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Neurocognition, Health-Related Reading Literacy, and Numeracy in Medication Management for HIV Infection

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Abstract

Successful medication management is an essential ingredient for effective treatment for HIV. Risk factors for poor medication adherence, including neurocognitive impairment and low health literacy, are common in HIV patients. To better understand the most salient risks for poor management of HIV medications, we tested the interrelation of neurocognitive functioning, reading literacy for health related information, and numeracy and their effect on self-management of a simulated HIV medication regimen. Cross-sectional data on 191 HIV-positive men and women recruited from HIV outpatient clinics in South Florida were collected. Exploratory factor analysis was conducted with literacy, numeracy, and neurocognitive scores and suggested that four factors were present representing executive skill, verbal memory, planning, and motor speed. Both the literacy and numeracy scores loaded on the executive factor. Adjusted analyses showed that executive and planning skills were significantly related to medication management. Findings suggest that patients must rely on higher order cognitive skills to successfully navigate medication self-management, and that efforts to simplify health information that merely lowers readability are likely to meet with limited success.

Introduction

Successful management of HIV infection requires strict adherence to antiretroviral therapy (ART). Several studies have implicated neurocognitive functioning and health literacy as important indicators of an individual's ability to correctly understand one's HIV medication regimen.[1–3] The cognitive dysfunction associated with HIV infection has been well described and affects domains such as executive functioning, working memory, learning, information processing speed, and psychomotor skills.[4–7] Despite the reduced prevalence of the more severe HIV-associated dementia following the advent of highly active antiretroviral therapies (HAART), the number of HIV positive individuals living with more mild forms of HIV associated neurocognitive disorders (HAND) appears to be increasing.[8,9] Multiple factors influence the benefits of HAART on neurocognitive function including HIV disease duration and severity, medication adherence, and genetic predisposing factors.[9] Therefore, clear estimates of neurocognitive impairment in the era of HAART are difficult to ascertain. In a sample of nonsubstance-abusing HIV-positive men and women with no history of head injury or major psychiatric illness, Heaton et al.[2] classified 37% of their sample as cognitively impaired. Others have shown similar results with one third of a study sample remaining cognitively impaired at 6–12 months of follow-up[10] and study incidence of cognitive impairment of 21%.[11]

Several studies have shown that cognitive impairment is associated with nonadherence over time.[12–14] Few studies, however, have assessed the relation of cognitive abilities with understanding ART prescription instructions independent of adherence. Albert et al.,[3] using the Medication Management Test (MMT), a simulated observed-performance test specifically tailored to antiretroviral regimens, reported that deficits in executive functions and psychomotor skills were related to inaccurate pill dispensing (correctly placing a week's supply of 5 medications into a pill box). Deficits in learning were related to poor performance on items that assessed anticipation of refills, understanding side effects, dosing instructions and determination of missed doses. Furthermore, Heaton et al.,[2] found that performance on a revised version of the MMT was significantly lower for HIV patients classified as globally neuropsychologically impaired. Skill deficits in executive skills (e.g., reasoning and mental flexibility) and learning/memory were the only ability domains significantly related to medication knowledge; information processing speed, motor

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skills, attention/working memory and delayed recall were not associated with management of the simulated regimen.

Likewise, health literacy, or the ability to complete basic reading and numerical tasks required to perform in the health care environment, has been shown to be related to adherence to antiretroviral medications among HIV patients.[15–17] The relation of health literacy to prescription knowledge was shown by Miller et al.,[1] to be predictive of poorer regimen knowledge 8 weeks after initiation of ART medications. Moreover, in non-HIV patient populations, several studies have associated poor reading literacy for health-related information with poor regimen knowledge.[18–20] Emerging research on health numeracy, the use of quantitative skill in a health context, has shown its importance in the management of chronic illness[21,22] and for adherence to HIV medications.[20]

In addition to the risk for neurocognitive impairment, HIV disproportionately affects persons at high risk for poor health literacy (e.g., low income, poor educational quality). Given the relationship between neurocognitive impairment and low health literacy and poor medication management, certain HIV patients may be at substantial risk for poor medication management. A better understanding of the interrelationship of health literacy and neurocognitive functioning on medication management can inform interventions developed from empirically derived data on the most salient component of successful medication management. We therefore tested the association of neurocognitive functioning, reading literacy for health related information and numeracy to management of a simulated HIV medication regimen.

Methods

Analyses from this dataset have been previously published[23] but did not include neuropsychological measures, but rather, focused exclusively on health literacy and numeracy. The current study differs from previous publications through its inclusion of domain specific neuropsychological skills and their relation to medication management. As discussed above, neuropsychological functioning has been shown to affect medication-taking behavior across a number of studies as has health literacy. Thus it is important to understand their impact on medication management as co-occurring entities.

Participants

Participants for this study were recruited from either the HIV care clinic at the University of Miami, Jackson Memorial Hospital or Florida Department of Health pharmacies serving individuals enrolled in the AIDS Drug Assistance Program (ADAP) in Miami-Dade County, Florida. Study enrollment took place from December 2005 through August 2008. Participants were primarily referred by their HIV care providers or learned of the study from posted flyers. Interested persons were screened in person or over the telephone. Those eligible for the study were 18 years of age, currently receiving antiretroviral treatment (ART) or medically "in-process" for their first course of ART, had no history of head injury or loss of consciousness lasting more than 30 min and no presence of psychotic symptoms at the time of enrollment. Additionally, eligible individuals self reported no use of heroin, cocaine or marijuana in the past 12 months. Both English- and Spanish-speaking individuals were enrolled and the study was conducted in the preferred language of the individual.

This study was approved by the Internal Review Boards of the University of Miami and the Florida Department of Health. Informed consent was obtained from each participant prior to initiation of study procedures. The study assessor was a master's level counselor trained and supervised by a licensed neuropsychologist involved in the study. All study procedures were completed in one session at a private office at the University of Miami medical campus located in a separate building from the HIV recruiting clinic. Testing procedures lasted no more than 2 h and participants were compensated $50 upon completion.[23]

Measures

Demographics. Participants answered basic demographic questions about age, education, race, and history of HIV infection.

Reading comprehension for health-related information. The Reading Comprehension subtest of the Test of Functional Health Literacy (TOFHLA)[24] was used to measure reading literacy. This test consists of 50 items that assess text comprehension using the modified cloze procedure.[25] Every fifth to seventh word in a health-oriented text passage is omitted and the reader selects the appropriate word from a list of four possible choices. Scores range from 0 to 50 and the percent correct was calculated. Although a short version of the test is available (36 items) the test developers recommend use of the full version in research studies.

Numeracy. The Applied Problems subtest of the Woodcock Johnson–III Tests of Achievement[26] was used to assess quantitative skills involving analyzing and solving math problems. To solve the problems, the person must listen to the problem (the test items are read aloud by the examiner), recognize the procedure to be followed, and then perform relatively simple calculations. Because many of the problems include extraneous information, the individual must decide not only the appropriate mathematical operations to use but also which numbers to include in the calculation. Applied Problems is a measure of quantitative reasoning, math achievement, and math knowledge. According to the test developers, low performance on this test may be a function of limited math skills, comprehension difficulties, or poor mathematical reasoning abilities. This test was chosen since it tapped abilities identified at "face value" to be similar to skills required for medication management capacity, including those identified in "document literacy" that require calculation problems and inference of the correct mathematical operation when one is not provided.[27]

Any test item may be repeated and the person is given a pencil and paper on which to make calculations. Although the test contains a total of 63 items, all items are not usually administered. This test has a ceiling criterion to determine discontinuation of the test. The ceiling is met when the subject responds incorrectly to 6 consecutively administered items or when the final item is administered.

Neuropsychological measures. Brief descriptions of each test are provided below. More detailed information on these measures can be found in Lezak[28] and Spreen and Strauss.[29]

The Color Trails Test (CTT)[30] uses colored circled numbers and alternately colored circled numbers to measure speed of

attention, sequencing, mental flexibility and visual search and motor functions. This test has been widely used with HIV-positive individuals and was developed by the World Health Organization to eliminate cultural bias. The time taken to complete the two portions of the CTT (CTT-1 and CTT-2) will be the variables of interest from this test.

The Tower of London Test[31] assesses higher order planning and problem solving. The test involves looking ahead to determine the order of moves necessary to rearrange three colored balls from their initial position on two of three upright sticks to a new set of predetermined positions on one or more of the sticks. The total number of moves and total correct scores will be the variables of interest for analyses.

The WHO/UCLA Auditory Verbal Learning Test (AVLT)[32] was used to assess verbal learning through 5 repeated trials of a 15-word list. A learning score was derived from the total number correct across the 5 trials. Delayed memory was assessed after asking for repetition of the original word list after a 20-min delay. Scores used in this study were total recall from trials 1 through 5, and the 20-min delayed recall score.

The Rey Complex Figure[33] was administered to measure visual memory and visuomotor skills. The copy score is derived following the presentation of a black and white image of a complex line drawing for copy. Delayed visual memory is assessed after the individual reproduces the design from memory after a 20- to 30-min delay. Scores used in this study were the total copy score and total delayed recall score.

The Purdue Pegboard Test[34] is a measure of fine eye–hand motor coordination and speed. This test consists of a board with cups for holding pins, washers and collars and two columns of holes. The test is taken over four trials. The first trial consists of taking small metal pins with the dominant hand (e.g., right) and placing them in the right-hand column of holes as quickly as possible within 30 seconds. The same procedure is followed in trial 2 with the nondominant hand. The third trial involves the participant using both hands simultaneously. The fourth trial is an "assembly" task requiring continuous alternating movements of the right and left hands, one picking up a pin, next a washer, then a collar. Participants complete as many assemblies as possible in 60 seconds. Total completed insertions for the nondominant hand, both hands and assembly tasks were scores of interest for the present study.

Outcome variable: medication management. A standardized test to measure one's ability to manage a simulated HIV medication regimen, the Columbia Medication Management Test (MMT),[3] was the outcome variable in this study. The test consists of 8 items with a total of 16 points. There are 5 "mock" HIV medications with labels (created for the test) based on typical ART medications and dosing schedules (e.g., zidovudine, lamivudine, and saquinavir; over-the-counter medications such as acetaminophen and vitamins were used in place of actual antiretroviral medications). An example of a medication label is "Take one tablet two times a day–Medication B 150 mg tablet 30 tablets." Another is "Take two tablets three times a day." The MMT also has a medication insert for loperamide, an antidiarrheal, which contains indications, contraindications, dosing instructions side effects, and warnings.

The test score is then based on answers to questions about the medication labels, the loperamide insert, the ability to correctly count out and place a week's supply of pills in a medication organizer, and to determine missed doses and refills. Example questions include "The next few questions are about Medication A. Assume that when you started taking Medication A, you had a 7-day supply and that you've been taking the medication for 3 days now. In other words, you should have taken the medication as prescribed for the last 3 days. Now show me what you would do to determine if you've missed any pills so far" and "For medication B, how many days will a new prescription last?" and "Please answer the following questions based on this package insert information for a common diarrhea medication. If you were suddenly experiencing diarrhea and began taking this medication, what's the maximum number of capsules you should take over a 2-day period?" The total percent correct was used in analyses.[23] The MMT has good reliability (Cronbach α range from 0.63 to 0.84) and is related to measures of adherence. In the validation study, low scores ($\leq$60% correct) were significantly more likely to report missing a dose of medication in the past 3 days.[3]

Data analysis

In order to understand the interrelationship of health literacy, numeracy, and neurocognitive skill, we developed a factor analytic model of the underlying ability domains employing exploratory factor analysis. Scores on the health literacy, numeracy, and neurocognitive measures described above were included in the factor analysis. Factor scores were retained and included in a hierarchical multiple regression analysis to test their relationship to medication management skill. Correlation analyses were conducted to test for potential covariance between demographic characteristics (e.g., age, gender, race, time since HIV diagnosis) and medication management scores. Only those characteristics significantly associated with medication management ($p < 0.05$) were included in the final regression model.

Results

A total of 191 participants completed this study. As shown in Table 1, 57% of participants were men and nearly 83% were African American. The majority of participants reported being heterosexual (78%) and nearly 22% reported being homeless during the past year with 14% reportedly living on the streets or in a homeless shelter at the time of the study while half of the participants lived in their own home or apartment. Most (75%) reported heterosexual sex as their risk factor for HIV infection. On average, participants were about 45 years old (range, 23–67 years) and had been diagnosed with HIV for 9.98 years (range, <1 year to 25 years). Study participants averaged less than 12 years of education (11.5 years of school; range, 5–20 years of school); 6% had 8 years or less of school, 36% had a high school degree (12 years of education) and 27% had some college or technical training.

Table 2 presents average test performance of study participants. To be able to describe here participants' neurocognitive performance in relation to "average" performance, test scores, except those for the TOFHLA, were converted into demographically corrected z scores (with a mean of 0 and standard deviation of ± 1) based on each test's published normative data. On the reading comprehension portion of the TOFHLA, participants answered 77% of test items correctly

Table 1. Sociodemographic Characteristics of Participants ($N = 191$)

	Study subjects
Characteristics	
Gender	
Men	108 (57%)
Women	83 (43%)
Race/ethnicity	
African American	159 (83%)
Hispanic	21 (11%)
White	8 (4%)
Other	3 (2%)
Sexual orientation	
Heterosexual	144 (78%)
Gay	25 (13%)
Bisexual	13 (7%)
Not sure	3 (2%)
Mean age	44.81 (8.43)
Mean years of education	11.56 (2.25)
Mean years since HIV diagnosis	9.98 (6.73)
Mean years taking ART	3.4 (3.5)
Living situation	
In own home	96 (52%)
Someone else's home	41 (22%)
Rented room	9 (5%)
Shelter, car or street	26 (14%)
Treatment facility/halfway house	13 (7%)
Homeless in the last year	40 (22%)
Unemployed (yes)	154 (81%)
Receiving public assistance (yes)	105 (43%)

on *average*. Examination of z scores for all other measures shows that only average scores for the Tower of London were above the normative mean (z score = 0.60). All other scores were below average. Numeracy scores averaged more than 1 standard deviation below the mean and scores on the Purdue Pegboard Test (motor speed) and the copy of the Rey Complex Figure (visuoconstruction) averaged more than 2 standard deviations below the normative mean.

Results of exploratory factor analysis with varimax rotation (using raw test scores) revealed that four factors should be retained and interpreted based on the eigenvalue greater than 1 criterion and inspection of the scree plot. The first factor accounted for 35.4% of the common variance, factor two accounted for 12.7% of the common variance, the third factor accounted for 11.8% of the common variance, and factor four accounted for 11.0% of the common variance. Measures with high loadings on factor one included scores from the TOFHLA, Applied Problems test, Rey Complex Figure copy and recall, and time to complete trials 1 and 2 of the Color Trails Test. We named this first factor "Executive Skill" since it appears to represent a number of higher order mental processes tapped by these various measures including working memory, organizing, sequencing, and monitoring. Measures with high loadings on factor two, "Verbal Memory," included total number of words recalled across trials 1 through 5 and on the delayed recall trial of the Auditory Verbal Learning Test. The third factor, "Planning," included the total number of moves and the total correct scores from the Tower of London. Finally, the fourth factor, "Psychomotor," included scores from the Purdue Pegboard insertion with both hands and assembly tasks. Rotated factor loadings are presented in Table 3.

Table 2. Mean Neuropsychological Test Performance (z scores)

Neuropsychological test score	*Mean z score*
Rey Copy Total	−2.23
Rey Delayed Total	−0.77
Color Trails 1	−0.73
Color Trails 2	−0.57
Tower of London total moves	−0.94
Tower of London total correct	0.65
Purdue Pegboard both hands	−2.08
Purdue Pegboard Assembly	−2.05
AVLT learning (total of trials 1-5)	−0.87
AVLT delayed recall	−0.65

AVLT, Auditory Verbal Learning Test.

Next, gender, African American versus non-African American race, and time since HIV diagnosis were entered into the first step of a multiple regression analysis. These variables were significantly related to medication management score, explaining 10% of the variance in those scores ($R^2 = 0.103$, $p < 0.001$). All three of the variables were significant with female gender, African American race, and living with HIV longer being associated with poorer medication management. Next, the four ability factors were entered into the model. The addition of these factors accounted for a significant increase in variance in the model 1 ($R^2\Delta = 0.276$, $p < 0.001$). The two steps in the model together explained 38% of the variance in medication management scores. The Executive and Planning factors were significantly associated with medication management ($p < 0.05$). With the inclusion of the four factors, the association of gender, race, and time since HIV diagnosis with medication management diminished to nonsignificance. Examination of standardized beta weights shows that Executive Skill accounted for the greatest amount of variance (Table 4).

Discussion

This study tested the effects of neurocognitive functioning, reading literacy for health-related information and numeracy on the ability to manage a simulated HIV medication regimen. Although studies have found each of these skill areas to be related to medication management, no study to date has evaluated how these skills may relate to one another and to understanding medication instruction. Our findings showed that tests of reading comprehension and mathematical reasoning shared common traits with neuropsychological measures that require working memory, mental flexibility, visual scanning, and organization. This set of executive skills was highly associated with successfully managing the simulated HIV regimen. Similarly, planning skills were demonstrated to be important for completion of this task as well. A number of studies have shown impairment in cognitive function and executive skill in particular to affect medication adherence in individuals with HIV infection.[12,43,44]

Executive function is a broad term that encompasses a number of higher order skills necessary for independent, goal-directed behavior, including holding and manipulat-

Table 3. Exploratory Factory Analysis

Variable	Factor			
	Executive	*Verbal Memory*	*Planning*	*Psychomotor*
TOFHLA	**0.655**	0.140	0.206	0.005
Applied Problems	**0.620**	0.191	0.310	0.029
Rey Copy Total	**0.659**	0.168	0.052	0.057
Rey Delayed Total	**0.455**	0.280	0.025	0.179
Color Trails 1	**−0.663**	−0.060	−0.018	−0.126
Color Trails 2	**−0.708**	−0.027	−0.141	−0.146
AVLT learning (total of trials 1-5)	0.289	**0.784**	0.178	0.108
AVLT delayed recall	0.127	**0.872**	0.042	0.091
Tower of London total correct	0.098	0.023	**0.859**	0.063
Tower of London total moves	−0.252	−0.168	**−0.767**	−0.084
Purdue Pegboard both hands	0.103	0.064	0.054	**0.977**
Purdue Pegboard Assembly	0.146	0.114	0.076	**0.658**

TOFHLA, Test of Functional Health Literacy; AVLT, Auditory Verbal Learning Test.
Bold values represent variables with higher loadings on each factor.

ing information in working memory, planning/sequencing multistep tasks, and ascertaining the "big picture" from a complicated set of details.[45] Recent studies have emerged to describe the contribution of executive skill to reading comprehension.[46,47] Although deficits in single-word decoding, fluency, and reading proficiency explain a portion of reading comprehension deficits, they do not account for all problems with reading comprehension and for those whose single word reading is intact. Studies have shown that children with dyslexia display working memory deficits in both verbal and visual domains.[48] Verbal working memory has been linked to reading comprehension across a number of studies[49–51] and is thought to "...facilitate comprehension through the availability of ample cognitive resources to simultaneously engage in multiple reading processes including decoding of unfamiliar words, retrieving semantic knowledge of familiar words, recalling previously read text, and anticipating where the passage is going."[47] Moreover, reasoning and critical analysis are also thought to influence reading comprehension[52] and those with good reading comprehension are more likely to use cognitive and metacognitive strategies.[53] On measures requiring an organized response, children with reading comprehension difficulties tend to produce less organized and less structured copies of geometric figures (similar to the Rey Complex Figure task used in the present study) and require longer planning times on visual problem solving tasks.[48,54] Sesma et al.[47] demonstrated that executive skills (measured by the Tower of London, and Arithmetic and Digit Span tests that are working memory components of the Wechsler Intelligence Scale for Children) were associated with reading comprehension but not single word recognition in children. Arithmetic measures that require computation and inference of mathematical operands are also strongly associated with attention and working memory. The arithmetic subtest from the Wechsler Intelligence Scales[55] contains similar task demands to those of the Applied Problems test used in the present study, with the exception that scoring is based partially on speed of response. In a factor analysis, the arithmetic test loads on an IQ index termed "Freedom from Distractibility" tapping attention, working memory, and organizing skill sets.[56]

This evidence lends support to the present study showing that executive skills are inherently involved in reading comprehension and numeracy. Although planning skill did not

Table 4. Hierarchical Multiple Regression of Numeracy, Reading Literacy for Health Information, and the Four Neurocognitive Domains on Medication Management Scores

Variable	Model 1			Model 2		
	B	*SE B*	*β*	*B*	*SE B*	*β*
Gender	−1.427	0.663	−0.164[a]	−1.036	0.627	−0.119
HIV diagnosis[b]	−0.008	0.004	−0.153[a]	−0.007	0.004	−0.138
Race[c]	−2.322	0.911	−0.191[a]	−1.167	0.881	−0.096
Executive				2.317	0.315	0.476[c]
Verbal Memory				0.418	0.322	0.085
Planning				1.045	0.312	0.218[d]
Psychomotor				0.163	0.273	0.038
R^2		0.103			0.379	
F for change in R^2		6.329[d]			14.020[d]	

[a] $p < 0.05$.
[b] HIV diagnosis = time since HIV diagnosis.
[c] Race = African American vs. non-African American.
[d] $p < 0.001$.

load on the same factor as the literacy, numeracy and other executive skills, its association with medication management as well suggests that it too is an important, higher order cognitive process that is necessary to carry out rather complex day-to-day health behaviors such as medication management. In the context of earlier research, a number of studies found the TOFHLA and other reading tests (e.g., the REALM) to be related to medication understanding and adherence.[15–20] Moreover, interventions stemming from such findings have used nonwritten communication strategies such as pictorial medication cards, to communicate medication instructions.[19] Although these interventions have met with some success, the findings presented herein suggest that successful medication management for low health literate individuals involves a broader and more complex array of skills than only reading ability.

A recent study found HIV perinatally infected adolescents to have significantly lower receptive language and word recognition skills than those who were perinatally exposed to HIV but did not seroconvert. Moreover, their performance was well below that of age appropriate expectations. Unfortunately, executive skill was not assessed in this study and so the contribution of executive deficits to language deficiencies cannot be measured. The findings emphasize that HIV may have a significant effect on language skill that should be accounted for in care programs for this population.[57]

The generalizability of this study is limited since the study sample was not randomly selected and was comprised mostly of African Americans. However, executive and planning skills are a universal human ability that would be equally important to those who confront the task of medication management regardless of background, level of education, or nationality. Second, contemporary HIV regimens often contain fewer total medicines than the five used in our simulated regimen. This may decrease generalizability for less complex regimens which are associated with poorer management.[40] However, in addition to antiretroviral medicines, many HIV patients are also prescribed prophylactic medications, vitamins, and supplements that also require adequate adherence for maximum effectiveness. Therefore, we believe these findings to still be relevant for many HIV-positive patients. It also noteworthy to consider the present findings within the parameters of health numeracy put forth by Ancker and Kaufman.[26] They purport that productive use of quantitative health information, such as completion of a medication regimen, depends in part on the health numeracy abilities of the individual. It also depends on the ability of the communication device, whether through an individual expert or information artifact, to effectively communicate clear, "cognitively manageable" information.[26] Poorly communicated information can handicap even those with advanced numeracy skill whereas effectively communicated health information can help to compensate for weak individual skill. The findings from the present study constitute only a portion of the dynamic of functional health literacy by measuring individual-level ability. A number of other factors untested in the present study may also impact self-management of one's medications such as drug use,[12] disease knowledge,[16] support of family or caregivers,[41] and self-efficacy for medication taking.[42] Nonetheless, these findings help to underscore individual skill sets of particular relevance for managing medications. The optimal point of intervention based on these findings, whether with the individual, provider, healthcare system, or some combination thereof, should be evaluated in further intervention research.

These findings hopefully increase provider awareness of the complexity of higher order cognitive processes on which patients must rely to successfully navigate medication self-management. Although reading and arithmetic are key elements for understanding prescription instructions, they are carried out via metacognitive processes that may be more challenging to identify. In diseases such as HIV/AIDS that produce cognitive dysfunction, the need to assess for cognitive dysfunction as well as reading and numeric literacy is further illustrated here. Based on these findings, efforts to simplify health information that merely lowers readability are likely to meet with limited success.

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