Neuroscience Letters 661 (2017) 1–4

Contents lists available at ScienceDirect

Neuroscience Letters

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

Research article

Impaired decision making under risky conditions in the acute phase of Graves' thyroitoxicosis

Fang Dai[b,1], Lili Yuan[a,1], Juan Fang[c], Qiu Zhang[b,*], Kai Wang[c,*]

[a] Department of Neurology, The First Affiliated Hospital of Wannan Medical College, Wuhu, Anhui Province, PR China
[b] Department of Endocrinology, The First Hospital of Anhui Medical University, Hefei, Anhui Province, PR China
[c] Department of Neurology, The First Hospital of Anhui Medical University, Hefei, Anhui Province, PR China

ARTICLE INFO

Keywords:
Graves' disease
Hyperthyroidism
Thyroid hormones
Decision making
Game of Dice Task

ABSTRACT

The patients with Graves' thyroitoxicosis often complain that they have neuropsychiatric symptoms and impaired cognitive function. Decision making is important and complex process involving the interaction and integration of a series of cognitive components. In the 31 newly diagnosed patients with Graves' thyroitoxicosis and 30 healthy controls, we used the Hamilton Anxiety Rating Scale (HAMD), Hamilton Depression Rating Scale (HAMD) and The Game of Dice Task (GDT) to assess the emotion and decision making under risky conditions. The patients with Graves' disease had higher score on HAMA and HAMD, and had poorer performance in GDT than healthy controls. A negative correlation was found between utilization of negative feedback and score of HAMA in the patients with Graves' disease. Our findings in Graves' disease might be association with the extensive brain disorders including prefrontal cortex and the limbic system, and dopamine dysfunction.

1. Introduction

Graves' disease is an autoimmune thyroid disease caused by thyroid stimulating hormone receptor antibodies (TRAb), which stimulates the thyroid to synthesize and secrete the excess thyroid hormone, and it reportedly is the most common cause of hyperthyroidism [1]. Laboratory tests reveal positive TRAb, increased serum level of thyroid hormone (TH) and decreased level of serum TSH among the patients with Graves' disease. Clinical presentation of Graves' disease often includes heat intolerance, sweating, exophthalmos, weight loss, tremor, irritable and impulsive. The signs and symptoms depend on the duration of disease, magnitude of hormone excess and the age of the patients [2].

In the acute phase of Graves' disease, patients often complain that they have neuropsychiatric symptoms, including anxiety, depression, a loss in attention and memory, and difficult to solve the complex problem [3–8]. Some studies investigating affective symptoms in patients with Grave' disease have shown that their scores of anxiety and depression were higher than the general population using self-rating scales and other-rating scales, including Zung Self-Rating Anxiety Scale (Z-SAS), Hamilton Anxiety Rating Scale (HAMD), Hamilton Depression Rating Scale (HAMD), Hospital Anxiety and Depression Scale (HAD) and so on [9]. Engum and his colleagues claimed no statistical association between hyperthyroidism and the presence of depression or anxiety disorder by the research of a large, unselected population [10].

Since 1835, clinical neurologists acknowledged that the patients with Graves' disease might have the impairments of psychiatric and cognitive function. The large-scale survey of the patients with Grave' disease had found many of them experience anxiety, dysphoria, irritability, fatigue, hopelessness and anger. They showed the poor executive function and had difficult to control their inappropriate behavior and negative emotion [11–13]. Accumulating lines of evidence have demonstrated impairments of attention, memory, executive function, planning, controlling, and learning ability in the patients with Grave' disease. Graves' thyroitoxicosis leads to a metabolic imbalance through excessive thyroid hormones secretion. The high levels of thyroid hormones are related to oxidative stress and necrotic death of neurons. Early studies have found that the patients with excessive thyroid hormones appear the changes of cerebral metabolism and neurotransmitter systems using neuroimaging and neurochemistry techniques [14–19].

Decision making is important and complex process involving the interaction and integration of many cognitive components. Compulsive control disorders are believed to affect the balance between an impulsive system and a reflective system, and impair the decision-making process. Decisions under ambiguity and risk conditions are the 2 different decision-making situations which differ in mainly their explicitness of probabilities for winning and losing [20,21]. In decision-making

* Corresponding authors.
E-mail addresses: aynfmk@163.com (Q. Zhang), wangkai1964@126.com (K. Wang).
[1] These two authors contributed equally to this work.

http://dx.doi.org/10.1016/j.neulet.2017.08.058
Received 23 March 2017; Received in revised form 27 July 2017; Accepted 26 August 2017
Available online 30 August 2017
0304-3940/

under ambiguity, the explicit knowledge about the consequences or the probabilities for gains and losses are not provided to decision maker. Whereas, in decision-making under risk, the probabilities for gains and losses are obvious, and decision maker can reason which is high-risk and which is low-risk from beginning [22]. According to the literature, these two types of decision-making might be related to specific cerebral regions. In general, decision-making under ambiguity strongly relies on ventromedial prefrontal cortex and anterior cingulate cortex, and decision-making under risk involves the dorsolateral prefrontal cortex, basal ganglia and amygdala [20,23–25]. Dopaminergic system plays a major role in decision-making [26,27]. Two different type of Decisions-making are dissociated in obsessive-compulsive disorder (OCD), narcolepsy-cataplexy (NC), Parkinson's disease (PD) and so on [28–30].

The Game of Dice Task (GDT) is usually used to assess decision-making under risk conditions. In previous study we have observed that patients with hyperthyroidism had the decision-making impairment under ambiguous condition, most of whom suffered from Graves' disease [31]. Do the patients with Graves' thyroitoxicosis also have impaired decision-making under risk? If the answer is yes, we speculate the patients with Graves' disease might have the global, not dissociated decision-making impairment and explore the possible mechanism of decision making characteristics. In our study, the patients with hyperthyroidism were asked to perform the GDT.

2. Methods

2.1. Subjects

The current study included 31 newly diagnosed patients with Graves' thyroitoxicosis, 18–50 years of old, from the First Affiliated Hospital of Anhui Medical University. Laboratory tests showed these patients had abnormally increased serum levels of T3 (> 2.79 nmol/L) and T4 (> 161.30 nmol/L) and abnormally decreased TSH (< 0.550 μIU/mL). Their educational background ranged from 5 to 16 years, and their scores of Mini-Mental State Examination (MMSE) score were greater than or equal to 26. The exclusion criteria included addiction to psychoactive substances, anxiety and depressive state (Hamilton Anxiety Scale, HAMA > 14, or Hamilton Depression Scale, HAMD > 17), neurologic or psychiatric disorders, and other endocrine disease.

We also recruited 30 healthy controls, 20–48 years of old, from the society. They had normal serum T3, T4, and TSH levels. Their age, gender and educational level were matched to the patients with Graves' thyroitoxicosis. Exclusion criteria of healthy controls were MMSE < 26, affective disorder (HAMA > 14, or HAMD > 17) serious physical disease or mental illness revealed in anamnesis. All subjects, including the patients and healthy controls, were right-handed, and had normal hearing, understanding communication skills and normal or corrected-to-normal vision.

All subjects were told the whole study procedures and some announcements. They had good compliance, and provided written informed consent. This study was approved by the ethics committee of Anhui Medical University.

2.1.1. Laboratory measurements

After venepuncture, blood was immediately sent to the Endocrinology Laboratory of the First Affiliated Hospital, Anhui Medical University and samples were assayed using chemiluminescence immunoassay. For the level of 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.

2.1.2. Neuropsychological background tests

For each participant, the Mini-Mental State Examination (MMSE) was a simple assessment instrument to measure global cognitive performance including orientation, memory, attention, calculation, verbal repetition, reading comprehension and visual spatial function. The HAMA and HAMD were to assess anxiety and depressive levels. The HAMA includes 14 items investigating both physical and psychological symptoms. In our study, the 17-item version of HAMD was used. All the neuropsychological background tests were performed by a trained physician within 24 h of the blood draw.

2.1.3. Decision making task: GDT

The computerized GDT is usually to measure decision making under risky conditions. Subjects sat in the front of a computer screen and watched the throwing virtual dice. All subjects were asked to do their best to win as much capital as possible with fictive starting capital of €1000 by 18 rounds. There were four different alternatives: a single number or a combination of two, three, or four numbers. Each choice was associted with explicit probabilities for gains and losses: €1000 gain/loss for choosing a single number (winning probability 1:6), €500 gain/loss for a combination of two numbers (winning probability 2:6), €200 gain/loss for a combination of three numbers (winning probability 3:6), €100 gain/loss for a combination of four numbers (winning probability 4:6). Before each throw, subjects were required to guess which number would appear and made a choice. Every choice would add or subtract corresponding amount on the basis of the starting capital, and residual captial was presented on the screen. For instance, if a subject chose the combination "three", "four" and "five", he would gain €200 when a "three", "four", or "five" was thrown; conversely, he would loss €200 when none of the chosen numbers was thrown. The gain or lose was indicated by distinct colors and acoustic signals. According to the winning probability, the choice of 1 or 2 numbers was classified as "high-risk" or advantageous choices (winning probability < 50%), and the choice of 3 or 4 numbers as "low-risk" disadvantageous choices (winning probability ≥ 50%). Among them, a single number is highest-risk option and a combination of 4 numbers is lowest-risk option.

We analyzed data as follows: (1) final capital (remained capital on the screen when the GDT ended); (2) frequency of choosing the 4 different options; (3) overall net score (the number of advantageous choices minus the number of disadvantageous choices) and risk score (the number of highest-risk choice minus the number of lowest-risk choice); (4) use of negative feedback (the frequency of shifting to choose an advantageous option when receiving the loss after choosing a disadvantageous option).

2.1.4. Statistical analysis

The statistical analyses were performed using Statistical Product and Service Solutions (SPSS, version 13.0) for Windows. All data were examined for normality with the Kolmogorov-smirnov statistic and for homogeneity of variance with the Levene test. Independent sample *t*-test was used to compare background data (with the exception of gender) and GDT data which were normally distributed between the patients with Grave's disease and healthy controls. Nonparametric statistics was used to analyze GDT data, which were not normally distributed. The statistical significance of the differences in gender was detected using a Chi-square test. Correlation analysis between the performance of GDT and clinical and neuropsychological data were examined using Pearson and Spearman correlation analysis. For all tests, the level of significance was $p < 0.05$.

3. Results

Results of the demographic, clinical and neuropsychological test data are summarized in Table 1. No significant differences in age, gender, education or MMSE, was observed between the patients with Graves' disease and healthy controls. There were the significant differences in T3, T4 and TSH between 2 groups. The patients with Graves' disease had higher score on the HAMA and HAMD than healthy controls.