

The Impact of Rheumatoid Arthritis in Neuropsychology, Depression and Anxiety. A Case-Control Study, with 90 Portuguese Female Subjects.

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Resumen

Objetivos: The study of the impact of Rheumatoid Arthritis in cognitive functions has not been well documented in Portugal. So, with this original article we tried to clarify this reality in this particular country. **Methods:** We assessed the results of 45 Rheumatoid Arthritis female patients (intervention group), comparing each patient in a case control paired strategy (years in school and age), with control subjects (n = 45, in a total of 90 subjects). All subjects were evaluated with Paced Auditory Selective Attention Test, Word List Generation Test, Luria Nebraska Neuropsychological Battery, a Portuguese depression screening test (IACLIDE), STAI (anxiety trace and trait test) and the Mini Mental state examination. **Results:** The results show, for the first time in Portuguese patients, the presence of major deficits in terms of cognitive function and symptoms of depression and anxiety. **Conclusion:** This article strengthens the argument of the necessity to pay attention in psycho-educational, psychotherapeutic and cognitive stimulation as well as neuropsychological intervention in these types of patients.

Key-words: Neuropsychological assessment, inflammatory / rheumatic diseases; depression, anxiety.

Resumen

Objetivos: El estudio del impacto de la Artritis Reumatoidea en las funciones cognitivas no ha sido bien documentado en Portugal. En este trabajo tratamos de aclarar esta realidad en este país en particular. **Métodos:** Evaluamos los resultados de 45 pacientes femeninas con Artritis Reumatoidea (grupo de intervención), comparando cada paciente en estrategia pareada de caso control (años en la escuela y edad), con sujetos controles (n=45, en total 90 sujetos). Todos los sujetos fueron evaluados con Prueba de Atención Auditiva Selectiva, Test de Generación de Palabras, Batería Neuropsicológica de Luria, Evaluación Portuguesa de Depresión, STAI (anxiety trace and trait test) y examen de Estado Mínimo Mental. **Resultados:** Los resultados demuestran, por primera vez en pacientes portugueses, la presencia de déficits mayores en términos de función cognitiva y síntomas de depresión y ansiedad. **Conclusión:** Este artículo fortalece el argumento de la necesidad de prestar atención en la estimulación psico-educacional, psicoterapéutica y cognitiva, así como la intervención neuropsicológica en este tipo de pacientes.

Palabras clave: evaluación neuropsicológica, enfermedades inflamatorias /reumáticas, depresión, ansiedad.

Rev. Ecuat. Neurol. Vol. 21, N° 1-3, 2012

Introduction

Since the first unpublished description of Rheumatoid Arthritis (RA), from Landré-Beauvais, in 1800,¹ the knowledge about this condition increased dramatically. Known since Hippocrates as gout, after 1800 RA started to be seen as a particular etiological entity. Generally RA is considered a progressive and disabling auto-immune disease,² provoking severe physical, emotional and financial problems.³ RA is characterized by inflammation of the lining at the joints, and this can provoke long term injury, chronic pain, limited daily activity,⁴ and familiar emotional distress.⁵ It is estimated that in USA there is a prevalence of approximately 1 in 108 or 0.92% (2.5 million people in USA),⁶ and almost ninety seven thousand in Portugal.

As time passed, patients and clinicians started to be aware with other kind of symptoms that seem to affect RA patients in a very marked way: chronic fatigue,⁷ psychiatric disorders,⁸ with major incidence of Depression and Anxiety,⁹⁻¹³ and others.

From another point of view, one particular point that we would like to bring to discussion, is the relation of depressive and anxiety symptoms with neuropsychological data in RA patients. A cognitive and neuropsychological deficit pattern in RA has been reported in several studies in the last years of clinical research.¹⁴

Methodology

We assessed 90 subjects (45 rheumatoid subjects and 45 control subjects, paired by age more or less 3 years,

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and years in School, more or less 3 years). The intervention group was collected in different centers (institutions) for specialized care in Rheumatic patients, in the Center Region of Portugal. Control subjects were selected by statistical convenience method.

Short description of tests

- Paced Auditory Serial Addition Test (PASAT) is a measure of cognitive function, developed by Gronwall in 1977,¹⁵ which expressly assess acoustic information processing swiftness and plasticity, as well as computation ability. The patient has to execute a serial summation of numbers (61 items and 60 calculations) that are given in a CD voice support, in a rate of 2 or 3 seconds. The results could vary in a range of 0 to 60. Scores lower than percentile 5, considering the normal population, are usually considered to be in the compromised range.

- The Word List Generation procedure assess the ability to produce and access semantic knowledge, through the process of naming words of a particular category or starting with a particular letter.¹⁶ The subject is expected to be able to present, as a minimum, 10 items (names of vegetables, animals and words that starts with the letter P). A result indicating less than 10 items is considered very poor.

- Mini Mental State Examination was developed by Folstein et al¹⁷⁻¹⁸ as a brief test used to screen cognitive impairment. In the Portuguese version, the test has 30 items and the results of this test could range from 0 (severe cognitive deterioration), to 30 (no signal of cognitive deterioration).

- The Luria Nebraska Neuropsychological Battery (LNNB) allows study and analyzes neuropsychological performance of control and patient subjects, both genders, adults (aged 18-65) from different academic levels. The principal neuropsychological functions assessed were Motor, Rhythm, Tactile, Visual, Receptive Speech, Expressive Speech, Writing, Reading, Arithmetic, Memory and Intellectual Processes.^{19, 20} The test is composed by more than 740 different items / tasks, with different ways of correction. For each subject (and in each scale) we have to calculate a value ("Critical Value") considering the age and years in school. This Critical Value will serve, individually, to identify if the subject is above or not a T note of normality (results lower than T = 60 represents normality).

- The State-Trait Anxiety Inventory (STAI) was conceptualized as a study instrument to explore anxiety in adults.²¹ The test is composed by two scales (trait and state). Each scale is composed by 20 items that should represent the way the subject is feeling in the moment of test taking. Using a 4 points range for each item, the results in the test varies from 20 to 80. Higher results represent higher levels of anxiety in both scales (State and Trait)

- IALCIDE – It is a test adapted to Portuguese population to assess Depressive Symptoms.²² The test is composed by 21 items that should represent the way the subject is feeling in the moment of test taking (using a five point range 0-4). Results may vary from 0 to 84. Results lower than 20 represent normality. Then, the level of depression indicators increases as the sum of items provides a higher result. For instance a result of 25 could represent light indication of depression, but a result of 75 represents a strong indication of Severe Depression.

Results

In Table I we can see that the mean age for control subjects are 40,76, with a standard deviation of 10,05, and the mean for years in school are 10,64, with a standard deviation of 4,09. Regarding to the intervention group (RA patients), the mean age is 41,07, with a standard deviation of 9,68 and the mean for years in School are 10,16, with a standard deviation of 4,03. None of these differences are statistically significant (Age: $t = -1,016$; $p = ,315$; Years in school: $t = 1,830$; $p = 0,074$).

In Table II we can see that the mean results in PASAT test for control subjects are 30,51 with a standard deviation of 10,76 and the mean for intervention group is 17,69 with a standard deviation of 10,76, being this difference statistically significant ($t = 10,004$; $p = 0,023$). We also verified that the mean results in WLG for control subjects is 17,69 with a standard deviation of 3,24 and the mean for intervention group is 9,07 with a standard deviation of 3,12, being this difference statistically significant ($t = 14,600$; $p = 0,034$). Finally, in Table II we verify that the mean results in MMSE for control subjects is 28,86 with a standard deviation of 1,44 and the mean for intervention group is 27,86 with a standard deviation of 2,56, being this difference statistically significant ($t = 2,396$; $p = 0,021$).

In Table III we can see that the mean results in STAI (anxiety) test for control subjects are 41,11 with a standard deviation of 6,0, and the mean for intervention group is 57,40 with a standard deviation of 8,83, being this difference statistically significant ($t = -13,869$; $p = 0,013$). Regarding to depressive symptoms (Ialide Test) we can see that the mean results for control subjects were 11,16 with a standard deviation of 11,03 and the mean results for intervention group were 20,91 with a standard deviation of 9,04, being this difference statistically significant ($t = -5,913$; $p = 0,010$).

In Table IV we can see the mean results in all Clinical Scales of Luria Nebraska Neuropsychological Battery (LNNB). In the Motor Functions C1 Scale, the Control subjects present a mean punctuation of 9,02 with a standard deviation of 8,76 and the mean for intervention group is 15,14 with a standard deviation of 12,82, being this difference statistically significant ($t = -3,404$; $p = 0,001$).

Table I. Different average in Age and Years in School.

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Age Controls	40,76	45	10,05	1,50
	Age Intervention Group	41,07	45	9,68	1,44
Pair 2	Years in School Controls	10,64	45	4,09	,61
	Years in School Intervention Group	10,16	45	4,03	,60

Table II. Different average in PASAT, WLG and MMSE.

		Mean	N	Std. Deviation	Std. Error Mean
Pair 3	PASAT Controls	30,51	45	10,76	1,60
	PASAT Intervention Group	17,69	45	7,77	1,16
Pair 4	WLG Controls	17,69	45	3,24	,48
	WLG Intervention Group	9,07	45	3,12	,47
Pair 5	MMSE Controls	28,86	42	1,44	,22
	MMSE Intervention Group	27,86	42	2,56	,40

Table III. Different average in STAI (Anxiety) and Depressive Symptoms.

		Mean	N	Std. Deviation	Std. Error Mean
Pair 6	STAI Controls	41,11	45	6,04	0,90
	STAI Intervention Group	57,40	45	8,83	1,32
Pair 7	laclide Depression Controls	11,16	44	11,03	1,66
	laclide Depression Intervention Group	20,91	44	9,04	1,36

In Rhythm Functions C2 Scale, the Control subjects present a mean punctuation of 1,62 with a standard deviation of 1,89 and the mean for intervention group is 3,67 with a standard deviation of 2,74, being this difference statistically significant ($t = -3,855$; $p = 0,012$).

In Tactile Functions C3 Scale, the Control subjects present a mean punctuation of 4,69 with a standard deviation of 4,90 and the mean for intervention group is 7,24 with a standard deviation of 5,88, being this difference statistically significant ($t = -2,690$; $p = 0,010$).

In Visual Functions C4 Scale, the Control subjects presents a mean punctuation of 6,74 with a standard deviation of 3,41 and the mean for intervention group is 10,43 with a standard deviation of 4,60, being this difference statistically significant ($t = -4,930$; $p = 0,021$).

Table IV. Different average in Clinical scales of Luria Nebraska Neuropsychological Battery.

		Mean	N	Std. Deviation	Std. Error Mean
Pair 8	C1 Motor Functions Controls	9,02	42	8,76	1,35
	C1 Motor Functions Intervention Group	15,14	42	12,82	1,98
Pair 9	C2 Rhythm Controls	1,62	42	1,89	,29
	C2 Rhythm Intervention Group	3,67	42	2,74	,42
Pair 10	C3 Tactile Functions Controls	4,69	42	4,90	,76
	C3 Tactile Functions Intervention Group	7,24	42	5,88	,91
Pair 11	C4 Visual Functions Controls	6,74	42	3,41	,53
	C4 Visual Functions Intervention Group	10,43	42	4,60	,71
Pair 12	C5 Receptive Speech Controls	4,83	42	4,66	,72
	C5 Receptive Speech Intervention Group	7,50	42	5,64	,87
Pair 13	C6 Expressive Speech Controls	6,55	42	5,58	,86
	C6 Expressive Speech Intervention Group	10,86	42	8,25	1,27
Pair 14	C7 Writing Controls	1,88	42	2,70	,42
	C7 Writing Intervention Group	3,67	42	3,29	,51
Pair 15	C8 Reading Controls	1,67	42	1,73	,27
	C8 Reading Intervention Group	2,40	42	2,37	,37
Pair 16	C9 Arithmetic Controls	3,90	42	2,80	,43
	C9 Arithmetic Intervention Group	5,81	42	5,13	,79
Pair 17	C10 Memory Controls	5,17	42	3,98	,61
	C10 Memory Intervention Group	9,10	42	5,05	,78
Pair 18	C11 Intellectual Processes Controls	19,83	42	10,79	1,67
	C11 Intellectual Processes Intervention Group	27,02	42	10,89	1,68

In Receptive Speech Functions C5 Scale, the Control subjects presents a mean punctuation of 4,83 with a standard deviation of 4,66 and the mean for intervention group is 7,50 with a standard deviation of 5,64, being this difference statistically significant ($t = -3,082$; $p = 0,004$).

In Expressive Speech Functions C6 Scale, the control subjects present a mean punctuation of 6,55 with a standard deviation of 5,58 and the mean for intervention group is 10,86 with a standard deviation of 8,25, being this difference statistically significant ($t = -4,792$; $p = 0,007$).

In Writing Functions C7 Scale, the control subjects present a mean punctuation of 1,88 with a standard deviation of 2,70 and the mean for intervention group is 3,67 with a standard deviation of 3,29, being this difference statistically significant ($t = -4,930$; $p = 0,021$).

tion of 2,70 and the mean for intervention group is 3,67 with a standard deviation of 3,29, being this difference statistically significant ($t = -3,868$; $\rho = 0,012$).

In Reading Functions C8 Scale, the control subjects present a mean punctuation of 1,67 with a standard deviation of 1,73 and the mean for intervention group is 2,40 with a standard deviation of 2,37. This difference is not statistically significant ($t = -1,728$; $\rho = 0,091$).

In Arithmetic Functions C9 Scale, the control subjects presents a mean punctuation of 3,90 with a standard deviation of 2,80 and the mean for intervention group is 5,81 with a standard deviation of 5,13, being this difference statistically significant ($t = -2,199$; $\rho = 0,034$).

In Memory Functions C10 Scale, the control subjects presents a mean punctuation of 5,17 with a standard deviation of 3,98 and the mean for intervention group is 9,10 with a standard deviation of 5,05, being this difference statistically significant ($t = -4,932$; $\rho = 0,032$).

In Intellectual Processes Functions C11 Scale, the control subjects presents a mean punctuation of 19,83 with a standard deviation of 10,79 and the mean for intervention group is 27,02 with a standard deviation of 10,89, being this difference statistically significant ($t = -4,341$; $\rho = 0,024$).

Discussion

In this article we tried to assess a particular set of intervention subjects with Rheumatoid Arthritis, in a case control study. We verified, in this original Portuguese study that in the majority of the evaluated constructs, the intervention group presented worse results than paired control subjects considering statistical significance.

Due to a good paired strategy, we can see that the mean age for control subjects doesn't differ from patient's mean age, as well as for the years in school. This guarantee to us that the verified differences presented in the several test utilized should not be attributed to differences in age, academic level and gender (this last variable was a constant).

Regarding to differences in anxiety and depression, confirming prior studies, our intervention group presented more psychiatric symptoms, which are considered as two concurrent pathologies that produce strong deficits in daily life tasks, as well as in quality of life.²³⁻³⁸

Regarding to neuropsychological results, our data is in concordance with several studies that support that RA patients present a strong deficit in attention and executive functions when measured with these types of tests.³⁹ Several investigators also reported deficits in intervention group with RA on tasks requiring differentiation of similar letter and pattern comparison tests of information processing speed in connection with upper levels of pain and depression,⁴⁰ as we will approach latter.

Like in prior international publications, this original study found neuropsychological deficits in RA Portuguese patients. In a study realized to define the inci-

dence of cognitive impairment in patients with RA, 40 patients with RA and 40 healthy controls were evaluated. The major conclusion was that cognitive impairment was not connected to clinical and treatment types or disability once it appears as an independent deficit (not related with the well-known relation between RA, Depression and Anxiety disorders).⁴¹

Other recent study using the Automated Neuropsychological Assessment Metrics (ANAM) shows that RA patients, when compared with healthy matched controls, present 61% more neuropsychological deficits.⁴²

Conclusions

Our results, confirms, in a very structured way, what Portuguese Rheumatologists already know, as reported by official websites of Portuguese Rheumatologists.⁴³ RA produces strong deficits not only in somatic, emotional and cognitive experiences, but also in Neuropsychological reality.

This is the first Portuguese Study with RA patients demonstrating strong deficits in Neuropsychological dimensions of daily life, (as well as the already known relation with depressive and anxiety constructs).

So, this article strengthens the necessity to pay attention to psychoeducational, psychotherapeutic and cognitive stimulation as well as neuropsychological intervention in this type of patients.

Acknowledgements

The author is grateful to the participants and reports no potential conflicts of interest.

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