Association between testosterone and cognition in men and women over 60 years of age living in contexts of social vulnerability.

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Abstract

The aim of the present study was to analyse associations between testosterone and cognitive domains in men and women 60 years of age or older. A quantitative, cross-sectional study was conducted with a sample of 190 older people stratified by sex and age group registered at Family Health Units in an area of social vulnerability. Data were collected on sociodemographic characteristics, cognitive performance (Mini Mental State Examination) and hormone levels (thyroid-stimulating hormone, prolactin, estradiol, total testosterone and calculated free testosterone). Total testosterone levels changed with the increase in age. Correlations were found between total testosterone and cognition in the temporal orientation (r=-0.910; p=0.00) and evoked recall (r=0.740; p=0.03) domains for men aged 80 years or older as well as the attention/calculation domain for women aged 60 to 69 years (r=0.307; p=0.01) and 80 years or more (r= -0.691; p=0.03). For longer-lived women, a correlation was also found with language (r=0.694 p= 0.03). Correlations between calculated free testosterone and cognition were found for evoked recall in men aged 60-69 years (r=0.323; p=0.05) as well as attention/calculation in women aged 60-69 years (r=0.335; p=0.01). The present findings indicate correlations between testosterone levels and cognition influenced by sex and age among older people in contexts of social vulnerability.

Keywords: Elderly, Testosterone, Cognition, Primary health care, Social vulnerability.

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Introduction

The older population in Brazil has increased at an accelerated pace and the number of individuals aged 60 years or older is expected to reach 31.8 million by 2025, making it the sixth largest population of older people in the world. This increased longevity is accompanied by a greater frequency of health problems typical to this age group including [1] dementias. A projected 130 million cases of dementia are expected by 2050, making this an important public health problem [2,3].

Cognitive performance is influenced by different factors, such as an advanced age, a low level of schooling, the female sex, inadequate nutritional status, physical inactivity, and low income [4-6]. The literature has also shown associations between cognition and levels of hormones, such as testosterone, in both men and women, although the findings are inconclusive [7,8].

Thus, studies on hormonal and cognitive aspects in older people are of considerable importance. Testosterone levels diminish with the increase in age and low endogenous levels of this hormone may be related to a reduction in cognitive capacity [8]. One study analysed the association between cognitive function in men over 50 years of age and serum concentrations of total and bioavailable testosterone as well as other factors, such as sex hormone-binding globulin (SHBG). The findings showed that men with higher levels of bioavailable testosterone performed better on cognitive tests, whereas worse scores were associated with high levels of SHBG [9]. Moreover, cognitive performance may differ between women and men. Cherrier and collaborators state that men generally outperform women regarding spatial skills, but the increase in age is accompanied by reductions in cognitive capacity and memory as well as testosterone levels [10].

A randomized study evaluated verbal episodic memory, spatial memory, and incidental learning among women in surgically induced menopause and who received estradiol valerate combined with either testosterone undecanoate or placebo. Evaluations were conducted at the onset of the study, at cross-over, and after the end of treatment. The authors found that the addition of testosterone to estrogen treatment exerted a negative effect on immediate verbal recall in comparison to estrogen combined with placebo, whereas other memory functions were not compromised [11]. Another randomized study found no significant improvement in verbal fluency, verbal recall, or spatial skills after hormone replacement therapy compared to a placebo [12]. Thus, further studies are needed to assess the

association between cognitive performance and hormone levels according to sex, especially in older people [13,14].

Considering the longevity and heterogeneity of the population, studies that consider different age groups and the context of social vulnerability in which older people live are needed and could broaden knowledge on this topic. Therefore, the aim of the present study was to analyse correlations between testosterone levels and cognitive performance in men and women in three age groups (60-69, 70-79, and 80-89 years) registered at services affiliated with the Family Health Support Center in a region of high social vulnerability in a city in the state of São Paulo, Brazil.

Materials and Methods

A quantitative, cross-section study was conducted. This study was linked to the research project "Monitoring Tool for Frailty Levels in Older People in Primary Care": Assessment of effectiveness and efficiency", known as the PPSUS project, which was funded by São Paulo State Research Foundation (FAPESP) (Process nº. 2016/152351) and approved by the Research Ethics Committee (Opinion No.2,424,616 / 2017, CAAE: 66076017.30000.5504).

Setting

The study was conducted in the city of São Carlos, which is located in the central region of the state of São Paulo, Brazil. Data were collected from the homes of the participants, who were registered at one of the five Family Health Units of the city. The health units were in the area of coverage of the Family Health Support Center in the neighbourhood of Cidade Aracy, which, according to the Paulista Social Vulnerability Index, is a region of high social vulnerability.

Participants

The initial sample was composed of 345 older people registered with Family Health Units of the Cidade Aracy Family Health Support Center who participated in the PPSUS project. After the application of the exclusion criteria (severe cognitive, language, and communication impairment that impeded answering the data collection instruments; thyroid-stimulating hormone values higher than 10 µUI/mL; and the use of anticonvulsants, glucocorticoids, opioids, finasteride, estrogen, androgen, anti-androgen, and benzodiazepine), the final sample was selected based on age and sex and was composed of 76 men and 114 women.

Data collection procedures

Volunteers who agreed to participate in the study signed a statement of informed consent and were submitted to individual home interviews for the collection of the variables of interest (sociodemographic characteristics, cognitive performance, and testosterone levels). Blood was collected during morning hours by trained professionals and the analysis of the biological material was performed by a laboratory affiliated with city hall. Data collection occurred between March and August 2018 during business hours at the participants' homes. The interviewers were duly trained undergraduate and graduate students.

Data collection instruments and measures

Sociodemographic characteristics: A questionnaire was created for the characterization of the sample in terms of age (in years), sex (male; female), marital status (married or living with partner; widowed; single), schooling (in years), and family income (in Brazilian currency).

Mini Mental State Examination (MMSE): Cognitive function screening instrument composed of 30 items distributed among the following domains: attention and orientation; memory; verbal fluency; language; and visuospatial skill. The cut-off points recommended [15] were adopted for the present study: 17 for illiterate individuals; 22 for those with one to four years of schooling; 24 for those with five to eight years; and 26 for those with nine or more years of schooling. A score below the cut-off point is indicative of cognitive deficit.

Laboratory analysis of sex hormones: Blood was collected for the determination of levels of thyroid-stimulating hormone (TSH), prolactin, estradiol, total testosterone, and calculated free testosterone. The levels were determined between 8 and 11 am using chemiluminescence. The level of free testosterone was calculated based on the level of sex hormone-binding globulin (SHBG) using Vermeulen's formula. Normal values were considered to be 29 to 112 pg/mL for men and 0.34 to 5.6 pg/mL for women between 47 and 91 years of age.

Data analysis procedures

The data were entered into the Excel 2010 software (Microsoft Corp, Redmond, WA, USA) by two blinded independent typists. The statistical analyses were performed with the aid of SPSS version 21.0 (IBM Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was used to confirm the adherence of the data to normality ($p>0.05$). The databank was divided into male and female participants. In the two databanks, subgroups were created based on age (60-69 years; 70-79 years; 80-89 years). Sociodemographic characteristics, cognitive performance, and hormone levels were expressed as mean and standard deviation values for the different subgroups. Comparisons among the three age groups were performed using one-way analysis of variance (ANOVA) for independent samples with Tukey's post hoc test (pairwise comparisons). The significance level was set at 5% ($p \leq 0.05$). Pearson's correlation coefficients were calculated to determine the presence/absence of correlations between cognitive performance and free testosterone level. The magnitude of the correlations was classified based on Levin, Fox, and [16] Forbe < 0.3=weak; 0.3 to 0.59=moderate; 0.6 to 0.9=strong; and 1.0=perfect. The data are presented in tables stratified by sex and age group.

Results

One hundred ninety older people participated in the present study: 76 men (40%; n=34 in the 60-to-69-year-old age group, n=33 in the 70-to-79-year-old age group, and n=8 in the 80-to-89-year-old age group) and 114 women (60%; n=59 in the 60-to-69-year-old age group, n=47 in the 70-to-79-year-old age group, and n=9 in the 80-to-89-year-old age group). The men had a mean age of 71.04 ± 6.0 years and mean schooling of 3.2

± 2.9 years; 72% were married or lived with a partner; family income was approximately R$2613.32 ± 1321.4. The women had had a mean age of 70.6 ± 6.0 years and mean schooling of 2.7 ± 2.8 years; 53.0% were married or lived with a partner; family income was approximately R$1983.50 ± 1262.0. Mean schooling of the male participants was significantly higher in the youngest age group (p=0.001).

Higher percentages of normal TSH were found in both the men and women and among the age groups (men: p=0.394; women: p=0.658). The same was found for prolactin (men: p=0.034; women: p=0.380), with only some differences among the age groups in the men. Most estradiol values did not differ significantly (men: p=0.297; women: p=0.025). The only exception was a lower mean (8.78 ± 5.56 pg/ml) in women 80-89 years of age compared to the other groups. Although no significant difference in total testosterone was found among the different age groups in either the men (p=0.206) or women (p=0.142), serum total testosterone in the men diminished with age, especially above 80 years of age (259.13 ± 94.65 ng/dl). No significant difference in free testosterone was found among the age groups (Tables 1 and 2).

Tables 3 and 4 displays the cognitive performance results measured using the MMSE. The mean was 23.1 ± 4.90 points for men and 22.2 ± 3.72 points for women; 31.6% of the men and 39.5% of the women scored below the expected cut-off point, indicating cognitive deficit. Younger men and women

Table 1. *Hormone levels in men stratified by age group. São Carlos, 2018. (n = 76).*

Variables	Men (n=76)			
	60-69 (n=35) a	70-79 (n=33) b	80-89 (n=8) c	P¹
Hormone				
TSH, mean ± SD. *in µUl/ml*	2.57 ± 2.07	2.88 ± 1.74	2.38 ± 1.03	.0394
Normal, n (%)	30 (85.7)	31 (93.9)	8 (100)	
Altered, n (%)	5 (14.3)	2 (6.1)	-	
Prolactin, mean ± SD, *in ng/ml*	9.09 ± 3.92	10.83 ± 5.03	6.00 ± 2.33	.034
Normal, n (%)	34 (97.1)	22 (66.7)	3 (37.5)	
Altered, n (%)	1 (2.9	11 (33.3)	5 (62.5)	
Estradiol, mean ± SD*, in pg/ml*	41.31 ± 20.32	46.91 ± 28.15	40.25 ± 24.30	.297
Normal, n (%)	26 (74.3)	22 (66.7)	6 (75.0)	
Altered, n (%)	9 (25.7.)	11 (33.3)	2 (25.0)	
Total testosterone, mean ± SD, *in ng/dl*	427.97 ± 143.95	330.82 ± 166.15	259.13 ± 94.65	.206
Normal, n (%)	33 (94.3)	27 (81.8)	5 (62.5)	
Altered, n (%)	2 (5.7)	6 (18.2)	3 (37.5)	
Free testosterone, mean ± SD*, in pg/ml*	70.06 ± 23.86	67.15 ± 60.06	35.88 ± 18.20	.712
Normal, n (%)	33 (97.1)	32 (97.0)	6 (100)	
Altered, n (%)	1 (2.9)	1 (3.0)	-	
¹ANOVA one-way com Tukey Post hoc test. Men - Prolactin: a=b; a=c; b≠c. Testosterone total: a≠b; a=c; b=c.				

Table 2. *Hormone levels in women stratified by age group. São Carlos, 2018. (n=114)*

Variables	Women (n=114)			
	60-69 (n=59) a	70-79 (n=47) b	80-89 (n=9) c	P¹
Hormone				
TSH, mean ± SD*, in µUl/ml*	3.16 ±1.80	2.81 ± 1.78	1.89 ± 1.36	.658
Normal, n (%)	48 (81.4)	40 (85.1)	11 (100)	
Altered, n (%)	11 (18.6)	7 (14.9)	-	
Prolactin, mean ± SD*, in ng/ml*	9.22 ± 7.45	10.1 ± 11.22	7.22 ± 3.19	.380
Normal, n (%)	48 (82.8)	39 (83.0)	9 (100)	
Altered, n (%)	10 (17.2)	8 (17.0)	-	
Estradiol, mean ± SD*, in pg/ml*	23.76 ± 20.34	29.98 ± 20.89	8.78 ± 5.56	.025
Normal, n (%)	52 (89.7)	37 (78.7)	9 (100)	
Altered, n (%)	6 (10.3)	10 (21.3)	-	
Total testosterone, mean ± SD*, in ng/dl*	47.50 ± 63.09	40.13 ± 25.30	29.11 ± 13.57	.142
Normal, n (%)	52 (89.7)	41 (82.2)	9 (100)	
Altered, n (%)	3 (10.3)	6 (12.8)	-	
Free testosterone, mean ± SD*, in pg/ml*	7.64 ± 12.96	5.47 ± 3.86	3.44 ± 2.60	.085
Normal, n (%)	39 (66.1)	28 (59.6)	8 (72.7)	
Altered, n (%)	20 (33.9)	19 (40.4)	3 (27.3)	
¹ANOVA one-way com Tukey Post hoc test. Men - Prolactin: a=b; a=c; b≠c. Testosterone total: a≠b; a=c; b=c.				

Table 3. *Cognitive performance of men stratified by age group. São Carlos, 2018. (n=76)*

Variables	Men (n=76)			
	60-69 (n=34) a	70-79 (n=33) b	80-89 (n=8) c	P[1]
Cognition				
Temporal orientation, mean ± SD	4.49 ± 1.09	4.27 ± 1.08	4.63 ± 0.74	.726
Spatial orientation, mean ± SD	4.57 ± 0.97	4.58 ± 0.96	4.88 ± 0.35	.306
Immediate recall, mean ± SD	2.83 ± 0.56	2.94 ± 0.24	3.00 ± 0.00	.029
Attention/calculation, mean ± SD	3.43 ± 1.52	2.09 ± 1.91	2.50 ± 1.91	.144
Evoked recall, mean ± SD	1.80 ± 1.05	1.00 ± 1.25	1.25 ± 0.70	.141
Language, mean ± SD	7.03 ± 1.52	6.39 ± 1.36	6.75 ± 0.88	.465
Visual construct, cap.. mean ± SD	049 ± 0.50	0.24 ± 0.43	0.00	.000*
MMSE, mean ± SD	24.63 ± 5.23	21.52 ± 4.62	23.00 ± 2.00	.280
Normal, n (%)	27 (77.1)	18 (54.5)	7 (87.5)	
Altered, n (%)	8 (22.9)	15 (45.5)	1 (12.5)	

[1]ANOVA one-way com Tukey Post hoc test. Men. AC: a≠b; a=c; b=c. ME: a≠b; a=c; b=c. CCV: a=b; a≠c; b=c. MMSE: a≠b; a=c; b=c. Women - MEEM: a=b; a≠c.

Table 4. *Cognitive performance of women stratified by age group. São Carlos, 2018. (n = 114)*

Variables	Women (n=114)			
	60-69 (n=59) a	70-79 (n=47) b	80-89 (n=9) c	P[1]
Cognition				
Temporal orientation, mean ± SD	4.50 ± 0.88	4.55 ± 0.88	3.56 ± 1.23	.133
Spatial orientation, mean ± SD	4.69 ± 0.62	4.64 ± 0.64	4.11 ± 1.05	.001*
Immediate recall, mean ± SD	2.78 ± 0.56	2.87 ± 0.44	2.89 ± 0.33	.154
Attention/calculation, mean ± SD	1.62 ± 1.44	1.55 ± 1.70	0.56 ± 0.72	.010
Evoked recall, mean ± SD	1.72 ± 0.89	1.64 ± 1.05	1.44 ± 0.88	.188
Language, mean ± SD	6.88 ± 1.39	6.72 ± 1.13	6.44 ± 1.33	.869
Visual construct, cap.. mean ± SD	0.41 ± 0.49	0.36 ± 0.48	0.11 ± 0.33	.000*
MMSE, mean ± SD	22.60 ± 3.31	22.34 ± 4.01	19.11 ± 3.58	.399
Normal, n (%)	41 (70.7)	26 (55.3)	2 (22.2)	
Altered, n (%)	17 (29.3)	21 (44.7)	7 (77.8)	

[1]ANOVA one-way com Tukey Post hoc test. Men. AC: a≠b; a=c; b=c. ME: a≠b; a=c; b=c. CCV: a=b; a≠c; b=c. MMSE: a≠b; a=c; b=c. Women - MEEM: a=b; a≠c.

had a better cognitive performance than older individuals for visual constructive capacity (p=0.000 for both). Among the women, the performance regarding spatial orientation was also better in the youngest age group (p=0.001). For cognitive level, no significant differences among the age groups were found for men or women (p=0.280 and .399, respectively).

Tables 5 and 6 displays the correlation data for total testosterone and cognitive performance of the sample stratified by sex and age group. For men aged 80 years or older, a strong negative correlation was found in the temporal orientation domain (r = -0.910; p=0.00) and a strong positive correlation was found in the evoked recall domain (r=0.740; p=0.03). For women aged 60 to 69 years, a moderate positive correlation was found in the attention/calculation domain (r=0.691; p=0.03) and a strong positive correlation was found in the language domain (r=0.694; p=0.03).

Tables 7 and 8 displays the correlation data for calculated free testosterone and cognitive performance of the sample stratified by sex and age group. For men aged 60 to 69 years, a moderate positive correlation was found in the evoked recall domain (r=0.323; p=0.05). For women aged 60 to 69 years, a moderate positive correlation was found in the attention/calculation domain (r=0.335; p=0.01).

Discussion

The sample of the present study was composed predominantly of women, married individuals (with a higher percentage of widowed individuals among the longest lived), and schooling between one and four years, which was higher among men aged 60 to 69 years. A previous study involving 8556 participants with a mean age of 63.7 ± 9.9 years at baseline of the Longitudinal Study on the Health of Older Brazilians (ELSI-Brasil) also had a higher percentage of women (56%). The literature has pointed out the phenomenon of feminization in old age [17-21]. These data show the influence of socioeconomic and cultural factors, especially in regions of high social vulnerability, as well as the issue of gender in the education of older people.

Regarding hormones, TSH was altered in only 9.2% of the men and 15.7% of the women. These findings are similar to those described in a study conducted with 123 older people divided among three age groups (60-69, 70-79, and ≥ 80 years), which found a predominance of the female sex (71.5%) and the majority of participants exhibited normal thyroid function [22]. According to the Consensus on Thyroid Disease of the Brazilian Society of Endocrinology, normal TSH values range from 0.34 to 5.60 μUI/mL. The increase in TSH that occurs with aging seems to have a cardioprotective effect, which is not yet fully

Table 5. *Correlations between testosterone and performance on MMSE stratified by sex and age. São Carlos, 2018. (n=76)*

Variables	Participants		
	Men (n=76)		
Performance on MMSE × testosterone level	60-69 years	70-79 years	80 – 89 years
Temporal orientation r (p)	-.207 (0.23)	. -112 (0.53)	-.910 (0.00) *
Spatial orientation r (p)	-.079 (0.65)	-.058 (0.75)	.099 (0.81)
Immediate recall r (p)	-.315 (0.06)	-.010 (0.95)	-
Attention/calculation r (p)	-0.44 (0.80)	-.009 (0.96)	-.594 (0.12)
Evoked recall r (p)	0.22 (0.19)	.218 (0.22)	.740 (0.03) *
Language r (p)	-.197 (0.25)	-.216 (0.22)	.133 (0.75)
Visual construct, cap, r (p)	-.071 (0.68)	.035 (0.84)	-
Total MMSE, r (p)	-.125 (0.47)	-.044 (0.80)	-.420 (0.30)
Pearson's correlation test. *p significant correlation			

Table 6. *Correlations between testosterone and performance on MMSE stratified by sex and age. São Carlos, 2018. (n=114)*

Variables	Participants		
	Women (n=114)		
Performance on MMSE × testosterone level	60-69 years	70-79 years	80-89 years
Temporal orientation r (p)	.094 (0.48)	-.048 (0.74)	-.094 (0.81)
Spatial orientation r (p)	.097 (0.46)	.164 (0.27)	.410 (0.27)
Immediate recall r (p)	.058 (0.66)	0.178 (0.23)	.224 (0.56)
Attention/calculation r (p)	307 (0.01)	.057 (0.70)	-.691 (0.03) *
Evoked recall r (p)	-.032 (0.81)	-.019 (0.90)	.361 (0.34)
Language r (p)	.041 (0.75)	-.055 (0.71)	.694 (0.03) *
Visual construct. cap. r (p)	-0.35 (0.79)	-.036 (0.81)	-.390 (0.30)
Total MMSE r (p)	.191 (0.15)	.035 (0.81)	1.00 (0.46)
Pearson's correlation test. *p significant correlation			

Table 7. *Correlations between calculated free testosterone and performance on MMSE stratified by sex and age. São Carlos, 2018. (n=76)*

Variables	Participants		
	Men (n=76)		
Performance on MMSE × testosterone level	60-69 years	70-79 years	80-89 years
Temporal orientation r (p)	-.174 (0.31)	.037 (0.83)	-.626 (0.09)
Spatial orientation r (p)	-.108 (0.53)	-.069 (0.70)	-.269 (0.51)
Immediate recall r (p)	-.190 (0.27)	-.269 (0.51)	-
Attention/calculation r (p)	.251 (0.14)	015 (0.93)	-.574 (0.13)
Evoked recall r (p)	.323 (0.05) *	-.157 (0.38)	.624 (0.09)
Language r (p)	-.165 (0.34)	.121 (0.50)	.015 (0.97)
Visual construct. cap. r (p)	-.032 (0.85)	-.119 (0.51)	-
Total MMSE r (p)	.009 (0.95)	-0.14 (0.94)	-.459 (0.25)
Pearson's correlation test. *p significant correlation			

Table 8. *Correlations between calculated free testosterone and performance on MMSE stratified by sex and age. São Carlos, 2018 (n = 114).*

Variables	Participants		
	Women (n=114)		
Performance on MMSE × testosterone level	60-69 years	70-79 years	80 – 89 years
Temporal orientation r (p)	.119 (0.37)	.101 (0.49)	-.164 (0.67)
Spatial orientation r (p)	.113 (0.39)	.211 (0.15)	.344 (0.36)
Immediate recall r (p)	.025 (0.85)	.123 (0.40)	.208 (0.59)
Attention/calculation r (p)	.335 (0.01) *	.102 (0.49)	-.543 (0.13)
Evoked recall r (p)	.044 (0.74)	-0.32 (0.82)	.339 (0.37)
Language r (p)	.048 (0.72)	-.104 (0.48)	.548 (0. 12)
Visual construct. cap. r (p)	-.001 (0.99)	-.023 (0.88)	-.352 (0.35)

Total MMSE r (p)	.236 (0.07)	.072 (0.62)	.208 (0.59)
Pearson's correlation test. *p significant correlation			

understood. However, levels higher than 10 may be associated with a greater risk of cognitive impairment [23]. Therefore, individuals with TSH above this threshold were excluded from the present study. Mean prolactin levels were normal, except among longer-lived men, which may be associated with the use of medications, especially antiemetics, anticonvulsants, and antidepressants, or hypothyroidism [23]. No significant alterations were found regarding estradiol levels, with the exception of women between 80 and 89 years of age, in whom the mean was lower (8.78 ± 5.56 pg/ml) compared to the other groups, likely due to the advanced age [24].

Although no significant differences were found in total testosterone (TT) levels among the different age groups in either the men or women, serum TT levels diminished with age, especially after 80 years of age. This finding is likely to do the greater sensitivity of the exam, as Vermeulen's formula was used, including SHBG, which increases with age and diminishing serum testosterone levels. Previous studies also report lower TT levels in individuals at more advanced ages [25,26]. No significant alterations in calculated free testosterone (FT) levels were found in the different groups.

Regarding the cognitive profile, a significant portion of the sample (31.5% of the men and 39.4% of the women) scored below the cut-off point on the MMSE. Cognitive performance was better among the younger age groups. This is similar to data described in a previous Brazilian study, which found a lower percentage of cognitive deficit (18.2%) among younger seniors compared to those aged 80 years or older [27]. The reduction in the number of neurons, especially in the region of the hippocampus, and neurochemical (cholinergic and dopaminergic) losses can lead to a reduction in cognition with age, especially among women, who live longer than men. Therefore, the present finding is similar to data described in national and international studies [28,29] showing that age is related to cognitive impairment among older people, although a high percentage of normal results on the MMSE was found among the participants in the present study. We also found differences between the sexes for some cognitive domains, which is also in agreement with data described in the literature, such as the better performance of men compared to women regarding the attention and calculation domain [27].

No correlations were found between testosterone (TT and FT) and the total MMSE score. In a double-blind, placebo-controlled study conducted in the USA, 308 men aged 60 years or older with low TT and FT levels were divided into two groups. One group underwent testosterone replacement therapy for 36 months and the other group received a placebo. Despite the increase in serum TT and FT levels in the hormone therapy group, testosterone did not have any effect on the results of the cognitive tests, as no improvements on the different domains were found in comparison to the control group [30].

Although negative correlations were found in the oldest age group (≥ 80 years) regarding the temporal orientation domain (men) and the attention/calculation domain (women) and positive correlations were found regarding evoked recall (men) and language (women) in the same age group, testosterone levels were withing the normal range, despite being comparatively lower in relation to the other age groups. Another important aspect regards the small number of participants in this group, which may have influenced the result. In the analysis of calculated FT, positive correlations were found for both men (evoked recall) and women (attention/calculation) in the 60-to-69-year-old age group, which may be explained by the higher levels of testosterone in younger age groups.

Few studies have evaluated the association between testosterone levels and cognition in women. The side effects of androgen hormones, such as acne, the emergence of body hair, and hair loss, end up limiting its use. A randomized, double-blind, placebo-controlled study evaluated the association between sex steroid levels and cognitive function among 200 women between 50 and 65 years of age in natural menopause. The participants were divided into three groups, each of which was submitted to a different replacement treatment (estradiol, testosterone, or placebo) for four weeks. The authors analysed TT, FT, and estradiol levels as well as cognitive functions (verbal fluency, verbal memory, and spatial skills) before and after treatment and concluded that neither testosterone nor estradiol had any significant effect on these domains [12].

Another study evaluated 643 healthy women not in hormone replacement therapy who were in menopause for either less than six years or more than ten years. Estradiol, estrone, progesterone, free testosterone, and SHBG levels were determined and the women were submitted to a neuropsychological evaluation of episodic verbal memory, executive functions, and global cognition. The linear regression analysis revealed no associations between the steroids and the cognitive domains. The only exception was SHBG, which was positively associated with verbal memory [31]. This was likely due to the increase in SHBG that occurs with aging, diminishing its bond to testosterone, which can then act freely on brain or through its conversion into estradiol, as the literature has shown a possible association between these hormones [31].

The present study has limitations that should be considered. The cross-sectional design does not enable the establishment of cause- and-effect relations among the variables studied. Despite the potential for comparisons to other areas of high vulnerability, the findings were restricted to the sample analysed and cannot be generalized. The number of individuals in the 80-to-89-year-old age range was small in both the male and female groups. Future studies should include a larger number of participants with an advanced age. The present study is of extreme importance, as it involved male and female older people in different age groups, including long-lived individuals. Few studies have been conducted with this age range and with women.

Conclusions

The results of the research allow us to conclude that regarding the sociodemographic characteristics the profile of the participants was similar to that described in the literature, that is, elderly women aged 60-69 years, married and with low education. Most of the men and women participating in this study had cognitive performance as expected.

Levels of total testosterone in men and estradiol in women were lower in older elderly people, despite being within normal limits. The results of the relationship between total testosterone and cognition showed that there was a negative correlation both for the Temporal Orientation domain in men and for the Attention and Calculation domain in women aged 80-89 years and in this same group, there was a positive correlation for the domain Evocation Memory in men and Language for women. The Attention and Calculation domain also showed a positive correlation in younger elderly women. The data evaluated between free testosterone and cognitive performance, showed a positive correlation only in the Evocation Memory domain in men and Attention and Calculation in women, in the age group of 60-69 years.

This study evaluated associations between testosterone and cognitive function in older men and women (≥ 60 years), revealing no significant differences, although age was found to be a risk factor for the reduction in cognitive performance among older people. As the side effect of testosterone therapy in older people limit its application and considering the population aging phenomenon due to the increase in life expectancy, broader knowledge is needed through the conduction of studies on adequate treatments or prevention measures that can avoid or revising cognitive impairment.

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