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Age- and education-matched comparison of aging HIV+ men who have sex with men to general population on common neuropsychological assessments

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Abstract

Little is known about the impact of HIV and aging on cognitive functioning. This New York City cross-sectional study of aging HIV-positive gay and bisexual men assessed their neuropsychological state. Working memory and verbal abstract reasoning were relatively intact. After 55 years of age, attention abilities were impaired. Executive function impairment was present regardless of age and education. Results suggest the need for HIV-specific norms, and the use of neuropsychological assessments (i.e. baseline and over time) as a cost-effective way to assess HIV-related cognitive decline in developed and under-developed countries.

Keywords

age, AIDS, cognitive, HIV, men's health, neuropsychological

Introduction

The epidemiology of neurocognitive disorders among HIV-positive individuals has evolved over the course of the epidemic as a result of more effective antiretroviral (ARV) therapies that have extended the average life expectancy and slowed the progression of serious cognitive dysfunction (Goodkin et al., 2001). Concurrently, ARV therapies contribute to what has been called an "accelerated-aging process," meaning that HIV-positive people are experiencing metabolic and cardiovascular sequalae, including cognitive decline, typically experienced in people approximately 5–15 years old (Justice, 2010). Because HIV-related neurocognitive disorders are similar to cardiovascular-related dementias, we can learn from the prevention and cognitive rehabilitation efforts used with other populations (Vance, 2013; Vance et al., 2013). However, the accelerated-aging process suggests that utilizing existing neuropsychological norms gathered from similarly aged

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people may be inappropriate for use among seropositive people and may result in over-reporting of cognitive dysfunction. Developing HIV-specific, age- and education-matched neuropsychological norms is imperative, given that the proportion of HIV-seropositive adults ages 50 years and older is expected to increase exponentially (Centers for Disease Control and Prevention DHAP (CDC), 2012). Understanding the antecedents of HIV-related cognitive disorders and how impacted cognitive domains are similar and different from other dementing illnesses will inform prevention and individual-level (e.g. cognitive rehabilitation and pharmacological) and public health interventions (Herlihy et al., 2012; Vance, 2013; Vance et al., 2013).

Degenerative brain dysfunction related to both HIV and aging has been associated with neuronal loss, physiological impairments, reduced neurotransmitter production, and inflammation (Morgan et al., 2012a, 2012b; Vance, 2010; Vance et al., 2011a). Research suggests that both older age and HIV-seropositive status are independent risk factors for global neurocognitive impairment and specifically impair attention, working memory, motor skills, verbal fluency, information processing speed, reaction time, learning, and executive functioning (Gonzalez et al., 2010; Heaton et al., 2011; Manly et al., 2011; Scott et al., 2011; Thames et al., 2011; Wendelken and Valcour, 2012). These neurocognitive impairments may negatively impact activities of daily living, such as ARV adherence, medical management, mental health, and other behavioral-risk factors such as sexual decision making and substance use (Becker et al., 2011; Blackstone et al., 2012a, 2012b; Cavaleri et al., 2010; Cook et al., 2011; Ettenhofer et al., 2010; Halkitis et al., 2009, 2013; Homer et al., 2013; Lee et al., 2011; Slavin et al., 2011; Vance et al., 2010; Malspina et al., 2011; Woods et al., 2009, 2011; Zogg et al., 2012). Despite the widespread use and efficacy of ARV therapies in slowing cognitive decline, some researchers have found that 30–88 percent of HIV-positive adults perform in the impaired range on neuropsychological batteries (Abrass et al., 2011; Harezlak et al., 2011; Heaton et al., 2011; Margolin et al., 2002; Martin et al., 2008). Other researchers have found no differences or mixed results in neurocognitive performance between HIV-positive and HIV-negative people (Cysique et al., 2011; Kissel et al., 2005). These mixed results regarding the cognitive state of aging seropositive populations will become more pressing as the proportion of HIV-positive people age 50 years and older aggregates.

Globally, more than 34 million people live with HIV/AIDS, and in 2011, 2.5 million were newly diagnosed with HIV (American Foundation for AIDS Research (AMFAR), 2012). Additionally, from 2009 to 2015, the proportion of seropositive people in the United States who are aged 50+ is expected to rise from 32.7 percent to 50 percent (CDC, 2012; Shah and Mildvan, 2006). This shift is attributed to increased life expectancy and new HIV infection rates among older adults (Palella et al., 2006). While extant literature is robust in describing the relation between aging and neurocognitive diseases such as Alzheimer's and Parkinson's diseases, much less is understood about neurocognitive decline among older HIV-positive individuals (High et al., 2012; Solomon and Budson, 2011). Age-specific normative data for HIV-seropositive adults are missing from the literature (Cysique et al., 2011). Therefore, this article will characterize the neurocognitive state of an HIV-positive sample of men who have sex with men (MSM) aged 50 years and older, and compare their performance to age-matched normative data.

Methods

Study design

Project Global Opportunities for Leadership Development (GOLD) was a two-phase study from May to August 2010 (Phase I) and March to August 2011 (Phase II). All protocols, forms, and Institutional Review Board (IRB) training

were approved by the New York University IRB. Researchers were also training on the administration of neuropsychological measures. Our sample ($N = 199$) of HIV-positive gay, bisexual, and other MSM, who were aged 50 years and older were recruited through a variety of in-person and online outreach methods. Because HIV has disproportionately impacted racial and ethnic minorities (CDC, 2011), we oversampled MSM of color and utilized targeted sampling to achieve recruitment goals.

Eligible participants were (1) 50 years or older, (2) HIV-positive, (3) born biologically male, and (4) male-identified. Additionally, written informed consent was obtained from all eligible participants in Project GOLD. The study included a computer-based survey, and face-to-face neuropsychological measures, which were administered at the research center. Participants received a US$50 incentive upon survey completion.

Measures

This cross-sectional study obtained data on a range of individual-level factors and neurocognitive indicators.

Demographic factors. Demographic data included information on age, race/ethnicity, and educational attainment (i.e. "High school or less" and "More than a high school education").

Traumatic brain injuries indicators. Utilizing the Ohio State University Traumatic Brain Injury Identification Method Short Form (OSU TBI-ID), participants self-reported information regarding head injuries (Corrigan and Bogner, 2007). Those with a moderate-severe brain injury (i.e. unconscious for greater than 30 minutes) were excluded from analyses to mitigate the risk of reporting suboptimal neurocognitive scores (Gerberding and Binder, 2003; Kay et al., 1993).

Neurocognitive assessments. Neuropsychological tests used measured cognitive domains known to be impacted by HIV. The battery assessed global cognitive functioning through the Mini-Mental State Examination (MMSE) (Folstein et al., 1975), executive functioning (Trail B) (Reitan and Wolfson, 1985), attention and working memory (Trail A and Wechsler Adult Intelligence Scale (WAIS-III) Digit Span subtest) (Reitan and Wolfson, 1985; Wechsler, 1997), verbal comprehension, and abstract reasoning (WAIS-III Similarities subtest) (Wechsler, 1997).

Sample results were compared to population norms outlined in Crum et al. (1993) for the MMSE, in Tombaugh (2004) for Trails-Making A & B, and in Wechsler (1997) for the WAIS-III Digit Span and Similarities subtests. Additionally, the WAIS-III protocols require the conversion of raw scores to scaled scores ranging from 1 to 19 ($M = 10$, standard deviation (SD) = 3) to allow for easy interpretation.

Data analysis

Descriptive, bivariate, and multivariate analyses were conducted utilizing IBM Statistical Package for Social Sciences (SPSS) Statistics 20.

Results

Study sample

Project Gold consisted of 199 HIV-positive MSM, aged 50–69 years. After excluding 30 participants that reported a moderate or severe TBI, the demographics of the analytic sample ($N = 169$) was proportional to the total sample ($N = 199$) (see Table 1). Overall, the analytic sample consisted of predominantly racial/ethnic minority MSM ($n = 124$, 73.3%). The mean age was 55.78 years ($SD = 4.60$) and mean number of years living with HIV was 17.76 ($SD = 6.41$). Most participants indicated an educational attainment higher than high school ($n = 91$, 53.80%) and identified as gay or bisexual ($n = 157$, 92.9%). Additionally, most participants perceived their socioeconomic status as middle class ($n = 75$, 44.4%). Most men

Table 1. Social and demographic characteristics among 169 HIV-positive MSM aged 50 years and over, New York City, 2010–2011.

Participant characteristics	Number (%) of study participants	
	Study sample (*N* = 199)	Analytic sample (*n* = 169)
Age, mean (standard deviation)	55.49 (4.54)	55.78 (4.60)
Years living with HIV, mean (standard deviation)	18.14 (6.31)	17.76 (6.41)
Race		
Black	93 (46.7)	80 (47.3)
White	46 (23.1)	42 (24.9)
Latino	28 (14.1)	21 (12.4)
Mixed race/other	29 (14.6)	23 (13.6)
Education		
Less than high school	23 (11.6)	16 (9.5)
High school/GED	71 (35.7)	62 (36.7)
Associate's degree	37 (18.6)	30 (17.8)
Bachelor's degree	47 (23.6)	40 (23.7)
Graduate degree	21 (10.6)	21 (12.4)
Sexual orientation		
Gay	149 (74.9)	130 (76.9)
Bisexual	36 (18.1)	27 (16)
Straight	4 (2.0)	4 (2.4)
Other	10 (5.0)	8 (4.7)
Perceived socioeconomic status		
Lower	26 (13.1)	23 (13.6)
Lower middle	55 (27.6)	50 (29.6)
Middle	92 (46.2)	75 (44.4)
Upper middle	25 (12.6)	20 (11.8)
Upper	1 (0.5)	1 (0.6)
Traumatic brain injury		
Improbable	84 (42.21)	83 (49.1)
Possible	38 (19.1)	35 (20.7)
Mild	48 (24.1)	51 (30.2)
Severe	29 (14.6)	0 (0.0)
Self-reported CD4 count, mean (standard deviation)	488.31 (259.71)	482.51 (260.83)
Self-reported viral load count		
Undetectable	149 (74.9)	122 (72.2)
Under 500	15 (7.5)	14 (8.3)
500–5000	18 (9.0)	17 (10.1)
Over 5000	13 (6.5)	12 (7.1)
HIV treatment (lifetime)		
No	12 (6.0)	10 (5.9)
Yes	187 (94.0)	159 (94.1)
Opportunistic infection (lifetime)		
No	75 (37.7)	69 (40.8)
Yes	124 (62.3)	100 (59.2)

Table 1. (Continued)

Participant characteristics	Number (%) of study participants	
	Study sample (N = 199)	Analytic sample (n = 169)
Self-reported physical health		
Poor	6 (3.0)	2 (1.2)
Fair	41 (20.6)	36 (21.3)
Good	77 (38.7)	71 (42.0)
Very good	50 (25.1)	44 (26.0)
Excellent	25 (12.6)	16 (9.5)

MSM: men who have sex with men; GED: General Equivalency Diploma.

reported ever receiving some form of HIV medication treatment (n = 159, 94.1%) and rated their health as good or better (n = 131, 77.5%). The mean self-reported CD4 count was 482.51 (SD = 260.83) and 122 had undetectable viral loads (72.2%).

MMSE. The MMSE evaluated overall cognitive functioning. Using the established cut score of 24, 23 percent (n = 22) were deemed to have mild cognitive impairment/early dementia or greater cognitive impairment (Folstein et al., 1975). The MMSE scores for the men in Project GOLD were as follows: (1) age 50–54 years (M = 27.17, SD = 3.25), (2) age 55–59 years (M = 27.33, SD = 2.96), and (3) age 60–69 years (M = 27.39, SD = 3.17). Analysis of variance (ANOVA) and t-test determined that age and education were not significant. Most of the sample MMSE scores by age and education attainment were within 1 SD of the population mean (Crum et al., 1993). See Table 2 for a side-by-side, age- and education-related comparison (Crum et al., 1993). However, the 65–69 years of age cohort with a "high school education or less" only had 1 participant and therefore results were discarded due to inadequate cell size.

Trails-Making Test A. Using the Trails-Making Test A norms (i.e. attention) and age cohorts outlined by Tombaugh (2004), 21 percent (n = 35) of our sample performed worse (i.e. had slower times) than 90 percent of the people in the normative sample. Scores by age revealed significant differences ($F(3) = 3.35$, $p < .05$), with those aged 50–54 years (M = 35.26, SD = 13.01) having lower average times on Trails A than men aged 55–59 years (M = 43.51, SD = 22.81) and 60–64 years (M = 45.22, SD = 20.92). An ANOVA determined that there were no differences in times on Trails A by education. Moreover, those aged 50–54 years, regardless of educational attainment, and men aged 55–59 years with "more than a high school education" had times on Trails A that were within a SD of the norms (Tombaugh, 2004). However, participants aged 55+ years had more difficulty paying attention than those in the general population. Further, men aged 55–59 years with a "high school education or less" and 60–64 years regardless of educational attainment had times greater than 1 SD from population norms (Tombaugh, 2004). In addition, there were significant differences between the norms and those aged 65–69 years. However, due to the limited cell size, these differences should be interpreted with caution. To determine whether age, education, and the age–education interaction influenced the scores on Trails A, a two-way ANOVA was utilized. Participant scores on Trails A (i.e. attention) were not influenced by age and educational attainment nor the interaction of age and education.

When comparing Trails A times to other HIV-positive populations, our sample had similar times to those identified as both asymptomatic

Table 2. Comparison of neurocognitive scores by age cohort and dichotomized education level to general population norms.

Neurocognitive measures, age cohort (number of participants)	High school or less		More than high school education	
	Sample (*M* (*SD*); *n*)	General population norms (*M* (*SD*))	Sample (*M* (*SD*); *n*)	General population norms (*M* (*SD*))
MMSE[a]				
50–54; *n* = 78	27.18 (3.54); *n* = 44	28 (2.2)[a]	27.15 (2.89); *n* = 34	29 (1.9)[a]
55–59; *n* = 55	26.45 (2.96); *n* = 20	28 (2.2)[a]	27.83 (2.89); *n* = 35	29 (1.5)[a]
60–64; *n* = 27	26.38 (3.75); *n* = 13	28 (1.7)[a]	28.36 (2.21); *n* = 14	29 (1.3)[a]
65–69; *n* = 9	21.00 (N/A); *n* = 1	28 (1.4)[a]	28.13 (2.59); *n* = 8	29 (1.0)[a]
Trails A*,[b]				
50–54; *n* = 78	35.16 (11.89); *n* = 44	31.78 (9.93)[b]	35.38 (14.52); *n* = 34	31.78 (9.93)[b]
55–59; *n* = 55	48.65 (29.87); *n* = 20	35.1 (10.94)[b]	40.57 (17.42); *n* = 35	31.72 (10.14)[b]
60–64; *n* = 27	48.85 (27.53); *n* = 13	33.22 (9.10)[b]	41.86 (12.25); *n* = 14	31.32 (6.96)[b]
65–69*; *n* = 9	55.00 (N/A)*; *n* = 1	39.14 (11.84)[b]	34.38 (6.87)*; *n* = 8	33.84 (6.69)[b]
Trails B***[b]				
50–54; *n* = 78	111.61 (68.76); *n* = 44	63.76 (14.42)[b]	100.47 (54.61); *n* = 34	63.76 (14.42)[b]
55–59; *n* = 55	120.10 (69.62); *n* = 20)	78.84 (19.09)[b]	111.77 (65.60); *n* = 35	68.74 (21.02)[b]
60–64*; *n* = 27	173.00 (81.34)*; *n* = 13	74.55 (19.55)[b]	111.71 (34.18); *n* = 14	64.58 (18.59)[b]
65–69***; *n* = 9	250.00 (N/A)***; *n* = 1	91.32 (28.89)[b]	86.00 (28.10)***; *n* = 8	67.12 (9.31)[b]
Digit span[c]				
50–54; *n* = 78	8.59 (3.4); *n* = 44	10 (3)[c]	8.91 (3.27); *n* = 34	10 (3)[c]
55–64; *n* = 82	8.91 (2.74); *n* = 33	10 (3)[c]	9.82 (3.03); *n* = 49	10 (3)[c]
65–69; *n* = 9	6.00 (N/A); *n* = 1	10 (3)[c]	9.88 (3.00); *n* = 8	10 (3)[c]
Similarities**[c]				
50–54**; *n* = 75	7.81 (2.45)**; *n* = 42	10 (3)[c]	9.18 (1.78)**; *n* = 33	10 (3)[c]
55–64**; *n* = 81	8.88 (2.80)**; *n* = 32	10 (3)[c]	10.82 (2.84)**; *n* = 49	10 (3)[c]
65–69*; *n* = 9	7.00 (N/A)*; *n* = 1	10 (3)[c]	11.50 (1.60)*; s*n* = 8	10 (3)[c]

MMSE: Mini-Mental State Examination; *SD*: standard deviation.
[a]Crum et al. (1993).
[b]Tombaugh (2004).
[c]Wechsler (1997).
***$p < .001$, **$p < .01$, *$p < .05$.

and symptomatic HIV (Margolin et al., 2002). Furthermore, our sample had faster times when compared to other HIV-positive populations including those with AIDS (Fazeli et al., 2011; Margolin et al., 2002; Vance et al., 2011b). However, mean times reported by both Fazeli et al. (2011) and Margolin et al. (2002) included seropositive people of all ages.

Trails-Making Test B. Our sample demonstrated that 55 percent (n = 93) had times on Trails-Making B that were worse (i.e. slower) than 90 percent of the normative sample (Tombaugh, 2004). The mean sample score on Trails B was 114.75 (SD = 65.36; range = 35–300). Significant differences ($t(167) = 2.05$, $p < .05$) were found by the education variable, with "more than a high school education" (M = 105.27, SD = 54.90) having faster times than those with a "high school education or less" (M = 125.79, SD = 74.61). Additionally, the average times on Trails B were all greater than 1 SD from age-specific population norms, with those having a "high school education or less" having times that were 2–5 SDs above the norms (Tombaugh, 2004) (see Table 2). Trails B times appeared to be sensitive to the influences of age and the education variable ($F(3) = 5.51$, $p < .001$) and the age–education interaction using a two-way ANOVA. Those with "more than a high school education" had faster and more consistent times as they were aged than those with "high school degree or less," who were more likely to experience increases in time on Trails B as they aged. Additionally, those with a "high school degree or less" demonstrated significantly different times on Trails B by age, with those aged 60–69 years (M = 178.50, SD = 80.81) taking significantly longer to complete the test than those aged 50–59 years (M = 114.27, SD = 68.59). Comparing Trails B times to another HIV-positive population, the times were similar to those with symptomatic HIV and AIDS (Margolin et al., 2002). In contrast, participants had faster times on Trails B than seropositive participants aged 50 years and older in other studies (Fazeli et al., 2011; Vance et al., 2011b).

WAIS-III Measures

Digit span. Working memory was assessed using the Digit Span subtest of the WAIS-III. No differences in Digit Span scaled scores were found by age or educational attainment. Only 16 percent (n = 27) of participants had scaled scores greater than 1 SD (M = 10, SD = 3) below the age-related population norm. The mean overall sample scaled score was 9.12 (SD = 3.11) and the age-specific averages were as follows: (1) ages 50–54 years (M = 8.73, SD = 3.29), (2) 55–64 years (M = 9.45, SD = 2.93), and (3) 65–69 years (M = 9.44, SD = 3.09). Norms are compared to sample means in Table 2. Those with a "high school education or less" had scores similar to another study of older seropositive people (Vance et al., 2011a), whereas those with "more than a high school education" had scores similar to those from Fazeli et al. (2011). However, neither study published scores by age or education (Fazeli et al., 2011; Vance et al., 2011a).

Similarities. Insight into the abstract reasoning or verbal abstraction ability was ascertained from the WAIS-III Similarities subtest. The proportion with scaled scores greater than 1 SD (M = 10, SD = 3) below the age-related population norm was 11.5 percent (n =19). The overall scaled score was 9.36 (SD = 2.76). There were significant differences by age for the Similarities test ($F(2,162) = 9.38$, $p < .001$), with those aged 50–54 years scoring lower than men aged 55–64 years and 65–69 years. The age-specific scaled scores for the Similarities subtest were as follows: (1) ages 50–54 years (M = 8.41, SD = 2.27), (2) 55–64 years (M = 10.05, SD = 2.97), and (3) 65–69 years (M = 11.00, SD = 2.12). Similarities scores are compared to the norms in Table 2 (Wechsler, 1997). The education variable ($t(163) = -5.02$, $p < .001$) was significant. Men with "more than a high school education" (M = 10.28, SD = 2.54) had higher scaled scores than those with a "high school education or less" (M = 8.25, SD = 2.63). To determine whether age, education, and the age–education interaction relationship were

significant, a two-way ANOVA was utilized. Evaluating the education variable ($F(5) = 8.16$, $p < .001$) yielded significant results. However, the age–education interaction term was not significant, whereas the age and education were each significant.

Discussion

Researchers have analyzed cognitive functioning across a wide age range of HIV-positive people (Fazeli et al., 2011; Vance et al., 2011b). However, only Vance et al. (2011b) reported results on those aged 50 years and older. This is the first study of HIV-positive MSM aged 50 years and older, specifically, to document cognitive functioning using common neuropsychological measures. Overall, the proportion of participants with test scores in the impaired range (11.5%−55%) were lower than the 30−88 percent cited in prior studies (Abrass et al., 2011; Harezlak et al., 2011; Heaton et al., 2011; Margolin et al., 2002; Martin et al., 2008; Woods et al., 2004).

Regarding overall cognitive functioning, working memory, and verbal abstract reasoning, our sample had scores within the normal range (Crum et al., 1993; Wechsler, 1997). Prior to the age of 55 years, attention was within normal range, regardless of education. However, after the age of 55 years, those without some college education were more likely to demonstrate impaired attention. Moreover, men had consistently longer times on Trails-Making B when compared to the norms, regardless of age and education, which suggests possible impairment in executive functioning (Tombaugh, 2004).

Limitations

Due to the cross-sectional design of the study, we were unable to ascertain premorbid (i.e. pre-HIV or pre-ARV therapy) cognitive functioning or current intellectual capability (i.e. IQ), which is necessary to fully measure cognitive decline over time. Additionally, because we utilized single-faceted measures, assumptions can only be made regarding the current cognitive performance on those specific measures. Moreover, we did not use nonparametric tests to compare our sample to the population norms, which limited our ability to report significant difference. However, comparing individual scores to published population means and *SD*s is how clinicians determine whether scores are within the "normal range." Furthermore, results are mixed as to whether the MMSE is sensitive enough to detect cognitive decline among the seropositive people (Abrass et al., 2011; Vance et al., 2013).

Vance (2010) argued that researchers overestimate the prevalence of cognitive decline in HIV populations because study incentives attract people who are unemployed, mentally unstable, substance users, or have low educational attainment. However, to mitigate the risk of reporting suboptimal cognitive states, those with moderate-severe TBI were removed from analyses. Additionally, race/ethnicity, substance use, and recruitment venue quotas were enacted to ensure diversity of sampling. Additionally, because the proportion of cognitive impairment was lower than other studies, we believe the recruitment quotas and removing those with TBIs addressed the concerns outlined by Vance (2010).

Conclusion

Neuropsychological assessment may be a cost-effective alternative to magnetic resonance imaging (MRI) and computer axial tomography (CT or CAT) scan for early detection of cognitive decline among HIV-positive people living in developed and developing countries. Early detection of cognitive decline would allow practitioners to investigate biological, psychological, and pharmacological causes and develop solutions. In addition, adding a neuropsychological evaluation to the baseline assessment of biological markers (i.e. CD4 counts and viral load) at the time of seroconversion would allow clinicians to assess for premorbid cognitive functioning, possibly detect future cognitive decline.

Impairment in attention and executive functioning on the individual level can fuel HIV-treatment noncompliance (i.e. medication and medical appointment), which can result in future medication resistance, increased sexual risk, and substance use, as well as suboptimal health, mental health, and neuropsychological and psychosocial outcomes. From a policy perspective, increased cognitive impairment may contribute to disease transmission and increased healthcare costs. Further longitudinal research to document the trajectory of HIV-specific cognitive decline and intervention research testing efficacy of cognitive rehabilitation on HIV-positive populations is imperative. Both early detection and intervention can mitigate the impact cognitive impairment, thereby allowing older seropositive individuals to maintain their independence as they continue to live longer.

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