Utility of the Montreal Cognitive Assessment (MoCA) and its subset in HIV-associated neurocognitive disorder (HAND) screening

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ABSTRACT

Objectives: The Montreal Cognitive Assessment (MoCA) is a useful screening tool for mild cognitive impairment. We aimed to know whether the full MoCA and subsets of the full test are effective for detecting HIV-associated neurocognitive disorder (HAND).

Methods: We examined the socio-demographic, clinical, functional, and neuropsychological levels of 194 HIV-infected patients. We compared total scores and scores from each cognitive domain of MoCA between patients with and without HAND. We also examined the utility of subsets of the full test using a few selective domains. The diagnostic accuracies of MoCA and subset composition were evaluated.

Results: The total scores of MoCA ($P < 0.001$) and scores from Trail Making Test-B ($P = 0.020$), attention domain ($P = 0.005$), and immediate ($P = 0.003$) and delayed recall ($P = 0.002$) differed between patients with and without HAND. A subset composed of Trail Making Test-B, rescored serial subtraction, and immediate/delayed recall showed a 69.2% accuracy.

Conclusions: Our results suggest that the MoCA and its subsets alone are not sufficient in screening for HAND. Further studies will be needed to develop a simpler and easier screening tool for HAND based on this study.

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1. Introduction

HIV-associated neurocognitive disorder (HAND) is still prevalent in the HIV-infected population, although the most severe form of HAND (i.e., HIV-associated dementia) is decreasing due to the use of combination antiretroviral therapy (cART) [1–4]. Since neurocognitive deficits may affect medication compliance [5,6] and mortality [7,8] in patients with HIV, it is important for clinicians to identify the presence of cognitive impairment in these patients for appropriate management to be started without delay [9]. A HIV-specific screening tool for

neurocognitive impairment such as the HIV dementia scale [10] has been reported to be effective in detecting HIV-associated dementia. However, insufficient research had been performed on the screening tool for milder forms of HAND, especially in Asia.

The Montreal Cognitive Assessment (MoCA) [11] is a screening tool used for mild cognitive impairment that measures multiple cognitive domains in a relatively short time (about 10 min). Some researchers have applied it to screening for HAND [12–19]. Nonetheless, the entire MoCA may be difficult to use in a HIV clinic, because physicians must assess many other medical conditions within a limited time. Therefore, in a hectic clinical situation, a simpler and rapider screening measure would be valuable to assess the need for neuropsychiatric consultation.

In a previous study [20] we reported the prevalence and risk factors of HAND in Korea, and observed that the Grooved Pegboard Test and the Wisconsin Card Sorting Test were useful for diagnosing HAND. This result may reflect the fact that impairments of motor speed and executive function are common among patients with HAND [4,9,21]. However, such complex neuropsychological tests require specialized instruments and relatively prolonged administration time. In addition, either of the two tests alone could not measure memory impairment itself (learning

and recall), which were detected in 48% of our sample [20]. Memory is an important predictor of employment status, medication compliance, and driving performance in individuals with HIV [5].

In this study, therefore, we focused on designing a simple paper-based tool using subsets of the MoCA covering multiple cognitive domains. We aimed to identify 1) which items of the MoCA predicted HAND in our Korean sample, and 2) whether a subset of MoCA could be used to substitute for the full MoCA in HAND screening.

2. Methods

2.1. Study sample

We recruited 200 HIV-infected patients who were 18 years old or older and being treated at HIV clinics in two university hospitals in Seoul, South Korea. Exclusion criteria were the following: (1) recent or significant traumatic brain injury, (2) neurological disorders not related to HIV infection, (3) infections that affect the CNS, (4) significant CNS opportunistic infections based on history and/or neurological examination, (5) symptoms of current or active infection, a body temperature of >38.5 °C at the time of recruitment, and current treatment for a serious or systemic infection within 3 months, (6) current or past psychotic or affective disorder, (7) significant substance use, (8) color blindness, and (9) hearing deficits that appeared to affect auditory comprehension. Among the 200 patients, five with confounding comorbidities including major depression and one with early withdrawal from the study were excluded. Finally, a total of 194 patients participated in the study. This study was approved by the Institutional Review Board of each hospital. All participants provided informed consent.

All participants at both study sites underwent socio-demographic, clinical, and comprehensive neuropsychological assessments alongside functional level evaluations. The evaluation of functional level was assessed using the Karnofsky Performance Status Scale [22] and additional functional questions based on the suggestions of Antinori et al. [23]. The additional functional questions were as follows [20]: "Is it hard to take medication in the correct dosages at the correct time?"; "Is it hard to manage financial matters independently (budgeting, writing checks, paying rent and bills, going to the bank)?"; "Is it hard to perform household tasks alone or with occasional assistance?"; "Do you have trouble managing your daily schedule?"; "Do you make more mistakes in your work?"; "Do you need more time than before to do the same amount of work?"; "Do you find it more difficult than before to carry out tasks successfully?"; "Are you less able to produce your best work?".

2.2. Neuropsychological evaluation

Along with assessments of daily functioning, a comprehensive neuropsychological battery was performed to diagnose HAND. The battery included assessments of the following cognitive domains commonly affected by HIV [1,3,4,23]: speed of information processing (Wechsler Adult Intelligence Scale [WAIS]-digit symbol subtest, Trail Making Test-A [TMT-A]), learning and memory (Auditory Verbal Learning Test, Complex Figure Test), executive functions (Wisconsin Card Sorting Test, WAIS-similarity subtest, Trail Making Test-B [TMT-B]), verbal/language (WAIS-vocabulary subtest), sensory-perceptual/motor skills (Grooved Pegboard Test), and attention/working memory (WAIS-digit span subtest). Norms of each test were based on results of the HIV-negative Korean population [24–28]. According to the Frascati criteria for HAND [23], neurocognitive impairment was defined as 1 SD below the mean for demographically corrected norms over at least 2 cognitive domains.

2.3. Montreal Cognitive Assessment (MoCA)

The MoCA is a screening test that measures the following domains: (1) memory—short-term delayed memory recall (5 points);

(2) visuospatial abilities—clock-drawing (3 points) and 3-dimensional cube copy (1 point); (3) executive functions—modified TMT-B (1 point) and verbal abstraction (2 items); (4) attention and concentration—target detection using tapping (1 point), serial subtraction (3 points), and digits forward and backward (2 points); (5) language—naming of animals (3 points), repetition of sentences (2 points), and phonemic fluency (1 point); and (6) orientation (6 points) [11]. This test is scored from 0 to 30 points, with higher scores indicating better cognitive function. Although the scores of immediate recall items (i.e., 1st and 2nd trial) are not included in the total scores of MoCA, we deliberately scored each item of immediate recall to explore its utility in screening for HAND. The Korean version of the MoCA that was used in this study was previously validated in patients at a memory clinic in Korea [29].

2.4. Data analysis

We first compared the socio-demographic factors and crude scores of MoCA and its items between patients with and without HAND using independent *t*-tests and chi-square tests when appropriate. Considering that, in this study, our focus was on comparing the score of each cognitive domain between the two groups, we did not adjust them by adding 1 point to the total MoCA scores in subjects of ≤6 years of education according to the original Korean MoCA scoring method [29]; rather we used the "crude" scores of MoCA in the descriptive analyses. In addition, while the serial subtraction item was scored from 0 to 3 points in the original MoCA, there were actually 5 trials of serial subtraction. We also counted each trial as 1 point and compared the rescored serial subtraction scores (total 5 points) between the two groups. Next, we performed an analysis of covariance (ANCOVA) or nonparametric ANCOVA to compare MoCA scores between two groups adjusting for potential confounders (i.e., age, sex, and education).

To explore the utility of a subset consisting of several items from the MoCA and to determine how simplified subsets corresponded to results for the full MoCA, we combined items that showed significant differences between the two groups. The sensitivity, specificity, and positive and negative predictive values were calculated in comparison with the reference diagnosis, which was based on cases with HAND. We then performed receiver operating characteristic (ROC) curve analyses to identify the predictive accuracy of the screening tests. The area under the curve (AUC) and the 95% confidence interval (CI) were also calculated. Two-tailed $P < 0.05$ indicates statistical significance. Data were analyzed using the SPSS version 20 (SPSS Inc., Chicago, IL, USA).

3. Results

Participant age (mean ± SD) and educational years were 45.1 ± 11.0 and 13.4 ± 3.3 years, respectively. The majority of patients were male (93.8%) and were receiving cART (86.6%). The viral loads of patients were suppressed (mean ± SD = 2.0 ± 1.4 $\log_{10}$ HIV-1 RNA copies/mL). The current and nadir CD4$^+$ T-cell count were 481.4 ± 236.0 and 187.0 ± 138.0 cells/mm^3, respectively.

We found that 26.3% (51 of 194) of participants met the criteria for HAND, of which 27 and 24 patients had asymptomatic neurocognitive impairment and mild neurocognitive disorder, respectively. There were no individuals with HIV-associated dementia. Age, sex, and education were not significantly different between patients with and without HAND. Compared to patients without HAND, HAND patients showed significant impairment in total scores of MoCA and in its attention and delayed recall domains (Table 1). In detail, among items within each domain, serial subtraction (attention domain) was impaired in HAND patients. There was a trend of lower TMT-B scores (visuospatial/executive domain) and repetition of sentences (language domain) in HAND patients (Table 1). After adjustments for age, sex, and education, TMT-B scores were significantly different ($F[1192] = 5.484$, $P = 0.020$),