Tittle: Sex differences on anxiety and depression in older adults and their relationship with cognitive impairment: gendered implications.

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Ethical concerns

This study was approved by the Research Ethics Committee of the Spanish Autonomous Community of Aragón, protocol number (CEICA PI11/90). Personal data protection regulations were respected. All the participants were informed about the study objectives and signed informed consent. The deontological norms recognized by the

Declaration of Helsinki and good clinical practice norms were followed, and current legislation was complied with.

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Abstract

Introduction: Subjective memory complaints (SMC) in elderly adults could express cognitive decline in the future. A consensus has been reached about how these SMC relate to mood variables, but further research is required to determine which socio-demographic, cognitive, functional and occupational factors will act as predictors in elderly adults.

Objetive: To analyze, through a descriptive observational study, the relationship between anxiety/depression and sex ~~gender~~, age and occupation, with cognitive/functional performance in 367 older adults with SMC, but without objective cognitive impairment in a primary healthcare center.

Methods: The cognitive variables were measured by applying the Spanish version of Mini-Mental State Examination (MEC-35) and Set-Test for verbal fluency. To measure functional level, the Barthel index and Lawton and Brody scales were employed. Physical occupational status and mental occupational status were measured based on three levels, low, medium and high, according to the American Occupational Therapy Association.

Results: Low educational and occupational physical and mental levels were related to anxiety and depression. In addition, differences by sex were found on anxiety and depression related to different factors. In men, anxiety was related to higher cognitive level, and in women to higher functional performance in IADLs. On the contrary, depression in men was related to lower cognitive level and higher performance in ADLs.

Conclusions: It is important to maintain a sex-gender perspective on the study of anxiety and depression in elderly, taking into account social roles and the traints of the work environment, in order to avoid cognitive and functional impairment.

Keywords: Aging; Cognitive mini-exam; Cognitive impairment; Occupational therapy; Physical occupation; Mental occupation; Mental health.

Título: Diferencias por sexo en ansiedad y depression en personas adultas mayores y su relación con el deterioro cognitivo~~: implicaciones para el análisis de género.~~

Resumen

Introducción: Las quejas subjetivas de memoria (SMC) en adultos mayores podrían expresar un daño cognitivo en el futuro. Existe consenso sobre la relación de estas SMC con variables del estado de ánimo pero se necesita más investigación, para determinar qué factores sociodemográficos, cognitivos, funcionales y ocupacionales serían los predictores en los adultos mayores.

Objetivo: Analizar la relación entre ansiedad y depresión con el sexo, edad y ocupación, así como con el desempeño cognitivo y funcional en 367 adultos mayores con QSM, en un centro de atención primaria.

Métodos: Las variables cognitivas se midieron mediante la version Española del Mini-Mental State Examination (MEC-35) y Set-Test para la fluidez verbal. Para medir el nivel funcional se utilizaron el índice de Barthel y la escala de Lawton y Brody. El estado ocupacional físico y mental fueron medidos en base a tres niveles (bajo, medio y alto) según la American Occupational Therapy Association.

Resultados: Los niveles educativos y ocupacionales físicos y mentales bajos se relacionaron con ansiedad y depresión. Además, se encuentran diferencias por sexo en los factores relacionados con la ansiedad y depresión. En los hombres, la ansiedad se relacionó con un mayor nivel cognitivo y en las mujeres con mayor desempeño funcional en las AIVD. Por el contrario, la depresión en los hombres se relacionó con menor nivel cognitivo y un mayor desempeño en las ABVD.

Conclusiones: Es importante mantener la perspectiva sexo-género en el análisis de la ansiedad y depresión en personas mayores, teniendo presentes los roles sociales y características del entorno laboral, para evitar el deterioro cognitivo y funcional.

Palabras clave: Envejecimiento; Mini examen cognitive; Deteroiro cognitive; Terapia Ocupacional; Ocupación física; Ocupación mental; Salud mental.

Tittle: Sex differences on anxiety and depression in older adults and their relationship with cognitive impairment.

INTRODUCTION

Aging and longevity depend on psycho-cultural aspects like level of education and performing activities with a positive mental status, emotions and positive experiences [1].

Subjective memory complaints (SMC) are one of the elderly's key concerns Their range of prevalence is 25-50% and they depend on socio-demographic (age, education, gender), psychological and mood (anxiety and depression) and cognitive performance factors. In turn, these SMC are linked with higher rates of multimorbidity, pain, polypharmacy, functional dependence and poor self-perceived health. Consequently, this age group resorts more to health services [2-3].

In socio-demographic terms, these SMC clearly rise with age from 24% in the 65-69 age group to 57% in the 90 years or older age group for those with a low level of education and for being female [2]. Older cognitively intact men tend to better resist the psychopathological processes of Alzheimer's disease than women [4].

Subjective memory complaints are defined as common daily concerns about having problems remembering recent events or spatially locating objects. It is increasingly acknowledged that people's subjective perception of their cognitive capacity can be substantially relevant even though this does not coincide with the results of objective cognitive tests as they could express future cognitive decline [5].

A consensus has been reached about the relation between SMC and mood variables like anxiety and depression, and about the negative impact that they could have on elderly people's functional capacity and quality of life [3]. Evidence to date indicates that when SMC are present, these associations must be considered in order to assess the risk of cognitive impairment and to know when follow up needs to be carried out [2].

Conversely, it has been argued that SMC reflect affective symptoms like anxiety and depression, and a slower mental pace instead of real cognitive problems.

Hence the importance of considering affective factors in people with SMC because they could indicate an expression of general impairment feelings caused by depression [6].

Moreover, other studies have indicated that adults with anxiety/depression disorders worse perform in complex attention cognitive domains, executive/social cognition functions, and their processing rate is slower. These findings suggest that cognitive impairment in psychological aspects cannot be ruled out in patients with SMC, rather both constructs can be potentially useful for identifying high-risk populations for interventions and prevention trials to enrich our understanding of the pathogenesis of neurocognitive disorders [7-8].

Different studies have shown the need to include a gender perspective to study health and determining situations for people SMC in order to also focus on identifying the predictor factors of gender differences in depression during old age [8-9].

Considerable evidence can be found for occupational participation helping older adults to maintain their cognitive function toward old age, especially those with better intellectual requirements [9]. Predominantly manual occupational activities are related to being at higher risk of presenting cognitive impairment and/or dementia according to some studies, whereas other authors indicate that being male and doing manual work can contribute significantly to the cognitive/physical function after retirement [9-10].

Nevertheless, a knowledge gap exists lives about anxiety and depression in olde age between the level of mental and physical occupation that developed during working. This indicates the need for more studies to be conducted that analyse the characteristics of job posts and subsequent cognitive/mental impairment, and the mechanisms involved in these associations [11-12].

This study aimed to analyze the relation between anxiety/depression and gender, age and physical/mental occupation, and to cognitive/functional performance in elderly adults with SMC.

METHODOLOGY

Study design

Observational descriptive cross-sectional study conducted in a primary healthcare center in a provincial capital city.

Study population

Participants in the study were people over 65 years recruited in two primary health centers in the provincial capital. These centers serve a total of 36,215 people, with those over 65 years of age accounting for 49.44% of the total in both centers. The study population selected for the sudy was composed of 367 older adults with SMC who attended this primary healthcare service and received the usual therapy and nursing care. The participants received information about the project from informative posters placed on the doors of all the medical consultation rooms and where their family doctors worked.

Inclusion/exclusion criteria

The inclusion criteria were as follows: ≥ 65 years with the Spanish version of Mini-Mental State Examination (MEC-35) score between 24 and 35 points suffering from SMCs. The exclusion criteria were as follows: institutionalization and cognitive stimulation in the past 12 months.

Sampling technique

Given the characteristics of the design, as it is a descriptive study in which it is intended to make inferences to population values from a sample, a convenience sampling was carried out to facilitate accessibility to the participants. The sample size for this type of study was calculated with the basic requirements for parameter estimation. These primary health centers were considered because they are quite representative of the average for the province and the city.

Sample size calculation

Considering a population size of around 1,000,000 individuals with a margin of error of 5% and a confidence level of 95%, a sample size of around 380

individuals was estimated, taking into account that the population of the province is less than a million people, our sample of 367 individuals would be representative of the population under study.

Furterhmore, the sample size was calculated with 95% confidence interval, to estimate the mean of the Spanish version of the Mini-Mental State Examination (MEC-35) in the population, considering a deviation of three points and allowing an error of approximately 0.3.

Study variables

The following socio-demographic variables were studied: gender, age, level of education, marital status, and mental/physical occupational status. An analysis of the subgroups was considered according to level of education (primary/higher), physical/mental occupational status based on three levels, low, medium and high (for each one) [12], and by differentiating cognitive and motor skills according to the American Occupational Therapy Association (AOTA) [13].

Instruments used

The existence of SMCs was evaluated with the question “Do you have complaints about your memory?” (dichotomous response (yes/no) [14].

The main psychological variables were: The Goldberg Anxiety Subscale [15] and the Yesavage Geriatric Depression Scale with the 15-point version [16].

Goldberg Anxiety Subscale

It is a subscale of the Goldberg questionnaire, with nine dichotomous response items (yes/no). One point is awarded per affirmative response on each item. The cut-off value is ≥ 4. It has a specificity of 91% and a sensitivity of 86% [17].

Yesavage Geriatric Depression Scale (GDS), the 15-point version

It is considered an appropriate scale for older people in the community. Scores range from 0 to 15, and a total score > 5 is interpreted as "probable depression". It has a sensitivity of 71.8% and a specificity of 78.2%. [18].

The secondary cognitive variables were the Spanish version of MMSE (MEC-35) [17] and the Set-Test to measure verbal fluency [18]. The functional variables were the Barthel index [19] and the Lawton and Brody scale [20].

The Spanish version of MMSE (MEC-35)

MEC-35 is considered one of the most widely used short cognitive tests to study cognitive capacities in primary care. In Spain it is common to resort to the adaptation of the MMSE, more adapted to the cultural level. It evaluates eight components: spatio-temporal orientation (10 points), fixation memory (3 points), attention (3 points), calculation (5 points), short-term memory (3 points), language and praxis (11 points). Its sensitivity and specificity are respectively 85-90% and 69%. With this questionnaire, global cognition and cognitive functions were evaluated [19].

Set-test

Set-test measures verbal fluency in four categories: colors, animals, fruits, cities. Scores range from 0 (minimum score) to 40 (maximum score), with 0 being the minimum score and 40 the maximum with a cut-off point of 27 points. It has a documented sensitivity of 79% and a specificity of 82% [18].

Barthel Index (BI)

This tool measures independence in 10 basic activities of daily living (BADL). The maximum score is 100 points and scores ≥ 60 indicate mild dependence. The sensitivity of this test ranges from 76% to 99.8% and its specificity from 46% to 97%. [19].

Lawton and Brody scale (LB)

It measures autonomy in eight instrumental activities of daily living (IADLs). Scores range from 0 (dependent) to 8 (independent). The sensitivity of this scale is 57% and its specificity is 82% [20].

The evaluation process was performed by occupational therapists after receiving the corresponding training to guarantee the homogeneous application of evaluation instruments.

Statistical Analysis

The statistical analysis was performed with the IBM SPSS Statistics Package, v.22.(SPSS Inc., Chicago, IL, USA). The descriptive statistics are shown according to the nature of each variable: mean (m) and standard deviation (SD) or the number of participants in each category (n) and the proportion of patients in relation to the total (%). The normality of the variables was verified by the Kolmogorov–Smirnov test.

An inferential analysis was performed to analyze the cognitive characteristics for each gender with the non parametric Mann-Whitney U test. The Kruskal–Wallis H-test was applied to the cognitive characteristics and mental occupation status. Level of significance was set at 5%.

Ethical Considerations

This study was approved by the Regional Research Ethics Committee. Personal data protection regulations were respected. All the participants were informed about the study objectives and signed informed consent. The deontological norms recognized by the Declaration of Helsinki and good clinical practice norms were followed, and current legislation was complied with.

RESULTS

This study included 367 older adults who scored 24-35 points in the Spanish version of MMSE (MEC-35). Table 1 includes the socio-demographic and occupational characteristics of the study participants per gender and age group. Of them all, 66.48% (244) were women and 53.67% (197) were in the younger age group of 65-74 years. Their mean age was 73.85 years (SD: 5.99), 76.8% had completed Primary Education and 67% were married. Their physical occupational status was low in 20.2% of the cases, average in 43.6% and high in 36.2%. Their mental occupational status was low in 59.1% of the cases, average in 35.1% and high in 5.7%.

In gender terms, mens' level of education and physical/mental occupational status were higher than for women, where differences were statistically significant ($p<0.001$). Nonetheless for age group, differences were found only in the younger age group (65-74 years), which included more married people ($p=0.001$).

The participants' psychological measures determined that 37.2% had anxiety and 19.89% had depression. Table 2 lists their distinguishing psychological characteristics per gender, age and physical/mental occupational status. Women had higher levels of anxiety and depression than men ($p<0.001$). However, there were no differences in anxiety and depression for either age group or mental occupational status during their working lives before they retired. It was noteworthy that a higher proportion of anxiety/depression was found in those with lower levels of mental occupational status, while having a lower physical occupational status during their working lives presented a higher proportion of anxiety ($p=0.030$) after they retired.

Table 3 shows the relation between anxiety and the cognitive level of verbal and functional fluency. In overall cognitive terms, differences were found for gender, and men with anxiety obtained higher cognitive outcomes with 1.12 points more than women ($p=0.001$).

According to the cognitive domains, men with anxiety were related to higher temporal orientation levels ($p=0.006$), but lower anxiety levels were related to better attention and calculation scores ($p<0.001$ in both cases).

In functional terms and in relation to BADL, people without anxiety generally do better with the Barthel Index ($p=0.001$), especially men without anxiety *versus* women ($p=0.003$). For IADL, however, people with anxiety present higher levels than those without anxiety ($p=0.014$), especially women ($p<0.001$).

Finally, Table 4 offers the analysis of the relation between depression and the cognitive/functional level according to gender. No overall cognitive differences appear in the table depending on whether subjects had depression or not. However, men scored lower when they had depression with statistically significant differences ($p=0.001$)

For the cognitive domains, people with depression indicated that their fixed memory was more affected (p=0.045) and men without depression performed better in attention (p=0.001), calculations (p<0.001) and language (p=0.039) than women.

In functional terms, people without depression and men better performed BADL (both with p<0.001), while women without depression did IADL better (p <0.001).

DISCUSSION

This study explored anxiety and depression, the characteristics related to the occupational, physical and mental profiles, and the socio-demographic and functional factors of older adults living in the community, with SMC and attended to in a primary healthcare center in Spain.

As in other studies, we found that being older and female and having a low level of education were associated with frequently having memory problems. Both married people and those with higher levels of education had lower cognitive and functional impairment levels [2] and, despite longitudinal studies indicating that these benefits are cancelled after a 10-year follow-up, education is believed to be the most consistent predictor of the cognitive level and is modulated by cerebral plasticity [21].

We found gender differences in occupational terms. Women performed mental/physical occupations worse than men. The literature traditionally indicates that women are assigned less physically demanding tasks owing to sexual differential impositions at work and gender roles, and these differences are reflected in the opportunities of performing occupational tasks [22]. Grotz et al [12] worked with a sample whose socio-demographic characteristics were similar to those in the present study, and they also identified lower mental occupation levels for women.

Meanwhile women have been found to have higher anxiety/depression levels than men; like other studies, SMC are more present in women, particularly during life periods marked by psychosocial stress factors. However, depression levels

in men seem to be influenced more by their health and cognitive functioning, and their participation in social activities [23].

The present study found no differences in anxiety and depression per age group. Nevertheless, other authors indicate that younger people with depression and anxiety tend to evaluate neutral stimuli as negative, but processing emotions during aging is subject to a "positivity effect" insofar as older adults pay more attention to positive stimuli than to negative ones [24].

Lower mental occupational levels are associated with a more marked tendency to anxiety and depression in old age. The literature indicates that long-term mental work stimulation in adulthood will offer potential benefits for cognition in old age [9], which will protect people of both genders from cognitive impairment and depression, and will contribute to successful aging given the increased cognitive reserve that takes place. For anxiety, a wide knowledge gap still exists in relation to mental occupation [6,25].

Low physical activity levels are related to increased anxiety, and depression in old age also tends to grow. Although physical activity has been shown to play a key role in treating mental health diseases [25], other authors indicate that occupational physical demands are related mostly to physical health benefits, and psychological demands are associated with mental health benefits [26].

In order to lower anxiety and depression levels in old age, strategies and interventions in the workplace should be promoted in adulthood that include complex cognitive and physical activities that are significant for these workers [26]. It has been reported that participating in a range of occupational activities that engage more than one domain can afford relevant mental health benefits [23,27].

In cognitive terms, anxiety in men is related to better temporal orientation outcomes. People without anxiety, especially men, perform better in attention and calculations. Our result coincide with those reported by other authors who indicated that milder anxiety symptoms can be related to obtaining higher MMSE scores until an optimum level is reached when the beneficial influence lowers and, therefore, severer anxiety is related to worse cognitive function [27], while

temporal orientation is associated with fewer SMC and better cognitive performance [2].

Our study also found that people without depression had higher cognitive levels for fixed memory, and men without depression better performed attention, calculation and language. For memory, other studies have indicated that SMC are associated with lower subject memory test scores regardless of affective disorders [28]. However, more recent studies have shown that increased anxiety or depression leads to worse memory performance [7].

Although a relation has been found between having higher levels of education and better performing calculations to a higher mental occupation level, which could be marked by biological-type sexual differences, it is essential to bear in mind that the cognitive aspect of attention is one of the most vulnerable domains to cognitive impairment, which is marked by gender inequalities that could pose fewer opportunities for women at work and in their later old age [29].

Finally in functional terms, and according to our results, older adults without anxiety and depression, particularly men, better peformed BADL, while IADL were performed better by older adults without depression, but with anxiety, especially women. Depressive symptoms and being older, along with having SMC, have generally been identified as risk factors of funcional impairment [3].

Functional impairment seems to progress differently in men and women. The fact that women show more autonomy for performing IADL could be explained by gender inequalities in sharing out household chores, which would make men more environmentally dependent [30].

In this case, it would once again seem necessary to bear in mind the possible existence of gender biases in strategies that measure functionality in the elderly because socialization in traditional gender roles can determine instrumental activities, where women obtain higher scores, but this does not actually establish that women's health is better [3].

Limitations

Our first limitation is not contemplating other factors, such as pain, comorbidities and polypharmacy, physical exercise, self-perceived health or hospitalizations.

The second limitation lies in our patients not generally presenting high anxiety/depression levels. Finally, this study includes no control group without SMC, not having performed such an analysis could be considered a bias in our study.

Nevertheless, our strong points include it analyzing the different variables that impact the elderly's psychological well-being, such as socio-demographic, gender, cognitive and occupational variables, and the gender study. Therefore, we consider that the novel study characterizing the population with SMC includes physical/mental occupational demands, and the psychological, cognitive and functional benefits, which can be obtained. Finally, the representativeness of our sample allows the research outcomes to be transferred to other healthcare centers with similar characteristics.

Conclusions

We found that women with SMC had higher anxiety/depression levels than men, a lower level of education, and their physical/cognitive occupation level was also lower. Having anxiety and depression was related to functionally performing BADL worse. Depression comes with cognitive symptoms that start with less fixed memory. Although anxiety is not excessively high, it favors improved temporal orientation and better performing IADL.

Preventing anxiety and depression in old age is important for avoiding functional and cognitive impairment from a gender perspective. Likewise, during working lives, cognitive tasks and challenges must be combined with physical activities. Future studies should explore if participating in physical, cognitive and social activities can help to improve older people's mental and cognitive health and their functional independence.

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Table 1. Patients' socio-demographic and occupational characteristics by sex and age.

	Patients' socio-demographic and occupational characteristics							
	SEX				AGE			
	Total (n = 367) n (%)	**Men (n = 123) n (%)**	**Women (n = 244) n (%)**	**p-value**	**Total (n=367) n (%)**	**65-74 years (n=197) n (%)**	**>75 years (n=170) n (%)**	**p-value**
Level of education								
Primary	282 (76.8)%	82 (66.7%)	200 (82%)	**<0.001****	282 (76.8%)	144 (73.1%)	138 (81.2%)	0.067
Higher	85 (23.2%)	41(33.3%)	44 (18%)		85 (23.2)%	53 (26.9%)	32 (18.8%)	
Marital status								
Single	19 (5.2%)	2(1.6%)	17(7.0 %)		19 (5.2%)	10 (5.1%)	9 (5.3 %)	
Married	246 (67%)	104 (84.6%)	142 (58.2%)	**<0.001****	246 (67%)	145 (73.6%)	101 (59.4%)	**0.001***
Widowed	90 (24.5%)	13 (10.6%)	77(31.6%)		90 (24.5%)	33 (16.8%)	57 (33.5%)	
Separated	12 (3.3%)	4 (3.3%)	8 (3.3%)		12 (3.3%)	9 (4.6%)	3 (1.8%)	
Physical occupational								
Low	74 (20.2%)	26 (21.1%)	48 (19.7%)		74 (20.2%)	43 (21.8%)	31 (18.2%)	
Medium	160 (43.6%)	40 (32.5%)	120 (49.2%)	**<0.001****	160 (43.6%)	88 (44.7%)	72 (42.4%)	0.455
High	133 (36.2%)	57 (46.3%)	76 (31.1%)		133 (36.2%)	66 (33.5%)	67 (39.4%)	
Mental occupational								
Low	217(59.1%)	48 (39%)	169 (69.3%)		217(59.1%)	112 (56.9%)	105 (61.8%)	
Medium	129 (35.1%)	59 (48%)	70 (28.7%)		129 (35.1%)	75 (38.1%)	54 (31.8%)	0.424
High	21(5.7%)	16 (13.2%)	5 (2%)	**<0.001****	21(5.7%)	10 (5.1%)	11(6.5%)	
No	343 (93.5%)	113 (91.9%)	230 (94.3%)		343 (93.5%)	184 (93.4%)	159 (93.5%)	

p: Pearson's Chi square p-value.
*p < 0.05 **p<0.001

Table 2. Differential psychological characteristics by sex, age and mental/physical occupation (average and standard deviation).

SEX	Total (n=367)	Men (n=123)	Women (n=244)	p-value
Anxiety	2.76 (2.41)	2.08 (2.07)	3.09 (2.50)	**<0.001***
Depression	2.70 (2.51)	1.90 (1.94)	3.11(2.66)	**<0.001***
AGE	**Total (n=367)**	**65-74 years (n=197)**	**>75 years (n=170)**	**p-value**
Anxiety	2.76 (2.41)	2.90 (2.43)	2.58 (2.37)	0.128*
Depression	2.70 (2.51)	2.70 (2.44)	2.70 (2.59)	0.688*

OCCUPATION	Total (n=367)	Mental occupation study			p-value
		Low (n=217)	Average (n=129)	High (n=21)	
Anxiety	2.76 (2.41)	2.92 (2.44)	2.52 (2.37)	2.40 (2.27)	0.213**
Depression	2.70 (2.51)	2.80 (2.49)	2.50 (2.40)	2.40 (2.79)	0.354**

OCCUPATION	Total (n=367)	Physical occupation study			p-value
		Low (n=74)	Average (n=160)	High (n=133)	
Anxiety	2.75 (2.41)	3.26 (2.62)	2.87 (2.42)	2.34 (2.22)	0.030**
Depression	2.70 (2.51)	3.00 (2.77)	2.80 (2.48)	2.41 (2.40)	0.239**

*p: Mann-Whitney U p-value; **p: Kruskal-Wallis H p-value

Table 3. Relation of anxiety to the cognitive/functional levels and verbal fluency by sex.

	Total (n=367)	Without anxiety (n=230)	With anxiety (n= 137)	p-value
MEC-35	29.48 (3.18)	29.32 (3.11)	29.74 (3.30)	0.217*
	Men	30.28 (3.02)	30.61 (3.29)	**0.001****
	Women	28.67 (3.01)	29.49 (3.27)	
Temporal Orientation	4.39 (0.92)	4.27 (0.99)	4.60 (0.74)	**0.001***
	Men	4.27 (1.04)	4.71 (0.53)	**0.006****
	Women	4.27 (0.97)	4.57 (0.79)	
Spatial Orientation	4.66 (0.62)	4.66 (0.60)	4.66 (0,63)	0.746*
	Men	4.65 (0.69)	4.74 (0.45)	0.917**
	Women	4.66 (0.55)	4.63 (0.68)	
Fixed Memory	3.00 (0.05)	3.00 (0,07)	3.00 (0.00)	0.440*
	Men	3.00 (0.00)	3.00 (0.00)	0.646**
	Women	2.99 (0.09)	3.00 (0.00)	
Attention	1.74 (1.22)	1.77 (1.21)	1.71 (1.23)	0.664*
	Men	2.20 (1.15)	1.84 (1.27)	**<0.001****
	Women	1.48 (1.17)	1.67 (1.23)	
Calculation	4.38 (1.00)	4.36 (0.99)	4.40 (1.03)	0.475*
	Men	4.78 (0.61)	4.61 (0.96)	**<0.001****
	Women	4.08 (1.10)	4.34 (1.05)	
Short-term memory	1.60 (1.09)	1.57 (1.09)	1.64 (1.09)	0.614*
	Men	1.49 (1.18)	1.65 (1.05)	0.824**
	Women	1.63 (1.04)	1.63 (1.12)	
Language	5.28 (0.84)	5.28 (0.83)	5.29 (0.87)	0.739*
	Men	5.42 (0.79)	5.45 (0.77)	0,075**
	Women	5.18 (0.85)	5.25 (0.89)	
Praxis	4.42 (0.70)	4.42 (0.69)	4.42 (0.73)	0.718*
	Men	4.48 (0.67)	4.61 (0.56)	0,257**
	Women	4.38 (0.70)	4.37 (0.76)	
SET-TEST	37.34 (3.79)	37.13 (4.04)	37.69 (3.30)	0.181*
	Men	37.04 (3.86)	37.19 (3.41)	0.251**
	Women	37.18 (4.18)	37.83 (3.27)	
BARTHEL	96.76 (6.54)	97.59 (5.66)	95.38 (7.61)	**0.001***
	Men	97.88 (5.25)	96.53 (7.21)	**0.003****
	Women	97.39 (5.92)	95.05 (7.73)	
LAWTON	7.10 (1.45)	6.94 (1.56)	7.36 (1.20)	**0.014***
	Men	6.22 (1.62)	6.32 (1.60)	**<0.001****

	Women	7.42 (1.34)	7.66 (0.85)	

p: Mann-Whitney U p-value for differences according to anxiety and the Kruskal Wallis test for gender differences. *p: Mann-Whitney U p-value; **p: Kruskal-Wallis H p-value

Table 4. Relation of depression to the cognitive/functional levels and verbal fluency by sex.

	Total (n=367)	Without depression (n=230)	With depression (n= 137)	p-value
MEC-35	29.48 (3.18)	29.60 (3.18)	28.99 (3.19)	0.139*
	Men	30.48 (2.98)	29.53 (3.70)	**0.001****
	Women	29.09 (3.18)	28.84 (3.07)	
Temporal Orientation	4.39 (0.92)	4.40 (0.92)	4.34 (0.94)	0.484*
	Men	4.39 (0.97)	4.33 (0.90)	0.915**
	Women	4.41 (0.89)	4.34 (0.97)	
Spatial Orientation	4.66 (0.62)	4.67 (0.60)	4.59 (0,68)	0.447*
	Men	4.66 (0.66)	4.80 (0.41)	0.566**
	Women	4.68 (0.56)	4.53 (0.73)	
Fixed Memory	3.00 (0.05)	3.00 (0,00)	2.99 (0.18)	**0.045***
	Men	3.00 (0.00)	3.00 (0.00)	0.149**
	Women	3.00 (0.00)	2.98 (0.13)	
Attention	1.74 (1.22)	1.77 (1.21)	1.66 (1.25)	0.485*
	Men	2.16 (1.17)	1.73 (1.28)	**0.001****
	Women	1.54(1.18)	1.64 (1.25)	
Calculation	4.38 (1.00)	4.42 (0.97)	4.21 (1.15)	0.475*
	Men	4.74 (0.73)	4.73 (0.59)	**<0.001****
	Women	4.23 (1.04)	4.07 (1.23)	
Short-term memory	1.60 (1.09)	1.61 (1.08)	1.55 (1.17)	0.749*
	Men	1.56 (1,15)	1.27 (1.10)	0.657**
	Women	1.63 (1.03)	1.62 (1.18)	
Language	5.28 (0.84)	5.31 (0.81)	5.19 (0.95)	0.501*
	Men	5.46 (0.78)	5.20 (0.77)	**0.039****
	Women	5.22 (0.82)	5.19 (0.99)	
Praxis	4.42 (0.70)	4.43 (0.70)	4.40 (0.70)	0.744*
	Men	4.52 (0.65)	4.47 (0.64)	0.340**
	Women	4.37 (0.73)	4.38 (0.72)	
SET-TEST	37.34 (3.79)	37.44 (3.76)	36.90 (3.89)	0.160*
	Men	37.07 (3.75)	37.13 (3.80)	0.099**
	Women	37.66 (3.77)	36.84 (3.93)	
BARTHEL	96.76 (6.54)	97.64 (5.38)	93.25 (9.15)	**<0.001***
	Men	98.15 (4.36)	93.17 (11.20)	**<0.001****
	Women	97.34 (5.88)	93,27 (8.66)	
LAWTON	7.10 (1.45)	7.09 (1.47)	7.12 (1.37)	0.867*

	Men	6.29 (1.59)	6.00 (1.77)	**<0.001****
	Women	7.56 (1.17)	7.40 (1.09)	

p: Mann-Whitney U p-value for differences according to depressionand the Kruskal Wallis test for gender differences. *p: Mann-Whitney U p-value; **p: Kruskal-Wallis H p-value