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Aging, Prospective Memory, and Health-Related Quality of Life in HIV Infection

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Abstract

HIV infection and older age are each independently associated with lower health-related quality of life (HRQoL) and deficits in prospective memory (PM), which is a distinct aspect of cognition involving the ability to "remember to remember" to do something at a future occasion. The present study investigated associations between PM and HRQoL in 72 older (≥ 50 years) and 41 younger (≤ 40 years) HIV-infected adults. Self-reported PM complaints predicted HRQoL across the entire sample, but there was a significant interaction between performance-based PM and age group on HRQoL, such that lower time-based PM was associated with lower HRQoL only in the younger cohort. Within the younger group, time-based and self-reported PM significantly predicted mental HRQoL independent of other risk factors (e.g., depression). These findings suggest that PM plays a unique role in HRQoL outcomes among younger persons living with HIV infection and support the examination of other age-related factors (e.g., effective use of compensatory strategies) that may regulate the adverse impact of PM on everyday functioning.

Keywords

AIDS Dementia Complex; Aging; Prospective memory; Quality of life; Functional status; Health status

INTRODUCTION

Since the advent of combined antiretroviral therapy (cART) in 1996, an increasingly larger proportion of HIV-infected individuals are living into later years of life. As of 2008, older adults (at least 50 years old) comprised nearly 25% of individuals living with HIV infection in the United States [1], and this number is expected to rise to 50% by 2015 [2]. While cART has successfully improved overall HIV disease outcomes [3], older infected individuals still face a host of medical (e.g., hepatitis C co-infection, neuropathy), psychosocial (e.g., stigma, functional autonomy), and neuropsychiatric (e.g., neurocognitive impairment) complications that may adversely impact health-related quality of life (HRQoL). HRQoL is defined as a multidimensional concept that describes one's well-being and includes physical, mental, emotional, and social functioning. HIV-infected individuals have considerably lower HRQoL levels than the general population [4], and older HIV+ adults are at particular risk in that regard. In fact, even among seronegative individuals,

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older adults self-report more overall unhealthy days, physically unhealthy days, and activity limitation days than their younger counterparts [5]. Compared to younger adults, older persons with HIV have a greater overall number of risk factors for lower HRQoL, including more advanced HIV disease (e.g., more rapid progression to AIDS), as well as risks of age-related comorbid conditions (e.g., cardiovascular disease). Thus, not only are older HIV-infected adults likely to be at particular risk for experiencing lower HRQoL, but the specific predictors of HRQoL declines may also differ in older versus younger persons.

Nevertheless, very few studies have specifically examined the prevalence and predictors of HRQoL in younger versus older HIV-infected adults. Among persons living with HIV in the pre-cART era, older age was significantly associated with worse HRQoL scores in the domains of physical function, social function, and health perception [4]. In the cART era, older HIV-infected adults tend to report less social support and evidence greater distress than younger persons with HIV [6]. Older HIV-infected adults with more advanced disease may be particularly vulnerable in this regard, potentially increasing isolation from personal and community support systems due to greater fatigue and diminished participation in social activities [7, 8, 9, 10, 11]. Accordingly, identification of potentially modifiable predictors of HRQoL has emerged as an important clinical and public health issue for younger and older adults infected with HIV.

One important HRQoL factor not well understood in the context of aging in HIV is neurocognitive impairment. Although the occurrence of HIV-associated dementia has markedly decreased [12], milder forms of HIV-associated neurocognitive disorders (HAND) are still highly prevalent, affecting as many as one half of infected individuals [13]. Older HIV-infected adults evidence HAND at disproportionately higher rates [HAD; 14, 15, 16, 17] and show the greatest impairment in the domains of psychomotor speed, executive functions (e.g., complex attention and problem-solving), and memory [18, 19, 20, 21]. Among older adults, HAND may be particularly detrimental for everyday functioning outcomes [22]; for example, older adults with HIV-associated neurocognitive impairment evidence poorer medication [23] and financial [24] management as compared to younger individuals. A handful of studies report that declines in specific neurocognitive domains are predictive of lower HRQoL among younger and middle-aged HIV-infected adults, including psychomotor speed, executive functions, and memory [25, 26].

Such findings raise the interesting possibility that prospective memory (PM), which is an ecologically relevant aspect of memory with strong executive demands, may be a robust predictor of HRQoL in HIV. PM describes one's ability to "remember to remember", examples of which include remembering to attend a medical appointment, take a medication as prescribed, or pay a bill on the first of the month. Successful PM requires several steps, including forming an intention (e.g., taking a medication at bedtime), maintaining the intention during other activities (e.g., daily life), detecting the appropriate cue to retrieve the intention (e.g., preparing for bed), and finally, retrieving and executing the correct intention (e.g., taking the medication as prescribed). The cues that trigger the retrieval of the PM intention may be based on the passage of time (e.g., return a telephone call in an hour) or the occurrence of an event (e.g. return a telephone call when you arrive at home). Time-based PM cues are hypothesized to have stronger executive (i.e., strategic monitoring and cue detection) demands than event-based PM cues [27]. PM is served by both executive functions and retrospective memory abilities, but is also separable from both of these cognitive domains at the neurobiological, cognitive, and functional levels [28, 29].

Persons living with HIV infection endorse more PM complaints in their daily lives than do their seronegative counterparts [30]. HIV is also associated with deficits in objective, laboratory-based measures of both time- and event-based PM [31, 32]. The profile of HIV-

associated PM deficits is suggestive of impairment in the strategic (i.e., executive) aspects of executing future intentions, particularly for time-based cues [27]. Older HIV-infected adults may be especially vulnerable to declines in PM, particularly on tasks with strong executive demands [33, 34]. Of clinical interest, HIV-associated PM impairment is a unique predictor of functional outcomes, such as declines in instrumental activities of daily living [35], nonadherence to antiretroviral medications [36, 37, 38], and unemployment [39]. Importantly, PM possesses incremental value in predicting functional status in HIV, meaning it explains variance in these everyday functioning outcomes independent of well-established clinical risk factors, such as psychiatric comorbidities, demographics, substance dependence, HIV disease severity [35]. Accordingly, it is reasonable to posit that PM may play an important role in HRQoL in HIV infection.

The present study was therefore designed to examine the interrelationships between PM, aging, and HRQoL within an HIV-positive cohort. We hypothesized that both laboratory-based PM deficits and self-reported PM complaints would be associated with lower mental and physical HRQoL across the lifespan. Moreover, we were interested in the possibility that PM may be differentially predictive in younger versus older HIV-infected persons. Considering prior evidence that older adults with HAND may be especially vulnerable to worse functional outcomes [22, 24], we expected to see the strongest relationship between PM and HRQoL in the older cohort, who is also at greatest risk for lower PM and HRQoL. We also predicted that the associations between PM and HRQoL would not be better explained by known contributors, including HIV disease severity, HAND diagnoses, or psychiatric comorbidities.

METHODS

Participants

This study was approved by the institution's human research protections program. Participants were recruited from the San Diego community and local HIV clinics. The primary inclusion criteria were a diagnosis of HIV infection determined by enzyme-linked immunosorbent assays and confirmed by a Western Blot test as well as age ≥ 50 ("Older"; n=72) or ≤ 40 ("Younger"; n=41) years. Although the "older" sample represents a relatively more youthful cohort than is typically studied in geropsychology, the use of 50 years as the cutoff age is nevertheless consistent with the nature of the HIV epidemic [40] and National Institutes of Health (NIH) recommendations for aging neuroAIDS research [41]. All subjects were enrolled in an NIH-funded R01 to study the combined effects of HIV and aging on PM that used this same discrepant age classification approach (i.e., no subject between the ages of 41 and 49 were enrolled in the parent study). Exclusion criteria included a diagnosis of a severe psychiatric illness (e.g., schizophrenia), neurological disease (e.g. seizure disorders, closed head injury with loss of consciousness greater than 15 minutes, or active CNS opportunistic infections), a verbal IQ estimate of <70 based on the Wechsler Test of Adult Reading [WTAR; 42], diagnosis of substance dependence within the 6 months of evaluation, urine toxicology screen positive for elicit drugs on the day of evaluation (excluding marijuana), or a Breathalyzer test positive for alcohol.

Table 1 shows the demographic, psychiatric, and HIV disease characteristics of the study samples. The older sample had a higher proportion of Caucasians, more years of formal education, and a higher rate of hepatitis C co-infection (ps < .05). HIV disease-related differences included lower nadir CD4 cell counts, longer estimated durations of infection, and higher rates of AIDS diagnoses in the older group (ps < .05).

Materials and Procedure

After providing written, informed consent, participants completed a comprehensive neuropsychological, psychiatric, and medical evaluation.

Quality of life assessment—To assess HRQoL, participants were administered the RAND 36-Item Short Form Health Survey (SF-36). The SF-36 is a generic assessment of quality of life consisting of 36 questions [43]. An individual's responses to these questions are combined to form eight subscales of HRQoL, including physical functioning, social functioning, physical role, emotional role, mental health, vitality, bodily pain and general health due to physical and emotional problems, emotional well-being, pain, and vitality [44]. Each of these dimensions receives a score of 0 to 100 (with higher scores indicating better HRQoL). For the purposes of this study, the eight dimensions were summarized into two subscales of HRQoL: physical health and mental health [45]. These two component scores have been well-validated in HRQoL literature [45], and while investigating their separate relationships with PM was not a hypothesis-driven endeavor, it was nevertheless warranted in light of prior literature showing possible differential predictors of physical and mental HRQoL in a variety of clinical populations. Each subscale was given a score ranging from 0 to 100, with higher scores indicating better HRQoL. Prior studies support the reliability and construct validity of the SF-36 for use in investigations of HIV infection [46, 47].

PM assessment—Participants were administered the research version [48] of the Memory for Intentions Screening Test (MIST) [49], which is a standardized, performance-based measure of PM. Prior research supports the reliability and construct validity of the MIST in individuals with HIV infection [28, 48]. The MIST consists of eight trials during which the participant completes at least one word search puzzle as the ongoing task. The MIST trials are counterbalanced on the following characteristics: (1) a 2-min or 15-min delay; (2) a verbal (e.g., "In 2 min, ask me what time this session ends today") or a physical (e.g., "In 15 min, use that paper to write down the number of medications you're currently taking") response; and (3) a time-based (e.g., "In 15 min, tell me that it is time to take a break") or an event-based (e.g., "When I show you a postcard, self-address it") cue. On each of these six subscales, scores range from 0 to 8 points, with a total MIST score range of 0 to 48 points. Consistent with previous studies, errors were coded as follows: (1) no-response (i.e., no reaction to a PM cue); (2) loss of time (i.e., executing a correct response ≥ 15% of the target time); (3) task substitution (i.e., responding incorrectly to the cue); or (4) loss of content (i.e., awareness that a response is required but failure to recall the correct intention). After the MIST was completed, participants were administered an eight-item, three-choice recognition task (range = 0 to 8).

Self-reported PM was assessed using the Prospective and Retrospective Memory Questionnaire [50]. The PRMQ is a 16-item measure that assesses the frequency of memory complaints in everyday life, using a 5-point Likert-type scale that ranges from 1(*never*) to 5 (*very often*). This study focused on the 8-item PM subscale, which is comprised of 4 self-cued PM complaints (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 4 environmentally-cued PM complaints (e.g., "How often do you forget to buy something you planned to buy, like a birthday card, even when you see the shop?"). Total scores on the PRMQ PM scale range from 0 to 40, with higher scores indicating poorer self-reported PM. Prior research supports the reliability [51] and construct validity [52] of the PRMQ.

General neuropsychological assessment—Participants received a comprehensive neurocognitive assessment in accordance with Frascati research guidelines for assessing HAND [53]. The neuropsychological battery was comprised of several standardized and

well-validated research tests, including the following: Trail Making Test A & B [TMT; 54], Action Fluency [55], California Verbal Learning Test – 2nd Edition [CVLT-II; 56], Logical Memory (LM) Subtest of the Wechsler Memory Scales Third Edition [WMS-III; 57], Tower of London – Drexel [ToL^{DX}; 58], Digit Span subtest and Digit Symbol subtest of the Wechsler Adult Intelligence Scale – Third Edition [WAIS-III; 55], and Grooved Pegboard Test [GP; 59]. For further details, see [27]. A global clinical rating score was generated from participants' neurocognitive test scores across these seven domains of cognitive functioning (i.e., executive functions, learning, memory, attention, verbal fluency, information processing speed, and motor skills), which range from 1 (above average) to 9 (severely impaired). Global clinical rating scores greater than or equal to 5 were used to determine a HAND diagnoses [60].

Psychiatric assessment—Participants received structured psychiatric interviews, conducted using the Composite International Diagnostic Interview [CIDI version 2.1; 61], which is based on the Diagnostic and Statistical Manual of Mental Disorders criteria [62]. The CIDI provided lifetime and current diagnoses of major depressive disorder, generalized anxiety disorder, and substance use disorders. These modules were chosen for their prevalence in HIV disease and potential relevance to HAND. Additionally, participants completed the Profile of Mood States questionnaire [POMS; 63], a 65-item self-report measure of current mood states (covering the week prior to evaluation) in areas including tension/anxiety, depression/dejection, anger/hostility, vigor/activity, fatigue/inertia, and cognitive/confusion. The POMS also provides a total mood disturbance score, whereby higher scores on any variable indicate greater distress.

RESULTS

As shown in Table 2, we conducted four primary multiple regression analyses to examine the relationship between PM, aging, and HRQoL. In each regression, the SF-36 summary score for either mental or physical HRQoL (M-QoL and P-QoL, respectively) served as the criterion. In the first two models, we focused on the self-initiated and strategic aspects of PM by examining the MIST time-based (TB) PM and PRMQ PM Self-Cued scales as predictors of HRQoL, along with their interactions with age group. In the last two models, we focused on the associative and more automatic aspects of PM by examining the MIST event-based (EB) PM and PRMQ PM Environmentally-Cued scales as predictors of HRQoL, as well as their interactions with age group. Additionally, in each model, we included as covariates the five variables shown in Table 1 that differed across age groups (i.e., education, ethnicity, HCV status, duration of infection, and AIDS status). Although the older group also had a significantly lower nadir CD4 counts, we only included AIDS diagnosis in these regressions because of the collinear relationship between these two variables. Nevertheless, our findings remained the same when nadir was used instead of AIDS status in the four hierarchical regressions predicting HRQoL from PM variables.

Age Group, PM cues, and HRQoL

Table 2 shows the results of two separate hypothesis-driven multiple regression analyses to concurrently predict both M-QoL and P-QoL from TB and EB MIST performance and PRMQ PM scales. In the regression predicting M-QoL from strategic (i.e., time-based) PM, the overall model was significant ($F(10, 94) = 10.00$, $p < .001$, adjusted $R^2 = .46$), with the age by MIST TB interaction ($p = .04$) and PRMQ Self-Cued score ($p < .001$) as sole predictors. A similar result emerged in the model predicting P-QoL from strategic PM, such that the overall model was significant ($F(10, 96) = 5.32$, $p < .0001$, adjusted $R^2 = .29$), with PRMQ Self-Cued score ($p < .001$) and the age by MIST TB interaction ($p = .05$) emerging as the only predictors (although the latter was at trend-level). Follow-up analyses showed

that MIST TB PM was associated with both M-QoL (Spearman's ρ = .39, p = .01) and P-QoL (Spearman's ρ = .36, p = .02) in the younger HIV-positive group, but not in the older HIV-positive group (ps >.10). The PRMQ Self-Cued score was associated with HRQoL in both groups as a main effect (ps < .01). In the entire sample (N = 113), PRMQ Self-Cued score was strongly correlated to M-QoL (Spearman's ρ = −.65, p < .001) and P-QoL (Spearman's ρ = −.56, p < .001). Within the younger HIV-positive group alone, the PRMQ Self-Cued score was associated with both M-QoL (Spearman's ρ = −.63, p < .001) and P-QoL (Spearman's ρ = −.38, p = .02). A similar finding emerged in the older HIV-positive group, in which PRMQ Self-Cued score was also associated with both M-QoL (Spearman's ρ = −.61, p < .001) and P-QoL (Spearman's ρ = −.61, p < .001).

In the regression predicting M-QoL from associative (i.e., event-based) PM, the overall model was significant (F(10, 95) = 6.74, p < .001, adjusted R^2 = .35), with PRMQ Environmentally-Cued score as the sole predictor (p < .001). A similar result occurred in the regression predicting P-QoL from associative PM, with the overall model being significant (F(10, 97) = 4.73, p < .001, adjusted R^2 = .26), and the PRMQ Environmentally-Cued score as the sole predictor (p < .001). Within the entire sample (N = 113), the PRMQ Environmentally-Cued score was strongly correlated to M-QoL (Spearman's ρ = −.60, p < .001) and P-QoL (Spearman's ρ = −.55, p < .001). Within the younger HIV-positive group alone, the PRMQ Environmentally-Cued score was associated with both M-QoL (Spearman's ρ = −.59, p < .001) and P-QoL (Spearman's ρ = −.50, p < .001); a similar finding emerged in the older HIV-positive group, in which PRMQ Self-Cued score was also associated with both M-QoL (Spearman's ρ = −.59, p < .001) and P-QoL (Spearman's ρ = −.57, p < .001)

PM and HRQoL in the Younger Cohort

Table 3 shows the results of two follow-up multiple regression analyses in the younger HIV-positive group to examine the statistical independence of MIST TB PM and the PRMQ PM total as predictors of M-QoL and P-QoL, above and beyond other established risk factors for low HRQoL (i.e., current Major Depressive Disorder, CD4 cell count, lifetime Substance Dependence, and HAND diagnosis) (see Table 3). In the model predicting M-QoL, the overall amount of variance accounted for was significant (F(6, 33) = 9.04, p < .001, adjusted R^2 = .55), with MIST TB PM performance (p = .02), PRMQ PM total score (p < .001), and current MDD (p = .01) as the only significant predictors. In the analysis predicting P-QoL, the overall model was significant (F(6, 33) = 3.26, p = .01, adjusted R^2 = .26), with only PRMQ PM total score (p = .05) and current Major Depressive Disorder (p = .06) emerging as trend-level predictors.

PM Components and HRQoL in the Younger Cohort

To examine component cognitive processes that relate to HRQoL in the younger HIV-positive group, we looked at correlations between M-QoL, P-QoL, and the following MIST variables: error types (i.e., Omission, Loss of Time, Loss of Content, and Task Substitution), distracter task performance (i.e., total items found on the word search distracter task), recognition task total score, and the 24-hour delay task. Only Omission errors were significantly associated with M-QoL (Spearman's ρ = −.32, p = .02) and P-QoL, but at a trend-level finding (Spearman's ρ = −.29, p = .07). No other correlations were significant (ps >.10).

DISCUSSION

Consideration of HRQoL has become increasingly important for persons living with HIV infection in the era of cART. The current study extends a nascent literature on

neurocognitive predictors of HRQoL in HIV to the domain of PM in the context of aging. Results from this cross-sectional study revealed that self-reported PM was a unique and robust predictor of HRQoL in HIV; specifically, elevated PM complaints were associated with lower mental and physical HRQoL across the lifespan. Notably, this association was not better explained by other known predictors of HRQoL, including disease-related factors (i.e., current CD4 cell count, duration of infection, AIDS diagnoses), current major depressive disorder, lifetime substance dependence, and HAND diagnoses. This predictive value of self-reported PM is consistent with other indices of daily functioning within HIV infection, including declines in instrumental activities of daily living [IADL; 35] and self-reported medication management [37]. However, another interpretive possibility of this finding is that individuals who experience lower HRQoL are simply more likely to complain about declines in higher-level cognitive abilities, which tend to correlate strongly with one another [51], thereby raising questions about the possibly specificity of the self-reported PM findings reported herein.

Age Effects and the Association Between Laboratory PM and HRQoL

Contrary to our *a priori* hypotheses, results revealed a differential predictive value of PM across older and younger HIV-infected adults; that is, performance-based, specifically time-based, PM was associated with lower HRQoL only in the younger cohort. These findings suggest that PM is a potentially important risk factor for poorer HRQoL in younger, but not older HIV-infected individuals. These data directly conflict with prior studies suggesting that older adults with HAND may be especially vulnerable to functional declines [22]. Findings are unlikely to be an artifact of group differences in HIV disease severity or psychiatric factors, as these variables were included in the statistical models. Moreover, we used age-corrected SF-36 variables, thereby reducing the likelihood that group differences in HRQoL factors could explain the discrepant PM predictions.

One possible interpretation of our finding is that the younger population is less likely than older adults to use compensatory mechanisms (e.g., external reminders, request assistance from others) in their daily lives to help overcome PM-related deficits. To that end, a recent study from our group found that older HIV-infected adults who successfully completed a naturalistic PM task (i.e., telephoning the laboratory the day after the exam) were more likely to use external and PM compensatory strategies in their daily lives than were younger HIV-infected adults [33]. This reasoning would be commensurate with a phenomenon termed “the age-prospective memory paradox” which demonstrates that, even though older adults evidence greater deficits than younger adults on PM laboratory-based tasks, they perform comparably (or sometimes even better than) younger adults on naturalistic PM tasks [33]. Tempering this interpretation is the apparent discrepancy with self-reported PM, which was predictive of HRQoL in across both age groups. This finding is consistent with prior research showing weak correlations between performance-based and self-report PM measures [30], even though both methods are sensitive to HIV and are independently predictive of many everyday functioning outcomes [35]. Another possible (and not necessarily unrelated) mechanism that could be driving this paradoxical relationship is that of metacognitive awareness; that is, older adults have more experience with PM in their daily lives than younger adults do, and are thus more aware of their PM deficits and more likely to proactively compensate for them [64, 30]. Prospective studies are needed to directly evaluate the possible moderating effects of meta-cognitive awareness and compensatory strategy use on the associations between PM and everyday functioning outcomes in older and younger persons living with HIV infection.

PM, Functional Outcomes, and HRQoL

Taken together, these findings raise broader questions about precisely *how* PM may impact HRQoL in HIV infection. Given that these data are commensurate with data on PM and functional outcomes, including medication adherence [38], unemployment [39], and IADLs [35], one possible explanation is that HRQoL may be mediated by functional deficits secondary to PM impairment. In fact, this suggestion resonates with the influential conceptual model of HRQoL by Wilson and Cleary [65]. In the context of this linear model, biological vulnerabilities (e.g., immunovirological burden and neural injury) result in the expression of PM impairment that adversely impacts everyday functioning outcomes, which in turn lead to reduced personal health perceptions and lower HRQoL. Integrating this model with the age-prospective memory paradox described above, one might predict that the use of targeted compensatory strategies to alleviate the functional deficits could ultimately improve health perceptions and thus better HRQoL. Nevertheless, such conceptual musings are somewhat preliminary as our study did not directly assess Wilson & Cleary's model and omitted several key elements in that regard, including assessments of general health perceptions and of the individual's personal characteristics and environment (i.e., symptom amplification, personality motivation, value preferences, and psychological/social/economic support systems). Future studies with larger samples, more sophisticated statistical models, and the inclusion of questionnaires that directly query participants about the impact of perceived PM deficits on HRQoL may shed some light on these issues.

PM Across Mental and Physical HRQoL

One interesting observation from this study that was not predicted in our *a priori* hypotheses was the finding that performance-based PM was found to be more strongly associated with mental HRQoL than physical HRQoL. While time-based PM was correlated with both mental and physical HRQoL in the younger HIV-infected sample, follow-up multiple regression analyses including other salient predictors (e.g., depression) revealed that this effect persisted only for mental HRQoL. In contrast, self-reported PM predicted both mental and physical HRQoL in the larger models. Although these findings were derived from exploratory (but still planned) analyses, it may be possible that PM ability (cf. complaints) may be more clinically relevant to mental versus physical HRQoL in younger HIV+ adults, though interpretations of this differential association clearly warrants further investigation. While deficits in time- and event-based PM are broadly comparable in HIV infection, the cognitive architecture of these two aspects of PM may diverge, with time-based PM being more strongly affected by certain aspects of cognitive dyscontrol, including strategic monitoring and self-initiated retrieval processes [27]. To this end, other studies from our group have found time-based PM to be an especially valuable predictor of everyday functioning [32, 35]. Nevertheless, we cannot exclude the possibility that event-based PM tasks with greater strategic demands (e.g., under conditions of high cognitive load) may be associated with lower HRQoL.

Limitations

As with all clinical investigations, several limitations exist in interpreting the findings from the current study. First, while the SF-36 is broadly used and well-validated within HIV [46, 47], it nevertheless provides a generic assessment of HRQoL and is not tailored to assess specific aspects of HIV-related QoL. This limitation, for example, may have played a role in the relatively weak associations observed between the demographic and clinical characteristics (e.g., HIV disease severity) of our groups and physical HRQoL as measured by the SF-36 in this study. As concerns the study design, the parent study used cross-sectional, discrepant age-based group classifications rather than examining age as a continuous variable. Although this approach is arguably more powerful in detecting age-related effects and is quite common in studies on aging and cognition among healthy adults,

is nevertheless not without limitations or controversy. Most notably, this approach does not permit us to generalize our findings to individuals aged 41–49 years, who represent a large proportion of the HIV epidemic. Moreover, we cannot exclude the possibility that our findings simply reflect cohort effects, rather than aging *per se*. Relatedly, our sample also consisted of mostly well-educated Caucasian men with relatively well-controlled HIV disease (e.g., median current CD4 cell count was 556). As such, these findings may not generalize to other HIV-infected populations, including women and ethnic minorities, populations in which the number of incident AIDS cases are increasing [66]. Additionally, we did not include data on socioeconomic status, which may have implications for HRQoL outcomes. Finally, our exclusion criteria included factors that have been linked to lower HRQoL, including traumatic brain injury [67], current substance dependence [68], and severe mental illness [69].

In summary, findings from this study indicate that PM deficits and complaints are associated lower HRQoL in younger HIV-infected adults. These data highlight the potential benefits of including assessments of PM in neuropsychological evaluations of persons living with HIV. Additionally, cognitive rehabilitation techniques aimed at lessening the executive demands of PM in this at-risk population might improve HRQoL outcomes. For example, techniques could include training an individual for improvement in different aspects of PM, from lessening distraction during the delay interval to making the PM cue more salient (e.g., a large pillbox placed in a prominent place) to enhance the likelihood of detection. Given that associations have been found between PM and several aspects of daily functioning, it may also prove beneficial to educate individuals on the day-to-day risks of PM deficits, which may increase usage of compensatory mechanisms. Of course, whether any of these rehabilitation techniques targeted toward PM improvement may in fact improve daily functioning and HRQoL is an empirical question and warrants investigation in future research.

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References

1. Centers for Disease Control. HIV/AIDS surveillance report, 2005. Atlanta: U.S. Department of Health and Human Services, CDC; 2007. p. 1-63.

2. Smith, G. Aging hearing: HIV over fifty, exploring the new threat. Washington, DC: Senate Committee on Aging; Statement of Senator Gordon H. Smith. Available from: http://www.aging.senate.gov/events/hr141gs.pdf
3. Kitahata MM, Gange SJ, Abraham AG, et al. Effect of early versus deferred antiretroviral therapy for HIV on survival. N Engl J Med. 2009; 360:1815–1826. [PubMed: 19339714]
4. Piette J, Wachtel TJ, Mor V, Mayer K. The impact of age on the quality of life in persons with HIV infection. J Aging Health. 1995; 7(2):163–17. [PubMed: 10165953]
5. Zahran HS, Kobau R, Moriarty DG, et al. Health-related quality of life surveillance—United States, 1993–2002. MMWR Surveill Summ. 2005; 54:1–35. [PubMed: 16251867]
6. Chesney MA, Chambers DB, Taylor JM, Johnson LM. Social support, distress, and well-being in older men living with HIV infection. J Acquir Immune Defic Syndr. 2003; 33(Suppl 2):S185–S193. [PubMed: 12853868]
7. Avis NE, Smith KW. Quality of life in older adults with HIV disease. Res Aging. 1998; 20(6):822–845.
8. Hays RB, Catania JA, McKusick L, Coates TJ. Help-seeking for AIDS-related concerns: a comparison of gay men with various HIV diagnoses. Am J Community Psychol. 1990; 18(5):743–55. [PubMed: 2075900]
9. Fleishman JA, Sherbourne CD, Crystal S, et al. Coping, conflictual social interactions, social support, and mood among HIV-infected persons. HCSUS Consortium. Am J Community Psychol. 2000; 28(4):421–53. [PubMed: 10965385]
10. Swindells S, Mohr J, Justis JC, et al. Quality of life in patients with human immunodeficiency virus infection: impact of social support, coping style and hopelessness. Int J STD AIDS. 1999; 10(6):383–91. [PubMed: 10414881]
11. Schmitz MF, Crystal F. Social relations, coping, and psychological distress among persons with HIV/AIDS. J Appl Soc Psychol. 2000; 30(4):665–685.
12. Heaton RK, Franklin DR, Ellis RJ, et al. HIV-associated neurocognitive disorders before and during the era of combination antiretroviral therapy: differences in rates, nature, and predictors. J Neurovirol. 2011; 17(1):3–16. [PubMed: 21174240]
13. Heaton RK, Franklin D, Clifford D, et al. Persistence and progression of HIV-associated neurocognitive impairment (NCI) in the era of combination antiretroviral therapy (CART) and the role of comorbidities: The CHARTER Study. J Neurovirol. 2009; 15(Suppl 1):34–35.
14. Becker JT, Lopes OL, Dew MA, Aizenstein HJ. Prevalence of cognitive disorders differs as a function of age in HIV virus infection. AIDS. 2004; 18:S11–18. [PubMed: 15075493]
15. Larussa D, Lorenzini P, Cingolani A, et al. Highly active antiretroviral therapy reduces the age-associated risk of dementia in a cohort of older HIV-1 infected patients. AIDS Res Hum Retroviruses. 2006; 22:386–392. [PubMed: 16706614]
16. Valcour B, Shikuma C, Shiramizu B, et al. Higher frequency of dementia in older HIV-1 individuals: The Hawaii Aging with HIV Cohort. Neurology. 2004; 63:822–827. [PubMed: 15365130]
17. Valcour B, Shikuma C, Shiramizu B, et al. Age, apolipoprotein E4, and the risk of HIV dementia: The Hawaii HIV with Aging Cohort. J Neuroimmunol. 2004; 157:197–202. [PubMed: 15579298]
18. Cherner M, Ellis RJ, Lazzaretto D, et al. Effects of HIV-1 infection and aging on neurobehavioral functioning: preliminary findings. AIDS. 2004; 18(Suppl 1):S27–34. [PubMed: 15075495]
19. Sacktor N, Skolasky R, Selnes OA, et al. Neuropsychological test profile differences between young and old human immunodeficiency virus-positive individuals. J Neurovirol. 2007; 13(3):203–9. [PubMed: 17613710]
20. Sacktor N, Skolasky RL, Cox C, et al. Longitudinal psychomotor speed performance in human immunodeficiency virus-seropositive individuals: impact of age and serostatus. J Neurovirol. 2010; 16(5):335–41. [PubMed: 20726699]
21. Woods SP, Moore DJ, Weber E, Grant I. Cognitive neuropsychology of HIV-associated neurocognitive disorders. Neuropsychol Rev. 2009; 19(2):152–168. [PubMed: 19462243]
22. Barclay TR, Hinkin CH, Castellon SA, Mason KI, Reinhard MJ, Marion SD. Age-associated predictors of medication adherence in HIV-positive adults: Health beliefs, self-efficacy, and neurocognitive status. Health Psychol. 2007; 26:40–49. [PubMed: 17209696]

23. Ettenhofer ML, Foley J, Behdin N, Levine AJ, Castellon SA, Hinkin CH. Reaction time variability in HIV-positive individuals. Arch Clin Neuropsychol. 2010; 25(8):791–8. [PubMed: 20798183]
24. Thames AD, Kim MS, Becker BW, et al. Medication and finance management among HIV-infected adults: The impact of age and cognition. J Clin Exp Neuropsychol. 2011; 33(2):200–9. [PubMed: 20694873]
25. Tozzi V, Balestra P, Galgani S, et al. Neurocognitive performance and quality of life in patients with HIV infection. AIDS Res Hum Retroviruses. 2003; 19(8):643–52. [PubMed: 13678465]
26. Osowiecki DM, Cohen RA, Morrow KM, et al. Neurocognitive and psychological contributions to quality of life in HIV-1-infected women. AIDS. 2000; 14(10):1327–32. [PubMed: 10930146]
27. Zogg JB, Woods SP, Weber E, Doyle K, Grant I. the HNRC Group. Are time- and event-based prospective memory comparably affected in HIV infection? Arch Clin Neuropsychol. 2011; 26:250–59. [PubMed: 21459901]
28. Gupta S, Woods SP, Weber E, Dawson MS, Grant I. the HNRC Group. Is prospective memory a dissociable cognitive function in HIV infection? J Clin Exp Neuropsychol. 2010; 32(8):898–908. [PubMed: 20425662]
29. Woods SP, Morgan EE, Marquie-Beck J, et al. Markers of macrophage activation and axonal injury are associated with prospective memory in HIV-1 disease. Cogn Behav Neurol. 2006; 19(4):217–21. [PubMed: 17159619]
30. Woods SP, Carey CL, Moran LM, et al. Frequency and predictors of self-reported memory complaints in individuals infected with HIV. Arch Clin Neuropsychol. 2007; 22(2):187–95. [PubMed: 17289343]
31. Carey CL, Woods SP, Rippeth JD, Heaton RK, Grant I. the HNRC Group. Prospective memory in HIV-1 infection. J Clin Exp Neuropsychol. 2006; 28(4):536–48. [PubMed: 16676475]
32. Martin EM, Nixon H, Pitrack DL, et al. Characteristics of prospective memory deficits in HIV-seropositive substance-dependent individuals: Preliminary observations. J Clin Exp Neuropsychol. 2007; 29(5):496–504. [PubMed: 17564915]
33. Weber E, Woods SP, Delano-Wood L, et al. An examination of the age-prospective memory paradox in HIV-infected adults. J Clin Exp Neuropsychol. In press.
34. Woods SP, Dawson MS, Weber E, Grant I. the HNRC Group. The semantic relatedness of cue-intention pairings influence event-based prospective memory failures in older adults with HIV infection. J Clin Exp Neuropsychol. 2010; 32(4):398–407. [PubMed: 19763997]
35. Woods SP, Iudicello JE, Moran LM, et al. HIV-associated prospective memory impairment increases risk of dependence in everyday functioning. Neuropsychology. 2008; 22(1):110–117. [PubMed: 18211160]
36. Contardo C, Black AC, Beauvais J, Dieckhaus K, Rosen MI. Relationship of prospective memory to neuropsychological function and antiretroviral adherence. Arch Clin Neuropsychol. 2009; 24:547–54. [PubMed: 19648150]
37. Woods SP, Moran LM, Carey CL, et al. Prospective memory in HIV infection: Is “remembering to remember” a unique predictor of self-reported medication management? Arch Clin Neuropsychol. 2008; 23(3):257–270. [PubMed: 18243645]
38. Woods SP, Dawson MS, Weber E, et al. Timing is everything: Antiretroviral non-adherence is associated with impairment in time-based prospective memory. J Int Neuropsychol Soc. 2009; 15(1):42–52. [PubMed: 19128527]
39. Woods SP, Weber E, Weisz M, Twamley EW, Grant I. the HNRC Group. Prospective memory deficits are associated with unemployment in persons living with HIV infection. Rehabil Psychol. 2011; 56(1):77–84. [PubMed: 21401289]
40. Center for Disease Control. HIV/AIDS surveillance report, 2007. Atlanta: U.S. Department of Health and Human Services, CDC; 2009. p. 1-54.
41. Stoff DM. Mental health research in HIV/AIDS and aging: problems and prospects. AIDS. 2004; 18(Suppl 1):S3–S10. [PubMed: 15075492]
42. The Psychological Corporation. Manual for the Wechsler Test of Adult Reading (WTAR). San Antonio, TX: Author; 2001.
43. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care. 1992; 30(6):473–83. [PubMed: 1593914]

44. Ware, JE., Jr; Snow, KK.; Kosinski, M.; Gandek, B. SF-36 Health survey: manual and interpretation guide. Boston: The Health Institute, New England Medical Center; 1993.
45. Ware, JE.; Kosinski, M.; Keller, SD. SF-36 Physical and mental health summary scales: a user's manual. Boston: The Health Institute, New England Medical Center; 1994.
46. Lamping DL. Methods for measuring outcomes to evaluate interventions to improve health-related quality of life in HIV infection. Psychol Health. 1994; 9(1–2):31–49.
47. Hsiung PC, Fang CT, Chang YY, Chen MY, Wang JD. Comparision of WHOQOL-bREF and SF-36 in patients with HIV infection. Qual Life Res. 2005; 14(1):141–150. [PubMed: 15789948]
48. Woods SP, Moran LM, Dawson MS, Carey CL, Grant I. the HNRC Group. Psychometric characteristics of the Memory for Intentions Screening Test. Clin Neuropsychol. 2008; 22(5):864–78. [PubMed: 18756389]
49. Raskin, S.; Buckheit, C.; Sherrod, C. Memory for Intentions Test (MIsT). Lutz, FL: Psychological Assessment Resources, Inc; 2010.
50. Smith G, Della Sala S, Logie RH, Maylor EA. Prospective and retrospective memory in normal ageing and dementia: a questionnaire study. Memory. 2000; 8(5):311–2. [PubMed: 11045239]
51. Crawford JR, Smith G, Maylor EA, Della Sala S, Logie RH. The Prospective and Retrospective Memory Questionnaire (PRMQ): Normative data and latent structure in a large non-clinical sample. Memory. 2003; 11(3):261–75. [PubMed: 12908675]
52. Smith HJ, Taylor R, Mitchell A. A comparison of four quality of life instruments in cardiac patients: SF-36, QLI, QLMI, and SEIQoL. Heart. 2000; 84(4):390–4. [PubMed: 10995407]
53. Antinori A, Arendt G, Becker JT, et al. Updated research nosology for HIV-associated neurocognitive disorders. Neurology. 2007; 69(18):1789–99. [PubMed: 17914061]
54. Reitan, RM.; Wolfson, D. The Halstead-Reitan Neuropsychological Test Battery: Theory and Clinical Interpretation. Tucson, AZ: Neuropsychology Press; 1985.
55. Woods SP, Carey CL, Tröster AI, Grant I. the HNRC Group. Action (verb) generation in HIV-1 infection. Neuropsychologia. 2005; 43(8):1144–51. [PubMed: 15817172]
56. Delis, DC.; Kramer, JH.; Kaplan, E.; Ober, BA. The California Verbal Learning Test. 2. San Antonio, TX: The Psychological Corporation; 2000.
57. Psychological Corporation. WAIS-III and WMS-III technical manual. San Antonio, TX: Author; 1997.
58. Culbertson, WC.; Zillmer, EA. The Tower of London DX (TOL-DX) manual. North Tonawanda, NY: Multi-Health Systems; 2001.
59. Kløve, H. Grooved pegboard. Indiana: Lafayette Instruments; 1963.
60. Woods SP, Rippeth JD, Frol AB, et al. Interrater reliability of clinical ratings and neurocognitive diagnoses in HIV. J Clin Exp Neuropsychol. 2004; 26(6):759–78. [PubMed: 15370374]
61. World Health Organization. Composite International Diagnostic Interview (CIDI, version 2.1). Geneva, Switzerland: World Health Organization; 1998.
62. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4. Washington, DC: Author; 1994.
63. McNair, DM.; Lorr, M.; Droppleman, LF. Manual for the Profile of Mood States. San Diego, CA: Educational and Industrial Testing Services; 1981.
64. Kliegel, M.; Jager, T.; Altgasen, M.; Shum, D. Clinical neuropsychology of prospective memory. In: Kliegel, M.; McDaniel, MA.; Einstein, GO., editors. Prospective Memory: Cognitive, Neuroscience, Developmental, and Applied Perspectives. New York: Taylor and Francis Group/ Lawrence Erlbaum Associates; 2008. p. 283-308.
65. Wilson IB, Cleary PD. Linking clinical variables with health-related quality of life. A conceptual model of patient outcomes. JAMA. 1995; 273(1):59–65. [PubMed: 7996652]
66. Centers for Disease Control. HIV/AIDS surveillance report, 2005. Atlanta: U.S. Department of Health and Human Services, CDC; 2007. p. 1-63.
67. Dijkers MP. Quality of life after traumatic brain injury: a review of research approaches and findings. Arch Phys Med Rehabil. 2004; 85(4 Suppl 2):S21–35. [PubMed: 15083419]

68. Smith KW, Larson MJ. Quality of life assessments by adult substance abusers receiving publicly funded treatment in Massachusetts. Am J Drug Alcohol Abuse. 2003; 29(2):323–35. [PubMed: 12765209]

69. Holloway F, Carson J. Quality of life in severe mental illness. Int Rev Psychiatry. 2002; 14(3): 175–184.

Table 1

Demographic, Psychiatric, and Medical Characteristics of the Study Participants

Characteristics	Young (n=41)	Old (n=72)	p
Demographics			
Age (years)	30.9 (5.2)	55.9 (5.6)	<.001
Education (years)	12.9 (2.3)	14.0 (2.6)	.013
WTAR verbal IQ	100.2 (10.2)	101.5 (11.1)	.542
Sex (% female)	17.1	18.1	.895
Ethnicity (% Caucasian)	43.9	70.8	.005
Psychiatric			
Lifetime major depression (%)	58.5	54.2	.653
Lifetime generalized anxiety (%)	12.2	19.4	.322
Lifetime substance dependence (%)	48.8	56.9	.403
POMS total[a]	38 (27, 72)	51 (26, 78)	.363
Medical			
Hepatitis C (%)	4.9	35.2	<.001
HIV Disease			
HIV duration (years)	6.4 (5.5)	16.5 (7.2)	<.001
AIDS (%)	31.7	59.7	.004
HAART (%)	82.9	91.7	.263
Nadir CD4[a] (cells/μl)	249 (165, 350)	177 (65, 300)	.006
Current CD4[a] (cells/μl)	547 (404, 809)	558 (386, 803)	.975
HIV RNA $\log_{10}$ (% detectable)	26.8	14.3	.103

Note. WTAR = Wechsler Test of Adult Reading. POMS = Profile of Mood States. HAART = highly-active antiretroviral therapy.

[a]Median (interquartile range)

Table 2

Multiple regressions concurrently predicting mental and physical HRQoL from TB and EB PM after controlling for demographics, psychiatric/medical, and cognitive factors.

	Mental HRQoL				Physical HRQoL			
	B	***B* 95% CI**	***β***	**Adj R^2**	***B***	***B* 95% CI**	***β***	**Adj R^2**
Strategic PM				0.46***				0.29***
Education	−0.09	−0.89, 0.71	−0.02		0.34	−0.53, 1.20	0.07	
Ethnicity	−0.96	−2.95, 1.02	−0.08		−0.07	−2.19, 2.05	−0.01	
HCV serostatus	0.33	−2.20, 2.87	0.02		0.57	−2.06, 3.21	0.04	
Duration of HIV infection	−0.13	−0.40, 0.15	−0.08		−0.16	−0.45, 0.14	−0.11	
AIDS status	−0.94	−2.79, 0.92	−0.08		−1.14	−3.12, 0.83	−0.10	
Age	2.18	−0.50, 4.87	0.17		1.75	−1.19, 4.69	0.15	
MIST TB PM	0.84	−0.44, 2.12	0.12		0.85	−0.53, 2.24	0.13	
MIST TB PM x Age	−1.32	−2.59, −0.06	−0.18*		−1.36	−2.74, 0.01	−0.19†	
PRMQ SC PM Scale	−0.98	−1.24, −0.71	−0.67***		0.61	−0.90, −0.33	−0.45***	
PRMQ SC PM Scale x Age	0.09	−0.17, 0.34	0.06		−0.14	−0.42, 0.13	−0.10	
Associative PM				0.41***				.33***
Education	−0.12	−0.98, 0.74	−0.03		0.13	−0.74, 1.00	0.03	
Ethnicity	−0.71	−2.87, 1.45	−0.06		0.37	−1.78, 2.51	0.03	
HCV serostatus	0.64	−2.07, 3.35	0.04		0.84	−1.78, 3.46	0.06	
Duration of HIV infection	−0.13	−0.43, 0.18	−0.08		−0.14	−0.44, 0.17	−0.10	
AIDS status	−0.96	−2.98, 1.06	−0.08		−1.14	−3.15, 0.87	−0.10	
Age	1.58	−1.25, 4.40	0.13		1.73	−1.15, 4.61	0.15	
MIST EB PM	0.55	−0.89, 1.98	0.08		1.00	−0.43, 2.43	0.15	
MIST EB PM x Age	−0.26	−1.65, 1.13	−0.04		−0.89	−2.29, 0.50	−0.13	
PRMQ EC PM Scale	−0.92	−1.20, −0.64	−0.61***		−0.69	−0.98, −0.40	−0.48***	
PRMQ EC PM Scale x Age	0.06	−0.21, 0.34	0.04		−0.05	−0.32, 0.23	−0.03	

Note. Adj = adjusted; *B* = beta weight; β = standardized beta weight; MIST = Memory for Intentions Screening Test; TB PM = time-based prospective memory; SC = self-cued; EB PM = event-based prospective memory; EC = environmentally-cued; PRMQ = Prospective and Retrospective Memory Questionnaire;

† $p < .10$.

*$p < .05$.

**$p < .01$.

***$p < .001$.

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Table 3

Multiple regression predicting mental and physical HRQoL from TB PM in the younger HIV+ sample, controlling for demographics, psychiatric/medical, and cognitive factors.

	Mental HRQoL				Physical HRQoL			
	B	***B*** **95% CI**	***β***	**Adj R^2**	***B***	***B*** **95% CI**	***β***	**Adj R^2**
Entire Model				0.55***				0.26*
HAND	0.11	−3.25, 3.47	<0.01		2.44	−1.79, 6.66	0.19	
Current MDD	4.76	1.02, 8.50	0.29*		4.66	−0.04, 9.36	0.29†	
Current CD4 count	<0.01	−0.01, 0.01	0.03		<0.01	−0.01, 0.01	<0.01	
LT Substance Dependence	0.39	−2.32, 3.09	0.03		1.07	−2.33, 4.48	0.10	
MIST TB PM	2.62	0.47, 4.77	0.31*		1.78	−0.92, 4.48	0.21	
PRMQ PM total score	−1.04	−1.49, −0.59	−0.54***		−0.56	−1.13, <0.01	−0.30†	

Note. Adj = adjusted; *B* = beta weight; β = standardized beta weight; HAND = HIV-associated neurocognitive disorder; MDD = Major Depressive Disorder; LT = lifetime; TB PM = time-based prospective memory; PRMQ = Prospective and Retrospective Memory Questionnaire;

† $p < .10$.

* $p < .05$.

** $p < .01$.

*** $p < .001$