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Functional Status of Thyroid and Cognitive Functions after Menopause

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Background: Thyroid activity plays a role in cognition. However, the relation between the functional state of thyroid and neuropsychiatric changes proceeding with age among people without clinical symptoms of thyroid dysfunction is still unknown. The aim of this study was analysis of cognitive function levels in reference to thyroid examination: thyroid-stimulating hormone (TSH), total thyroxin (TT4), triiodothyronine (TT3), free thyroxin (FT4), free triiodothyronine (FT3), thyroperoxidase antibodies (TPO-AB), and thyroglobulin antibodies (Tg-AB), TSH receptor antibodies (AB-TSHR) in women after menopause.

Material/Methods: A group of 383 women was recruited for the study. The inclusion criteria were: minimum two years after the last menstruation and no dementia signs on Montreal Cognitive Assessment (MoCA). Computerized battery of Central Nervous System Vital Signs (CNS VS) test was used to diagnostic cognitive functions. The blood plasma values were determined: TSH, FT3, FT4, TT3, TT4, TPO-AB, Tg-AB, and AB-TSHR. Statistical analysis was performed using Pearson's correlation coefficient and analysis of variance in STATISTICA software.

Results: In women after menopause, TSH was negatively correlated with NCI results, executive functions, complex attention, and cognitive flexibility. FT4 was positively correlated with results of psychomotor speed. TT3 and TT4 were negatively correlated with results of memory and verbal memory. Furthermore, TT4 was negatively correlated with NCI, executive functions, and cognitive flexibility. TPO-AB was negatively correlated with results of memory, verbal memory, and psychomotor speed. Tg-AB was positively correlated with results of reaction time. AB-TSHR was negatively correlated with NCI results, memory, executive functions, psychomotor speed, complex attention, and cognitive flexibility.

Conclusions: Our study supports the importance of thyroid functionality in cognitive functioning in a group of women after menopause. The values of TSH, TT3, TT4, TPO-AB, and AB-TSHR were higher and FT4 was lower in examined women. The results were poorer in examination of cognitive functions measured with a battery of CNS-VS tests.

MeSH Keywords: Antibodies • Cognition • Menopause • Thyroid Function Tests • Thyroid Hormones

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Background

The relationship between the functional state of the thyroid gland and the risk of lowering cognitive functions and dementia, particularly Alzheimer's disease, was examined many times in the last twenty years. The great majority of these studies concluded that increased levels of TSH (thyrotropin hormone) are connected with dysfunctions in cognitive functions [1,2]. Van Osch et al., on the basis of their own research, suggested that low values of TSH can be an independent risk factor because in their studies low TSH was connected with increased risk of Alzheimer's disease [3]. In the research called 'The Framingham Study' it was stated that both low and high levels of TSH are connected with increased risk of Alzheimer's disease in women [4]. However prospective this may be, observations in population studies suggest that levels of TSH and FT4 (free thyroxin) in the serum were not directly connected with dysfunctions of cognitive functions [5].

Despite the fact that it has been established that thyroid activity plays a role in cognition, the relationship between state of the thyroid gland and neuropsychiatric symptoms in patients without clinical signs of thyroid dysfunction or in euthyreosis was not clear.

It has been demonstrated that thyroid hormones influence the brain metabolism, modulate gene expression, and influence transfer of signals between cells, among others, through the synthesis of enzymes needed for neurotransmitters production [6]. There is a known influence of thyroid hormones on neurotransmitter networks: noradrenergic, serotonergic and GABA-ergic. The impact of thyroid hormones on the brain in adults probably occurs through their activity regulation and G proteins synthesis. Deficiency of thyroid hormones depresses signal transferring by adenylate cyclase and phosphoinositol [7].

Experimental studies demonstrated that thyroid hormones modulate the development of glial cells, have an influence on proliferation processes and migration of nerve cells, proper synaptogenesis, growth of axons and creation of arborescent branching [8–11], and they also participate in a processes of myelinization of nerve cells [12].

In a mature brain, the effects of thyroid hormones actions are less known than in the foetal brain, but even a short break in de-iodination within a period of fetal life can cause local dysfunction of thyroid hormones synthesis in later age [13]. Thyroid hormones have an impact on neurotransmitter networks in the mature brain: noradrenergic, serotonergic and GABA-ergic, and they also participate in the repair processes [7,14]. According to the latest hypothesis, thyroid hormones regulate brain functioning through their impact on catecholamine release regulation [8].

Recent years have seen a growth of interest in studies on determinants of changes in cognitive functions [15,16]. The appearance of menopause is combined with the appearance of many diseases, which are directly linked with hormonal changes during this period. Women after menopause have lower efficiency in cognitive functions, which is below average as compared to the general population. It has been shown that women after menopause obtained worse results within a range of processing speed, cognitive flexibility, and executive functions. The best ones were obtained within a range of verbal memory and visual memory [17]. In the literature it is suggested that lowering of oestrogen levels is responsible for cognition and psychical dysfunctions observed in this period of life. However, research findings on the influence of estrogen replacement therapy on cognition functioning were contradictory [18,19]. Therefore, it seems that the problem is more complicated than only estrogen deficiency. Numerous controversies in the research results indicate that there is a need for further exploration of health and social aspects, which could improve cognition functioning in this population. Research on the above issues seems to be worthwhile as there are other unexplained dysfunctions in other endocrine organs, which are related to dysfunction of cognitive functions during this period. In the literature it is stated that there is a change of functioning with age of the hypothalamus-pituitary gland-thyroid and potential influence of this axis on cognitive functions.

The aim of this study was to analyze cognitive functions levels according to thyroid examinations: thyroid-stimulating hormone (TSH), total thyroxin (TT4), triiodothyronine (TT3), free thyroxine (FT4), free triiodothyronine (FT3), thyroperoxidase antibodies (TPO-AB) and thyroglobulin antibodies (Tg-AB), and TSH receptor antibodies (AB-TSHR) in women after menopause.

Material and Methods

Study group

The study was conducted in 2012 and 2013 at the Institute of Rural Health in Lublin. The study group included women from south-eastern Poland. The criteria of inclusion in the study were as follows: age 50–65, good general health, education level at least completed elementary. The women were also qualified into the study group based on clinical symptoms – minimum 2 years after the last menstrual period. The criteria for exclusion from the study were as follows: chronic diseases, particularly of liver and kidneys, active cancerous disease within the period of five years before recruitment; mental diseases in medical history, including depressions before menopause; addiction to drugs and alcohol; diagnosed nosology unit with the symptoms of dementia. Women under examination were not using hormonal replacement therapy. At the stage of qualification

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for the study, a brief The Montreal Cognitive Assessment scale was conducted in order to include the patients who did not show the symptoms of dementia [20]. The Montreal Cognitive Assessment scale for evaluation of cognitive functions was designed as a quick screening instrument for the evaluation of mild cognitive dysfunctions, with a Polish adaptation of the scale by Magierska et al. The maximum number of scores in this test is 30; and the result of 26 or more scores is considered as normal. All the women included in the study obtained more than 26 scores in the MoCA test.

Four hundred and six women volunteered to take part in the research, three hundred and eighty six were accepted. Twenty three women did not comply with the criteria.

Neuropsychological assessment

Cognitive functions were evaluated with the help of the diagnostic instrument Central Nervous System-Vital Signs (CNS-VS) (Polish version) [21] with software by CNS Vital Signs (1829 East Franklin St., Bldg. 500, Chapel Hill, NC 27514, USA). The instrument in the form of a battery of computer tests is standardized, has been subjected to the full validation procedure, and possesses a Polish adaptation. The entire research procedure with the use of a computer was performed in Polish. The report concerning test results is published in English. CNS-VS covers the following tests: Verbal Memory Test – VBM, the test examining motor functioning – Finger Tapping Test – FTT, Symbol Digit Modalities Test – SDMT, Stroop Test – ST, Shifting Attention Test – SAT, The Continuous Performance. CNS-VS assess nine cognitive functions: memory, verbal memory, visual memory, processing speed, executive functions, psychomotor speed, reaction time, complex attention, and cognitive flexibility. Based on five of these functions: memory, psychomotor speed, reaction time, complex attention, and cognitive flexibility, the Neurocognition Index (NCI) is calculated. The computer data from the CNS-VS test provides: raw results, standardized results, percentiles, and evaluations according to the 5-point scale for each of the nine cognitive functions examined and the Neurocognitive Index. These evaluations are as follows: above average (more than 109 standardized scores), average (90–109), below average (80–89), low (70–79), very low (less than 70).

Laboratory tests

The blood of the examined women was collected to mark such parameters as: thyroid-stimulating hormone (TSH), total thyroxin (TT4), triiodothyronine (TT3), free thyroxine (FT4), free triiodothyronine (FT3), thyroperoxidase antibodies (TPO-AB), and thyroglobulin antibodies (Tg-AB), TSH receptor antibodies (AB-TSHR). Blood samples were immediately delivered to the laboratory. Marking was carried out in accredited SYNEVO laboratory. The normal range for specific tests: TSH: 0.27–44 mU/l; TT4: 66–181 nmol/l; TT3: 1.3–3.1 nmol/l; FT4: 12–22 pmol/l; FT3: 3.1–6.8 pmol/l; TPO-AB: 0–34 IU/l; Tg-AB: 0–115 IU/l; AB-TSHR: 0–1.5 IU/l.

Statistical analysis

The statistical analysis and diagrams were done in STATISTICA software. In the tables there are absolute numbers (*n*) and relative ones (relation of units number having particular feature variant to the sample size, given in%), minimum and maximum values, arithmetic mean (*M*), reflecting average level and standard deviations (*SD*), measuring the level of measurements dispersion around arithmetic mean, analysis of variance F test, Pearson's correlation coefficient, which shows the strength and direction of correlation between two quantitative characteristics, and also empirical values of statistical tests and critical significance level p. It is the lowest (in given results of the sample) significance level, the null hypothesis can be rejected. In statistical tests there has been established a 0.05 significance level.

The sample size was 383. Because of the large sample size, normal distribution of parameters' estimators was assumed.

Consent for the study was obtained from the Bioethical Committee at the Institute of Rural Health in Lublin.

Results

Total 383 women after menopause were examined. Their average age was 56.4±3.4 years. The most numerous groups in terms of education included women with a secondary (47%) and higher (43%) levels of education. About 10% had basic vocational education. Over two-thirds (67.36%) were white-collar workers and 15.67% were blue-collar workers. The rest of the women under examination (16.97%) performed mixed intellectual-physical jobs.

The examined women's TSH ranged from 0.27 to 7.38 mU/l, on average 1.91±1.35 mU/l. Levels of free and total thyroid hormones in the examined group were: FT3 on average 4.03±0.63 pmol/l, FT4 14.76±2.34 pmol/l, TT3 1.85±0.31 nmol/l and TT4 99.12±16.98 nmol/l. Average values of anti-thyroid antibodies were: 64.74±125.04 IU/l for TPO-AB, 100.69±161.56 IU/l for Tg-AB and 1.40±0.56 IU/l for AB-TSHR (Table 1).

The examined women obtained neurocognitive index at the average level of 84.4 points, meaning the evaluation of cognitive functions is below average (Table 2).

The examined women obtained the worst results in the test evaluating cognitive flexibility (78.64 points at an average), processing speed (79.25 points at an average), and executive

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Table 1. Laboratory tests of thyroid function in examined women.

Marked Parameter	mU *	Min	Max	M**	SD***	Me****	Q1#	Q3##	V### (%)
TSH	mU/l	0.27	7.36	1.91	1.35	1.40	0.93	2.55	71
FT3	pmol/l	2.61	6.49	4.03	0.63	3.95	3.56	4.48	16
FT4	pmol/l	9.32	22.16	14.76	2.34	14.75	13.06	16.30	16
TT3	nmol/l	1.08	2.88	1.85	0.31	1.84	1.64	2.05	17
TT4	nmol/l	62.99	146.70	99.12	16.98	97.32	87.71	109.50	17
TPO-AB	IU/l	5.00	600.00	64.74	125.04	14.90	9.40	28.30	193
Tg-AB	IU/l	8.00	800.20	100.69	161.56	30.90	16.84	103.90	160
AB-TSHR	IU/l	0.31	3.80	1.40	0.56	1.36	1.03	1.72	40

* Unite of measure; **average; *** standard deviation; ****median; # lower quartile; ## upper quartile; ### coefficient of variation.

Table 2. Cognitive functions of examined women.

Cognitive functions	Min–Max	M±SD*	Scores				
			Very low	Low	Low average	Average	Above
			n (%)	n (%)	n (%)	n (%)	n (%)
NCI**	29–115	84.41±16.24	65 (16.97)	77 (20.10)	58 (15.14)	178 (46.48)	5 (1.31)
Memory	44–128	90.15±15.65	32 (8.37)	69 (18.02)	93 (24.28)	124 (32.38)	65 (16.97)
Verbal memory	42–125	91.22±17.75	38 (9.92)	56 (14.62)	64 (16.71)	148 (38.64)	77 (20.10)
Visual memory	47–125	93.37±15.03	22 (5.74)	40 (10.44)	96 (25.07)	179 (46.74)	46 (12.01)
Processing speed	26–117	79.25±14.35	85 (22.19)	101 (26.37)	92 (24.02)	99 (25.85)	6 (1.57)
Cognitive functioning	18–124	79.75±25.08	113 (29.50)	45 (11.75)	63 (16.45)	123 (32.11)	39 (10.18)
Psychomotor speed	22–116	83.42±18.07	70 (18.28)	55 (14.36)	93 (24.28)	144 (37.60)	21 (5.48)
Reaction time	36–121	86.87±16.72	44 (11.49)	65 (16.97)	101 (26.37)	155 (40.47)	18 (4.70)
Complex attention	6–121	82.24±28.64	92 (24.02)	48 (12.53)	49 (12.79)	142 (37.08)	52 (13.58)
Cognitive flexibility	18–125	78.64±26.08	101 (26.37)	59 (15.40)	64 (16.71)	122 (31.85)	37 (9.66)

* Average ±standard deviation; ** neurocognition index.

functions (79.75 points at an average), which indicated low evaluation of these cognitive functions. The results were better in the tests evaluating complex attention (82.24 points at an average) and psychomotor speed (83.42 points at an average) and better still – reaction time (86.87 points at an average), meaning the cognitive functions to be below average. The best results were obtained in tests evaluating memory (90.15 points at an average), including verbal (91.22 points at an average) and visual (93.37 points at an average), which indicates average evaluation of these cognitive functions (Table 2).

There were no correlations between results of cognitive functions and age in the group of women under study. There was a correlation between level of education and results of tests that determined neurocognitive index and four cognitive domains: memory, verbal memory, psychomotor speed, and reaction time. The scores of women in these domains have improved with level of education. The type of job was significantly correlated with neurocognitive index and all cognitive domains but not visual memory. In all of these domains the best scores were achieved by white-collar women (Table 3).

It has been established that in the women after menopause, the level of TSH was negatively correlated with results of NCI, executive functions, complex attention, and cognitive flexibility.

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Table 3. Cognitive functions (standardized results) according to age, education and type of job of women under examination.

Domena	Age (years) (correlation coefficients)		Level of education			Significance of differences		Type of job			Significance of differences	
			Basic vocational	Secondary school	University			Physical	Intelectual	Physical-intelectual		
	r****	p***	M±SD*	M±SD*	M±SD*	F**	p***	M±SD*	M±SD*	M±SD*	F**	p***
NCI	–0.004	0.939	80.08 ±16.76	83.13 ±16.34	86.78 ±15.74	**3.678**	**0.026**	76.33 ±17.86	87.09 ±15.05	81.22 ±16.43	**12.958**	**<0.001**
Memory	–0.072	0.160	85.46 ±18.20	88.77 ±16.51	92.72 ±13.59	**4.675**	**0.010**	86.40 ±15.35	91.58 ±15.15	87.94 ±17.20	**3.492**	**0.031**
Verbal memory	–0.070	0.172	83.78 ±18.86	89.93 ±19.43	94.31 ±14.73	**6.405**	**0.002**	85.60 ±17.56	93.55 ±17.15	87.15 ±18.59	**7.172**	**0.001**
Visual memory	–0.043	0.405	90.76 ±20.47	92.80 ±14.35	94.58 ±14.31	1.224	0.295	91.77 ±18.41	93.53 ±14.19	94.17 ±14.98	0.447	0.640
Processing speed	–0.004	0.943	75.78 ±14.08	78.54 ±12.93	80.81 ±15.72	2.284	0.103	76.92 ±13.52	80.92 ±13.21	74.78 ±18.00	**5.825**	**0.003**
Executive function	0.027	0.598	79.54 ±23.93	78.36 ±25.51	81.33 ±24.90	0.603	0.548	70.13 ±26.66	83.05 ±23.88	75.55 ±25.67	**7.827**	**<0.001**
Psychomotor speed	–0.047	0.359	74.97 ±21.18	83.22 ±17.87	85.55 ±17.06	**5.311**	**0.005**	72.98 ±21.42	86.66 ±15.22	80.23 ±21.03	**16.368**	**<0.001**
Reaction time	–0.058	0.255	75.24 ±18.89	85.57 ±15.92	90.90 ±15.69	**15.357**	**<0.001**	77.63 ±19.77	89.30 ±15.18	85.77 ±16.70	**12.752**	**<0.001**
Complex attention	0.036	0.480	81.32 ±31.28	79.94 ±29.60	84.96 ±26.85	1.345	0.262	73.22 ±32.51	86.07 ±26.77	75.34 ±29.32	**7.418**	**0.001**
Cognitive flexibility	0.029	0.566	79.27 ±24.55	76.85 ±26.42	80.46 ±26.06	0.838	0.433	68.95 ±28.02	82.26 ±24.56	73.23 ±27.27	**8.326**	**<0.001**

* Mean ±standard deviation; ** F-test; *** significance level; **** correlation coefficient.

Table 4. Correlation coefficient between cognitive domains (standard stores) and TSH (m/Ul) in examined women

Cognitive functions	TSH (mU/l)	
	r*	p**
NCI***	**–0.104**	**0.042**
Memory	–0.024	0.646
Verbal memory	0.026	0.611
Visual memory	–0.064	0.209
Processing speed	–0.002	0.962
Cognitive functioning	**–0.145**	**0.005**
Psychomotor speed	–0.058	0.260
Reaction time	–0.083	0.106
Complex attention	**–0.136**	**0.008**
Cognitive flexibility	**–0.128**	**0.012**

* Correlation coefficient; ** significance level; *** neurocognition index.

On average, higher values of TSH were combined with worse results in the above-mentioned domains (Table 4).

The level of FT3 was not linearly correlated with NCI and other analyzed cognitive functions in the examined women. However, the level of FT4 was positively correlated with the results for

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Table 5. Correlation coefficient between cognitive domains (standard stores) and free thyroid hormones (pmol/l) in examined women.

Cognitive functions	FT3 (pmol/l)		FT4 (pmol/l)	
	r*	p**	r	p
NCI***	0.033	0.516	0.039	0.449
Memory	–0.023	0.649	0.021	0.678
Verbal memory	0.030	0.561	0.043	0.398
Visual memory	–0.066	0.196	–0.013	0.797
Processing speed	–0.021	0.677	0.002	0.966
Cognitive functioning	0.051	0.321	–0.010	0.847
Psychomotor speed	0.053	0.300	**0.126**	**0.013**
Reaction time	0.005	0.927	0.058	0.258
Complex attention	0.041	0.428	0.019	0.712
Cognitive flexibility	0.027	0.605	–0.007	0.890

* Correlation coefficient; ** significance level; *** neurocognition index.

Table 6. Correlation coefficient between cognitive domains (standard stores) and total thyroid hormones (nmol/l) in examined women.

Cognitive functions	TT3 (nmol/l)		TT4 (nmol/l)	
	r*	p**	r	p
NCI***	–0.040	0.437	**–0.106**	**0.038**
Memory	**–0.106**	**0.039**	**–0.125**	**0.014**
Verbal memory	**–0.118**	**0.021**	**–0.120**	**0.019**
Visual memory	–0.027	0.594	–0.048	0.346
Processing speed	0.024	0.644	0.036	0.477
Cognitive functioning	–0.001	0.981	**–0.124**	**0.015**
Psychomotor speed	–0.086	0.092	–0.054	0.297
Reaction time	0.000	0.997	–0.041	0.429
Complex attention	–0.015	0.767	–0.089	0.082
Cognitive flexibility	–0.016	0.750	**–0.123**	**0.016**

* Correlation coefficient; ** significance level; *** neurocognition index.

psychomotor speed. This means that together with growth of FT4 level, the examined women obtained better results on average within a range of this cognitive function (Table 5).

There were significant negative correlations between TT3 level and the results for memory and verbal memory. As the level of TT3 in the examined women was higher, the results on average were worse within a range of these two mentioned functions.

With the level of TT4, the results for memory and verbal memory were negatively correlated, besides that of NCI, executive functions, and cognitive flexibility. This means that the higher the level of TT4 in the examined women, on average, the lower the results within a range of NCI and these 4 functions (Table 6).

There were also significant negative correlations between a level of TPO-AB and results for memory, verbal memory, and

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Table 7. Correlation coefficient between cognitive domains (standard stores) and anti-thyroid antibodies (IU/l) in examined women.

Cognitive functions	TPO-AB (IU/l)		Tg-AB (IU/l)		AB-TSHR (IU/l)	
	r*	p**	r	p	r	p
NCI***	–0.069	0.176	0.042	0.409	**–0.169**	**0.001**
Memory	**–0.144**	**0.005**	–0.001	0.993	**–0.113**	**0.026**
Verbal memory	**–0.183**	**0.000**	–0.001	0.986	–0.084	0.101
Visual memory	–0.069	0.177	–0.050	0.327	–0.077	0.133
Processing speed	–0.046	0.368	0.073	0.152	0.062	0.229
Cognitive functioning	–0.042	0.417	–0.003	0.953	**–0.177**	**0.001**
Psychomotor speed	**–0.112**	**0.028**	0.047	0.358	**–0.154**	**0.003**
Reaction time	–0.005	0.921	**0.123**	**0.016**	–0.066	0.195
Complex attention	–0.066	0.198	–0.015	0.769	**–0.171**	**0.001**
Cognitive flexibility	–0.034	0.505	0.005	0.916	**–0.172**	**0.001**

* Correlation coefficient; ** significance level; *** neurocognition index.

psychomotor speed. The higher the levels of antibodies in the examined women, on average, the lower the results for the 3 mentioned functions.

The level of Tg-AB was positively correlated only with the results for reaction time in the examined group. This means that the higher the level of Tg-AB in the examined women, on average, the better the results for reaction time.

However, the levels of antibodies of TSH receptor were negatively correlated with NCI results, memory, executive functions, psychomotor speed, complex attention, and cognitive flexibility. On average, the higher the levels of AB-TSHR in the examined women, the lower the NCI results and the above-mentioned cognitive functions (Table 7).

Discussion

The aim of this study was to examine the relation between different parameters of thyroid functioning and cognitive functions in women after menopause without clinical symptoms of thyroid diseases. Not only TSH and thyroid hormones were considered (FT3, FT4, TT3, and FT4), but also anti-thyroid antibodies (TPO-AB, Tg-AB, and AB-TSHR).

None of the examined women were diagnosed with a thyroid disease or were on thyroid hormones in the past. This is important, as in the obtained results the maximum levels of TPO and Tg-AB amounted to 600 and 800 IU/1, respectively. The maximum levels of THS in the examined group were 7.38 uIU/ml and were higher than the average (maximum from 4.27 to 5.0 depending on the test). They were qualified for the examined group because the accepted level of TSH after 60 cannot be higher than 10.

In the examined group of women after menopause, the level of TSH was negatively correlated with NCI results, executive functions, complex attention, and cognitive flexibility. In the study, the level of FT4 was non-linearly correlated with NCI and other analyzed cognitive functions in the examined women. However, the level of FT4 was positively correlated with results for psychomotor speed.

There was also a significant negative correlation between the level of TT3 and the results for memory and verbal memory. Levels of TT4 were negatively correlated with results of memory and verbal memory, NCI, executive functions, and cognitive flexibility.

In the studies of the Italian authors carried out on a group of 337 seniors without clinical dysfunctions of thyroid gland examined in respect to cognitive functions with Mini Mental State Examination (MMSE) tests, Prose Memory Test (PMT) and Matrix Test (MT), it has been demonstrated that tests results were significantly lower among people with subclinical hypothyreosis as compared with people that had clinical euthyreosis. There has been also a negative dependence between TSH and MMSE, PMT, and MT results, which confirms the results of this study. However, there was no correlation between the levels of FT4 and FT3 and MMSE, PMT, and MT tests results [22]. These results cannot be referred to this particular study because an average age of the examined women was 74.3, i.e., about 20 years more than in this material.

In the research carried out on a group of 122 healthy women, with average age of 51, higher concentration of FT3 correlated positively with longer time of Trail Making Test performance

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(test of linking the points) - Part A (p=0.006), Part B (p=0.032) and Tower of London test (ToL) (p=0.002). There were no correlations observed between the levels of thyroid hormones and the mood, verbal memory, and working memory. The authors suggest that possible influence of thyroid hormones on cognitive functions takes place in the middle of frontal cortex and areas connected with executive functions [23].

On the basis of data obtained from Healthy Aging in Neighborhoods of Diversity Across the Life Span (HANDLS) Study, the cognitive functions were assessed using 13 tests of cognitive functions, including such domain as learning, memory, verbal memory, attention, visual memory, psychomotor speed, executive functions, and others. It was stated that the increased concentration of FT4 correlated with better results of women in tests of spacial perception in the whole examined group, and also in a sub-group of women. Higher concentration of FT4 correlated positively with abilities of assimilation and memory in a sub-group of women. Higher concentrations of TT4 correlated with better results within a range of psychomotor speed (people without intensified symptoms of depression); however, higher concentration of FT4 and TT4 correlated with better results in verbal tests in a group of men. Higher levels of T3 correlated with better results of spacial perception and psychomotor speed in white people. Concentrations of TSH below reference values correlated with better results in tests of psychomotor speed and concentration [24]. Results of this study confirm the results obtained in self-study in a group of women where TSH values correlated negatively with the results of executive functions, cognitive flexibility, complex attention; however, the level of FT4 was positively correlated with the results of psychomotor speed.

In studies of Prinz et al., carried out on healthy, older men, concentrations of TT4 in a range of correct values correlated positively with general efficiency of cognitive functions, but the levels of TT3 were not connected with any results of cognitive functions [25]. In this study opposite results were obtained; the level of TT4 correlated negatively with the results for cognitive functions, suggesting that biologically active hormones cause positive effects on cognitive functions, where higher values of total hormones can confirm higher amount connected with transport proteins, and lower amount of free, active forms. The conclusion is that they should be strongly considered in the evaluation examinations of the transport proteins level.

Similar results to the results of this study were obtained by Gunnarsson et al., in which lowering of memory was negatively correlated with the concentration of T3 and T4 in serum. In those studies significant improvement of memory during treatment of thyroid hormones deficiency was observed [26].

The above-mentioned results were confirmed by studies of van Boxtel et al. carried out in a group of 120, age 49-71 years. They indicated negative correlation between level of TSH and memory. As the level of TSH was higher in the examined people, the memory was weaker. The obtained results were independent of age [27].

In this study among women after menopause, there was also analysis of the relationship between anti-thyroid antibodies levels and the dysfunction of cognitive processing. On the one hand it is significant, because as the literature states, above age of 60, there is a higher sensibility for autoimmune diseases [28], including autoimmunological thyroid diseases, which in reality are the main reason for its hypo-functioning. On the other hand, menopause can modify clinical expression of some thyroid diseases, particularly autoimmunological [29]. The autoimmunological occurrences in the thyroid cannot be excluded, regardless of their impact on thyroid functioning since they can play a role in discrimination of cognitive state observed in older people with sub-clinical hypothyreosis [30].

In our study there were significant negative correlations between levels of TPO-AB and results of memory, verbal memory, and psychomotor speed. Levels of Tg-AB correlated positively with results of reaction time. The level of antibodies of TSH receptor correlated negatively with results of NCI, memory, executive functions, psychomotor speed, complex attention, and cognitive flexibility.

In the research of Grigorov et al. mentioned earlier, there was similar evaluation of the impact of anti-thyroid antibodies level on cognitive functions. They concluded that higher concentrations of anti-thyroglobulin antibodies correlated positively with greater errors in Trail Making Test Part B in the Word Fluency test and in Design Fluency test [23].

Many other studies confirm the negative impact on the results of cognitive functions of high antibodies of thyroglobulin peroxidase [31,32], which would confirm the result obtained by our research stating that the positive impact on reaction time results with high thyroglobulin antibodies. Despite the information presented above, Regal states that after correcting the data for multiple comparisons in variance analysis, there was no correlation between denominations of thyroglobulin antibodies and thyroglobulin peroxidase antibodies in analyzed cognitive test [33].

Conclusions

Our studies confirm the significance of the state of activity of the thyroid gland for cognitive functioning in a group of women after menopause. As the values of TSH, TT3, TT4, TPO-AB, and AB-TSHR were higher and FT4 was lower, then the results were worse in examination of cognitive functions measured with a battery of CNS-VS tests.

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