Neuroscience Letters 574 (2014) 26–30

Contents lists available at ScienceDirect

Neuroscience Letters

journal homepage: www.elsevier.com/locate/neulet

Impairment of attention networks in patients with untreated hyperthyroidism

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HIGHLIGHTS

- Attention networks in untreated hyperthyroid patients were explored using ANT task.
- Hyperthyroid patients had deficits in the alerting and executive control networks.
- Value of executive network was positively correlated with the T4 level in patients.
- These deficits may be involved in extensive brain and neurotransmitters disorders.

ARTICLE INFO

Article history:
Received 23 January 2014
Received in revised form 29 April 2014
Accepted 8 May 2014
Available online 20 May 2014

Keywords:
Hyperthyroidism
Thyroid hormones
Cognition
Attention Network Test

ABSTRACT

Attention disorders are common symptoms in patients with untreated hyperthyroidism. Nevertheless, it is unknown whether they represent a global attention deficit or selective impairment of attention networks. Thirty-seven patients with hyperthyroidism were recruited and underwent the Attention Network Test (ANT), which provided measures of three independent attention networks (alerting, orienting and executive control), before being treated with methimazole. This study demonstrated that patients with untreated hyperthyroidism had significant deficits in the alerting and executive control networks. Interestingly, a significant positive association was also found between T4 level and the value of the executive network in patients with hyperthyroidism. These results suggest that the patients with hyperthyroidism may not just exist a specific impairment of attention networks, and there was some relationship between the level of T4, not T3 or TSH, and the value of the executive control network in patients with hyperthyroidism.

1. Introduction

Hyperthyroidism is a common endocrine disease. Most evidence indicates that patients with hyperthyroidism have affective symptoms [1–4]. However, studies regarding effects of hyperthyroidism on cognition are variable [4,5]. Some studies have provided evidence that hyperthyroidism is associated with cognitive dysfunction, on the basis that patients demonstrated abnormal cerebral metabolism [6] and changes in brain size [7].

Hyperthyroidism is typically characterized by a decreased serum thyroid-stimulating hormone (TSH) level in association with increased serum levels of thyroid hormone (TH) including triiodothyronine (T3) and thyroxine (T4). As an indicator of thyroid function, TH and TSH also play a key role in adult brain function [8–11]. Abnormal TH and TSH levels are even thought to be a risk factor for dementia [10,12,13]. Previous studies have demonstrated that excessive thyroxine can induce oxidative stress and damage neurons [13]. Claustre et al. [14] showed that hyperthyroidism altered the amount of central catecholamine including norepinephrine and dopamine by influencing the concentration of tyrosine hydroxylase that is the rate-limiting enzyme in the synthetic pathway of catecholamine, and these neurotransmitters could lead to cognitive dysfunction.

Attention is an important cognitive function. Posner and Petersen [15] have proposed the Attention Network Theory in which the attention systems can be subdivided into three distinct brain networks, namely, an alerting network, an orienting network and an executive network. The alerting network is defined as achieving and maintaining a state of high sensitivity to incoming

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http://dx.doi.org/10.1016/j.neulet.2014.05.016
0304-3940/

stimuli. The orienting network is the process of selecting information from sensory input by shifting the attentional focus from one area or object to another in the visual field. The executive network concerns resolution of response conflicts between competing information. These three networks are related to specific anatomies and neurotransmitters. The right hemisphere systems and norepinephrine are involved in the alerting system, while posterior areas and the cholinergic system play a critical role in the orienting network. The anterior cingulate cortex and frontal cortical regions are implicated in the executive network which is modulated by dopamine.

These evidences have indicated impairments of attention in patients with hyperthyroidism [3,6,16]. However, the underlying mechanism by which hyperthyroidism is harmful to attentional function is unclear. Alvarez et al. [16] considered that increased metabolism resulting from hyperthyroidism might generate an increase in the synthesis and degradation of neurotransmitters that regulate attentional processes. The Attentional Network Test (ANT) developed by Fan et al. [17] provides measures of the three different attention components in a single task. This test is useful to explore whether the patients with hyperthyroidism have generalized attention deficits or a selective attentional network disorder.

In this study, adults with newly diagnosed hyperthyroidism, who were not yet being treated with anti-thyroid drugs, were asked to perform the ANT. The purpose of this study was to determine whether the attention networks are widely impaired in patients with hyperthyroidism.

2. Methods

2.1. Participants

Thirty-seven patients with hyperthyroidism (21 women and 16 men, age range: 19–46 years) took part in the current study. Their educational background ranged from 5 to 17 years. Inclusion criteria were as follows: (1) All patients had abnormally high serum T3 (>2.79 nmol/L) and T4 (>140.60 nmol/L) level and abnormally low TSH (<0.550 μIU/mL). (2) All patients' age ranged from 18 to 50 years. (3) All patients had a new diagnosis of hyperthyroidism and had not been treated with anti-thyroid drugs. (4) All patients had an MMSE score > 24. Exclusion criteria were as follows: addiction to psychoactive substances, other severe neurological and/or psychiatric illness, and head injury were revealed in anamnesis. Forty-two healthy subjects (21 women and 21 men, ages range: 19–49 years) with normal serum T3, T4, and TSH levels, matched to the patients with hyperthyroidism for age, sex and education level, were recruited. None of the controls had current or a history of neurologic or psychiatric disorder or endocrine disease. For both the hyperthyroid group and healthy subjects, basic requirements of the study required that all participants were right-handed, had the ability to understand the study procedures, and had normal or corrected-to-normal vision. Following an explanation of the study objective, all the subjects provided written informed consent. This study was approved by the ethics committee of Anhui Medical University.

2.2. Serum measurements

For each participant, serum hormone levels – T4, T3 and TSH – were measured using a chemiluminescence immunoassay performed at the Endocrinology Laboratory of the First Affiliated Hospital, Anhui Medical University. For T4, the normal range was 58.10–140.60 nmol/L; for T3, the normal range was 0.92–2.79 nmol/L; and for TSH, the normal range was 0.550–4.780 μIU/mL.

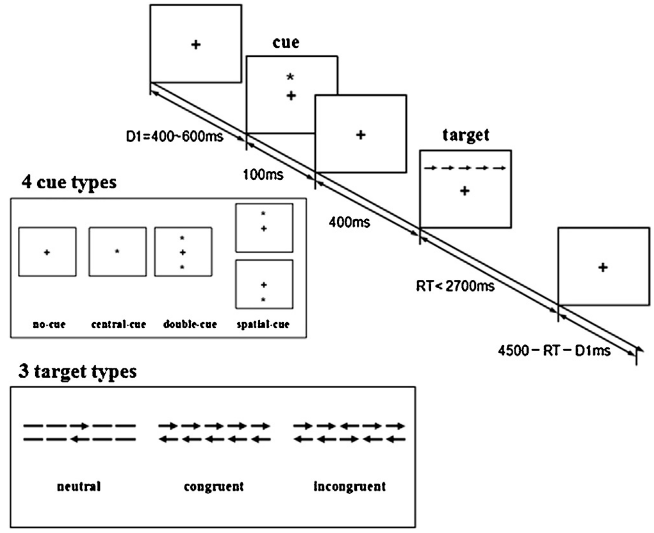

Fig. 1. Experimental paradigm of the ANT.

2.3. Neuropsychological background tests

The Mini-Mental State Examination (MMSE) was administered to each subject to assess global cognitive functions. The digit span test (forward and backward) was employed to quantify attention and short-term memory.

2.4. Attention Network Test

The ANT task [17] is usually used to investigate three different attention networks. The participants were required to gaze at a central cross shown on a computer screen throughout the task. The target item was presented at the center of the field and flanked by stimuli from three possible conditions: neutral condition, congruent condition and incongruent condition. Participants' task was to indicate the direction of the target arrow and to respond as quickly and accurately as possible by pressing one button for the left direction or another button for the right direction. The first fixation duration was varied randomly (400–1600 ms). The second fixation, with or without a warning cue, lasted for 100 ms. Following a third fixation period (400 ms), the target and flankers appeared simultaneously until the subject responded via pressing a button. The duration for the target display only remained for a maximum of 2700 ms. The duration of the post-target fixation period was based on the duration of the first fixation and the RT. The test had four cue conditions: no-cue, central-cue, double-cue, and spatial-cue (Fig. 1).

The ANT task consisted of a 24-trial practice set, where the subject received feedback regarding whether the response was accurate or inaccurate, and three experimental sets with no feedback. Each experimental set consisted of 96 trials (48 conditions: 4 cue types × 2 target locations × 2 target directions × 3 flanker conditions, with two repetitions). The order of the trials was randomized for all subjects.

2.5. Calculation of attention network efficiencies

The efficiencies of the alerting, orienting, and executive control networks were measured according to the differences in RTs under the different testing conditions. The mean RT was computed for each condition and there were 12 conditions in total: 4 cue types by 3 target types. The efficiency of the alerting network was calculated using the mean RTs of the no-cue condition minus the mean RTs of the double-cue condition averaging across three target types.

Table 1
Demographic, clinical, and neuropsychological characteristics of the patients with hyperthyroidism and healthy subjects.

Characteristic	Patients with hyperthyroidism	Healthy subjects
n	37	42
Age (years)	30.65 ± 8.80	30.88 ± 8.61
Sex (male/female)	16/21	21/21
Education (years)	11.22 ± 3.62	11.90 ± 3.12
T3	7.12 ± 3.92*	1.88 ± 0.46
T4	271.06 ± 93.06*	97.94 ± 23.06
TSH	0.02 ± 0.04*	2.18 ± 0.73
MMSE	28.22 ± 1.00	28.26 ± 1.29
Digit span test (forward)	7.24 ± 1.09	7.33 ± 0.87
Digit span test (backward)	5.16 ± 1.28	5.64 ± 1.16

* $p < 0.01$.

The orienting efficiency was calculated using the mean RTs of the center-cue condition minus the mean RTs of the spatial-cue condition. The efficiency of the executive control network was calculated by subtracting the mean RTs of the congruent target condition from the mean RTs of the incongruent target condition averaging across four cue types.

2.6. Data analyses

The Statistical Product and Service Solutions (SPSS, version 13.0) (SPSS Inc., Chicago, IL, USA) was used for the analysis of data. A 2 (group: patients with hyperthyroidism, health subjects) × 4 (cue type: no-cue, central-cue, double-cue, and spatial-cue) × 3 (target type: neutral, congruent, and incongruent) mixed factors ANOVA on RT was carried out. The statistical significance of the differences (with the exception of sex) between the patients with hyperthyroidism and healthy controls was compared using an independent sample *t*-test. The statistical significance of the differences in sex was detected using a Chi-square test. Correlation analysis between the values of three networks and thyroid hormone and TSH were examined using Pearson's correlation analysis. For all tests, the level of significance was defined as $p < 0.05$.

3. Results

3.1. Demographic data, clinical information, and neuropsychological findings

The means and standard deviations of the demographic characteristics and clinical of patients with hyperthyroidism and healthy subjects are summarized in Table 1. No significant differences in age, sex, educational level, MMSE and digit span test score was found between the two groups (Table 1). There were significant differences between the two groups in terms of T3 [$t(77) = 8.089$, $p < 0.01$], T4 [$t(77) = 11.021$, $p < 0.01$], and TSH [$t(77) = -19.106$, $p < 0.01$]. None of the patients with hyperthyroidism had severe deficits in cognitive function as measured by the neuropsychological background tests.

Table 3
Attention network reaction time (RT) and accuracy (%) of patients with hyperthyroidism and healthy subjects.

	Patients with hyperthyroidism ($n = 37$)	Healthy subjects ($n = 42$)
Alerting RT (ms)	20.62 ± 22.41*	35.14 ± 16.71
Orienting RT (ms)	37.73 ± 23.92	45.83 ± 26.76
Executive conflict RT (ms)	115.68 ± 40.81*	93.29 ± 28.43
Overall mean RT (ms)	649.35 ± 88.64	663.36 ± 95.27
Accuracy (%)	98.62 ± 1.30	98.43 ± 1.17

* $p < 0.01$.

3.2. Efficiencies of the three networks

The mean RTs under each condition of the two groups are summarized in Table 2. The main effect of group was not significant [$F(1, 77) = 0.387$, $p = 0.536$]. The main effect of cue types and target types were significant [$F(3, 231) = 229.097$, $F(2, 154) = 772.630$, respectively; $p < 0.01$]. There were significant interactions between group and target types [$F(2, 154) = 3.120$, $p < 0.01$], and cue types and target types [$F(6, 462) = 19.467$, $p < 0.01$]. No significant interactions were found between group and cue types [$F(3, 231) = 8.494$, $p = 0.031$]. The three-way interaction between group, cue types and target types was also not significant [$F(6, 462) = 1.444$, $p = 0.210$]. The efficiencies of the alerting, orienting, and executive control networks were calculated according to the differences in RTs under the different conditions. The value of the alerting network in the patients with hyperthyroidism was significantly lower than that of the healthy subjects [$t(77) = -3.289$, $p < 0.01$]. The mean RTs difference in the incongruent condition and congruent condition averaging across 4 cue types, which provides a measure of the executive control network, was significantly longer in the patients with hyperthyroidism relative to the healthy subjects [$t(77) = 2.856$, $p < 0.01$]. No significant difference was found between the two groups for the efficiency of orienting network [$t(77) = -1.411$, $p = 0.162$]. In addition, there were no significant differences in the overall mean RT [$t(77) = -0.674$, $p = 0.503$] or global accuracy [$t(77) = -0.695$, $p = 0.489$] between the two groups (Table 3).

3.3. Correlations

The relationships between the scores for the three networks and T3, T4, and TSH were examined. A positive correlation was found between T4 level and the value of the executive control network in patients with hyperthyroidism ($r = 0.402$, $p = 0.014$) (Fig. 2), whereas T3 and TSH levels were not correlated with the value of the executive control network ($r = 0.260$, $r = -0.209$, respectively; $p = 0.120$, $p = 0.215$, respectively). There was also no evidence that T3, T4 and TSH levels were correlated with the values of the alerting ($r = 0.115$, $r = 0.112$, $r = 0.203$, respectively; $p = 0.498$, $p = 0.511$, $p = 0.229$, respectively) and orienting ($r = -0.210$, $r = -0.281$, $r = 0.089$, respectively; $p = 0.213$, $p = 0.092$, $p = 0.599$, respectively) networks in patients with hyperthyroidism. For healthy subjects, there were no significant

Table 2
Mean reaction time (RT) under each condition in patients with hyperthyroidism and healthy subjects.

Group	Target type	Cue type			
		Center	Double	None	Spatial
Mean RTs (ms) and standard deviations					
Patients with hyperthyroidism	Congruent	643.35 ± 98.15	634.38 ± 95.66	662.59 ± 97.54	608.43 ± 93.70
	Incongruent	771.76 ± 91.83	761.90 ± 99.47	770.65 ± 92.07	710.32 ± 112.53
	Neutral	556.65 ± 78.56	562.35 ± 90.69	592.70 ± 90.00	538.49 ± 88.42
Health subjects	Congruent	654.50 ± 105.18	648.43 ± 104.01	685.02 ± 100.49	614.31 ± 101.80
	Incongruent	762.40 ± 103.94	749.14 ± 103.62	765.90 ± 102.68	698.36 ± 111.16
	Neutral	594.19 ± 86.42	587.55 ± 86.68	644.19 ± 87.77	564.98 ± 89.55

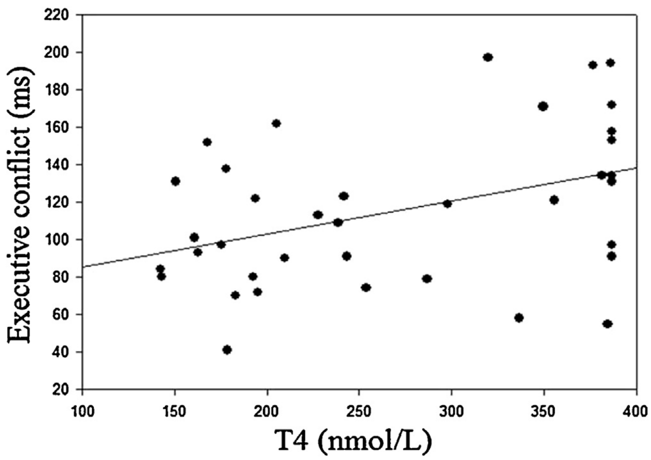

Fig. 2. Association between thyroxine (T4) levels and the value of executive control network in patients with hyperthyroidism.

correlations between T3, T4, and TSH levels and the values of the alerting ($r = 0.234$, $r = 0.199$, $r = -0.288$, respectively; $p = 0.136$, $p = 0.207$, $p = 0.065$, respectively) and orienting ($r = 0.024$, $r = 0.087$, $r = -0.110$, respectively; $p = 0.882$, $p = 0.582$, $p = 0.487$, respectively) and executive control ($r = -0.269$, $r = -0.286$, $r = 0.288$, respectively; $p = 0.085$, $p = 0.066$, $p = 0.064$, respectively) networks. No correlations were demonstrated between T3, T4, and TSH levels and the values of the alerting ($r = -0.174$, $r = -0.177$, $r = 0.214$, respectively; $p = 0.125$, $p = 0.118$, $p = 0.058$, respectively) and orienting ($r = -0.221$, $r = -0.217$, $r = 0.152$, respectively; $p = 0.051$, $p = 0.055$, $p = 0.180$, respectively) and executive control ($r = 0.220$, $r = 0.217$, $r = -0.218$, respectively; $p = 0.052$, $p = 0.055$, $p = 0.053$, respectively) networks in the complete sample.

4. Discussion

4.1. Summary of findings

The current study demonstrated that the patients with hyperthyroidism had abnormalities in the alerting and executive control networks, although they had normal performance in the mean RTs under each condition, overall mean RT and global accuracy. The difference in value of orienting network between the two groups was not significantly different. A positive correlation between the level of T4, not T3 or TSH, and the value of the executive control network in patients with hyperthyroidism was also found.

4.2. Three networks of attention

The patients with hyperthyroidism had significantly lower efficiency in the alerting network than healthy subjects. Fukui et al. [18] demonstrated that a patient with hyperthyroidism had deficits in vigilance. The alerting system is related to right hemisphere systems and norepinephrine. Schreckenberger et al. [3] found significantly reduced metabolism in the right-hemispheric limbic system of patients with hyperthyroidism using a brain fluorodeoxyglucose positron emission tomography (PET). From previous literature, level of norepinephrine decreased in hyperthyroidism [19,20].

The patients with hyperthyroidism have a significantly deficit in the executive control network when resolving conflicts. This conclusion is consistent with early study that patients with hyperthyroidism had executive function impairments using the Wisconsin card sorting tests [21]. Previous study suggested that executive control activity is localized to the midline frontal cortex and anterior cingulate cortex, and executive control network is modulated by dopamine [22]. Using magnetic resonance spectroscopy (MRS), patients with hyperthyroidism have been shown to have abnormal cerebral metabolism in midfrontal regions [6,23]. Rastogi and Singhal [11] found the levels of dopamine in hyperthyroid rat brain, are altered by the excess thyroid hormone.

Our study demonstrated that the differences between two groups for the value of orienting network were not statistically significant, although a case report indicated that the elderly patient with hyperthyroidism suffered from orientation impairment [18]. The reason in causing the inconsistent result might be that the patients we recruited in the study were younger than that of the earlier research.

The earlier study has found attention impairment in the patients with hyperthyroidism [16,18]. In the present study, the patients with hyperthyroidism had normal performance in the overall mean RT and global accuracy comparing with healthy subjects. It is supposed that the patients entering our study have a new diagnosis of hyperthyroidism and short disease duration.

4.3. Associations between attention networks and TH or TSH

From the previous literature, it is controversial whether there was an association between TH or TSH and the cognitive impairment. Our study found a positive correlation between level of T4 and the value of the executive control network in patients with hyperthyroidism, but not in the healthy subjects or in the complete sample. This is similar to results from Prinz et al. [24] who reported associations between T4, but not TSH, and both verbal and global cognitive functioning. De Jong et al. [25] also reported that higher T4 levels, but not TSH, were associated with an increased risk of dementia. However, Wahlin et al. [26] found an association between TSH, but not T4, and episodic memory and Livner et al. [10] found that TSH levels were related to prospective memory function, while T4 levels were unrelated to their deficits. In our study, it is likely that excessive T4 could induce executive network disorders by regulating the metabolism of the midfrontal brain areas and dopamine. Particularly worth mentioning is that T4 levels need to exceed the normal range before they effectively affect the value of executive control network.

5. Conclusions

To our knowledge, this is the first study to examine the attention networks of adults with hyperthyroidism using the ANT task. In view of the current results, it is clear that the patients with hyperthyroidism may not just have a specific impairment of attention networks. Further investigation is needed to explore whether attention deficits reverse when patients reach a euthyroid state after antithyroid treatment.

Conflict of interest

The authors declared no conflict of interest.

Acknowledgements

This work was supported by grants from the National Natural Science Foundation of China (Grants no. 81100806, no. 91232717), National Basic Research Program of China (Grant no. 2011CB707805). We also thank the doctors and research staff involved in our study.

References

[1] D.J. MacCrimmon, J.E. Wallace, W.M. Goldberg, D.L. Streiner, Emotional disturbance and cognitive deficits in hyperthyroidism, Psychosom. Med. 41 (1979) 331–340.
[2] M.M. Demet, B. Ozmen, A. Deveci, S. Boyvada, H. Adiguzel, O. Aydemir, Depression and anxiety in hyperthyroidism, Arch. Med. Res. 33 (2002) 552–556.
[3] M.F. Schreckenberger, U.T. Egle, S. Drecker, H.G. Buchholz, M.M. Weber, P. Bartenstein, Positron emission tomography reveals correlations between brain metabolism and mood changes in hyperthyroidism, J. Clin. Endocrinol. Metab. 91 (2006) 4786–4791.
[4] A. Vogel, T.V. Elberling, M. Hording, J. Dock, A.K. Rasmussen, U. Feldt-Rasmussen, Affective symptoms and cognitive functions in the acute phase of Graves' thyrotoxicosis, Psychoneuroendocrinology 32 (2007) 36–43.
[5] D.F. Zhu, Z.X. Wang, D.R. Zhang, Z.L. Pan, S. He, X.P. Hu, fMRI revealed neural substrate for reversible working memory dysfunction in subclinical hypothyroidism, Brain 129 (2006) 2923–2930.
[6] T.V. Elberling, E.R. Danielsen, A.K. Rasmussen, U. Feldt-Rasmussen, G. Waldemar, C. Thomsen, Reduced myo-inositol and total choline measured with cerebral MRS in acute thyrotoxic Graves' disease, Neurology 60 (2003) 142–145.
[7] A. Oatridge, M.L. Barnard, B.K. Puri, S.D. Taylor-Robinson, J.V. Hajnal, N. Saeed, Changes in brain size with treatment in patients with hyper- or hypothyroidism, AJNR Am. J. Neuroradiol. 23 (2002) 1539–1544.
[8] L.A. Desouza, U. Ladiwala, S.M. Daniel, S. Agashe, R.A. Vaidya, V.A. Vaidya, Thyroid hormone regulates hippocampal neurogenesis in the adult rat brain, Mol. Cell Neurosci. 29 (2005) 414–426.
[9] A. Wahlin, D. Bunce, T.B. Wahlin, Longitudinal evidence of the impact of normal thyroid stimulating hormone variations on cognitive functioning in very old age, Psychoneuroendocrinology 30 (2005) 625–637.
[10] A. Livner, A. Wahlin, L. Backman, Thyroid stimulating hormone and prospective memory functioning in old age, Psychoneuroendocrinology 34 (2009) 1554–1559.
[11] R.B. Rastogi, R.L. Singhal, Influence of neonatal and adult hyperthyroidism on behavior and biosynthetic capacity for norepinephrine, dopamine and 5-hydroxytryptamine in rat brain, J. Pharmacol. Exp. Ther. 198 (1976) 609–618.
[12] M.P. van Boxtel, P.P. Menheere, O. Bekers, E. Hogervorst, J. Jolles, Thyroid function, depressed mood, and cognitive performance in older individuals: the Maastricht Aging Study, Psychoneuroendocrinology 29 (2004) 891–898.
[13] E. Hogervorst, F. Huppert, F.E. Matthews, C. Brayne, Thyroid function and cognitive decline in the MRC Cognitive Function and Ageing Study, Psychoneuroendocrinology 33 (2008) 1013–1022.
[14] J. Claustre, C. Balende, J.F. Pujol, Influence of the thyroid hormone status on tyrosine hydroxylase in central and peripheral catecholaminergic structures, Neurochem. Int. 28 (1996) 277–281.
[15] M.I. Posner, S.E. Petersen, The attention system of the human brain, Annu. Rev. Neurosci. 13 (1990) 25–42.
[16] M.A. Alvarez, A. Gomez, E. Alavez, D. Navarro, Attention disturbance in Graves' disease, Psychoneuroendocrinology 8 (1983) 451–454.
[17] J. Fan, B.D. McCandliss, T. Sommer, A. Raz, M.I. Posner, Testing the efficiency and independence of attentional networks, J. Cogn. Neurosci. 14 (2002) 340–347.
[18] T. Fukui, Y. Hasegawa, H. Takenaka, Hyperthyroid dementia: clinicoradiological findings and response to treatment, J. Neurol. Sci. 184 (2001) 81–88.
[19] T. Mano, H. Sakamoto, K. Fujita, M. Makino, H. Kakizawa, M. Nagata, Effects of thyroid hormone on catecholamine and its metabolite concentrations in rat cardiac muscle and cerebral cortex, Thyroid 8 (1998) 353–358.
[20] A.C. Swann, Thyroid hormone and norepinephrine: effects on alpha-2, beta, and reuptake sites in cerebral cortex and heart, J. Neural Transm. 71 (1988) 195–205.
[21] K. Jablkowska, M. Karbownik-Lewinska, K. Nowakowska, R. Junik, A. Lewinski, A. Borkowska, Working memory and executive functions in hyperthyroid patients with Graves' disease, Psychiatr. Pol. 42 (2008) 249–259.
[22] M.S. Lidow, F. Wang, Y. Cao, P.S. Goldman-Rakic, Layer V neurons bear the majority of mRNAs encoding the five distinct dopamine receptor subtypes in the primate prefrontal cortex, Synapse 28 (1998) 10–20.
[23] V.S. Bhatara, R.P. Tripathi, R. Sankar, A. Gupta, S. Khushu, Frontal lobe proton magnetic-resonance spectroscopy in Graves' disease: a pilot study, Psychoneuroendocrinology 23 (1998) 605–612.
[24] P.N. Prinz, J.M. Scanlan, P.P. Vitaliano, K.E. Moe, S. Borson, B. Toivola, Thyroid hormones: positive relationships with cognition in healthy, euthyroid older men, J. Gerontol. A: Biol. Sci. Med. Sci. 54 (1999) 111–116.
[25] F.J. de Jong, K. Masaki, H. Chen, A.T. Remaley, M.M. Breteler, H. Petrovitch, Thyroid function, the risk of dementia and neuropathologic changes: the Honolulu-Asia aging study, Neurobiol. Aging 30 (2009) 600–606.
[26] A. Wahlin, T.B. Wahlin, B.J. Small, L. Backman, Influences of thyroid stimulating hormone on cognitive functioning in very old age, J. Gerontol. B: Psychol. Sci. Soc. Sci. 53 (1998) 234–239.