Published in final edited form as:

AIDS Care. 2012 ; 24(9): 1126–1135. doi:10.1080/09540121.2012.687813.

NEUROCOGNITIVE DEFICITS IN HIV-INFECTED WOMEN AND VICTIMS OF CHILDHOOD TRAUMA

G Spies¹, C Fennema-Notestine^{3,4}, SL Archibald³, M Cherner³, and S Seedat^{1,2}

¹South African Research Chairs Initiative (SARCHI), PTSD program, Department of Psychiatry, University of Stellenbosch, Cape Town, South Africa

²MRC Unit on Anxiety and Stress Disorders, Department of Psychiatry, University of Stellenbosch, Cape Town, South Africa

³Department of Psychiatry, University of California San Diego, La Jolla, CA, USA

⁴Department of Radiology, University of California San Diego, La Jolla, CA, USA

Abstract

Objectives—The study investigated the behavioral and brain effects of childhood trauma and HIV-infection, both separately and in combination, and assessed potential interactions in women who were dually affected.

Methods—83 HIV-positive and 47 matched HIV-negative South African women underwent neuromedical, neuropsychiatric and neurocognitive assessments. Univariate tests of significance assessed if either HIV infection or childhood trauma, or the combination, had a significant effect on neurocognitive performance.

Results—The majority of women were Black (96%) and had an average age of 30. An analysis of covariance revealed significant HIV effects for the Hopkins Verbal Learning Test (HVLT) learning and delay trials ($p < .01$) and the Halstead Category test ($p < .05$). A significant trauma effect was seen on the HVLT delay trial ($p < .05$).

Conclusion—The results provide evidence for neurocognitive dysfunction in memory and executive functions in HIV-infected women and memory disturbances in trauma exposed women.

Keywords

HIV/AIDS; childhood trauma; memory; executive functions; neurocognition

Introduction

In South Africa, 5.63 million individuals were infected with HIV in 2009. Of these, 3.3 million were females (UNAIDS, 2010). Women's vulnerability to HIV/AIDS is largely attributable to biological factors and to socio-economic inequalities. High rates of gender-based violence (GBV) such as intimate partner violence (IPV), rape, and childhood abuse

have been reported (Andersson, Cockcroft, & Shea, 2008; Jewkes, Penn-Kekana, Levin, Ratsaka, & Schrieber, 2001; Kalichman & Simbayi, 2004). Studies suggest that high rates of childhood emotional (51.9%), physical (51.1%), and sexual (41.6%) abuse have been reported in HIV-positive individuals (Walton et al., 2011). Few studies have assessed the influence of GBV on neurocognition in South Africa. Among existing studies, high rates of GBV and revictimisation have been reported in South African women (Dunkle et al., 2004; Jewkes, Dunkle, Nduna, Jama, & Puren, 2010; Jewkes, Levin, Mbananga, & Bradshaw, 2002).

HIV is capable of penetrating the blood-brain barrier (BBB) early in the course of infection and can be highly neurovirulent (Woods, Moore, Weber, & Grant, 2009). Risk for a significant brain involvement is highest with more advanced disease staging (Centers for Disease Control and Prevention, 1993; Heaton et al., 1995). In diagnosing HIV effects on the central nervous system (CNS), neuropsychological (NP) assessments remain the most important tools, especially in resource-limited settings where modern neuroimaging technology is often unavailable (Robertson, Liner, & Heaton, 2009). HIV is frequently associated with deficits in higher order brain function. Disturbances with memory, psychomotor speed, executive functions, and problems with attention are frequent (Grant, 2008). Neurocognitive disorders in HIV are related to disease staging and range from less severe to its worst form, HIV associated dementia (HAD) (Grant, 2008). Collectively, these disorders are referred to as HIV-associated neurocognitive disorders (HAND). They consist of asymptomatic neurocognitive impairment (ANI), mild neurocognitive disorder (MND), and HAD (Antinori et al., 2007). HAND occurs globally and across the various genetic clades of the virus (Joska, Fincham, Stein, Paul, & Seedat, 2010). Findings from the CHARTER study suggest that milder forms of cognitive impairment remain predominant, even among those receiving combined antiretroviral therapies (cART). CHARTER data indicate that 33% of the cohort met criteria for ANI, 12% for MND, and only 2% for HAD (Heaton et al., 2010; Heaton et al., 2011).

Few studies have examined neurocognitive deficits and HAND in South Africa. In one study, of 536 individuals screened with the HIV Dementia Scale (HDS), 23.5% met criteria for HDS defined HAND (Joska et al., 2010). In a separate study, of 170 individuals, 43 (25%) met criteria for HAD, while 72 (42%) had MND, and 15 (9%) met criteria for ANI using the ANN criteria (Joska et al., 2010). HAND, specifically HAD is associated with increased morbidity and mortality in infected patients, especially in countries where access to antiretroviral medications is poor (Sacktor, 2002).

There is evidence for deficits in memory and executive functions among individuals with PTSD (Clark et al., 2003; Jelinek et al., 2006; Lagarde, Doyon, & Brunet, 2010). Studies examining neurocognitive outcomes of early life adversities are limited and inconsistent. Impairments in intellectual development, language, verbal learning, spatial working memory, and psychomotor speed have been reported in individuals exposed to childhood trauma (Choi, Jeong, Rohan, Polcari, & Teicher, 2009; Majer, Nater, Lin, Capuron, & Reeves, 2010; Palmer et al., 1997). However, other studies did not report any neurocognitive impairments (Jelicic, Geraerts, & Merckelbach, 2008; Saigh, Yasik, Oberfield, Halamandaris, & Bremner, 2006; Yasik, Saigh, Oberfield, & Halamandaris, 2007). An

increased risk of HIV-related morbidity and mortality, and poorer cognitive functioning in individuals who have a history of childhood trauma, acute stress, and PTSD has been documented (Leserman et al., 2007; Leserman et al., 2005). To our knowledge, there are currently no published studies investigating the additive effects of HIV and childhood trauma on neurocognitive function. HIV infected women who have a history of childhood trauma may be especially vulnerable to psychiatric and neurocognitive dysfunction secondary to the additive or interaction effects of HIV and childhood trauma. Therefore, the study hypothesized that a synergistic relationship between HIV and childhood trauma would be evident. This synergistic relationship with respect to impact on neurocognition has not been previously documented.

Methods

Participants

The study cohort consisted 83 (64%) HIV-positive and 47 (36%) HIV-negative women. Forty eight HIV-positive women were exposed to childhood trauma. Among controls, 20 had been exposed to childhood trauma. Eligibility criteria included: willingness and ability to provide written informed consent, ability to read and write in either English or Afrikaans at 5th grade level, aged between 18 and 65 years, medically well enough to undergo neuropsychological testing and MRI scanning. Exclusions included: a current or past history of schizophrenia, bipolar disorder or other psychotic disorders, current substance or alcohol abuse or dependence, significant previous head injury, demonstrated frank dementia on the HIV Dementia Scale, current seizure disorders of any cause, history of CNS infections of neoplasms, hepatitis B positive status, and current use or use within the last month of any psychotropic medication.

Procedure

The study was approved by the ethics committee of the University of Stellenbosch, South Africa. All participants were recruited through community health care facilities in and around Cape Town. Participants underwent neuromedical, neurocognitive and childhood trauma exposure assessments.

Measures

Demographic and clinical characteristics—Age, gender, marital status, ethnicity, years of education and employment status were captured. A comprehensive history was obtained from, and a general physical examination conducted in, all patients. Virologic markers of disease progression (CD4 lymphocyte count and viral loads) were obtained from blood samples.

Psychiatric morbidity—Current and lifetime psychiatric disorders were evaluated using the MINI- International Neuropsychiatric Interview- Plus (M.I.N.I.-Plus) (Sheehan et al., 1998).

Self-report behavioural instruments—Participants were assessed for depressive symptomatology using the Center for Epidemiologic Studies Depression Scale (CES-D)

(Radloff, 1977). Trauma symptomatology was assessed using the Davidson Trauma Scale (DTS) (Davidson et al., 1997).

Childhood trauma—The Childhood Trauma Questionnaire Short Form (CTQ-SF), a 28-item self-report inventory that provides valid screening for histories of abuse and neglect was administered (Bernstein et al., 2003). It assesses five types of maltreatment including, emotional, physical, and sexual abuse, and emotional and physical neglect. These five subscales each consist of 5 items with scores ranging from 5 to 25. The overall trauma score ranges from 25 to 125 with higher scores indicating higher levels of childhood trauma (score of 25-31 = no trauma, score of 41-51 = low to moderate, 56-68 = moderate to severe, and 73-125 = severe to extreme).

Neurocognitive assessment—The battery included 17 individual test measures thought to be especially vulnerable to the effects of HIV. It was compiled by the HIV Neurobehavioral Research Center (HNRC) at the University of California, San Diego (Table 1) and administered by a trained research psychologist. Appropriate cultural modifications were made to the HVLT-R. The precious stone semantic category was replaced with vegetables.

Data Analyses—Age and education corrected z-scores were calculated from all raw neuropsychological (NP) data and grouped into domains (motor, verbal fluency, working memory, speed, learning, recall, and executive functions). This was done by running a regression analysis on all raw NP data ($n = 130$) using test scores as the outcome and age and education as predictors. The residual was then saved and a studentized residual was calculated. Within each domain, the studentized residual for each test was summed to obtain a domain z score. Univariate tests of significance (ANOVA and ANCOVA) were applied to all domain and raw scores to determine if either HIV infection or childhood trauma, or the combination, had a significant effect on neurocognitive performance. In looking at the raw scores, age and education were added as covariates in the model. Separate ANOVAs were carried out for each ability domain and separate ANCOVAs were carried out on each individual test (raw scores). Given that several tests are grouped within each ability domain, it may be possible to miss effects. This was the rationale behind examining both domain and raw scores. Corrections for multiple testing (Fisher LSD) were carried out. A multiple regression analysis was performed. Self-report instruments and demographic and clinical variables were entered into the analysis to determine whether or not they could explain variance in the significant dependent variables.

Results

Demographic characteristics of the sample (see Table 2 and 5)

The control group was significantly younger and more educated. Age and education were significantly correlated with most neuropsychological tests and were therefore included as covariates in the analyses.

Clinical characteristics of the HIV-positive sample (see Table 2)

The mean CD4 lymphocyte count was 405 cells/mm³ (range 35-1529 cells/mm³). The mean HIV viral load was 105169.5 copies/ml, ranging from below the detectable limit to 3,200 000 copies/ml. The lower limit for detection was 40 copies/ml. The predominant HIV clade was subtype C (76%). The majority of women were antiretroviral therapy naïve, with only 13 (15.5%) HIV-positive women on antiretroviral treatment.

Childhood trauma

The type of childhood trauma most frequently endorsed was emotional neglect ($M = 11.7$, $SD = 4.92$). Mean scores for the remaining four sub-scales were as follows: emotional abuse ($M = 10.2$, $SD = 5.73$), physical neglect ($M = 9.24$, $SD = 3.55$), physical abuse ($M = 8.20$, $SD = 5.09$), and sexual abuse ($M = 6.93$, $SD = 4.52$).

Analysis of Covariance (ANCOVA) of neurocognitive variables

Results revealed no HIV or childhood trauma effects on any of the other ability domains except the recall domain. A significant HIV effect was evident for the recall domain, which consists of the HVLT-R and BVMT-R delay recall trials ($F = 4.19$, $p < .05$). Univariate tests of significance using age and education as covariates were conducted on all NP raw data (Table 3). Significant HIV effects were evident for the following neurocognitive tests: HVLT-R [total learning] ($F = 7.16$, $p < .01$), HVLT-R [delay] ($F = 13.0$, $p < .01$), and the Halstead Category test ($F = 4.77$, $p < .05$). HIV-positive women scored lower on all three trials of immediate learning ($M = 23.18$, $SD = 4.28$) and delayed learning of the HVLT-R ($M = 8.11$, $SD = 1.85$) compared to HIV-negative women ($M = 25.40$, $SD = 3.97$; $M = 9.37$, $SD = 1.68$). Similarly, HIV-positive women had more errors on the Halstead Category Test ($M = 75.97$, $SD = 26.6$) compared to HIV-negative women ($M = 65.86$, $SD = 20.7$). A significant childhood trauma effect was evident on the HVLT-R [delay trial] ($F = 4.90$, $p < .05$). Women with a history of childhood trauma scored lower on the delay trial of the HVLT-R ($M = 8.37$) compared to women without a history of childhood trauma ($M = 9.11$). A significant interaction effect was evident of the WAIS-III Symbol Search task ($F = 5.00$, $p < .05$). There was however very little difference in mean scores between HIV-positive ($M = 18.75$, 7.81) and HIV-negative women ($M = 18.88$, $SD = 7.27$). Women with a history of childhood trauma performed better ($M = 20.21$, 7.97) than those without a history of childhood trauma ($M = 17.42$, 7.58).

Multiple Regression Analysis

Significant neurocognitive variables in the univariate tests were included (WAIS-III Symbol Search, HVLT-R, HVLT-R [delay trial] and the Halstead Category Test). Predictor variables included HIV status, age, education, CTQ total score, DTS total score, and the CES-D total score. The percentage of variance explained by the model for each neurocognitive variable is as follows: WAIS-III Symbol Search (29%), HVLT-R (14%), HVLT-R delay trial (17%), and Halstead category test (22%). See table 4.

Discussion

Although the present study did not find evidence for a combined effect of HIV and trauma, it does provide evidence for the separate effects of both HIV and trauma on neurocognitive outcomes and the importance of these findings should be explored in future studies aimed at teasing out the discriminating effects of early adversity by trauma type and the effects HIV by disease stage.

Significant HIV effects in learning and delayed memory, and executive functions were evident. Similarly, a trauma effect was evident in memory recall. HIV-positive women scored lower on all trials of the HVLT-R compared to HIV-negative women. The HVLT-R tests one's ability to learn and immediately recall verbal information, as well as the ability to retain, reproduce, and recognise this information after a delay. The finding that HIV influences memory is in keeping with previous studies. Memory disturbances in particular tend to be most prominent (Grant, 2008). HIV-related deficits in memory have been consistently reported in the both the developed world (Grant et al., 1987; Heaton et al., 1995; Heaton et al., 2011; Maki et al., 2009; Mason et al., 1998; Saykin et al., 1991; Tozzi et al., 2005) and the developing world (Cysique et al., 2007; Gupta et al., 2007; Kanmogne et al., 2010; Lawler et al., 2010; Robertson et al., 2007; Sacktor et al., 2006; Wong et al., 2004; Yephthomi et al., 2006). However, participant characteristics, methodological aspects, and instrumentation have varied widely among studies and women have been under-represented in these studies. The majority of all-female studies have been conducted in areas where clade B predominates. In South Africa, clade C predominates and whether the neurocognitive profile differs among the different strains of HIV is still largely under investigation. Moreover, antiretroviral (ARV) naïve samples have been rare. Of all the studies mentioned above, only two were all female case-control studies (Maki & Martin-Thormeyer, 2009; Maki et al., 2009; Mason et al., 1998). Three studies consisted of all male samples (Grant et al., 1987; Heaton et al., 1995; Saykin et al., 1991) and others consisted of more males than females (Cysique et al., 2007; Heaton et al., 2011; Tozzi et al., 2005; Yephthomi et al., 2006).

HIV-positive women had significantly more errors on the Halstead Category Test compared to HIV-negative women. The finding that HIV influences executive functions is in keeping with previous studies. HIV is highly neurovirulent and is frequently associated with deficits in higher order brain functions. Executive function disturbances are frequent among HIV patients (Grant, 2008). HIV-related deficits in executive functioning have been consistently reported in the both the developed world (Grant et al., 1987; Grant, 2008; Heaton et al., 2011; Richardson et al., 2002) and the developing world (Cysique et al., 2007; Kanmogne et al., 2010; Robertson et al., 2007; Sacktor et al., 2006; Yephthomi et al., 2006) but as previously mentioned, women have been under-represented in neurocognitive studies of HIV. Except for the present study, only two all-female studies to date have demonstrated impairments in abstraction using the Colour Trails Tests. However, these studies differed from the present study with regard to demographic and clinical characteristics. Women with a history of childhood trauma scored lower on the delay trial of the HVLT-R compared to women without a history of childhood trauma. The finding that trauma is associated with deficits in memory recall is in keeping with previous studies. Studies assessing stressful life

events, acute stress, and/or PTSD have found evidence for memory deficits (Clark et al., 2003; Jelinek et al., 2006; Lagarde et al., 2010; Yasik et al., 2007).

Memory deficits in individuals with PTSD have also been shown to be associated with small hippocampal volumes (Bremner et al., 1995; Bremner, 2006; Heim & Nemeroff, 2009). However, findings have been inconsistent and some studies have not found memory deficits in PTSD patients (Horner & Hamner, 2002; Isaac, Cushway, & Jones, 2006; Twamley, Hami, & Stein, 2004). A recent study examined brain morphometry in female victims of intimate partner violence (IPV) with and without PTSD. Results revealed smaller mesial temporal lobe gray matter volumes in IPV subjects, regardless of PTSD status. The gray matter abnormalities were associated with executive functioning and auditory working memory tasks (Fennema-Notestine, Stein, Kennedy, Archibald, & Jernigan, 2002). Although some studies assessing early life trauma did not find evidence for memory deficits (Jelicic et al., 2008), others did (Choi et al., 2009; Majer et al., 2010).

The results also revealed a significant interaction effect between HIV status and trauma status on the WAIS-III Symbol Search Task. However, there was very little difference in the mean scores between HIV-positive and HIV-negative women. Women with a history of childhood trauma performed better than those without a history of childhood trauma. Although impairments in psychomotor speed have been reported in the childhood trauma literature (Palmer et al., 1997), studies have also reported the contrary. The finding that HIV negative controls with a history of childhood trauma scored the highest on the WAIS-III Symbol Search Task, compared to all other groups, is indeed unexpected and inconsistent; however, they are in keeping with a recent study (Majer et al., 2010). One possible explanation for this unexpected finding is that psychomotor speed may not be a particularly sensitive or discriminating test of childhood trauma in healthy adults. The highest mean score on the CTQ was evident on the emotional neglect sub-scale ($M = 11.7$, $SD = 4.92$). Taking the socio-economic status of the sample into account, everyday living conditions apparent in peri-urban/township areas might be mistaken for, or regarded as, emotional neglect. This might account for the high scores on the emotional neglect subscale. It is plausible that this trauma type may not have influenced neurocognitive outcomes or that the influence may have been too subtle. The type and severity of childhood abuse may, therefore, play an important role in influencing neurocognitive outcomes and needs careful evaluation in future research. In a similar vein, HIV disease stage is also known to play a role (Heaton et al., 1995). The majority of the women in this sample were medically asymptomatic and ARV-naïve (83.3%).

Cross-sectional study designs preclude longer-term assessment of neurocognitive outcomes, future research should therefore be prospective in nature and should better delineate the nature, severity, and temporal relationship of childhood trauma to neurocognitive outcomes, as well as the mediators and moderators of these outcomes.

Acknowledgements

This research was supported by the South African Research Chairs Initiative of the Department of Science and Technology and National Research Foundation, Centers for AIDS Research and Claude Leon Foundation. Professor Kidd provided statistical assistance and Nonkuthalo Ludwaba recruited participants.

References

- Andersson N, Cockcroft A, Shea B. Gender-based violence and HIV: Relevance for HIV prevention in hyperendemic countries of southern africa. *AIDS*. 2008; 22(Suppl. 4):73–86.
- Antinori A, Arendt G, Becker JT, Brew BJ, Byrd DA, Cherner M, et al. Updated research nosology for HIV-associated neurocognitive disorders. *Neurology*. 2007; 69(18):1789–1799. [PubMed: 17914061]
- Bernstein DP, Stein JA, Newcomb MD, Walker E, Pogge D, Ahluvalia T, et al. Development and validation of a brief screening version of the childhood trauma questionnaire. *Child Abuse & Neglect*. 2003; 27(2):169–190. [PubMed: 12615092]
- Bremner JD. The relationship between cognitive and brain changes in posttraumatic stress disorder. *Annals of the New York Academy of Sciences*. 2006; 1071:80–86. [PubMed: 16891564]
- Bremner JD, Randall P, Scott TM, Bronen RA, Seibyl JP, Southwick SM, et al. MRI-based measurement of hippocampal volume in patients with combat-related posttraumatic stress disorder. *The American Journal of Psychiatry*. 1995; 152(7):973–981. [PubMed: 7793467]
- Centers for Disease Control and Prevention. Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. 1993. Retrieved February, 18, 2011, from <http://www.cdc.gov/mmwr/preview/mmwrhtml/00018871.htm>
- Choi J, Jeong B, Rohan ML, Polcari AM, Teicher MH. Preliminary evidence for white matter tract abnormalities in young adults exposed to parental verbal abuse. *Biological Psychiatry*. 2009; 65(3):227–234. [PubMed: 18692174]
- Clark CR, McFarlane AC, Morris P, Weber DL, Sonkilla C, Shaw M, et al. Cerebral function in posttraumatic stress disorder during verbal working memory updating: A positron emission tomography study. *Biological Psychiatry*. 2003; 53(6):474–481. [PubMed: 12644352]
- Cysique LA, Jin H, Franklin DR Jr, Morgan EE, Shi C, Yu X, et al. Neurobehavioral effects of HIV-1 infection in china and the united states: A pilot study. *Journal of the International Neuropsychological Society*. 2007; 13(5):781–790. [PubMed: 17697409]
- Davidson JRT, Book SW, Colket JT, Tupler LA, Roth S, David D, et al. Assessment of a new self-rating scale for post-traumatic stress disorder. *Psychological Medicine*. 1997; 27(01):153–160. [PubMed: 9122295]
- Dunkle KL, Jewkes RK, Brown HC, Yoshihama M, Gray GE, McIntyre JA, et al. Prevalence and patterns of gender-based violence and revictimization among women attending antenatal clinics in soweto, south africa. *American Journal of Epidemiology*. 2004; 160(3):230–239. [PubMed: 15257996]
- Fennema-Notestine C, Stein MB, Kennedy CM, Archibald SL, Jernigan TL. Brain morphometry in female victims of intimate partner violence with and without posttraumatic stress disorder. *Biological Psychiatry*. 2002; 52(11):1089–1101. [PubMed: 12460692]
- Grant I. Neurocognitive disturbances in HIV. *International Review of Psychiatry*. 2008; 20(1):33–47. [PubMed: 18240061]
- Grant I, Atkinson JH, Hesselink JR, Kennedy CJ, Richman DD, Spector SA, et al. Evidence for early central nervous system involvement in the acquired immunodeficiency syndrome (AIDS) and other human immunodeficiency virus (HIV) infections. *Annals of Internal Medicine*. 1987; 107(6):828–836. [PubMed: 3688675]
- Gupta JD, Satishchandra P, Gopukumar K, Wilkie F, Waldrop-Valverde D, Ellis R, et al. Neuropsychological deficits in human immunodeficiency virus type 1 clade C-seropositive adults from south india. *Journal of Neurovirology*. 2007; 13(3):195–202. [PubMed: 17613709]
- Heaton RK, Clifford DB, Franklin DR Jr, Woods SP, Ake C, Vaida F, et al. HIV-associated neurocognitive disorders persist in the era of potent antiretroviral therapy: CHARTER study. *Neurology*. 2010; 75(23):2087–2096. [PubMed: 21135382]
- Heaton RK, Franklin DR, Ellis RJ, McCutchan JA, Letendre SL, Leblanc S, et al. HIV-associated neurocognitive disorders before and during the era of combination antiretroviral therapy: Differences in rates, nature, and predictors. *Journal of Neurovirology*. 2011; 17(1):3–16. [PubMed: 21174240]

- Heaton RK, Grant I, Butters N, White DA, Kirson D, Atkinson JH, et al. The HNRC 500--neuropsychology of HIV infection at different disease stages. HIV neurobehavioral research center. *Journal of the International Neuropsychological Society*. 1995; 1(3):231–251. [PubMed: 9375218]
- Heim C, Nemeroff CB. Neurobiology of posttraumatic stress disorder. *CNS Spectrums*. 2009; 14(Suppl. 1):13–24. [PubMed: 19169190]
- Horner MD, Hamner MB. Neurocognitive functioning in posttraumatic stress disorder. *Neuropsychology Review*. 2002; 12(1):15–30. [PubMed: 12090717]
- Isaac CL, Cushway D, Jones GV. Is posttraumatic stress disorder associated with specific deficits in episodic memory? *Clinical Psychology Review*. 2006; 26(8):939–955. [PubMed: 16481082]
- Jelicic M, Geraerts E, Merckelbach H. No evidence for verbal learning impairments in women with a history of childhood abuse. *Psychiatry Research*. 2008; 157(1-3):299–302. [PubMed: 17935794]
- Jelinek L, Jacobsen D, Kellner M, Larbig F, Biesold KH, Barre K, et al. Verbal and nonverbal memory functioning in posttraumatic stress disorder (PTSD). *Journal of Clinical and Experimental Neuropsychology*. 2006; 28(6):940–948. [PubMed: 16822734]
- Jewkes R, Penn-Kekana L, Levin J, Ratsaka M, Schriber M. Prevalence of emotional, physical and sexual abuse of women in three south african provinces. *South African Medical Journal*. 2001; 91(5):421–428. [PubMed: 11455808]
- Jewkes RK, Dunkle K, Nduna M, Jama PN, Puren A. Associations between childhood adversity and depression, substance abuse and HIV and HSV2 incident infections in rural south african youth. *Child Abuse & Neglect*. 2010; 34(11):833–841. [PubMed: 20943270]
- Jewkes R, Levin J, Mbananga N, Bradshaw D. Rape of girls in south africa. *The Lancet*. 2002; 359(9303):319–320.
- Joska J, Fincham D, Stein D, Paul R, Seedat S. Clinical correlates of HIV-associated neurocognitive disorders in south africa. *AIDS and Behavior*. 2010; 14(2):371–378. [PubMed: 19326205]
- Joska JA, Westgarth-Taylor J, Myer L, Hoare J, Thomas KG, Combrinck M, et al. Characterization of HIV-associated neurocognitive disorders among individuals starting antiretroviral therapy in south africa. *AIDS and Behavior*. 2010 10.1007/s10461-010-9744-6.
- Kalichman SC, Simbayi LC. Sexual assault history and risks for sexually transmitted infections among women in an african township in cape town, south africa. *AIDS Care*. 2004; 16(6):681–689. [PubMed: 15370057]
- Kanmogne G, Kuete C, Cysique L, Fonsah J, Eta S, Doh R, et al. HIV-associated neurocognitive disorders in sub-saharan africa: A pilot study in cameroon. *BMC Neurology*. 2010; 10(1):60–70. [PubMed: 20626870]
- Lagarde G, Doyon J, Brunet A. Memory and executive dysfunctions associated with acute posttraumatic stress disorder. *Psychiatry Research*. 2010; 177(1-2):144–149. [PubMed: 20381880]
- Lawler K, Mosepele M, Ratcliffe S, Seloilwe E, Steele K, Nthobatsang R, et al. Neurocognitive impairment among HIV-positive individuals in botswana: A pilot study. *Journal of the International AIDS Society*. 2010; 13:15–23. [PubMed: 20406460]
- Leserman J, Pence B, Whetten K, Mugavero M, Thielman N, Swartz M, et al. Relation of lifetime trauma and depressive symptoms to mortality in HIV. *The American Journal of Psychiatry*. 2007; 164(11):1707–1713. [PubMed: 17974936]
- Leserman J, Whetten K, Lowe K, Stangl D, Swartz MS, Thielman NM. How trauma, recent stressful events, and PTSD affect functional health status and health utilization in HIV-infected patients in the south. *Psychosomatic Medicine*. 2005; 67(3):500–507. [PubMed: 15911916]
- Majer M, Nater UM, Lin JM, Capuron L, Reeves WC. Association of childhood trauma with cognitive function in healthy adults: A pilot study. *BMC Neurology*. 2010; 10:61–70. [PubMed: 20630071]
- Maki PM, Cohen MH, Weber K, Little DM, Fornelli D, Rubin LH, et al. Impairments in memory and hippocampal function in HIV-positive vs HIV-negative women: A preliminary study. *Neurology*. 2009; 72(19):1661–1668. [PubMed: 19433739]
- Maki PM, Martin-Thormeyer E. HIV, cognition and women. *Neuropsychology Review*. 2009; 19(2):204–214. [PubMed: 19430907]

- Mason KI, Campbell A, Hawkins P, Madhere S, Johnson K, Takushi-Chinen R. Neuropsychological functioning in HIV-positive african-american women with a history of drug use. *Journal of the National Medical Association*. 1998; 90(11):665–674. [PubMed: 9828581]
- Palmer LK, Armsworth M, Swank PR, Bush G, Frantz C, Copley J. The neuropsychological sequelae of chronically psychologically traumatized children. *Archives of Clinical Neuropsychology*. 1997; 12(4):379–380.
- Radloff SF. The CES-D scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement*. 1977; 1(3):385–401.
- Richardson JL, Martin EM, Jimenez N, Danley K, Cohen M, Carson VL, et al. Neuropsychological functioning in a cohort of HIV infected women: Importance of antiretroviral therapy. *Journal of the International Neuropsychological Society : JINS*. 2002; 8(6):781–793. [PubMed: 12240742]
- Robertson K, Liner J, Heaton R. Neuropsychological assessment of HIV-infected populations in international settings. *Neuropsychology Review*. 2009; 19(2):232–249. [PubMed: 19455425]
- Robertson KR, Nakasujja N, Wong M, Musisi S, Katabira E, Parsons TD, et al. Pattern of neuropsychological performance among HIV positive patients in uganda. *BMC Neurology*. 2007; 7:8–14. [PubMed: 17411437]
- Sacktor N. The epidemiology of human immunodeficiency virus-associated neurological disease in the era of highly active antiretroviral therapy. *Journal of Neurovirology*. 2002; 8(Suppl 2):115–121. [PubMed: 12491162]
- Sacktor NF, Nakasujja NF, Skolasky RF, Robertson KF, Wong MF, Musisi SF, et al. Antiretroviral therapy improves cognitive impairment in HIV+ individuals in sub-saharan africa. *Neurology*. 2006; 67(2):311–314. [PubMed: 16864825]
- Saigh PA, Yasik AE, Oberfield RA, Halamandaris PV, Bremner JD. The intellectual performance of traumatized children and adolescents with or without posttraumatic stress disorder. *Journal of Abnormal Psychology*. 2006; 115(2):332–340. [PubMed: 16737397]
- Saykin AJ, Janssen RS, Sprehn GC, Kaplan JE, Spira TJ, O'Connor B. Longitudinal evaluation of neuropsychological function in homosexual men with HIV infection: 18-month follow-up. *The Journal of Neuropsychiatry and Clinical Neurosciences*. 1991; 3(3):286–298. [PubMed: 1821245]
- Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, et al. The mini-international neuropsychiatric interview (M.I.N.I.): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *The Journal of Clinical Psychiatry*. 1998; 59(Suppl. 20):22–33. [PubMed: 9881538]
- Tozzi V, Balestra P, Lorenzini P, Bellagamba R, Galgani S, Corpolongo A, et al. Prevalence and risk factors for human immunodeficiency virus-associated neurocognitive impairment, 1996 to 2002: Results from an urban observational cohort. *Journal of Neurovirology*. 2005; 11(3):265–273. [PubMed: 16036806]
- Twamley EW, Hami S, Stein MB. Neuropsychological function in college students with and without posttraumatic stress disorder. *Psychiatry Research*. 2004; 126(3):265–274. [PubMed: 15157752]
- UNAIDS. Worldwide HIV & AIDS statistics. 2010. Retrieved February 03, 2011, from <http://www.avert.org/worldstats.htm>
- Walton G, Co SJ, Milloy MJ, Qi J, Kerr T, Wood E. High prevalence of childhood emotional, physical and sexual trauma among a canadian cohort of HIV-seropositive illicit drug users. *AIDS Care*. 2011 10.1080/09540121.2010.525618.
- Wong M, Robertson K, Nakasujja N, Musisi S, Katabira E, McArthur J, et al. HIV-associated neurological complications among HIV-seropositive individuals in uganda. *Neurology*. 2004; 62(7):A444.
- Woods SP, Moore DJ, Weber E, Grant I. Cognitive neuropsychology of HIV-associated neurocognitive disorders. *Neuropsychology Review*. 2009; 19(2):152–168. [PubMed: 19462243]
- Yasik AE, Saigh PA, Oberfield RA, Halamandaris PV. Posttraumatic stress disorder: Memory and learning performance in children and adolescents. *Biological Psychiatry*. 2007; 61(3):382–388. [PubMed: 16920073]
- Yepthomi T, Paul R, Vallabhaneni S, Kumarasamy N, Tate DF, Solomon S, et al. Neurocognitive consequences of HIV in southern india: A preliminary study of clade C virus. *Journal of the International Neuropsychological Society*. 2006; 12(3):424–430. [PubMed: 16903135]

Table 1**HNRC Neuropsychological Testing Battery**

Neuropsychological domain	Neuropsychological test
Speed of Information Processing	WAIS-III Digit Symbol WAIS-III Symbol Search Trail Making Test Part A
Attention/Working Memory	Paced Auditory Serial Addition Test WMS-III Spatial Span
Abstraction/Executive Functioning	Wisconsin Card Sorting Test - computer version Color Trails 1 and 2 Stroop Color Word Test Halstead Category Test – computer version
Learning and Delayed Recall (2 domains)	Hopkins Verbal Learning Test, Revised Brief Visuospatial Memory Test, Revised
Language	Controlled Oral Word Association Test (FAS) Category Fluency (Animals, Action)
Motor	Grooved Pegboard Test (both hands)
Screening for effort	Hiscock Digit Memory Test

Table 2

Demographic and clinical characteristics of the cohort (N = 130)

		N	f	%	M	SD	Range
Participants		130		100			
	HIV-positive		83	64			
	HIV-positive with trauma		48	37			
	HIV-negative		47	36			
	HIV-negative with trauma		20	15			
Gender	Female	130		100			
Age (years)		130		100	29.6	7.0	18-50
Ethnicity		130		100			
	Black		125	96			
	Coloured		5	4			
Home language		130					
	Xhosa		115	88			
	Afrikaans		6	5			
	English		4	3			
	Other		5	4			
Handedness		130					
	Right		121	93			
	Left		9	7			
Marital status		130					
	Single		93	71			
	Married		26	19.8			
	Cohabiting		3	2.3			
	Separated		4	3.1			
	Divorced		3	2.3			
	Widowed		1	0.8			
Education		130			10.7	1.2	7-14
	Grade 8		7	5			
	> Grade 8		123	95			
	Attended high school but did not complete		94	71			
	Completed high school		31	24			
	Tertiary education		4	4			
Employment		130		100			
	Employed		46	35			

		N	f	%	M	SD	Range
	Unemployed		84	65			
Breadwinner		130		100			
	Yes		51	39			
	No		79	61			
Annual household income (South African Rand)		130		100			
	< R10 000		103	79			
	R10 000 – R20 000		21	16			
	R20 000 – R40 000		1	1			
	R40 000 – R60 000		2	2			
	R60 000 – R100 000		1	1			
	> R100 000		2	2			
CD4 lymphocyte count		83		64	405	259.8	35-1529
	< 200 cells/mm ³		18	13.8			
	> 200 cells/mm ³		65	50.2			
Viral load		83		64	105169.5	407459.5	Below the detectable limit - 3,200 000 cells/mm ³
	Below the detectable limit		6	4.6			
HIV Clade		83		64			
	Clade C		64	76			
	Negative		15	18			
	No sequence		1	1.2			
	Possible recombinant sequence		3	3.6			
Antiretroviral treatment							
	Yes		13	15.5			
	No		70	83.3			

Table 3

Analysis of covariance (N = 130)

Dependent variables	HIV		Childhood Trauma		HIV*Childhood trauma	
	F	p	F	P	F	p
Pegs (dominant hand)	0.45	<i>ns</i>	0.18	<i>ns</i>	2.04	<i>ns</i>
Pegs (non-dominant hand)	0.42	<i>ns</i>	0.33	<i>ns</i>	1.79	<i>ns</i>
COWAT (FAS)	0.95	<i>ns</i>	3.49	<i>ns</i>	0.03	<i>ns</i>
Category Fluency (Animals)	0.60	<i>ns</i>	0.79	<i>ns</i>	0.03	<i>ns</i>
Category Fluency (Actions)	0.03	<i>ns</i>	0.96	<i>ns</i>	0.62	<i>ns</i>
PASAT	0.04	<i>ns</i>	1.73	<i>ns</i>	0.01	<i>ns</i>
Trails A	0.02	<i>ns</i>	0.73	<i>ns</i>	0.09	<i>ns</i>
Color Trails 1	0.45	<i>ns</i>	0.04	<i>ns</i>	0.01	<i>ns</i>
Color Trails 2	0.03	<i>ns</i>	0.27	<i>ns</i>	0.09	<i>ns</i>
Digit Symbol	0.12	<i>ns</i>	3.38	<i>ns</i>	0.22	<i>ns</i>
Symbol Search	0.01	<i>ns</i>	5.04	<i>ns</i>	5.00	< .05
Spatial Span	0.50	<i>ns</i>	2.46	<i>ns</i>	1.00	<i>ns</i>
BVMT-R	0.02	<i>ns</i>	0.91	<i>ns</i>	0.18	<i>ns</i>
BVMT-R (delay)	1.08	<i>ns</i>	0.99	<i>ns</i>	0.57	<i>ns</i>
HVLT-R	7.16	< .01	0.33	<i>ns</i>	0.68	<i>ns</i>
HVLT-R (delay)	13.0	< .01	4.90	< .05	0.99	<i>ns</i>
HCT	4.77	< .05	0.18	<i>ns</i>	0.79	<i>ns</i>
WCST	0.15	<i>ns</i>	0.75	<i>ns</i>	0.84	<i>ns</i>
Stroop Word	0.14	<i>ns</i>	2.27	<i>ns</i>	0.13	<i>ns</i>
Stroop Color Naming	0.00	<i>ns</i>	0.05	<i>ns</i>	0.01	<i>ns</i>
Stroop Color Word	1.04	<i>ns</i>	1.57	<i>ns</i>	0.51	<i>ns</i>

ns = not statistically significant

Table 4

Summary of Multiple Regression Analysis (N = 130)

DV	Predictor	R ²	Adj. R ²	β	p
WAIS-III Symbol Search		0.29	0.25		< .01
	HIV Status			0.27	<i>ns</i>
	Age			−0.41	< .01
	Education			1.95	< .01
	CTQ			0.04	<i>ns</i>
	DTS			−0.02	<i>ns</i>
	CES-D			−0.02	<i>ns</i>
HVL-T-R		0.15	0.11		< .01
	HIV Status			−2.36	< .01
	Age			−0.01	<i>ns</i>
	Education			0.85	< .01
	CTQ			−0.01	<i>ns</i>
	DTS			−0.01	<i>ns</i>
	CES-D			0.04	<i>ns</i>
HVL-T-R (Delay)		0.17	0.13		< .01
	HIV Status			−1.32	< .01
	Age			0.01	<i>ns</i>
	Education			0.32	< .05
	CTQ			−0.01	<i>ns</i>
	DTS			0.00	<i>ns</i>
	CES-D			0.01	<i>ns</i>
HCT		0.22	0.18		< .01
	HIV Status			10.4	< .05
	Age			−0.09	<i>ns</i>
	Education			−7.85	< .01
	CTQ			0.08	<i>ns</i>
	DTS			0.00	<i>ns</i>
	CES-D			−0.06	<i>ns</i>

ns = not statistically significant

Table 5

Demographic and Clinical Characteristics of the HIV & Trauma Groups

Variable		HIV-positive without childhood trauma (n = 35)	HIV-positive with childhood trauma (n = 48)	HIV-negative without childhood trauma (n = 27)	HIV-negative with childhood trauma (n = 20)
Mean age (SD)		31.5 (6.03)	31.7 (6.85)	25.0 (5.72)	27.7 (7.72)
Mean Education (SD)		10.6 (1.26)	10.5 (1.23)	11.4 (0.93)	10.6 (1.34)
Mean CD4 count		684	601	N.A.	N.A.
Mean Viral load		40425	528046	N.A.	N.A.
HIV Subtype C (N)		25	39	N.A.	N.A.
On ART (N)		9	4	N.A.	N.A.
Handedness (N)	Left	2	2	3	2
	Right	33	46	24	18
Ethnicity (N)	Black	33	47	25	20
	Coloured	2	1	2	0
Marital status (N)	Single	23	32	23	15
	Married	9	8	4	5
Home language (N)	Xhosa	32	42	24	17
	Afrikaans	2	2	2	0
	English	1	3	0	0
Employed (N)		20	32	18	14
Breadwinner (N)		16	23	6	6
Annual household income (N)		< R10 000	25	38	21
				19	

N.A = Not Applicable