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Characteristics of the neuropsychological performance in patients with HIV infection

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Objective. Objective. To describe the characteristics of the neuropsychological performance of patients with HIV infection in the different stages of the infection.

Methods. A clinical sample made up of 122 patients was obtained: asymptomatic seropositive subjects: Stage A (n = 30), Stage B (n = 17), Stage C or AIDS: Stage C (n = 41) and seronegative subjects: Control Group (n = 34). All the subjects underwent the same evaluation procedure: neuropsychological assessment, an interview on sociodemographic and clinical aspects. The results were compared based on the serological situation and clinical stage.

Results. Performance of the seropositive subjects was lower than that of the seronegative ones (Group Control) in all the studied factors: 1) Visual memory (F = 12.83; p < 0.000); 2) Attention/psychomotor speed (F = 18.25; p < 0.000); 3) verbal intelligence/abstract reasoning (F = 11.97; p < 0.000); 4) Verbal memory for texts (F = 6.43; p < 0.000); and 5) verbal memory for digits and words (F = 6.27; p < 0.001). Inside the group of seropositive subjects, the patients with AIDS (Phase C) presented the lowest levels of execution in all the factors. The functions demonstrating the worse performance were those of: Attention/psychomotor speed, visual memory and verbal intelligence/abstract reasoning.

Conclusions. Neuropsychological performance is clearly diminished in the advanced phases of the disease, this not being as clear in the asymptomatic phases. In view of the characteristics of the neuropsychological performance observed in the early stages of the infection, we consider that these cannot be used as reliable predictors of more severe future neuropsychological alterations characteristic of the most advanced phases of HIV infection.

Key words:

HIV. AIDS. Neuropsychological performance. Clinical stages.

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Características del rendimiento neuropsicológico de pacientes infectados por VIH

Objetivo. Describir las características de la ejecución neuropsicológica de pacientes con infección por VIH en las diferentes fases de la infección.

Métodos. Se reclutó una muestra clínica compuesta por 122 pacientes: seropositivos asintomáticos: fase A (n = 30), seropositivos con sintomatología menor: fase B (n=17), sujetos con SIDA: fase C (41) y seronegativos: grupo control (34). Todos los sujetos fueron sometidos al mismo proceso de evaluación (examen neuropsicológico, entrevista sobre aspectos sociodemográficos y clínicos. Contrastando los resultados en base a la situación serológica y el estadio clínico.

Resultados. Los sujetos seropositivos tuvieron un rendimiento inferior a los seronegativos (grupo control), en todos los factores estudiados: 1) Memoria visual (F = 12,83; p < 0,000); 2) Atención/velocidad psicomotora (F = 18,25; p < 0,000); 3) Inteligencia verbal/pensamiento abstracto (F = 11,97; p < 0,000); 4) Memoria verbal para textos (F = 6,43; p < 0,000); y 5) Memoria verbal para dígitos y palabras (F = 6,27; p < 0,001). Dentro del grupo de sujetos seropositivos, los pacientes con SIDA (fase C) presentaron los niveles de ejecución más bajos en todos los factores, siendo las funciones que evidenciaron peor rendimiento las referidas a atención/velocidad psicomotora, memoria visual e inteligencia verbal/pensamiento abstracto.

Conclusiones. El rendimiento neuropsicológico se ve claramente disminuido en las fases avanzadas de la enfermedad, no siendo tan claro en las fases asintomáticas. A la vista de las características del rendimiento neuropsicológico observado en las fases tempranas de la infección, consideramos que estas no pueden utilizarse como predictores confiables de futuras alteraciones neuropsicológicas más graves, propias de las fases más avanzadas de la infección por VIH.

Palabras clave:

VIH. SIDA. Rendimiento neuropsicológico. Estadio clínico.

INTRODUCTION

The study of the neuropsychological consequences of HIV-1 infection during asymptomatic stages has been characterized by the variety and discrepancy of the results.¹⁻² However, no one questions that there is neuropsychological deterioration in the symptomatic or advanced stages of the disease. Nonetheless, an important attempt must be made to establish an adequate estimation of the grade of cognitive deterioration in the different stages of HIV-1 infection in order to understand the relationship existing between the HIV-1 associated minor cognitive complex and HIV-1 associated dementia. This is because it is currently unknown if both diagnoses represent different stages of the same disorder or if they are really independent clinical conditions.³

Several studies have tried to analyze the reasons for the variety and discrepancy of the results,⁴⁻⁷ especially found in the asymptomatic stages. They have identified a series of methodological features that may be the cause of this inequality of results, among them: 1) the criteria used for the inclusion and exclusion of the subjects; 2) the presence and adequacy of the control groups; 3) the nature and representativeness of the neuropsychological assessment instruments used and 4) the different methods used to analyze and interpret the data obtained as a result of the neuropsychological evaluation.

The pattern of neuropsychological involvement observed in the asymptomatic seropositive patients presents great variability and also has a very heterogeneous prevalence and severity.⁸ Patients with subclinical neuropsychological disorders generally have deficits in attention, memory, abstract thinking and slow-down in data processing speed.⁹⁻¹⁰ In general, the neuropsychological performance of AIDS patients is qualitatively similar to that of the asymptomatic ones,¹¹ observing worse performance when the subjects have to cope with tasks with limited time, problem solving, visual recognition and understanding, visuomotor integration and alternance between several series of stimuli.¹¹

In spite of the abundant international research, few studies have been conducted in our setting. Thus, the question, the purpose of the present study, is to describe the neuropsychological performance of patients with HIV infection based on the clinical stage variable, in agreement with the diagnostic criteria of the Centres for Disease Control and Prevention.¹²

METHOD

The sample is made up of 122 subjects, men and women, 88 seropositive heterosexual subjects who received medical care in the Complejo Hospitalario of Orense (Spain): 30 asymptomatic subjects in Stage A, 17

with minor symptoms in Stage B, 41 with AIDS, in Stage C, and 34 seronegative heterosexual subjects with no background of substance abuse, who made up the Control group.

For the selection of the seropositive subjects, the following criteria were taken into account: being HIV-1 infected, not being coinfecting with HIV-2, not having been hospitalized in the last 30 days, not having consumed drugs in the last 3 months, although being in methadone maintenance programs was permitted, not having presented a picture of chronic and severe alcohol abuse in the last 6 months, not having other CNS conditions, caused by opportunistic pathogens, opportunistic neoplasms or systemic disorders, not presenting peripheral nervous system and muscle conditions that could affect neuropsychology performance of the subject, not having any severe psychiatric neurological background or those that require psychopharmaceutical treatment or that alter the awareness level or behavior of the subject and having been infected by heterosexual transmission or through parenteral drug consumption.

Regarding the enrolment of subjects from the control group, those subjects who had no background of drug dependence, who belonged to the social-familial setting of the HIV infected persons or who were at risk of infection, matching them with seropositive patients, of similar age, gender, school level and hand dominance were selected.

All the subjects selected were previously informed of the purpose of the research and were asked for their consent. Then they were given an appointment for the application of the tests that had to coincide with the day in which the control analyses were performed. In this way, we could obtain reliable measurements of the CD4, viral load and other clinical-biological parameters through an economical procedure.

The same evaluation procedure was used for all the subjects. This consisted in the administration of a semistructured interview on sociodemographic, toxicological and clinical aspects and a neuropsychological evaluation using an «integrated battery» designed *ad hoc* for this study. The neuropsychological battery was made up of a combination of tests, of wide tradition in the neuropsychological study. These evaluated a wide range of cognitive functions. The functions were regrouped according to the results of a factorial analysis (Kaiser Varimax method) that resulted in a grouping of five factors. The factors accounted for 73.34% of the variance, according to that stated in previously published works.¹³ The factors were: 1) Visual memory (Benton Visual Retention Test,¹⁴ successes and errors; Rey Complex Figure Test,¹⁵ reproduction of memory and copy); 2) Attention/psychomotor speed (Trail making test,¹⁶ parts A and B; Digit Coding Subtest of WAIS-R,¹⁷ and Toulouse Pieron¹⁸); 3) Verbal intelligence/abstract thinking (WAIS-R subtests,¹⁷ Vocabulary, Comprehension and Similarities); 4) Verbal

memory for texts (History of Backcock,¹⁹ immediate and delayed recall and 5) Verbal Memory for Digits and Words (Rey Auditory-Verbal Test of Rey²⁰; successes; and direct and inverse Digit subtest of WAIS-R¹⁷).

For the data processing, an analysis of comparison of means was done using the ANOVA and Chi Square statistical test. Comparisons were made between the seropositive subjects (who were, in turn, subdivided into three groups according to the diagnostic criteria of the Centres for Disease Control and Prevention:¹² Stage A, Stage B and Stage C) and between these and the Control group. All the neuropsychological tests were applied and scored with standardized procedures, their gross scores being transformed into T scores.

Version 14 of the statistical program for social sciences SPSS-PC was used for the data processing.

RESULTS

Sociodemographical and clinical characteristics of the sample

As can be seen in tables 1a and 1b, once the contrast of variables used for the Control of homogenization is performed between the Control group and the seropositive patient group, both were equivalent in all the variables used: age, gender, schooling level and hand dominance (Table 1a and 1b).

In regards to the seropositive patient group, as was expected, statistically significant differences were found regarding the variables (tables 1a and 2b): *number of CD₄/mm³* ($\chi^2_{(2)}=22.72$; $p < 0.000$), *post hoc* analyses (Tukey method) identified the existence of significant differences

Variables	Stage A (n = 30)	Stage B (n = 17)	Stage C (n = 41)	Control group (n = 34)	F Value
Age	33.07 (5.67)	34.76 (5.57)	34.00 (4.69)	32.60 (6.16)	0.85
Education level	10.30 (3.74)	9.47 (2.07)	9.39 (2.05)	9.89 (2.39)	1.61
Viral load	25943.83 (54454.56)	69867.65 (188975.99)	152380.00 (398115.55)	---	1.77
CD ₄ /mm ³	511.36 (291.92)	298.64 (149.97)	181.02 (133.90)	---	22.72***

Variables	Stage A (n = 30)	Stage B (n = 17)	Stage C (n = 41)	Control Group (n = 34)	Value χ^2	
Gender	Men (%)	53.30	76.50	68.30	52.95	4.73
	Women (%)	46.70	23.50	31.70	47.05	
Dominance Hand	Right- hand (%)	93.30	100.00	100.00	88.90	4.02
	Left-hand (%)	6.70	0.00	0.00	11.10	
Background Consumption Drugs	Never consumed (%)	26.70	17.60	24.40	---	0.69
	Abstinent IDU (%)	40.00	41.20	36.60	---	
	MMP (%)	33.30	41.20	39.00	---	
Treatment Antiretroviral	Yes (%)	63.30	94.10	92.70	---	12.41**
	No (%)	36.70	5.90	7.30	---	

Abbreviations: IDU: Intravenous drug user; MMP: Methadone maintenance program.
*p < 0.05; **p < 0.01; ***p < 0.001.

between the patients of stage A and stage B ($p < 0.003$) and with those of stage C ($p < 0.000$). However, this did not occur between the patients of stage B and C or AIDS stage ($p > 0.119$). Antiretroviral treatment ($\chi^2_{(2)} = 12.41$; $p < 0.001$), the *a posteriori* analyses indicated differences between stage A patients with those of stage B ($\chi^2_{(1)} = 5.41$; $p < 0.020$) and with those of stage C ($\chi^2_{(1)} = 9.43$; $p < 0.002$), but not between clinical stages B and C patients ($\chi^2_{(1)} = 0.04$; $p > 0.844$).

Neuropsychological performance

In the first place, for the analysis of neuropsychological performance based on the clinical stage, the contrast of each one of the mean scores of the seropositive subject group (1 = Stage A; 2 = Stage B and 3 = Stage C) and the Control Group was used. After, the mean scores obtained in each factor within the seropositive patient group was contrasted (Figure 1).

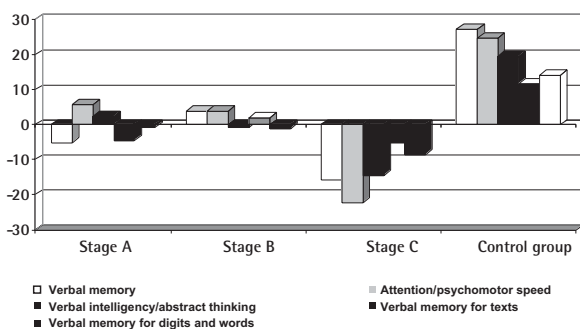


Figure 1 Levels of neuropsychological performance based on clinical stage variable.

The level of performance of the subjects in the factor that evaluated Visual Memory showed statistically significant intergroup differences ($F_{(3)} = 12.83$; $p < 0.000$). The subjects of the Control Group obtained higher scores on this factor than the other groups, the differences in regards to the stage A or asymptomatic subjects ($p < 0.000$) and those of stage C or AIDS stage ($p < 0.000$) being statistically significant. No differences in the performance in this factor ($F_{(2)} = 2.64$; $p > 0.077$) were found in regards to the analysis of the neuropsychological performance within the group of seropositive patients.

The seropositive patients obtained significantly lower scores than those of the control group in the factor that measured Attention/Psychomotor Speed ($F_{(3)} = 18.27$; $p < 0.000$). The *a posteriori* tests (Tukey Method) found significant differences between the Control Group and those subjects included in clinical A ($p < 0.039$) and C ($p < 0.000$) categories. On the other hand, statistically significant dif-

ferences ($F_{(2)} = 9.93$; $p < 0.000$) were found between the performance of those forming the clinical A and C ($p < 0.000$) and between B and C ($p < 0.005$) categories, but not between the patients of stages A and B ($p > 0.971$).

Statistically significant intergroup differences were detected ($F_{(3)} = 11.97$; $p < 0.000$) in the Factor that evaluated tasks related with Abstract Thinking / Verbal Intelligence. Performance of the Control Group subjects was superior to that of the other groups, with significant differences regarding performance of the subjects included in categories A ($p > 0.028$), B ($p < 0.027$) and C ($p < 0.000$). In addition, significant differences were found between the performance levels of seropositive patients ($F_{(2)} = 4.60$; $p < 0.013$), but only between those included in clinical categories A and C ($p < 0.015$).

In regards to the tests that evaluated Verbal Memory for Texts, the analysis of variance detected statistically significant intergroup differences ($F_{(3)} = 6.43$; $p < 0.000$), while the *a posteriori* significance tests revealed differences in performance between the subjects of the Control group and those forming the clinical categories of A ($p < 0.003$) and C ($p < 0.001$). On the contrary, the analysis of neuropsychological performance of the seropositive patients in this factor revealed the absence of statistically significant differences ($F_{(2)} = 1.07$; $p > 0.349$).

Finally, significant intergroup differences were found in the tests that were included in the factor of Verbal Memory for Digits and Words ($F_{(3)} = 6.27$; $p < 0.001$). Once again, the control group obtained the best performance levels, the differences being statistically significant regarding the patients of the clinical categories A ($p < 0.043$) and C or AIDS stage ($p < 0.000$). In regards to the seropositive patients, no statistically significant differences were found in the neuropsychological performance in this factor between patients of the difference clinical stages ($F_{(2)} = 1.63$; $p > 0.202$).

DISCUSSION

The analysis of the data shows that seropositive patients as a whole obtained lower levels of neuropsychological performance in all the factors studied, differences that were statistically significant regarding the control group. Within the seropositive group, the AIDS patients presented lower performance levels in all the factors studied. However, statistically significant differences were only found regarding the patients of clinical stages A and B in two factors: attention/psychomotor speed and verbal intelligency/abstract thinking.

On the other hand, although no significant differences were found between the performance of asymptomatic patients (Stage A) and patients with minor symptoms (Stage B), it is true that the latter had better performance in the tests

that constituted the factors for visual memory and verbal memory for texts. The fact that the stage B patients were receiving antiretroviral treatment in a larger proportion may have induced improvements in the neuropsychological performance of these factors since, as has been reported in several studies, antiretroviral therapy may improve the neuropsychological performance of HIV-infected subjects.²¹⁻²⁴

One important feature deduced from the analysis of the data from this study refers to the fact that we have not found that neuropsychological performance describes a pattern of progressive worsening, parallel clinical and biological deterioration observed as the HIV infection advances. Great variability in the neuropsychological performance of seropositive patients without AIDS was also reflected.⁴⁻⁸ Thus, it does not seem that the neuropsychological alterations observed in the early stages of the infection serve as reliable predictors of future severe neuropsychological alterations characteristics of the more advanced stages of the disease.³⁻²⁵

In synthesis, our data are consistent with those of Price, Brew, Sidtis et al.²⁶ who state that the neuropsychological performance of AIDS patients is qualitatively similar to that of asymptomatic subjects, this been more clearly seen when the subject has to cope with tasks against the clock, problem solving or tasks that require recognition and processing of visual information. Furthermore, the type of deficits observed is consistent with the hypothesis of a pattern of affection that involves the subcortical frontal systems. This is characterized by difficulties of performance of complex cognitive tasks and slow-down of data processing.¹⁰⁻²⁷

In summary, the data reported in this research support the thesis that the AIDS stage regarding other clinical stages of HIV-1 infection is associated to lower neuropsychological performance levels. This aspect has been widely and consistently reported in the international literature²⁸⁻³² and in the few studies performed in our setting.³³⁻³⁴ In addition, both symptomatic and asymptomatic seropositive subjects present a significantly lower neuropsychological performance than seronegative ones. This confirms the influence of HIV on neuropsychological functioning.³³⁻³⁵

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