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## ABSTRACT

The aims of this paper were to explore the relationship between depressive symptoms and neuropsychological performance in a sample of HIV-infected women, and to examine the contribution of demographic, HIV-related variables, and depressive symptoms to neurocognitive performance. In this cross-sectional study, a sample of 103 HIV-infected women, recruited from February to December 2010, was assessed for depressive symptoms [with the Beck Depression Inventory] and neurocognitive performance [with the HIV Dementia Scale]. Severe depressive symptoms were reported by 31.1% of the women. Findings indicated that severe levels of depressive symptoms were significantly associated with reduced cognitive functioning in HIV-infected women, particularly in domains of attention, psychomotor speed, and construction. Older age and low education level were significantly associated with neurocognitive impairment in univariate analyses. In the multivariate model, only depressive symptoms were a significant independent risk factor for neurocognitive impairment. Compared to participants with none/minimal depressive symptoms, those with moderate and severe depressive symptoms had an odds ratio (OR) of 5.03 (95% CI, 1.33-18.99) and 3.22 (95% CI, 1.15-9.06), respectively. These findings support continued investigation of the presence of neurocognitive impairment, particularly among women, and may help mental health providers with early detection, planning, and implementation of more effective interventions.

Keywords: Depressive symptoms; HIV/AIDS; Neurocognition

#### **INTRODUCTION**

Living with HIV often includes co-morbidity with several psychiatric conditions, and one of the most prevalent is depression (Ciesla & Roberts, 2001; Treisman & Angelino, 2007). This high prevalence exists across countries, despite cultural differences and differences in diagnostic criteria, measures, and samples (Rabkin, 2008). Since the introduction of Highly Active Antiretroviral Therapy (HAART), in 1996, a decrease in depression has been suggested (Judd et al., 2000); however, depression remains significantly associated with poorer treatment outcomes, lower adherence and increased mortality (Hinkin et al., 2002).

The growing number of new HIV infections among women has focused more research on depressive symptoms in this population (Benton, 2008). As in general population studies (e.g., Kessler et al., 2003), depression rates among HIV-infected women are high, and evidence suggest that women may be more vulnerable than men to the onset of depression during HIV disease (Ickovics et al., 2001; Morrison et al., 2002; Valverde et al., 2007). In HIV samples, the literature has shown significant differences, with more women reporting depressive symptoms than men (Pereira & Canavarro, 2011; Valverde et al., 2007; Wisniewski et al., 2005), and a recent study focusing on serodiscordant and seroconcordant couples has shown that women reported higher levels of depressive symptoms, regardless of their partner's HIV status (Li, Liang, Lee, & Farmer, 2012). However, in the HIV literature, there also evidence of no gender differences in depressive symptoms (Haug et al., 2005).

HIV/AIDS also has detrimental effects on neurocognitive function (Gibbie et al., 2006; Grant, 2008), most particularly in the domains of motor function, attention, speed of information processing, executive functioning, and memory (Woods, Moore, Weber, & Grant, 2009). Also, neuropsychological studies have confirmed that cognitive impairment occurs in a substantial (15-50%) proportion of patients (Schouten et al., 2011). Worldwide, the knowledge of neurocognitive complications of HIV infection is fundamentally based on studies involving men, and women are still under-represented in neuropsychological studies of HIV (Maki & Martin-Thormeyer, 2009). Therefore, it is critical to gather additional information about women's neurocognitive performance to improve their mental health, quality of life, and adherence to treatment.

In addition, one study (Faílde-Garrido, Alvarez, & Simón-Lopez, 2008) reported a different pattern of neuropsychological impairment among HIV-infected men and women: men reported worse results in visual memory, attention, psychomotor speed, and abstracting reasoning, and women reported greater impairment on attention, verbal memory for the texts, and psychomotor speed. Thus, and consistent with the recent observation of Martin et al. (2011), different patterns of performance cannot always be generalized from men to women.

There is some evidence that women may be more vulnerable to the development of neurocognitive disorders, particularly due to greater psychiatric morbidity, lower socioeconomic level, and lower cognitive reserve due to lower education and premorbid intelligence (Basso & Bornstein, 2000; Farinpour et al., 2003; Satz et al., 1993). However, a review of studies by Maki and Martin-Thormeyer (2009) has revealed a paucity of studies of HIV and neurocognitive performance involving all-female samples. The authors have identified six studies that involved a cross-sectional design and compared HIV-infected women with seronegative controls. Overall, some studies have reported no evidence of impairment among HIV-infected women (Mason et al., 1998; Stern et al., 1998), and other studies have found that impairment was most evident on psychomotor tasks (Durvasula et al., 2001; Richardson et al., 2002). Richardson et al. (2005) have shown that the risk of cognitive impairment was greater among HIV and Hepatitis C virus (HCV) co-infected women.

Depressive symptoms are a risk factor for neurocognitive impairment in HIV-infected individuals (Bragança & Palha, 2011; Vásquez-Justo et al., 2003; Waldrop-Valverde et al., 2005); however, research has produced mixed findings, with some studies being unable to identify any significant association between depressive symptoms and neurocognitive impairment (Applebaum et al., 2010; Ammassari et al., 2004; Carter et al., 2003; Cysique et al., 2007) or identifying only a minimal association (Goggin et al., 1997). Although these studies have examined the combined effect of HIV and depressive symptoms on neurocognitive performance, to our knowledge, none of these studies examined this specific relationship in an all-female sample.

Depressive symptoms, however, are not the only factor associated with impaired neurocognition. In fact, several demographic and HIV-related factors have been associated with neurocognitive impairment. These include: older age (Fazeli et al., 2011; Lopardo et al., 2009; Richarson et al., 2002), lower education (De Ronchi et al., 2002; Tozzi et al., 2007; Waldrop-Valverde et al., 2010), professional situation (Heaton et al., 2011; Woods et al., 2011), ethnicity (Durvasula et al., 2001; Manly et al., 2011), and HIV/HCV co-infection (Hinkin et al., 2008; Richardson et al., 2005). Although inconsistent, some studies have also found an association between neurocognitive impairment and lower CD4 count (De Ronchi et al., 2002; Fazeli et al., 2011; Njamnshi et al., 2009; Osowiecki et al., 2000), and higher plasma viral load (Marcotte et al., 2003; Tate et al., 2011). However, although there is a clear improvement of the understanding of HIV-associated neurocognitive disorders, and it was well established that HIV can cause a cognitive decline due to its direct action in the brain (Woods et al., 2009), it is important to know if depressive symptoms and other factors (particularly, demographic and clinical variables) also contributes to the prevalence of neurocognitive impairment. In addition, since studies that have examined the combined contribution of these factors among HIV-infected women are scarce, examining such factors from a female perspective can help health professionals to identify the underlying risk and protective factors that may predict neurocognitive impairment, which is important to improve disease management and clinical care, and to facilitate treatment decision making.

Therefore, the aims of this study were: (1) to assess the presence of depressive symptoms and neurocognitive impairment and to explore the association between severity of depressive symptoms and neurocognitive performance; and (2) to examine the influence of demographic and HIV-related variables on neurocognitive performance. We hypothesized that: (1) HIV-infected women with depression would show more impairment on neurocognition than those without depression; and (2) neurocognitive impairment would be associated with both demographic and clinical variables, particularly, older age, lower education, unemployment, HIV/HCV co-infection, and lower CD4 T cells count.

#### METHODS

#### Study Participants

Consecutive patients who attended the Infectious Diseases Service (IDS) of the Portuguese National Health System Hospital (Lisbon), between February 2010 and December 2010 were approached and invited to participate in the study by the first author (n = 156). Eleven participants

were considered ineligible because of administrative reasons (illegal situation). Of those eligible, 21 participants refused to participate in the study (refusal rate = 13.5%; the main reasons for not participating was lack of interest and lack of time), and 21 participants were excluded because of missing data > 20% in Beck Depression Inventory. The final sample consisted of 103 participants, representing a response rate of 71% among eligible patients. The women excluded from the analyses did not differ in age or sociodemographic characteristics from those who participated in the study. The general inclusion criteria were age (over 18 years) and enough knowledge of Portuguese to complete the assessment protocol. Those participants who presented, or had presented neurological or medical pathologies (including psychiatric disorders, such as schizophrenia, bipolar disorder, etc.) that could affect the CNS, and had current use of illegal drugs were excluded from the study. These criteria were found consulting the individual medical records and by a brief pre-assessment interview conducted by the first author. The assessment protocol was administered by a trained psychologist (first author) in one 45-minute session.

All participants invited to the study signed a letter of consent presenting the objectives of the study, as well as their roles and the researchers' obligations. The Ethics Committee of the Hospital provided ethical approval for the study protocol.

#### Measures

The following demographic variables were assessed: age, education, ethnicity, marital status, employment status, time since HIV diagnosis, HIV status disclosure (categorized as disclosed to no-one; disclosed to at least one person), HAART adherence, current CD4+ T cell count, and current viral load. HIV-related information was obtained from the medical records.

*Depressive Symptoms*. The Portuguese version of the Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961) was used to assess the prevalence and severity of depressive symptoms. Respondents were required to rate 21 items from 0 to 3, according to how they had felt during the previous two weeks. The total scores ranged from 0 to 63. Using summated BDI scores, and according to the cut-off scores of the Portuguese version (Vaz Serra & Pio Abreu, 1973), participants were categorized into one of the three depressive symptom groups: (1) none/minimal depression (BDI scores of 0-9); (2) mild/moderate depression (BDI scores of 10-29); and (4) severe

depression (BDI scores of 30-63). The BDI is widely used and numerous studies have demonstrated its reliability and validity for assessing depressive symptoms in clinical and non-clinical samples.

*Neurocognitive performance*. The HIV Dementia Scale (HDS; Power et al. 1995) is a brief screening measure designed for the detection of dementia in HIV-infected individuals. The HDS is comprised of four tasks that evaluate the domains of memory (recall of four items at five minutes), attention (antisaccadic errors), psychomotor speed (timed written alphabet), and construction (cube copy time). A subscore and sum score were calculated for each domain. A score  $\leq 10$  points is suggestive of HIV associated cognitive impairment or dementia and would warrant additional neurologic assessment.

#### Data Analysis

Data were analyzed using the Statistical Package for Social Sciences (IBM SPSS 20.0). To describe the characteristics of the sample, analysis of frequencies, mean (M), median, and standard deviations (SD) were first performed. A two-way contingency analysis ( $\chi^2$ ) was conducted to assess whether impaired or unimpaired patients differed on categorical variables, and Student's t test or Mann-Whitney test were performed to compare both groups in continuous variables. Univariate analysis of variance (ANOVA), and multivariate analysis of variance (MANOVA) were also performed. MANOVA was used to test for group differences (categories of depressive symptoms as between-participant's factors) in the different HDS sub-tests. Subsequent ANOVAs were conducted to identify the source of the multivariate effect. The combined contribution of demographic, HIV-related characteristics and depressive symptoms on neurocognitive impairment were assessed through a stepwise multiple logistic regression model. Potential confounders, identified as those significantly associated with the dependent variable at p < 0.25 in univariate analyses or theoretically linked to the dependent variable, were entered into the multivariable model. Two steps were conducted: demographic and HIV-related variables were entered in the first step, while depression categories were entered in the second step. The results are shown as odds ratios (OR) with 95% confidence intervals (CIs). The model's goodness of fit was measured with the Hosmer-Lemeshow test.

Using the G\* Power program (Faul, Erdfelder, Lang, & Buchner, 2007), post hoc power calculations demonstrated that with a significance level of .05 and power  $\geq$  .80, the achieved sample

size allowed for the detection of medium to large effects. Effect sizes are presented for all analyses (small effects:  $\eta^2 \ge 0.01$ , Cohen's  $d \ge 0.20$ , Cramer's  $V \ge 0.01$ ; medium effects:  $\eta^2 \ge 0.06$ , Cohen's  $d \ge 0.50$ , Cramer's  $V \ge 0.03$ ; large effects:  $\eta^2 \ge 0.14$ , Cohen's  $d \ge 0.80$ , Cramer's  $V \ge 0.05$ ) (Cohen, 1992).

## RESULTS

#### Sample characteristics

The sample consisted of 103 HIV-infected women, with a mean age of 43.86 years (range: 22-80). Most of these women had been infected through sexual contact (95.1%). The overall sample characteristics are presented in Table 1. All women were receiving HAART therapy at the time of enrolment, and 82.5% (n = 85) have reported to fully adhere to treatment. Twenty-eight women (27.2%) had not yet disclosed their HIV status to anyone. The  $\chi^2$  analyses did not reveal significant differences of participants' characteristics by level of depressive symptoms.

## [Insert\_Table\_1]

### Depressive symptoms

The prevalence of depressive symptoms was examined through analysis of total BDI scores. The mean BDI score among participants was 22.35 (SD = 11.59; range: 0-50). Using the previously mentioned cut-off values, 17 participants (16.5%) had minimal or no depressive symptoms, 54 (56.4%) had mild/moderate depressive symptoms, and 32 (31.1%) had severe depressive symptoms. *Neurocognitive performance* 

Using a cut-off score of 10 or less on the HDS, 59 HIV-infected women (57.3%) met criteria for neurocognitive impairment. The scores of neurocognitive impairment were statistically different by level of depressive symptom severity [41.2% vs. 50% vs. 78.1% respectively; (2, N = 103) = 8.65, p =0.013, Cramer's V = 0.29], that is, the proportion of women with neurocognitive impairment was significantly higher in the category of severe depressive symptoms.

### Relationship between depressive symptoms and neurocognitive performance

When applying MANOVA, results showed a significant multivariate effect (Wilks' Lambda = .75, F(4, 98) = 3.76, p < 0.001). Follow-up univariate tests showed significant differences in attention, psychomotor speed, and construction (Table 2). Overall, women with severe depressive symptoms reported lower scores on these HDS subtests than women with none/minimal to moderate depressive

symptoms. No differences were found regarding memory recall. Post hoc analysis also showed no significant differences between the two first groups (minimal or no depressive symptoms *versus* mild/moderate depressive symptoms). Regarding the total score, a significant difference was also found, and the same pattern was observed, that is, women with severe depressive symptoms were more impaired than those with none/minimal to moderate depressive symptoms.

## [Insert\_Table\_2]

#### Neurocognitive performance according to demographic and HIV-related variables

Of all the variables analyzed, only age and education were associated with neurocognitive impairment. The total score was higher among younger and highly educated women. None of the other variables revealed a statistically significant difference, although a marginal difference was observed regarding employment status (see Table 3). Regarding the subtests, older age was significantly associated with lower psychomotor speed, F(1, 101) = 7.38, p = 0.008, and marginally associated with lower scores on attention, F(1, 101) = 3.87, p = 0.052. Lower education was significantly associated with lower scores on psychomotor speed, F(1, 101) = 4.31, p = .040, and memory recall, F(1, 101) =8.53, p = 0.004. Marital status, professional situation, ethnicity, time since diagnosis, HIV/HCV coinfection, self-reported adherence, CD4 count, and viral load were not significantly associated with HDS subtests.

## [Insert\_Table\_3]

Finally, a multivariate logistic regression was carried out to assess if any of the variables analysed (demographic, HIV-related, and depressive symptoms) were independent risk factors for a lower score on the HDS. The total score was categorized according to the cut-off score (< 10 and  $\geq$ 10), and was considered the dependent variable. Only factors associated with neurocognitive impairment at *p* < .25 in the bivariate analyses were included in the multivariable model. The overall logistic regression model was significant,  $\chi^2 = 13.80$ ; *df* = 6; *p* = 0.032, and the results of the Hosmer-Lomeshow's goodness-of-fit test indicated that the multivariable model fit the data well,  $\chi^2 = 7.89$ ; *df* = 7; *p* = 0.343.According to the multivariate model, only depressive symptoms stood out as a significant risk factor for neurocognitive impairment (see Table 4).

#### DISCUSSION

The aim of this study was to examine the presence of depressive symptoms and neurocognitive impairment in a sample of HIV-infected women, and to assess the association between the severity of depressive symptoms and neurocognitive performance. In addition, we intended to examine the influence of several demographic and HIV-related variables on neurocognitive performance. Determining such influence may be beneficial in detecting future cognitive impairments and, focusing on a female perspective, may also help to target specific areas for psychological intervention. Overall, the results of our study only partially confirm our hypothesis. Although preliminary, this study offers an important contribution to the field, especially because women are still under-represented in neuropsychological studies of HIV (Maki & Martin-Thormeyer, 2009), despite the fact that over the course of the HIV epidemic the proportion of women has drastically increased, with women now accounting for approximately half of the adults living with HIV and AIDS (UNAIDS, 2010).

Firstly, our findings indicate that HIV-infected women experience high levels of depressive symptoms. These findings are consistent with prior work that revealed a significant prevalence of depression among HIV-infected patients (Leserman, 2003, Ciesla & Roberts, 2001), and particularly among women (Bragança & Palha, 2011; Pereira & Canavarro, 2011; Ickovics et al., 2001; Rabkin, 2008; Valverde et al., 2007). In our study the percentage of HIV-infected women showing severe depressive symptoms (31.1%) was higher than that found in past studies (Mello, Segurado, & Malbergier, 2010; Morrison et al., 2002). Accordingly, we believe that this high prevalence rate is disturbing, and highlights the importance of women's early engagement with HIV-specific mental health infrastructures.

The percentage of women with neurocognitive deficits was 57.3%. This rate was considerably higher than found in prior studies (Ganasen et al., 2008; Gibbie et al., 2006) or all-female samples (Wojna et al., 2007). Because all women were receiving HAART treatment, we did not expect as many to meet criteria for neurocognitive impairment on a screening measure such as the HDS. Also, we did not expect that the higher percentage of women with none or minimal depressive symptoms who showed neurocognitive impairment (41.2%). It is possible that these findings could be related to

the direct action of the HIV in the brain, but also to the sum of different demographic and clinical variables, which may act synergistically. In fact, the sample of this study represents a group of women living with HIV and having low levels of education, lack of financial and other resources of support (nearly 30% had never disclosed their HIV status), and who are, in general, severely depressed. In this context, education is particularly important, because education is an important protective factor for neurocognitive impairment (De Ronchi et al., 2002). In addition, non-disclosure of a positive HIV status may be a barrier to women receiving the support they need to cope with their disease (Serovich et al., 2000).

Consistent with the first hypothesis, severe depressive symptoms in HIV-infected women were significantly associated with decreased cognitive performance, particularly in the domains of attention and psychomotor speed, suggesting that severe levels of depressive symptoms may increase the tendency for cognitive impairment in this population. These findings were consistent with studies conducted with all-female samples (Durvasula et al., 2001; Richardson et al., 2005), and reinforce the notion that patterns of performance, as well as risk factors, cannot always be generalized from men to women. Also, in our study, depressive symptoms were not significantly associated with memory, which is consistent with a prior study conducted in Portugal (Bragança & Palha, 2011).

As previously mentioned, neurocognitive impairment among HIV-infected patients is influenced by several risk factors. However, some of these risk factors are not well known in female patients. In our study, in univariate analysis, only age and education were significantly associated with neurocognitive performance. These findings are consistent to findings of prior studies (De Ronchi et al., 2002; Lopardo et al., 2009; Tozzi et al., 2007), suggesting that older age and lower education are associated with an increased risk of neuropsychological impairment. In our study, neither marital status, ethnicity, employment status, HIV/HCV co-infection, time from diagnosis of HIV infection, self-reported HAART adherence, current CD4 count, and viral load were associated with neurocognitive performance.

In the multivariate analysis, age and education were not determining factors, and only depressive symptoms stood out as an independent risk factor for neurocognitive impairment in logistic regression analysis. In prior research, depression has been found not to account completely for neurocognitive impairment among HIV-infected individuals (Ammassari et al., 2004; Cysique et al., 2007; Goggin et al., 1997), although some studies had suggested that depression co-exists with neurocognitive impairment, as well as being associated with severity (Bragança & Palha, 2011; Gibbie et al., 2006). However, given that most of these studies were conducted in predominantly male samples, this finding is particularly important because depression occurs frequently in HIV-infected women. Indeed, given the higher prevalence of depression among women (Wisniewski et al., 2005), it is possible, as pointed out by Maki and Martin-Thormeyer (2009), that the effects of depression on neurocognitive functions are more pervasive among women. In addition, women with mild/moderate and severe depressive symptoms were, respectively, five and three times more likely to present neurocognitive impairment than non depressed women. This finding was unexpected, and may be related with specific characteristics of the sample. Specifically, in a further analysis, although without statistical significance, women with mild/moderate depressive symptoms were older, lived without partner, had lower CD4 count, and have reported lower adherence to HAART. Therefore, as previously mentioned, it is possible that the cumulative effect of these variables may account for these results.

This study had a number of limitations that should be acknowledged. Firstly, potential limitations imposed by a sample of convenience, the absence of a seronegative and/or male comparison groups. Secondly, the cross-sectional study design prohibited assessment of temporal relations, must also be considered when generalizing these results. Thirdly, the small sample size limited the power to detect small but potentially important differences. In fact, following Cohen (1992), post hoc power calculations demonstrated that the achieved sample size only allowed for the detection of medium to large effects. Additionally, despite our inclusion of several demographic and HIV-related variables, other variables that may have affected neurocognitive performance were not included. These include variables such as nadir CD4 count, cerebrospinal fluid viral load, and questions on antiretroviral treatment and duration of HAART. In particular, the duration of HAART and the adherence levels were not fully reported, thereby making it difficult to assess the real effects of antiretroviral therapy on neurocognition. Finally, a noteworthy limitation of this study was the non-use of a full battery of neuropsychological tests to confirm the results of the HDS screening test. It is

possible that this brief measure is less sensitive than those tests employed in earlier studies and, as suggested by some authors (e.g., Bottiggi et al., 2007), the HDS may not be accurate in detecting neurocognitive impairment as a more thorough neuropsychological examination. Additionally, given that psychological and neurocognitive problems can intersect, that is, patients with psychiatric problems may have underlying organic causes and patients with neurocognitive impairments may have their impairments worsen as a consequence of emotional distress (Gibbie et al., 2006), it is also possible that depressed women in our study may have obtained false positives in this test. Thus, replication of these findings in a longitudinal study with a larger sample, and a more detailed neuropsychological and psychiatric assessment is needed, to determine if our results can be generalized to all HIV-positive women, and may help to clarify the relationship between depressive symptoms and neurocognition.

Despite these limitations, our results broaden the understanding of the effect of depressive symptoms on neurocognitive performance among HIV-infected women. In this study, it is particularly worrying that HIV-infected patients remain at significant risk of depressive symptoms and neurocognitive impairment, factors that may interfere with adherence to HAART (Hinkin et al., 2004; Valcour et al., 2011), significantly affect quality of life (Parsons et al., 2006; Osowiecki et al., 2000; Tozzi et al., 2004), and may hasten progression to AIDS. Accordingly, these results underscore the importance of early diagnosis and monitoring of depressive symptoms in this vulnerable population. In addition, neurocognitive impairment should be assessed early in the course of HIV infection, especially because it is a potentially treatable condition with antiretroviral therapy (Cysique et al., 2009; Heaton et al., 2010; Lopardo et al., 2009; Wright, 2009).

Further studies with larger samples are needed to address neurocognitive aspects of HIV among women, to identify the spectrum of risk factors that contribute to neurocognitive performance, and to identify the clinical relevance of cognitive impairment, and the real impact of neurocognitive aspects on overall functioning. Overall, these findings offer health providers with additional considerations that may increase the extent to which HIV health services are responsive to particular issues (and contexts) faced by women living with HIV. Therefore, it would be important to develop tailored interventions for some of the factors contributing to cognitive dysfunction, and provide more systematic mental health support for this population. This would be of crucial importance because women usually present multiple factors, where interactions and cumulative effects may well increase their vulnerability to the effects of HIV on neuropsychological functioning.

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Variable		M (SD)
Age		43.86 (12.36)
Education		9.68 (4.71)
Time since HIV diagnosis		8.04 (5.02)
		n (%)
Marital status	Living with partner	67 (65.0)
	Living alone	36 (35.0)
Ethnicity	White/Caucasian	81 (78.6)
	Black	22 (21.4)
Professional Status	Employed	63 (61.2)
	Unemployed/Retired	40 (38.8)
HIV/HCV co-infection	No	81 (78.6)
	Yes	22 (21.4)
Viral Load	Detectable	50 (51.0)
	Undetectable (< 50 copies)	48 (49.0)
CD4 T cell count	$\leq$ 200 cells/mm <sup>3</sup>	10 (10.1)
	201-499 cells/mm <sup>3</sup>	44 (44.4)
	$\geq$ 500 cells/mm <sup>3</sup>	45 (45.5)

Sociodemographic and HIV-related characteristics of the sample (N = 103)

	None/minimal	Mild/moderate	Severe	<i>F</i>	$\eta^2$
	M (SD)	M (SD)	M(SD)	_ I'	
Attention	2.88 (1.17)	2.63 (1.07)	1.69 (1.15)	9.33***	0.16
Psychomotor speed	3.65 (1.27)	3.07 (1.56)	1.72 (1.51)	11.81**	0.19
Memory recall	2.65 (0.94)	2.56 (0.90)	2.50 (0.98)	0.16	0.00
Construction	1.12 (0.70)	0.94 (0.71)	0.50 (0.57)	6.27**	0.11
HDS total	10.29 (2.66)	9.20 (3.17)	6.41 (2.89)	12.26***	0.20

*Mean scores (and SD) of the HDS by categories of depressive symptoms (N* = 103)

\* p < 0.05; \*\* p < 0.01; \*\*\* p < 0.001

Variable	Categories	п	M(SD)	р	Cohen's d
Age (years)	20-44 years	59	9.08 (3.48)	0.043	0.41
	45-80 years	44	7.75 (2.97)		
Education (years)	< 10 years	55	7.73 (3.27)	0.009	-0.52
	$\geq$ 10 years	48	9.42 (3.18)		
Marital status	Living with partner	67	8.76 (3.56)	0.306	-0.21
	Living alone	36	8.06 (2.82)		
Ethnicity <sup>a</sup>	White/Caucasian	81	8.57 (3.40)	0.756	0.08
	Black	22	8.32 (3.08)		
Professional Status	Employed	63	8.98 (3.50)	0.072	0.38
	Unemployed/Retired	40	7.77 (2.91)		
Time since diagnosis	< 8 years	49	8.69 (3.13)	0.634	0.09
	$\geq 8$ years	53	8.38 (3.54)		
HIV/HCV co-infection <sup>a</sup>	No	81	8.74 (3.39)	0.186	0.33
	Yes	22	7.68 (2.98)		
HAART adherence <sup>a</sup>	No	18	8.17 (3.05)	0.550	0.13
	Yes	85	8.59 (3.39)		
Viral Load	Detectable	50	8.50 (3.39)	0.928	-0.02
	Undetectable (< 50 copies)	48	8.56 (3.40)		
CD4 T cell count	$\leq$ 499 cells/mm <sup>3</sup>	54	8.24 (3.25)	0.395	-0.17
	$\geq$ 500 cells/mm <sup>3</sup>	45	8.82 (3.52)		

Neurocognitive impairment according to demographic and HIV-related characteristics

<sup>a</sup> Mann-Whitney test

Variables associated with neurocognitive impairment

Variable	Categories	OR	95% CI	р
Age (years)	20-44 years	1 (reference)		
	45-80 years	1.64	0.65-4.17	0.299
Education (years)	< 10 years	1 (reference)		
	$\geq 10$ years	0.89	0.37-2.17	0.798
Professional Status	Employed	1 (reference)		
	Unemployed/Retired	1.76	0.73-4.27	0.211
HIV/HCV co-infection	No	1 (reference)		
	Yes	1.91	0.60-6.08	0.276
BDI categories	Non depressed	1 (reference)		
	Mild/moderate depression	5.03	1.33-18.99	0.017
	Severe depression	3.22	1.15-9.06	0.026