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Prevalence of “organic brain syndrome” in a Southern European population in two different time periods. The *ZARADEMP* Project

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ABSTRACT – Background: Comparative studies of dementia in different time periods are quite limited in the international literature, but might be useful to test environmental hypotheses. The aim of this study is to compare the prevalence of “organic brain syndrome”, as a measure of dementia, in the elderly living in the same community in two different time periods and using the same methods.

Methods: Representative samples of the elderly in the *Zaragoza Study* or *ZARADEMP 0* (n= 1,080), completed the past decade, and now in *Wave I* of the *ZARADEMP Project* or *ZARADEMP I* (n= 4,803) were interviewed. The *Geriatric Mental State* (GMS) was the main case-finding instrument and the results were analysed using the *AGECAT* diagnostic package to generate diagnoses.

Results: Adjusted, total prevalence of “organic brain syndrome” in individuals aged 65 years and older has not varied from the previous decade. It was 8.4% in *ZARADEMP I*, and 7.4% in *ZARADEMP 0* (prevalence ratio, PR = 0.83; CI 0.65-1.07). Adjusted preva-

lence among men was lower in *ZARADEMP I* (3.6%) when compared to *ZARADEMP 0* (5.5%), although the differences do not reach statistical significance ($PR=0.65$; $CI\ 0.41-1.05$). However, in support of the working hypothesis, the differences were more marked, and we consider they reach statistically significant proportions in the age group 80-84 years.

Conclusions: The prevalence of "organic brain syndrome" has not increased from the previous decade. On the contrary, the prevalence tends to be lower in men, and the differences reach statistical significance in the age group 80-84 years. New analysis using diagnostic criteria of dementia in the same sample are required to confirm these findings.

Introduction

A similarity of the overall prevalence estimates of dementia in different countries has been reported when only studies using similar methods were compared, such as in the EURODEM reports (Hofman *et al.* 1991, Lobo *et al.* 2000). The similarity of estimates was also apparent in a cross-cultural comparison conducted the previous decade between the cities of Liverpool and Zaragoza (*Zaragoza Study* or *ZARADEMP 0*) when the Geriatric Mental State (GMS) - AGE CAT criteria of "organic brain syndrome" were used as a measure of dementia (Lobo *et al.* 1992). However, epidemiological conjectures were stimulated in both EURODEM reports, which included preliminary data from Zaragoza, by the appearance of some disparities in rates of dementia among men. Furthermore, contrary to most epidemiological enquiries, in *ZARADEMP 0* we found a relative increase in the prevalence of dementia (DSM-III-R criteria, American Psychiatric Association, 1987) in men when compared to women, particularly in the age groups between 70 years and 84 years (Lobo *et al.* 1995).

Comparative studies in different time periods, which are quite limited in the inter-

national literature (Kokmen *et al.* 1993), might also test environmental hypotheses. Since we have conducted during the *ZARADEMP Project*, as described in a previous paper (Lobo *et al.* 2005a), a reappraisal of the age and sex distribution of dementia in the same city, we could compare the findings with data collected in the same city the previous decade and using the same methods. We now hypothesize that, compared to *ZARADEMP 0*, a decreased prevalence of GMS-AGE CAT "organic brain syndrome" in men will be found in *ZARADEMP I*, particularly in the age groups between 70 years and 84 years.

Method

Similar methods were used in both studies, but there were differences in the sampling frame due to the different objectives in both investigations. The background, objectives and general methodology of the *ZARADEMP Project* are described in previous articles (Lobo *et al.* 2005a, Lobo *et al.* 2005b). In brief, this is an epidemiological study with three waves, but only the results of *Wave I* (*ZARADEMP I*), the baseline, cross-sectional study will be used here. A

random sample of individuals aged 55 and over, stratified by age and sex was drawn from municipal census lists (Spanish census, 1991). Ultimately 4,803 people were interviewed (years 1994-1996), but for comparative purposes in this study only the people aged 65 and over will be considered. The interviewers were senior medical students, and their training was carried out by one of the authors (A.L.) who had been trained in the use of the GMS in Liverpool (Lobo *et al.* 1992).

Similar methods were used in *ZARADEMP 0* (Lobo *et al.* 1995). In brief, a random sample of individuals aged 65 and over, stratified by age and sex was drawn from municipal inhabitants lists. Ultimately 1,080 people were interviewed (years 1988-1989). The interviewers were also medical students having the same training than in the other study.

In both studies, all interviews were carried out using shortened community versions of the GMS schedule (Copeland *et al.* 1976). This instrument, of which a more detailed description is given in the methods paper, has been used extensively in epidemiological studies in English speaking, as well as non-English speaking countries. A careful process of translation and validation of the Spanish version of the GMS has previously been carried out. The results were analysed using the AGE CAT computerized diagnostic package (Copeland *et al.* 1986), which is also described in the previous paper, to generate diagnoses. The authors have reported the validity of the Spanish version of AGE CAT (Saz *et al.* 1996). AGE CAT diagnostic cases of "organic brain syndrome" nominated by Stage II were used as a measure of dementia. The AGE CAT diagnosis of "organic brain syndrome" has been shown (Copeland *et al.* 1990) to correspond to

diagnoses of dementia made according to the rules of DSM-III-R (American Psychiatric Association, 1987).

Results

The age-sex distribution of the two samples is shown in Table I. The table also shows the prevalence of "organic brain syndrome" for each five-year age band for each gender, as well as the global prevalence data. The expected steep rise of prevalence with age in *ZARADEMP I* is seen, similarly to *ZARADEMP 0*, but the rise is more regular in the former. The total prevalence, adjusted by age in *ZARADEMP I* was 8.4% (CI 7.6-9.3) (Table I), and there were no significant differences with the previous study (prevalence ratio, PR = 1.14; CI 0.90-1.44) (Table II). For comparative purposes, in view of the progressive aging of city dwellers in Zaragoza and changes in the population structure over the last, approximately ten years, adjusted total prevalence has been calculated. It was 7.3% (CI 5.7-9.0) in *ZARADEMP 0* and 6.1% (CI 5.3-6.7), in *ZARADEMP I*, the differences being non-significant (Table II).

Contrary to the previous study, the prevalence of "organic brain syndrome" in *ZARADEMP I* was significantly higher in women (10.5%, CI 9.2-11.8) when compared to men (5.5%, CI 4.3-6.6), PR = 1.92; CI 1.52-2.43) (Tables I and III), and the differences are also significant if total prevalence is adjusted by age (Tables I and III).

No significant differences in the prevalence of "organic brain syndrome" in women, total or adjusted, were observed between *ZARADEMP 0* and *ZARADEMP I*

Table I

Prevalence of "organic brain syndrome" (AGECAT criteria), by sex and age, and study

	Women			Men			Total		
	N	Prevalence	% of total sample	N	Prevalence	% of total sample	N	Prevalence	% of total sample
ZARADEMP 0:									
65-69	9	5.8	14.3	2	1.8	10.3	11	4.2	24.5
70-74	3	1.8	15.4	5	3.7	12.5	8	2.7	27.9
75-79	13	8.3	14.4	8	8.1	9.2	21	8.2	23.6
80-84	12	12.1	9.2	7	12.1	5.4	19	12.2	14.5
85+	17	24.3	6.5	4	12.5	3.0	21	20.6	9.4
Total									
prevalence		8.4 (6.2-10.5)			6.0 (3.7-8.2)			7.4 (5.8-9.0)	
Adjusted prevalence (CI95%)		8.5 (6.2-10.8)			5.5 (3.3-7.6)			7.3 (5.7-9.0)	
ZARADEMP I:									
65-69	4	0.8	12.8	8	2.0	10.5	12	1.4	23.3
70-74	23	4.7	13.2	9	2.6	9.3	32	3.8	22.5
75-79	25	6.7	10.0	8	3.3	6.6	33	5.3	16.6
80-84	41	14.0	7.9	9	4.8	5.1	50	10.4	12.9
85+	138	24.2	15.3	49	14.1	9.3	187	20.4	24.7
Total									
prevalence		10.5 (9.2-11.8)			5.5 (4.3-6.6)			8.4 (7.6-9.3)	
Adjusted prevalence (CI95%)		7.7 (6.6-8.8)			3.6 (2.7-4.5)			6.1 (5.3-6.7)	

Table II

Prevalence Ratio (PR) of "organic brain syndrome", *ZARADEMP I* vs. *ZARADEMP 0*, by sex and age

Age group	Women		Men		Total	
	PR	CI 95%	PR	CI 95%	PR	CI 95%
65-69	0.14	0.05-0.39	1.14	0.24-5.27	0.33	0.15-0.72
70-74	2.59	0.83-8.06	0.70	0.24-2.06	1.44	0.67-3.07
75-79	0.81	0.42-1.54	0.40	0.16-1.02	0.65	0.38-1.10
80-84	1.16	0.64-2.11	0.40	0.16-1.00	0.86	0.52-1.42
85+	1.00	0.64-1.55	1.13	0.44-2.91	0.99	0.66-1.48
Total	1.25	0.95-1.66	0.92	0.60-1.41	1.14	0.90-1.44
Adjusted	0.91	0.68-1.21	0.65	0.41-1.05	0.83	0.65-1.07

Table III

Prevalence Ratio (PR) of dementia, women vs. men, by study

Study	PR	CI 95%
ZARADEMP 0		
Total	1.40	0.89-2.19
Adjusted*	1.56	0.98-2.48
ZARADEMP I		
Total	1.92	1.52-2.43
Adjusted*	1.49	1.13-1.98

* Ratio of adjusted (by age) prevalence

(Tables I and II). The prevalence among men in *ZARADEMP I* (5.5%, CI 4.3-6.6) was lower than in the previous, *ZARADEMP 0* study (6.0%, CI 3.7-8.2) (Table I), but the differences were non significant (PR = 0.92 (CI 0.60-1.41) (Table II). Similarly, the between studies differences were non significant among men if prevalence data are adjusted by age: it was 3.6% (CI 2.7-4.5) in *ZARADEMP I* and 5.5% (CI 3.3-7.6) in *ZARADEMP 0* (Table I); PR = 0.65 (CI 0.41-1.05) (Table II) .

However, in support of the working hypothesis, the between studies differences of prevalence in men were more marked, and we believe they reach statistically significant proportions in the age group 80-84 years (PR = 0.40; CI 0.16-1.00) (Table II).

Discussion

Prevalence of "organic brain syndrome"

The final results of the baseline, cross sectional study in *ZARADEMP I* confirm in a large, representative community sample that a considerable proportion of the elderly community has an "organic brain syndrome" (prevalence 8.4%, CI 7.6-9.3), a measure of dementia. (The overall prevalence in the *ZARADEMP I* sample, including the individuals below 65 years, was 6.7%, CI 6.0-7.4). They also confirm the expected, steep rise of prevalence with age, which has been reported in dementia studies across Europe (Hofman *et al.* 1991, Lobo *et al.* 2000) and, in fact, unanimously in the international literature (Gallo and Lebowitz 1999).

Prevalence rate of "organic brain syndrome" in two different time periods

An important objective in this study was to compare the prevalence of "organic brain syndrome" involving two different periods of time in the same city and using the same methods. We are not aware of previous comparative studies of this kind, which might throw some light in view of beliefs in relation to the epidemic proportion of dementia (Plum 1979). Furthermore, comparative studies in different time periods also have the potential to test environmental hypotheses. While a follow-up study of hospital cases done in Minnesota suggested an increase in the relative incidence of DAT (Kokmen *et al.* 1993), the issue needs further exploration. The results of this study suggest that prevalence rates are similar in *ZARADEMP 0* and *ZARADEMP I* and, therefore, the prevalence of "organic brain syndrome", a measure of dementia has not increased in a period of approximately seven years.

However, the main objective of this report was related to our previous observation in *ZARADEMP 0* of a relative, non-significant increase of the prevalence of dementia in men compared to women, when using DSM-III-R diagnostic criteria (Lobo *et al.* 1995). This relative increase of prevalence in men was observed in all age groups until the age of 90 years, and the finding is contrary to most reports in the literature (Jorm *et al.* 1987, Hofman *et al.* 1991). While the final results of *ZARADEMP 0* when using AGE CAT diagnostic criteria reported now do not confirm this relative increase of "organic brain syndrome" in men, the issue merits some further examination in view of the different criteria used and the limited number of

cases in some age subgroups. Our results tend to confirm the hypothesis that, compared to *ZARADEMP 0*, a decreased prevalence in men would be found in *ZARADEMP I*, particularly in some age sub-groups. First, contrary to *ZARADEMP 0*, the prevalence of dementia in women in *ZARADEMP I* is significantly higher than in men. Second, contrary to the observation in women, the total prevalence in men was higher in *ZARADEMP 0* in relation to *ZARADEMP I*, although the differences were not statistically significant. And third, a higher prevalence of dementia in men was seen in all age groups between the ages of 70 and 84 years in *ZARADEMP 0*, when compared to *ZARADEMP I*, and we take these differences as being statistically significant in the age group 80-84 years.

The two time points for comparison between samples are too close together to detect differences in exposure in this particular study, but the relative increase in the prevalence of dementia found in men in *ZARADEMP 0* merits some discussion. Environmental influences have been suggested in cross-national studies reporting more differences among men than among women on the prevalence of both, global dementia and DAT (Hofman *et al.* 1991, Rocca *et al.* 1991). Geographical differences in these studies might also be influenced by factors such as the rate of institutionalization or survival in different countries, but this potential bias is not influencing our comparative study, completed in the same city. Furthermore, the potential educational bias is minimized here, since the case-finding instruments used had been standardized in this specific, Spanish elderly population, and the proportion of the elderly with limited education (primary, complete or incomplete) was similar in *ZARADEMP 0* (82.8%) and

ZARADEMP I (83.8%). Other environmental factors could be considered, such as childhood exposure to infectious agents (Pyles 2001); higher smoking or toxin exposure during adulthood (Suay and Ballester 2002, Juan *et al.* 2004); or dietary deprivation at some point in the development (Esposito *et al.* 2002). However, men in the age groups with higher than expected prevalence of "organic brain syndrome" in *ZARADEMP 0* were in military age during the Spanish civil war. Important demographic movements related to that period of time have been documented, as well as adverse social outcomes (Cabr and Prez 2004). Cognitive impairment has been associated in some studies to both, social disengagement (Bassuk *et al.* 1999) and, in particular, to stress related to the war (Sutker *et al.* 1990). These hypotheses must be tested in new analysis of the prevalence of dementia using DSM criteria, since "organic brain syndrome" is not equivalent to dementia. In particular, the hypotheses must be tested on incidence data in this same *ZARADEMP Project*, since prevalence studies are not adequate to study risk factors.

Other limitations of the study

Both studies in the same city, in this comparative report, fulfil present day requirements in psychiatric epidemiology, such as the investigation of representative community samples which include institutionalized and non-institutionalized elderly, standardized structured methods of assessment specifically developed for the elderly and standardized diagnostic criteria and case levels of illness (Kaelber and Regier 1995, Copeland *et al.* 1999). Among the limitations of the study, it may be argued that the sampling methods are not totally

comparable, since *ZARADEMP 0* used random sampling with replacement. On the contrary, *ZARADEMP 1* used a random sample, with size corrected for potential losses. However, the response rate was similar in both studies, and in *ZARADEMP 0* no differences of prevalence were observed between the full sample interviewed and the sample selected as the first choice (Lobo *et al.* 1995). Therefore, we feel the results are broadly comparable. Other limitations in *ZARADEMP 1* could be related to higher non-response rate due to refusals in women (Lobo *et al.* 2005b). Underestimation of prevalence rates of dementia might occur, since most studies have reported higher epidemiological rates of dementia among women (Copeland *et al.* 1999, Andersen *et al.* 1999). However, this potential underestimation would be limited and should not affect the main conclusions of the study, which are related to comparisons of prevalence rate of "organic brain syndrome" in men.

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