Original Article

Prospective and Retrospective Memory Complaints in HIV-Infected Individuals

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Abstract

Background and Purpose: Deficits of retrospective memory and prospective memory, which are two primary components of episodic memory, have been reported in prior studies in HIV-infected individuals. The present study aimed to further elucidate the characteristics of prospective and retrospective memory complaints in HIV-infected individuals.

Materials and Methods: We recruited 50 HIV-uninfected individuals from the general community, and 67 HIV-infected people who were under the treatment of antiretroviral therapy in Imam Khomeini Hospital of Tehran, Iran in 2016. Analysis of variance (ANOVA) was used to inspect the differences between HIV-infected and seronegative volunteers.

Results: The results of ANOVA showed that HIV-infected individuals had more complaints of in long-delayed ProM ($p=0.049$), short-delayed RetM ($p=0.016$), and long-delayed RetM ($p=0.009$) than seronegative volunteers. No difference was observed in the complaints of short-delayed ProM between HIV-infected and the seronegative volunteers ($p=0.921$). The results of paired sample t-test also revealed that ProM complaints did not differ with RetM complaints among HIV-infected individuals ($p=0.55$), but ProM complaints were more frequent than RetM complaints among seronegative volunteers ($p<0.001$).

Conclusion: Through understanding the characteristics of ProM/RetM complaints in HIV-infected individuals, we will be able to provide appropriate rehabilitation programs which correctly target their ProM/RetM deficits.

Keywords: Prospective memory; Retrospective memory; Memory complaint; PRMQ; HIV; AIDS

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1. Introduction

With acquiring HIV-infection, opportunist infections enter into the central nerves system (CNS), causing cognitive impairment in people living with HIV (PLWH) (1). HIV-associated neurocognitive disorders (HAND) can range from severe forms of HIV-associated dementia (HAD) to minor neurocognitive disorder (MND), to milder forms known as asymptomatic neurocognitive impairment (ANI) (2). Recently, using anti-retroviral (ARV) treatment has decreased HIV-associated dementia, but other types of cognitive impairments are still significant barriers to the treatment of HIV infection (3).

Memory complaints are of most common problems that PLWH report (4-6). Deficits of retrospective and prospective memory, which are two primary components of episodic memory, have been reported in previous studies in PLWH (4-9). Retrospective memory (RetM) is the recollection of past experiences in response to overt prompts (10). RetM was the main focus of memory research in HIV. A prior study found that PLWH report more complaints of RetM (4). Similarly, another study found that HIV serostatus predicts immediate and delayed verbal episodic memory, working memory, and visual memory (5).

Prospective memory (ProM) has recently received high amount of attention in HIV population. ProM or "remembering to remember" refers to the execution of future intentions (e.g. eating prescribed medication at right time in the future). ProM contains a series of cognitive processes including: (a) forming an intention which pairs with a specific retrieval cue, (b) maintaining intention-cue pairing over a delay interval while engaging another task, (c) detecting the cue, (d) retrieving content of the intention from retrospective memory, and (e) executing the intention (6).

ProM deficits have also been reported in PLWH in prior studies (7, 10). A prior study has indicated that PLWH report more time-based and even-based ProM problems compared to healthy comparison volunteers, but in cognitive deficits task, the difference was not meaningful (9). Another study has investigated the characteristics of ProM in HIV seropositive substance-dependent subjects, and reported that they have more problems in time-based long-delayed ProM tasks but not in event-based ProM tasks (7). Similarly, another study found that PLWH had more problems in time-based long-delayed ProM tasks, in addition to long-delayed self-reported ProM. They found no difference between objectives and self-reported measures of ProM among HIV seropositive and healthy individuals (8).

Although a growing body of literature has examined the objective deficits of ProM and RetM in PLWH, a few other studies have examined whether PLWH report subjective failures of ProM in their day to day activities. We hypothesized that; (1) PLWH report more complaints of short-delayed ProM than seronegative volunteers (2) PLWH report more complaints of long-delayed ProM than seronegative volunteers (3) PLWH report more complaints of short-delayed RetM than seronegative volunteers (4) PLWH report more complaints of long-delayed RetM than seronegative volunteers (5) Complaints of ProM were more frequent than complaints of RetM in PLWH. Therefore, the present study aimed to further elucidate the subjective failures of ProM in HIV-infected individuals, and compare the complaints of ProM and RetM

complaints between the HIV-infected individuals and the seronegative volunteers.

2. *Materials and Methods*

In a cross-sectional study, we recruited 50 HIV-uninfected individuals from the general community and 67 HIV-infected people who were under the treatment of antiretroviral therapy (ART) in Imam Khomeini Hospital of Tehran, Iran in 2016. The researchers took convenience sampling method, and asked the patients who referred to Imam Khomeini Hospital to participate in the study. The inclusion criteria were adult patients' ages more than 18 years. The participants who were under the surgical treatment or admission to the hospital were excluded from HIV positive sample, and all participants signed a voluntarily informed consent form, and all information were kept confidential.

2.1. *Instruments*

Prospective/retrospective assessment: Participants completed prospective-retrospective memory questionnaire (PRMQ). PRMQ was designed by Crawford, Smith (11) to assess self-reported complaints of memory, and has two major domains including retrospective and prospective memory. This scale has four subscales including short-delayed ProM, long-delayed ProM, short-delayed RetM, and long-delayed RetM. Each domain is comprised of eight items, and participants were asked to answer the questions in a five-point Likert scale in which one (i.e. "never") shows strong disagreement and five (i.e. "very often") shows strong agreement. Participants got a score between16 to 80. We used Farsi version of PRMQ with its published evidences of reliability and validity (12). In our study, the Cronbach's alpha was found to be 0.90 which showed a good internal consistency of the scale.

2.2. *Medical assessment*

HIV serostatus was determined by two ELISA tests and confirmed by western blot test. Standard flow cytometry methods were used to assess the CD4 count in blood samples. The PARTEC kit (Germany) and whole blood were used as a sample for CD4 counting.

Viral loads were then measured by a referral laboratory using quantitative ultrasensitive polymerase chain reaction (PCR). For the viral load assay, QIAGEN kit was used to extract the RNA from the plasma of people living with HIV. The buffers used in the test were: AVL buffer contains RNA carrier and, AW1 and AW2 buffer for third and fourth passes and AVE buffer for the last pass in a centrifuge.

2.3. *Data analyses*

Analysis of variance (ANOVA) was used to inspect the differences in PRMQ subscales in HIV-infected individuals and seronegative volunteers after screening the data for assumptions of using ANOVA. Paired sample t-test was used to assess the differences in ProM and RetM complaints.

This study was in accordance with the ethical rule of Tehran University of Medical Sciences (TUMS), and all processes and instruments were proved by ethical committee of TUMS. The ethical code was IR.TUMS.REC.1394.1349.

3. *Results*

The demographic and clinical characteristics of the participants who voluntarily participated in the study are shown in Table 1.

Table 1. Participants' demographic information and HIV disease characteristics

Variable	HIV infected	HIV uninfected
Age (years)	39.85 (8.38)	35.18 (13.56)
Sex		
Men	31 (46.26)	20 (40.00)
Women	36 (53.73)	30 (60.00)
Education		
Primary school	8 (11.94)	---
Secondary school	21 (31.34)	7 (14.00)
High school	31 (46.26)	25 (50.00)
University	7 (10.44)	18 (36.00)
HIV disease characteristics		
Duration of using ARV (months)	56.31 (55.51)	
Current CD4 count (cells/µl)	509.87 (267.51)	
Nadir CD4 count (cells/µl)	236.44 (177.31)	
Baseline CD4 count (cells/µl)	202.02 (184.49)	
Plasma viral load (copies/ml)	2312.36 (3178.48)	

CD4: cluster of differentiation 4; ARV: anti-retroviral

Firstly, we investigated the assumptions of using ANOVA. No univariate and multivariate outliers were detected. The results of Kolmogorov-Smirnov test proved the normality of distribution in all variables (P>0.05). Levene's test was also found to be not significant in all variables (P>0.05), which showed that variances were equal in all variables. The results of ANOVA are shown in Table 2 which showed that the group differences were significant in long-delayed ProM (F (1, 101) = 3.78, p=0.049, partial η2 = 0.036), but no group differences were observed in short-delayed ProM between HIV-infected and seronegative volunteers (F (1, 101) =0.010, p=0.921, partial η2 = 0.001). Furthermore, group differences were significant for short-delayed RetM (F (1, 101) = 5.99, P=0.016, partial η2 = 0.056) and long-delayed RetM (F (1, 101) = 7.10, p=0.009, partial η2 = 0.066).

Table 2. Results of ANOVA for group differences in short-delay and long-delay ProM and RetM, Tehran, 2016

Variable	Mean square	F	Sig.	Partial Eta Squared	Observed Power
Short-delay ProM	0.134	0.010	0.921	0.000	0.051
Long-delay ProM	44.333	3.781	0.049	0.036	0.487
Short-delay RetM	74.346	5.995	0.016	0.056	0.679
Long-delay RetM	85.197	7.104	0.009	0.066	0.752

Table 3 demonstrates mean scores of long-delay and short-delay ProM and RetM for HIV-infected and seronegative volunteers. HIV-infected individuals had higher mean scores in long-delayed ProM complaints than seronegative volunteers (M=9.14, SD=3.88). Similarly, HIV-infected individuals had higher mean scores of short-delayed RetM complaints (M=9.51, SD=4.22) and long-delayed RetM complaints (M=9.51, SD=4.22) than seronegative volunteers.

Table 3. PRMQ subscale for HIV-infected and seronegative volunteers, Tehran, 2016

Measures	HIV-infected individuals (Mean, SD) N=67	Seronegative Volunteers (Mean, SD) N= 50	P	Cohen's d
Short-delayed ProM	10.06 (4.11)	10.17 (2.76)	0.921	0.03
Long-delayed ProM	9.13 (3.80)	7.75 (2.55)	0.055	0.44
Short-delayed RetM	9.47 (4.16)	7.86 (2.11)	0.016	0.48
Long-delayed RetM	9.46 (4.05)	7.70 (1.87)	0.009	0.55

Our results of paired sample t-test also revealed that ProM complaints did not differ with RetM complaints among HIV-infected individuals (t=0.593, p=0.555), but ProM complaints were more frequent than RetM complaints among seronegative volunteers (t= 4.02, p=0.0001).

4. Discussion

In the current study, it was found that complaints of ProM and RetM were significantly more frequent in HIV-infected individuals currently taking ARVs than in seronegative volunteers. HIV-infected individuals reported more complaints of long-delayed ProM, short-delayed RetM, and long-delayed RetM, but no group differences were observed in short-delayed ProM complaints between HIV-infected individuals and seronegative comparison group. Our results were commensurate with previous studies showing that HIV-infected individuals reported more complaints of episodic (retrospective) memory than seronegative volunteers (4, 5). To this end, the prior study in Hong Kong on a sample of 90 HIV-infected individuals showed that HIV-infected individuals experienced more subjective problems of retrospective memory (4). Another study on a sample of 164 participants showed that individuals were comorbid with HIV-infection and alcoholism, face problems of delayed, and immediate episodic memory (5). To assess episodic memory, they asked subjects to read and remember a name and address. They also presented two short narratives to the participants, and following each story, the subjects were presented with multiple choice questions.

Our findings also converged with previous studies showing that HIV-infected individuals experienced more problems with ProM than seronegative volunteers (7, 8, 10). To this end, a prior study reported objective and self-reported deficits in long-delayed and short-delayed ProM tasks in HIV-associated neurocognitive disorders (HAND) (8). They used memory for intention screening test (MIST) to assess prospective memory and consistent with our findings, they observed no difference between HIV-infected and seronegative volunteers in objective and subjective measures of ProM tasks. In other studies, deficits of ProM have been reported but they focused on other types of ProM (i.e. time-based and event-based). One study investigated ProM impairments on a sample of 31 individuals who were comorbid with HIV-infection and drug dependence and 35 seronegative volunteers(7). They found that HIV-infected individuals showed deficits of

time-based ProM compared to healthy control volunteers, but no significant difference was observed in event-based ProM between the two groups. Another study compared ProM in 42 HIV-infected individuals and 29 seronegative volunteers using MIST and found that HIV-infected individuals showed more deficits of time-based and event-based ProM than healthy comparison volunteers(9). Similarly, another study investigated the frequency and predictors of self-reported prospective memory in HIV-infected individuals on a sample of 75 HIV-infected and 60 healthy control volunteers using PRMQ(10). They found that HIV-infected individuals reported more complaints of time-based ProM.

Prospective/retrospective memory deficits are part of HIV associated neuropsychological disorders (HAND) that occur within the early hours and days of initial infection when HIV enters the brain early after systemic infection and crosses blood-brain barriers (BBB), and causes neurophysiologic changes in basal ganglia, frontal neocortex, hippocampus, and cerebral white matter (3, 13, 14).

PRMQ can be used to assess individuals ProM/RetM complaints and could be used to identify issues to be followed up in a clinical interview and objective measures of ProM and RetM (11). Although a prior study reported that subjective measures of PRMQ are not valid to assess ProM and RetM (15), but PRMQ is a measure of meta prospective/retrospective memory, and therefore cannot be treated as a direct measure of prospective memory performance, and contains helpful information. For example, a person with real deficits of ProM and RetM and average or above average scores in PRMQ, indicate lack of insight that may be more serious in its consequences than the deficits themselves.

Our data also found no significant difference between ProM and RetM complaints among HIV-infected individuals. Our results were then not in line with a prior study (10) which found that complaints of ProM were more frequent than RetM in HIV-infected individuals. They suggested that ProM may be more germane than RetM memory to self-perceptions regarding day-to-day memory functioning, but our findings did not support this assertion.

While finding out the association between ProM/RetM and HRQoL and everyday functioning (6, 16), future studies should focus on the effects of ProM/RetM rehabilitation on changes in everyday functioning and HRQoL. Examples of rehabilitation techniques include using retrospective memory strategies, prospective memory training, meta-memory training (to educate patients for their MetaProM/MetaRetM deficits and its adverse consequences), or utilizing external aids, such as using an appointment book for important daily tasks or a programmable electronic device that notifies the patients to take their medication on time. Through knowing that memory deficit is one of the barriers of adherence to HIV medication regimen (17-20), ProM and RetM rehabilitation will play a significant role in the medication adherence of HIV-infected individuals.

Prior limitation of the current study was the lack of control over the other factors influencing the self-reported ProM and RetM in HIV-infected individuals, such as controlling for psychiatric variables. Another limitation was the cross-sectional nature of the study. Despite these limitations, our findings added to the

understanding about the features of ProM and RetM in HIV-infected individuals. Figuring out the characteristics of ProM/RetM complaints in PLWH, we will then be able to provide appropriate rehabilitation programs which target correctly their ProM/RetM deficits.

5. Conclusion

In summary, this study indicated that complaints of ProM and RetM were significantly more frequent in HIV-infected individuals than in seronegative volunteers. Complaints of long-delayed ProM, long-delayed RetM, and short-delayed RetM were significantly higher in HIV-infected individuals than in seronegative volunteers, but no difference was observed in short-delayed RetM between the two groups. Our data also indicated no difference between ProM and RetM complaints among HIV-infected individuals, but ProM complaints were found to be more frequent than RetM complaints among healthy control volunteers.

Ethics approval

Our study was approved by the Tehran University of Medical Sciences (TUMS) Moral Committee of Tehran, Iran. No animal was used in this study. Our study was in accordance with ethical standards of the Helsinki declaration of 1975, which was revised in 2008.

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Conflict of interests

The authors report no real or perceived vested interests related to this article that could be construed as a conflict of interest.

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