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Performance by South African Adults on Semantic Fluency Tests: Effects of home language, educational attainment, and HIV infection

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Author Note

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Supervisor: Kevin Thomas
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   Main Body: [6382]
Abstract

Research emerging from the global north suggests that semantic fluency test performance (a) is influenced by level of educational attainment and by the language in which the test is administered, and (b) discriminates reliably between HIV-infected individuals and healthy controls. Given that the South African population is marked by wide disparities in educational attainment, that the country has 11 official languages, and that it houses the world’s largest number of HIV-infected individuals, local research on the use of semantic fluency tests is imperative. The current investigation sought to meet this imperative. Study 1 ($N = 114$) assessed semantic fluency performance in two groups of healthy adults (those administered tests in English ($n = 54$), and those administered tests in Xhosa ($n = 60$)). Independent-sample $t$-tests detected no significant between-group differences. Hierarchical regression analyses indicated that education was a significant predictor of performance on both animal and fruit-and-vegetable category tests, and that sex was a significant (but weaker) predictor of performance on the fruit-and-vegetable test. Based on these findings, we used regression-based techniques to produce preliminary normative data, stratified by the appropriate demographic variables, for South African adults on semantic fluency tests. Study 2 investigated whether performance on these tests discriminated between HIV-infected individuals ($n = 102$) and healthy matched controls (the Study 1 sample, $n = 114$). Independent-sample $t$-tests detected no significant between-group differences. Together, these results suggest that, in South African adults, (a) educational attainment, but not language of administration, affects semantic fluency performance, and (b) semantic fluency tests do not discriminate HIV-infected individuals from healthy controls. The first result is consistent with those from in previous research conducted in the global North, and highlights the importance of considering educational level as a factor influencing semantic fluency scores. This factor is particularly relevant in South Africa, where educational levels vary substantially across age cohorts and regions. The data also indicate that semantic fluency tests should not be included in batteries seeking to detect the presence of HIV-related cognitive impairment in South Africa adults. Given the high rates of infection in the country, this result is of great practical significance.

Keywords: education; HIV; normative data; semantic fluency; South Africa; HIV-associated neurocognitive impairment.
Since their development and introduction into literature more than 70 years ago, verbal fluency tests have become one of the most important forms of cognitive assessment within both clinical neuropsychological practice and experimental neuropsychological research (Rosselli et al., 2002). These tests include those measuring semantic (or category) fluency (e.g., the number of animals, fruits and vegetables, or girls’ names the test-taker can name within a given time limit) and action fluency (i.e., the number of verbs the test-taker can name within a given time limit; Strauss, Sherman, & Spreen, 2006).

Poor performance on verbal fluency tests can be attributed to either disease-related (i.e., HIV, Alzheimer’s, or Parkinson’s) or non-disease-related factors. Because of the former, these tests are used frequently in the assessment of neurodegeneration associated with, for instance, Alzheimer’s pathology or HIV infection (Shao, Janse, Visser, & Meyer, 2014; Snitz et al., 2009). It is only relatively recently, however, that the psychological literature has begun to examine whether performance differences on verbal fluency tests might be attributable to non-disease-related factors (e.g., age, sex, education, or language of test administration).

The balance of impairment attributable to disease-related versus non-disease-related factors might vary from person to person, and hence it is imperative for research to distinguish clearly (a) the roles of each of those factors in performance, and (b) which non-disease-related factors might play particular roles in the performance of specific individuals. The current study used South African samples to (a) examine the influence of four non-disease-related factors (age, sex, educational attainment, and language of test administration) on semantic fluency performance, (b) generate locally appropriate normative data for semantic fluency tests, and (c) examine the influence of a disease-related factor, HIV infection, semantic fluency test performance.

Non-disease-related Influences on Semantic Fluency Performance

A relatively consistent finding in this literature is that age is significantly negatively associated, and level of educational attainment is significantly positively associated, with performance on semantic fluency tests (see, e.g., Brickman et al., 2005; Esteves et al., 2015; Fichman et al., 2009; Strauss et al., 2006; Troyer, 2000). For instance, in a large normative study ($N = 1300$) using cognitively intact individuals aged 16-95 years with 0-21 years of education, Tombaugh, Kozak, and Rees (1999) showed that both age and education
(13.6%) accounted for a significant proportion of the variance in number of words generated to the category cue of animals. Similarly, Crossley, D’Arcy, and Rawson (1997) reported that older adults (aged 65 years and older) who had completed 13 or more years of formal education generated more than double the amount of words compared to those who had completed 6 or fewer years. More recently, Zimmermann, Parente, Joanette & Fonseca (2014) found, using a Brazilian sample of healthy individuals aged 19-75 years, that (a) older adults (60-75 years) performed more poorly than middle-aged (40-59) and young adults (19-39), (b) those with higher levels of education (7 years or more) performed better than those with lower levels (2-6 years), and (c) there was an age x education interaction suggesting that, among older adults, level of education was less predictive of performance than among younger adults.

The effects of biological sex on semantic fluency performance are not as clear-cut, however. In the Tombaugh et al. (1999) normative study, there were sex differences in overall semantic fluency performance, but the variable contributed a small amount (1%) to variance in outcomes. More recently, Esteves et al. (2015) found, using a Brazilian sample (N = 265) of adults older than 60 years, no effect of sex on animal category fluency.

Regarding language of test administration, knowing the language history of the test-taker is crucial to understanding variations in performance on cognitive tasks, including verbal fluency tests (Soh, 2014; Whiteside et al., 2015). Although the test-taker’s language history is of obvious importance in all assessment contexts and for all neuropsychologists, most of the literature on this topic has emerged from the global north. Specifically, due to the rapidly increasing Spanish-speaking population in the United States, a large literature has developed around neuropsychological assessment of Latino individuals in the United States because of the need for such assessment to be structured appropriately for these individuals (see, e.g., Rosselli et al., 2000; Mack et al., 2005).

There is a relative paucity of literature on the effects of language of test administration in African clinical contexts. More such studies are needed because, across the continent, most individuals are, at least, bilingual, and many are multilingual (Ansaldo, Marcotte, Scherer, & Raboyeau, 2008; Foxcroft, 2011). South Africa has 11 official languages, and according to the South African Schools Act 84 of 1996, all primary and high school students must have formal classes in at least two of those. Hence, most citizens of the country are at least partially multilingual (Government of the Republic of South Africa, 1996).
Code switching is a common phenomenon appearing in those familiar with more than one language. This term refers to an instance of when a speaker alternates between two or more languages within a single conversation. The frequency with which people code switch depends on their proficiency in both the imminent language and the one in which they switch to (Rodriguez-Fornells, Krämer, Lorenzo-Seva, Festman, & Münte, 2012). Although the ability to code switch is associated with mature executive control processes (Yim & Bialystok, 2012), it is sometimes seen in children or in individuals with a limited vocabulary in the imminent language (i.e., those without a fully-fledged lexicon in one language might switch to a different language in order to describe a concept; Genesee, Crago, & Paradis, 2004; Grosjean, 1982).

Those who code switch in the course of ordinary conversation tend to do so with equal frequency during administration of verbal fluency tasks (Rodriguez-Fornells et al., 2012). For instance, Yim and Bialystok (2012) demonstrated that participants ($N = 78$ English-Cantonese speakers) who employed more code-switching during a semi-structured conversation switched between languages more swiftly on a semantic fluency task than those who did not.

Another key language-related problem for cross-cultural neuropsychologists is whether participants deliver better performance if tested in their home language or in the language in which they received most of their education (Kempler et al., 1998; Ardila et al., 2000; Soh, 2014). A South African study assessing reading literacy performance of Grade 4 students showed that students who were administered the test in their home language (e.g., Sesotho, Zulu, Xhosa) achieved lower scores than those who were administered the test in their medium of academic instruction (e.g., English or Afrikaans; Van Staden, Bosker, & Bergbauer, 2016). There are no published studies examining this question with regard to semantic fluency performance, however.

A Disease-related Influence on Semantic Fluency Performance: HIV infection

Semantic fluency tests are often a core component of HIV neuropsychology batteries (Robertson, Liner, & Heaton, 2009; Heaton et al., 2011; Sacktor et al., 2009, 2013), primarily because performance on these tests has, in many previous studies, distinguished HIV-infected from HIV-negative samples (see, e.g., Iudicello, Woods, Parsons, Moran, Carey, & Grant, 2012; Millikin, Trépanier, & Rourke, 2004). For instance, Iudicello, Woods, Deutsch, Grant & HNRP Group (2012), in a US-based study, reported that HIV-infected older adults (age ≥ 50 years) performed more poorly than HIV-infected younger adults (age < 40 years) and than HIV-negative adults of all ages. In contrast, a Master’s thesis by van Wyk (2014) reported no
significant differences in performance between HIV-infected and HIV-negative South African participants. This latter study remains unpublished, however, and the finding has yet to be replicated despite the fact that the long-lasting effects of the HIV pandemic mean South African clinical psychologists and neuropsychologists must be particularly conscious of psychometric means to distinguish between infected and uninfected individuals (Albert, & Martin, 2014; Foley, Ettenhofer, Wright, & Hinkin, 2008; Woods, Moore, Weber, & Grant, 2009).

**The Current Research**

The present research comprised two studies. Study 1 examined the influence of four non-disease-related factors (age, sex, educational attainment, and language of test administration) on semantic fluency performance in healthy South African adults, and, on the basis of those findings, established appropriately stratified preliminary normative data for the local population. Study 2 assessed whether impaired semantic fluency performance distinguished HIV-infected South African adults from their HIV-negative counterparts.

**Study 1:**

**Sociodemographic influences on semantic fluency performance in South Africa**

Although a large and robust literature describes the effects of language of test administration on cognitive test performance (see, e.g., Coady, 2010; Gasquoine & Gonzalez, 2012; Lehman Blake, Ott, Villanyi, Kazhuro, & Schatz, 2015), and despite the fact that most South Africans do not have English as a first language, yet often have cognitive tests administered to them in that language (Ferrett et al., 2014; Shuttleworth-Edwards, 2012; Watts & Shuttleworth-Edwards, 2016), very few of those studies have been conducted in this country. Furthermore, no previously published study has directly examined the effects of language of test administration on semantic fluency performance.

The present study aimed to fill that knowledge gap. We used a South African sample of healthy, cognitively intact adults to assess the effects of language of test administration (English or isiXhosa) on semantic fluency performance. We then built regression models to examine the contribution of other non-disease-related factors (viz., age, sex, level of educational attainment) to (a) test performance, and (b) code switching during test completion. Although previous studies (see, e.g., Esteves et al., 2015; Fichman et al., 2009; Strauss et al., 2006) suggest that those sociodemographic variables have important effects on semantic fluency performance, most of those studies were conducted in the industrialized countries of the global north. There are no published studies on the topic emerging from low-
or middle-income countries in the global south. Finally, we used the results of analyses to produce preliminary normative data for South African adults on semantic fluency tests.

In summary, the present study tested the following hypotheses:

1. Those taking the test in English will generate more words on semantic fluency tests than those taking the test in isiXhosa. We made this prediction because (a) it is likely that most participants will have received much of their formal education in English, and so those taking the test in this language might have a larger pool of appropriate words upon which to draw, and (b) it is likely that the English language contains more words describing animals, and fruits and vegetables, than isiXhosa.

2. Participants who are younger, and/or who have higher levels of educational attainment, will (a) perform better on both semantic fluency tests and (b) have more instances of code switching than those who are older and/or have completed fewer years of formal education. We made this prediction because higher levels of education are associated with larger vocabularies, and with more mature executive control processes (Bialystok, Craik, & Luk; 2008), and because younger adults tend to have more robust generativity processes than older adults (Kempler et al., 1998). We predicted no significant sex differences because the literature is equivocal on this matter (see, e.g., Crossley et al., Esteves et al., Tombaugh et al., 1999)

**Methods**

**Design and setting.** This cross-sectional study aimed to assess performance of two groups of participants (those administered tests in English, and those administered tests in isiXhosa) on two semantic verbal fluency tests (an animal category test and a fruits-and-vegetables category test). We used data from a larger research programme that investigated the use of mobile technology in the routine screening of HIV-associated cognitive impairments (Gouse et al., 2017; Robbins et al., 2015). Data collection for that parent study ran between May 2014 and April 2016 in Town II Clinic, Khayelitsha, Cape Town (Robbins et al., 2015).
Participants. The final sample for whom data were analyzed consisted of 114 adults (56 men, 58 women). All were recruited from Town II Clinic, where they had just tested negative on a routine HIV test.

To be eligible for participation, these HIV-negative individuals had to be (1) between the ages of 18 and 75 years, (3) either English- or isiXhosa-speaking, (4) willing to participate and give consent, (5) willing to allow access to their medical records by the study nurse, (6) medically healthy (i.e., not have any illnesses that may negatively affect neurocognitive functioning), and (7) willing to undergo a psychiatric and neuropsychological evaluation. Individuals with a current psychotic disorder or significant suicidal ideation, or who showed severe cognitive impairment that would make giving consent and participation impossible, were excluded from participation.

Power analysis. We used G*Power (Faul, Erdfelder, Buchner, & Lang, 2009) to calculate a series of a priori power analyses. The first set of analyses was relevant to the first hypothesis, and so we set the following parameters for a one-tailed independent-samples $t$-test with two equal-sized groups: $\alpha = .05$, desired power = a minimum of .80, and Cohen’s $d = 0.20$ (small), 0.50 (medium), or 0.80 (large). The recommended sample sizes were $N = 620$, 102, and 42, respectively. The second set of analyses were relevant to the second hypothesis, and so we set the following parameters for a two-tailed fixed-effects linear multiple regression model: $\alpha = .05$, desired power = a minimum of .80, predictors = 3, and Cohen’s $f^2 = .15$, .35, or .50. Here, the recommended sample sizes were $N = 55$, 25, and 19, respectively. Hence, we argue that the study was adequately powered to explore its aims.

Measures. In the parent study, tests of semantic verbal fluency were part of a comprehensive neuropsychological test battery that aimed to assess cognitive impairment across multiple domains. Administration of that test battery took 2-3 hours to complete. Verbal fluency tests were administered as the 7th of 9 tests within the battery. All tests were administered in either English or isiXhosa, with the participant choosing his or her preferred language of administration. Sixty participants were administered the tests in isiXhosa, and 54 in English.

Regarding the current versions of the semantic fluency tests, the test administrator instructed the participant to generate the names of as many animals as possible within 60 seconds. After completing that test, the administrator repeated the same instructions for the semantic category of fruits and vegetables.

For each of these two tasks, the test administrator recorded each word onto a scoring sheet and summed the number of correct words, repetitions/perseverations (the repetition of a
word said previously instead of generating a new word), and intrusions (generating a word unrelated to the category, e.g., generating the word coffee on the animal fluency task). The scoring sheet divided each 60-s time frame into four 15-s intervals so that pace of generation could be captured. Subsequently, we reviewed these scoring sheets and recorded each code-switching occurrence.

Procedure. All participants completed an informed consent document and the comprehensive neuropsychological test battery in a private room at the Town II Clinic. At the beginning of the session, participants read and signed the consent form, and were given verbal information as to the nature of the study as well as the activities set to take place during the test session. Thereafter, a fully-trained and bilingual (isiXhosa-English) female psychometrist administered the test battery. If a participant was unable, for any reason, to complete the battery, the psychometrist scheduled a second test session to take place within the next 7 days.

Data Management and statistical analyses. We used SPSS (version 24) for all data analyses, with the threshold for statistical significance set at $\alpha = .05$, unless otherwise stated. The analyses proceeded across four steps. First, we generated a complete set of descriptive statistics that allowed us to examine the normality of data distributions, and to test the assumptions underlying subsequent inferential statistical analyses. Second, to test Hypothesis 1, two independent-sample $t$-tests assessed whether participants who took the semantic fluency tests (animals, fruits and vegetables) in English generated more words than those who took the test in isiXhosa. Third, to test Hypothesis 2a, two separate hierarchical regression models described the influence of age, sex, and level of educational attainment on (i) animals category test total score, and (ii) the fruits and vegetables category test total score. Fourth, to test Hypothesis 2b, two separate hierarchical regression models described the influence of age, sex, and level of educational attainment on (i) code switching during the animals category test, and (ii) code switching during the fruits and vegetables category test. In all of the regression models, we entered sex first, then age, then education.

Results

Sample characteristics. Most participants were aged between 20 and 50 years and had at least some high school education. Of the 144 participants, 113 identified isiXhosa as their home language and 1 identified their home language as isiZulu. Some, however, had received a significant amount of their formal education in English. Analyses detected significant between-group differences in terms of age and education, but no such differences in terms of sex distribution across groups (see Table 1).
Testing Hypothesis 1. Analyses detected no significant between-group differences in performance on either the animals category test or the fruits and vegetables category test (see Table 1). Because of these non-significant results, and because of the types of analyses conducted in testing subsequent hypotheses, we did not run analyses of covariance to examine whether the significant between-group age and education differences had any bearing on the pairwise comparisons.

Table 1
Between-group Differences: Demographic characteristics and test performance (N = 114)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th></th>
<th>t / χ²</th>
<th>p</th>
<th>ESE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>isiXhosa</td>
<td>English</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>M (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>39.40 (11.81)</td>
<td>30.98 (10.50)</td>
<td>-4.01</td>
<td>&lt; .001***</td>
<td>0.75</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>18-54</td>
<td>18-64</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td></td>
<td></td>
<td>1.69</td>
<td>.19</td>
<td>.12</td>
</tr>
<tr>
<td></td>
<td>26:34</td>
<td>30:24</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education (years)</td>
<td>M (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10.28 (1.48)</td>
<td>10.85 (1.28)</td>
<td>2.18</td>
<td>.032*</td>
<td>0.41</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>7-13</td>
<td>8-13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Semantic Fluency</td>
<td></td>
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</tr>
<tr>
<td>Animals</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>M (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>14.54 (3.22)</td>
<td>13.32 (3.81)</td>
<td>1.85</td>
<td>0.066</td>
<td>0.35</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8-23</td>
<td>7-25</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fruits and Vegetables</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>M (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>13.47 (3.79)</td>
<td>14.65 (3.29)</td>
<td>1.77</td>
<td>0.080</td>
<td>0.33</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6-22</td>
<td>9-23</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note. Means are presented, with standard deviations in parentheses. ESE = effect size estimate (in this case, Cohen’s d for t-tests and Cramer’s V for chi-squared tests).

* p < .05. ** p < .01. *** p < .001.

Testing Hypothesis 2. The first set of regression models suggested that level of educational attainment was a consistently strong predictor of semantic fluency performance, regardless of the category in which the participant was generating words (see Table 2). Age and sex were not significant predictors of performance on the animal category task, but sex was a significant predictor of performance on the fruits-and-vegetables category task, explaining 9.1% of the variance in the outcome. Education explained an additional 12.4% of the variance in this outcome. Table 3 presents the consequent regression equations that can serve to produce preliminary normative data for performance of South African adults on the two semantic fluency tests.

The second set of regression models suggested that none of the sociodemographic variables was a significant predictor of code switching during the animal category task, but
that both sex ($R^2 = .050$) and age ($R^2 = .126$) were significant predictors of code switching during the fruits-and-vegetables category task.
<table>
<thead>
<tr>
<th>Table 2</th>
<th>Hierarchical Regression Analyses: Predictors of outcomes and performance characteristics on semantic fluency tests (N = 114)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subtest / Outcome variable</td>
<td>Significant predictor(s)</td>
</tr>
<tr>
<td>Animal fluency: Total score</td>
<td>Education</td>
</tr>
<tr>
<td>Fruits and vegetables fluency: Total score</td>
<td>Sex, Education</td>
</tr>
<tr>
<td>Animal fluency: Code switching</td>
<td>Education</td>
</tr>
<tr>
<td>Fruits and vegetables fluency: Code switching</td>
<td>Sex, Age</td>
</tr>
</tbody>
</table>

*p < .05. **p < .01. ***p < .001

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Regression-based Normative Data: Semantic fluency tests (N = 114)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subtest / Outcome variable</td>
<td>Regression equation</td>
</tr>
<tr>
<td>Animal fluency: Total score</td>
<td>$Y = 7.80 + (0.578*\text{Education})$</td>
</tr>
<tr>
<td>Fruits and vegetables fluency: Total score</td>
<td>$Y = 3.238 + (2.476*\text{Sex}) + (0.903*\text{Education})$</td>
</tr>
</tbody>
</table>

*Note. In the equations, for Sex we code the categorical variable as 0 for men and 1 for women, and for Education we code the continuous variable as number of years of completed education.*
Study 2:

Semantic fluency performance in HIV-infected South African adults

The HIV pandemic has hit South Africa harder than any other country in the world. Recent estimates suggest that about 1 of every 5 HIV-infected people lives in this country, a number that exceeds 7 million people (12% of the country's population). In 2016, 270 000 South Africans were infected with HIV, whilst 110 000 died from HIV/AIDS-related illnesses (UNAIDS, 2017).

A significant proportion of those infected individuals (more than 60%, according to one of the few local prevalence studies) experience at least mild HIV-associated cognitive impairment (Joska et al., 2010). Hence, South African clinical psychologists and neuropsychologists are often required to assess whether, and to what degree, HIV-infected patients experience cognitive impairment, and how that impairment impacts on their ability to complete everyday functional activities (Joska, Fincham, Stein, Paul & Seedat, 2009; Joska et al., 2010; Robbins et al., 2014; Heaton et al., 2004).

Numerous studies suggest that semantic fluency tasks are sensitive to the cognitive impairments present in HIV-infected participants, especially as these relate to changes in frontal circuitry (see, e.g., González-Scarano & Martín-García, 2005; Woods et al., 2009). In South Africa, a study by Joska et al. (2011) showed that there was a statistically significant difference in performance of adults (age range = 18-40) on the both the animal and fruit and vegetable category between the HIV-negative participants ($n = 94$) and the HIV-infected participants ($n = 96$) with the HIV-negative participants performing better on these tests than the HIV-infected group. However, van Wyk (2014) reported that HIV-infected ($n = 30$) and HIV-negative ($n = 70$) South African adolescents (age range = 13-16) did not perform significantly differently on animals and fruit-and-vegetables category fluency tests. Those findings are yet to be replicated in a sample of South African adults, however. Moreover, a significant limitation of that study is that there was no objective verification of participants’ HIV status: Those assigned to the HIV-infected group were deemed so because they belonged to a local clinic’s HIV programme, whereas those assigned to the HIV-negative group were simply sampled from a local school and reported they were not HIV-infected. There was no blood testing for HIV/AIDS.

Hence, Study 2 aimed to contribute to the extant literature by comparing semantic fluency performance in terms of total words generated on the animal category test, and on the
fruit-and-vegetable category test) in a sample of HIV-infected South African adults to that in a sample of demographically matched HIV-negative controls.

**Methods**

**Design and setting.** This study was cross-sectional and quasi-experimental in design, with a primary focus on comparing HIV-infected to HIV-negative participants. The data we analyzed were collected from the same research programme described in Study 1, with the exception that HIV-infected participants were recruited from two different clinics (Town II Clinic in Khayelitsha and Mzamomhle Clinic in Mitchell’s Plain) after they completed a 12-month parent-study visit (Gouse et al., 2017; Robbins et al., 2015).

**Participants.** The final sample for whom data were analysed consisted of 102 HIV-infected adults (19 men and 83 women, all of whom identified their home language as isiXhosa) and 114 HIV-negative adults (56 men, 58 women; the Study 1 sample).

Regarding eligibility criteria for inclusion in the HIV-infected group, individuals had to be (1) HIV-positive, as determined by testing within the parent study, (2) between the ages of 18 and 75 years, (3) either English- or isiXhosa-speaking, (4) willing to participate and give consent, (5) willing to allow access to their medical records by the study nurse, (6) eligible (following South African government guidelines) to initiate ART, (7) willing to undergo a psychiatric and neuropsychological evaluation, (8) ready to initiate mandatory counselling prior to ART initiation, (9) willing to bring a support partner to the intervention, and (10) willing to use Wisepill (Haberer, 2010; Pellowski et al., 2014) to store and dispense HIV medication during the duration of the study. Individuals who had a current psychotic disorder or significant suicidal ideation, or who showed severe cognitive impairment that would make giving consent and participating impossible, were excluded from the study.

**Measures and procedure.** The semantic fluency tests were administered and scored using the same procedures as described in Study 1. Among the HIV-infected participants, 97 were administered the tests in isiXhosa and 5 in English. Given Study 1’s non-significant findings regarding effects of language of test administration on semantic fluency performance, we simply combined the data from these individuals into a single HIV-infected group.

**Data management and statistical analyses.** As in Study 1, we used SPSS (version 24) for all data analyses, and set the threshold for statistical significance at $\alpha = .05$, unless otherwise stated. We began our analysis by creating standardized data that was stratified by the appropriate demographic variables. This was done through the use of the regression equations derived from the regression analysis in study 1 (Table 3). First, we ran the
regression equation analysis for all participants in order to get their expected scores. Second, we deducted the expected score from the participants actual score and divided that by the residual standard deviation in order to arrive at the standardized data (Z-scores) that would be used in study 2. As in Study 1, we generated a complete set of descriptive statistics for the outcome variables. These descriptive statistics allowed us to examine the normality of data distributions, and to test the assumptions underlying subsequent inferential statistical analyses. Thereafter, two separate independent-sample $t$-tests assessed whether, on average, the group of HIV-infected participants generated significantly fewer words on the semantic fluency tests (animals, fruits and vegetables) than the group of HIV-negative participants.

**Results**

**Sample characteristics.** Analyses detected no significant between-group differences in terms of age and education (see Table 4). Most participants in both groups were aged between 25 and 45 years and had at least some high school education. Regarding sex distribution, analyses detected a significant between-group difference, with a much larger proportion of women in the HIV-infected group. We did not run an ANCOVA with sex as a covariate because we used regression equations to generate standardized outcome variables. Finally, although all participants had a home language of Xhosa, the ratio of those administered the test in Xhosa to those administered the test in English was much higher in the HIV-infected group. Again, however, because Study 1 results indicated no significant effects of language of test administration, we did not use this variable as a factor in subsequent analyses.

**Between-group comparisons.** Analyses detected no significant between-group differences in performance on either the animal category test or the fruits-and-vegetables category test (see Table 4).
Table 4
Sample Characteristics (N = 216)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>HIV-negative (n = 114)</th>
<th>HIV-infected (n = 102)</th>
<th>t / χ²</th>
<th>p</th>
<th>ESE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td>1.90</td>
<td>.059</td>
<td>.23</td>
</tr>
<tr>
<td>M (SD)</td>
<td></td>
<td>35.41 (11.93)</td>
<td>32.80 (7.46)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Range</td>
<td></td>
<td>18-64</td>
<td>18-56</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education (years)</td>
<td></td>
<td></td>
<td></td>
<td>1.32</td>
<td>.188</td>
<td>.22</td>
</tr>
<tr>
<td>M (SD)</td>
<td></td>
<td>10.55 (1.42)</td>
<td>10.25 (1.99)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td></td>
<td>7-13</td>
<td>2-13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td>22.09</td>
<td>&lt; .001***</td>
<td>.32</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td>58 (50.88%)</td>
<td>83 (81.37%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td>56 (49.12%)</td>
<td>19 (18.63%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Language of test administration</td>
<td></td>
<td></td>
<td></td>
<td>49.9</td>
<td>&lt; .001***</td>
<td>.48</td>
</tr>
<tr>
<td>Xhosa</td>
<td></td>
<td>60 (52.63%)</td>
<td>97 (95.01%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td>54 (47.37%)</td>
<td>5 (4.9%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Semantic Fluency</td>
<td></td>
<td></td>
<td></td>
<td>-0.31</td>
<td>.173</td>
<td>.04</td>
</tr>
<tr>
<td>Animals</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M (SD)</td>
<td></td>
<td>-.001(1.0)</td>
<td>-.04(1.86)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td></td>
<td>-1.91-2.97</td>
<td>-2.36-1.78</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fruits and Vegetables</td>
<td></td>
<td></td>
<td></td>
<td>-0.24</td>
<td>.661</td>
<td>-.03</td>
</tr>
<tr>
<td>M (SD)</td>
<td></td>
<td>-.0001(1.0)</td>
<td>.03(1.99)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Range</td>
<td></td>
<td>-2.99-2.25</td>
<td>-2.37-2.84</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note. For the variables Sex and Language of Test Administration, counts are presented with percentages in parentheses. ESE = effect size estimate (in this case, Cohen’s d for t-tests, Cramer’s V for chi-squared tests). ***p < .001.

General Discussion

Performance on semantic fluency tests (i.e., tests that require oral generation of words to a category cue) is susceptible to the influence of variation in non-disease-related factors (e.g., age, education, home language) and to the presence of disease-related impairment (e.g., HIV infection). Because South Africa is a demographically heterogeneous society, with regionally specific language variation and great disparities in educational attainment and socioeconomic power, and because the country is home to the world’s largest population of HIV-infected individuals, research on semantic fluency performance is particularly relevant for local clinical purposes. Hence, the current study used South African samples to (a) examine the influence of four non-disease-related factors (age, sex, educational attainment, and language of test administration) on semantic fluency performance, (b) generate locally appropriate normative data for semantic fluency tests, and (c) examine the influence of HIV infection on semantic fluency test performance.
Results from Study 1 suggested that, in a sample of participants who were isiXhosa
home-language speakers, and most of whom had some high school education, those who
were administered the semantic fluency tests in English performed no differently than those
who were administered the tests in isiXhosa. Vast differences on performance between tests
administered in different languages may speak to the validity of the test; that is whether it
measures verbal fluency or lexicon of words belonging to a category (animals or fruit and
vegetables) in a specific language. These results are of particular importance in multilingual
South Africa because there is need of culturally corrected tests that do not have a language
bias. Moreover, this suggests that clinicians can administer these tests in different South
African languages without concern that it may negatively influence the test-takers
performance. This is consistent with Pekkala et al. (2009) who found that English-speaking

group (n=30, M (SD) 19.9 (3.8)) performed no differently than the Finnish-speaking group
(n=30, M (SD) 18.9, (4.7) on the semantic fluency task (animals), p=.423.

Study 1’s results further suggested that level of educational attainment was a strong
predictor of performance on both the animal and fruits-and-vegetables category tasks. This
finding is consistent with previous research suggesting that education is positively associated
with performance on semantic fluency tests (i.e., the higher level of education one attains, the
better one will perform on the tests; see, e.g., Bento-Torres et al., 2017; Brickman et al.,
2005; Esteves et al., 2015; Fichman et al., 2009; Parisi et al., 2012; Schneeweis, Skirbekk, &
Winter-Ebmer, 2014; Strauss et al., 2006; Troyer, 2000). One account of this association is
that more years of exposure to formal education provides individuals with a greater
foundation of the necessary knowledge and skills to engage in and successfully complete
cognitive processes (e.g., the retrieval of memory traces required in verbal fluency tasks), and
with a larger and more diverse vocabulary.

In contrast, age was not a significant predictor of performance on either semantic
fluency test. This is inconsistent with previous literature that describes a strong negative
correlation of age with performance-the younger you are the better you should perform on the
semantic fluency test (see, e.g., Brickman et al., 2005; Esteves et al., 2015; Fichman et al.,
2009; Strauss et al., 2006; Troyer, 2000) as well as Tombaugh et al (1999) who found age to
be the strongest predictors of performance, accounting for a variance of 23.4% in the
semantic fluency tests. However, it can be attributed to our age range (18-64) which in
comparison to Tombaugh et al. (1999) (age range = 16-95) and other studies (see, e.g.,
Cavaco et al., 2013; Elgamal, Roy and Sharratt, 2011; Gladsjo et al., 1999; Kavé, 2005;
Zimmermann et al., 2014, is considerably small. This means that age is more likely to be a significant predictor in studies that have a larger age range.

Moreover, sex was not a significant predictor of performance on the animal category task, but was a significant (albeit minor, compared to education) predictor of performance on the fruits-and-vegetables category task (women performed better than men). This result is partially consistent with Tombaugh et al. (1999), who found small sex differences (in favour of men) in performance on a semantic fluency task. This can be attributed to the large sample size in the Tombaugh et al. (1999) as well as the large number of participants with higher levels of education of up to 21 years of educational attainment. Of the 734 participants who took part in their study, 29.5% had educational levels ranging from 13-21 years and this had a great influence because education accounts for a bigger variance in performance than sex. Both the current data and those reported by Tombaugh et al. (1999) are not, however, consistent with Esteves et al. (2015), who reported no effects of sex on semantic fluency performance. Inconsistency with the Esteves et al. (2015) study could be directed at the fact that they had an uneven distribution between sexes in their study (men = 101 (38%); women = 164 (62%) whereas our study had a more even distribution of 56 (49%) and 58 (51%), respectively.

Regression modelling further suggested that none of the sociodemographic variables was a significant predictor of code switching during the animal category task, but that both sex and age were significant predictors of code switching during the fruits-and-vegetables category task. These results disconfirm our hypothesis that higher educational attainment (because of a consequent larger vocabulary) would be associated with more instances of code-switching. These results are particularly important because most people are bilingual, if not multilingual and receive most of their education in English which will likely result in them code-switching. Therefore, it is important to have psychometrists know the language history of the test-taker as well as understand these language so as to avoid incorrect scoring of the participant and making the semantic fluency test a test of language instead. No studies have examined educational attainment as a predictor for code-switching in semantic fluency tests, however one study by Yim and Bialystok (2012) argued that those who code-switched during conversations were more likely to code switch in semantic fluency tasks. In South Africa, fruits and vegetables are largely referred to in English despite the language spoken by individuals at that given time and this can be a result of age and sex being predictors for code-switching in that it is expected that younger adults will have greater exposure to societal
constructs (language) and our study found that females perform better which gives reason to why these two are predictors to code-switching.

Tests assessing semantic verbal fluency tap into neural processes and circuits centred on the frontal and temporal lobes (see, e.g., Baldo et al., 2006; Meinzer et al., 2009; Shao et al., 2014). Because damage to this circuitry appears to underlie HIV-associated cognitive impairment (González-Scarano & Martín-García, 2005; Woods et al., 2009), research exploring the sensitivity of semantic fluency to HIV infection, and to the trajectory of cognitive decline following infection, is critical. Because South African research is equivocal on the ability of semantic fluency tests to detect HIV-associated cognitive impairment (see, e.g., Joska et al. (2009); van Wijk, 2013). Study 2 of the current research compared semantic fluency performance in a sample of HIV-infected South African adults to that of demographically matched HIV-negative controls.

Analyses detected no significant between-group differences in performance on either of the semantic fluency tests. Most people in the world (including South Africa) are infected with the HIV-1 virus (Hemelaar, Gouws, Ghys, & Osmanov., 2011). HIV-1 comprises of three groups (Robertson, 2000), with 90% of infections globally being attributable to Group M (M for major), which is comprised of different clades (A-K). Clade B accounts for approximately 10% of all infections worldwide, and is prominent in North and Central America, Western and Central Europe, and Australia, whereas, Clade C is prominent in Southern and Eastern Africa and South Easter Asia (Hemelaar et al., 2006; Liner, Hall, & Robertson, 2007; Osmanov Pattou, Walker, Schwardländer, & Esparza, 2002; Smith, Kuiken & Korber, 2003) and accounts for up to 50% of global infections. For the significance of HIV neuropsychology, several studies suggest that HIV-associated neurocognitive deficits are more evident in Clade B than in Clade C (Tyor, Fritz-French & Nath, 2013). Our study was based on participants with HIV Clade C, whereas previous studies that found a significant difference conducted the study on HIV Clade B which is more neurovirulent (Langford, Letendre, Larrea & Masliah, 2006; Sacktor et al., 2001), therefore accounting for the inconsistencies in comparison to our results.

Limitations and Directions for Future Research

The conclusions one might draw from this research are limited by two sample-related factors. First, although our sample was large enough to power the study adequately, we only recruited participants from the Western Cape, and therefore the languages we considered in the first part of Study 1 were limited to a small proportion of the languages spoken in South
Africa as a whole. Future research should extend participant recruitment to other parts of South Africa, and/or to participants who have other home languages.

Second, in Study 2 there was a much larger number of women than men in the HIV-infected group. Future research should therefore attempt to include equal numbers of men and women to ensure that data is equally distributed according to sex.

Third, although South Africa generally has a lower life expectancy (men = 59.7; women = 65.1 yoe) (Statistics South Africa, 2016) compared to the US (men = 77; women = 82) (WHO, 2015), it is important to have a wider age range in order to account for performance among the oldest and the youngest participants. Our study, unfortunately, fell short of this, however it is important for future research to consider getting older or younger participants than what we had.

Summary and Conclusion

Our research aimed to examine the influence of language of test administration, age, sex, level of education, and HIV infection on semantic verbal fluency performance. We found no differences in performance on the semantic fluency tasks between those who took the tests in English and those who took the tests in isiXhosa. Furthermore, education was a consistently strong predictor of performance across both semantic fluency tests (animals and fruits-and-vegetables) These results are particularly relevant for South African clinicians and researchers, who operate in an assessment context where educational levels vary substantially across age cohorts and regions. The data from Study 2 suggest that semantic fluency tests should not be a core component of neuropsychological test batteries seeking to detect the presence of HIV-related cognitive impairment in South Africa adults. Given the high rates of infection in the country, this result is of great practical significance. Overall, this study is important, especially in the South African context of diverse languages, varying educational levels and high HIV-infection because it examines how these factors affect performance on this important cognitive assessment- something that has not been done before in Africa.
References


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Sacktor, N., Nakasujja, N., Okonkwo, O., Skolasky, R., Robertson, K., Musisi, S., & Katabira, E. (2013). Longitudinal neuropsychological test performance among HIV


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We would like to thank our supervisor, Kevin Thomas, for the endless hours spent editing, commenting, bringing in new ideas and responding to our last-minute questions. Our co-supervisor, Michelle Henry, for helping us with all the statistical analysis the data. Hetta Gouse and Reuben Robbins for their contribution to this paper. We are truly grateful for the part you played in making this a success.
Appendix A
Ethics Approval Letter

14 October 2014
HREC/REF: 596/2014

A/Prof J Joska
Psychiatry & Mental Health
J-block
GSH

Dear A/Prof Joska

Project Title: A MOBILE APP FOR LMIC LAY HEALTH WORKERS TO SCREEN FOR NEUROCOGNITIVE IMPAIRMENT

Thank you for your response letter dated 07 October 2014, addressing the issues raised by the Human Research Ethics Committee (HREC).

It is a pleasure to inform you that the HREC has formally approved the above mentioned study.

Approval is granted for one year until the 30 October 2015.

Please submit a progress form, using the standardised Annual Report Form, if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

Please note that the on-going ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the HREC REF in all your correspondence.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS

Federal Wide Assurance Number: PWA00001637.
Institutional Review Board (IRB) number: IRB00001938

HREC/REF: 596/2014
This serves to confirm that the University of Cape Town Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.

The Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.
Appendix B
Amended Ethical Approval letter
We are requesting to make an amendment to our protocol 298/2014, "A Mobile App for LMIC Lay Health Workers to Screen for Neurocognitive Impairment." We would like to add a matched sample of 100 healthy, HIV-uninfected adults. This will not change or alter study aims. Adding the control group will enhance the precision of the sensitivity and specificity estimates that will be generated for the app’s ability to detect neurocognitive impairment for Aim 2 of the study. Further, we believe that adding the control group will make our findings more generalisable.

We would also like to add five more, standard, brief, neuropsychological tests to the full neuropsychological test battery being administered in the study. We would like to add the Montreal Cognitive Assessment (MoCA), the CLOX test, Judgment of Line Orientation, the Paced Auditory Serial Addition Test, and Action Fluency – all well-established and commonly used neuropsychological tests. All of these tests are brief, and we estimate that the addition of them will increase the study visit no more than 20-30 minutes. We also believe that the compensation remains fair given the increased burden. In our experience, the current test battery takes, on average, just under 2.5 hours to complete. Adding 20-30 minutes would still keep the study visit within the 3-hour maximum as stated in the consent form. Only the control group would receive these extra tests, as we will achieve our target sample size of 100 HIV-infected adults within the next 2-3 weeks.

Adding the control group and additional tests will change or recruitment strategy, inclusion criteria, consent form, and assessment instruments. We have updated the following sections (all changes have been bolded):

Lay Summary
Description of Subject Population
Recruitment Procedures
Inclusion/Exclusion Criteria #2
Consent Procedures
Assessment Instruments

We have also included a new Consent Form specifically for the control participants. We have included a version with tracked changes and a version with accepted changes.

Please do not hesitate to contact me if you have any additional questions or need additional information.

Sincerely,

John Joska.

Principal Investigator to complete the following:

1. Protocol information
Appendix C
Semantic Fluency Administration Sheet

Category/Semantic Fluency

Animals:
I want to see how many animals you can say in one minute. They can be wild or tame animals. Name them as quickly as possible.

Fruits and Vegetables:
Now tell me the names of as many fruits and vegetables as you can. Name them as quickly as possible.

Each category timed for 1 minute. Record each response given.

<table>
<thead>
<tr>
<th>Records</th>
<th>Animals</th>
<th>Fruits and Vegetables</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 15s</td>
<td>Bear, Cat, Lion, Tiger, Crocodile</td>
<td>Apple, Banana, Avocado, Tomato, Cabbage, Corn</td>
</tr>
<tr>
<td>16 - 30s</td>
<td>Rabbit, Snake</td>
<td>Orange, Strawberries, Pomegranate</td>
</tr>
<tr>
<td>31 - 45s</td>
<td>Chicken, Cucumbers, Zucchini</td>
<td>Palm, Potatoes</td>
</tr>
<tr>
<td>46 - 60s</td>
<td>Spider, Cake</td>
<td></td>
</tr>
</tbody>
</table>

Correct Words: 14
Repeats/Perseverations: 1
Intrusions: 0

Correct Words: 13
Repeats/Perseverations: 0
Intrusions: 0