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The role of decision-making ability in HIV/AIDS: Impact on prospective memory

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Abstract

Background—Prospective memory (ProM), a form of episodic memory related to execution of future intentions, is important for everyday functioning. Among persons living with HIV (PLWH), executive dysfunction is implicated in ProM impairments. However, specific subcomponents of executive functioning involved in ProM deficits remain poorly understood. Unlike more "traditional" neurocognitive (NC) measures of executive functioning associated with dorsolateral prefrontal cortex (i.e., conceptual reasoning, abstraction), those associated with medial orbitofrontal/ventromedial prefrontal (mOF/vmP) cortex (i.e., decision making, inhibitory control, goal-oriented behavior) have yet to be examined in ProM.

Method—This study characterized ProM ability in a sample of 89 HIV-seropositive adults and examined the unique role of decision-making ability in ProM. Participants completed a standard NC battery, the *Iowa Gambling Task* (IGT; a decision-making measure), and the *Memory for Intentions Screening Test* (MIST; a ProM measure).

Results—Correlational analyses revealed that both traditional executive functioning measures and the IGT were associated with ProM. Regression analyses revealed that the IGT significantly predicted ProM, even after accounting for NC measures. Among all NC measures, only executive functioning significantly contributed to ProM.

Discussion—Further examination of mOF/vmP-sensitive executive dysfunction within this population is needed as PLWH may require more tailored treatment recommendations due to specific decision-making difficulties that can impact medication management.

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Keywords

Prospective memory; Neurocognition; HIV/AIDS; Decision making; Executive function

Prospective memory (ProM) is a unique and dissociable form of episodic memory that encompasses the execution of future intentions, or "remembering to remember." It is essential for forming, monitoring, and carrying out behaviors based on internal or external cues within the context of ongoing distractions (Raskin, Buckheit, & Sherrod, 2010). Imaging studies suggest that intact ProM performance not only requires medial temporal lobe involvement, but is also associated with prefrontal cortex activation (Burgess, Quayle, & Frith, 2001; Burgess, Scott, & Frith, 2003; Poppenk, Moscovitch, McIntosh, Ozcelik, & Craik, 2010) indicating involvement of both memory and executive functioning abilities. Not surprisingly, ProM deficits have been reported in individuals with frontal neuropathology, such as HIV (Carey et al., 2006; Contardo, Black, Beauvais, Dieckhaus, & Rosen, 2009; Gupta et al., 2010; Martin et al., 2007; Weber et al., 2011; Woods, Carey, et al., 2007; Woods, Dawson, et al., 2009; Woods, Iudicello, et al., 2008; Zogg, Woods, Weber, Doyle, Grant, & HNRC Group, 2011; Zogg et al., 2010), and are associated with important real-world outcomes among persons living with HIV (PLWH), including impaired objective and self-reported medication adherence (Contardo et al., 2009; Woods, Dawson, et al., 2009; Woods, Moran, Carey, et al., 2008).

HIV infection is associated with synaptic degeneration and neuronal atrophy in frontal regions and subcortical structures; these neuropathological changes affect frontostriatal circuits and the subcortical nuclei to which they connect (Contardo et al., 2009; Ellis, Calero, & Stockin, 2009; Hardy, Hinkin, Castellon, Levine, & Lam, 2006; Pfefferbaum et al., 2009). Subsequently, the most commonly reported neurocognitive (NC) deficits among PLWH include poor executive function, processing speed, learning and memory, attention/working memory, verbal fluency, and motor coordination (Contardo et al., 2009; Ellis et al., 2009; Heaton et al., 2010; Heaton et al., 1995; Rivera Mindt et al., 2008). As a result of HIV-related NC deficits, PLWH often experience significant difficulties in areas of everyday functioning (Heaton, Marcotte, et al., 2004; Rivera Mindt et al., 2003), including impairments in prospective memory (ProM; Woods, Carey, et al., 2007).

Although prior research suggests that executive dysfunction is related to ProM in PLWH, these studies have only examined "traditional" measures of executive function (i.e., measures typically associated with dorsolateral prefrontal cortex (DLPFC) such as the Wisconsin Card Sorting Test (WCST) or Trail Making Test–Part B (Carey et al., 2006; Contardo et al., 2009; Gupta et al., 2010; Zogg et al., 2011). DLPFC is associated with executive functions of conceptual reasoning, abstraction, and cognitive flexibility. Studies examining the relationship between ProM and DLPFC-related executive function have yielded contradictory results, with some suggesting a strong association between traditional measures of executive function and ProM measures (Carey et al., 2006; Zogg et al., 2011), one finding no correlation between these variables (Contardo et al., 2009), and several suggesting that ProM is a dissociable construct from more general DLPFC executive

function abilities (Contardo et al., 2009; Gupta et al., 2010). Therefore, ProM may rely on executive functioning abilities beyond those associated with DLPFC functioning.

Deciphering which aspects of executive function are involved in ProM is necessary to better understand the potential neuroanatomical substrates of real-world functioning, such as medication adherence, for PLWH. Executive function related to decision-making, inhibitory control, and goal-oriented behavior tend to be associated with medial orbitofrontal/ventromedial prefrontal (mOF/vmP) cortex involvement (Labudda et al., 2008). Interestingly, developmental studies have shown that mOF/vmP circuitry differentially develops from other prefrontal regions (Hooper, Luciana, Conklin, & Yarger, 2004), indicating a dissociation between mOF/vmP functioning and DLPFC functioning. These mOF/vmP-mediated executive functions have yet to be examined in ProM. Both ProM and decision making involve multiple cognitive processes, particularly those involving planning, initiation of action, and judgment based on future outcomes. Therefore, intact decision making (i.e., making advantageous choices in the face of risk and uncertainty; Bechara, 2007) and intact ProM ability are potentially mediated by shared neuroanatomical structures.

From a neuroanatomical perspective, decision-making ability is associated with mOF/vmP cortex. Neuroimaging evidence demonstrates that the mOF region plays a role in monitoring, learning, and recalling a reward, whereas vmP function plays a role in integrating information about rewards into decision making (Kringelbach & Rolls, 2004). These structures are integral for monitoring rewards, monitoring response contingencies, responding to fearful stimuli, and integrating information to guide decision making (Bechara, Damasio, & Damasio, 2000; Bechara et al., 2001; Bechara, Tranel, & Damasio, 2000; Lawrence, Jollant, O'Daly, Zelaya, & Phillips, 2009). Further, Bechara, Tranel, and Damasio (2000) found that individuals with lesions in the vmP cortex have difficulty delaying immediate rewards, indicating an "insensitivity to future consequences." Given that ProM relies on the execution of future intentions, it is possible that mOF/vmP are also implicated in ProM.

Relatively recent research indicates that poor decision making and risky behavior are aspects of executive dysfunction often found in PLWH (Gonzalez et al., 2005; Hardy et al., 2006; Martin et al., 2004). Martin et al. (2004) found that substance-dependent PLWH made significantly more disadvantageous (i.e., risky) choices on a decision-making gambling task (the Iowa Gambling Task, IGT; Bechara, 2007) than did substance-dependent HIV-seronegative individuals, indicating poorer decision-making ability and higher levels of cognitive impulsivity. Among non-substance-dependent PLWH, Hardy et al. (2006) found that poorer performance on inhibition (Stroop) and verbal recall (California Verbal Learning Test, CVLT) were associated with poorer IGT performance. Taken together, decision making is likely to be impaired in PLWH and could be an integral factor in ProM in this population. In order to better inform our understanding of ProM, there is a need to examine the unique role of mOF/vmP-mediated executive functioning, specifically decision-making.

The IGT, a task involving decision making, is a multifactorial task that involves numerous abilities related to frontal lobe functioning. What makes this measure unique is that it also taps into decision making, which is a construct that is not directly measured by traditional

executive functioning tasks (e.g., Trails B, Wisconsin Card Sorting Task). In fact, a recent review of the relationship between IGT performance and traditional measures of executive functioning (e.g., inhibition, working memory, set-shifting, etc.) found that the majority of studies reported no significant correlations between IGT performance and these cognitive abilities (Toplak, Sorge, Benoit, West, & Stanovich, 2010). This supports the distinction between decision making on the IGT and traditional measures of executive functioning. However, it is important to consider that these constructs of traditional executive functioning and decision-making ability are not mutually exclusive. Both tasks require frontal lobe involvement; however, the contribution of specific frontal lobe areas to these tasks have yet to be disentangled.

Clinical studies have shown that patients with mOF or vmP cortex lesions cannot successfully perform the IGT (Bechara, Damasio, Damasio, & Anderson, 1994; Bechara, Damasio, Damasio, & Lee, 1999; Bechara, Tranel, Damasio, & Damasio, 1996). These patients continue to opt for the high-risk, disadvantageous decks, suggesting that they are guided by the prospect of immediate short-term gains rather than adverse long-term consequences (Bechara et al., 1996). Functional imaging of healthy individuals has also revealed an association between performance on the IGT and mOF and vmP cortex activation (Li, Lu, D'Argembeau, Ng, & Bechara, 2010). These studies demonstrate the sensitivity of the IGT to mOF/vmP functioning. Of note, these findings do not imply a specificity of the IGT to the mOF/vmP areas; however, given this association between the IGT (a task involving decision making), inhibitory control, and goal-oriented behavior with mOF/vmP function, the effects of decision-making ability on ProM is of interest in HIV/AIDS considering the frontal involvement in HIV-related neuropathology.

In sum, given the prevalence of ProM and executive function deficits in the HIV/AIDS population, there is a need to clarify the association between NC functioning and ProM, focusing on subcomponents of executive functioning. Understanding these associations is particularly important given the potential real-world impact of ProM on medication adherence. For instance, individuals with HIV/AIDS with ProM difficulties may require specialized and tailored treatment recommendations. Therefore, the aim of this study was to examine the relationship between ProM performance, traditional NC measures, and a decision-making task in a population of PLWH in order to better understand HIV symptomology and to better tailor treatment recommendations with this group. Of note, the focus of this study was not to identify an HIV effect between those with and those without HIV, as that has been previously accomplished (see Carey et al., 2006). Rather, this study's aim was to extend prior literature by examining those individuals who may be most at risk for ProM difficulties within an HIV-seropositive population based on neurocognitive performance. Therefore, the focus of this study was a within-group design.

To our knowledge, no prior studies have investigated ProM performance, traditional NC measures, and a decision-making task within an HIV-seropositive group. Given the high rate of poor medication adherence among PLWH, it is imperative to determine the factors contributing to poor adherence. It was hypothesized that: (a) HIV-seropositive individuals with impaired decision making on a gambling task would have worse ProM performance

than those not impaired on this task of decision making; and (b) decision-making performance would predict ProM performance, above and beyond traditional NC measures.

METHOD

Participants

The current study sample included 89 adults with HIV-infection who were participating in an NIMH-funded medication adherence study. Participants were primarily recruited via community outreach (in New York City, particularly the Harlem area) and self-referral. Additional recruitment occurred through clinics and related studies at the Icahn School of Medicine at Mount Sinai (ISMMS) in New York City. HIV-serostatus was confirmed by medical records. This study was approved by the Institutional Review Boards of ISMMS and Fordham University.

Inclusion criteria for the current study consisted of documented HIV-seropositive status, more than 6 years of completed education, current stable anti-retroviral medication regimen for at least 12 weeks, aged 18–68 years, Hispanic or non-Hispanic white, and English language proficiency. Participants were excluded for a history of schizophrenia, active psychosis, bipolar disorder, loss of consciousness greater than 12 hours, acute intoxication and/or a non-HIV-related neuromedical diagnosis impacting cognition (e.g., epilepsy, multiple sclerosis, Parkinson's disease, Huntington's disease, Alzheimer's disease, end-stage renal disease).

Procedure

This study was conducted at the ISMMS in New York City between years 2008 and 2011. Participants completed all study measures at ISMMS over the course of two visits. During the first visit, voluntary, informed consent was obtained from all participants prior to administration of any study measures. All participants completed neuromedical, psychiatric, and neurocognitive evaluations and a measure of ProM. All measures were administered, scored, and double scored in a standardized manner by trained psychometrists. All study procedures and scoring were supervised by a board-certified clinical neuropsychologist (M.R.M.).

Measures

Neuromedical evaluation—The neuromedical evaluation consisted of a blood draw for CD4 count and HIV viral load (measures of immunosuppression and disease severity), evaluation of the current medication regimen through patient interview, and urine toxicology for acute substance use.

Psychiatric and substance abuse evaluation—Psychiatric evaluations assessed for exclusion criteria of a history of schizophrenia and active psychosis and bipolar disorder. Current and past substance abuse history was also assessed. These evaluations were administered by trained examiners using well-validated, clinician-administered instruments that yielded diagnoses in accordance with the *Diagnostic and Statistical Manual–Fourth Edition (DSM–IV*; American Psychiatric Association, 1994). The majority of participants

completed the *Composite International Diagnostic Interview* (CIDI; World Health Organization, 1998). The remainder of participants (n = 14) completed the *Psychiatric Research Interview for Substance Use and Mental Disorders* (PRISM; Hasin et al., 1996). Current depressive symptomology within a two-week period from the date of testing was assessed with the Beck Depression Inventory–2nd edition (BDI–II; Beck, Steer, & Brown, 1996), a 21-question, multiple-choice, self-report inventory.

Neurocognitive evaluation—Table 1 summarizes the comprehensive NC battery that all participants completed. This battery includes assessment of the following seven theoretically derived domains: executive function, learning, memory, attention/working memory, processing speed, verbal fluency, and motor functioning. The NC measures included in this battery were chosen because of their well-validated use in HIV samples, as well as strong psychometric characteristics (Antinori et al., 2007; Carey et al., 2004; Heaton et al., 2010; Rivera Mindt et al., 2008; Woods et al., 2004). Total completion time of the NC battery was approximately two to three hours. Sample-specific z scores were calculated per our study aim of analyzing NC functioning and decision-making within PLWH.

Decision-making evaluation—The *Iowa Gambling Task (IGT;* Bechara, 2007) has often been used to study decision-making differences across various clinical and developmental populations (Toplak et al., 2010). The IGT is a computerized test of decision making in which participants are hypothetically given $2,000 with which to gamble. Gambling is based on choosing one card at a time from four decks of cards on a computer screen. Two decks are disadvantageous and result in large immediate rewards but an overall net loss of money, while the other two decks are advantageous and result in small immediate rewards but an overall net gain of money. Participants are told that some decks are better than others and that the goal of the game is to win as much money as possible. Participants are instructed to treat their hypothetical money as if it were real money. Individuals without neurological dysfunction typically learn to choose from the advantageous decks over the course of the game and are able to complete the task with a net gain (Bechara, 2007). Raw total net score was calculated by the difference between the number of cards selected from advantageous decks and disadvantageous decks. Raw scores were then converted to T-scores. The IGT net total score was used for this study, and participants with an IGT net total T-score ≤44 were considered to have impaired decision making, as based on the IGT manual cutoff scores (Bechara, 2007). There is minimal research examining IGT performance discrepancies between ethnic minority groups. However, Cauffman et al. (2010) reported no significant differences on IGT performance between ethnicities in a diverse sample population. As such, a cutoff score of T-score <44 was deemed appropriate for this study. The IGT has been previously validated with HIV samples (Gonzalez et al., 2005; Hardy et al., 2006; Martin et al., 2004).

Prospective memory evaluation

Memory for Intentions Screening Test *(MIST*; Raskin et al., 2010): *Memory for Intentions Screening Test (MIST;* Raskin et al., 2010) is a 30-min test used to assess a person's ability to remember to perform tasks in the future. Participants are instructed to complete eight tasks of ProM: four verbal responses and four action responses. ProM tasks

are categorized by length of delay (2-minute or 15-minute delay) and cue type (event based or time based). Participants are oriented to a clock placed on the table to assist them with keeping track of time. Participants work on distractor tasks (i.e., word search puzzles) continuously throughout the entire test. Following the administration of the eight ProM tasks, multiple-choice recognition trials are given for those ProM tasks that the participant did not complete correctly. Lastly, participants are given a 24-hour ProM task in which they are instructed to call the examiner the following day at the same time to report the number of hours they slept the night after the assessment.

For each of the eight tasks, participants can receive a score of two for full completion of the task at the correct time; one for partial completion of the tasks or correct completion of the task but at the wrong time; or zero if the task is not completed, and no response is given at the correct time. Errors are categorized are as follows: prospective memory failure; task substitution; loss of content; place losing; omission; repetition; and random error. The overall total comprises the raw score of the eight prospective memory tasks resulting in the MIST summary score, ranging from 0–48 and adjusted for length of delay, type of cue, and type of response. This raw score is then converted to a *z* score based on age and education. Prior research has found that the subscales, errors, and retrieval index for the MIST are strongly correlated with the summary score (Woods, Moran, Dawson, et al., 2008). Therefore, the MIST summary *z* score was the only MIST outcome variable analyzed to maintain parsimony. The MIST has strong internal validity and convergent reliability with tasks of everyday functioning (Raskin, 2004; Woods, Moran, Dawson, et al., 2008).

Estimated premorbid IQ—The reading subtest of the *Wide Range Achievement Test–3rd Edition* (WRAT–3; Wilkinson, 1993*)* was used to assess estimated premorbid IQ (Strauss, Sherman, & Spreen, 2006). This test measures reading ability through oral reading of a progressively difficult list of words. Raw scores were calculated for total number of correctly pronounced words and were then converted to age-corrected standard scores.

Statistics

Raw scores were used to create *z* scores for all NC measures. Domain average *z* scores were derived from the mean *z* scores of the individual tests in that particular domain, and the global NC average *z* score is the mean of all individual NC test *z* scores. Impairment for the IGT was determined by a T-score of ≤44, as indicated in the IGT manual (Bechara, 2007).

First, a series of analyses (i.e., correlations, chi-squares, and *t* tests) were conducted to examine the relationship between demographic, medical, and psychiatric (i.e., depression) variables with the MIST summary *z* score. The results of these analyses revealed that none of these factors were significantly associated with the MIST summary *z* score (all *p*s > .10). Second, correlational and *t* test analyses were conducted to examine the relationships of the NC and IGT variables with the MIST summary *z* score. To test our hypotheses and examine the unique contribution of traditional NC measures and IGT net total scores in the prediction of the MIST summary *z* score, a series of hierarchical regression analyses were computed. All analyses were conducted using SPSS Version 22 software, and alpha was set at .05.

RESULTS

Sample characteristics

As summarized in Table 2, 78% of participants were Latina/Latino, 21% were non-Hispanic white, 69% were male, and 86% were right-handed. The mean age of participants was 46.6 years (*SD* = 8.7), and mean years of completed education was 12.9 years (*SD* = 2.7). All participants were HIV-seropositive with a median CD4 lymphocyte count of 486 (interquartile range, IQR: 326, 721). Approximately 12% of the participants were immunosuppressed (i.e., CD4 lymphocyte count <200 cells μL^{-1}). At the time of the assessment, 42% of the participants produced a positive urine toxicology for an illicit substance. The results of a series of *t* tests revealed that there were no significant differences between participants who tested positive or negative on urine toxicology on any of the following measures: MIST summary *z* score and IGT total score (all *p*s > .10). Furthermore, *t* tests analyzing substance abuse history based on the CIDI found that current and past drug-abusing and drug-dependent individuals did not perform significantly differently from nonusers on the MIST summary *z* score and the IGT total score (all *p*s ≤.10).

Table 3 summarizes the overall neurocognitive, prospective memory, and decision-making test performance of the participants.

Neurocognitive performance—Average global NC functioning and average NC domain T-scores all fell within normal limits. Participants endorsed a minimal level of depressive symptoms as evidenced by group average BDI–II total raw score of 10.1 (*SD* = 9.2). WRAT–3 Reading subtest group mean was 89.1 (*SD* = 14.9) indicating low average estimated premorbid IQ for the group. Depressive symptomology (BDI–II total score), premorbid IQ (WRAT–3 Reading), or current/past substance use (based on urine toxicology and CIDI assessment) were not significantly related to MIST summary *z* score (all *p*s > .10).

MIST performance—The average MIST summary score for the group was 32.9 (*SD* = 10.3) with an average MIST summary *z* score of –0.5 (*SD* = 1.4). Median MIST total errors was 3 and ranged from 0–7. For the 24-hour ProM task, only 20% of participants called the next day. Of the 22 participants who completed this task, only 13 (59%) participants called at the correct time.

IGT performance—The overall average IGT net total score was within normal limits for the sample (IGT total score: *M* = 45.3, *SD* = 10.1). However, further examination of IGT net total revealed that 50% of the participants scored in the impaired range (T-score ≤ 44). A series of independent-sample *t* tests were then conducted to compare participants with impaired versus nonimpaired IGT performance on global NC and NC domain scores, as well as ProM measures. Of note, there were no differences between these two groups on relevant demographic, medical, or depression variables (all *p*s >.10). There were also no between-group differences on average global or domain NC *z* scores (all *p*s > .05). However, the impaired IGT group performed significantly worse than the nonimpaired IGT group on MIST summary *z* score, $t(87) = 2.09$, $p < .01$.

Correlational analyses with the MIST and IGT—As shown in Table 4, a series of bivariate Pearson correlational analyses were calculated to analyze the association of MIST summary *z* score to global and domain-specific NC average *z* scores. MIST summary *z* score was significantly positively correlated with global NC function and the domains of executive function and attention/working memory (all *p*s < .05).

Correlational analyses were also computed to examine the associations between IGT and traditional NC measures (i.e., average global and domain NC *z* scores). The results revealed that the IGT net total was significantly associated only with executive function, $r = .27$, $p = .01$. Global NC, $r = .15$, $p = .15$, and all other domain associations were not significant (all *p*s > .05). It should be noted that executive functioning significantly correlated with all other NC domains (all *p*s < .05) except motor. The fact that IGT net total has a more specific relationship to executive functioning is indicative of a unique contribution distinct from traditional measures of executive functioning.

Hierarchical regression analysis with the MIST

A hierarchical regression analysis was conducted to examine whether decision making (i.e., IGT net total) provided a unique contribution to the prediction of ProM (i.e., MIST summary *z* score) after accounting for traditional measures of NC functioning. A measure of multicollinearity, the variance inflation factor (VIF), indicated that a very low level of multicollinearity was present for all NC domains entered in the first step [i.e., executive functioning (VIF = 1.60), learning (VIF = 4.41), memory (VIF = 4.22), attention/working memory (VIF = 1.95), processing speed (VIF = 1.28), verbal fluency (VIF = 1.44), and motor (VIF = 1.06)]. In the second step of the model, IGT Net Total score (VIF = 1.20) was entered. Missing cases were excluded listwise, resulting in a total of 82 participants included in the regression model.

As illustrated in Table 5, the overall model accounted for 6% of the variance, $F(8, 73) = 1.70$, $p = .11$. Among the seven NC domains entered in the first step, only executive function served as a significant predictor [$\beta = 0.29$, $t(81) = 2.11$, $p = .04$]. In Step 2, IGT net total score was added to the model in order to determine whether IGT net total provided a unique contribution over and above the effects of the NC domain scores. Following Step 2, the omnibus model showed a significant association with the MIST summary *z* score and accounted for 15.7% of the variance ($R^2 = .157$, $p = .03$). The addition of the IGT net total score provided a unique contribution to the model [$R^2_\Delta = .05$, $F_\Delta(1, 73) = 4.71$, $p = .03$], serving as a significant predictor of MIST summary *z* score [$\beta = 0.26$, $t(81) = 2.17$, $p = .03$]. Executive function did not remained a significant contributor to the model [$\beta = 0.31$, $t(81) = 2.02$, $p = .05$] when the IGT net total score was added, further highlighting the dissociation and unique contribution of the IGT.

DISCUSSION

The aim of the present study was to add to the conceptual understanding of ProM by examining the contributory roles of both traditional NC measures and decision making (e.g., making advantageous choices in the context of risk and uncertainty) to ProM. Assessment of decision-making ability (assessed with the IGT) was used to examine the role of the

mOF/vmP in ProM in an attempt to disentangle specific frontal lobe processes involved in "remembering to remember." In terms of the main hypothesis of this study, we expected that executive functioning skills involving decision-making ability would predict ProM functioning above and beyond traditional NC abilities associated with DLPFC function. Consistent with this hypothesis, decision making on the IGT among PLWH was significantly and positively related to overall ProM performance and was also predictive of accurately recalling future information. Even after accounting for the variance of NC domains (using traditional measures of executive function, learning, memory, etc.), executive functioning skills involving decision-making ability uniquely contributed to ProM in this cohort of PLWH. We also found a significant contribution of traditional executive functioning measures to ProM, which contradicts previously mentioned studies (Contardo et al., 2009; Gupta et al., 2010) and supports others (Carey et al., 2006; Zogg et al., 2011). That being said, the contribution of traditional executive function abilities was no longer significant once IGT was introduced. We were able to show a unique contribution of decision-making performance to ProM that was not accounted for by traditional measures of executive functioning thought to be more strongly related to DLPFC functioning. These findings have important implications for PLWH with ProM difficulties, as they may suggest that cognitive interventions targeting decision making may improve ProM performance and, importantly, real-world correlates like adherence.

Examination of the effects of the NC domains (using traditional measures of executive function, learning, memory, attention/working memory, processing speed, verbal fluency, and motor skills) revealed that only executive function significantly predicted ProM performance. Our variable of executive function included measures of mental flexibility, inhibition, and sequencing, and the findings suggest that these abilities are important for overall ProM functioning. These results extend previous studies' findings that decision making has its own distinct contribution to ProM (Gupta et al., 2010; Poppenk et al., 2010). The current findings also add to the literature by suggesting that ProM is a distinct type of memory that relies on higher order cognitive functioning, including decision making, for appropriate execution. Although imaging studies suggest that intact ProM performance requires both medial temporal and prefrontal cortical processes (Burgess et al., 2001, 2003; Poppenk et al., 2010), the NC functions related to medial temporal processes (i.e., learning and memory) were not significantly correlated with or predictive of ProM in this study. Instead, the NC functions associated with multiple frontal processes (i.e., both mOF/vmP and DLPFC circuitries) proved to be the only significant functions in ProM within this cohort. These findings support recent research indicating that ProM is dissociable from retrospective memory (Gupta et al., 2010; Zogg et al., 2011) and extend prior research by disentangling the subcomponents of executive function involved in ProM.

In terms of decision-making ability as assessed by the IGT, there was a high rate of impairment, with approximately half of the sample performing in the impaired range on the task of decision making. There were small-to-moderate associations between overall IGT performance with the traditional measures of executive function and processing speed, suggesting a frontostriatal linkage with decision-making ability. Also of note, although participants with impaired decision-making ability did not significantly differ on traditional NC domains when compared to participants without impaired decision-making abilities,

participants with impaired decision-making ability performed significantly worse on the ProM measure than those with intact decision making. These findings extend prior research on decision making in HIV (Gonzalez et al., 2005; Martin et al., 2004) by highlighting the high rate of impaired decision-making ability in this population and the integral role of decision-making ability in ProM. Together, these findings point to the need to expand standard assessment of executive function in HIV/AIDS to include evaluation of decision-making ability.

The limitations of the current study include a relatively small sample size and a sample limited to HIV + adults. Studies have previously shown that HIV-seropositive individuals performed significantly more poorly than healthy controls on the MIST (Carey et al., 2006). This study sought to examine more nuanced differences of ProM performance within an HIV-seropositive group. Therefore, we focused on within-group comparisons of HIV-seropositive adults to provide insight into beneficial treatment recommendation for those most at risk for poor ProM within this group. Related to these factors, it is unclear whether the lack of findings regarding learning and memory in the multivariate analyses were related to a lack of power, or to a unique characteristic of the sample, as these were the only domains in which group average performance was deficient, suggesting pervasive deficits that may limit discriminant analysis. Additionally, the mean sample's premorbid IQ was 89, which may play a role in the variability observed in test performance. Of note, low average IQ is typical of this population based on prior research (Ryan, Baird, Rivera Mindt, Byrd, & Monzones, 2005).

Further, it is unclear whether these findings would generalize to other neurologic or racial/ethnic minority groups, as this study's population was specific to HIV and comprised predominantly Latinos/Latinas. Future studies would benefit from a larger, more diverse sample including other neurologic disorders to both increase power of the analyses (particularly with regard to learning and memory measures) and the generalizability of the study. It would also be interesting to expand on this research with neuroimaging techniques to more accurately determine brain activation during tasks of ProM. Moreover, future studies should further examine the real-world implications of both ProM and decision making on tasks of everyday functioning, such as medication adherence.

Finally, it is important to mention the potential emotional effects of decision-making performance, which have been considered to involve "hot cognition" as opposed to "cold cognition." Hot cognition is believed to be related to motivated reasoning, in which a person's thinking is influenced by their internal emotional state (Westen, Blagov, Harenski, Kilts, & Hamann, 2006). The fact that ProM is related to forming, monitoring, and carrying out behaviors based, in part, on internal cues may make it more aligned with what is traditionally considered "hot cognitions" mediated by orbital prefrontal cortex (OPC) than more traditional measures of executive function, which are considered "cold cognitions" mediated by DLPFC (Krain, Wilson, Arbuckle, Castellanos, & Milham, 2006). This is an area for future research.

Despite the aforementioned limitations of this study, the results add to the conceptual understanding of ProM in PLWH and have significant functional implications. An additional

strength of the current study includes a focus on an understudied ethnic minority population (Latinas/Latinos) for which medication adherence has been found to be particularly poor (Murphy, Roberts, Hoffman, Molina, & Lu, 2003). Research with predominantly Caucasian samples has found that among HIV-seropositive individuals, those with poorer prospective memory also had poor adherence (Woods, Dawson, et al., 2009). Considering the poorer rates of medication adherence reported in the Latina/Latino population, it is pertinent to examine the impact of ProM on medication adherence in this population. A specific focus within this ethnic minority sample is needed as little has been done to examine ProM within Latinas/Latinos who are at disproportionate risk for a number of neurologic disorders, including those associated with HIV/AIDS. The importance of health disparities and marginalization in underrepresented groups cannot be overlooked when developing treatment recommendations. Finally, this study applies a more fine-grained analysis of executive function involvement in ProM.

In conclusion, these findings expand on the limited and inconsistent research examining the NC contributions to ProM in PLWH. We found that among multiple traditional measures of NC domains (executive function, processing speed, attention/working memory, learning, memory, verbal fluency, and motor skills) and decision-making ability on a gambling task, only executive function and decision making significantly predicted ProM performance within an HIV population. This highlights the critical role of both mOF/vmP and DLPFC circuitry in ProM separate from traditional measures of frontotemporal functioning. Because of the strong implications of ProM on medication adherence in HIV, it is important to fully understand those individuals most susceptible to ProM difficulties. Practitioners especially need to assess and be aware of ProM problems in their HIV-seropositive patients because of its real-world effects on medication adherence. Patients with ProM difficulties may require more specialized and tailored treatment recommendations.

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TABLE 1

Neurocognitive test battery by seven major ability areas

Neuropsychological domain and test
Executive functioning
Wisconsin Card Sorting Task–64 Item
Trail Making Test (Part B)
Iowa Gambling Task
Attention/working memory
WAIS–III Letter Number Sequencing
PASAT total correct
Learning
Hopkins Verbal Learning Test–Revised
Brief Visuospatial Memory Test–Revised
Delayed recall
Hopkins Verbal Learning Test–Revised
Brief Visuospatial Memory Test–Revised
Motor
Grooved Pegboard time
Speed of information processing
WAIS–III Digit Symbol
WAIS–III Symbol Search
Trail Making Test (Part A)
Verbal fluency
Controlled Oral Word Association Test (FAS)
Semantic (animal) fluency

Note. WAIS = Wechsler Adult Intelligence Scale; PASAT = Paced Auditory Serial Arithmetic Test.

TABLE 2

Participant demographic and clinical characteristics

Characteristics	*M*	*SD*	*n*	*%*
Age, years	46.6	8.7		
Education, years	12.9	2.7		
CD4 count, total	564	334		
Median (interquartile range)	486	326–721		
% <200	12.0			
HIV viral load log10, total	1.98	1.14		
Median (interquartile range)	1.38	1.38–1.91		
Latino/Latina			67	78.8
Non-Hispanic white			18	21.2
Male			62	69.7
Right-handed			77	86.5
Positive urine toxicology			38	42.7

Note. $N = 89$.

TABLE 3

Neurocognitive and psychological characteristics

	Characteristics			
Estimated premorbid IQ	***N***	***Mean***	***SD***	***Range***
WRAT–3 Reading subtest	88	89.1	14.9	55 to 119
NC domain (z-score)				
Global	88	−0.01	0.48	−1.2 to 0.9
Executive function	88	−0.02	0.89	−4.0 to 0.4
Learning	88	0	0.83	−1.8 to 0.7
Memory	88	0	0.85	−2.0 to 0.5
Attention & working memory	86	−0.04	0.84	−2.9 to 0.0
Processing speed	88	0.01	0.34	−2.0 to 0.5
Motor	87	0	0.93	−4.3 to 0.2
Verbal fluency	86	0.02	0.89	−2.2 to 0.9
Iowa Gambling Task (T-score)				
Net total	89	45.3	10.1	23 to 71
Prospective memory				
MIST summary score (raw)	89	32.9	10.3	3 to 48
MIST summary *z* score	89	−0.5	1.4	−5.2 to 0.5
MIST total errors (raw)	89	2.9	1.7	0 to 7
Depression symptomology				
BDI total	87	10.1	9.2	0 to 43

Note. WRAT–3 = Wide Range Achievement Test–Third Edition; BDI = Beck Depression Inventory; NC = neurocognitive; MIST = Memory for Intentions Screening Test.

TABLE 4

Pearson bivariate correlations for neuropsychological functioning, decision making, and prospective memory

Bivariate correlations	MIST summary *z* score (*n* = 89)	IGT net total (*n* = 89)
Global	.24*	.15
Executive functioning	.23*	.27*
Learning	.12	.1
Memory	.09	−.11
Attention/working memory	.24*	.21
Processing speed	.18	.18
Motor	.16	.07
Verbal fluency	.13	.16

Note. IGT = Iowa Gambling Task; MIST = Memory for Intentions Screening Test.

* $p < .05$.

TABLE 5

Hierarchical regression analysis of neurocognitive functioning and decision making to predict overall prospective memory

	MIST summary z score			
Independent variable	***SE B***	***sr***	***R^2***	***R^2 change***
Step 1			.10	
Executive functioning	.21	.24*		
Learning	.36	0.4		
Memory	.34	−.04		
Attention/working memory	.26	.04		
Processing speed	.47	.06		
Motor	.16	.05		
Verbal fluency	.20	−.11		
Step 2			.16	.05
Executive functioning	.21	.16		
Learning	.36	.01		
Memory	.35	.02		
Attention/working memory	.25	.03		
Processing speed	.46	.04		
Motor	.16	.04		
Verbal fluency	.19	−.13		
IGT net total	.02	.25*		

Note. IGT = Iowa Gambling Task; MIST = Memory for Intentions Screening Test; sr = semipartial correlation. Dependent variable (DV) = MIST summary *z* score; $n = 82$.

*$p < .05$.