CHARTER Study: Asymptomatic Cognitive Problems 'Harbinger' for Future Neurologic Decline

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Numerous studies have noted increasing rates of neurological disorders in people living with HIV, but many of the cases included in these findings involve patients with cognition problems that don't affect daily functioning—data often dismissed as being statistical artifacts or meaningless measurements. However, new data presented at the 19th Conference on Retroviruses and Opportunistic Infections in Seattle suggest they are clinically important and predictive of worsening symptoms.

According to study presenter Robert Heaton, MD, of the University of California at San Diego, HIV-associated neurocognitive disorders (HAND) have been reported in up to half of people living with HIV, despite use of combination antiretroviral therapy. The most common HAND diagnosis is asymptomatic neurocognitive impairment (ANI)—signs of cognitive impairment, but without deficits in functioning—occurring in 33 percent of HAND cases, according to a 2010 report.

Heaton noted, however, that there are lingering questions regarding ANI diagnoses, notably: Since ANI does not affect everyday function, is it relevant? Does it have concurrent or predictive validity?

In an effort to provide answers, Heaton and his colleagues examined data from the CHARTER study, one of the world's largest and most intensive studies on the cognitive effects of HIV. Specifically,

Heaton's team examined the records of 347 participants followed for an average of 45 months and for up to 90 months. Included in the analysis were 226 "neurocognitively normal" (NML) people living with HIV—those without documented cognitive or functional impairments—and 121 ANI cases. All participants completed a battery of neuromedical, laboratory, neurocognitive evaluations, along with self-report and performance-based measures of everyday functioning approximately every six months.

Ages averaged 43 in the NML group and 45 in the ANI group. Slightly more than 80 percent of both groups were male, roughly half were white, and roughly 70 percent had a history of illicit drug use. ANI subjects tended to be slightly better educated and were also more likely to have a

comorbidity, such as viral hepatitis coinfection.

Heaton also noted that more than half of patients in both groups had a history of an AIDS diagnosis. Average CD4 cell counts were above 400 at the start of the analysis, with no significant difference between the two groups, but those in the ANI group were significantly more likely to have a lower lowest-ever (nadir) CD4 count compared with those in the NML group (162 versus 201 cells, respectively).

The CHARTER volunteers included in the analysis had been on ARV therapy for an average of 10 years.

Looking solely at self-reported measures of function impairment—including memory, language and cognition complaints, along with problems completing basic tasks such as housekeeping, cooking and managing finances—Heaton's group found that individuals with ANI were significantly more likely to progress to symptomatic HAND (noticeable worsening of cognition and functioning) compared with those in the NML group. Among those with ANI, the relative risk of progressing to symptomatic HAND during 80 months (6.6 years) increased roughly 130 percent.

After looking at performance-based functional impairment data—structured tasks related to medication management (for example, placing pills in a pill organizer according to a prescription schedule) and work—Heaton's group again found that ANI study volunteers were significantly more likely to progress to symptomatic HAND compared with NML patients. Here, the relative risk of developing symptomatic HAND after receiving a diagnosis of ANI increased nearly 400 percent during a 90-month period (7.5 years).

Even after adjusting the data for demographic differences—such as education level, reading scores and comorbidities—the relative risk increases were more or less the same: Both self-report and performance-based measures indicated that those diagnosed with ANI were significantly more likely to develop symptomatic HAND over the follow-up period.

As for demographic predictors, Heaton reported that those who progressed to symptomatic HAND tended to be slightly older, slightly less educated and were more likely to be women, have a history of substance use and have a comorbidity (notably hepatitis C coinfection). Those with a history of an AIDS diagnosis and low CD4 cell count were also more likely to experience neurocognitive decline in the study, compared with those who did not.

"In conclusion," Heaton said, "individuals with ANI tend to progress to symptomatic HAND more frequently than those with normal cognitive functioning." He added that "ANI may be a harbinger of future HAND worsening and therefore warrants increased monitoring."
