# Multivariate base rates of low score on neuropsychological tests of individuals with coca paste use disorder

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## Abstract

**Objective:** The aim of this study was to determine the prevalence of low scores on eight commonly used neuropsychological tests to evaluate learning and memory, language, and executive functions in individuals with coca paste use disorders (CPUD) and to identify the differences with respect to a group of healthy nonconsuming subjects (HCs). **Methods:** 162 Colombian adults with CPUD and a group of 162 Colombian adult HCs participated in this comparative study. Eight tests (eighteen test scores) were grouped into three categories: learning and memory, language, and executive functions. Each participant was categorized based on the number of low scoring tests in specific percentile cut-off groups (25$^{th}$, 16$^{th}$, 10$^{th}$, 5$^{th}$, and 2$^{nd}$). **Results:** In the learning and memory domain, 89.5% of individuals with CPUD and 55.6% of HCs scored below the 25$^{th}$ percentile on at least one of the five test scores, in the language domain, 80.7% of individuals with CPUD and 58% of HCs and in the executive function domain, 92% of individuals with CPUD and 67.3% of HCs. Having two or more scores below the 10th percentile or 10 or more at the 5th percentile shows an optimal cut-off for determining the sensitivity and specificity for discriminating between the two groups. **Conclusions**: The individuals with CPUD had a higher percentage of low scores than the HCs in the domains of learning and memory, language, and executive function. It is important for clinicians to be aware of low scores in individuals with CPUD to avoid false-positive diagnoses of cognitive impairment.



***Keywords:*** Coca paste; Substance abuse; Neuropsychology; Diagnosis, Psychometrics.

## 1. Introduction

Cocaine use disorders are considered a public health problem (United Nations Office on Drug and Crime [UNODC], 2021). The consumption of cocaine has negative consequences that can affect the activities of daily life and the quality of life of those who consume it (European Monitoring Centre for Drugs and Drug Addiction [EMCDDA], 2021, González-Saiz & Vergara-Moragues, 2021). The literature shows how the systematic and acute consumption of cocaine can cause short- and long-term cognitive deficits in attention, impulsivity, verbal learning/memory, and working memory (Potvin et al., 2014). These deficits are caused by changes in the metabolic and structural levels of the prefrontal regions (Alonso-Matías et al., 2019; Volkow et al., 2014). In 2018, Frazer et al. published a meta-analysis concluding that a general cognitive impairment in chronic cocaine users could not be confirmed due to the heterogeneity of the studies and methodological problems, pointing out the importance of further research on this topic, especially to deepen our understanding of the different routes of administration of this drug (de la Fuente et al., 2021).

The most frequent route of administration is sniffing (insufflated cocaine), but there is also a large consumption of smoked cocaine (e.g., coca paste or crack). Coca paste is a nonrefined product of cocaine mixed with other chemical impurities, which has a rapid and intense effect, generating a great dependence (López-Hill et al., 2011). In addition, the consumption of coca paste (smoked cocaine) is widespread in people with a low sociodemographic status, especially adolescents, and is very popular in Latin America (Castaño, 2000; Fukushima et al., 2014; Galvalisi et al. 2015; Schwarzkopf et al. 2018). It seems that the consumption of coca paste has effects that may be harmful to the person who consumes it (Meikle et al., 2009; Pérez, 2003). A few studies have found that cognitive impairment could result from continued use of coca paste (or smoked cocaine). De la Fuente et al. (2021) indicated that cognitive impairment has been found in different areas, such as attention, executive functions, memory, language, and social cognition. In addition, they have found differences with other consumption pathways where they have found worse attention scores in subjects consuming coca paste compared to insufflated cocaine (de la Fuente et al., 2021). Another study by Vallejo-Reyes (2019) showed lower learning scores in individuals who used coca paste and the presence of frontal behavioural syndromes (dorsolateral syndrome (executive dysfunction) and orbitofrontal syndrome (disinhibition)) compared to healthy subjects. The main problem with these studies is that the study samples were very small (fewer than 30 individuals). In Vergara-Moragues et al.'s (2021) study, compared with healthy controls, coca paste consumers have more deficits in learning and memory, language and executive functions. The consequences of presenting cognitive deficits in coca paste users may create difficulties during the rehabilitation process (Alonso-Matías et al., 2019). There is evidence that cognitive alterations in consumers are related to a worse response to treatment, leading to higher relapse rates and a higher probability of not completing treatment (Vergara-Moragues et al., 2017).

The neuropsychological evaluation of individuals who consume coca paste is very important to understand the strengths and weaknesses of these individuals; however, no universally accepted system exists for determining cognitive impairment. Consequently, low scores and the definition of impairments are inconsistently applied by clinical neuropsychologists in the area of substance abuse. Recently, there was an attempt to reach consensus on some specific recommendations for the application of uniform performance testing and for the definition of impairments, but we still need more studies in this area

(Guilmette et al., 2020). A common source of misinterpretation is that when a neuropsychological evaluation is carried out in people with substance use disorders, a large number of neuropsychological tools are used and may overestimate the possible cognitive alterations. Likewise, another mistake is to draw inferences about cognitive performance based on a single score of a neuropsychological test rather than an analysis of performance across all measures simultaneously (Brooks & Iverson, 2010; Rivera et al., 2021). Identifying these possible neuropsychological deficits in coca paste users compared to the expected cognitive functions in a nonconsuming population will be key to the implementation of future treatments (Brooks et al., 2016, Karr et al., 2017). Until now, neuropsychology professionals have understood that a low score on neuropsychology tests could be related to reduced cognitive performance. However, recent research has shown that when a group of adults is assessed with a battery of neuropsychological tests, the result may give a considerable prevalence of low scores, which could be mistakenly interpreted as low cognitive performance (Brooks et al., 2016; Guilmette et al., 2020; Oltra-Cucarella et al., 2021; Schretlen et al., 2008; Steinberg et al., 2005). A proven fact is that as the number of tests administered increases, the probability of obtaining a poor score increases, a fact demonstrated through various studies that are investigating the base rates of low scores (called multivariate base rates) (Binder et al., 2009; Brooks & Iverson, 2010; Schretlen et al., 2008). To avoid this outcome, in pediatric and adult sample groups, multivariate base rate analysis has begun to be used to control the interpretations of false-positives in assessments and to reduce the likelihood of mistakenly diagnosing individuals with cognitive deficits (Brooks et al., 2016; Crawford et al., 2012; Karr et al., 2017; Rivera et al., 2021; Rivera et al., 2019;). However, as far as we know, no studies exist that have used multivariate base rate analysis in samples with addictive disorders in general and coca paste in particular.

The present manuscript aims to fill the gap in the literature by studying the multivariate base rate among individuals with coca paste use disorder. The goal of the present study was to determine the prevalence of low scores on eight neuropsychological commonly used tests to evaluate learning and memory, language and executive functions in an individual with CPUD and to identify the differences with respect to HC adults. It is hypothesized that the CPUD group will have a higher percentage of low scores than HC adults in cognitive test performance.

## 2. Materials and methods

### *2.1. Participants*

The sample consisted of two groups (comparative design). The first group consisted of 162 Colombian adults with CPUD who at the time of the study were hospitalized in different therapeutic institutions of Bogotá and had been abstinent for 1 month. The second group consisted of 162 Colombian HC adults with a nonhistory of consumption of an illicit substance and were selected to compare their performance on the neuropsychological tests. Descriptive analyses show that the healthy sample did not differ from the individuals with CPUD in terms of age, gender, and education. The participants included in both samples were mainly men (HC n=92; 56.8% and CPUD n=108; 63.7%). The sociodemographic characteristics of both groups are presented in Table 1.

Insert Table 1.

The inclusion criteria in both groups were as follows: (a) age between 18 and 45 years old, (b) born and currently living in Colombia, (c) spoke Spanish as their native language, (d) had completed at least one year of formal education and (e) were able to read and write at the time of evaluation. The inclusion criteria for individuals with CPUD were (a) diagnosis of cocaine use disorder, accompanied by a request for treatment for addiction to coca paste as the main substance and (b) ability and willingness to sign the informed consent form. The exclusion criteria for individuals with CPUD were (a) a history of diagnosis of psychiatric conditions (schizophrenia, schizophreniform disorder, schizoaffective disorder, or delusional disorder), (b) intoxication or serious organic disease at the time of the interview, (c) history of neurological alterations not related to the consumption of psychoactive substances, (d) immediate family history of psychosis, (e) history of learning disabilities and developmental disorders or (f) concomitant use of marijuana. The exclusion criteria for the HC were (a) history of neurological or psychiatric conditions, (b) daily consumption and/or use of an illicit substance, (c) history of chronic disease (e.g., diabetes mellitus), (d) regular use of pain-killers or other medications that may impact cognitive performance, (e) severe visual and/or hearing deficit or (f) history of learning disabilities and developmental disorders. More details regarding the participants and procedure of this study have been described elsewhere in Vergara-Moragues et al. (2021). 14.2% of the individuals with CPUD have also consumed alcohol, 13.6% cannabis, 12.3% cocaine (nasal, oral, or smoked), 3.1% heroin and 1.9% inhalants.

### *2.2. Measures*

A wide range of neuropsychological tests have been applied, all of which are frequently used in research and clinical practice (Arango-Lasprilla et al., 2017). The tests were grouped into three cognitive domains (a total of 18 test scores): learning and memory, language, and executive function (Table 2).

Insert Table 2

*2.3. Procedure*

The coca paste consumer group was identified in three addictive treatment centres of Bogota, Colombia. Potentially eligible people were informed of the study goals, and once these individuals agreed to participate, they were interviewed, and the neuropsychiatric questionnaires were administered by specialized personnel. The HC group was obtained from a larger study to generate normative data for Spanish-language neuropsychological tests for the Colombian population controlling for age and educational level (Arango-Lasprilla & Rivera, 2015; Guàrdia-Olmos et al., 2015). All the ethical standards of the Declaration of Helsinki for research with people were followed. The research protocol was approved by the Research and Ethics Committee at the University of San Buenaventura (Bogota, Colombia)

*2.4. Data Analysis*

Kolmogorov–Smirnov tests were applied to evaluate normal distribution in quantitative variables (demographic and test scores) in both groups. Since most of the test scores, age, and education did not have a normal distribution, the Wilcoxon rank-sum test was used to verify that the samples did not differ either in age or in the number of years of education of the primary caregivers. The chi-square test was used to compare qualitative variables. Raw scores were converted to percentiles $(Pc_i)$ using the normative data published for HVLT-R and ROCF by Rivera et al. (2019), for M-WCST, SDMT, TMT, Stroop test by Rivera et al. (2020) and BNT, VFT by Olabarrieta-Landa et al. (2019). Percentiles $(Pc_i)$ were utilized to estimate the number of low scores (base rate low score) at various cut-off percentiles: below the 25$^{th}$, 16$^{th}$, 10$^{th}$, 5$^{th}$ and 2$^{nd}$, in each cognitive domain (learning and memory, language and executive function; see Table 2). For all comparison analyses, the effect size (*r*) for the nonparametric test was estimated (Field et al., 2012, p. 665) with a cut-off point of 0.20 as small, 0.50 as medium, and 0.80 as large effect sizes (Cohen 1992). In the chi-square test case, the effect size was estimated using the Phi correlation coefficient ($\varphi$).

To examine the discrimination of the proposed neuropsychological battery between both CPUD and HC participants, a series of receiver operating characteristic (ROC curves) studies were conducted using the number of low scores for each cut-off point (below the 25$^{th}$, 16$^{th}$, 10$^{th}$, 5$^{th}$, and 2$^{nd}$ percentiles). The area under the curve (AUC) was examined to calculate the accuracy of the ROC curve. Additionally, the Youden Index ($J$) and Index of Union (IU) were calculated to determine the optimal cut-off point for the number of low scores below the 10$^{th}$ percentile and below the 5$^{th}$ percentile to discriminate CPUD or HC participants. IU shows the optimal cut-off point (*c*) that has the maximum values of sensitivity (Se) and specificity (Sp) at the same time, minimizing the differences between them (Unal, 2017). According to Youden (1950), it is a measure that summarizes the ROC curve, and it is used to measure how effective a diagnostic marker is and allows the selection of an optimal cut-off point for that marker. Its value ranges from 0 to 1. Analyses were performed using R 4.0.5 (R Development Core Team, 2021). The *pROC* package (Robin et al., 2011) was used for analysing ROC curves.

## 3. Results

The base rates of low test scores in learning and memory, language and executive functions are presented in Table 3. The results show that HCs tend to have a lower cumulative percentage of low scores than the CPUD in learning and memory (Figure 1), in language (Figure 2) and in executive function (Figure 3) at the different cut-off points (in the 25th, 16th, 10th, 5th and 2nd percentiles) (more information in supplementary data).

Insert Figure 1

Insert Figure 2

Insert Figure 3

The Wilcoxon rank-sum test showed significant differences in the distributions of the number of low scores between the CPUD and HC participants (*p's*<.001; see Table 4), where the CPUD group presented a higher number of low scores at each percentile cut-off (25, 16, 10, 5 and 2). All comparisons showed large effect sizes (*r's*.>.48). The AUCs (see Table 4) indicated a moderate degree of accuracy in discriminating between individuals with CPUD and HCs at each percentile cut-off. ~~(25th percentile [AUC=.747; CI=.694.800], 16th percentile [AUC=.747; CI=.694.747], 10th percentile [AUC=.716; CI=.661.772], 5th percentile [AUC=.735; CI=.681.790], and 2nd percentile [AUC=.755; CI=.703.808]).~~

Insert Table 3

The Youden Index ($J$) and the Union Index (IU) are used to indicate the effectiveness of a variable and to minimize the differences between sensitivity and specificity. In this study, both $J$ and IU were used to calculate the optimal cut-off point to discriminate between HC and CPUD subjects based on the number of low scores (see Table 5). The cut-off points with the maximum Youden Index $J$ and the minimum IU showed that the optimal cut-off points for the 5th percentile were ≥10 (sensitivity =.69 and specificity =.67). For the 10th percentile, the optimal cut-off point was ≥2 (sensitivity =.75 and specificity =.60).

Insert Table 3

## 4. Discussion

The aim of this study was to determine the prevalence of low scores on eight neuropsychological commonly used tests to evaluate learning and memory, language and executive functions in individuals with CPUD and to find the differences with respect to HC adults. The results show that individuals with CPUD have greater proportions of low scores than nonusers of substances in the three cognitive domains studied. Currently, research has been conducted with samples of healthy adults from different Latin American countries with measurements of different cognitive domains (de la Fuente et al., 2021; Vallejo-Reyes, 2019), but to our knowledge, no study has used multivariate base rates of low scores in the coca paste-consuming population.

Neuropsychological assessment in people with substance use disorders is one of the fundamental aspects when considering an intervention with this population because those with cognitive alterations may not benefit from treatments in the same way. However, the precise measurement of cognitive domains must be done through normative data and with measures that minimize the probability of finding false-positives in the use of neuropsychological batteries (Rivera et al., 2021). For this, new well-established psychometric methods, such as the multivariate base rates of low scores, are needed to avoid overdiagnosis of cognitive impairment (Brooks et al., 2010). In this study, eight neuropsychological tests were applied, and a total of 18 scores were obtained, which could overestimate cognitive impairment in coca paste users. Our study confirms that, even considering the percentage of low scores in the healthy population, chronic cocaine-paste consumers present more low scores that could be evidence of the presence of cognitive deficits in this population.

In the study of De la Fuente et al. (2021), despite not using the multivariate analysis base rates of low scores, many neuropsychological tests were applied to 25 subjects who smoked cocaine. Specifically, they used a total of 19 scores, 5 of them of memory, using the same tests as in our study. They found deficits in learning and memory, but this case could overestimate the extent of neuropsychological impairment. Similar results were obtained in the study by Vallejo-Reyes (2019), where differences in the learning scores were found between coca paste users and a group of HCs. Interesting data from the study conducted by de la Fuente et al. (2021) is that they have also used a comparison group of insufflated cocaine users (another route of administration), reaching the conclusion that there are no differences in memory impairment between the two forms of cocaine administration (smoked vs. insufflated), but there are differences with respect to nonusers.

In the domain of language, the results show that there are more differences in the highest percentiles (no low score and scores below the 25th percentile). With a more stringent criterion to diagnose deficits (below the 16th percentile, below the 10th percentile and below the 2nd percentile), coca paste users have a similar percentage of low scores in language as healthy nonusers. A total of 80.7% of subjects with CPUD had one or more scores below the 25th percentile, while healthy subjects had 58%. When diagnosing the deficit with scores below the 10th percentile, the results indicate 47.8% in individuals with CPUD, compared to 33.3% in healthy subjects, even having very close values if we set as a limit the scores below the 2nd percentile (90.7% in individuals with CPUD vs. 93.8% in HCs). It is therefore important to take these results into account when diagnosing language deficits. These results may explain the contradictory results found in previous studies. In the study by de la Fuente et al. (2021), lower scores were found in language compared to healthy subjects; in contrast, in the study by Vallejo Reyes (2019), no such differences were found (measured through verbal fluency).

In the executive function domain, previous studies (De la Fuente et al., 2021; Vallejo Reyes, 2019) have confirmed alterations in this domain, although in the study by Vallejo Reyes (2019), differences were only found in the prefrontal behaviour scale, where high scores were obtained in the executive dysfunction scales (dorsolateral prefrontal syndrome) and in the disinhibition scale (orbitofrontal prefrontal syndrome). No differences were found in cognitive performance tests (Trail Making Test, STROOP, Wisconsin Card Sorting Test and Iowa Gambling Task).

The negative effects of cocaine use have already been widely demonstrated (Frazer et al., 2018; Potvin et al., 2014), but it is important to test whether the effects on cognitive performance differ according to the type of chemical composition (coca paste is a nonrefined product of cocaine mixed with other chemical impurities) and the form of administration (smoked vs. insufflated). In the study by de la Fuente et al. (2021), they found differences in the level of attention between users of smoked cocaine (coca paste) and insufflated cocaine. Subjects who consumed coca paste had lower scores in attention and executive functions (only in verbal fluency) than subjects who consumed cocaine insufflated. The authors confirm that these differential deficits are due to abnormalities detected at the brain level both at the structural level (reduction in grey matter density in the caudate nucleus) and at the functional level, producing alterations in the connectivity of the regions of the caudate-frontal circuit, which are responsible for attentional tasks and executive functions. In addition, they hypothesize that the differences may be due to the presence of active adulterants, such as cocaine, which may particularly affect the caudate-frontal neural network. According to the results found by Prieto (2020) with animal models, caffeine acts as an enhancer of the reinforcing effect of coca paste and causes changes at both the functional and molecular levels in the brain. No differences were found in the rest of the cognitive areas (neither in memory nor in language) in this study. Studies with adolescent coca paste users have identified a hyperfusion of the prefrontal circuit and limbic structures, especially in the dorsolateral prefrontal area, which may explain the cognitive deficits identified in coca paste users compared to other cocaine users (Delgado Vivas, 2011; Ferrando et al., 2009). These alterations in these areas coincide with the prefrontal behavioural syndromes detected in the study by Vallejo Reyes (2019), in which elevated scores for dorsolateral prefrontal (executive dysfunction) and orbitofrontal (disinhibition) syndrome in consumers of coca paste (smoked cocaine) were found.

In the present study, significant differences were found with the HCs regardless of the cut-off; in all of them, the CPUD group showed a greater number of scores below the cut-off than the HC group. It is important to note that in cut-offs below the $25^{th}$ percentile, the CPUD group showed a median of 7 test scores below that criterion, while the HC group showed a median of 3 (a difference of 4 scores). The same difference is shown in the $5^{th}$ and $2^{nd}$ percentiles. On the other hand, the cut-off points showing the least difference are the 16th percentile (difference of 3 scores) and the 10th percentile (difference of 2 scores). This indicates that the tests administered to evaluate the domains of learning and memory, language and executive function were sensitive to detecting the effects of consumption of coca paste. In addition, as far as we know, this is the first study of individuals with coca paste use disorder with neuropsychological impairment that has shown a strong ability to discriminate between individuals with CPUD and HCs. Specifically, having two or more scores below the $10^{th}$ percentile or 10 or more at the 5th percentile shows an optimal cut-off for determining the sensitivity and specificity to discriminate between the two groups. This demonstrates the importance of evaluating the three domains to assess cognitive deficits in coca paste users, which is essential to elaborate the appropriate therapeutic and rehabilitation goals to ensure the best recovery and avoid relapses. Additionally, these findings revealed that the neuropsychological battery is a significant classifier of CPUD versus HC, and the consideration of these base rates may be useful in making clinical inferences and reducing the likelihood of misdiagnosing cognitive impairments (Rivera et al., 2022).

The present study has several limitations that should be pointed out. The cutoff values to differentiate these groups will only be clinically applicable when these specific tests are administered. Also, in the present study, there were no differences between groups in terms of age and education. However, the IQ of the participants was not measured, which could influence the number of low scores in both groups since high IQ has been related to the presence of some low scores. Future studies should also match both groups on IQ to reduce this bias. In addition, it would have been useful to register the duration and intensity of the users' coca paste consumption as well as the comorbidity of the consumption of other substances, which may affect the cognitive development of the sample group. Performance validity measures have also not been administered. Despite these limitations, as far as the authors know, there have been no studies that have considered, in depth, the cognitive functioning of coca paste users compared to healthy groups considering sociodemographic characteristics with a large sample of coca paste-consuming subjects. No previous studies sought to establish the prevalence of low scores in the cognitive measures of both sample groups using multivariate base rate analysis. Similarly, the results obtained indicate directions for future studies. Until now, studies have shown that substance users have lower scores in cognitive functions than control groups. However, as shown in this study, it would be necessary to carry out further research using multivariate base rate analysis to avoid overestimating cognitive deficits (especially in language) by not considering that the sample of nonusers may also produce a percentage of low scores. This line of study would help identify, in a more detailed way, the real deterioration of the population of substance users.

In conclusion, our study confirms that individuals with CPUD have a higher percentage of low scores than HCs at all percentiles analysed (from the 25th to the 5th percentiles), assessing the domains of memory and learning, language, and executive functions. Clinicians working with people with substance use disorders should consider the higher probability of low scores when evaluating neuropsychological processes using several sets of scores to reduce false-positive diagnoses of cognitive deficits and reduce the likelihood of misdiagnosis. In addition, the prioritization of assessing the domains of memory and learning, language and executive function when assessing deficits in coca-pasta users is important, constituting a useful diagnostic tool for the clinical neuropsychologist when assessing cognitive deficits in this type of population.

**Declaration of interest statement**

The authors report there are no competing interests to declare.

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**Table 1.**

*Sample distribution by age, education, and Gender.*

| Variable | Group | Median | Min - Max | Statistic | *p* value | Effect size |
|---|---|---|---|---|---|---|
| Age | HC | 31 | 18-47 | 12 298 | .328 | 0.05 |
| | CPUD | 28 | 18-47 | | | |
| Education | HC | 11 | 5-13 | 25 501 | .131 | 0.08 |
| | CPUD | 11 | 5-13 | | | |
| Sex | HC | Female 70 (43.2%) | Male 92 (56.8%) | 3 345 | .067 | 0.10 |
| | CPUD | Female 54 (33.3%) | Male 108 (63.7%) | | | |

*Note*: HC: healthy control; CPUD: coca paste user disorder

**Table 2.** *Neuropsychological test applied in the study*

| Domain | Tests | Scores |
|---|---|---|
| Learning and memory | Hopkins Verbal Learning Test–Revised (HVLT-R) (Brandt, 1991) | Total recall<br>Delayed recall<br>Recognition |
| | Rey–Osterrieth Complex Figure (ROCF) | Copy<br>Immediate recall |
| Language | Verbal fluency test (VFT) (Strauss et al., 2006) | Total number of words (letter M)<br>Total number of words (letter A)<br>Total number of words (letter S)<br>Total number of words in animal category<br>Total number of words in fruit category |
| | Boston Naming Test (BNT) (Kaplan et al., 1983), | Number of correct items |
| Executive Functions | Modified Wisconsin Card Sorting Test (M-WCST) (Schretlen, 2010) | Number of correct categories obtained |
| | Stroop Color-Word Interference Test (Golden, 2007) | Words<br>Colors<br>Interference (word-color task) |
| | The Trail Making Test (TMT) (Reitan, 1992; Tombaugh, 2004) | Time (seconds) in TMT-A<br>Time (seconds) in TMT-B |
| | Symbol Digit Modalities Test (SDMT) | Final score corresponds to the number of correct substitutions registered (Smith, 2002). |

**Figure 1.** *Cumulative proportion of adults with the specified number of adjusted learning and memory low scores below the specified percentile cutoff by CPUD and HC.*

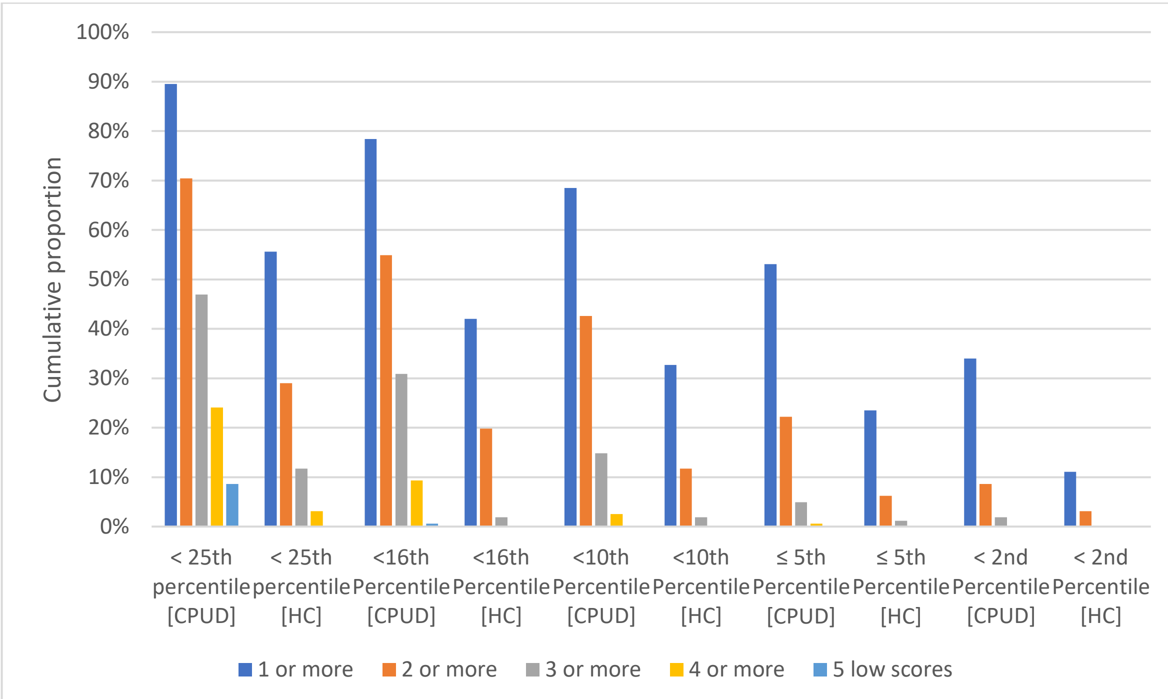

**Figure 2.** *Cumulative proportion of adults with the specified number of adjusted language scores below the specified percentile cutoff by CPUD and HC.*

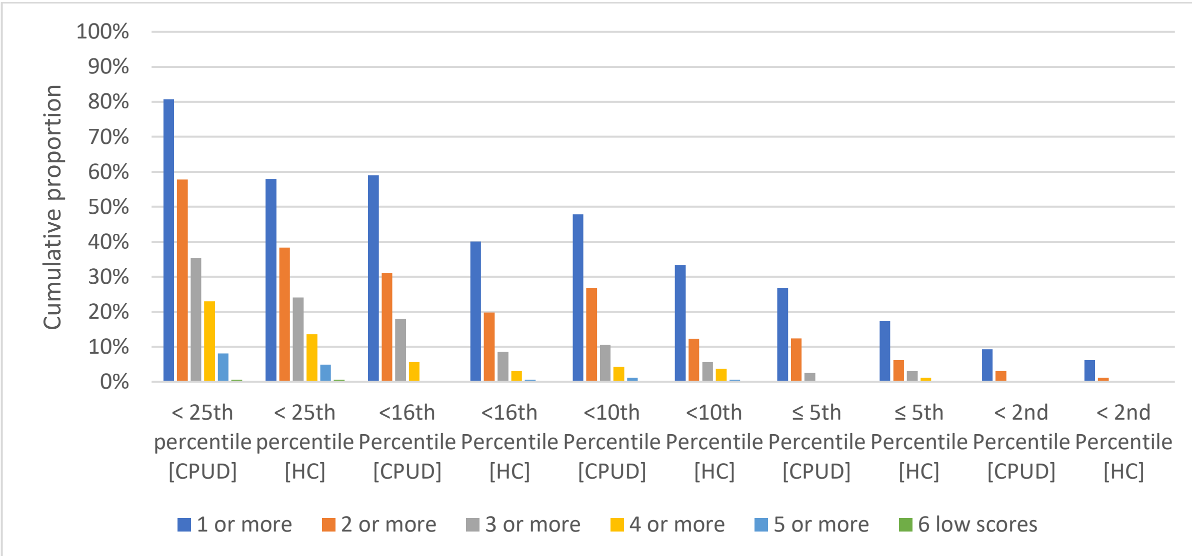

**Figure 3.** *Cumulative proportion of adults with the specified number of adjusted executive functions scores below the specified percentile cutoff by CPUD and HC.*

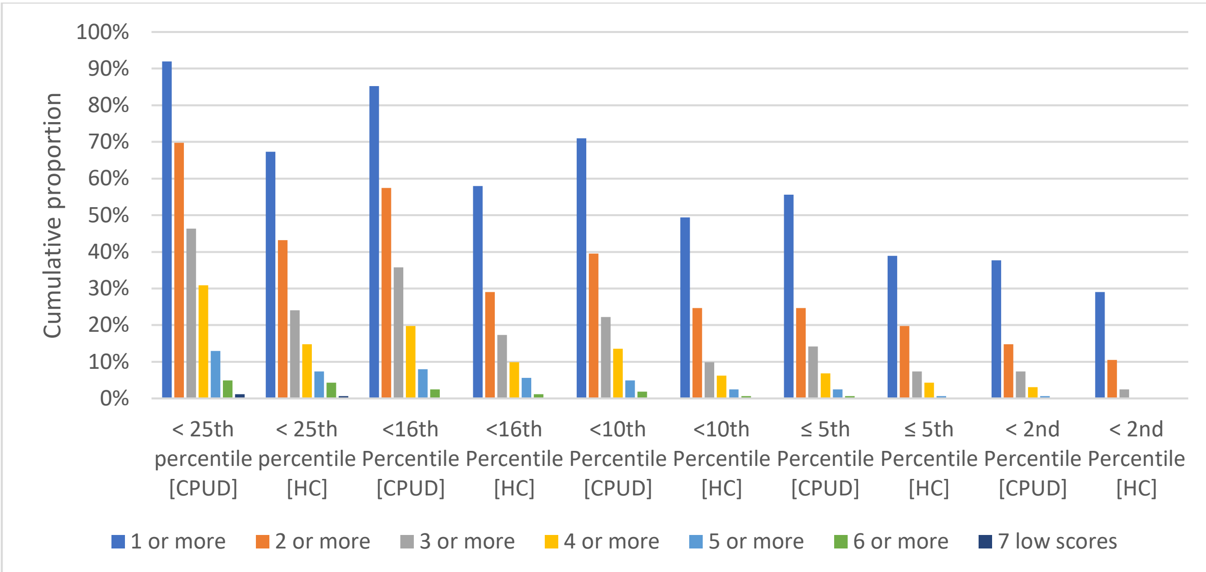

**Table 3.**

*Comparison between groups on the number of test scores falling below specified percentile cutoffs and associated ROC Curve characteristics*

| Cutoff | Group | Median | Min. | Max. | W | *p value* | Effect size (r) | ROC | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | AUC | Lower bound | Upper bound |
| **<25th percentile** | **HC** | 3 | 0 | 14 | 19 622.0 | <.001 | 0.54††† | .747 | .694 | .800 |
| | **CPUD** | 7 | 0 | 14 | | | | | | |
| **<16th percentile** | **HC** | 2 | 0 | 12 | 19 624.0 | <.001 | 0.54††† | .747 | .694 | .800 |
| | **CPUD** | 5 | 0 | 13 | | | | | | |
| **<10th percentile** | **HC** | 1 | 0 | 11 | 18 805.0 | <.001 | 0.48†† | .716 | .661 | .772 |
| | **CPUD** | 3 | 0 | 12 | | | | | | |
| **<5th percentile** | **HC** | 8 | 0 | 18 | 19 308.5 | <.001 | 0.52††† | .735 | .681 | .790 |
| | **CPUD** | 12 | 3 | 17 | | | | | | |
| **<2nd percentile** | **HC** | 2 | 0 | 14 | 19 838.5 | <.001 | 0.56††† | .755 | .703 | .808 |
| | **CPUD** | 6 | 0 | 13 | | | | | | |

*Note:* HC = Healthy Control; ID = Intellectual Disability; Min = Minimum; Max = Maximum; ††† = Large effect; †† = Medium effect; Lower bound and upper bound refer to the 95% confidence intervals of the AUC.

**Table 4.**

*Cut-points and associated sensitivity and specificity values*

| Threshold | **<10th percentile** | | | | **<5th percentile** | | | |
|---|---|---|---|---|---|---|---|---|
| | Sensitivity | Specificity | Youden | IU | Sensitivity | Specificity | Youden | IU |
| ≥1 | .56 | .78 | 0.34 | 0.22 | .04 | 1.00 | 0.04 | 0.96 |
| ≥2 | .75 | .60 | 0.35 | 0.14 | .07 | 1.00 | 0.07 | 0.93 |
| ≥3 | .81 | .48 | 0.30 | 0.33 | .12 | .99 | 0.12 | 0.87 |
| ≥4 | .86 | .33 | 0.19 | 0.52 | .21 | .98 | 0.19 | 0.77 |
| ≥5 | .90 | .27 | 0.17 | 0.63 | .28 | .96 | 0.24 | 0.67 |
| ≥6 | .93 | .17 | 0.09 | 0.76 | .39 | .92 | 0.31 | 0.53 |
| ≥7 | .94 | .08 | 0.02 | 0.86 | .48 | .85 | 0.33 | 0.38 |
| ≥8 | .98 | .05 | 0.03 | 0.93 | .54 | .80 | 0.35 | 0.26 |
| ≥9 | .99 | .04 | 0.02 | 0.95 | .61 | .74 | 0.35 | 0.13 |
| ≥10 | .99 | .01 | 0.01 | 0.98 | .69 | .67 | 0.35 | 0.12 |
| ≥11 | 1.00 | .01 | 0.01 | 0.99 | .78 | .54 | 0.32 | 0.25 |

*Note: Se = Sensitivity; Sp = Specificity; J =Youden index; IU = Index of Union.*

**Supplementary data**

*Cumulative proportion of adults with the specified number of adjusted learning and memory, language and executive functions low scores below the specified percentile cutoff by CPUD and HC.*

| | | Cumulative percent with low scores below the cutoffs | | | | | |
|---|---|---|---|---|---|---|---|
| | | **Number of Low Scores** | **< 25th percentile** | **<16th Percentile** | **<10th Percentile** | **≤ 5th Percentile** | **< 2nd Percentile** |
| Learning and memory | CPUD | No low Scores | 10.5% | 21.6% | 31.5% | 46.9% | 66.0% |
| | | 1 or more | 89.5% | 78.4% | 68.5% | 53.1% | 34.0% |
| | | 2 or more | 70.4% | 54.9% | 42.6% | 22.2% | 8.6% |
| | | 3 or more | 46.9% | 30.9% | 14.8% | 4.9% | 1.9% |
| | | 4 or more | 24.1% | 9.3% | 2.5% | 0.6% | -- |
| | | 5 low scores | 8.6% | 0.6% | -- | -- | -- |
| | HC | No low Scores | 44.4% | 58.0% | 67.3% | 76.5% | 88.9% |
| | | 1 or more | 55.6% | 42.0% | 32.7% | 23.5% | 11.1% |
| | | 2 or more | 29.0% | 19.8% | 11.7% | 6.2% | 3.1% |
| | | 3 or more | 11.7% | 1.9% | 1.9% | 1.2% | -- |
| | | 4 or more | 3.1% | -- | -- | -- | -- |
| | | 5 low scores | -- | -- | -- | -- | -- |
| Language | CPUD | No low Scores | 19.3% | 41.0% | 52.2% | 73.3% | 90.7% |
| | | 1 or more | 80.7% | 59.0% | 47.8% | 26.7% | 9.3% |
| | | 2 or more | 57.8% | 31.1% | 26.7% | 12.4% | 3.1% |
| | | 3 or more | 35.4% | 18.0% | 10.6% | 2.5% | -- |
| | | 4 or more | 23.0% | 5.6% | 4.3% | -- | -- |
| | | 5 or more | 8.1% | -- | 1.2% | -- | -- |
| | | 6 low scores | 0.6% | -- | -- | -- | -- |
| | HC | No low Scores | 42.0% | 59.9% | 66.7% | 82.7% | 93.8% |
| | | 1 or more | 58.0% | 40.1% | 33.3% | 17.3% | 6.2% |
| | | 2 or more | 38.3% | 19.8% | 12.3% | 6.2% | 1.2% |
| | | 3 or more | 24.1% | 8.6% | 5.6% | 3.1% | -- |
| | | 4 or more | 13.6% | 3.1% | 3.7% | 1.2% | -- |
| | | 5 or more | 4.9% | 0.6% | 0.6% | -- | -- |
| | | 6 low scores | 0.6% | -- | -- | -- | -- |
| Executive Functions | CPUD | No low Scores | 8.0% | 14.8% | 29.0% | 44.4% | 62.3% |
| | | 1 or more | 92.0% | 85.2% | 71.0% | 55.6% | 37.7% |
| | | 2 or more | 69.8% | 57.4% | 39.5% | 24.7% | 14.8% |
| | | 3 or more | 46.3% | 35.8% | 22.2% | 14.2% | 7.4% |
| | | 4 or more | 30.9% | 19.8% | 13.6% | 6.8% | 3.1% |
| | | 5 or more | 13.0% | 8.0% | 4.9% | 2.5% | 0.6% |

| | | | | | | |
|---|---|---|---|---|---|---|
| | 6 or more | 4.9% | 2.5% | 1.9% | 0.6% | -- |
| | 7 low scores | 1.2% | -- | -- | -- | -- |
| HC | No low Scores | 32.7% | 42.0% | 50.6% | 61.1% | 71.0% |
| | 1 or more | 67.3% | 58.0% | 49.4% | 38.9% | 29.0% |
| | 2 or more | 43.2% | 29.0% | 24.7% | 19.8% | 10.5% |
| | 3 or more | 24.1% | 17.3% | 9.9% | 7.4% | 2.5% |
| | 4 or more | 14.8% | 9.9% | 6.2% | 4.3% | -- |
| | 5 or more | 7.4% | 5.6% | 2.5% | 0.6% | -- |
| | 6 or more | 4.3% | 1.2% | 0.6% | -- | -- |
| | 7 low scores | 0.6% | -- | -- | -- | -- |

*Note*: HC: healthy control; CPUD: coca paste user disorder