Original Research Article

Gender Differences in Verbal and Visuospatial Working Memory Tasks in Patients with Mild Cognitive Impairment and Alzheimer Disease

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Abstract

Background/Aims: To date, there are few studies on gender differences in patients with mild cognitive impairment (MCI) and Alzheimer disease (AD). In the present study, the existence of differences between sexes in verbal and visuospatial working memory tasks in the evolution of cognitive and pathological aging was examined. ***Method:*** Ninety participants took part in this study: 30 AD, 30 MCI, and 30 healthy elderly participants (50% men and 50% women). ***Results:*** There were no significant differences between men and women with AD in visuospatial tasks, whereas these differences were found within the MCI group, with the average of men achieving significantly higher results than women. In verbal tasks, there were no differences between sexes for any of the groups. ***Conclusion:*** Execution in visuospatial tasks tends to depend on gender, whereas this does not occur for verbal tasks.

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Introduction

Working memory (WM) dysfunctions can be found among the difficulties that appear in the functioning of the memory of patients with Alzheimer disease (AD) [1]. Although there are several models of WM, the model proposed by Baddeley and Hitch [2, 3] is one of the most used in the neuropsychological research of cognitive aging. According to this model, the WM system includes 4 components: the phonological loop, which holds verbal information; the

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visuospatial sketchpad, which holds visual and spatial information; an episodic buffer that links the two prior components with long-term memory, and a central executive in charge of the attentional control of information.

The verbal component of WM has been one of the most studied in AD patients. In Huntley and Howard's [4] review of WM and AD, there were more studies showing significant differences in WM verbal tasks between healthy elderly and Alzheimer patients in early stages of the disease [5], or between mild and moderate phases [6], than studies not showing such differences. However, in relation to visuospatial WM tasks, research has shown that they are clearly affected in Alzheimer patients [7] and that this involvement can be found in patients with mild cognitive impairment (MCI) [8, 9] and even in healthy elders [10].

However, there are currently very few studies investigating the effect of gender on verbal and visuospatial WM tasks in patients with AD and MCI. Regarding AD, Heun and Kockler [11] found that women, on average, had more difficulties in visuoconstructive skills compared to men. Moreover, women had greater deficits in verbal skills; a difference which was not expected a priori, which – according to the authors – is probably explained by a pattern of differential neuronal degeneration in men and women. These findings are collected in a meta-analysis [12] where the analysis of 253 publications showed a greater overall deterioration in women with AD compared to men. Regarding gender differences in MCI, the scarcity of research is even greater. One study [13] reported that men performed better in visuospatial tasks than women, but in verbal tasks, women were better than men. The lack of research on gender differences in MCI is still greater than in AD, and to date, there are no definitive studies on this issue.

The objective of the present research was to study the effect of gender on the performance of verbal and visuospatial WM tasks in MCI and AD patients. It was based on a previous study [14], in which a greater deterioration in the visuospatial component than in the verbal component of the WM of Alzheimer patients was obtained, without finding significant differences between sexes. Subsequently, the cognitive deterioration was enlarged with a MCI sample and also by including new verbal and visuospatial tasks. The following hypotheses were considered: (1) the performance in visuospatial tasks will be more affected in women than in men in each of the groups (AD, MCI, and normal aging); (2) the performance in verbal tasks will be more affected in women in the more advanced stages of cognitive impairment.

Methods

Participants

The study sample consisted of 90 participants. There was a group of 30 patients (15 men and 15 women) diagnosed with dementia due to probable AD (according to NIA-AA criteria [15]). As some patients had a very low level of schooling (>2 standard deviations) and were unable to complete all of the study's tests, 14 men and 13 women were finally included. There was another group of 30 patients (15 men and 15 women) diagnosed with MCI according to Albert criteria [16].

The inclusion criteria were, in the AD group, MMSE scores <23 and Geriatric Dementia Scale (GDS) scores of 4–5. They met criteria for dementia due to probable AD in the category of amnestic presentation. In the MCI group, participants had MMSE scores between 27 and 24 and GDS scores of 3–4. Participants with AD and MCI were recruited from a sample of patients who attended the Neuropsychology Unit of the Geriatric and Palliative Care Service of Badalona Serveis Assistencials.

In the healthy elderly control group, there were 30 participants (15 men and 15 women). They had obtained an MMSE score >27 and/or a GDS score of 2.

The exclusion criteria for all participants who were taken into account were other concomitant central nervous system pathologies, chronic disabling diseases, psychiatric disorders, or severe sensory deficiencies. All patients in the AD group had been taking cholinesterase inhibitors for more than 4 weeks. Neuropsychological testing was administered under standardized conditions; a differential medication effect is therefore not expected. Patients were able to perform activities of daily living; they were not clinically depressed and they were not taking medication for it. All participants included in the study signed informed consent and participated voluntarily.

Cognitive Assessment

Mini-Mental State Examination (MMSE) [17]. This is a measurement of the general cognitive status. It consists of 30 items that include spatiotemporal orientation, repetition, attention, calculation, memory, denomination, reading, writing, and visoconstructive functions. Its scores range from 0 to 30 points.

Standard Corsi Block-Tapping Test [18]. The task is to repeat a visual sequence of fixed blocks on a board that the participant touches with his/her finger. The series start with a sequence of two blocks initially and increase at a rate of 1 per level of amplitude or difficulty (each level consists of 3 series) until the participant fails at least 2 series in 1 level. The total number of correct blocks remembered was scored.

Corsi Block-Tapping Task (with Inhibition) [14]. The participant must inhibit (not repeat) the second block of each trial, then he/she must recall the rest of the sequence in the same order. The total score of the number of correct blocks remembered was obtained.

Hooper Visual Organization Test (HVOT) [19, 20]. This visuoperceptive test measures object recognition. It consists of 30 sheets which contain drawings of everyday objects that have been cut into several pieces and placed in different positions. The participant is asked to recognize and say the name of the represented object. The scores range from 0 to 30 points.

Wechsler Memory Scale Revised [21]. The test consists of reading increasing series of digits that the subject must remember later, in serial order. The score of the total number of correct digits remembered was obtained.

Digits Task (with Inhibition) [14]. The participant must inhibit (not repeat) the second digit of each trial by recalling the whole sequence in the same order. The score of the total number of correct digits remembered was obtained.

Semantic Verbal Fluency Subtest: Animals from the Barcelona Test (TB) [22]. This classic test measures the total number of named animals belonging to a semantic category during 1 min.

Statistical Analysis

To compare sociodemographic characteristics and cognitive impairment (MMSE) among AD, MCI, and healthy elderly patients, and to verify if there were differences, Student *t* tests were performed for independent samples (Tables 1, 2). The results indicated significant differences in MMSE scores between the 3 groups, as expected (Table 1). As there were age differences between patients with AD and the healthy elderly, as well as between AD and MCI patients, age was used as a covariate in all ANOVAs that were performed. No significant differences were found in years of education. There were no significant differences in the variables age, years of education, and MMSE in the comparison between men and women in each group.

We then performed mixed analyses of variance (ANOVA) for the visuoperceptive tests (Corsi and HVOT cubes) and verbal tests (Digits and Semantic Fluency) with group (AD vs. MCI vs. controls) and sex (female vs. male) as inter-subject factors and content (visuospatial vs. verbal) and suppression status (without vs. inhibition) as intra-subject factors.

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Table 1. Sociodemographic variables of the sample for each group

	AD	MCI	Control	AD vs. control	AD vs. MCI	MCI vs. control
Age, years	78.37±5.77	74.43±7.42	74.63±5.51	$t = 2.5$ $p = 0.02*$	$t = 2.22$ $p = 0.03*$	$t = -0.12$ $p = 0.906$
Education, years	9.63±2.79	9.3±3.74	9.53±2.73	$t = 0.13$ $p = 0.896$	$t = 0.37$ $p = 0.71$	$t = -0.28$ $p = 0.784$
MMSE score	21.89±1.95	26.03±1.45	28.13±1.67	$t = -15.72$ $p < 0.00*$	$t = -9.17$ $p < 0.00*$	$t = -7.25$ $p < 0.00*$

Values are expressed as means ± standard deviations. Independent-samples t tests test were used in comparisons between groups. * $p < 0.05$.

Table 2. Sociodemographic variables of the sample by gender in each group

	AD		MCI		Controls	
	males ($n = 14$)	females ($n = 13$)	males ($n = 15$)	females ($n = 15$)	males ($n = 15$)	females ($n = 15$)
Age, years	76.64±6.11	80.23±4.93	76.20±7.74	72.67±6.87	74.87±5.23	74.40±5.95
Education, years	8.64±2.89	10.69±2.32	8.73±3.67	9.87±3.85	10.13±2.42	8.93±2.96
MMSE score	21.21±2	22.62±1.66	26.53±1.18	25.53±1.55	28.80±1.08	27.47±1.92

Values are expressed as means ± standard deviations.

Results

The results of the present study indicated that, in the Corsi Block-Tapping test without inhibition, there were main effects of the group [F(2, 80) = 3.83, MC = 1,942.173, $p < 0.05$, $\eta^2_p = 0.09$] and of sex [F(1, 80) = 6.28, MC = 3,187.183, $p < 0.05$, $\eta^2_p = 0.07$], as well as for the interaction between these variables [F(2, 80) = 5.38, MC = 2,731.880, $p < 0.05$, $\eta^2_p = 0.12$]. Pairwise comparisons applying the Bonferroni correction indicated that there was a significant trend between the MCI groups (69.13) and the controls (84.83) ($p < 0.08$). Among the AD patients (70.70) and the healthy elderly, a significant trend was also found ($p < 0.10$) (Table 3). Regarding the differences between sexes, significant differences were found between men (81.16) and women (68.77) ($p < 0.01$), with the average performance of women being significantly lower than that of men. Regarding the differences between sexes within each group (Table 3), these differences were only significant between men (84.55) and women (51.08) ($p < 0.01$) in the MCI group.

As can be observed in Table 3, the performance of women was also lower than that of men in the healthy elderly group, although this difference was not found to be significant. However, in the AD group, the performance of women was curiously higher than that of men. It is likely that the fact that female AD patients had a higher educational level than male AD patients may be influencing this relatively good performance of female AD patients in the visuospatial Corsi Block-Tapping test (we shall comment further on this issue in the Discussion section). Therefore, taking into account the results of the average performance of women and the average performance of men in the Corsi test without inhibition for each of the 3 groups,

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Table 3. Performance of men and women in the 6 tests used with AD and MCI patients as well as healthy elders

	AD		MCI		Controls	
	males (n = 14)	females (n = 13)	males (n = 15)	females (n = 15)	males (n = 15)	females (n = 15)
Visuospatial						
Blocks without inhibition	69.43±15.42	72.08±25.51	84.07±31.45	54.20±18.84	89.20±25.26	80.47±19.39
Blocks with inhibition	24.57±16.15	32.62±16.55	40.80±26.72	24.53±15.03	51.00±23.7	42.67±16.66
HOVT	11.75±3.75	15.54±3.24	16.93±4.72	14.63±4.77	17.73±4.47	19.43±4.55
Verbal						
Digits without inhibition	97.79±21.52	98.31±28.53	91.53±29.97	96.73±33.65	125.93±54.59	107.13±34.99
Digits with inhibition	38.14±24.08	44.92±23.52	58.67±36.54	39.33±20.4	77.60±47.73	63.20±25.92
Semantic fluency	9.71±5.15	10.62±3.82	14.07±3.86	14.27±5.06	16.73±5.46	13.87±3.62

Values are expressed as means ± standard deviations.

it can be stated that the first hypothesis was partially confirmed. There were no other significant effects.

In the analysis of the results obtained in the Corsi Block-tapping test with inhibition, ANOVA indicated that there were main effects of group [$F(2, 80)$ = 5.64, MC = 1,976.73, $p <$ 0.05, η^2_p = 0.124] and of the interaction between group and sex [$F(2, 80)$ = 4.97, MC = 1,741.287, $p < 0.05$, η^2_p = 0.11]. Bonferroni paired comparison showed significant differences between the AD group (28.44) and the healthy elderly (46.83) ($p < 0.01$) as well as between the MCI group (32.67) and the healthy elderly ($p < 0.01$). Regarding the group-by-sex interaction, significant differences were found in the MCI group between men (41.31) and women (21.29) ($p < 0.01$). As can be observed in Table 3, the performance of female MCI patients was lower than that of male MCI patients, confirming the first hypothesis. However, in the AD group, there was a trend towards significance in the differences between men (25.55) and women (37.4), again finding that the average of women was higher than that of men ($p < 0.10$). There were no other significant effects.

The ANOVA results of the HVOT test showed main effects of group [$F(2, 80)$ = 7.41, MC = 131.513, $p < 0.05$, η^2_p = 0.16], as well as for the group-by-sex interaction [$F(2, 80)$ = 5.193, MC = 92.167, $p < 0.05$, η^2_p = 0.115]. Once again, significant differences were found in the Bonferroni paired comparisons between the AD group (13.57) and the healthy elderly (18.58) ($p < 0.01$). In addition, there was a trend towards significance between the MCI group (15.78) and the control group ($p < 0.010$). In the group-by-sex interaction, significant differences were found in the AD group between men (11.75) and women (15.54) ($p < 0.05$). There was also a clear trend toward significance in the MCI group between men (16.93) and women (14.63) ($p < 0.07$). As can be observed, these results would go in the same direction as the results found previously in the other two visuospatial tests, as will be further commented in the Discussion section. There were no other significant effects.

As for the Standard Digits test without inhibition, significant differences were observed in ANOVA only for the group factor [$F(2, 80)$ = 3.2, MC = 4,107.9, $p < 0.05$, η^2_p = 0.074]. Bonferroni paired comparisons showed significant differences between patients with MCI (94.13) and controls (116.53) ($p < 0.05$). There was also a significant trend between the AD group (98.04) and the controls ($p < 0.08$) (Table 3). There was no main effect of sex or of the interaction between group and sex.

In the Digits test with inhibition, ANOVA only yielded significant effects for the group factor [$F(2, 80)$ = 5.63, MC = 5,509.68, $p < 0.05$, η^2_p = 0.123]. Significant differences were

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obtained between the AD patients (41.41) and the controls (70.40) ($p < 0.05$) as well as between the MCI patients (49) and the controls ($p < 0.05$), confirming the previous pattern of results found in the Digits test without inhibition.

The third test (the Semantic Fluency test) used to examine the verbal component between the two sexes in each group showed main effects for the group factor [$F_{(2, 80)}$ = 7.145, MC = 151.719, $p < 0.05$, η^2_p = 0.16]. Significant differences were found between the AD group (10.15) and the controls (15.30) ($p < 0.01$) as well as between the MCI group (14.17) and the controls ($p < 0.05$). Therefore, the results of the 3 tests used, in which the verbal component was examined, showed that this component also had a greater deterioration as cognitive deterioration increased in the AD and MCI groups, compared to the execution of the healthy elderly. There was no main effect of sex or of the interaction between group and sex, indicating that in this test the group of women did not perform worse in the more advanced phases of cognitive impairment, unlike the predictions made in the second hypothesis.

Discussion

In the absence of research on gender differences that include the entire array of normal and pathological aging, this study provides relevant data on the differences between sexes in patients with MCI and AD compared with healthy elderly and in relation to significantly lower performance in visuospatial and verbal tasks associated with the evolution of cognitive impairment.

Regarding gender differences, according to the literature, it was expected that the visuospatial component would be more affected in the group of women than in the group of men in each of the groups of deterioration. The results obtained in the present study showed a partial confirmation. There were no differences in the AD group, the scores of women being, in general, higher than those of men. A possible interpretation to explain this result may be the fact that the sample of AD women presented, curiously, an average level of years of schooling higher than that of men, although the differences in years of schooling were not statistically significant. It is possible that the higher level of schooling of AD women may compensate, to some extent, the visuospatial deficits that had been hypothesized for this group. Further studies between male and female AD patients would be necessary to see if these results are corroborated or not.

Nevertheless, these differences were found in the MCI group: women had a much lower performance than men in visuospatial tasks, which would contribute to the results of Elosúa et al. [14] – where MCI participants were not included – that state that in this stage of cognitive impairment differences between sexes appear. The results of the present research corroborate those previously found by other authors [10, 14]; yet, this study has expanded the visuospatial tasks in the MCI group and has added the differences between sexes that were obtained.

Regarding the differences between the sexes in the healthy elderly group, both in the present study and in the study by Elosúa et al. [14], a lower average performance was obtained in the group of women than in the group of men, although in neither study were these differences significant. These results point in the same direction as other previous studies [12, 23–25].

Considering all the results, it could be pointed out that the visuospatial component of WM (with the exception of the AD group) appears to be more affected in women than in men, in line with what was indicated by previous studies, although differences have not always been significant [11, 12, 14, 25].

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Regarding the verbal component, where differences between sexes were expected to appear in the more advanced stages of deterioration, the results of this study showed that they did not appear in the healthy elderly group, nor in the AD or the MCI groups. In the work performed, both in the Standard Digits test without inhibition and with inhibition and in the Semantic Fluency, the results obtained indicated that women and men maintained a quite similar performance, even in the AD group, where the cognitive impairment was more pronounced. In the study by Elosúa et al. [14], lower scores were found in the average performance of AD females, compared to that of males, in the 2 verbal tasks (standard digits and digits with inhibition), although the differences were not significant. In the present study, after increasing and pairing the number of men and women in the 3 groups (AD, MCI, and healthy elderly), no significant differences appeared. Even though certain studies have found differences between sexes in verbal tasks similar to those in our study [12, 26], it is noteworthy that other studies did not, in line with the results obtained in our research [12, 26, 27, 28].

Conclusion

This study reports findings showing that performance in visuospatial tasks tends to depend on sex, while verbal tasks do not. However, it is possible that an Alzheimer population that has a higher degree of deterioration (MMSE score) may either maintain or change this pattern of results. More studies are warranted, with a larger sample of women and men diagnosed with MCI and AD, to better observe whether these results are replicated or not.

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Disclosure Statement

The authors have no conflicts of interest to disclose. The sponsors had neither a role in the analysis or interpretation of these data, nor in the content of the article.

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