Cause Analysis and Control of Thyroid Disease Based on Cognitive Behavior Science

Yan Zhao¹*, Jiajing Le², LiFeng Zhu³, Ming Zuo³

ABSTRACT
Due to the accelerated pace of life, thyroid function problems have become increasingly prominent, affecting human health. With ERP method, this study deals with the cognitive function of thyroid patients by comparing the data between thyroid patients and healthy people based on signal task and game experiment. The results show that there are significant differences in the accuracy rate and the error rate between the two groups in the signal task experiment and the healthy group performs better than the hyperthyroidism group. In the first three stages of the game experiment, the net score of the hyperthyroidism group increases more than that of the healthy control group and the executive function of the hyperthyroidism subjects is significantly impaired. For the control group, FRN difference wave has certain statistical significance under different feedback intensities, but the FRN difference is not obvious for the hyperthyroidism group. The sensitivity of hyperthyroidism patient reduces accordingly, thus their response to the stimulus with high and low feedback intensity tends to be similar. In the stop signal task, the N2 amplitude of patients with hyperthyroidism is significantly lower than that of the healthy control group, and the impairment of prefrontal lobe function is associated with the decrease of N2 amplitude, especially in patients with hyperthyroidism, which is accompanied by the decrease of frontal lobe metabolism.

Key Words: Cognitive Behavior, Thyroid Disease, Brain Mechanism
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Introduction
Due to rapid economic development and accelerated pace of life, endocrine problems have become more prominent, especially in the aspect of thyroid function (Nakagawa et al., 2011; Annunziata, 2003; Wykes, 2008). Much attention has been paid to the relationship between thyroid gland and cognitive function, but there are few studies on the relationship between thyroid gland and cognitive dysfunction (Cuijpers et al., 2008; Hollon et al., 2005; Agras et al., 2000). In a complex environment, it is necessary to reduce the impact of the neighborhood by performing functions to achieve the set goals. It is found in the clinic that the thyroid disease patients’ executive function is relatively weak, which may have the certain correlation with the frontal lobe function disorder (Siegle et al., 2006; Andersson et al., 2015).

As a new research method, ERP (Event Related Potential) is applied to the study of executive function in the study of the brain mechanism (Leichsenring, 2003; Barrowclough et al., 2001). ERP, also known as cognitive potential, is a special type of brain evoked potential, which has the temporal resolution of teaching and can reveal the neural electrophysiological changes of the brain through cognitive processing, thus discovering the possible mechanism of brain cognitive activity (Pike et al., 2003; Fava et al., 2004; Felmingham et al., 2010).

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Although ERP has been applied to the study of executive function, it is rarely applied to the cognitive function of hyperthyroidism (Smith et al., 2005; Coates and Lewis, 1984; Durlak et al., 1991). With ERP method, this study investigates the executive ability of thyroid patients, and analyzes the brain nerve mechanism of hyperthyroid patients with impaired executive function based on signal task and game experiment.

**Methods**

**Selection of subjects**

(1) A total of 25 patients, 7 males and 18 females, who have been diagnosed with hyperthyroidism in the hospital as yet untreated within 2 years are selected as subjects.

(2) A total of 20 healthy people in the same age range are also selected as subjects, 6 males and 14 females, without any mental disease found through corresponding examination.

**Experimental procedure**

(1) Signal task

The signal task requires the subjects to perform the task quickly and accurately during the test, which is a unique version of a classical approach to measuring response inhibition (Liddle et al., 2008; Tarrier et al., 2008). Specifically, it is implemented in two aspects: one is that the subjects are required to respond to the provided reaction signals by pressing buttons; the other is the stop signal task, wherein the subjects are required to respond to the stop signals that appear after the response task finishes by pressing the button. Through these two aspects, the subjects’ response and inhibition behavior are analyzed.

At the beginning, white circles appear on the experimental screen, prompting the subjects to prepare for the reaction, followed by white arrows with left-pointed or right-pointed direction, namely the reaction signals, which the subjects are required to respond to. Then the red arrow appears, that is, the stop signal, which requires the subject to stop pressing button immediately, and then finally the screen becomes black, indicating the end of the experiment.

During the experiment, the reaction and the stop experiment appear at random, and the intermediate rest time is provide for the subjects, who are informed between the experiments that there is no need to specifically wait for a stop signal to delay the reaction time.

(2) Game experiment

In this study, the game experiment is improved accordingly to meet the demand for collecting potential data. After improvement, it is possible to analyze the feasibility of the subject to adjust his behavior in a timely manner under negative feedback with unknown probability.

At first, two boxes appear on the screen, with numbers, 50 and 100 in them respectively, representing the equivalent amount of RMB. The figure below the boxes is the total obtained amount statistically. After the subject chooses one of them, he will be informed the outcome of the selection, then this round of experiment ends. This cycle is repeated.

Before each experiment, each subject will be informed that he has a total score of 1,000 which is equal to the same amount of RMB. He can choose between 50 and 100 each time. In the end, the equivalent amount of money will be given to the subjects according to their statistical score to ensure that they can attach enough attention to the experiment.

During the experiment, the winning and losing rate for the two options are different, as winning rate for the number 50 is 60%, while 40% for 100. But the subjects are not informed of the information that “50” is the favorable option, while “100” is the unfavorable one. They need to make their own judgment and adjust their own options through feedback mechanism.

(3) ERP experiment

Through the ERP experiment, the brain mechanism of the subjects is studied. The experimental environment is quiet and electrically shielded, with dark light, wherein the testers and the subjects are isolated to avoid mutual interference.

a. Preparation before experiment

Before starting the experiment, the subjects will be informed of the flow of the experiment and the safety of the experiment, so as to avoid the influence of unnecessary tension on the result of the experiment. The subject’s head is fitted with an electrode cap, and the contact area is rubbed with abrasive and alcohol to reduce electrical resistance. During the experiment, it is necessary for the subjects to control their head movement in order to obtain the ideal waveform.

b. Acquisition and processing of ERP data

In the signal task, it is necessary to superimpose the average data of the two tasks, and then measure the features of N2, P2, and P3 in
the ERP. Nine electrode points are selected in this article, including FZ, F3, F4, CZ, C3, C4, PZ, P3, and P4.

In the game experiment, a total of 4 items, the average winning and losing data for the options 50 and 100 are superimposed, FRN and P300 features in ERP are measured, and Fz, FCz, and Cz are selected for the measurement of FRN amplitude.

**Data Analysis**

**Signal task**
The analysis is mainly focus on P2, N2 and P3 components. Electrode positions for both reaction and stop signals are defined as intra-group factors, and amplitude and latency of P2, N2 and P3 are analyzed. The electrode points for analysis include FZ, F3, F4, CZ, C3, C4, PZ, P3, and P4.

**Game experiment**
The analysis is mainly focus on FRN and P3 components. The type, size and electrode position of the feedback are defined as intra-group factors, and the average wave amplitudes of the FRN and P300 original waves are analyzed. FZ, FCz and Cz are selected for FRN, and FZ, F5, F6, CZ, C5, C6, PZ, P5 and P6 are selected for P3.

**Results**

**Behavioral results**

(1) Signal task
No significant difference is found between the two groups of SI by independent sample t. The difference of CR and MR between the two groups is found to be statistically significant by non-parametric test of independent samples. Details are shown in Table 1.

(2) Game experiment
Through the analysis of variance of repeated measurements, it is found that the main effects of feedback size, type and electrode position of FRN component are significant, and notably that the interaction effects of feedback size, type and group are significant, as shown in Figures 7 and 8. Through the effect analysis, it can be seen that the interaction effects of the size and type of feedback of the healthy contrast group are significant, while it is opposite in the case of the thyroid patient group. In the case of winning or losing of money, the main effects of electrode position and the feedback intensity of the FRN difference wave are more significant. The interaction effects of feedback group and intensity are significant, and the main effects of feedback intensity are

**Table 1.** Comparison of stopping signal tasks in hyperthyroidism group and healthy comparison group

<table>
<thead>
<tr>
<th></th>
<th>SI</th>
<th>CR</th>
<th>MR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperthyroidism</td>
<td>51.60±9.00</td>
<td>94.87±14.39</td>
<td>5.13±14.39</td>
</tr>
<tr>
<td>group</td>
<td></td>
<td></td>
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<tr>
<td>Health comparison</td>
<td>55.88±7.52</td>
<td>99.55±0.45</td>
<td>0.45±0.45</td>
</tr>
<tr>
<td>group</td>
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<tr>
<td>p value</td>
<td>0.096</td>
<td>0.003</td>
<td>0.003</td>
</tr>
</tbody>
</table>

(2) Game experiment
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significant in healthy control group. The wins and losses of 100 belong to high intensity, while that of 50 belong to low intensity, FRN difference wave of low intensity is significantly lower than that of high intensity. But the main effects of feedback intensity in hyperthyroidism group are not significant, as shown in Figures 9 and 10.

**Figure 2.** Total mean diagram evoked by different tasks at FZ in two group (hyperthyroidism group)

**Figure 3.** Total mean diagram evoked by different tasks at FZ in two group (health comparison group)

**Figure 4.** Total mean diagram evoked by different tasks at FZ in two group (response task)

**Figure 5.** Total mean diagram evoked by different tasks at FZ in two group (stopped task)

**Figure 6.** N2 amplitude comparison between response and stopped task (hyperthyroidism group and healthy comparison group)

**Figure 7.** Total mean diagram evoked by different tasks at FCZ in two group (Hyperthyroidism Group)
In P3, the main effects of feedback size, type, and electrode position are significant. The position of CZ electrode shows the maximum amplitude of P3, and the interaction effects of feedback group, size and type are not significant.

**Discussions**

It is found through experiment that the performance of the healthy control group is better than that of the hyperthyroidism group in the signal task, and there is a significant difference in the accuracy rate and the error rate in the response experiment between the two groups. In the game experiment, in the first three stages, the increase in the net score of the hyperthyroidism group is greater than that in the healthy control group, but no significant differences in the behavioral statistics are found. Although both methods are experiments on executive ability, but their emphases are different. From the aspect of behavior, hyperthyroidism subjects’ executive function is significantly impaired in the absence of emotional factors.

In the game experiment, the subjects will evoke FRN. In this study, it is found that the FRN difference wave is statistically significant in the cases with different feedback intensities in the healthy control group, but it is not significant in the hyperthyroid subjects, indicating that under normal conditions, people’s responses to stimulus with high intensity and to that with low feedback intensity are different, but if they suffer from hyperthyroidism, their sensitivity will decrease accordingly, thus the hyperthyroidism patients’ responses to stimulus with high intensity and to that with low feedback intensity are basically the same. This may be due to DA system disorder caused by excessive thyroid hormone.

During the signal task, it is found through ERP that the amplitude of N2 in the hyperthyroidism group is significantly lower than that in the healthy control group in the stop signal task and executive function is closely related to N2 and P3 of the ERP components. However, in this experiment, the comparison of P3 is not significant. The study finds that after the inhibition of a stop-task stimulus, N2 with a large amplitude is recorded, mainly originating from the prefrontal cortex. Impairment of prefrontal lobe function is associated with a decrease in N2 amplitude, especially in patients with hyperthyroidism, which is often accompanied by a decrease in frontal lobe metabolism. In this study, objective evidence for impaired executive function in patients with hyperthyroidism has been found by means of neuroelectrophysiology.

ERP can be used to study the correlation between thyroid function and brain function in invasive cases. However, it should be noted that the study of thyroid dysfunction by
neurophysiology is relatively rare and the physiological mechanism of ERP and its changes cannot be fully understood.

Conclusions
With ERP method, this study deals with the cognitive function of hyperthyroidism patients by comparing the data between hyperthyroidism patients and healthy people based on signal task and game experiment. The results are as follows: In the signal task experiment, there is a significant difference in the accuracy rate and the error rate between the two contrast groups and the performance of the healthy control group is superior to that of the hyperthyroidism group. In the first three stages of the game experiment, the net score of the hyperthyroidism group increases more than that of the healthy control group and the executive function of the hyperthyroidism subjects is significantly impaired.

For the healthy control group, the FRN difference wave is statistically significant under the different feedback intensities, but it is not significant for the hyperthyroidism subjects. Under normal conditions, people's responses to stimulus with high intensity and to that with low feedback intensity are different, but the sensitivity of the hyperthyroidism patients decreases accordingly, thus their responses to stimulus with high intensity and to that with low feedback intensity are similar.

In the stop signal task, the N2 amplitude of the hyperthyroidism group is significantly lower than that of the healthy control group. The impairment of prefrontal lobe function is associated with the decrease of N2 amplitude, especially in patients with hyperthyroidism, which is accompanied by the decrease of frontal lobe metabolism.

References


Annuzinta P. Blood-brain barrier changes during invasion of the central nervous system by hiv-1. old and new insights into the mechanism. Journal of Neurology 2003; 250(8): 901-06.


