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.

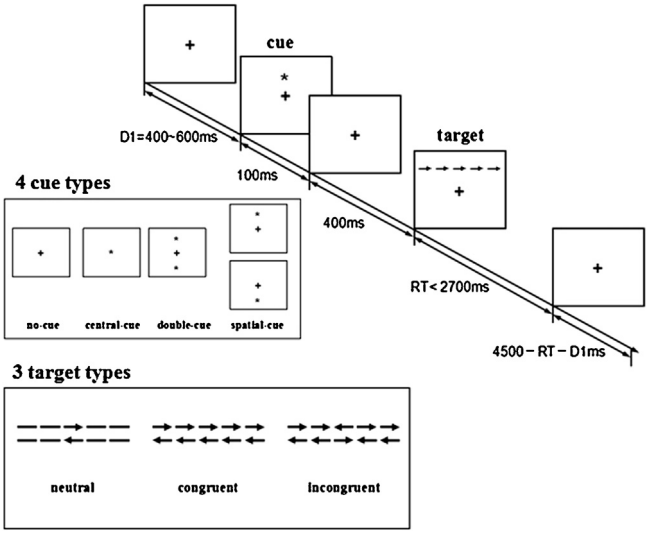

Fig. 1. Experimental paradigm of the ANT.

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.