Research Article

Lower prospective memory is associated with higher neurocognitive dispersion in two samples of people with HIV: A conceptual replication study

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Abstract

Objectives: People living with HIV (PLWH) often experience deficits in the strategic/executive aspects of prospective memory (PM) that can interfere with instrumental activities of daily living. This study used a conceptual replication design to determine whether cognitive intraindividual variability, as measured by dispersion (IIV-dispersion), contributes to PM performance and symptoms among PLWH. **Methods:** Study 1 included 367 PLWH who completed a comprehensive clinical neuropsychological test battery, the Memory for Intentions Test (MIsT), and the Prospective and Retrospective Memory Questionnaire (PRMQ). Study 2 included 79 older PLWH who completed the Cogstate cognitive battery, the Cambridge Prospective Memory Test (CAMPROMPT), an experimental measure of time-based PM, and the PRMQ. In both studies, a mean-adjusted coefficient of variation was derived to measure IIV-dispersion using normative T-scores from the cognitive battery. **Results:** Higher IIV-dispersion was significantly associated with lower time-based PM performance at small-to-medium effect sizes in both studies (mean $r_s = -0.30$). The relationship between IIV-dispersion and event-based PM performance was comparably small in magnitude in both studies ($r_s = -0.19, -0.20$), but it was only statistically significant in Study 1. IIV-dispersion showed very small, nonsignificant relationships with self-reported PM symptoms in both samples ($r_s < 0.10$). **Conclusions:** Extending prior work in healthy adults, these findings suggest that variability in performance across a cognitive battery contributes to laboratory-based PM accuracy, but not perceived PM symptoms, among PLWH. Future studies might examine whether daily fluctuations in cognition or other aspects of IIV (e.g., inconsistency) play a role in PM failures in everyday life.

Keywords: memory for intentions; infection; executive functions; variability; neuropsychological assessment; human immunodeficiency virus

Introduction

People living with HIV (PLWH) commonly experience difficulties with prospective memory (PM; Avci et al., 2017), which involves the capacity to carry out an intended action that is executed in response to a particular cue (McDaniel & Einstein, 2000; Rummel & McDaniel, 2019). Everyday tasks that involve PM include remembering to take prescribed medications, attend scheduled appointments, or pay household bills. As compared to seronegative individuals, PLWH report higher frequencies of PM symptoms in their daily lives (Avci et al., 2017; Woods et al., 2007), exhibit lower accuracy on clinical measures of PM (Carey et al., 2007), and are more likely to fail naturalistic PM tasks (Carey et al., 2007). HIV-associated PM deficits are clinically relevant since they are reliably associated with dependence in everyday functioning (Woods et al., 2008a), including unemployment (Woods et al., 2011) and medication mismanagement (Woods et al., 2009). Therefore, it is important to understand the cognitive mechanisms that underlie PM failures in HIV, which can inform

both internal mnemonic and external compensatory approaches to improve PM among PLWH (Woods et al., 2020, 2021).

Most of the research on PM in HIV has been guided by the Multiprocess framework (McDaniel & Einstein, 2000; Scullin et al., 2013). Broadly, the Multiprocess framework argues that the cognitive resource demands of PM encoding, retention, monitoring, and cue detection can range from highly strategic/executive processes that are primarily reliant on the frontoparietal network (e.g., Lamichhane et al., 2018) to largely automatic/spontaneous processes that rely on mediotemporal systems (e.g., Gordon et al., 2011). For example, a time-based PM cue with a highly demanding ongoing task (e.g., remembering to take a medication at 2 pm during a busy afternoon of meetings) is strategically/executively demanding, whereas a more focal, salient event-based PM cue with a minimally demanding ongoing task (e.g., remembering to brush your teeth while in the bathroom and getting ready for a dental appointment) would involve more automatic/spontaneous processes. Given that HIV tends to disrupt the frontostriatal

networks (Ellis et al., 2009), it follows that PLWH exhibit deficits on PM tasks with higher strategic/executive demands (e.g., Doyle et al., 2013), but not on those that involve primarily automatic/spontaneous processes (e.g., Woods et al., 2010). The effect size of HIV on the more strategically/executively demanding time-based PM across the literature is nearly double that which is observed for relatively more automatic/spontaneous event-based PM (Avci et al., 2017). HIV-associated deficits in the strategic/executive aspects of PM are driven by difficulties with monitoring (e.g., Doyle et al., 2013), correlate with measures of executive functions (e.g., Zogg et al. 2011), and can improve when strategic/executive supports are provided (Woods et al., 2020, 2021).

The current study extends our understanding of the cognitive architecture of PM in HIV by examining the contribution of cognitive intraindividual variability (IIV; Bunce et al., 1993). While some degree of within-person variability in cognitive performance is quite normal, higher levels of IIV can suggest that an individual experiences difficulty maintaining consistent cognitive task execution over time (e.g., Stuss et al., 2003; Hultsch et al., 2002). When considered in the context of the Multiprocess framework, it is clear how greater variability in cognitive task execution could disrupt the strategic/executive aspects of PM, particularly the encoding and planning aspects of the cue-intention pairing and the complex process of monitoring for the PM cue vis-à-vis a complex, nonfocal ongoing task.

IIV is commonly measured by calculating the variability within repeated measures of the same cognitive test (i.e., IIV-inconsistency, typically in response time) or by variability across different cognitive tests (i.e., IIV-dispersion). In this study, we focus on IIV-dispersion, which is associated with increased risk of incipient cognitive decline (e.g., Jones et al., 2018) and is elevated in cross-sectional samples of older adults (e.g., Hilborn et al., 2009) and in persons with Huntington's disease (Musso et al., 2015), traumatic brain injury (TBI; Hill et al., 2013), Dementia with Lewy Bodies (Webber et al., in press), and viral infection (Morgan et al., 2012; Sheppard et al., 2020). Higher IIV-dispersion has been linked to poorer microstructural integrity of white matter pathways in older adults (Halliday et al., 2019) and persons with mild TBI (Sorg et al., 2021), particularly the genu and the superior longitudinal fasciculus. Higher IIV-dispersion is also related to poorer global cognition (Morgan et al., 2011), executive dysfunction (Sullivan et al., 2018), and difficulties multitasking (Fellows & Schmitter-Edgecombe, 2015). Taken together, there is both a conceptual and empirical basis to suggest that IIV-dispersion may measure an aspect of cognition that is important to PM in PLWH.

Indeed, there has been growing research interest in IIV-dispersion in PLWH over the past decade (Vance et al., in press). Historically, the pattern of neuropsychological deficits in HIV is heterogeneous across resource demanding tasks (Dawes et al., 2008), which some investigators hypothesize may reflect abnormal IIV-dispersion (Morgan et al., 2011). Indeed, HIV is associated with higher IIV-dispersion (Morgan et al., 2011) that may be exacerbated by older age (Morgan et al., 2011) and substance use (Arce Rentería et al., 2020). Higher IIV-dispersion increases risk of HIV-associated neurocognitive impairment and death (Anderson et al., 2018). Neuroimaging studies in HIV show that higher IIV-dispersion is related to lower white and gray matter volumes (Hines et al., 2016) and fractional anisotropy in some frontoposterior white matter tracts (Jones et al., 2018). Of clinical relevance, IIV-dispersion is associated with self-reported declines in activities

of daily living (Morgan et al., 2012) and suboptimal medication adherence (e.g., Thaler et al., 2015) among PLWH.

Yet the relationship between IIV-dispersion and PM in HIV is not known. We are aware of six studies that have examined the association between different types of IIV and event-based PM, all of which have been conducted in healthy adults. Experimental studies show that the addition of PM intention can increase IIV-inconsistency during the ongoing task (e.g., Ball & Brewer, 2018; Joly-Burra et al., 2018). Correlational studies suggest that higher IIV-inconsistency is independently associated with lower event-based PM accuracy for both focal (e.g., Haynes et al., 2018; Schmitter-Edgecombe et al., 2020) and nonfocal (e.g., Ihle et al., 2017; Sullivan et al., 2018) cues. One study reported that IIV-dispersion is also negatively associated with time-based PM; specifically, Sullivan et al. (2018) demonstrated that higher variability in scores across the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS; Randolph et al., 1998) showed a small, but independent association with poorer time-based PM in the laboratory and in daily life among 194 older Australians. Furthermore, Sullivan et al. provided evidence for the convergent and concurrent validity of IIV-dispersion with an independent composite of executive measures.

Building on the literature reviewed above, the present study examined the hypothesis that higher IIV-dispersion is associated with worse PM in the laboratory and in daily life among PLWH. We examined the unique contribution of IIV-dispersion across a battery of neuropsychological tests to PM as measured by both laboratory performance-based tasks and self-reported symptom ratings. We conducted these analyses in two, separate retrospective samples of PLWH that used different neurocognitive batteries and different measures of laboratory performance-based PM. This design affords a *conceptual replication* of the hypothesized association between PM and IIV-dispersion in HIV (Lynch et al., 2015; Sullivan et al., in press); in other words, we tested the same hypothesis in different samples using different measures of the same construct, which provides direct evidence of the external validity of the findings.

Study 1

Study 1 participants

The sample for Study 1 included 367 participants with HIV aged 18–79 years who were enrolled in a memory study at the University of California San Diego (UCSD) HIV Neurobehavioral Research Program, which recruits from community-based organizations, local clinics, and regional advertisements. Aspects of these data have been reported previously (e.g., Sheppard et al., 2020), but the associations between IIV and PM are novel. The exclusion criteria for this study were an estimated verbal IQ score less than 70 on the Wechsler Test of Adult Reading (WTAR; The Psychological Corporation, 2001), or prior diagnosis of any of the following: (1) severe psychiatric disorder (e.g., schizophrenia), (2) central nervous system opportunistic infection, (3) seizure disorder, (4) head injury with loss of consciousness for more than 30 min, (5) stroke with neurological sequelae, or (6) presence of a non-HIV major neurocognitive disorder. Individuals were also excluded if they had current substance dependence as measured by the Composite International Diagnostic Interview (CIDI; World Health Organization, 1998) or tested positive on a breathalyzer or urine toxicology

Table 1. Demographic and clinical information for the two study samples of adults with HIV disease

Variable	Sample 1 ($n = 367$)	Sample 2 ($n = 79$)
Sociodemographic		
Age (years)	45.5 (11.6)	57.0 (6.1)
Gender (% men)	86.1	82.3
Education (years)	13.5 (2.6)	14.5 (2.7)
WTAR VIQ	102.2 (11.8)	—
Race/ethnicity (%)		
White	58.3	59.5
Black/African American	23.2	21.5
Hispanic/Latino	16.3	17.7
Other	2.2	1.3
Psychiatric		
Major depressive disorder (%)	57.8	73.4
Generalized anxiety disorder (%)	14.0	22.8
Substance use disorder (%)	54.5	70.9
Medical		
Hepatitis C virus (%)	17.9	25.3
HIV duration (years)	13.1 (8.1)[1]	21.7 (8.5)
Plasma RNA detectable (%)	25.8[1]	2.7[1]
Current CD4 count (cells/µL)	570.5 (363.0, 769.5)[1]	707.1 (531.8, 850.3)[1]
Nadir CD4 count (cells/µL)	213.7 (55.0, 322.0)	187.7 (26.0, 299.0)
AIDS (%)	56.0[1]	68.4
Prescribed ART (%)	85.6	93.6[1]

Note. Values are Means (standard deviation) or valid sample % values.

HIV, human immunodeficiency virus; WTAR VIQ, Wechsler test of adult reading verbal IQ estimate; RNA, ribonucleic acid; CD4, cluster of differentiation 4 cell; AIDS, acquired immune deficiency syndrome; ART, antiretroviral therapy.

[1]In all cases, no more than 8 participants were missing data.

screen for illicit drugs (except marijuana) on the day of testing. The demographic and disease characteristics for the Study 1 sample are shown in Table 1.

Study 1 materials and procedure

Participants provided written, informed consent prior to completing a comprehensive medical, psychiatric, and neuropsychological research evaluation for which they received nominal financial compensation. The human research ethics office at UCSD approved the study procedures. The research in this study was completed in accordance with Helsinki Declaration.

Neuropsychological evaluation

Participants were administered a comprehensive neuropsychological test battery by research assistants who adhered to the published manuals. Eleven indices drawn from seven tests were used to generate a measure of dispersion (Morgan et al., 2011), including (1) the Digit Span and Logical Memory I subtests from Wechsler Memory Scale, third edition (WMS-III; Wechsler, 1997); (2) the Total Moves and Total Execution Time scores of the Tower of London Drexel Version (Culbertson & Zillmer 1999); (3) Total time scores from Parts A and B of the Trail Making Test (Army Individual Test Battery 1944; Heaton et al. 2004); (4) Total Trials 1–5 of the California Verbal Learning Test, second edition (CVLT-II; Delis et al. 2000); (5) Total completion time from the dominant and nondominant hand trials of the Grooved Pegboard Test (Heaton et al. 2004; Kløve 1963); (6) Total score from the Boston Naming Test (BNT; Kaplan et al. 1983; Heaton et al., 2004); and (7) Total correct words generated on the Action (verb) Fluency Test (Piatt et al. 1999; Woods et al. 2005). Raw scores were converted to demographically adjusted T-scores to provide a common metric for the generation of a coefficient of variation (CoV-dispersion; Wisdom et al., 2012) to measure IIV-dispersion. The intraindividual mean (IM; sample

range = 33.1–64.9) and intraindividual standard deviation (ISD; sample range = 3.7–16.8) of the 11 T-scores were calculated for each participant. The CoV-dispersion was generated by dividing the ISD by the IM, which adjusts variability for overall level of performance. A higher CoV-dispersion indicated greater within-person variability across the battery of tests (sample range = 0.1–0.4).

Prospective memory

Performance-based PM was assessed with the research version (Woods et al., 2008b) of the Memory for Intentions Test (MIsT; Raskin, 2009). The MIsT is a standardized, performance-based measure that includes four time-based (e.g., "*In 15 min, tell me that it is time to take a break*") and four event-based (e.g., "*When I show you a postcard, self-address it*") cues that are counter-balanced on response modality (i.e., action vs. verbal) and delay (i.e., 2-min vs. 15-min). Participants were informed that they could use a wall clock to monitor time, but the clock was placed out of their immediate view. The ongoing task is a series of word search puzzles (range of correct words = 3–40). Two possible points are awarded for each MIsT trial: one for responding to the appropriate cue and one for providing the correct response. The individual trials are then summed across cue type to create time-based and event-based subscales (ranges = 0–8). Spearman's rho (r_s) between time-based MIsT and event-based MIsT scores in the current sample was 0.491, $p < .001$. We also generated scores for the following error types: (1) omissions (i.e., failure to respond to the PM cue); (2) task substitutions (e.g., responding to a cue with a commission error); (3) loss of content (e.g., I know I'm supposed to do something, but I don't know what to do); and (4), loss of time (i.e., responding with the correct intention at the incorrect time). Participants completed an 8-item, three-choice intention recognition trial immediately following the completion of the MIsT (range = 0–8).

Participants were also administered the 24-hr naturalistic task from the MIsT, which asks them to call the examiner the day after

testing to report how many hours they slept. Participants are neither prohibited nor encouraged to use compensatory strategies. The MisT 24-hr task shows evidence of reliability in HIV (Kordovski et al., 2020) is associated with laboratory-based measures of PM, executive functions, and retrospective memory (Doyle et al., 2015; Kamat et al., 2014; Zogg et al., 2010), but is not reliably related to everyday functioning (e.g., Woods et al., 2009, 2011). Consistent with prior work, participants were classified into two groups based on whether they placed the call ($n = 144$) or failed to call ($n = 222$).

Self-report of PM symptoms in daily life was measured using the Prospective and Retrospective Memory Questionnaire (PRMQ; Smith et al., 2000). The PM scale includes 8 items that assess the frequency of PM failures (e.g., forget to deliver a message) based on responses that range from 1 ("never") to 5 ("very often"). Total scores ranged from 8 to 40 (sample Cronbach's $\alpha = 0.919$).

Study 1 data analysis

The primary analyses were conducted with a mixed linear regression, which used CoV-dispersion as the predictor variable and the time- and event-based subscales of the MisT as the within-subjects criterion variables. Note that, the vast majority of the PM study variables were not normally distributed (Shapiro–Wilk Test $ps < .001$), and thus the planned bivariate correlations were conducted with Spearman's rho rather than Pearson's r. However, findings did not change in significance or effect size magnitude if we used Pearson's r. Nominal logistic regression was used to examine the association between CoV-dispersion and the MIsT 24-hour naturalistic task. Across all models, covariates were selected using a data-driven confound approach (Field-Fote, 2019); that is, any variable listed Table 1 was included as covariate if it was related to both the predictor and the criterion at $ps < .05$. The critical alpha was set at .05, except for the exploratory bivariate correlations of component PM processes, which were Type I error adjusted with the Benjamini–Hochberg false discovery rate method (Benjamini & Hochberg, 1995).

Study 1 results

MIsT results

The WTAR estimated verbal IQ was the only variable from Table 1 that met our criteria for inclusion as a covariate. Significant main effects were observed in the expected direction for CoV-dispersion ($F(1,364) = 11.61$, $p < .001$), WTAR verbal IQ ($F(1,364) = 24.20$, $p < .001$), and PM cue type ($F(1,364) = 4.88$, $p = .028$). Post hoc analyses showed that higher CoV-dispersion was associated with lower scores on both the time- ($r_s = -0.15$) and event-based ($r_s = -0.19$) scales of the MIsT (see Figure 1). No significant interactions were evident between CoV-dispersion and PM cue ($F(1,364) = 1.23$, $p = .269$) or WTAR verbal IQ and PM cue ($F(1,364) = 0.69$, $p = .407$).

Next, we examined the univariable associations between CoV-dispersion and several component process subscales from the MIsT, including error types, the ongoing word search task, and the posttest intention recognition trial. Higher CoV-dispersion was significantly correlated with higher MisT task substitution ($r_s = 0.15$, *Benjamini-Hochberg* $p = .011$) and MIST loss of time ($r_s = 0.15$, *Benjamini-Hochberg* $p = .011$) errors, but not with omission ($r_s = 0.10$, *Benjamini-Hochberg* $p = .088$) or loss of content ($r_s = -0.01$ *Benjamini-Hochberg* $p = .930$) errors. Higher
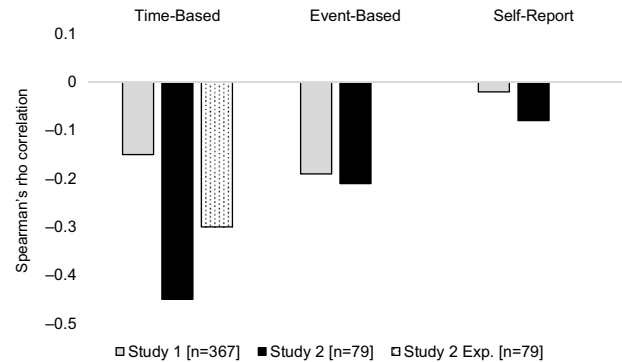

Figure 1. The bar chart displays the correlations between prospective memory (PM) and cognitive intraindividual variability in two samples of people with HIV. In Study 1, the gray time- and event-based bars represent correlations with the Memory for Intentions Test (MIsT). In Study 2, the black time- and event-based bars represent correlations with the Cambridge Prospective Memory Test, while the dotted bar represents the correlation with the experimental time-based PM task. In both studies, the self-report PM measure is the Prospective and Retrospective Memory Questionnaire. Exp. = Experimental time-based PM task.

CoV-dispersion was associated with fewer words identified during the ongoing task ($r_s = -0.21$, $p < .001$), but not with posttest intention recognition accuracy ($r_s = -0.05$, $p = .378$).

MIsT 24-hr trial results

The WTAR verbal IQ was the only variable that met our above-described criteria for inclusion as a covariate in the MIsT 24 hr trial analyses. The overall logistic regression model predicting MIsT 24 hr group from CoV-dispersion and WTAR verbal IQ was significant ($X^2 = 42.5$, $p < .0001$), but WTAR verbal IQ ($X^2 = 39.4$, $p < .001$) was the only contributor ($X^2 = 1.1$, $p = .295$).

PRMQ PM scale

No variable from Table 1 met inclusion for criteria as a covariate for the PRMQ, which showed a minimal and nonsignificant relationship with CoV-dispersion ($r_s = -0.02$, $p = .748$).

Study 2

Study 2 participants

The sample for Study 2 included 79 older adults with HIV aged 50–75 years who were enrolled in a memory experiment at UCSD (Woods et al., 2020, 2021). Aspects of these data have been reported previously (e.g., Matchanova et al., 2021), but the associations between IIV and PM are novel. Participants were included in the current study if they were at least 50 years of age, tested positive for HIV via MedMira, and completed the CogState (www.cogstate.com). The exclusion criteria for this study were comparable to Study 1. The demographic and disease characteristics of the Study 2 participants are shown in Table 1.

Study 2 materials and procedure

Participants provided written, informed consent prior to completing a comprehensive medical, psychiatric, and neuropsychological research evaluation for which they received nominal financial compensation. The human research ethics office at UCSD approved the study procedures. The research in this study was completed in accordance with Helsinki Declaration.

Neuropsychological evaluation

Participants were administered six subtests from the Cogstate (www.cogstate.com), a computer-based neuropsychological battery, by research assistants who adhered to the published manual. The subtests administered were Detection, Identification, One-Back, Two-Back, One Card Learning, and the Continuous Paired Associate Learning Task. Raw scores from the Cogstate were converted to demographically adjusted normative T-scores to provide a common metric for the generation of a CoV-dispersion. The IM (sample range = 21.9–58.7) and ISD (sample range = 2.7–16.5) of the 6 T-scores were calculated for each participant. The CoV-dispersion ratio score was calculated as ISD/IM for each individual, such that higher CoV indicated greater within-person variability across the battery of tests (sample range = 0.1–0.5).

Prospective memory

Performance-based PM was assessed with the Cambridge Prospective Memory Test (CAMPROMPT; Wilson et al., 2005). The CAMPROMPT includes three time-based trials (e.g., "When there are seven minutes left, I would like you to remind me not to forget my keys.") and three event-based trials (e.g., "When I tell you that the test is over, I would like you to remind me that I have hidden these [5] objects and tell me what they are and where they are hidden"). Participants were informed that they could use a wall clock to monitor time, but the clock was placed out of their immediate view. A series of paper and pencil puzzles serve as the ongoing task. Each PM trial is scored from 0 (item failed even after two prompts) to 6 (item recalled without prompt in response to the correct cue). The total range of scores for time-based and event-based PM scales was 0–18. Omission errors were recorded if the participant did not respond the PM cue. Finally, a 6-item, 3-choice posttest intention recognition trial was conducted (range = 0–6).

Participants also completed an experimental measure of time-based PM (see Woods et al., 2020) on which they were instructed to press a white response button at 2, 5, and 9 min during an ongoing language task. Responses were coded as accurate if participants pressed the correct response button within ±20 s of the instructed time (sample range = 0–100%). Participants could also press a blue response button to check a clock (sample range = 0–37 checks), but were instructed to do so minimally (Huang et al., 2014).

Self-report of PM symptoms was measured by the PRMQ as detailed in Study 1 (Study 2 sample range = 8–35, Cronbach's α = .904).

Study 2 data analysis

A series of linear regressions and bivariate correlations were conducted to examine the association between Cogstate CoV-dispersion and PM. For the CAMPROMPT, a mixed regression model was conducted with Cogstate CoV-dispersion as the predictor variable and the time- and event-based subscales of the CAMPROMPT as the within-subjects criterion variables. Similar to Study 1, the vast majority of the PM variables were not normally distributed (Shapiro-Wilk Test $ps < .001$) and were therefore examined using Spearman's rho. Note that the findings did not change in significance or effect size magnitude when Pearson's r was used instead. The critical alpha was set at .05, except for the exploratory bivariate correlations of component PM processes, which were Type I error adjusted (Benjamini & Hochberg, 1995). No variables in Table 1 met the *a priori* criteria for inclusion as a covariate in any of the models (as detailed in Study 1).

Study 2 results

CAMPROMPT

The regression model revealed a significant main effect of Cogstate CoV-dispersion ($F(1,77) = 7.91, p = .006$) on CAMPROMPT performance, which was tempered by a significant interaction between Cogstate CoV-dispersion and CAMPROMPT cue type ($F(1,77) = 7.36, p = .008$). Post hoc analyses showed that higher CogState CoV-dispersion was associated with lower scores on the time-based ($r_s = -0.45, p < .001$), but not event-based ($r_s = -0.21, p = .065$) scales of the CAMPROMPT.

Additionally, we examined the bivariate associations between Cogstate CoV-dispersion and several component process subscales from the CAMPROMPT, including error types, the ongoing task puzzles, and the posttest intention recognition trial. Higher Cogstate CoV-dispersion was significantly correlated with higher omission errors on the time-based ($r_s = 0.38$, Benjamini-Hochberg $p = .0024$), but not the event-based scale ($r_s = 0.15$, Benjamini-Hochberg $p = .178$). No significant correlations were observed between Cogstate CoV-dispersion and the number of ongoing task puzzles completed ($r_s = -0.17$, Benjamini-Hochberg $p = .175$) or post-task intention recognition accuracy ($r_s = -0.21$, Benjamini-Hochberg $p = .14$).

Experimental time-based PM

Results of correlational analyses showed that there was a significant, medium-sized relationship between higher CoV-dispersion and lower experimental time-based PM accuracy ($r_s = -.30, p = .008$). There was a very small and nonsignificant relationship between CoV-dispersion and clock checks ($r_s = .01, p = .956$).

PRMQ PM scale

Cogstate CoV-dispersion showed a weak, nonsignificant association with the PRMQ PM scale ($r_s = -0.08, p = .504$).

General discussion

PLWH commonly demonstrate PM deficits that disrupt daily activities (Woods et al., 2009) and are characterized by difficulties with the strategic/executive aspects of cue monitoring and detection (Doyle, et al., 2013). The present study extends our understanding of the cognitive underpinnings of PM in HIV by demonstrating its reliable association with IIV-dispersion, which is an indicator of an individual's variability in cognitive test performance across a battery. Thus, these data suggest that lower levels of laboratory-based PM performance in HIV are associated with greater difficulties in maintaining consistent cognitive task execution over time (e.g., Stuss et al., 2003; Hultsch et al., 2002). The findings from two separate HIV samples support this interpretation. In Study 1, higher IIV-dispersion on a battery of clinical neuropsychological tests had a significant, small association with worse performance on both time- and event-based PM scores from the MIsT among 367 PLWH. In Study 2, we observed significant, small-to-medium associations between IIV-dispersion on subtests of the Cogstate and worse time-based PM performance as measured by both an experimental computerized task and the CAMPROMPT in 79 older PLWH. Across both samples, the association between IIV-dispersion and PM was not confounded by sociodemographics nor by any of the medical and psychiatric factors that commonly accompany HIV. Our results are broadly consistent with studies showing that IIV-inconsistency in response

time is related to event-based PM functioning in healthy younger (e.g., Ball & Brewer, 2018; Ihle et al., 2017) and older (e.g., Schmitter-Edgecombe et al., 2020) adults and extend those findings to HIV and IIV-dispersion. Taken together, these studies suggest that higher levels of variability in execution within and across cognitive tasks may play a role in the completion of future intentions, perhaps by way of lapses in PM cue encoding, monitoring, and/or detection processes.

The association between IIV-dispersion and PM among PLWH in both studies was particularly robust for time-based cues on laboratory tasks. Higher IIV-dispersion was negatively related to three different measures of time-based PM in two separate samples at small-to-medium effect sizes. The magnitude, direction, and independence of the association between IIV-dispersion and time-based PM in the laboratory parallels prior findings using the RBANS and the MIsT in older healthy Australians (Sullivan et al., 2018). This provides further evidence for the generalizability of the relationship between IIV-dispersion and time-based PM, particularly because Sullivan and colleagues (2018) used the identical clinical PM task that we used in Study 1, but had a different cognitive battery from which their measure of IIV-dispersion was derived. In the current study, PLWH with greater IIV-dispersion in performance across a cognitive battery had difficulty strategically monitoring and detecting time-based PM cues on all three measures, which varied in their delay intervals, retrospective memory demands, ongoing tasks, and allowance of compensatory strategies. Interestingly, higher IIV-dispersion was associated with poorer ongoing task performance in Study 1, but not with clock checking in Study 2, which is a behavioral marker of strategic time monitoring. Thus, it is possible that IIV-dispersion may be particularly involved in cue detection more so than monitoring. Indeed, there may be a trade-off between ongoing task performance engagement and PM cue detection.

At a conceptual level, higher IIV is often interpreted to reflect fluctuations in "executive control" supported by the prefronto-striatal circuits (Stuss et al., 2003). This view of IIV broadly aligns nicely with the reliable association between IIV-dispersion and strategically/executively demanding aspects of PM in both the current studies. Nevertheless, this conceptual explanation is speculative because there can be variability in the underlying cognitive structure of different types of IIV (Stuss et al., 2003), and literature supporting the direct association between executive functions and IIV-dispersion specifically is quite limited. Two studies show a moderate association between IIV-dispersion and independent measures of executive functions in older adults (Fellows & Schmitter-Edgecombe, 2015; Sullivan et al., 2018). Yet, IIV-dispersion is also related to global cognition (e.g., Morgan et al., 2011), and elevations can be present in populations with diffuse brain injury (e.g., Hill et al., 2013). Future experimental studies are needed to better understand the psychometrics and cognitive architecture of IIV-dispersion, including the role of sustained attention, task factors, and different aspects of executive functions (e.g., cognitive control).

Interpreting the association between IIV-dispersion and event-based PM across these two studies of PLWH is a little more complicated. In terms of null hypothesis significance testing, IIV-dispersion was significantly related to event-based PM performance in the larger group of middle-aged PLWH, but not in the smaller group of older PLWH. However, a closer inspection of the observed effect sizes (see Figure 1) shows that the magnitude of the relationship between IIV-dispersion and event-based PM

was actually quite comparable across Study 1 ($\rho = -0.19$) and Study 2 ($\rho = -0.21$), despite their differences in sample size, demographics, and measurement. These small effect sizes are commensurate with findings from much of the extant literature on IIV-inconsistency and event-based PM in healthy adults (e.g., Haynes et al., 2018; Ihle et al., 2017). Taken together, these data suggest that IIV has a small, negative relationship with event-based PM that is observable across different measures of PM and IIV, in both cross-sectional and experimental study designs, and in different participant groups (Lynch et al., 2015). Therefore, the relationship between PM and IIV may not be highly dependent on the cue that triggers the retrieval of the intended action, as it is evident across both time- and event-based cues. Moreover, the relationship is observed across different dimensions of event-based cues, including both focal (e.g., Haynes et al., 2018; Schmitter-Edgecombe et al., 2020) and nonfocal (e.g., Ihle et al., 2017) cues. Given that IIV-dispersion is a nonspecific marker of task performance variability, it makes sense that people with higher scores on this measure would have difficulty reliably detecting PM cues under many different circumstances.

Another benefit of the conceptual replication study design is the confirmation of a null association between IIV-dispersion and PM symptoms in daily life. Specifically, we observed very small effect sizes for the relationship between IIV-dispersion and the PRMQ in both Study 1 and Study 2. These null associations align with the findings of Sullivan et al. (2018), who observed a near-zero correlation between the PRMQ and IIV-dispersion on the RBANS in a large sample of older Australians. Likewise, IIV-dispersion was not associated with naturalistic performance-based PM in this study. These findings suggest that dispersion in neurocognitive performance in the laboratory may not be associated with everyday PM failures, for which a variety of non-PM factors come into play (e.g., compensatory strategies, busyness, and routine). That said, it is possible that a different approach to measuring IIV in the laboratory (e.g., inconsistency in response time) or in the natural environment (e.g., ecological momentary assessment) may be more relevant to the types of PM failures people experience in daily life.

Although this investigation has many strengths, the findings are nevertheless interpreted in the context of the limitations of the design, sample, and measurement. First, we did not include HIV seronegative samples; therefore, the findings cannot be interpreted to explain HIV-associated deficits in PM nor can the association between IIV-dispersion and PM be considered specific to HIV. Indeed, the effects sizes observed here are comparable to other studies of IIV-dispersion and PM in healthy adults (e.g., Sullivan et al., 2018). Future work is needed to determine whether the presence of "impairment" in either IIV-dispersion or PM amplifies, dampens, or changes their association. Relatedly, the specificity of our findings to HIV is tempered by the inclusion of participants with various medical (e.g., hepatitis C, cardiovascular disease) and psychiatric (e.g., depression, substance use) comorbidities that can affect brain structure and function, including both IIV-dispersion and PM. Another limitation is that the samples consisted of mostly White men with some college education who were recruited into a memory study. Although subjective memory symptoms were not an inclusion criterion, recruitment bias is still possible. Moreover, the extent to which the observed associations between IIV and PM may differ in across sex and gender identity, ethnoracial groups, and socioeconomic strata remains to be determined. For example, premorbid verbal IQ was associated with both PM and IIV-dispersion in Study 1

and thus is a plausible moderator of our findings. To that end, one additional limitation is that Study 2 did not include a performance-based estimate of premorbid IQ, although education did not emerge as a confounding factor. One final limitation to consider is that IIV does not yet have normative data to establish "high" versus "low" variation or relationship to demographics other than age. Nevertheless, IIV provides a novel viewpoint of cognitive performance and can enhance our understanding of brain–behavior relationships beyond the traditional mean-based norms.

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