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# ANSIEDAD, DEPRESIÓN Y NEUROPSICOLOGÍA EN ARTRITIS REUMATOIDE EN 180 MUJERES PORTUGUESAS. UN ESTUDIO DE CASO-CONTROL

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## RESUMEN

**Objetivos:** En los últimos años hemos estado estudiando el impacto de la artritis reumatoide en funciones cognitivas una vez no que este fenómeno no es bien reconocido en Portugal. **Método:** Se evaluaron los resultados de 90 pacientes con artritis reumatoide femeninos, comparando cada paciente con una estrategia de casos y controles emparejados (años en edad escolar y sexo), con sujetos control normativos (n = 90, en un total de 180 sujetos). Se ha realizado un screening con una prueba portuguesa de sintomatología depresiva (IACLIDE), STAI (anxiety trace and trait test), Luria Nebraska Neuropsychological Battery, Mini Mental state examination, Paced Auditory Selective Attention Test e el Word List Generation Test. **Resultados:** Los resultados confirman nuestro estudio preliminar en pacientes portugueses, relativo a la incidencia de los principales déficits en el funcionamiento cognitivo (evaluado por una variedad de pruebas neuropsicológicas) y sintomatología depresiva y de ansiedad.

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*Conclusión:* Este artículo refuerza la necesidad de mejorar las estrategias psicoeducativas, estimulación cognitiva y psicoterapéutica y fortalecimiento de la intervención neuropsicológica en este tipo de pacientes.

**Palabras clave:** ansiedad, depresión, enfermedades reumáticas e inflamatorias, neuropsicología.

## ANXIETY, DEPRESSION AND NEUROPSYCHOLOGY IN RHEUMATOID ARTHRITIS, IN 180 PORTUGUESE FEMALE SUBJECTS. A CASE-CONTROL STUDY

### ABSTRACT

*Objectives:* In the last years we have been studying the impact of Rheumatoid Arthritis in cognitive functions once it has not been well acknowledged in Portugal. *Methods:* We assessed the results of 90 Rheumatoid Arthritis female patients (RA group), comparing each patient in a case control paired strategy (years in school and age), with control subjects (n = 90, in a total of 180 subjects). Subjects were assessed with a Portuguese depressive screening test (IACLIDE), STAI (anxiety trace and trait test), Luria Nebraska Neuropsychological Battery, Mini Mental state examination, Paced Auditory Selective Attention Test and Word List Generation Test. *Results:* The results confirm our preliminary study in Portuguese patients, showing the incidence of main deficits in cognitive functioning (assessed by a variety of neuropsychological tests), and depressive and anxiety symptomatology. *Conclusion:* This article reinforces the necessity to improve psychoeducational, psychotherapeutic and cognitive stimulation, and strengthening of neuropsychological intervention in these kinds of patients.

**Key words:** Anxiety, Depression, Inflammatory / Rheumatic Diseases, Neuropsychology.

Till the first unpublished report of Rheumatoid Arthritis (RA), by Landré-Beauvais, in 1800 (2004; Maia 2012), we saw that our knowledge about this illness was extremely amplified. Since Hippocrates that about 1800 named it as gout, RA started to be understood as a particular etiological entity. RA is considered a progressive and disabling auto-immune disease (National Rheumatoid Arthritis

Society, 2008; Maia, 2012), producing strong physical, emotional and financial problems (Markenson, 1991). RA is categorized by inflammation of the lining at the joints, and this can progress to long term damage, chronic pain, limitations in daily life activity (Arthritis Analysis, 2008), and familiar and emotional stress (Lam, Lehman, Puterman & DeLongis, 2009). Only in USA exists about 1 in 108 or 0.92% (2.5 million patients in USA), and approximately ninety seven thousand in Portugal (Maia, 2012).

A plethora of other kind of symptoms that apparently affected RA patients started to be studied: chronic fatigue (Stebbing, Herbison, Doyle, Treharne & Highton, 2010), psychiatric diseases (Lisitsyna, Veltishchev, Seravina, Kovalevskaya, Zeltyn, Fofanova, & Nasonov, 2009), with highest occurrence of Depression and Anxiety (Dirik & Karanci, 2010; Appenzeller, Bertolo, & Costallat; Gronwall, 1977; Ravdin, Katzen, Agrawal & Relkin, 2003).

Gradually, a cognitive and neuropsychological deficit pattern in RA was reported in several clinical investigation studies in the latest years (Appenzeller, Bertolo & Costallat, 2004; Maia, 2012).

## METHOD

Were evaluated 180 subjects (90 rheumatoid subjects and 90 control subjects, paired by age, more or less 3 years, and years in School, more or less 3 years). The RA Group was composed by patients of different centers (institutions) for specific care in Rheumatic patients, in the Center / Littoral Region of Portugal. Control subjects were selected by statistical convenience method (Maia, 2012).

### Tests.

- *Paced Auditory Serial Addition Test (PASAT)* measures cognitive function (Gronwall, 1977), that expressly assess acoustic information processing swiftness and plasticity, as well as computation ability (Maia, 2012). The subject as to perform serial summation of numbers (61 items and 60 calculations) that are presented in a CD voice support, in a rate of 2 or 3 seconds; the outcomes could

diverge in a range of 0 to 60. Scores lower than percentile 5, considering normal population, is usually considered to be in the compromised range (Maia, 2012).

- *The Word List Generation* accesses the ability to produce and access semantic knowledge, through the task of naming words of a particular category or starting words starting with a particular letter (Ravdin, Katzen, Agrawal & Relkin, 2003; Maia, 2012). The subject is expected to be able to present, as a minimum, 10 items (names of vegetables, animals and words that start with the letter P). A result indicating less than 10 items is considered very poor (Maia, 2012).

- *Mini Mental State Examination* was developed by Folstein, Folstein & Mchugh (1975) and Guerreiro, Silva & Botelho (1994) adapted it for Portuguese population, as a screening cognitive test. In the Portuguese version the test has 30 items and the results could range from 0 (severe cognitive deterioration), to 30 (no signal of cognitive deterioration) (Maia, 2012).

- *Luria Nebraska Neuropsychological Battery* (LNNB), studies neuropsychological performance of subjects, both genders, adults (aged 18-65) from different academic levels being the principal neuropsychological functions assessed Motor Functions, Rhythm Functions, Tactile Functions, Visual Functions, Receptive Speech Functions, Expressive Speech Functions, Writing Functions, Reading Functions, Arithmetic Functions, Memory Functions and Intellectual Processes Functions (Golden, Hammeke & Purisch, 1985; Maia, 2012; Maia, Loureiro, Silva, Vaz-Patto, Loureiro, Correia *et al.*, 2003). The Battery is constituted by more than 740 different items, with different ways of scoring. For each subject (and in each scale) we calculate a special value ("Critical Value") considering the age and years in school. This Critical Value serves, individually, to identify if the subject is above or not a normality T note (results lower than T = 60 represents normality) (Maia, 2012).

- *The State-Trait Anxiety Inventory* (STAI) – The test explore anxiety symptomatology in adults (Spielberger, Gorsuch & Lushene, 1970). It is composed by two scales (trait and state). Every scale is composed by 20 items that represent the way the subject is feeling in the moment of test administration. 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) (Maia, 2012).

- IALCIDE – A Portuguese test to assess Depressive Symptoms (Serra, 1995). It is composed by 21 items that represent the way the subject is feeling in the moment of test administration (using a five point range 0-4). Total results ranges from 0 to 84. Those results lower than 20 represent normality. From this point, the level of depression indicators increases as the summation of items provides a greater outcome. For example, a result of 25 represent light depression, and a result of 75 represents securely a strong indication of Severe Depression (Maia, 2012).

## RESULTS

In Table I we can see that the mean age for control subjects are 41,34, with a standard deviation of 9,20, and the mean for years in School are 10,45, with a standard deviation of 4,03. Regarding to RA group (patients), the mean age is 42,02, with a standard deviation of 9,30 and the mean for years in School are 10,21, with a standard deviation of 3,89. None of this differences are statistically significant (Age:  $t = -1,231$ ;  $p = ,379$ ; Years in school:  $t = 1,704$ ;  $p = ,073$ ).

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Age Controls	41,34	90	9,20	1,40
	Age RA group	42,02	90	9,30	1,34
Pair 2	Years in School Controls	10,45	90	4,03	,49
	Years in School RA group	10,21	90	3,89	,51

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

In Table II we can see that the mean results in PASAT test for control subjects are 30,03, with a standard deviation of 10,05, and the mean for RA group is 16,99, with a standard deviation of 8,95, being this difference statistically significant ( $t = 13,432$ ;  $p = ,031$ ).

According to Table II we verify that the mean results in WLG for control subjects is 17.64, with a standard deviation of 3,22, and the mean for RA group is

9,10, with a standard deviation of 3,12, being this difference statistically significant ( $t = 12,431; \rho = ,023$ ).

Finally, in Table II we verify that the mean results in MMSE for control subjects is 28,88, with a standard deviation of 1,49, and the mean for RA group is 27,93, with a standard deviation of 2,72, being this difference statistically significant ( $t = 2,400; \rho = ,023$ ).

		Mean	N	Std. Deviation	Std. Error Mean
Pair 3	PASAT Controls	30,03	90	10,05	1,46
	PASAT RA group	16,99	90	8,95	1,36
Pair 4	WLG Controls	17,64	90	3,22	,47
	WLG RA group	9,10	90	3,12	,44
Pair 5	MMSE Controls	28,86	90	1,49	,21
	MMSE RA group	27,93	90	2,72	,44

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

In Table III we can see that the mean results in STAI (anxiety) test for control subjects are 42,00, with a standard deviation of 5,99, and the mean for RA group is 56,99, with a standard deviation of 8,66, being this difference statistically significant ( $t = -11,743; \rho = ,010$ ). Regarding to depressive symptomatology (Iaclide Test) we can see that the mean results for control subjects were 10,97, with a standard deviation of 11,00, and the mean results for RA group were 21,00, with a standard deviation of 9,06, being this difference statistically significant ( $t = -4,900; \rho = ,009$ ).

	I	Mean	N	Std. Deviation	Std. Error Mean
Pair 6	STAI	42,00	90	5,99	,79
	Controls				
Pair 7	STAI RA group	56,99	90	8,66	1,25
	IACLIDE	10,97	90	11,00	1,53
	Depression Controls				
	IACLIDE	21,00	90	9,06	1,33
	Depression RA group				

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

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 presents a mean punctuation of 8,79, with a standard deviation of 8,87, and the mean for RA group is 15,03 with a standard deviation of 12,54, being this difference statistically significant ( $t = -3,003$ ;  $p = ,001$ ).

In Rhythm Functions C2 Scale the Control subjects presents a mean punctuation of 1,82 with a standard deviation of 1,78, and the mean for RA group is 3,64 with a standard deviation of 2,54, being this difference statistically significant ( $t = -3,532$ ;  $p = ,007$ ).

In Tactile Functions C3 Scale the Control subjects presents a mean punctuation of 4,44 with a standard deviation of 5,44 and the mean for RA group is 7,40 with a standard deviation of 5,78, being this difference statistically significant ( $t = -2,550$ ;  $p = ,010$ ).

In Visual Functions C4 Scale the Control subjects presents a mean punctuation of 6,43 with a standard deviation of 3,55, and the mean for RA group is 10,60 with a standard deviation of 4,10, being this difference statistically significant ( $t = -4,210$ ;  $p = ,016$ ).

In Receptive Speech Functions C5 Scale the Control subjects presents a mean punctuation of 4,60 with a standard deviation of 4,33, and the mean for RA

group is 7,80 with a standard deviation of 5,55, being this difference statistically significant ( $t = -2,941$ ;  $\rho = ,001$ ).

In Expressive Speech Functions C6 Scale the control subjects presents a mean punctuation of 6,30 with a standard deviation of 4,96, and the mean for RA group is 10,98 with a standard deviation of 8,54, being this difference statistically significant ( $t = -3,292$ ;  $\rho = ,004$ ).

In Writing Functions C7 Scale the control subjects presents a mean punctuation of 1,90 with a standard deviation of 2,66, and the mean for RA group is 3,73 with a standard deviation of 3,25, being this difference statistically significant ( $t = -2,862$ ;  $\rho = ,015$ ).

In Reading Functions C8 Scale the control subjects presents a mean punctuation of 1,74 with a standard deviation of 1,80, and the mean for intervention group is 2,54 with a standard deviation of 2,60. This difference is not statistically significant ( $t = -2,507$ ;  $\rho = ,076$ ).

In Arithmetic Functions C9 Scale the control subjects presents a mean punctuation of 3,99 with a standard deviation of 2,89, and the mean for intervention group is 5,90 with a standard deviation of 5,11, being this difference statistically significant ( $t = -2,086$ ;  $\rho = ,022$ ).

In Memory Functions C10 Scale the control subjects presents a mean punctuation of 5,15 with a standard deviation of 3,90, and the mean for intervention group is 9,46 with a standard deviation of 5,76, being this difference statistically significant ( $t = -3,002$ ;  $\rho = ,015$ ).

In Intellectual Processes Functions C11 Scale the control subjects presents a mean punctuation of 19,74 with a standard deviation of 10,55, and the mean for RA group is 27,97 with a standard deviation of 10,85, being this difference statistically significant ( $t = -4,700$ ;  $\rho = ,018$ ).



		Mean	N	Std. Deviation	Std. Error Mean
Pair 8	C1 Motor Functions Controls	8,79	90	8,87	1,12
	C1 Motor Functions Intervention group	15,03	90	12,54	1,64
Pair 9	C2 Rhythm Controls	1,82	90	1,78	,27
	C2 Rhythm Intervention group	3,64	90	2,54	,37
Pair 10	C3 Tactile Functions Controls	4,44	90	4,54	,63
	C3 Tactile Functions Intervention group	7,40	90	5,78	,75
Pair 11	C4 Visual Functions Controls	6,43	90	3,35	,49
	C4 Visual Functions Intervention group	10,60	90	4,10	,64
Pair 12	C5 Receptive Speech Controls	4,60	90	4,33	,52
	C5 Receptive Speech Intervention group	7,80	90	5,55	,78
Pair 13	C6 Expressive Speech Controls	6,30	90	4,96	,75
	C6 Expressive Speech Intervention group	10,98	90	8,54	1,23
Pair 14	C7 Writing Controls	1,90	90	2,66	,49
	C7 Writing Intervention group	3,73	90	3,25	,39
Pair 15	C8 Reading Controls	1,74	90	1,80	,24
	C8 Reading Intervention group	2,54	90	2,60	,38
Pair 16	C9 Arithmetic Controls	3,99	90	2,89	,41
	C9 Arithmetic Intervention group	5,90	90	5,11	,83
Pair 17	C10 Memory Controls	5,15	90	3,90	,51
	C10 Memory Intervention group	9,46	90	5,76	,85
Pair 18	C11 Intellectual Processes Controls	19,75	90	10,55	1,42
	C11 Intellectual Processes Intervention group	27,97	90	10,85	1,73

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

## DISCUSSION

Shin, Katz and Julian (2012) stresses the necessity of the understanding of “*perceived cognitive dysfunction and objective neuropsychological performance in persons with chronic diseases*” (unpublished abstract from accepted article).

We validated, in this Portuguese study that in the majority of the assessed constructs (somatic experiences, emotional and cognitive deficits but also in neuropsychological reality), RA group presented poorest results than paired control subjects, bearing in mind statistical significance (see also 2012).

Using a strong paired strategy, we verified 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 that the verified differences presented in utilized tests should not be credited to differences in age, academic level and gender (this last variable was a constant).

In terms of psychiatric symptoms (anxiety and depression), ratifying prior studies, our RA group presents more occurrence of psychiatric symptomatology, being measured as two concurrent pathologies that produce strong deficits in daily life tasks, as well as in quality of life of RA group (Abdel-Nasser, Abd El-Azim, Taal, El-Badawy, Rasker & Valkenburg, 1998; Belza, 1995; Brown, Glass & Park, 2002; Dicckens, McGowan, Clark-Carter & Creed, 2002; Dick, Eccleston & Crombez, 2002; Maia, 2012).

In terms of neuropsychological results, our records are in agreement with several studies that show that RA group presents a robust deficit in attention and executive functions when assessed with these types of tests (Dick, Eccleston & Crombez, 2002). Several researchers described similar deficits in RA patients on tasks demanding distinction of similar letter and pattern comparison tests of information processing speed in connection with upper levels of pain and depression (Brown, Glass & Park, 2002; Maia, 2012).

Hanly, Omisade, Su, Farewell & Fisk (2010) using the *Automated Neuropsychological Assessment Metrics* (ANAM) demonstrated that 61% RA patients, when compared with healthy and robust matched controls, presented more deficits in neuropsychological clinical capacities.

According to previous global studies, in our Portuguese RA studies, strong neuropsychological deficits were found. In a study realized to define the incidence of cognitive impairment in RA patients, 40 RA patients and 40 healthy controls was evaluated and the major inferences was that cognitive impairment was not related to clinical and

treatment natures or disability once it appears as an independent deficit (Appenzeller, Bertolo & Costallat, 2004; Maia, 2012).

Melo & Da-Silva (2012) demonstrated that this neuropsychological deficit occurs not only in RA but also in fibromyalgia, and systemic lupus erythematosus.

## CONCLUSION<sup>2</sup>

This study strength the knowledge about RA symptomatology, in a variety of dimensions that should be of interest of clinicians, psychiatrists, psychologists and obviously, Rheumatologists.

As previously stated (Maia, 2012) RA cause solid deficits not only in somatic dimensions, emotional and cognitive deficits but also in Neuropsychological reality.

These results are part of the first Portuguese Studies with RA patients (Maia, 2012) indicating robust deficits in Neuropsychological scopes of daily life, (as well as with depressive and anxiety symptoms).

This article reinforces the necessity to improve psychoeducational, psychotherapeutic and cognitive stimulation, and strengthening of neuropsychological intervention in these kinds of patients.

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