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# Utilizing the Color Figure Mazes Test to Assess Executive Functioning while Screening for HIV-Associated Neurocognitive Disorders in HIV-1 Seropositive Spanish-Speaking Adults

**Kimberly Smith[1], Alexander Joseph Steiner[1,2], Waguih William IsHak[1,3], Jessica Acosta[2], Bryce Erich[1], Lou D'Elia[3], Paula Cedillo[1,2] and Enrique López[1,3*]**

*[1]Department of Psychiatry and Behavioral Neurosciences, Cedars-Sinai Medical Center, Los Angeles CA, USA*
*[2]Department of Psychology, CSPP-Alliant International University, Los Angeles, CA, USA*
*[3]Department of Psychiatry and Biobehavioral Sciences, David Geffen School of Medicine, University of California Los Angeles (UCLA), Los Angeles CA, USA*

## Abstract

**Objective:** Spanish-speaking individuals are disproportionately impacted by HIV in the United States. There are limited selections of valid and reliable measures to accurately assess the presence of HIV-associated neurocognitive disorders (HAND) with this population. The dearth of available measures places this vulnerable population at risk for receiving assessments that utilizes measures that are not adequately translated, modified, normed, or culturally sensitive. The purpose of this study was to investigate the clinical utility and efficacy of the Color Figure Mazes (CFM), a nonverbal measure of attention, concentration, working memory and executive functioning, to screen for deficits that characterize a HAND profile in Spanish-speaking adults. We hypothesized the HAND group would perform significantly worse than the non-HAND group and control group as the CFM tasks increased with difficul-ty.

**Methods:** To explore the prevalence of HAND in Spanish-speaking individuals, we studied 100 HIV-1 seropositive participants (47 HAND; 53 non-HAND) who met criteria for the Center for Disease Control classification system category B or C and 27 HIV-seronegative controls. They were administered a comprehensive neuropsychological and psychosocial battery to assess for HAND.

**Results:** While controlling for Pre-Morbid Intellectual Functioning, ANCOVA revealed that the HAND group performed significantly worse than the non-HAND group and HIV-seronegative control group on measures that placed a greater demand on skills requiring executive functioning including set-shifting over short periods of time, mental flexibility, and higher order thought processes.

**Conclusion:** Our findings contribute to previous research by demonstrating that a brief, culturally sensitive measure, such as the CFM can help detect HAND in vulnerable populations, as is the case with Spanish speakers in the Unit-ed States. Furthermore, our results indicate that the CFM is sensitive in detecting executive function deficits associ-ated with HAND and may be culturally appropriate to use with HIV-seropositive Spanish-speaking adults.

**Keywords:** HIV; AIDS; Latino; Hispanic; Spanish-speakers; Neuropsychology; Executive Function; Neurocognitive; Screener; Ethnic Minorities

## Introduction

As HIV-related neuropathology results in significant complications with neural circuitry between the frontal lobes and basal ganglia, clinicians and medical professionals alike consider HIV-dementia as a subcortical dementia [1]. In consequence, the cognitive profile of HIV infection can manifest as difficulty with executive functioning, information processing speed, motor, and memory deficits [2]. One factor that complicates issues related to HAND and makes matters worse is that while individuals are living longer with HIV as a result of increased life expectancy, other neurocognitive disorders may develop as a result of a synergistic interaction between HIV and aging [3]. Most concerning recently is the virus's impact on executive functioning, as this is a domain that is commonly impacted by HIV-Associated Neurocognitive Disorders (HAND) in the post-HAART era, including skills like set-shifting and mental flexibility.

The U.S. Census Bureau [4] reported that approximately 50.5 million Hispanics currently live in the United States (U.S.), making America the world's fifth largest Hispanic population, while Mexico has the larger number with 117 million individuals speaking Spanish. In fact, recent estimates indicate that there has been a substantial increase of Spanish-speakers in the United States to 37.5 million and it continues to be the second most frequently spoken language other than English [5]. U.S. Census Bureau [4] expects the number of Hispanics in America to increase to over 100 million by the year 2050, equating to nearly 30 percent of the total U.S. population. As the number of U.S. Spanish-speaking citizens increases, there is a growing concern for clinicians to providing appropriate psychological services to individuals in the Spanish-speaking population [6-12].

Spanish-speakers in the U.S. are more likely to get tested in later courses of the, are more likely to have current opportunistic infection, and also are at greater risk for developing HAND [13]. In both the United States (US) and Los Angeles County (LAC), about a third of Hispanics test later for HIV in the course of their illness in comparison to the general population and are diagnosed with AIDS within one year of testing positive [14]. Collectively, Hispanics in LAC have less than a

***Corresponding author:** Enrique López, Assistant Professor, Department of Psychiatry and Behavioral Neurosciences at Cedars Sinai Medical Center, Thalians Health Center 8730 S Alden Dr., Room E-142, Los Angeles, CA 90048, USA, Tel: 310-993-8451; Fax: 310-423-8397; E-mail: lopeze@cshs.org

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high-school education and have the highest rates of poverty [4]. Within the adult age range, Spanish monolinguals tend to be foreign born, recent immigrants, and poorly educated. As a result, clinicians have been cautioned that it may be unethical to utilize certain instruments with U.S. Hispanic populations and to take this into consideration when interpreting test results [7]. Adding to the concern, there are still a limited number of neuropsychologists that are adequately trained and prepared to assess Spanish-speakers with HIV infection [15].

It is critical for clinicians to have adequate assessment tools that have been developed for Spanish-speaking populations living with HIV/AIDS [16]. As neurocognitive impairment and disorders are frequent complications of HIV infection, with a 50% incidence of HAND [17], a lack of studies assessing HAND in Spanish-speakers raises grave concerns for the overall health care of this population. Specifically, without full consideration of educational variables, neuropsychology runs the risk of finding brain pathology where merely educational differences exist [18], as it is generally agreed that literacy and educational levels may be reflected in psychoeducational and neuropsychological testing [19].

In an effort to reduce the impact of education and sociocultural variances in neuropsychological assessment of Human Immunodeficiency Virus-1 (HIV-1) positive individuals early in the epidemic, the World Health Organization (WHO) and University of California at Los Angeles (UCLA) created a neuropsychological battery that could be used cross-culturally in an ever-evolving global population [20]. The WHO and UCLA noted that this battery served to better investigate the nature and prevalence of HIV-1 related neurological, psychiatric and neuropsychological manifestations cross-culturally [20]. One of those measures was the Color Figure Mazes (CFM). The CFM was created to measure executive functioning that does not require the use of the alphabet, a number system, and/or having to read. Given the diversity of individuals with HIV in the United States, especially with a high-risk population such as Spanish speakers, this measure could be especially useful for individuals with limited exposure to traditional academic systems.

The CFM was created as a measure to assess executive functioning and is was modeled after both the Stroop and CTT. Briefly, the CFM has an individual sequence shapes and colors. At one point, the individual will have to alternate between sequencing both shapes and colors simultaneously, assessing set-shifting and mental flexibility. Unlike the CTT and the Stroop, the CFM does not utilize numbers and letters in the measure, removing educational biases for individuals that do not readily utilize Arabic numbers and/or the alphabet due to difference in formal educational attainment.

The present study examines utilizing the CFM in detecting HAND among Spanish-speaking individuals compared to traditionally used executive measures such as the Stroop and the Color Trails. We hypothesize that the CFM will be able to detect significant difference between individuals with HAND and those without HAND (non-HAND). Additionally, we hypothesize that the control participants will perform significantly better than those with HAND but not the non-HAND group.

## Method

### Participants

This study included 100 Spanish-Speaking HIV seropositive participants [(80 males, 11 females, 9 Transgender), mean age=44.95 years, SD=7.63, age range: 28-62 years; mean education=10.24 years, SD=3.36, education range: 1-20 years; mean Vocabulary subtest score=33.36SD=12.23; mean current CD4=479.93 SD=224.22; mean Beck Depression Inventory score=12.68, SD=9.81, mean Cognitive Difficulty Scale score = 54.14 SD=30.22, and 65.1% had an undetectable HIV viral load] living in the Los Angeles area at the time of assessment. Of this sample, the country of origin is as follows: Mexico 71%, Central America 23%, South America 6%. For the HIV seronegative controls the country of origin is as follows: Mexico 51.9%, Caribbean 3.7%, Central America 37%, South America 7.4%. For the demographic characteristics of the three different groups (HIV-, non-HAND and HAND) see Table 1.

### Procedures

All participants successfully pre-screened for the study were provided with an informed consent form approved by CSMC IRB. Eligible participants were assessed using two batteries (a comprehensive neuropsychological testing and a psychosocial battery). The neuropsychological battery consisted of the following: indicator of premorbid intelligence (Vocabulary WAIS-III [21]); auditory memory (Logical Memory [22], Rey Auditory Verbal Learning Test [23]); visual memory (Visual Reproduction [22], Picture Memory Interference Test (PMIT) [24]); working memory (N-Back [25]); Attention (Digit Span

| Characteristic | HIV- | NON-HAND | HAND | *p* |
|---|---|---|---|---|
| *N* | 27 | 53 | 47 | |
| Age (years) | 42.15 (12.10) | 44.72 (7.68) | 45.21 (7.66) | .502 |
| Education Level (years) | 11.78 (3.30) | 9.74 (2.62) | 10.81 (3.99) | .018 |
| Pre-morbid IQ (Vocabulary) | | 35.66 (11.44) | 30.77 (12.70) | .074 |
| CD4 Cell Count | - | 475.45 (232.50) | 484.51 (218.08) | .852 |
| CDS | 48.19 (27.43) | 53.89 (28.96) | 54.43 (31.88) | .652 |
| BDI | 9.41 (8.32) | 12.32 (10.05) | 13.09 (9.62) | .269 |
| Nondetectable Viral Load (%) | - | 51.8 | 48.2 | .651 |
| Gender (%) | | | | |
| Male | 70.4 | 79.2 | 80.9 | |
| Female | 18.5 | 11.3 | 10.6 | |
| MTF | 11.1 | 9.4 | 8.5 | |

Note. Means (Standard Deviations) and %. CDS = Cognitive Difficulty Scale. ND=Non-detectable (≤50). BDI=Beck Depression Inventory. MFT =Transgender Identity Male-to-Female. *Statistically significant at $p<.05$

**Table 1:** Sociodemographic and Medical Characteristics of the Participant Groups and Analysis of Variance (ANOVA) and Chi-Squares p values for Characteristic differences between HIV-, NON-HAND and HAND Groups infected with HIV.

and Spatial Span forward and backward [21], Continuous Performance Test II (CPT-II) [26]); Frontal Lobe functioning (Color Trails [27], Color Figure Mazes [24], Wisconsin Card Sorting Test (WCST) [28], and the Stroop Test [29]); Visuospatial Skills (WAIS-III Block Design and Matrices [21]); Verbal Fluency (COWAT) [30]; language (Boston Naming Test [31]); Processing Speed (WAIS-III Symbol Search and Digit Symbol [21]); Fine and Gross motor functioning (Grooved Pegboard [32], Finger Tapping Test [33], Timed Gait [34]).

In addition, participants completed psychosocial measures and a structured clinical psychiatric interview. The psychosocial battery consisted of a demographic measure, SCID-I (SCID) [35], the State Trait Anxiety Inventory (STAI) [36], the Profile of Mood States (POMS) [37]; the Structured Interview Guide for Hamilton Depression and Anxiety Scales (SIGH-AD) [38], Beck Depression Inventory (BDI) [39], self-report of the Cognitive Difficulties Scale (CDS) [40], adherence measures, substance and drug abuse history questionnaire, smoking questionnaire, a questionnaire of daily activities, bilingualism questionnaire, and the Marin-Marin Acculturation Scale [41].

Participants in the study were recruited from AIDS Service Organizations (ASO), including UCLA, Harbor-UCLA Medical Center, AIDS Project Los Angeles (APLA), and local physicians that provided their patients with the study's contact information. In addition, participants contacted CSMC in response to research advertisements in the community. All participants successfully pre-screened for the study were provided with an informed consent form written in Spanish approved by CSMC IRB. The study inclusion criteria included the following: 1) primary Spanish-speaking women and men, ages ≥ 18 years of age and willing to provide documentation of HIV-1 serostatus; 2) Spanish as their primary language in terms of speaking, reading and writing and 3) late symptomatic CDC clinical disease stages B and C of HIV-1 infection per patient report and/or medical record of opportunistic infection. The exclusion criteria in this study were:1) systemic, acute opportunistic infection or tumor requiring chemotherapy; 2) CNS infections or tumors associated with HIV infection that would interfere with NP testing or completion of the study procedures; 3) severe HAD as indicated by American Academy of Neurology 2007 criteria [42]; 4) non-HIV-associated neurological disease [e.g., history of epilepsy; non-correctable visual or hearing impairments; prior cerebrovascular accident; Alzheimer's disease]; 5) history of or current major psychiatric disorder [e.g., schizophrenia; bipolar affective disorder; major depressive disorder with melancholia]; 6) mental retardation, learning disorders, and pervasive developmental disorder; 7) current alcohol or substance dependence (per the standardized psychiatric interview [35] modified for the DSM-IV as well as a history of alcohol or substance abuse within the past three months; 8) collagen vascular disease; 9) severe chronic obstructive pulmonary disease (i.e., resting hypercarbia, O2 or steroid dependency); 10) severe congestive heart failure (class IV); 11) unstable angina; 12) myocardial infarction (within prior 6 months); 13) use of systemic steroids—catabolic or anabolic; 14) hepatic failure; 15) renal failure; and 16) use of immunostimulant therapies or participation in trials of non-FDA-approved antiretroviral medications.

Trained bilingual English and Spanish-speaking neuropsychologists and doctoral level clinical psychology students administered the comprehensive neuropsychological battery that was approximately 5-8 hours in duration. Participants were scheduled for a comprehensive neuropsychological assessment starting at approximately 9 AM to control for diurnal variation. Participants signed an informed consent before any procedures were initiated. Participants were compensated for completing the assessment and given a parking validation and meal voucher redeemable from the CSMC cafeteria for the day of assessment. The Institutional Review Board at Cedars Sinai Medical Center approved this study. Support for this study was provided from the National Institute of Mental Health (K23 MH087290) entitled: "HIV Neurocognitive Disorders among Primary Spanish-Speakers in Los Angeles."

## Classification of NON-HAND and HAND

To determine HAND status, the current recommended nosology for HIV-associated neurocognitive disorders was used [42]. HIV-associated asymptomatic neurocognitive impairment (ANI) and HIV-1-associated mild neurocognitive disorder (MND) require an individual's cognitive performance to be greater than one standard deviation but less than two standard deviations in at least two ability domains for age-education-appropriate norms on standardized neuropsychological testing and no evidence of another preexisting cause, with the only difference being that cognitive impairment does not interfere with daily function in the ANI group and mild impairment in daily functioning in the MND group. For a diagnosis of HIV-1-associated dementia (HAD), the individual's cognitive performance demonstrates marked impairment in at least two ability domains (with at least two standard deviations or greater in demographically corrected means), and marked interference with daily function in multiple areas (i.e., work, home life, social activities), without evidence of another preexisting cause for the dementia.

Participants were administered a comprehensive neuropsychological and psychosocial battery as previously mentioned to determine level of impairment. The cognitive and functional domains measured were the following: 1) attention/working-memory; 2) speed of information processing; 3) episodic memory; 4) abstraction/executive functioning; 5) language; 6) visuo-spatial abilities; 7) motor functioning; and 8) cognitive functional status. It is important to note that one domain may be represented by two or more measure. Per individual, each measure was compared to available normative data (see Table 3 for list of measures per domain and normative data used to compare each score). An impaired domain score then was derived by calculation if most measures in that domain were impaired (if the frequency of each measure was equal or greater than 50% in the impaired range). If participants met criteria for ANI, MND, or HAD they were classified as HAND. If they did not meet diagnostic criteria for any HAND disorder they were classified as Non-HAND.

## Measures

**Biological markers:** Participants were administered a comprehensive assessment battery that comprised three sections: a medical record review, a neuropsychological battery, and a psychosocial/psychiatric evaluation (see above list). Clinical laboratory measures used to confirm HIV-1 serostatus included in the medical record review were current plasma HIV-1 RNA load using the real time polymerase chain reaction technique (PCR) and CD4, including CD4 nadir, and CD8 counts (by flow cytometry), per medical record review.

### Executive neuropsychological measures

**Color figure mazes:** One of the measures in the WHO neuropsychological battery was the Color Figure Mazes (CFM) [24]. The CFM is a measure that integrates components of the Stroop Test and the Trail Making Test and Color Trail Test. The CFM is different in that it does not require individuals to be able to read the stimuli presented and to be familiar with Arabic numerals and the alphabet.

For example, the Trail Making Test requires individuals to sequence between number and letters, specifically the English alphabet. The traditional Stroop measures require individuals to read the stimuli. Even though certain modification have been done to correct the Stroop and the Trail Making Test by creating different language versions for diverse speaking populations, these modifications may still impact individuals with limited education who are not as familiar with the alphabet, numbers and reading. On the CFM, the individual is only required to alternate between figures and a sequence of colors, instead of connecting numbers and letters, or reading words. It requires participants to respond to progressively difficult non-verbal tasks that measure immediate attention, concentration and the ability to consciously alternate between two types of stimuli simultaneously. For CFM Trial A, the participant is simply required to connect a figure at the beginning of a maze to the last figure, assessing for gross motor writing skills. Trial B requires individuals to connect from one figure to the next until the end (measuring sustained attention). For Trial C, the participant is required to choose between squares and circles and alternate between them (assessing for selective attention). A sequencing task is required for Trial D, where the individual is required to complete the maze while in a sequence of three colors (pink, yellow and blue). Lastly, Trial E introduced the increased difficulty of having to complete the maze by selecting figures (i.e., squares and circles) while at the same time sequencing colors (i.e., pink, yellow and blue), requiring simultaneous set-shifting and the highest executive demand—divided attention (see Figure 1 for all trials). Again, strengths of the CFM is that it does not require knowledge of the US English alphabet and Arabic numeral in its applicability for use with linguistic minorities and is more culturally appropriate for individuals with low literacy levels and those with low educational levels.

**Stroop task:** The Stroop Color and Word Test [29] is based on the observation that individuals can read words with greater speed than they can identify and name colors. The cognitive dimension tapped by the Stroop is associated with cognitive flexibility, resistance to interference from outside stimuli, creativity, and psychopathology all of which influence the individual's ability to cope with cognitive stress and process complex input. The Stroop can be used as a screener or as part of a general battery, as it is quick and easy to administer. Further the Stroop's validity, and reliability make it a highly useful instrument.

The Stroop Color and Word Test consists of a Word Page (Part A) with the name of color words printed in black ink, a Color Page with 'Xs' printed in color, and a Color-Word Page with words from the first page printed in colors from the second page (the color and the word do not match). The examinee looks at each sheet and moves down the columns, reading words or naming the ink colors as quickly as possible. The test yields three scores based on the number of items completed on each of the three stimulus sheets per a 45 second interval. In addition, an Interference score, which is useful in determining the individual's cognitive flexibility, creativity, and reaction to cognitive pressure, can also be calculated.

**Color trails test:** The Color Trails Test [27] is often described as a culture-fair measure of visual attention, graphomotor speed and

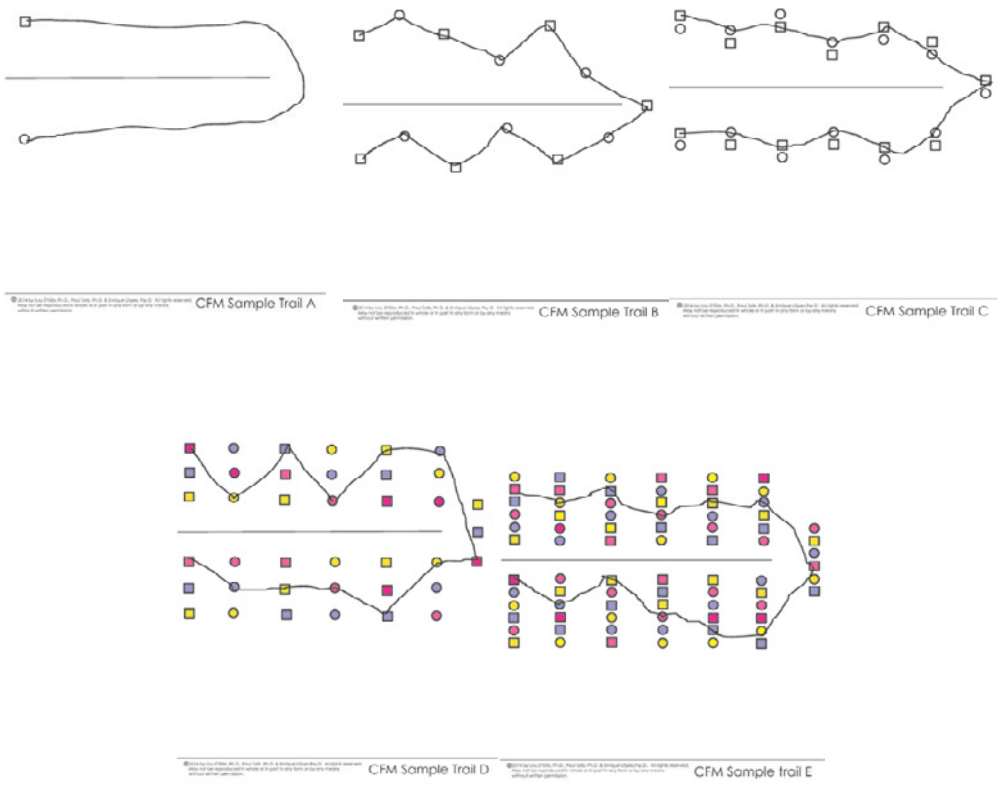


**Figure 1:** The participant is to alternate between Square-Circle, Square-Circle and etc., and Pink-Yellow-Blue, Pink-Yellow-Blue, and etc.

sequencing, as well as executive functioning as compared to the TMT [43]. Familiarity of the Arabic numeral and the English alphabet is mandatory for examinees, therefore individuals unable to count and whose written language does not include the English alphabet are precluded from taking the test. There are two parts to the CTT called Color Trails 1 and 2 (CT1, CT2).

In CT1 examinees are provided a page with scattered numbered circles from 1 to 25, with even-numbered circles colored yellow and odd-numbered circles colored a vivid pink. The examinee is required to connect the numbers as quickly as they can. During CT2, examinees are again provided a page with scattered numbered circles from 1 to 25 twice, with one sequence in yellow and the other in pink. The examinee is required to connect the numbered circles from 1 to 25 alternating between pink and yellow circles, while disregarding the numbers in circles of the alternate color.

### Statistical analysis

A number of control variables were examined for their influence on the outcome measure and for their potential utility as covariates. These included sociodemographic and clinical background characteristics (e.g., age, educational level, pre-morbid IQ, current CD4 cell count, current ART treatment per undetectable viral load, cognitive complaints, and depression). Transformations were employed, where possible and necessary, to ensure that distributional assumptions were met for the statistical tests used. Where normalization was not effective, non-parametric statistical tests were performed. The general linear model Analysis of Covariance (ANCOVA) used to statistically control for pre-morbid IQ (WAIS-III Vocabulary), because it a better indicator of an individual quality of education and pre-morbid cognitive abilities. When variability between groups was not equal (as determined by a Levine test), a modified *F* ratio (a Welch test) was calculated.

## Results

Demographic and clinical characteristics were compared between HIV-seronegative controls, HAND and non-HAND participants using a between factors one-way ANOVA (comparing group means) or Chi-square test of independence (comparing frequencies) (Table 1). No differences were found between groups with respect to age, pre-morbid IQ, current CD4 cell count, complaints of cognitive difficulties (Cognitive Difficulties Scale [CDS]), depression (Beck Depression Inventory II [BDI-II]) , and non-detectable plasma viral load (%). The HAND group was statistically different compared to the non-HAND group in years of education ($p$ = 0.018) as noted by the pre-morbid IQ. It is important to note that education was not statistically different between individuals with HAND versus those that did not meet the criteria for HAND. The only significant difference on years of education was between the non-HAND and the HIV-seronegative group.

On the NP measures that assess executive functioning, main results from the group comparisons are shown in Table 2. For the majority of test measures, there was a statistically significant difference between the HIV-seronegative, non-HAND, and HAND groups using an Analysis of Covariance (ANCOVA) statistically controlling for pre-morbid IQ. Means and standard deviations are also presented in all groups. Post-hoc analyses are included in Table 2 to show which groups significantly differed on each measure. A repeated-measure ANCOVA, controlling for pre-morbid IQ show a significant difference between the different groups across each level of the CFM trials (see Figure 2).

## Discussion

This study explored the prevalence of HAND in Spanish-

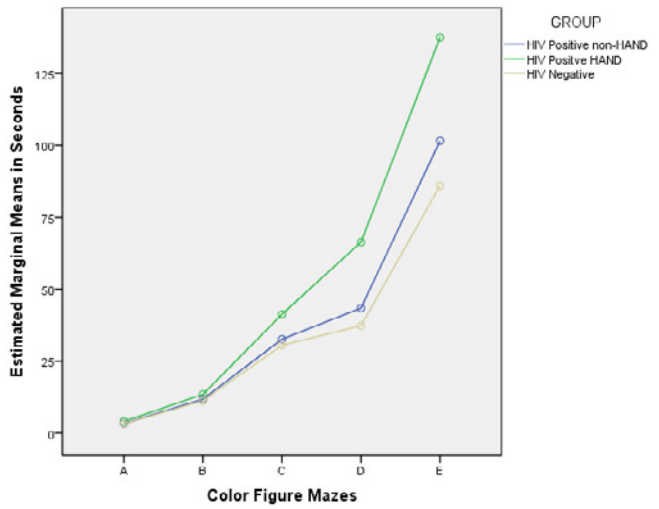


**Figure 2:** Mean difference values (seconds) for each trial of Color Figure Mazes (CFM) between the HIV-seronegative, non-HAND and HAND groups. Group differences were found on a Repeated Measures Analysis of Covariance controlling for pre-morbid IQ (p<.001, Partial Eta-Squared=0.179).

| Measure | HIV- | non-HAND | HAND | *p* | Effect Size |
|---|---|---|---|---|---|
| Color Trails 1 | 39.52 (10.18) | 42.26 (16.27) | 60.02 (24.36) | .001*[1,2,3] | .162 |
| Color Trails 2 | 99.33 (36.88) | 100.53 (33.76) | 142.74 (49.32) | .001*[2,3] | .173 |
| Stoop A | 94.19 (16.92) | 90.74 (15.36) | 78.32 (17.89) | .001*[2,3] | .106 |
| Stoop B[a] | 67.11 (13.37) | 66.04 (10.18) | 54.70 (10.69) | .001*[2,3] | .177 |
| Stroop C | 36.74 (11.07) | 37.47 (9.63) | 27.81 (8.75) | .001*[2,3] | .153 |
| CFM A | 3.15 (2.60) | 3.36 (1.79) | 4.36 (2.35) | .081 | .040 |
| CFM B | 11.19 (4.01) | 12.25 (3.89) | 14.40 (6.39) | .045* | .049 |
| CFM C | 30.07 (8.43) | 34.34 (15.00) | 44.87 (17.41) | .001*[2,3] | .112 |
| CFM D[a] | 35.37 (15.64) | 48.00 (41.10) | 78.04 (61.48) | .003*[2,3] | .092 |
| CFM E[a] | 84.00 (36.13) | 99.24 (43.78) | 141.52 (68.82) | .001*[2,3] | .144 |

*Note.* Means (Standard Deviations) for participant's Analysis of Covariance (ANCOVA) controlling for pre-morbid IQ (WAIS-III Vocabulary Subtest). CFM=Color Figure Mazes. Partial Eta-Squared was used for effect size. *Statistically significant at p<0.01. [a]Variances are not equal. Post-hoc analysis will be labeled by the following if significant: [1]HIV-seronegative versus non-HAND; [2]HIV-seronegative versus HAND; [3]non-HAND versus HAND.

**Table 2:** Means (Standard Deviations), Significance, and Effect Size using Analysis of Covariance (ANCOVA) for Neuropsychological Performance on Selected Measures while controlling for Pre-Morbid IQ (Vocabulary) raw scores.

| DOMAIN | NON-HAND | HAND | HIV- |
|---|---|---|---|
| Attention/Working Memory | | | |
| Digit Span (forward) | 7.26 (1.97) | 6.30 (1.40) | 7.89 (2.12) |
| Spatial Span (forward) | 8.08 (2.00) | 6.70 (1.49) | 8.41 (1.95) |
| CPT-II Omissions | 7.00 (14.72) | 11.05 (9.35) | 6.42 (12.25) |
| CPT-II Commissions | 10.33 (6.63) | 14.67 (7.98) | 12.38 (7.09) |
| Digit Span (backward) | 5.06 (1.93) | 3.87 (1.31) | 5.70 (2.22) |
| Spatial Span (backward) | 7.36 (1.91) | 5.32 (1.76) | 6.81 (2.08) |
| Speed of Info Processing | | | |
| Symbol Search | 23.34 (5.81) | 17.34 (8.44) | 24.44 (7.27) |
| Digit Symbol (Coding) | 53.15 (14.50) | 41.21 (14.23) | 54.30 (12.79) |
| CPT-II (Hit Rate) | 445.41 (92.82) | 456.93 (76.60) | 401.49 (49.67) |
| Episodic Memory | | | |
| RAVLT Long Delay | 9.53 (2.95) | 8.19 (2.20) | 9.11 (2.08) |
| Logical Memory Delay | 18.38 (7.21) | 12.91 (5.81) | 19.56 (5.85) |
| Visual Reproduction Delay | 29.08 (6.92) | 20.04 (8.99) | 29.26 (8.28) |
| PMIT 3 (TP) | 16.13 (2.77) | 15.27 (3.31) | 17.04 (2.03) |
| Abstraction/Executive | | | |
| Color Trails 2 | 100.53 (33.76) | 142.74 (49.32) | 99.33 (36.88) |
| WCST Perseverative Errors | 11.15 (5.39) | 16.30 (9.50) | 13.42 (6.96) |
| WCST Categories | 2.29 (1.35) | 1.76 (1.27) | 2.00 (1.52) |
| Stroop Interference | 37.47 (9.64) | 27.81 (8.75) | 36.74 (11.07) |
| Language | | | |
| Boston Naming Test | 52.81 (4.13) | 49.57 (6.50) | 52.15 (5.26) |
| COWAT (PMR) | 37.79 (9.91) | 27.66 (9.14) | 36.67 (7.93) |
| Category Fluency (Animals) | 18.21 (3.99) | 14.09 (4.31) | 17.00 (3.71) |
| Visuospatial Skills | | | |
| Block Design | 31.23 (10.76) | 21.74 (10.41) | 31.74 (8.42) |
| Matrices | 9.83 (4.31) | 7.68 (4.24) | 10.04 (4.74) |
| Motor Functioning | | | |
| Grooved Pegboard (Non-dom) | 74.60 (11.18) | 92.22 (32.42) | 78.11 (17.57) |
| Finger Tapping (Non-dom) | 45.41 (9.26) | 43.51 (11.51) | 43.49 (11.10) |
| Gait | 8.12 (1.48) | 8.71 (1.85) | 8.31 (1.98) |
| Functional Status | | | |
| MOS-HIV (Cognitive) | 16.77 (4.91) | 16.38 (4.61) | 15.92 (8.26) |
| Cognitive Difficulties Scale | 53.89 (28.96) | 54.43 (31.88) | 48.19 (27.43) |

*Note.* Means (Standard Deviations) for participant's. CPT-II=Conner's Continuous Performance Test-II. RAVLT=Rey Auditory Verbal Learning Test. PMIT=Picture Memory Interference Test. WCST=Wisconsin, Card Sorting Test.
COWAT=Controlled Oral Word Association Test. MOS-HIV=Dutch 4 Item Medical Outcomes Study-HIV.

**Table 3:** Means (Standard Deviations) for the comprehensive neurocognitive battery measures used to determine HAND status for Neuropsychological Performance.

speaking individuals, using a comprehensive neuropsychological and psychosocial battery. We further explored the utility of the CFM to detect HAND in HIV-1 seropositive individuals. The main findings in the study are: 1) Individuals with HAND performed significantly worse on the CFM compared to the no-HAND and controls; 2) there was no significant difference between the no-HAND group and the control group; and 3) The CFM appears to be as significant in detecting a difference much like the Stroop and CTT. It appears that the CFM becomes increasingly difficult for subjects to complete. This increased cognitive demand requires intact frontal lobe functioning, which appears to be impaired with individuals who were classified with HAND.

CTT and the Stroop test were included, as the CFM is an outgrowth of these two tests. As such, demonstrating convergent validity and the ability to detect HAND, in comparison to the CTT and Stroop was an important secondary outcome. As noted in the results, the CFM was as effective in detecting HAND as the CTT and Stroop, with the added component that it tends to be more culturally fair given that reading ability and Arabic numeral and alphabet knowledge are not required to perform the task. This significant finding highlights the applicability of the CFM test for use as a screener for HAND in HIV-1 seropositive Spanish speakers.

Adding to the concerns about a disproportionate and significantly increasing number of HIV infected Latinos in the United States [14], there is an additional layer of concern regarding assessment validity due to lack of adequate neuropsychological (NP) assessment instruments representing the spectrum of HAND amongst primary Spanish speakers. As neurocognitive impairment and disorders are frequent complications of HIV infection (with a 50% incidence of HAND, [44]), a lack of studies assessing HAND in Spanish raises grave concerns for the overall health care of this population. Specifically, without careful consideration of educational variables, neuropsychology runs the risk of finding brain pathology where there are only educational differences [18].

It is generally agreed that literacy and educational levels may be reflected in psycho educational and neuropsychological testing. Based on this, it can reasonably be assumed that psychometric measures of intelligence are strongly biased by education [19]. Intergroup differences are increasingly recognized in some neuropsychological measures by the inclusion of norms divided by demographic indices that include age, gender, educational level, and in some instances race and ethnicity [45]. Of note, the influence of sociocultural development and life experiences on cognitions is only recently being considered and studied systematically [46]. It has been argued that sociocultural and historical experiences influence the development of the nervous system, including cognition; and the brains, minds, and behaviors of individuals from different cultures are both similar and different [47]. Admittedly, clinical neuropsychology has not thoroughly responded to the increasing need of an ever-evolving and diverse society [7]. There is a dire need for neuropsychological literature and instruments that are designed for and norm referenced with Latinos living in the United States [6,9].

For various reasons, including socioeconomic and political, Hispanics have not achieved the level of educational attainment typically seen in the U.S. even when compared to other traditionally under-served and under-represented groups [48]. Test performance in monolingual Spanish-speakers and individuals with low educational attainment and from a low socioeconomic status can have various clinical manifestations, depending on the developmental history, quality of education, and exposure to new experiences.

These clinical manifestations may also be compounded by HIV, as is true for the participants in this study. Individuals with HAND may develop cognitive difficulties in executive functioning, processing speed, memory, language, gait, and visual disturbances. However, identifying HAND for this specific population is difficult as there are still very few neuropsychological tools created for, standardized, and normed on Spanish-speaking individuals living with HIV.

Our findings add to the literature by providing a culturally responsive measure that can be used as a source of data to detect HAND among Spanish speaking individuals. The development and use of the CFM as a screener to detect HAND is consistent with both the American Psychological Association [49] and the American

Psychiatric Association [50,51] ethical guidelines to the field for the use of appropriate norms when using neurocognitive testing to be inclusive of more than broad populations, where people should not be evaluated in a language differing from their primary language and culture. There were significant findings on the CFM in the non-HAND versus HAND group with this measure. Despite the growth of ethnic and linguistic minorities, neuropsychology as a field, whether in the clinical or research setting, has had a delayed response to the needs of these individuals [52].

Overall, CFM appears to be a sensitive measure of HAND in HIV-1 seropositive individuals indicating its utility as an HAND screening measure. As the few prior studies validating HAND screeners in a Spanish-speaking population involved only women, this validation study included both men and women, further enhancing it utility [53]. Non-significant findings on the early trials of the CFM (Trial A) may represent the ease of the test (gross motor component). Therefore, future studies may focus on expanding the sample size and heterogeneity of Hispanics, as well as include more women, and transgender individuals. Notably, the CFM can potentially have global utility to detect HAND, especially in lower resource countries.

### Study limitations

One limitation from the current study is that participants were recruited from the Los Angeles area and may not fully represent a heterogeneous sample of Spanish-speakers. Considering the majority of our participant's countries of origin consist of individuals from Mexico and Central America, a more inclusive sample of Spanish-speakers could potentially yield different results. Additionally, the difficulty of recruiting research subjects with HAD to participate in a study is relatively challenging, as our exclusion criteria required all individuals to complete the comprehensive neuropsychological assessment. It is possible these individuals' cognitive difficulties (i.e., memory, executive functioning) was a barrier to enrolling in the study, as they were required to contact the researchers independently. Further studies are encouraged to include individuals with HAND to determine the clinical utility of the CFM to aid in clarifying the degree of impairment severity between Spanish-speakers with ANI, MND, and HAD.

## Conclusion

Overall, the results from this study demonstrate that the CFM is sensitive in detecting HIV-associated neurocognitive disorders in a Spanish-speaking population with the additional benefit of being less cultural biased. The measure's ability to differentiate between the various levels of HAND is an additional benefit to diagnostic clarification within this unique cohort. The ease of administration would suit clinicians and researchers alike.

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