people, neurocognitive dysfunction remains a common problem, as several recent studies continue to show persistence and progression of cognitive impairment and brain injury.<sup>2,3</sup>

The study by Sacktor and colleagues<sup>4</sup> further supports the importance of this problem but also highlights some interesting differences. In the Multicenter AIDS Cohort Study (MACS), HIV-associated neurocognitive disorder (HAND) occurred in 25%–33% of participants—a rate somewhat lower than that observed in other recent studies (e.g., approximately 40%–50% in CNS HIV Antiretroviral Therapy Effects Research [CHARTER] and HIV Neuroimaging Consortium [HIVNC]),<sup>2,5</sup> probably reflecting demographic and clinical differences among these cohorts. These include less racial-ethnic diversity, less baseline disease severity (e.g., higher nadir CD4), and a greater proportion of gay/bisexual men than people with substance abuse in the MACS, which may also partially explain the lower progression rate. The mean age of the cohort (46 years) may also have some bearing on this issue, as declines in learning and memory may occur primarily among HIV-infected people over 55 years of age, whereas seronegative adults in this age range tend not to exhibit substantial declines.<sup>6</sup> As progression between HAND stages requires a discrete shift between diagnostic categories that partly depends on the determination of activities of daily living impairment, it is possible that a proportion of the cohort may have experienced subtle cognitive and functional declines that do not manifest as a shift in HAND severity in the short term.

Despite these limitations, the MACS study adds to a growing body of evidence for the persistence and progression of HAND in the cART era. As pointed out by the authors, further research is needed to evaluate these problems over a longer time period and the mechanisms underlying their persistence.

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