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HIV-associated Prospective Memory Impairment Increases Risk of Dependence in Everyday Functioning

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Abstract

HIV infection is associated with impairments in prospective memory (ProM), an aspect of episodic memory that refers to the ability to execute a future intention, such as remembering to take a medication at a specific time. The current study sought to examine the relationship between HIV-associated ProM impairment and the successful management of independent activities of daily living (IADLs). In a cohort of 66 HIV-infected individuals, ProM accounted for a significant proportion of variance in self-reported IADL dependence over and above that which was explained by retrospective memory and current affective distress. Analysis of component cognitive processes revealed that the relationship between HIV-associated ProM deficits and IADL dependence was driven by impaired cue detection and self-initiated intention retrieval. Results were not better explained by demographic factors, HIV disease severity, psychiatric comorbidity, or substance use. Collectively, these data support the potential incremental ecological validity of ProM as a predictor of dependence in IADLs among persons living with HIV infection.

Keywords

Human immunodeficiency virus; neuropsychological assessment; episodic memory; activities of daily living

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The human immunodeficiency virus (HIV) crosses the blood-brain barrier and often leads to neuropathological changes (e.g., syncytia and synaptodendritic injury), which primarily affect the basal ganglia, frontal neocortex, hippocampus, and cerebral white matter (González-Scarano, & Martín-García, 2005). Although widespread use of effective antiretroviral therapies

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has improved systemic disease outcomes and diminished the incidence of frank dementia among persons infected with HIV, the prevalence of milder forms of HIV-associated neurocognitive impairment remains a significant public health problem (McArthur, 2004). The neurobehavioral syndrome of HIV infection is most consistent with dysregulation of fronto-striato-thalamo-cortical circuits and is typically marked by mild-to-moderate bradyphrenia, bradykinesia, executive dysfunction, and deficits in episodic memory (e.g., Reger, Welsh, Razani, Martin, & Boone, 2002). As many as one-half of individuals with HIV-associated neurocognitive impairment experience problems independently managing their instrumental activities of daily living (IADLs; Heaton et al., 2004). Neuropsychological impairment contributes to decrements in medication management (e.g., Albert et al., 1999), automobile driving (Marcotte et al., 1999), and vocational functioning (e.g., van Gorp, Baerwald, Ferrando, McElhiney, & Rabkin, 1999), even after considering the effects of HIV disease severity and psychiatric distress (e.g., depression).

Deficits in episodic memory are among the strongest neuropsychological predictors of IADL declines in HIV (e.g., Andrade et al., 2005; Benedict, Mezhir, Walsh, & Hewitt, 2000; Heaton et al., 1994; van Gorp et al., 2007). Episodic memory impairment is evident in approximately 50% of individuals infected with HIV (e.g., Heaton et al., 1995) and is typically characterized by deficits in higher-level encoding (e.g., Murji, Rourke, Donders, Carter, Shore, & Rourke, 2003) and retrieval (e.g., Delis et al., 1994) strategies. Whilst the literature demonstrates a clear link between HIV-associated episodic memory impairment and IADL declines, such research has been limited to the construct of retrospective memory (RetM); that is, the recollection of past events in response to an explicit prompt (e.g., recalling a physician's specific instructions regarding medication usage upon being asked), which is the putative ability measured by most standard clinical tests of memory (e.g., list learning and recall). In contrast, the contribution of prospective memory (ProM), which is another aspect of episodic memory, to IADL dependence in persons living with HIV infection has not yet been evaluated.

ProM is a multifaceted cognitive construct involving the ability to execute a future intention, or "remembering to remember." Successful ProM requires the formation of an intention, maintenance of the intention-cue pairing over time (during which time both active and automatic monitoring may occur), detection and recognition of the cue (which may be based on time or a specific event), search and retrieval from RetM for the paired intention, and execution of the intention. A recent series of studies has begun to elucidate the nature and extent of ProM impairment in HIV. Self-reported ProM complaints are elevated in HIV, particularly on daily tasks that require self-initiated cue detection and retrieval (Woods et al., 2007a). Objective ProM performance is also impaired in HIV infection and is characterized by mild-to-moderate deficits in both time- (Carey et al., 2006; Martin et al., in press a) and event-based (Carey et al., 2006) ProM. HIV-1 associated ProM deficits reflect impaired strategic encoding and retrieval of future intentions, as evidenced by increased rates of task substitution and no response errors in the setting of normal recognition of cue-intention pairings (Carey et al., 2006). Paralleling research in healthy adults (e.g., West, Bowry, & Krompinger, 2006), HIV-associated ProM impairment may be singly dissociable from RetM; that is, intact RetM is a necessary, but not sufficient condition for normal ProM. Despite utilizing similar underlying retrieval processes and neural systems, ProM places greater demands on lateral and medial prefrontal networks than does RetM (e.g., Simons, Scholvinck, Gilbert, Frith, & Burgess, 2006; West & Krompinger, 2005; West et al., 2006). Among persons with HIV infection, self-reports of ProM complaints are more common and severe than RetM complaints (Woods et al., 2007a). Moreover, HIV-associated ProM deficits are only modestly correlated with RetM impairment (e.g., Carey et al., 2006; Martin et al., in pressa), indicating that these constructs are not exceedingly interdependent. Finally, HIV biomarkers of macrophage activation (e.g., monocyte chemoattractant protein-1) and neuronal injury (e.g., tau) are

associated with ProM, but not RetM deficits, suggesting that the neuropathogenesis of HIV-associated ProM impairment may be separable from RetM (Woods et al., 2006b).

Given evidence of a possible single dissociation between ProM and RetM, as well as the frequency with which tasks critical to successful daily functioning impose demands on ProM encoding and retrieval abilities, it is commonly posited that ProM may play a differential, and possibly more crucial role in IADLs than RetM. For instance, remembering to take a medication at a particular time of day (i.e., ProM) may be more essential to independent functioning than is recalling the exact name of the medication after being queried (i.e., RetM). In other words, a thorough assessment of ProM and its relation to IADLs may provide a unique glimpse into an aspect of cognition that is ever-present in daily life and critical to independent living, but is nevertheless not assessed by traditional clinical tests of learning and memory. Thus, the primary aim of the current study was to evaluate the possible incremental ecological validity of ProM versus RetM impairment in predicting IADL dependence in HIV infection.

Additionally, we sought to evaluate which component processes of HIV-associated ProM impairment were driving the risk of IADL dependence, most notably, problems with intention retrieval, task substitutions, and cue detection (i.e., no response errors).

Method

Participants

Sixty-six volunteers with HIV infection were recruited from the general community and local HIV clinics. The demographic, HIV disease, and psychiatric characteristics of the overall study sample are displayed in Table 1. HIV status was determined by enzyme linked immunosorbent assays and confirmed by a Western Blot test. Potential participants with histories of severe psychiatric illness (e.g., schizophrenia or bipolar disorder), neurological disease (e.g., seizure disorders, closed head injuries with loss of consciousness greater than 15 minutes, and central nervous system neoplasms or opportunistic infections), or verbal IQ estimates < 70 (based on the Wechsler Test of Adult Reading; Psychological Corporation, 2001) were excluded. Individuals with diagnoses of substance-related disorders within six months of evaluation as determined by the Composite International Diagnostic Interview (CIDI version 2.1; World Health Organization, 1998) were also excluded. All participants underwent a urine toxicology screen for illicit drugs (other than marijuana) on the day of evaluation to confirm recent abstinence. Finally, individuals with IADL declines that were attributed solely to gross physical limitations (e.g., ambulation disabilities) were excluded.

Materials and Procedure

After providing written, informed consent, all participants completed comprehensive neuropsychological, psychiatric, and medical research evaluations for which they received financial compensation. CD4+ lymphocytes were counted in blood using flow cytometry and HIV RNA levels were quantified in plasma using RT-PCR (Amplicor, Roche Diagnostics, Indianapolis, IN).

Measurement of ProM—The Memory for Intentions Screening Test (MIST; Raskin, 2004) is a standardized, performance-based measure of ProM with scores ranging from 0 to 48. Prior research supports the reliability (Raskin, 2004) and construct validity of the MIST in healthy adults (Carey et al., 2006), schizophrenia (Woods, Twamley, Dawson, Narvaez, & Jeste, 2007), and HIV infection (Carey et al., 2006; Woods et al., 2006; Woods et al., 2007a). The reader is referred to Carey et al. (2006) and Woods et al. (2007b) for a more comprehensive description and information regarding administration and scoring of the MIST. In brief, the MIST is comprised of eight ProM tasks counterbalanced on the following characteristics: 1) a 2-min or 15-min delay; 2) a verbal (e.g., “In 2 minutes, ask me what time this session ends”)

or physical (e.g., “In 15 minutes, use that paper to write down the number of medications you are currently taking”) response; and 3) a time-based (e.g., “In 15 minutes, tell me that it is time to take a break”) or event-based (e.g., “When I hand you a postcard, self-address it”) cue. Word search puzzles are provided as a distracter task to prevent unimpeded rehearsal of the prescribed intentions. The following error types were also coded (see Carey et al., 2006 for further details): (1) No Response (e.g., no reaction to a ProM cue); (2) Task Substitution (e.g., substitution of an action response for a verbal task); (3) Loss of Content (e.g., vague acknowledgment that a response is required to a ProM cue); and (4) Loss of Time (e.g., executing a correct intention 10% away from the appropriate response time). Note that, there were insufficient numbers of Place Losing Omissions ($n = 0$) and Random Errors ($n = 2$) to permit meaningful analyses. Finally, a 3-choice recognition trial was administered following the completion of all eight ProM tasks (range = 0–8), from which a Retrieval Index was derived by subtracting free recall accuracy (range = 0–8) such that higher scores indicate a greater retrieval deficit (see Carey et al., 2006; Woods et al., 2007b).

Self-reported ProM was assessed with the Prospective and Retrospective Memory Questionnaire (PRMQ; Smith, Della Sala, Logie, & Maylor, 2000), which is a 16-item questionnaire on which perceived memory difficulties are rated on a 5-point Likert-type scale that ranges from 1 (“*never*”) to 5 (“*very often*”). Prior research supports the internal consistency (Cronbach’s alphas = .80), factor structure (Crawford, Smith, Maylor, Della Sala, & Logie, 2003), and construct validity (Smith et al., 2000; Zeintl, Kliegel, Rast, & Zimprich, 2006; Woods et al., 2007a) of the PRMQ. The PRMQ includes eight items that target ProM complaints, which are separated into four self-cued (e.g., “*How often do you forget appointments if you are not prompted by someone else or by a reminder, such as a diary or a calendar?*”) and four environmentally-cued (e.g., “*How often do you forget to buy something you planned to buy, like a birthday card, even when you see the shop?*”) ProM complaints. Total scores on the PRMQ ProM Scale range from 8 to 40.

Measurement of RetM—Participants also completed three clinical tests of RetM, including: (1) Rey-Osterreith Complex Figure (Stern et al., 1999); (2) California Verbal Learning Test – Second Edition (CVLT-II; Delis, Kramer, Kaplan, & Ober, 2000); and (3) Logical Memory subtest from the Wechsler Memory Scale – Third Edition (WMS-III; Psychological Corporation, 1997). The delayed free recall scores from these three measures were converted to sample-based z-scores ($n = 66$) and then averaged to create a composite measure of RetM. Self-reported RetM was measured with the RetM scale of the PRMQ (described above). The 8-item PRMQ RetM scale is separated into four self-cued (e.g., “*How often do you forget something that you were told a few minutes before?*”) and four environmentally-cued (e.g., “*How often do you look at something without realizing you have seen it moments before?*”) RetM complaints. Consistent with its ProM counterpart, scores on the PRMQ RetM Scale range from 8 to 40.

Measurement of Affective Distress—The Profile of Mood States (POMS; McNair, Lorr, & Droppleman, 1981) was administered to assess overall affective distress over the week prior to evaluation. The POMS is a 65-item, self-report measure of current mood states in which participants rate various adjectives (e.g., “unhappy”) on a five-point Likert-type scale ranging from 0 (“*not at all*”) to 4 (“*extremely*”). The POMS Total score was used for all analyses.

Measurement of IADL Dependence—All participants completed a modified version of the Lawton and Brody (1969) ADL scale (see Heaton et al., 2004 and Woods et al., 2006a), which consists of numerous daily tasks (e.g., managing finances, grocery shopping, housekeeping, medication adherence, and employment) for which participants rated their current and best prior levels of functioning. The primary dependent variable of interest was the summed total severity of declines reported in current versus past functioning on all of the

IADL items (range = -29 to 0). To evaluate the clinical relevance of ProM as a predictor of IADLs, a second set of analyses was conducted in which participants were classified as IADL Dependent if they reported any current decline (relative to their best level of functioning) in their ability to independently perform two or more functional tasks (see Heaton et al., 2004 and Woods et al., 2006a). This classification system yielded 26 HIV-infected individuals with self-reported IADL dependence and 40 HIV-infected individuals who reported no IADL difficulties. As shown in Table 1, the IADL Dependent ($n = 26$) and Independent ($n = 40$) subgroups were generally comparable for HIV disease severity (e.g., AIDS status), demographic characteristics, and estimated verbal IQ (all $ps > .10$). The groups did not differ in diagnoses of current or lifetime major depressive disorder or generalized anxiety disorder (all $ps > .10$), but the IADL Dependent group did endorse greater levels of overall affective distress on the POMS ($p < .01$). Also, the IADL Independent group had a slightly *higher* prevalence rate of lifetime substance-related disorders ($p < .10$).

Results

Table 2 displays the Spearman's rho (π) intercorrelations between the IADL Scale, MIST, PRMQ variables, RetM z-score, and POMS (note that, nonparametric statistics were used when indicated by the Shapiro-Wilk W Test of normality, $p < .05$). Of particular relevance, the IADL Scale was significantly correlated with the MIST summary score ($p = .013$), PRMQ ProM ($p < .0001$) and RetM ($p = .0004$) Scales, RetM Z-score ($p = .007$), and POMS Total ($p < .0001$) in the expected directions.

Next, a hypothesis-driven hierarchical linear regression was conducted to predict the IADL Scale from the two ProM measures after accounting for the effects of RetM and affective distress (see Table 3). In the first step that included the PRMQ RetM Scale, RetM Z-score, and POMS Total, the model accounted for a significant amount of variance in the IADL Scale, $R^2 = .34$, $F(3, 62) = 10.77$, $p < .001$. In the next step, the subsequent inclusion of the MIST and PRMQ ProM Scale resulted in a significant increase in the proportion of IADL variance explained, $R^2 = .46$, R^2 change = .12, $F(5, 60) = 10.11$, $p < .001$. Note that, although the PRMQ ProM and RetM Scales were highly correlated, results did not change when the PRMQ RetM Scale was excluded from the statistical model.

Table 4 displays the RetM and ProM data for both the IADL Dependent and Independent groups. The IADL Dependent group demonstrated worse RetM performance and reported a greater number of RetM complaints on the PRMQ than the Independent sample ($ps < .05$). The IADL Dependent group also reported more ProM complaints on the PRMQ, endorsing problems with both self- and environmentally-cued ProM in their daily lives ($ps < .001$). Regarding their objective ProM abilities, the IADL Dependent group performed significantly below the IADL Independent sample on the MIST summary score, as well as the time- and event-based subscales and retrieval index of the MIST ($ps < .05$). However, the groups did not differ in their performance on the word search or the post-test recognition exam ($ps > .10$). Evaluation of error types revealed significant between-groups differences on No Response errors ($p < .05$), but not on Task Substitutions, Loss of Content, or Loss of Time (all $ps > .10$).

Finally, the MIST, PRMQ ProM and RetM Scales, RetM z-score, and POMS Total score were entered into a binary logistic regression as predictors of membership in the IADL Dependent and Independent groups, yielding a significant overall model ($\chi^2 = 28.7$, $p < .0001$) to which the MIST ($\chi^2 = 4.7$, $p = .03$) and the PRMQ ProM Scale ($\chi^2 = 9.7$, $p = .002$) were the only significant independent contributors. As was the case with the hierarchical regression analyses above, the results of the logistic regression did not differ when the PRMQ RetM Scale was excluded from the statistical model. Finally, range odds ratios were generated to evaluate the relative predictive power of the ProM and RetM measures. The odds ratio for the MIST

summary score as a predictor of IADL Dependence was 30.9 (90% confidence interval = 1.5, 1372.3), versus 7.0 [0.4, 155.3] for the RetM z-score. Similarly, the PRMQ ProM Scale yielded a considerably larger range odds ratio (188.8 [1.1, 90243.1]) as compared to the PRMQ RetM Scale (0.4 [0.0, 58.4]).

Discussion

Consistent with our hypotheses, the present findings demonstrate that ProM plays an important and unique role in successful daily functioning in individuals infected with HIV. Specifically, HIV-associated ProM impairment and elevated ProM complaints were each independently associated with an increased risk of dependence in everyday functioning. Consistent with prior literature in HIV (e.g., Heaton et al., 2004), poorer RetM functioning, RetM complaints, and acute affective distress were also predictive of IADL dependence; however, ProM accounted for a significant proportion of IADL variance over and above that which was explained by these traditionally measured factors. In practical terms, MIST impairment was associated with more than a fourfold greater likelihood of IADL dependence (odds ratio = 30.9) relative to objective RetM deficits (odds ratio = 7.0). Accordingly, these data support the potential incremental ecological validity of ProM as a valuable independent predictor of dependence in IADLs among persons living with HIV infection. Thus ProM may capture a unique aspect of cognition that is ubiquitous in day-to-day life, but nevertheless not probed by commonly used memory assessment techniques.

Considering emerging evidence regarding the increased frequency of ProM complaints (Woods et al., 2007a), objective ProM impairment (Carey et al., 2006; Martin et al., in pressa), and their respective associations with IADL dependence in HIV, formal assessment of both self-reported and performance-based ProM may be essential to neuropsychological evaluations of persons living with HIV infection. Indeed, self-reported ProM complaints and objective ProM performance appear to capture relatively distinctive and independent aspects of IADL dependence. Only a small correlation was observed between the PRMQ ProM Scale and the MIST, suggesting that individuals with HIV infection may misjudge their actual ProM abilities, yet both measures accurately predicted IADL dependence. Woods et al. (2007a) hypothesized that “metaProM” deficits such as this might increase risk of IADL dependence in HIV; for instance, overestimation of ProM abilities may lead some individuals to not apply needed compensatory techniques, such as using active mnemonic strategies, deploying salient reminders, and/or seeking assistance from others (Knight, Harnett, & Titov, 2005).

On a more conceptual level, analysis of component processes of performance-based ProM revealed that the relationship between HIV-associated ProM impairment and IADL dependence was driven by deficient cue detection and self-initiated intention retrieval. The pattern of ProM performance was characterized by deficits in both time- and event-based trials, marked by increased No Response errors and retrieval failures, but normal performance on the distracter task (i.e., the word search) and recognition post-test. The absence of group differences in the distracter task, recognition test, and other error types (i.e., Task Substitutions, Loss of Content and Loss of Time errors) suggest that the ability to execute an intention that has been adequately formed, maintained, cued, and retrieved is broadly intact. Yet the IADL Dependent group was unable to properly monitor, notice, or react to the ProM cues during the word search task. One possibility is that the observed deficits reflect underlying difficulties allocating cognitive resources to properly manage the simultaneous burden of the distracter task and cue monitoring, regardless of whether such monitoring takes the form of automatic and/or strategic detection processes (see McDaniel & Einstein, 2000).

Overall, findings from this study converge with the cardinal neuropathological and neuropsychological sequelae of HIV disease. As noted above, HIV-associated

neuropathologies predominantly affect the fronto-striato-thalamo-cortical circuits (e.g., González-Scarano, & Martín-García, 2005), which are known to support normal ProM functioning (e.g., Simons et al., 2006). However, it is important to acknowledge the lack of specificity of these findings as concerns the prefronto-striatal loops. Recent studies implicate the contribution of hippocampal neuropathology to HIV-associated episodic memory deficits (e.g., Castelo, Sherman, Courtney, Melrose, & Stern, 2006; Moore et al., 2006) and demonstrate that ProM is impaired in conditions with prominent medial temporal lobe involvement, such as Alzheimer's disease (e.g., Ducheck, Balota, & Cortese, 2006). Indeed, neural systems models of ProM openly recognize the role of the medial temporal lobe and associated RetM functions as necessary, but not sufficient for successful ProM performance (e.g., Martin et al., in press b). Nevertheless, the profile of ProM impairment was broadly consistent with prior studies of ProM in HIV (Carey et al., 2006), which postulated that HIV-associated neural injury disrupts the executive aspects of encoding and retrieval of future intentions (Carey et al., 2006; Woods et al., 2007a). This hypothesis is also commensurate with the general episodic memory deficit characteristic of HIV (e.g., Murji et al., 2003) and other conditions with notable prefronto-striatal involvement (e.g., Parkinson's disease; Buytenhuijs et al., 1994).

Naturally, this clinical study is not without limitations to its internal and external validity. The ProM and RetM performance-based tasks were not matched on format or difficulty level, thereby rendering conclusions regarding the true dissociability of these constructs in HIV debatable (Chapman & Chapman, 1973). Secondly, the use of a self-report measure of IADL functioning might have introduced some bias due to mild anosagnosia (Woods et al., 2006a), which may be evaluated more directly in future studies by incorporating proxy-report questionnaires and direct measures of functional performance (e.g., Albert et al., 1999; Heaton et al., 2004). A third limitation is that no demographically-adjusted normative standards have been published for the MIST or PRMQ, nor was the RetM composite based on published norms, which restricts the immediate clinical relevance of our data. Clearly, research regarding the basic psychometric properties (e.g., demographic correlates and reliability) and construct validity in healthy and clinical populations is needed to enhance the clinical applicability of these ProM tasks. Also, this cross-sectional study did not evaluate the longitudinal predictive validity of ProM impairment in HIV, but rather provides evidence of concurrent ecological validity. Finally, the generalizability of these data are restricted by the demographic (i.e., largely well-educated, Caucasian, men) and HIV disease (i.e., relatively immunocompetent) characteristics of the relatively small study sample.

Despite these limitations, findings from this study highlight the potential clinical benefits of assessing ProM as part of the broader neuropsychological evaluation of persons infected with HIV. In particular, the pattern of ProM deficits may have implications for cognitive remediation and rehabilitation of HIV-associated neurocognitive disorders. For example, incorporation of individualized training plans designed to enhance strategic cue monitoring and minimize internal and external distractions may be effective in enhancing the independent performance of IADLs (e.g., Kurtz et al., 2001; Willis et al., 2006). Another, perhaps more straightforward, intervention would be to simply increase the saliency of external cues and/or use explicit reminders (e.g., from significant others or caregivers) regarding important daily tasks (e.g., medication dosing) whenever possible (e.g., Fish et al., in press). In a recent study, Andrade and colleagues (2005) reported that a programmable electronic prompting device significantly improved antiretroviral adherence among individuals with HIV who evidenced episodic memory impairment at baseline. Given the elevated rate of task substitution ProM errors in HIV (Carey et al., 2006), highly specific reminders (e.g., detailed text messages rather than nonspecific notifications) will likely enhance the effectiveness of such interventions. Further investigations into the role of HIV-associated ProM deficits in IADL dysfunction and its remediability are clearly needed, particularly those aspects of daily functioning that – at least

at face value – place considerable demands on ProM, such as medication adherence (e.g., Park & Kidder, 1996).

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Table 1
Demographic, HIV Disease, and Psychiatric Characteristics of the Study Participants

Variable	Total Sample (<i>N</i> = 66)	Dependent (<i>n</i> = 26)	Independent (<i>n</i> = 40)	<i>p</i> ^a
Demographic Characteristics				
Age (years)	45.0 (8.3)	46.3 (9.1)	44.2 (7.8)	0.351
Education (years)	13.4 (2.9)	12.7 (2.5)	13.8 (3.1)	0.140
Sex (% men)	90.9%	88.5%	92.5%	0.673
Ethnicity (% Caucasian)	68.2%	61.5%	72.5%	0.350
General Cognitive Functioning				
Estimated Verbal IQ ^b	105.5 (13.6)	102.0 (15.6)	107.8 (11.8)	0.176
Proportion NP Impaired (%) ^c	33.3%	42.3%	27.5%	0.215
HIV Disease Characteristics				
Current CD4 Count ^d	578.0 (461.8)	521.5 (453.0)	637.0 (507.0)	0.112
Nadir CD4 Count ^d	220.0 (273.5)	172.0 (232.3)	270.0 (264.0)	0.267
HIV RNA log ₁₀ ^d	1.7 (0.9)	1.9 (2.1)	1.7 (0.4)	0.152
Proportion with AIDS (%)	50.0%	57.7%	45.0%	0.314
Proportion on HAART (%)	77.3%	69.2%	82.5%	0.395
Psychiatric Characteristics				
Substance Dependence (%)	53.0%	38.5%	62.5%	0.056
Major Depressive Disorder (%)	48.5%	42.3%	52.5%	0.418
Generalized Anxiety Disorder (%)	6.1%	7.7%	5.0%	0.645
Profile of Mood States (Total)	26.9 (37.2)	43.8 (36.7)	16.0 (33.5)	0.003
Lawton & Brody IADL Scale				
“Best” Level of Functioning ^e	0.4 (0.8)	0.6 (1.1)	0.3 (0.7)	0.300
Overall Decline Severity	-2.6 (3.5)	-6.0 (2.2)	-0.3 (0.9)	<0.0001
Number of Areas Declined	1.5 (2.0)	3.6 (1.8)	0.2 (0.4)	<0.0001

^aNote. *p*-values represent between group comparisons for IADL Dependent versus IADL Independent.

^bVerbal IQ was derived from the Wechsler Test of Adult Reading (WTAR).

^cSee Woods et al. (2004) for details regarding the methodology for determining global neuropsychological (NP) impairment.

^dMedian (interquartile range).

^eSum of self-reported “best” level of IADL functioning across domains, which range in score from 0 (fully independent) to 4 (fully dependent).

Table 2
Correlations Between ProM, RetM, Affective Distress, and IADL Dependence (n = 66)

Variable	1	2	3	4	5	6
1. IADL Severity	----					
2. MIST Summary Score	0.31 [*]	----				
3. PRMQ ProM Scale	-0.51 ^{****}	-0.13 ^{**}	----			
4. RetM Z-score	0.33 ^{**}	0.41 ^{***}	-0.10 ^{****}	----		
5. PRMQ RetM Scale	-0.43 ^{****}	-0.17 ^{**}	0.89 ^{****}	-0.27 [*]	----	
6. POMS Total	-0.47 ^{****}	-0.11	0.48 ^{****}	-0.22	0.44 ^{***}	----

Note. IADL = instrumental activities of daily living; MIST = Memory for Intentions Screening Test; POMS = Profile of Moods States; PRMQ = Prospective and Retrospective Memory Questionnaire; ProM = prospective memory; RetM = retrospective memory.

^{*}
 $p < .05$.

^{**}
 $p < .01$.

^{***}
 $p < .001$.

^{****}
 $p < .0001$.

Table 3
Hierarchical Regression Analysis Predicting IADL Dependence

Variable	B	SEB	β	R^2	ΔR^2
Step 1				0.34***	
POMS	-0.04	0.01	-0.45		
PRMQ RetM Scale	0.84	0.51	0.18		
RetM Z-score	-0.06	0.07	-0.11		
Step 2				0.46***	.12**
PRMQ ProM Scale	0.12	0.05	0.24		
MIST Summary Score	-0.26	0.11	-0.48		

Note. IADL = instrumental activities of daily living; MIST = Memory for Intentions Screening Test; POMS = Profile of Moods States; PRMQ = Prospective and Retrospective Memory Questionnaire; ProM = prospective memory; RetM = retrospective memory.

**
 $p < 0.01$.

 $p < 0.001$.

Table 4
Prospective and Retrospective Memory in the IADL Dependent and Independent HIV+ Groups

Variable	Dependent (n = 26)	Independent (n = 40)	p	Cohen's d (95% CI)
Retrospective Memory				
PRMQ RetM Scale ^a	21.50 (6.05)	16.58 (5.20)	0.001	0.87 (0.35, 1.39)
Self-Cued	11.69 (3.47)	9.53 (3.37)	0.020	0.63 (0.13, 1.14)
Environmentally-Cued	9.81 (3.10)	7.05 (2.23)	0.0004	1.03 (0.51, 1.55)
RetM Z-score	-0.30 (0.75)	0.20 (0.71)	0.014	-0.68 (-1.19, -0.18)
Prospective Memory				
PRMQ ProM Scale ^a	25.08 (6.04)	18.75 (5.57)	<0.0001	1.08 (0.55, 1.61)
Self-Cued ^a	13.04 (3.08)	9.93 (2.86)	0.0003	1.03 (0.50, 1.55)
Environmentally-Cued ^a	12.03 (3.16)	8.83 (3.02)	0.0002	1.03 (0.50, 1.55)
MIST				
Summary Score	36.00 (8.53)	41.18 (5.43)	0.010	-0.75 (-1.26, -0.24)
Time-based Cues	5.42 (1.55)	6.25 (1.24)	0.039	-0.60 (-1.10, -0.09)
Event-based Cues	6.62 (1.72)	7.48 (0.88)	0.020	-0.67 (-1.17, -0.16)
Word Search	15.50 (4.22)	16.90 (4.40)	0.367	-0.32 (-0.82, 0.18)
Recognition Post-test	7.65 (0.56)	7.78 (0.48)	0.324	-0.23 (-0.73, 0.26)
Retrieval Index	2.62 (1.53)	1.65 (1.17)	0.017	0.72 (0.21, 1.23)
Errors				
No Response	1.08 (1.35)	0.38 (0.59)	0.012	0.72 (0.21, 1.23)
Task Substitution	0.69 (0.84)	0.38 (0.54)	0.155	0.47 (-0.03, 0.97)
Loss of Content	0.77 (0.82)	0.70 (0.85)	0.648	0.08 (-0.41, 0.58)
Loss of Time	0.35 (0.75)	0.33 (0.57)	0.770	0.03 (-0.46, 0.53)

Note. Data are presented as mean values with the standard deviation in parentheses. CI = confidence interval; IADL = instrumental activities of daily living; MIST = Memory for Intentions Screening Test; PRMQ = Prospective and Retrospective Memory Questionnaire; ProM = prospective memory; RetM = Retrospective memory.