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# Changes in cognitive function in women with HIV infection and early life stress

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## Abstract

**Introduction—**HIV is frequently associated with deficits in brain function, including memory, psychomotor speed, executive function, and attention. Early life stress (ELS) has also been shown to have a direct influence on neurocognitive performance. However, little is known about the combined impact of ELS and HIV on neurocognitive function over time. The aim of the present study was to follow a cohort of affected women, allowing us to assess the effects of HIV and childhood trauma on cognition and the change in cognition over time.

**Method—**A battery of neurocognitive tests was administered to 117 women at baseline and then a year later. The sample included a total of 67 $HIV^+$ and 50 $HIV^-$ women, 71 with ELS and 46 without ELS. Controlling for age, education and antiretroviral therapy (ART) at baseline and 12-month follow-up, raw scores were compared across groups using a repeated measures Analysis of Covariance (ANCOVA).

**Results—**More women were on ART at follow-up compared to baseline. Results revealed a significant combined HIV and childhood trauma effect over time on the Wisconsin Card Sorting Test ($p = 0.003$) and Category Fluency Test ($p = 0.006$). A significant individual HIV effect over time was evident on the WAIS-III Digit Symbol Test ($p = 0.03$) and the Controlled Oral Word Association Test ($p = 0.003$).

**Conclusion—**Findings suggest better performance in abstract reasoning, speed of information processing and verbal fluency over time. While all groups showed improvements that may correspond to practice effects, effects of HIV and childhood trauma remained evident at 12-month follow-up despite greater ART uptake and improved HIV disease status. This is the first study to assess the combined impact of HIV and trauma on neurocognitive function over time in an all-female cohort with more advanced disease.

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We have no conflict of interest to declare.

## Introduction

Sub-Saharan Africa has one of the most serious human immunodeficiency virus (HIV) epidemics in the world. An estimated 5.51 million South Africans infected with the virus in 2014 (Statistics South Africa, 2014). Women tend to be particularly affected by the epidemic and many of these infected women also have developmental trajectories characterised by trauma. High rates of intimate partner violence, rape, and childhood abuse have been reported (Andersson, Cockcroft, & Shea, 2008; Jewkes, Penn-Kekana, Levin, Ratsaka, & Schrieber, 2001; Jewkes, Levin, Mbananga, & Bradshaw, 2002; Kalichman & Simbayi, 2004). Such trauma has been associated with poor neurocognitive functioning and other neurologic and psychiatric sequelae (Malan-Muller et al., 2013; Spies et al., 2012; Spies, Fennema-Notestine, Archibald, Cherner, & Seedat, 2012; Troeman et al., 2011), and may exacerbate HIV-related deficits.

HIV infected individuals commonly have neurocognitive deficits characterised as HIV-associated neurocognitive disorders (HAND), ranging from mild to severe, and related to disease staging (Antinori et al., 2007; Grant, 2008). Disturbances with attention, memory, psychomotor speed and executive function are common (Grant, 2008). Due to increased access to and use of ART, $HIV^+$individuals are living longer lives, making it imperative to understand etiological factors associated with neurocognitive disorders in order to prevent and treat these disorders. In a recent cross-sectional study assessing a cohort of 1019 HIV-infected women, HIV was found to have an effect on cognition, although the effect was small (Maki et al., 2015). Reading level, age, years of education, and race were more strongly associated with cognitive performance than HIV status. HIV-infected women with low education, low CD4 counts, high viral load, or an AIDS-defining illness were more vulnerable to cognitive impairments, suggesting that low cognitive reserve might exacerbate deficits in cognition in $HIV^+$ individuals (Maki et al., 2015).

Although studies have been limited and inconsistent, impairments in intellectual development, language, verbal learning, spatial working memory and psychomotor speed have also been reported in individuals exposed to childhood trauma (Choi, Jeong, Rohan, Polcari, & Teicher, 2009; Majer, Nater, Lin, Capuron, & Reeves, 2010; Palmer et al., 1997). Women infected with HIV who also have a history of childhood trauma may be especially vulnerable to neurocognitive impairments secondary to the additive or interaction effects of HIV and childhood trauma. Prior studies have documented 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 posttraumatic stress disorder (Leserman et al., 2007; Leserman et al., 2005). In a previous cross-sectional study investigating the additive effects of HIV and childhood trauma on neurocognitive function in a cohort of South African women, we reported HIV effects in learning, delayed memory and executive function. Additionally, we reported a distinct trauma effect on memory recall (Spies et al., 2012).

The individual effects of HIV and trauma on neurocognition have therefore been documented. However, to our knowledge, there are currently no published studies investigating the additive effects of HIV and childhood trauma on neurocognitive function over time. The aim of the present study was to follow a cohort of affected women after one

year, allowing us to assess change in cognition over time. Given the HIV and trauma effects previously reported (Spies et al., 2012), $HIV^+$ women with developmental trajectories characterised by trauma may be especially vulnerable to neurocognitive dysfunction. Our hypothesis was two-fold. Firstly, we hypothesised that the effects of HIV and childhood trauma would remain evident at follow-up (i.e. that poorer neurocognitive functioning would be evident over time across groups). Secondly, we hypothesised that the HIV-infected women with a history of trauma would be most affected.

## Method

### Participants

The sample consisted of 67 (51.9%) $HIV^+$ and 50 (38.8%) $HIV^-$ women (Table 2). Fifty three $HIV^+$ women and 18 controls were exposed to childhood trauma (Table 2). Eligibility criteria included: willingness and ability to provide written informed consent, ability to read and write in English, Afrikaans, or isiXhosa 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, current seizure disorders of any cause, history of CNS infections of neoplasms, hepatitis B or C 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 Stellenbosch University, South Africa (ethics reference number: N07/07/153). All women included in the present study were tested for HIV status at their local health care facility or at the study site, with HIV status confirmed by means of ELISA. Participants were recruited directly from the community or through community health care facilities such as voluntary counselling and testing (VCT) sites and HIV units, in and around the Cape metropole of South Africa from 2008–2015 by a research nurse and assistant or with the help of doctors and adherence counsellors. Recruitment procedures did not differ across groups. All participants who consented were screened for eligibility, including childhood trauma exposure, either in person at their clinic or telephonically. Those who met initial screening criteria subsequently came to the Department of Psychiatry at Stellenbosch University and underwent neuromedical, neuropsychiatric, neurocognitive, and neuroimaging assessments at baseline and at 12 month follow-up. Participants were reimbursed for travel costs to and from assessments and provided with refreshments at each visit to the University.

### Measures

**Demographic and clinical characteristics—**Important demographic details such as age, marital status, ethnicity, years of education and employment status were captured. A general physical examination (which included comprehensive history taking) was conducted on all participants. Virologic markers of disease progression (CD4 lymphocyte count and viral loads) were obtained from blood samples.

### Childhood trauma

A history of childhood trauma was established using the Childhood Trauma Questionnaire Short Form (CTQ-SF), a 28-item self-report inventory that provides valid screening for histories of abuse and neglect (Bernstein et al., 2003). The CTQ-SF 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). The internal consistency of the CTQ-SF in the current sample was high, with a Cronbach alpha coefficient of 0.879 respectively.

### Neurocognitive assessment

Neurocognitive function was assessed using a comprehensive neuropsychological battery consisting of tests that have been used commonly in HIV research and cover seven ability domains (learning, delayed recall, processing speed, attention/working memory, executive function, verbal fluency, motor ability) (Heaton, Cysique et al., 2010) (Table 1). The battery was administered by a trained research psychologist and research nurse. Test instructions and stimuli were adapted as necessary to fit the cultural context of South Africa and translated into Afrikaans and isiXhosa using standard test adaptation techniques. This involved forward and back translations in the relevant languages. Appropriate cultural modifications were made to the Hopkins Verbal Learning Test-Revised (HVLT-R) and the Controlled Oral Word Association Task (COWAT). For the HVLT-R, the precious stone semantic category was replaced with vegetables. The category of precious stones included emerald, sapphire, opal and pearl, which are unfamiliar in the South African context. These words were replaced with vegetables (bean, lettuce, potato and corn). For the COWAT, letters used were FAS for English, LBS for Afrikaans and IBS for isiXhosa. Tests were administered in English, Afrikaans or isiXhosa according to the participants' self-report of home language. We have previously reported group differences using this test battery (Spies et al., 2012).

### Data analysis

All data were analysed using SPSS for Windows (version 22) and Statistica (version 12). Descriptive statistics were computed for all demographic and clinical information. We used analysis of variance (ANOVA) to assess group differences in age, education, and virologic markers of disease progression. We used Pearson Chi-Square tests to assess group differences on categorical variables such as handedness. Unadjusted neurocognitive raw scores were analysed by means of a mixed model repeated measures ANCOVA. Age, education, HIV, ART status, childhood trauma and time were included as fixed effects and subjects were treated as random effects.Posthoc corrections were applied to correct for multiple comparisons using the Least Significant Difference (LSD) test.

## Results

### Demographic characteristics

At baseline (Table 2), the mean age of participants was 32.8 years (minimum of 18 years, maximum of 50 years). The mean level of education was 10.3 years (minimum of 5 years, maximum of 14 years). The groups significantly differed in age and education, with $HIV^-$ participants younger and more educated than $HIV^+$ counterparts; thus we controlled for age and education in our statistical analyses. All the women self-identified as Black African and the majority were Xhosa speaking (97.4%), and right handed (95.7%). Further demographic details are presented in table 2 (baseline) and 3 (follow-up).

### Clinical characteristics

Clinical characteristics are presented in Table 2 (baseline) and 3 (follow-up). Of the $HIV^+$ women, 46 (68.7%) reported being on antiretroviral treatment (ART) at baseline. By follow-up, more women had initiated ART, with 54 (80.5%) of $HIV^+$ women reporting the use of ART. More HIV+ women with histories of childhood trauma were on ART at follow-up ($n$ = 46) compared to baseline ($n$ = 39). There were no significant group differences with respect to clinical variables such as CD4 lymphocyte count and viral load.

### Childhood Trauma

Seventy one participants reported a history of childhood trauma and 46 reported none (Table 4). There were no differences in trauma scores between baseline and follow-up. The overall mean score on the CTQ-SF was 53.58 (SD = 22.89) with a minimum of 25 and a maximum of 114. The most commonly reported childhood trauma type was emotional abuse with a mean of 12.88 (SD = 6.33), followed by emotional neglect (M= 11.58; SD = 6.17), physical neglect (M= 10.92; SD = 5.16), physical abuse (M= 10.46; SD = 7.17) and lastly, sexual abuse (M= 7.72; SD = 5.35).

### Neurocognitive functioning

Mean scores for all tasks at baseline (with the exception of Color Trails 1 and PASAT) and at follow-up (with the exception of WCST and Halstead Category Test) suggest poorer performance in the dually affected group ($HIV^+$ $trauma^+$) compared to all other groups (see Table 4).

Results revealed significant HIV effects over time on the WAIS-III Digit Symbol Test (F = 5.00, $p$ = 0.027) and the Controlled Oral Word Association Test [COWAT] (F = 9.35, $p$ = 0.003). $HIV^+$ women ($N$ = 67) showed improvement in scores at follow-up compared to baseline on the WAIS-III Digit Symbol Test and COWAT. However, compared to all $HIV^-$ women ($N$ = 50), $HIV^+$ women still performed worse at follow-up.

A combined HIV and childhood trauma effect (interaction) over time was evident on the Category Fluency Test [Actions] (F = 7.83, $p$ = 0.006) and the Wisconsin Card Sorting Test [WCST] (F = 8.08, $p$ = 0.003). The $HIV^+$ $trauma^+$ group ($n$ = 53) showed improvement in scores at follow-up compared to baseline on the Category Fluency Test and WCST. However, at follow-up, the $HIV^+$ $trauma^+$ group ($n$ = 53) still performed worse than the

HIV$^+$ trauma$^-$group ($n$ = 14).The HIV$^-$ trauma$^+$ group performed worse compared to the HIV$^-$ trauma$^-$ group on the Category Fluency Test at baseline and follow-up and on the WCST at follow-up (see Table 4).

In the unadjusted analyses, being on antiretroviral treatment (ART) at baseline was significantly correlated with scores on the WAIS-III Digit Symbol at baseline ($r$ = 0.328, $p$ = 0.000). Similarly, being on ART at follow-up was significantly correlated with scores on the WAIS-III Digit Symbol at follow-up ($r$ = 0.407, $p$ = 0.000) and the COWAT at follow-up ($r$ = 0.237, $p$ = 0.01). Being on ART was associated with better performance on the abovementioned measures. However, being on ART was not significantly correlated with scores on the Category Fluency Test or the WCST at baseline or at follow-up ($p$ > 0.05). Being on ART treatment at baseline did not show up significant for any of the above-mentioned tasks when included in the repeated measures ANCOVA ($p$ > 0.05).

## Discussion

At both baseline and follow-up, mean scores for most tasks suggest poorer performance in the dually affected group (HIV$^+$ trauma$^+$) compared to all other groups, a finding in support of the second hypothesis of the study. Several factors have been implicated in the increased risk for neurocognitive disorders in HIV$^+$ individuals, such as medical and psychosocial comorbidities like hepatitis C infection and substance abuse (Martin-Thormeyer & Paul, 2009). Early life stress (ELS) is another psychosocial factor which may be associated with increased risk for neurocognitive decline in HIV$^+$ individuals, yet it has received little attention. The findings of the present study may suggest that HIV-related abnormalities in neurocognitive functioning may be partially attributable to, or even compounded by, the effects associated with experiencing trauma in childhood.

We found individual HIV effects on a test of processing speed (WAIS-III Digit Symbol) and phonemic verbal fluency (COWAT)and a combined HIV and childhood trauma effect on tests of semantic verbal fluency (Category Fluency Test) and abstract reasoning (WCST).Together, these HIV effects on aspects of processing speed and executive function are in line with current literature (Grant, 2008; Grant, 2008; Heaton, Cysique et al., 2010; Heaton et al., 2011; Heaton et al., 2011).

For the individual HIV effects detected, all HIV$^+$ women (regardless of trauma status) performed slightly better at the 12 month follow-up compared to baseline. However, in comparison to all HIV$^-$ controls (regardless of trauma status), HIV$^+$ women had lower scores at follow-up compared to baseline for both tests. Impairments in brain function are common in HIV$^+$ individuals, including problems with information processing speed (Grant, 2008). It is widely recognised that slowing is one of the most common cognitive problems in individuals infected with HIV (Hardy & Hinkin, 2002). These impairments tend to worsen with increasing disease severity (Centers for Disease Control and Prevention, 1993; Heaton et al., 1995; Heaton et al., 2010). Evidence also suggests that milder forms of cognitive impairment persist, even among those receiving combined antiretroviral therapies (Heaton et al., 2010; Heaton et al., 2011). In the HIV$^+$ group as a whole, there was a slight increase in mean scores on the WAIS-III Digit Symbol and COWAT from baseline to follow-up. At

follow-up, this group had higher mean CD4 counts and lower mean viral loads in line with more individuals being on ART. This immune recovery and viral control may be associated with the better performance evident at follow-up, since being on ART at baseline and at follow-up was associated with better performance on the processing task (WAIS-III Digit Symbol) and with better performance on the verbal fluency task (COWAT) at follow-up, although causality cannot be inferred directly. Consistent with previous research, the $HIV^+$ women continued to perform more poorly relative to controls over time, confirming a continued effect of HIV infection on cognitive function.

For the combined HIV and trauma effect on verbal fluency (Category Fluency Test), $HIV^+$ women with histories of childhood trauma (i.e. dually affected women) performed slightly better at the 12 month follow-up compared to baseline. However, in comparison to $HIV^+$ women without histories of childhood trauma, dually affected women performed worse at follow-up compared to baseline. Similarly, the dually affected group performed more poorly than $HIV^-$ controls without childhood trauma, both at baseline and at follow-up. Such findings may implicate childhood trauma as a risk factor for developing more rapid decline over time in HIV-infected individuals. To our knowledge, there has only been one other study assessing the combined impact of HIV and ELS. This study was a cross-sectional investigation of brain morphometry and neurocognitive function in males and females with higher CD4 lymphocyte counts suggestive of milder disease (Clark et al., 2012). Clark et al. studied four groups of individuals with and without HIV-infection and/or trauma histories in the United States, where clade B HIV predominates and the majority of individuals are on antiretroviral treatment (Clark et al. 2012). Their findings supported an interaction between HIV status and ELS severity, such that larger amygdala volumes were evident in HIV-infected individuals with high levels of ELS. These abnormalities were associated with neurocognitive dysfunction on a test of processing speed (Clark et al. 2012). The aforementioned study examined relatively complex groups that differed with respect to education, current stress, depression, lifetime cocaine use, and HCV status, although these variables did not appear to account for the interaction of neurocognitive and neural findings. Like Clark et al., we previously reported smaller brain volumes in this cohort of women, with smaller brain volumes associated with poorer neurocognitive performance in the domains of processing speed, attention/working memory, executive function, motor skills, learning and verbal fluency. These findings were more pronounced in the $HIV^+$ $trauma^+$ group compared to all other groups, highlighting the potential contributory role of developmental trauma in brain morphological and neurocognitive aberrations in HIV-infected individuals (Spies, Ahmed-Leitao, Fennema-Notestine, Cherner, & Seedat, 2016).No other studies have investigated the HIV-trauma effect on cognition longitudinally.

On a test of executive function (WCST), $HIV^+$ women with histories of childhood trauma also performed better at 12 month follow-up compared to baseline, with fewer errors evident at follow-up relative to baseline. However, in comparison to $HIV^+$ women without histories of childhood trauma, these dually affected women performed even better at follow-up compared to baseline.

The improvement in the dually affected group could be because more of the these women were on ART by follow-up relative to the $HIV^+$ $trauma^-$ group, possibly implicating the use

of ART with improved or preserved cognition in this cohort over time. It has been suggested that incomplete viral suppression in the central nervous system (CNS) or possible drug toxicity, both of which could be related to the CNS penetration effectiveness (CPE) of differing ART regimens, may contribute to an increase in milder forms of neurocognitive impairment. A recent study in South Africa found that the use of ART improves or preserves cognition in HIV infected individuals after one year, irrespective of the regimen's CPE (Cross, Combrinck, & Joska, 2013). Another study, however, found evidence for a link between regional brain alterations and immune recovery, with the largest increases in abnormal white matter and subcortical grey matter volumes evident in subjects with CD4+ T cell increases of at least 50 cells/μl (Fennema-Notestine et al., 2013).These brain alterations have also been associated with negative neurocognitive outcomes in other studies (Clark et al., 2012; Moore et al., 2006; Paul, Cohen, Navia, & Tashima, 2002). The present study did not directly assess this. Evidence is therefore still limited and inconsistent and further longitudinal studies are needed. There was a treatment difference between the $HIV^+$ groups, with more women in the trauma group on ART compared with the group without trauma. The influence that this difference in treatment status has on findings needs further exploration. Moreover, the length of ART treatment and time since HIV infection were also not taken into account and should be explored in follow-up studies. Stratification of groups by these variables would require large sample sizes.

Improved scores at follow-up seen within groups could also be explained by the practice effect of serial neuropsychological testing (Dikmen, Heaton, Grant, & Temkin, 1999). Practice or learning effects are seen on most neuropsychological measures and are larger on tests of problem solving. In particular, learning continues over multiple exposures to tests of executive function, such as the WCST (Basso, Bornstein, & Lang, 1999). Practice effects can confound the detection of meaningful change (Dikmen et al., 1999). Improved mean raw scores on most tests in an HIV-specific neuropsychological testing battery with repeated measurements were recently reported (Sithinamsuwan et al., 2014). As such, this warrants further examination. While the ideal analysis would include corrections for practice effects, as has been done in a large longitudinal study of HIV effects (Cysique et al., 2011; Heaton et al., 2015), we are not able to generate such adjustments with our small sample size. While all groups showed improvements that may correspond to practice effects across the battery, effects of HIV and childhood trauma remained evident at 12-month follow-up despite greater ART uptake and improved HIV disease status - a finding in line with the first study hypothesis.

Significant individual and combined effects of HIV and trauma may have been influenced by sociodemographic differences between the study groups. It is well understood that formal education can influence performance on both verbal and non-verbal tests, and education may represent a proxy for other societal advantages or disadvantages that manifest in test performance. In a recent large cross-sectional study assessing a cohort of 1019 HIV-infected women and 502 $HIV^-$ women, reading level was the strongest predictor of cognitive function. $HIV^+$ women performed more poorly on cognitive testing than $HIV^-$counterparts, but HIV effects on cognitive testing were smaller than the effects of years of education, age, household income, ethnicity and reading level (Maki et al., 2015). It should be noted that education was controlled for in the present analyses as groups did differ on this variable.

Nevertheless, caution should be used when interpreting our findings, considering that years of education may not capture all pre-existing differences between the groups.

A limitation of the present study was the retrospective assessment of childhood trauma and its contribution to recall bias. Moreover, the CTQ-SF does not include any questions around whether the abuse reported was a single isolated event(s) or repeated exposures. This would be important to elucidate going forward.

To conclude, the present study found evidence for HIV effects on processing speed and verbal fluency and a combined HIV and childhood trauma effect on verbal fluency and executive function in a cohort of South African women. These findings highlight the need for trauma screening and for the integration of trauma focussed interventions in HIV care to improve outcomes in affected individuals. The experience of early life trauma deserves more attention in the clinical care of $HIV^+$ individuals. This is to our knowledge the first study to assess the combined impact of HIV and trauma on neurocognitive function over time in an all-female cohort with more advanced disease.

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**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 |
| | Colour Trails 1 and 2 |
| | Stroop Colour Word Test |
| | Halstead Category Test – computer version |
| Learning and Delayed Recall (2 domains) | |
| | Hopkins Verbal Learning Test, Revised (HVLT-R) |
| | Brief Visuospatial Memory Test, Revised (BVMT-R) |
| Language | |
| | Controlled Oral Word Association Test |
| | Category Fluency (Animals, Action) |
| Motor | |
| | Grooved Pegboard Test (both hands) |
| Screening for effort | |
| | Hiscock Digit Memory Test |

**Table 2**

**Socio-demographic and clinical characteristics at baseline**

| | **HIV+ trauma+ (*n* = 53)** | **HIV+ trauma− (*n* = 14)** | **HIV− trauma+ (*n* = 18)** | **HIV− trauma− (*n* = 32)** | **F** | **χ** | ***p*** |
|---|---|---|---|---|---|---|---|
| Age Mean (SD) | 34.75 (6.30) | 34.14 (8.06) | 32.55 (9.26) | 29.28 (8.11) | 3.668 | | 0.014* |
| Ethnicity (%) | | | | | | | |
| African | 53 (100) | 14 (100) | 18 (100) | 32 (100) | | | |
| Education Mean (SD) | 9.75 (2.07) | 10.64 (1.21) | 10.83 (1.82) | 11.00 (1.41) | 3.925 | | 0.010* |
| < grade 8 (%) | 14 (26) | 1 (7) | 1 (6) | 2 (6) | | | |
| >grade 8 (%) | 39 (74) | 13 (93) | 17 (94) | 30 (94) | | | |
| Right handedness (%) | 52 (98) | 14 (100) | 16 (89) | 30 (94) | | 3.726 | 0.293 |
| Home language (%) | | | | | | | |
| English | 1 (2) | 0 (0) | 0 (0) | 0 (0) | | 4.315 | 0.634 |
| isiXhosa | 52 (98) | 14 (100) | 17 (94) | 31 (97) | | | |
| Other | 0 (0) | 0 | 1 (6) | 1 (3) | | | |
| Household income | | | | | | | |
| > R40,000/$3714 | 0 (0) | 1 (7) | 1 (6) | 1 (3) | | 14.707 | 0.258 |
| Marital status | | | | | | 15.093 | 0.088 |
| Single | 42 (79) | 10 (71) | 11 (61) | 18 (56) | | | |
| Cohabiting/Married | 10 (19) | 4 (29) | 7 (39) | 14 (44) | | | |
| Separated/Divorced | 1 (2) | 0 (0) | 0 (0) | 0 (0) | | | |
| Employed (%) | 6 (11) | 11 (79) | 6 (33) | 9 (28) | | 1.257 | 0.739 |
| ARV treatment (%) | 39 (74) | 7 (50) | 0 (0) | 0 (0) | | | |
| CD 4 count | | | | | 0.148 | | 0.702 |
| Mean | 442.04 | 413.57 | -- | -- | | | |
| SD | 234.88 | 285.02 | -- | -- | | | |
| Minimum | 25 | 46 | -- | -- | | | |
| Maximum | 1026 | 1053 | -- | -- | | | |
| Viral load | | | | | 0.137 | | 0.713 |
| Mean | 61505.04 | 81169.93 | -- | -- | | | |
| SD | 174046.09 | 185206.44 | -- | -- | | | |
| Minimum | <40copies/ml | <40copies/ml | -- | -- | | | |

| | HIV+ trauma+ (*n* = 53) | HIV+ trauma− (*n* = 14) | HIV− trauma+ (*n* = 18) | HIV− trauma− (*n* = 32) | F | χ | *p* |
|---|---|---|---|---|---|---|---|
| Maximum | 1052380 | 641937 | -- | -- | | | |

* $p < 0.05$; F = Analysis of Variance (ANOVA); χ = Pearson Chi-Square; HIV+= HIV-positive; HIV−= HIV-negative; trauma+ = history of childhood trauma; trauma− = no history of childhood trauma; African = South Africans belonging to the Black racial group; isiXhosa = one of the official indigenous African languages spoken in South Africa

**Table 3**

**Socio-demographic and clinical characteristics at 12-month follow-up**

| | **HIV+ trauma+ (*n* = 53)** | **HIV+ trauma− (*n* = 14)** | **HIV−trauma+ (*n* = 18)** | **HIV− trauma− (*n* = 32)** | **F** | **χ** | ***p*** |
|---|---|---|---|---|---|---|---|
| Age Mean (SD) | 36.05 (6.42) | 35.35 (8.03) | 33.22 (9.62) | 30.37 (8.02) | 3.914 | | 0.011 * |
| Education Mean (SD) | 9.79 (2.08) | 10.78 (1.18) | 10.22 (3.00) | 11.06 (1.29) | 2.799 | | 0.043 * |
| Household income (%) | | | | | | 16.127 | 0.185 |
| > R40,000/$3714 | 0 (0) | 0 (0) | 1 (6) | 1 (3) | | | |
| Marital status (%) | | | | | | 18.821 | 0.222 |
| Single | 32 (60) | 9 (64) | 12 (67) | 17 (53) | | | |
| Cohabiting/Married | 18 (34) | 5 (36) | 5 (28) | 12 (38) | | | |
| Separated/Divorced | 2 (4) | 0 (0) | 1 (6) | 1 (3) | | | |
| Widowed | 1 (2) | 0 (0) | 0 (0) | 2 6) | | | |
| Employed (%) | 15 (28) | 6 (43) | 5 (28) | 11 (34) | | 1.323 | 0.724 |
| ARV treatment (%) | 46 (87) | 8 (57) | 0 (0) | 0 (0) | | | |
| CD 4 count | | | | | 2.081 | | 0.133 |
| Mean | 469.21 | 464.50 | -- | -- | | | |
| SD | 261.43 | 292.54 | -- | -- | | | |
| Minimum | 85 | 74 | -- | -- | | | |
| Maximum | 1213 | 1264 | -- | -- | | | |
| Viral load | | | | | 0.218 | | 0.805 |
| Mean | 25841.34 | 37975.14 | -- | -- | | | |
| SD | 70419.258 | 59518.193 | -- | -- | | | |
| Minimum | <40copies/ml | <40copies/ml | -- | -- | | | |
| Maximum | 370852 | 184624 | -- | -- | | | |

* $p < 0.05$; F = Analysis of Variance (ANOVA); χ = Pearson Chi-Square; HIV+= HIV-positive; HIV– = HIV-negative; trauma+ = history of childhood trauma; trauma– = no history of childhood trauma

**Table 4**

**Neuropsychological and childhood trauma (CTQ-SF) scores**

| | Baseline | | | | Follow-up | | | |
|---|---|---|---|---|---|---|---|---|
| | **HIV+ trauma+ (*n* = 53)** | **HIV−trauma+ (*n* = 18)** | **HIV+ trauma− (*n* = 14)** | **HIV− trauma− (*n* = 32)** | **HIV+ trauma+ (*n* = 53)** | **HIV− trauma+ (*n* = 18)** | **HIV+ trauma− (*n* = 14)** | **HIV− trauma− (*n* = 32)** |
| Childhood trauma (CTQ-SF) scores *n* (%) | | | | | | | | |
| Low to moderate trauma (41-55) | 9 (13%) | 10 (25%) | -- | -- | -- | -- | -- | -- |
| Moderate to severe trauma (56-72) | 16 (24%) | 6 (12%) | -- | -- | -- | -- | -- | -- |
| Severe to extreme trauma (73-125) | 28 (42%) | 2 (4%) | -- | -- | -- | -- | -- | -- |
| Neuropsychological scores (mean) | | | | | | | | |
| (HVLT-R) total learning | 22.1 | 22.9 | 22.2 | 22.6 | 23.3 | 24.7 | 24.0 | 24.6 |
| (HVLT-R) delay | 6.83 | 7.83 | 7.64 | 7.84 | 7.56 | 9.05 | 7.71 | 9.03 |
| (BVMT-R) total learning | 14.5 | 19.7 | 18.2 | 18.9 | 16.8 | 22.8 | 20.0 | 23.2 |
| (BVMT-R)delay | 5.47 | 7.66 | 7.50 | 8.06 | 6.71 | 9.44 | 7.92 | 8.87 |
| WAIS-III Digit Symbol | 39.0 | 47.8 | 47.5 | 52.0 | 41.9 | 51.4 | 47.8 | 58.2 |
| WAIS-III Symbol Search | 13.5 | 18.6 | 17.3 | 18.9 | 13.1 | 19.9 | 16.1 | 20.5 |
| Grooved Pegboard Test (dominant hand)* | 82.9 | 66.8 | 67.8 | 68.7 | 78.4 | 65.6 | 69.7 | 63.7 |
| Grooved Pegboard Test (non-dominant hand)* | 92.4 | 80.0 | 77.5 | 74.8 | 88.6 | 74.2 | 82.3 | 70.9 |
| Trails A* | 67.4 | 49.3 | 49.6 | 48.5 | 60.4 | 42.7 | 45.9 | 42.9 |
| Color Trails 1* | 63.7 | 60.0 | 64.7 | 55.9 | 62.7 | 43.9 | 49.8 | 42.3 |
| Color Trails 2* | 129.6 | 113.2 | 123.4 | 109.8 | 133.0 | 106.0 | 116.1 | 98.9 |
| WMS-III Spatial Span | 10.1 | 11.8 | 11.2 | 11.9 | 10.3 | 12.1 | 11.3 | 12.0 |
| COWAT | 23.0 | 22.9 | 26.2 | 24.5 | 24.1 | 29.2 | 26.3 | 29.5 |
| Category Fluency (animals) | 10.7 | 12.4 | 12.7 | 12.1 | 11.4 | 13.0 | 12.5 | 13.3 |
| Category Fluency (actions) | 9.11 | 10.1 | 12.4 | 10.6 | 9.69 | 10.1 | 10.5 | 12.3 |
| Stroop | 27.4 | 27.7 | 28.6 | 31.4 | 27.1 | 31.6 | 35.0 | 34.1 |
| PASAT | 20.8 | 23.7 | 19.5 | 25.1 | 21.4 | 25.2 | 21.8 | 28.6 |
| WCST Perseverations* | 19.7 | 15.8 | 11.9 | 15.8 | 14.7 | 18.2 | 15.5 | 10.9 |
| Halstead Category Test* | 86.5 | 83.1 | 78.5 | 83.2 | 84.7 | 87.6 | 77.7 | 74.4 |

Asterisk denotes that higher scores indicate poorer performance. HIV + = HIV positive; HIV – = HIV negative; HVLT-R = Hopkins Verbal Learning Test, Revised; BVMT-R = Brief Visuospatial Memory Test, Revised; WAIS-III = Wechsler Adult Intelligence Scale; WMS-III = Wechsler Memory Scale; COWAT = Controlled Oral Word Association Task (with letters FAS for English, LBS for Afrikaans and IBS for isiXhosa); Stroop = Stroop Color and Word Test; PASAT = Paced Auditory Serial Addition Test; WCST = Wisconsin Card Sorting Test (computerised version).

**Table 5**

**Repeated measures Analysis of Covariance**

| Effect | Category fluency (Actions) | | Category fluency (Animals) | | BVMT-R delay | | BVMT-R total | | Halstead Category Test | | Color Trails 1 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **F** | ***p*** | **F** | ***p*** | **F** | ***p*** | **F** | ***p*** | **F** | ***p*** | **F** | ***p*** |
| HIV | 0.03 | 0.84 | 1.10 | 0.29 | 1.88 | 0.17 | 1.38 | 0.24 | 2.71 | 0.10 | 0.43 | 0.50 |
| Childhood trauma | 5.11 | 0.02* | 1.03 | 0.31 | 0.20 | 0.64 | 0.08 | 0.83 | 0.13 | 0.71 | 0.00 | 0.99 |
| Time | 0.04 | 0.83 | 3.74 | 0.05 | 14.3 | 0.00* | 23.8 | 0.00* | 0.22 | 0.63 | 18.8 | 0.00* |
| HIV*Childhood trauma | 0.00 | 0.92 | 1.36 | 0.24 | 1.82 | 0.17 | 1.36 | 0.24 | 0.03 | 0.84 | 0.10 | 0.75 |
| HIV*time | 4.05 | 0.04* | 1.56 | 0.21 | 0.66 | 0.41 | 2.22 | 0.13 | 0.01 | 0.90 | 1.73 | 0.19 |
| Childhood trauma*time | 0.33 | 0.56 | 0.09 | 0.75 | 2.50 | 0.11 | 0.10 | 0.74 | 0.72 | 0.39 | 1.18 | 0.27 |
| HIV*Childhood trauma*time | 7.83 | 0.00* | 1.87 | 0.17 | 0.01 | 0.89 | 0.48 | 0.48 | 0.98 | 0.32 | 2.42 | 0.12 |

| Effect | Color Trails 2 | | WAIS-III Digit Symbol | | COWAT | | HVLT-R delay | | HVLT-R | | PASAT | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | F | *p* | F | *p* | F | *p* | F | *p* | F | *p* | F | *p* |
| HIV | 0.41 | 0.52 | 0.83 | 0.36 | 0.37 | 0.54 | 1.66 | 0.19 | 0.03 | 0.84 | 2.67 | 0.10 |
| Childhood trauma | 0.00 | 0.97 | 1.05 | 0.30 | 0.61 | 0.43 | 0.01 | 0.90 | 0.22 | 0.63 | 0.06 | 0.79 |
| Time | 2.49 | 0.11 | 19.0 | 0.00* | 14.3 | 0.00* | 6.46 | 0.01* | 22.5 | 0.00* | 8.31 | 0.00* |
| HIV*Childhood trauma | 0.01 | 0.90 | 0.02 | 0.86 | 0.01 | 0.91 | 0.03 | 0.85 | 0.02 | 0.88 | 1.63 | 0.20 |
| HIV*time | 1.03 | 0.31 | 5.00 | 0.02* | 9.35 | 0.00* | 1.60 | 0.20 | 0.36 | 0.54 | 0.64 | 0.42 |
| Childhood trauma*time | 1.03 | 0.31 | 0.00 | 0.98 | 0.49 | 0.48 | 0.30 | 0.58 | 0.40 | 0.52 | 1.90 | 0.16 |
| HIV*Childhood trauma*time | 0.24 | 0.61 | 2.95 | 0.08 | 0.02 | 0.88 | 0.24 | 0.61 | 0.16 | 0.68 | 0.01 | 0.91 |

| Effect | Grooved Pegboard dominant | | Grooved Pegboard non-dominant | | WMS-III Spatial span | | Stroop | | WAIS-III Symbol search | | Trails A | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | F | *p* | F | *p* | F | *p* | F | *p* | F | *p* | F | *p* |
| HIV | 0.32 | 0.57 | 0.92 | 0.33 | 1.17 | 0.28 | 0.08 | 0.77 | 2.38 | 0.12 | 0.53 | 0.46 |
| Childhood trauma | 0.24 | 0.62 | 0.67 | 0.41 | 0.05 | 0.81 | 1.40 | 0.23 | 0.08 | 0.77 | 0.76 | 0.38 |
| Time | 1.65 | 0.20 | 0.69 | 0.40 | 0.50 | 0.48 | 9.45 | 0.00* | 0.19 | 0.66 | 7.33 | 0.00* |
| HIV*Childhood trauma | 2.08 | 0.15 | 0.43 | 0.51 | 0.67 | 0.41 | 0.09 | 0.75 | 0.61 | 0.43 | 2.63 | 0.10 |
| HIV*time | 0.30 | 0.58 | 1.03 | 0.31 | 0.08 | 0.77 | 0.02 | 0.87 | 2.27 | 0.13 | 0.03 | 0.86 |

| Effect | Category fluency (Actions) | | Category fluency (Animals) | | BVMT-R delay | | BVMT-R total | | Halstead Category Test | | Color Trails 1 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **F** | ***p*** | **F** | ***p*** | **F** | ***p*** | **F** | ***p*** | **F** | ***p*** | **F** | ***p*** |
| Childhood trauma * time | 0.14 | 0.70 | 1.02 | 0.31 | 0.05 | 0.80 | 1.71 | 0.19 | 0.04 | 0.82 | 0.26 | 0.61 |
| HIV * Childhood trauma * time | 2.23 | 0.13 | 0.42 | 0.51 | 0.01 | 0.90 | 3.48 | 0.06 | 0.12 | 0.72 | 0.07 | 0.78 |

| Effect | WCST | |
|---|---|---|
| | F | *p* |
| HIV | 0.26 | 0.60 |
| Childhood trauma | 1.94 | 0.16 |
| Time | 0.45 | 0.50 |
| HIV * Childhood trauma | 0.03 | 0.85 |
| HIV * time | 0.03 | 0.84 |
| Childhood trauma * time | 0.05 | 0.81 |
| HIV * Childhood trauma * time | 8.08 | 0.00 * |

* $p < 0.05$; HVLT-R = Hopkins Verbal Learning Test, Revised; BVMT-R = Brief Visuospatial Memory Test, Revised; WAIS-III = Wechsler Adult Intelligence Scale; WMS-III = Wechsler Memory Scale; COWAT = Controlled Oral Word Association Task (with letters FAS for English, LBS for Afrikaans and IBS for isiXhosa); Stroop = Stroop Color and Word Test; PASAT = Paced Auditory Serial Addition Test; WCST = Wisconsin Card Sorting Test (computerised version).

## Table 6
**Summary of significant and non-significant findings over time**

| HIV effect | HIV and childhood trauma effect | No effects |
|---|---|---|
| WAIS-III Digit Symbol (processing speed) | Category Fluency Test [Actions] (verbal fluency) | Category fluency (Animals) |
| COWAT (phonemic verbal fluency) | WCST (executive function) | BVMT-R (total and delay trials) |
| | | HalsteadCategory Test |
| | | Color Trails 1 and 2 |
| | | HVLT-R (total and delay trials) |
| | | PASAT |
| | | Trail Making Test A |
| | | Stroop |
| | | Grooved Pegboard Test (both hands) |
| | | WMS-III Spatial Span |
| | | WAIS-III Symbol Search |

HVLT-R = Hopkins Verbal Learning Test, Revised; BVMT-R = Brief Visuospatial Memory Test, Revised; WAIS-III = Wechsler Adult Intelligence Scale; WMS-III = Wechsler Memory Scale; COWAT = Controlled Oral Word Association Task (with letters FAS for English, LBS for Afrikaans and IBS for isiXhosa); Stroop = Stroop Color and Word Test; PASAT = Paced Auditory Serial Addition Test; WCST = Wisconsin Card Sorting Test (computerised version).