Revista Latinoamericana de Psicología (2016) 48, 147–158

Revista Latinoamericana de Psicología

www.elsevier.es/rlp

ORIGINAL ARTICLE

Neuropsychological functioning in methadone maintenance patients with HIV☆

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Received 28 January 2015; accepted 24 June 2015
Available online 14 June 2016

KEYWORDS
HIV infection;
Neuropsychological performance;
Intravenous drug users;
Cognitive reserve;
Methadone maintenance

Abstract Although highly active antiretroviral therapy (HAART) has improved survival rates of HIV patients, HIV-associated neurocognitive disorders (HAND) still exist in a highly prevalent group of persons with this disease. In this study we seek to evaluate the influence of drug use in the neuropsychological performance of seropositive drug users. We carried out an extensive neuropsychological evaluation and compared the performance of seropositive drug users ($n = 90$) with that of a control group of seronegative drug users ($n = 48$). The results reveal that methadone maintenance programmes can make the seropositive subject neuropsychologically vulnerable. Likewise, we found that giving up drugs have a protective effect in the presence of neuropsychological alterations associated with HIV. These findings lead us to suggest that seropositivity is not sufficient to explain the neuropsychological alterations of seropositive drug users, noting that these alterations are multifactorial.

☆ Best Article of the Issue Award.
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http://dx.doi.org/10.1016/j.rlp.2015.06.008

PALABRAS CLAVE
Infección por VIH;
Rendimiento neuropsicológico;
Consumidores de drogas por vía intravenosa;
Reserva cognitiva;
Tratamiento de mantenimiento con metadona

Función neuropsicológica en el tratamiento de mantenimiento con metadona en pacientes con VIH

Resumen Aunque la terapia antirretroviral de gran actividad (TARGA) ha mejorado los índices de supervivencia de los pacientes infectados por el VIH, los trastornos neurocognitivos asociados con el VIH (TNAV) todavía existen en un grupo de personas altamente prevalente a esta enfermedad. En este estudio buscamos evaluar la influencia del consumo de drogas en el rendimiento neuropsicológico de los usuarios de drogas seropositivos. Llevamos a cabo una amplia evaluación neuropsicológica, y el rendimiento de los usuarios de drogas seropositivos (n = 90) se comparó con la de un grupo control de usuarios de drogas seronegativos (n = 48). Los resultados demuestran que los programas de tratamiento de mantenimiento con metadona pueden convertir en vulnerable a nivel neuropsicológico al individuo seropositivo. Asimismo, descubrimos que abandonar las drogas provoca un efecto protector frente a la existencia de alteraciones neuropsicológicas asociadas con el VIH. Estos resultados nos llevan a sugerir que la seropositividad no basta para explicar las alteraciones neuropsicológicas de los usuarios de drogas seropositivos, ya que estas alteraciones al parecer son multifactoriales.

The human immunodeficiency virus (HIV) infection is associated with a wide range of neuropsychological deficits: psychomotor functioning, information processing speed, attention, executive functioning, information processing speed, attention, executive functioning and working memory (Al-Khindi, Zakzanis, & Van Gorp, 2011; Blackstone et al., 2012; Cysique, Marruf, & Brew, 2006; Heaton et al., 2011;Vázquez-Justo, Piñón-Blanco, Vergara-Moragues, Guillén-Gestoso, & Pérez-García, 2014). The nature of these deficits is compatible with an affection of the frontal-subcortical brain disturbances, including cerebral metabolite abnormalities (Cohen et al., 2010; Paul et al., 2008) and white matter damage (Coughlin et al., 2014; Fellows, Byrd, & Morgello, 2014) and their prevalence varies considerably (Cohen et al., 2015; Heaton et al., 2010; Woods, Moore, Weber, & Grant, 2009).

The variability of the data on the prevalence of these alterations leads us to consider, as Anand, Springer, Copenhaver, and Altice (2010) put forward, that these may be modulated by the coexistence of factors other than HIV. No definitive risk factors are yet available to indicate the development of these neuropsychological alterations and, bearing in mind that the presence of cognitive disturbances is a risk factor of early death in all stages of the infection (Lescure et al., 2011; Sevigny et al., 2007), there is a pressing need to determine those factors, either related or foreign to HIV, which help to explain the intra-group differences that exist and which may also be associated with the development and progression of the dysfunction (Anand et al., 2010; Byrd et al., 2011; Muñoz-Moreno et al., 2008). The identification of these risk factors will help us to outline the characteristics of the seropositive subjects who are neuropsychologically more vulnerable.

Research dealing with this sphere of work has mainly studied the influence of variables related to the infection, such as the stage of infection (Selnes et al., 1997; Spudich & Ances, 2015), the level of immunosuppression (Farinpour et al., 2000; Grassi, Perin, Borlla, & Mangoni, 1999), the combined effects of HIV infection and APOE ε4 may lead to greater cognitive deficits, especially in those with greater neuroinflammation (Chang, Connaghan, Wei, & Li, 2014) and the viral load (Ellis et al., 1997; Muñoz-Moreno et al., 2008; Stankoff et al., 1999). However, they have also dealt with determining the influence of other variables such as depressed mood (Fellows et al., 2014; Vázquez-Justo, Rodríguez-Álvarez, & Carro-Ramos, 2003; Vázquez-Justo, Rodríguez Álvarez, & Ferraces Otero, 2003), history of neurological pathology (Hestad, Updike, Selnes, & Royal III, 1995) and of psychiatric pathology (Baldeweg et al., 1997); variables related to drug use (García-Torres, Vergara-Moragues, Piñón-Blanco, & Pérez-García, 2015; Rodríguez, 2000; Vázquez-Justo, Rodríguez Álvarez, & Rodríguez Salgado, 2000; Vergara-Moragues, Vergara de Campos, & Girón-González, 2008), high psychosocial stress and lower socioeconomic status (Rubin et al., 2015) and educational level (Satz et al., 1993). The findings of these studies reveal that the neuropsychological performance of seropositive subjects may vary according to their situation with respect to each of these variables, although the results are not consistent.

We know that HIV infection in drug users is associated with neuropsychological alterations that cannot be attributed to the history of drug abuse (Vázquez-Justo et al., 2003a, 2003b; Vergara-Moragues, Vergara de Campos, & Girón-González, 2010). When evaluating the neuropsychological performance of seropositive drug users, a variable that may affect their performance is their current situation with respect to drug consumption, i.e. whether they continue to use drugs or whether they are abstaining at the time of evaluation. In this sense, the current consumption of drugs is related to a poorer performance in neuropsychological tasks than abstinence (Ardila, Rosselli, & Strumwasser, 1991; Grassi et al., 1995). The Methadone Maintenance Programmes (MMP) offer us a suitable

framework for evaluating the neuropsychological consequences of the active consumption of opiates. For example, chronic crack cocaine use seems to disrupt general cognitive functioning (MMSE), verbal memory, and attentional resources, but findings suggest that some of these effects could be reversed by abstinence (De Oliveira et al., 2009). In addition, Vázquez-Justo et al. (2000) evaluated the cognitive functioning of drug users in MMP and noted a significantly poorer performance in these subjects as compared to those in abstinence. Likewise, Rodríguez (2000) pointed out that the rate of neuropsychological affection of seropositive subjects in MMP is double that of abstaining seropositive subjects, observing greater difficulty in attention, coordination and visual-motor speed, memory, conceptualisation and verbal fluency in the seropositive subjects in MMP than in those abstaining.

The aim of this study is not only to contribute to clarifying the effect of some factors in the neuropsychological performance of Spanish seropositive subjects but also to make progress in this line of research by providing evidence of the multifactorial nature of neuropsychological deterioration associated with HIV infection.

Method

In order to carry out this research, a sample comprising 138 male volunteers was used. All subjects provided written informed consent. These subjects were distributed in two groups: one group of drug users with HIV infection ($n = 90$), referred to as seropositive (HIV+), of this group of 48 subjects were on the drug-free treatment programme and 42 were on methadone maintenance programme. A second group of controls (HIV−), formed by HIV seronegative drug users ($n = 48$), of this group of 27 subjects were on the drug-free treatment programme and 21 were on methadone maintenance programme. The drug dependent subjects were recruited in the HIV services at Hospitals and at units for the care of drug users in Galicia (Spain). To be included in the study the intravenous drug users should be diagnosed as opiate-dependent according to DSM-IV criteria. Before starting on heroin, all had taken cannabis, amphetamines, cocaine, or barbiturics, either simultaneously or consecutively, without becoming dependents on any of these other drugs, and primary drug of choice was cannabis or alcohol for all the drug user subjects.

Diagnosis of seropositivity and the classification of the subjects regarding phase of infection was carried out according to standard procedures (Centers for Disease Control [CDC], 1992), and was based on the medical report from the hospitals where the subjects were recruited.

Those subjects who presented, or had presented, neurological or medical pathologies that could affect the CNS, including HIV-associated dementia, psychiatric disturbances (psychotic symptoms), history of craneo-encephalic trauma requiring hospitalization owing to neurological complication, and antisocial personality disorder according to DSM-IV criteria (American Psychiatric Association, 2002) were excluded from the study. Finally, taking as a basis the report from the units for the care of drug addicts, those dependent on drugs who were currently consuming psychotropic substances (illegal drugs or alcohol) other than methadone were excluded. In the other hand, three months drug-free was required to be considered in abstinence.

Examination of each subject consisted of a semi-structured interview on socio-demographic, clinical and toxicological aspects and a neuropsychological evaluation with a battery of tests designed for this study, chosen for their validity and for having been shown to be sensitive to neuropsychological deterioration in HIV-infected patients in other studies. The neuropsychological domains and tests and comprising the battery are as follows:

1. Attention
   Visual Search and Attention Test (VSAT) (Trenerry, Crosson, Beboe, & Leber, 1990).
2. Visual-motor integration:
   Block Design and Object Assembly subtests of the Wechsler Adult Intelligence Scale – WAIS – (Wechsler, 1999).
3. Motor coordination:
   Purdue Pegboard Test (Tiffin, 1948).
   Finger Tapper Test (Reitan, 1979).
4. Language:
   Comprehension subtest of the Wechsler Adult Intelligence Scale – WAIS – (Wechsler, 1999).
   Verbal Fluency Test (Cuadrado, Esteba-Castillo, Böhm, Cejudo-Bolívar, & Peña-Casanova, 2002).
   Boston Naming Test (Kaplan, Goodglass, & Weintraub, 2001).
5. Memory:
   Rey Auditory Verbal Learning Test – AVLT – (Rey, 1964).
   Rey Osterrieth Complex Figure – ROCF – (Rey, 1987).
   Benton Visual Retention Test – BVRT –: Form C, Administration A (Benton, 1981).
6. Executive Functions:
   Similarities, Digit Span, Digit Symbol subtests of the Wechsler Adult Intelligence Scale –WAIS – (Wechsler, 1999).
   Trail Making Test – TMT – (Tombaugh, 2004)
   Stroop Test (Golden, 1994).
   Wisconsin Card Sorting Test – WCST – (Heaton, Chelune, Talley, Kay, & Curtiss, 2001).
7. Cognitive reserve:
   Vocabulary subtest of the Wechsler Adult Intelligence Scale (WAIS) (Wechsler, 1999).
8. Handeness:
   Edinburgh Handedness Inventory (Oldfield, 1971).

Results

Bearing in mind the objectives posed, and in order to respond to them, diverse data analyses were carried out using the SPSS statistical packet for Windows.

Characteristics of the Sample

First, an analysis of variance (ANOVA), chi squared or Student *t* test was performed when needed in order to determine whether there were differences between the seropositive and seronegative groups in the different socio-demographic and clinical variables. Statistically significant differences were observed between the groups in age, addiction time

Table 1 Group comparisons on demographic and clinical variables.

$n = 138$	HIV+ $n = 90$		HIV− $n = 48$		Statistic	p	Bonferroni posthoc
	Drug-free treatment programme (FTP) $n = 48$	Methadone maintenance programme (MMP) $n = 42$	Drug-free treatment programme (FTP) $n = 27$	Methadone maintenance programme (MMP) $n = 21$			
Age (years)	33 (4.8)	34 (5.3)	26 (3.8)	32 (4.1)	$F = 18.7$	<.05	FTP/HIV+>FTP/HIV−; MMP/HIV+>FTP/HIV−; FTP/HIV−<MMP/HIV−
Education (years)	10 (3.4)	10 (2.9)	10.5 (2.7)	10 (2.3)	$F = 0.166$	>.05	–
Occupational attainment					$\chi^2 = 15.20$	.005*	–
Unemployed	24 (50)	36 (85.7)	13 (48.1)	13 (61.9)			
Employed	24 (50)	6 (14.3)	14 (51.9)	8 (38.1)			
Economic level					$\chi^2 = 1.339$	.720	–
Low	15 (32.6)	18 (43.9)	10 (37)	7 (33.3)			
Middle	31 (67.4)	23 (56.1)	17 (63)	14 (66.7)			
Manual dominance					$\chi^2 = 2.997$	.392	–
Right	44 (93.6)	35 (89.7)	27 (100)	19 (90.5)			
Left	3 (6.4)	4 (10.3)	–	2 (9.5)			
Addiction time (years)	8.7 (3.6)	10.7 (4.7)	6.1 (3.3)	10.9 (4.1)	$F = 8.603$	<.05	MMP/HIV+>FTP/HIV−; FTP/HIV−<MMP/HIV−
Age at onset drug use	16 (2.7)	16 (2.7)	15 (3.3)	16 (3.9)	$F = 0.405$	>.05	–
Months of abstinence	64.04 (41.22)	–	11.69 (8.89)	–	$t = 6.496$	.000*	–
Months in Methadone Maintenance Programme	–	30.81 (34.6)	–	23.38 (26.8)	$t = 939$	.392	–
CD4 count	358 (318.6)	298 (315.6)	–	–	$t = 851$	.397	–
Plasma viral loads					$\chi^2 = 0.254$	.614	–
Detectable	18 (52.9)	12 (60)	–	–			
Undetectable	16 (47.1)	8 (40)	–	–			
Antirretroviral therapy					$\chi^2 = 0.068$	.795	–
Receiving	27 (60)	22 (62.9)	–	–			
No Receiving	18 (40)	13 (37.1)	–	–			

Numbers express means and (standard deviations) for quantitative variables and percentages for qualitative variables.

* $p < .0$.

Table 2 Group comparisons on neuropsychological measures (Mean and SD) influence of the situation with respect to drug use.

Neuropsychological test	HIV+		HIV−		Statistic	*p*	Bonferroni posthoc
	Drug-free treatment programme (FTP) *n* = 48	Methadone maintenance programme (MMP) *n* = 42	Drug-free treatment programme (FTP) *n* = 27	Methadone maintenance programme (MMP) *n* = 21			
Neuropsychological domains							
Attention							
VSAT	123.48 (32.42)	104.36 (35.37)	140.22 (18.86)	132.67 (27.14)	$F = 8.78$	<.05	FTP/HIV+>MMP/HIV+; MMP/HIV+<FTP/HIV−; MMP/HIV+<MMP/HIV−;
Language							
WAIS: comprehension	13.98 (3.76)	14.10 (4.05)	17.37 (2.84)	16.81 (3.56)	$F = 7.52$	<.05	FTP/HIV+<FTP/HIV− FTP/HIV+<MMP/HIV−; MMP/HIV+<FTP/HIV−; MMP/HIV+/MMP/HIV−
Verbal fluency	29.69 (9.03)	26.93 (11.04)	34.00 (7.17)	33.71 (9.67)	$F = 4.11$	<.05	MMP/HIV+<FTP/HIV−;
Boston naming	53.38 (4.97)	52.28 (5.43)	54.44 (3.00)	53.76 (2.39)	$F = 1.35$	>.05	–
Memory							
AVLT, 5−6	1.85 (2.08)	1.93 (1.84)	2.07 (2.00)	2.67 (2.11)	$F = 0.87$	>.05	–
AVLT, total	42.38 (8.07)	37.24 (10.98)	45.19 (7.68)	49.00 (6.72)	$F = 9.60$	<.05	FTP/HIV +>MMP/HIV+; FTP/HIV +<MMP/HIV−; MMP/HIV+<FTP/HIV−; MMP/HIV+<MMP/HIV−;
BVRT, correct	6.90 (1.80)	5.55 (2.10)	7.15 (1.03)	6.76 (1.79)	$F = 6.14$	<.05	FTP/HIV +>MMP/HIV+; MMP/HIV+<FTP/HIV−;
BVRT, errors	4.83 (3.17)	7.81 (4.29)	4.11 (1.85)	4.71 (3.12)	$F = 9.15$	<.05	FTP/HIV+<MMP/HIV+; MMP/HIV+<FTP/HIV−; MMP/HIV+<MMP/HIV−
ROCF: copy	30.89 (3.26)	30.28 (4.24)	32.79 (2.43)	31.59 (3.33)	$F = 3.08$	<.05	MMP/HIV+<FTP/HIV−;
ROCF: delay	15.51 (6.30)	14.45 (5.03)	18.81 (6.68)	17.38 (5.63)	$F = 3.42$	<.05	MMP/HIV+<FTP/HIV−;
Visual-motor integration							
WAIS: block design	33.25 (8.53)	28.90 (8.76)	37.15 (7.41)	33.57 (7.14)	$F = 5.79$	<.05	MMP/HIV+<FTP/HIV−;

Table 2 (*Continued*)

Neuropsychological test	HIV+		HIV−		Statistic	*p*	Bonferroni posthoc
	Drug-free treatment programme (FTP) *n* = 48	Methadone maintenance programme (MMP) *n* = 42	Drug-free treatment programme (FTP) *n* = 27	Methadone maintenance programme (MMP) *n* = 21			
WAIS: object assembly	30.60 (7.38)	26.55 (9.24)	33.74 (6.18)	32.10 (6.83)	$F = 5.49$	<.05	MMP/HIV+<FTP/HIV−; MMP/HIV+<PMM/HIV−;
Motor coordination							
Purdue: dominant	13.85 (2.39)	12.79 (2.48)	15.15 (1.73)	14.52 (2.16)	$F = 6.61$	<.05	MMP/HIV+<FTP/HIV−; MMP/HIV+<PMM/HIV−
Purdue: nondominant	12.90 (2.42)	12.14 (2.04)	14.22 (1.69)	13.14 (1.56)	$F = 5.65$	<.05	MMP/HIV+<FTP/HIV−
Finger: dominant	43.62 (11.63)	39.85 (9.58)	49.05 (5.03)	46.00 (5.99)	$F = 5.83$	<.05	MMP/HIV+<FTP/HIV−;
Finger: nondominant	40.32 (9.02)	34.66 (8.49)	43.33 (5.49)	39.47 (6.94)	$F = 7.25$	<.05	FTP/HIV +<MMP/HIV+; MMP/HIV+<FTP/HIV−
Executive functions							
WAIS: similarities	13.63 (4.53)	12.02 (5.60)	16.63 (3.22)	16.48 (3.25)	$F = 7.89$	<.05	FTP/HIV +<FTP/HIV−; MMP/HIV+<FTP/HIV−; MMP/HIV+<MMP/HIV−
WAIS: direct digit span	6.15 (1.05)	5.62 (1.27)	6.44 (1.15)	6.48 (1.03)	$F = 4.10$	<.05	MMP/HIV+<FTP/HIV−; MMP/HIV+<MMP/HIV−
WAIS: indirect digit span	4.35 (1.08)	3.93 (0.95)	4.41 (1.05)	4.24 (1.26)	$F = 1.58$	>.05	–
WAIS: digit symbol	48.00 (11.66)	37.96 (15.40)	53.78 (9.22)	48.38 (14.14)	$F = 9.31$	<.05	FTP/HIV +>FTP/HIV−; MMP/HIV+<FTP/HIV−; MMP/HIV+<MMP/HIV−
Trails A	40.50 (15.75)	52.69 (25.44)	33.35 (10.12)	38.52 (18.05)	$F = 6.73$	<.05	FTP/HIV +<FTP/HIV−; MMP/HIV+>FTP/HIV−; MMP/HIV+>MMP/HIV−
Trails B	84.60 (34.63)	138.86 (79.74)	79.41 (27.30)	82.33 (32.81)	$F = 11.57$	<.05	FTP/HIV+<FTP/HIV−; MMP/HIV+>FTP/HIV−; MMP/HIV+>MMP/HIV−

Table 2 (*Continued*)

Neuropsychological test	HIV+		HIV−		Statistic	*P*	Bonferroni posthoc
	Drug-free treatment programme (FTP) *n* = 48	Methadone maintenance programme (MMP) *n* = 42	Drug-free treatment programme (FTP) *n* = 27	Methadone maintenance programme (MMP) *n* = 21			
Stroop 1	99.83 (15.75)	90.52 (21.85)	105.85 (11.18)	104.81 (11.86)	$F = 6.02$	<.05	FTP/HIV +>FTP/HIV−; MMP/HIV+<FTP/HIV−; MMP/HIV+<MMP/HIV−
Stroop 2	66.25 (12.97)	58.64 (17.77)	70.56 (11.75)	68.38 (11.24)	$F = 4.71$	<.05	MMP/HIV+<FTP/HIV−; MMP/HIV+<MMP/HIV−
Stroop 3	39.94 (10.12)	32.12 (13.80)	41.11 (9.32)	40.14 (8.28)	$F = 5.45$	<.05	FTP/HIV+>FTP/HIV−; MMP/HIV+<FTP/HIV−; MMP/HIV+<MMP/HIV−
Stroop: interference	0.23 (7.62)	−2.85 (7.41)	0.34 (7.74)	−1.13 (5.84)	$F = 1.64$	>.05	–
WCST – number of categories	4.29 (1.80)	3.00 (2.13)	5.33 (1.07)	4.81 (1.81)	$F = 10.65$	<.05	FTP/HIV+>FTP/HIV−; MMP/HIV+<FTP/HIV−; MMP/HIV+<MMP/HIV−
WCST – learning to learn	−6.18 (10.25)	−6.31 (9.39)	−2.12 (5.35)	−0.04 (5.60)	$F = 3.31$	>.05	–
WCST-% perseverative errors	18.85 (11.64)	23.06 (14.45)	13.30 (6.59)	13.59 (8.65)	$F = 5.35$	<.05	MMP/HIV+>FTP/HIV−; MMP/HIV+>MMP/HIV−
WCST-% nonperseverative errors	15.14 (9.39)	19.59 (12.52)	14.30 (7.26)	15.65 (13.77)	$F = 1.80$	>.05	–
WCST-failure to maintain set	0.83 (1.10)	1.07 (1.39)	0.63 (0.79)	1.19 (1.54)	$F = 1.15$	>.05	–
WCST-% conceptual level responses	55.01 (22.63)	42.59 (22.07)	63.79 (16.31)	64.42 (19.01)	$F = 7.94$	<.05	FTP/HIV+>FTP/HIV−; MMP/HIV+<FTP/HIV−; MMP/HIV+<MMP/HIV−
WCST-% perseverative responses	21.66 (14.67)	26.76 (19.26)	15.13 (8.86)	13.13 (6.94)	$F = 5.71$	<.05	MMP/HIV+>FTP/HIV−; MMP/HIV+>MMP/HIV−
Cognitive reserve							
WAIS: vocabulary	43.92 (11.61)	41.33 (13.20)	48.67 (7.62)	51.05 (10.85)	$F = 4.50$	<.05	MMP/HIV+<MMP/HIV−

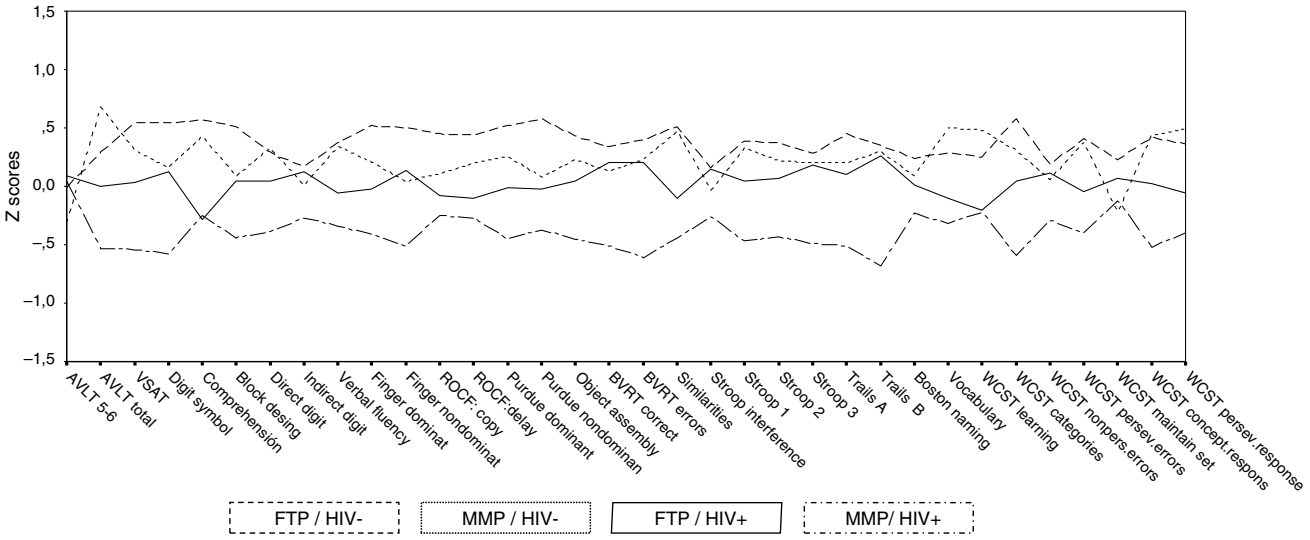

Figure 1 Neuropsychological *Z* scores for groups. Influence of the situation with respect to drug use.

and months of abstinence. Table 1 gives the mean scores and standard deviation in each group for these variables, and the significant differences observed are indicated. Moreover, Chi-square analyses revealed significant differences between occupational attainments.

Influence of the situation with respect to drug use

In order to determine the influence of the situation with respect to drug use in the neuropsychological performance of seropositive and seronegative drug users, the drug users were divided into two groups according to whether they were abstaining from drug use (Drug-free treatment programme [FTP]) or were included in a Methadone Maintenance Programme (MMP).

According to these results, we found differences between the groups in tests that assess attention, language, memory, visual-engine integration. Motor coordination and executive functions. In resume, the FTP/HIV-group performances the best and MMP/HIV+ group obtained the worst scores. Table 2 shows the mean scores and standard deviations obtained for the four groups in each measurement, and gives the significant differences noted in the ''post hoc'' multiple comparison tests. Figure 1 represents performance in the different neuropsychological tasks for each of the groups, after the direct scores were transformed to *Z* scores and their direction corrected.

Discussion

In this study we have attempted to be specially careful with some methodological aspects, hence we followed the recommendations made in the literature in this respect (Bornstein, 1994; Egan, Deary, & Brettle, 1992; Newman, Lunn, & Harrison, 1995; Stern, 1994; White, Heaton, Monsch, & The HNRC Group, 1995). Along these lines, we used a single risk group, that of intravenous drug users, taking into account that it has been pointed out that their neuropsychological performance could be different from that of other risk groups (Egan, Brettle, & Goodwin, 1992); the control groups have the same socio-demographic characteristics as the seropositive one (Bornstein, 1994); the size of the sample is greater than one hundred subjects, as recommended (Newman et al., 1995); and, finally, the criteria for inclusion and exclusion were carefully selected, without disregarding the importance of the representativeness of the sample (Bornstein, 1994).

In this research our aim was to study the group of intravenous drug users, first, because they represent the greatest percentage of HIV seropositive subjects and AIDS patients in Spain. Secondly, since most research studies use samples of homosexual and bisexual subjects, their results are not applicable to the risk group of intravenous drug users. With respect to sociodemographic characteristics and drug consumption history, the sample used in this research can be said to be representative of the population of intravenous drug users in Spain (Tables 1 and 2).

In order to be able to evaluate the neuropsychological consequences of HIV infection, it is important to determine the influence of other variables, whether related to the infection or not, which are also associated with the development of neuropsychological disturbances and which may make the seropositive subject more vulnerable neuropsychologically (Cohen et al., 2015; Rodríguez-Álvarez & Vázquez-Justo, 2002; Vázquez-Justo & Rodríguez-Álvarez, 2002;). One of the first studies in this line was that of Wilkins et al. (1990), who observed a significant relation between the degree of neuropsychological deterioration and the presence of contaminating factors. In our research we studied the influence of the current situation with respect to drug consumption on the neuropsychological performance of seropositive drug users, in order to help to clarify the influence of that factor on their neuropsychological performance.

With respect to the influence of drug use, several studies have disclosed that the use of drugs, past or present, can facilitate the appearance of neuropsychological disturbances (Albein-Urios, Marinez-González, Lozano, Clark, & Verdejo-García, 2012; Devlin et al., 2012; Ersche, Clark,

London, Robbins, & Sahakian, 2006; Fernandez-Serrano, Perez-Garcia, Schmidt Rio-Valle, & Verdejo-Garcia, 2010; López, Ravindran, Mrudula, & Priya, 2014; Lundqvist, 2005; Verdejo-García et al., 2012). Although there is no evidence that the use of opiates may be the direct cause of these disturbances, the poly-toxicomania pattern these subjects usually present, the high frequency of cranial traumatism and the nutritional deficiencies associated with their lifestyle makes them a risk group for neuropsychological impairment (Devlin et al., 2012; Ersche et al., 2006; Lundqvist, 2005; Rodríguez-Álvarez & Vázquez-Justo, 2002).

Bearing in mind that drug users who maintain current drug consumption showed poorer performance in neuropsychological tasks than those in abstinence (Grassi et al., 1995; Verdejo-García et al., 2012), chronic heroin-dependent subjects had widespread disruption of white matter structural connectivity located mainly in anterior and superior regions of the brain (Lin et al., 2013) and heroin users on MMP have low grey matter volume (GMV) in brain regions that are hypothesized to influence cognition and emotion, and the GMV findings might be involved comorbid disorders in the MMP group (Lin et al., 2012), we posit the interest of taking into account this situation when evaluating the neuropsychological performance of seropositive drug users. Along this line the MMP offer a suitable setting for evaluating the neuropsychological consequences associated with the active consumption of opiates.

In this research we sought to study the effect of the situation regarding drug consumption in seropositive drug users. These results reveal that the use of methadone is related to problems of attention, language, visual memory, motor speed, visual-motor integration and executives functions, along the lines of the results obtained in the works cited (Rodríguez, 2000; Vázquez-Justo et al., 2014). It has also been demonstrated, that the duration of MMP was associated with declining diffusion tensor image (DTI) indices in the superior longitudinal fasciculus and para-hippocampus (Lin et al., 2012).

Nevertheless, when we studied the influence of this variable on seronegative drug users we did not observe any differences between subjects in MMP and in period of abstinence in any of the tasks applied. These findings reveal that continuing in MMP makes the seropositive subjects more vulnerable neuropsychologically, but do not allow us to consider the use of methadone in itself as a risk factor for neuropsychological disturbances, inasmuch as we have not observed its influence in the group of seronegative drug users. Therefore we can consider it to be a risk factor for neuropsychological disturbances only in seropositive subjects.

Not only can the influence of the current situation as regards drug consumption on the neuropsychological performance of seropositive subjects be estimated by the differences observed in the two groups of drug users, but also important information can be provided by the comparison of the groups, taking into consideration not only seropositivity but also their situation regarding drug consumption. In this respect we noted that seropositive subjects in MMP showed a poorer performance than seronegative subjects in MMP and in period of abstinence, whereas the performance of seropositive subjects in abstinence is similar to that of seronegative subjects in MMP and in abstinence.

The interpretation of these results leads us to think that staying in MMP can be considered a risk factor for neuropsychological disturbances in seropositive subjects owing to the fact that seropositive subjects in MMP are those that show the poorest performance. These findings are in agreement with those studies that show a negative effect of current drug consumption on cognitive function (Egan, Deary, & Brettle, 1996; Grassi et al., 1995; Rodríguez, 2000; Vázquez-Justo et al., 2000).

While we identified methadone use as a risk factor in seropositive subjects, our results also reveal that giving up drugs seems to have a protective effect against the presence of neuropsychological disturbances associated with HIV. Once again we only identified its protective effect in seropositive subjects. This leads us to think that the situation with respect to drug consumption cannot in itself be considered a factor of risk or protection in the face of neuropsychological disturbances, inasmuch as its effect is only observed in seropositive subjects. We think that its influence may be due to a cumulative effect or to the effect of interaction with seropositivity. In any case, our data do not allow us to establish a causal relationship between the use of methadone and a poor neuropsychological performance, owing to the fact that, besides the direct effects of the substance on the organism, there could be other indirect effects related to lifestyle and/or the polyconsumption pattern so characteristic of the subjects in MMP.

This article shows some limitations, while assessment tools are widely used in other similar studies may have been advisable to include tests that deepen in very subtle aspects of cognitive change in the evolution of individuals in this type of methadone programmes, such as tests to discriminate processing speed, decision making, problem solving and reaction times. However it is appropriate to use batteries for attention and inhibitory control function that it was used in the sample. In addition, the sample size is not so broad as to allow conclusive findings but is interesting to continue this line of research.

Furthermore, the mechanisms by which the use of methadone makes a seropositive subject more vulnerable neuropsychologically remain to be determined. We posit, as a hypothesis to be confirmed in future studies, that the underlying mechanism may be related to the immune system, in which these two factors, seropositivity and methadone consumption, could be acting together and altering cognitive functioning in a way as yet unexplained.

To sum up, our results lead us to point out that there are certain factors that make the seropositive subject neuropsychologically vulnerable, regardless of seropositivity. We have identified some risk factors for seropositive drug users whose effects are not seen in seronegative drug users, such as the use of methadone. On the other hand, we identified two factors that protect against neuropsychological manifestations such as giving up drugs. The identification of these factors allows us to propose that seropositivity is not sufficient to explain the neuropsychological disturbances of seropositive drug users, suggesting that these may be of a multifactorial nature.

Hence, we feel that this research helps to clarify the lack of agreement in the literature on the presence of neuropsychological disturbances in seropositive subjects, thus revealing the importance of considering the

neuropsychological effect of multiple factors which, finally, are those that will determine the presence of these cognitive deficits inasmuch as they coexist with HIV itself. This lack of control over them in the research designs could explain, at least partly, the disparity of results in the abundant literature to this respect. Moreover, this study helps to outline the characteristics of the more neuropsychologically vulnerable seropositive subjects. The purpose of determining a profile of neuropsychological vulnerability in seropositive subjects is early detection with a view to preventing the manifestation of neuropsychological disturbances, and offer swift, suitable treatment. Furthermore, it can be used for planning intervention strategies not only in health or work behaviour but also in specific aspects related to infection.

References

Albein-Urios, N., Martinez-González, J. M., Lozano, O., Clark, L., & Verdejo-García, A. (2012). Comparison of impulsivity and working memory in cocaine addiction and pathological gambling: Implications for cocaine-induced neurotoxicity. *Drug Alcohol Dependence*, *126*(1–2). http://dx.doi.org/10.1016/j.drugalcdep.2012.03.008

Al-Khindi, T., Zakzanis, K. K., & Van Gorp, W. G. (2011). Does antiretroviral therapy improve HIV-associated cognitive impairment? A quantitative review of the literature. *Journal of the International Neuropsychology Society*, *17*, 956–969. http://dx.doi.org/10.1017/S1355617711000968

American Psychiatric Association. (2002). *Diagnosis statistical manual of mental disorders* (4th Rev. ed.). Washington, D.C.: American Psychiatric Association. DSM-IV-R.

Anand, P., Springer, S. A., Copenhaver, M. M., & Altice, F. L. (2010). Neurocognitive impairment and HIV risk factors: A reciprocal relationship. *AIDS Behaviour*, *14*(6), 1213–1226. http://dx.doi.org/10.1007/s10461-010-9684-1

Ardila, A., Roselli, M., & Strumwasser, S. (1991). Neuropsychological deficits in chronic cocaine abusers. *International Journal of Neurosciences*, *57*, 73–79.

Baldeweg, T., Catalan, J., Pugh, K., Gruzelier, J., Lovett, E., Scurlock, H., et al. (1997). Neuropsychological changes associated with psychiatric symptoms in HIV infected individuals without AIDS. *Biological Psychiatry*, *41*, 474–487.

Benito-Cuadrado, M. M., Esteba-Castillo, S., Böhm, P., Cejudo-Bolívar, J., & Peña-Casanova, J. (2002). Semantic verbal fluency of animals: A normative and predictive study in a Spanish population. *Journal of Clinical and Experimental Neuropsychology*, *24*(8), 1117–1122.

Benton, A. L. (1981). *(Visual retention test Benton) Test de retención visual de Benton*. Madrid, Spain: TEA.

Blackstone, K., Moore, D. J., Heaton, R. K., Franklin, D. R., Jr., Woods, S. P., Clifford, D. B., et al. (2012). Diagnosing symptomatic HIV-associated neurocognitive disorders: Self-report versus performance-based assessment of everyday functioning. *Journal of the International Neuropsychological Society*, *18*(1), 79–88. http://dx.doi.org/10.1017/S135561771100141X

Bornstein, R. A. (1994). Methodological and conceptual issues in the study of cognitive change in HIV infection. In I. Grant, & A. Martin (Eds.), *Neuropsychology of HIV infection* (pp. 146–160). New York, NY: Oxford University Press.

Byrd, D. A., Fellows, R. P., Morgello, S., Franklin, D., Heaton, R. K., Deutsch, R., et al. (2011). Neurocognitive impact of substance use in HIV infection. *Journal of Acquired Immune Deficiency Syndromes*, *58*(2), 154–162. http://dx.doi.org/10.1097/QAI.0b013e318229ba41

Centers for Disease Control. (1992). Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. *Morbidity and Mortality Weekly Report*, *41*(RR-17), 1–19.

Chang, S. L., Connaghan, K. P., Wei, Y., & Li, M. D. (2014). NeuroHIV and use of addictive substances. *International Review of Neurobiology*, *118*, 403–440. http://dx.doi.org/10.1016/B978-0-12-801284-0.00013-0

Cohen, R. A., Harezlak, J., Gongvatana, A., Buchthal, S., Schifitto, G., Clark, U., et al. (2010). Cerebral metabolite abnormalities in human immunodeficiency virus are associated with cortical and subcortical volumes. *Journal of Neurovirology*, *16*(6), 435–444. http://dx.doi.org/10.3109/13550284.2010.520817

Cohen, S., Ter Stege, J. A., Geurtsen, G. J., Scherpbier, H. J., Kuijpers, T. W., Reiss, P., et al. (2015). Poorer cognitive performance in perinatally HIV-infected children versus healthy socioeconomically matched controls. *Clinical Infectious Diseases*, *60*(7), 1111–1119. http://dx.doi.org/10.1093/cid/ciu1144

Coughlin, J. M., Wang, Y., Ma, S., Yue, C., Kim, P. K., Adams, A. V., et al. (2014). Regional brain distribution of translocator protein using [(11)C]DPA-713 PET in individuals infected with HIV. *Journal of Neuroviology*, *20*(3), 219–232. http://dx.doi.org/10.1007/s13365-014-0239-5

Cysique, L., Maruff, P., & Brew, B. (2006). The neuropsychological profile of symptomatic AIDS and ADC patients in the pre HAART era: A meta-analysis. *Journal of the International Neuropsychology Society*, *12*, 368–382.

De Oliveira, L. G., Barroso, L. P., Silveira, C. M., Sanchez, Z. V., De Carvalho Ponce, J., Vaz, L. J., et al. (2009). Neuropsychological assessment of current and past crack cocaine users. *Substance Use Misuse*, *44*(13), 1941–1957. http://dx.doi.org/10.3109/10826080902848897

Devlin, K. N., Gongvatana, A., Clark, U. S., Chasman, J. D., Westbrook, M. L., Tashima, K. T., et al. (2012). Neurocognitive effects of HIV, hepatitis C, and substance use history. *Journal of the International Neuropsychology Society*, *18*(1), 68–78. http://dx.doi.org/10.1017/S1355617711001408

Egan, V., Brettle, R. P., & Goodwin, G. M. (1992). The Edinburgh cohort of HIV-positive drug users: Pattern of cognitive impairment in relation to progression of disease. *British Journal of Psychiatry*, *161*, 522–531.

Egan, V., Deary, I. J., & Brettle, R. P. (1996). The Edinburgh Cohort of HIV-positive drug users: the effects of depressed mood and drug use upon neuropsychological function. *British Journal of Health Psychology*, *1*, 231–244.

Ellis, R. J., Hsia, K., Spector, S. A., Nelson, J. A., Heaton, R. K., Wallace, M. R., et al. (1997). Cerebrospinal fluid human immunodeficiency virus type 1 RNA levels are elevated in neurocognitively impaired individuals with acquired immunodeficiency syndrome HIV Neurobehavioral Research Center Group. *Annals of Neurology*, *42*, 679–688.

Ersche, K. D., Clark, L., London, M., Robbins, T. W., & Sahakian, B. J. (2006). Profile of executive and memory function associated with amphetamine and opiate dependence. *Neuropsychopharmacology*, *31*(5), 1036–1047.

Farinpour, R., Martin, E. M., Seindenberg, M., Pitrak, D. L., Pursell, K. J., & Harrow, M. (2000). Verbal working memory in HIV-seropositive drug users. *Journal of International Neuropsychological Society*, *6*, 548–555.

Fellows, R. P., Byrd, D. A., & Morgello, S. (2014). Effects of information processing speed on learning, memory, and executive functioning in people living with HIV/AIDS. *Journal of Clinical and Experimental Neuropsychology*, *36*(8), 806–817. http://dx.doi.org/10.1080/13803395.2014.943696

Fernandez-Serrano, M. J., Perez-Garcia, M., Schmidt Rio-Valle, J., & Verdejo-Garcia, A. (2010). Neuropsychological consequences of alcohol and drug abuse on different components of executive

functions. *Journal of Psychopharmacology*, *24*(9), 1317–1332. http://dx.doi.org/10.1177/0269881109349841

García-Torres, A., Vergara-Moragues, E., Piñón-Blanco, A., & Pérez-García, M. (2015). HIV-related neuropsychological impairment in patients with previous substance use: A preliminary study. *Revista Latinoamericana de Psicología*, *47*(3), 213–221. http://dx.doi.org/10.1016/j.rlp.2015.06.001

Golden, C. J. (1994). (*Test stroop color-word*) *Test de colores y palabras Stroop*. Madrid, Spain: TEA.

Grassi, M. P., Clerici, F., Perin, C., Zochetti, C., Borella, M., Cargnel, A., et al. (1995). HIV infection and drug use: influence on cognitive function. *AIDS*, *9*, 165–170.

Grassi, M. P., Perin, C., Borella, M., & Mangoni, A. (1999). Assessment of cognitive function in asymptomatic HIV-positive. *European Neurology*, *42*, 225–229.

Heaton, R. K., Chelune, G. J., Talley, J. L., Kay, G. G., & Curtiss, G. (2001). *WCST. Test de Clasificación de Tarjetas de Wisconsin*. Madrid, Spain: TEA Ediciones.

Heaton, R. K., Clifford, D. B., Franklin, D. R., Jr., Woods, S. P., Ake, C., Vaida, F., et al. (2010). HIV-associated neurocognitive disorders persist in the era of potent antiretroviral therapy: CHARTER study. *Neurology*, *75*(23), 2087–2096. http://dx.doi.org/10.1212/WNL.0b013e318200d727

Heaton, R. K., Franklin, D. R., Ellis, R. J., McCutchan, J. A., Letendre, S. L., & Leblanc, S. (2011). HIV-associated neurocognitive disorders before and during the era of combination antiretroviral therapy: differences in rates, nature and predictors. *Journal of Neurovirology*, *17*, 3–16. http://dx.doi.org/10.1007/s13365-010-0006-1

Hestad, K., Updike, M., Selnes, O. A., & Royal, W., III. (1995). Cognitive sequelae of repeated head injury in a population of intravenous drug users. *Scandinavian Journal of Psychology*, *36*, 246–255.

Kaplan, E., Goodglass, H., & Weintraub, S. (2001). *Boston naming test* (2nd ed.). Philadelphia, PA: Lippincott Williams and Wilkins.

Lescure, F. X., Omland, L. H., Engsig, F. N., Roed, C., Gerstoft, J., Pialoux, G., et al. (2011). Incidence and impact on mortality of severe neurocognitive disorders in persons with and without HIV infection: A Danish nationwide cohort study. *Clinical Infectious Diseases*, *52*(2), 235–243. http://dx.doi.org/10.1093/cid/ciq041

Lin, W., Li, Q., Zhu, J., Qin, Y., Zheng, Y., Chang, H., et al. (2013). White matter impairment in chronic heroin dependence: A quantitative DTI study. *Brain Research*, *19*(1531), 58–64. http://dx.doi.org/10.1016/j.brainres.2013.07.036

Lin, W. C., Chou, K. H., Chen, H. L., Huang, C. C., Lu, C. H., Li, S. H., et al. (2012). Structural deficits in the emotion circuit and cerebellum are associated with depression, anxiety and cognitive dysfunction in methadone maintenance patients: A voxel-based morphometric study. *Psychiatry Research*, *201*(2), 89–97. http://dx.doi.org/10.1016/j.pscychresns.2011.05.009

López, E., Ravindran, O. S., Mrudula, R. P., & Priya, G. (2014). Cognitive deficits in HIV infected children. *Indian Journal of Psychological Medicine*, *36*(3), 255–259. http://dx.doi.org/10.4103/0253-7176.135373

Lundqvist, T. (2005). Cognitive consequences of cannabis use: Comparison with abuse of stimulants and heroin with regard to attention, memory and executive functions. *Pharmacology, Biochemistry and Behavior*, *81*(2), 319–330.

Muñoz-Moreno, J. A., Fumaz, C. R., Ferrer, M. J., Prats, A., Negredo, E., Garolera, M., et al. (2008). Nadir CD4 cell count predicts neurocognitive impairment in HIV-infected patients. *AIDS Research and Human Retroviruses*, *24*(10), 1301–1307. http://dx.doi.org/10.1089/aid.2007.0310

Newman, S. P., Lunn, S., & Harrison, M. J. G. (1995). Do asymptomatic HIV-seropositive individuals show cognitive deficit? *AIDS*, *9*, 1211–1220.

Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia*, *9*(1), 97–113.

Paul, R. H., Ernst, T., Brickman, A. M., Yiannoutsos, C. T., Tate, D. F., Cohen, R. A., et al. (2008). Relative sensitivity of magnetic resonance spectroscopy and quantitative magnetic resonance imaging to cognitive function among nondemented individuals infected with HIV. *Journal of the International Neuropsychological Society*, *14*(5), 725–733. http://dx.doi.org/10.1017/S1355617708080910

Reitan, R. M. (1979). *Finger tapping test*. Arizona, AZ: Reitan Neuropsychology Laboratory.

Rey, A. (1964). (*The clinical psychological examination*) *L'examen clinique en psychologie*. Presses Universitaires de France Paris.

Rey, A. (1987). (*Copy test of complex figure*) *Test dc Copia de una Figura Compleja*. Madrid, Spain: TEA (original work published, 1959).

Rodríguez, D. (2000). *Afectación neuropsicológica temprana asociada a la infección por VIH en drogodependientes* Doctoral dissertation. Spain: University of Santiago de Compostela.

Rodríguez-Álvarez, M., & Vázquez-Justo, E. (2002). Influencia de factores relacionados con la infección en el rendimiento neuropsicológico de seropositivos al VIH. *Neurología*, *17*(6), 328–336.

Rubin, L. H., Cook, J. A., Weber, K. M., Cohen, M. H., Martin, E., Valcour, V., et al. (2015). The association of perceived stress and verbal memory is greater in HIV-infected versus HIV-uninfected women. *Journal of Neuroviology*, *21*(4), 422–432. http://dx.doi.org/10.1007/s13365-015-0331-5

Satz, P., Morgenstern, H., Miller, E. N., Selnes, O. A., McArthur, J. C., Cohen, B. A., et al. (1993). Low education as a possible risk factor for cognitive abnormalities in HIV-1: Findings from the multicenter AIDS cohort study (MACS). *Journal of Acquired Immune Deficiency Syndromes*, *6*, 503–511.

Selnes, O. A., Galai, N., McArthur, J. C., Cohn, S., Royal, W., III., Esposito, D., et al. (1997). HIV infection and cognition in intravenous drug users: Long term follow up. *Neurology*, *48*, 223–230.

Sevigny, J. J., Albert, S. M., McDermott, M. P., Schifitto, G., McArthur, J. C., Sacktor, N., et al. (2007). An evaluation of neurocognitive status and markers of immune activation as predictors of time to death in advanced HIV infection. *Archives of Neurology*, *64*(1), 97–102. http://dx.doi.org/10.1007/s13365-011-0053-2

Spudich, S. S., & Ances, B. M. (2015). CROI 2015: Neurologic complications of HIV Infection. *Topics in Antiviral Medicine*, *23*(1), 47–55.

Stankoff, B., Calvez, V., Suárez, S., Bassi, P., Rosenblum, O., Conquy, L., et al. (1999). Plasma and cerebrospinal fluid human immunodeficiency virus type-1 (HIV-1) RNA levels in HIV-related cognitive impairment. *European Journal of Neurology*, *6*(6), 669–675.

Stern, Y. (1994). Neuropsychological evaluation of the HIV patient. *Psychiatric Clinics of North America*, *17*, 125–134.

Tiffin, J. (1948). *Purdue pegboard*. Indiana, IN: Lafayette Instrument.

Tombaugh, T. N. (2004). Trail making test A and B: Normative data stratified by age and education. *Archives of Clinical Neuropsychology*, *19*(2), 203–214.

Trenerry, M. R., Crosson, B., Beboe, J., & Leber, W. R. (1990). *Visual search and attention test*. Florida, FL: Psychological Assesment Resources.

Vázquez-Justo, E., Piñón-Blanco, A., Vergara-Moragues, E., Guillén-Gestoso, C., & Pérez-García, M. (2014). Cognitive reserve during neuropsychological performance in HIV intravenous drug users. *Applied Neuropsychology Adult*, *21*(4), 288–296. http://dx.doi.org/10.1080/23279095.2013.813852

Vázquez-Justo, E., & Rodríguez-Álvarez, M. (2002). Influencia de factores no relacionados con la infección en el rendimiento neuropsicológico de seropositivos al VIH. *Revista de Neurología*, *35*, 474–480.

Vázquez-Justo, E., Rodríguez-Álvarez, M., & Carro-Ramos, J. (2003a). Neuropsychological performance in HIV/AIDS intravenous drug users. *Journal of Clinical and Experimental Neuropsychology*, *25*(6), 852–865.

Vázquez-Justo, E., Rodríguez-Álvarez, M., & Feraces-Otero, M. J. (2003b). Influence of depressed mood on neuropsychological performance in HIV seropositive drug users. *Psychiatry and Clinical Neurosciences*, *57*, 251–258.

Vázquez-Justo, E., Rodríguez-Álvarez, M., & Rodríguez-Salgado, D. (2000). Funcionamiento neuropsicológico en drogodependientes VIH/SIDA inmunodeprimidos: Importancia de la fase de la infección y del consumo de drogas. *Revista Española de Drogodependencias*, *25*, 263–278.

Verdejo-García, A., Betanzos-Espinosa, P., Lozano, O. M., Vergara-Moragues, E., González-Saiz, F., & Pérez-García, M. (2012). Self-regulation and treatment retention in cocaine dependent individuals: A longitudinal study. *Drug, Alcohol & Dependence*, *122*(1–2), 142–148. http://dx.doi.org/10.1016/j.drugalcdep.2011.09.025

Vergara-Moragues, E., Vergara de Campos, A., & Girón-González, J. A. (2010). Deterioro neuropsicológico asociado al síndrome de inmunoficiencia adquirida en pacientes expolitoxicómanos con exclusión social. *Enfermedades Infecciosas y Microbiologia Clinica*, *28*(5), 294–296. http://dx.doi.org/10.1016/j.eimc.2009.05.007

Wechsler, D. (1999). *Escala de inteligencia de Weschler para adultos*. Madrid, Spain: TEA.

White, D. A., Heaton, R. K., Monsch, A. U., & The HNRC Group. (1995). Neuropsychological studies of asymptomatic human immunodeficiency virus type-1 infected individuals. *Journal of the International Neuropsychological Society*, *1*, 304–315.

Wilkins, J. W., Robertson, K. R., Van Der Horst, C., Robertson, W. T., Fryer, J. G., & Hall, C. D. (1990). The importance of confounding factors in the evaluation of neuropsychological changes in patients infected with human immunodeficiency virus. *Journal of Acquired Immune Deficiency Syndromes*, *3*, 938–942.

Woods, S. P., Moore, D. J., Weber, E., & Grant, I. (2009). Cognitive neuropsychology of HIV-associated neurocognitive disorders. *Neuropsychology Review*, *19*(2), 152–168. http://dx.doi.org/10.1007/s11065-009-9102-5