Original Article

Study of cognitive functions in newly diagnosed cases of subclinical and clinical hypothyroidism

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Abstract

Introduction: Hypothyroidism is associated with significant neurocognitive deficits because hypothyroidism prevents the brain from adequately sustaining the energy consuming processes needed for neurotransmission, memory, and other higher brain functions. Hence, the study was done to assess the cognitive functions of newly diagnosed subclinical and clinical hypothyroid patients by evoked response potential P300. **Materials and Methods:** 75 patients each of newly diagnosed subclinical and clinical hypothyroid patients attending endocrinology clinic and 75 healthy age and sex matched euthyroid controls were considered for the study. P300 was recorded with Record Medicare System Polyrite, Chandigarh using auditory "oddball paradigm". The data was analyzed using ANOVA followed by post Tukey's test. **Results:** Newly diagnosed clinical hypothyroid patients showed a significant increase in P300 latency compared to control ($P < 0.05$) and subclinical cases ($P < 0.01$) while there was no significant difference between the P300 latency of subclinical cases and control group. Also, there was no significant difference in P300 amplitude among the three groups. **Conclusion:** P300 latency in case of newly diagnosed hypothyroid clinical cases is significantly increased compared to newly diagnosed subclinical cases and control.

Key words: Cognition, event related potentials, hypothyroidism, P300

INTRODUCTION

Low thyroid function irrespective of age has been found to have detrimental effect on cognitive functions because hypothyroidism prevents the brain from adequately sustaining the energy (glucose)-consuming processes needed for neurotransmission, memory and other higher brain functions. Low brain uptake of glucose is commonly associated with deterioration of cognition.[1] Hypothyroidism is associated with significant neurocognitive deficits involving attention and concentration, memory, perceptual function, defective language, executive functions, development of a range of intellectual, disorientation in space and time, loss of autonomy, emotional depersonalization and other mental defects.[2]

Hypothyroidism in non-demented older adults is associated with impairments in learning, word fluency, visual-spatial abilities, some aspect of attention, visual scanning and motor speed.[3] Cognitive functions can be assessed by evoked potential e.g., P300 wave of event related potential (ERP).[4] Some researchers have found that subclinical hypothyroidism is associated with changes in mood and cognitive functioning while other were of the opinion that no correlation exists between these two.[5,6]

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MATERIALS AND METHODS

The present study was conducted in the department of Physiology in collaboration with the department of Medicine, PGIMS, Rohtak, India. It included 75 patients of newly diagnosed clinical and subclinical hypothyroidism patients attending endocrinology clinic and 75 healthy age and sex matched euthyroid controls [Table 1]. The subjects were divided into three groups:

Group I: Comprised of age and sex matched 75 healthy euthyroid subjects
Group II: Comprised of 75 newly diagnosed patients of subclinical hypothyroidism of either sex below the age of 50 years
Group III: Comprised of 75 newly diagnosed patients of clinical hypothyroidism of either sex below the age of 50 years.

Inclusion criteria

Hypothyroidism was diagnosed by increased thyroid stimulating hormone (TSH) and decreased thyroid hormone level. To avoid the effect of aging over cognition, we have included subjects below 50 years of age.

For subclinical hypothyroidism TSH level > 5.1mIU/L and T_4 ≥57.9 nmol/L.

For clinical hypothyroidism TSH level > 5.1mIU/L and T_4 <57.9 nmol/L.[7]

Exclusion criteria

1. Patients with any other major medical disorder which can affect cognitive function, i.e. diabetes mellitus, anaemia, hypertension, chronic obstructive pulmonary disease, acute or chronic liver and kidney disease
2. History of drug abuse including alcoholism
3. Neurological or psychiatric illness
4. Altered sensorium
5. Patients who don't co-operate during the study period.

Recording electrodes for ERP P300

The volume conducted evoked responses were picked up from scalp by using disc type of $Ag/AgCl_2$ electrodes. Two reference electrodes was attached to left and right mastoid, designated as A_1 and A_2 respectively, one active electrode on vertex labeled as Cz and one as ground electrode to forehead termed as Fpz. All the electrodes were plugged to a junction box. Impedance between skin and electrode was monitored and kept below 5 K ohms. Recommended montages for ERP p300 were: Channel 1: Cz -A_1, Channel 2: Cz -A_2 and Ground: Fpz.

Procedure for P300

P300 was recorded in context of a standard auditory oddball paradigm. Target or rare tone and non target or frequent tone of 70 dB was applied on both ears simultaneously through headphones applied to ears of subject. Rare tone and frequent tone was of 2 KHz and 1 KHz respectively. Rare tone stimuli were given in 20% and frequent tone stimuli in 80% frequency in random. Stimulus frequency was 1 stimulus per two sec. Total numbers of stimuli given were 160. The signals were picked by electrodes and were filtered, amplified, averaged, displayed on the screen of RMS EMG EP MK2 and recorded. Latency and amplitude of P300 wave were measured.

Statistical analysis

All the data gathered were tabulated and were analyzed using SPSS 14th version. For analysis ANOVA was used followed by Tukey's test.

RESULTS

The TSH was significantly higher ($P < 0.001$) in clinical hypothyroid patients compared with subclinical and controls. While T4 was significantly lower ($P < 0.001$) in clinical hypothyroid patients when compared with subclinical and controls as shown in Table 1. On comparison between subclinical and control, TSH was significantly higher ($P < 0.001$) and T4 was significantly lower ($P < 0.05$) in subclinical group. Height and weight were comparable amongst the three groups.

Table 2 shows that newly diagnosed clinical hypothyroid patients showed a significant increase in P300 latency compared to control ($P < 0.01$) and subclinical cases ($P < 0.05$) while there was no significant difference between the P300 latency of subclinical cases and control group. Also, there was no significant difference in P300 amplitude among the three groups [Figures 1-3].

Table 3 shows that the correlation coefficient between P300 latency and T4 was negative (−0.546) and statistically significant, while with TSH, it was positive (0.267), though statistically non-significant. The correlation coefficient between P300 amplitude and T4 was positive (0.042)

Table 1: Height, weight matching along with hormone level

Parameters	Control	Subclinical	Clinical
Age (years)	38±6.6	36±11	36±9
Sex (M/F)	3/72	4/71	2/73
Height (in cms)	160±4.65	157±10	158±5.8
Weight (in kg)	62±6.5	62±16	60±10
TSH (mIU/L)	1.25±0.55	8.98±2.55*	99.84±57.1*#
T4 (nmol/L)	116.89±31.24	103.14±13.1@	29.43±16.23*#

*Very highly significant (P<0.001) compared with control, #Very highly significant (P<0.001) compared with subclinical, @Significant (P<0.05) compared with control, TSH: Thyroid stimulating hormone

Table 2: Comparison of ERP P300 values of subclinical clinical and control cases

Parameters	Control	Subclinical	Clinical
P300 latency (ms)	281.84±9.76	283.14±19.97	295.98±16.52*#
P300 amplitude (μV)	7.18±1.85	6.91±3.75	6.30±2.66

*Highly significant (P<0.01) compared with control, #Significant (P<0.05) compared with subclinical

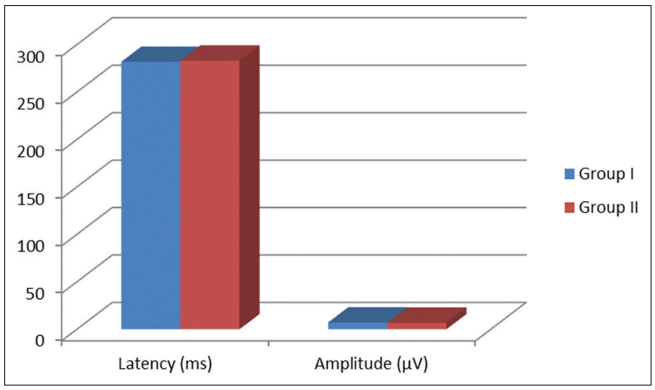

Figure 1: Comparison of P300 latency and amplitude between control (Group I) and newly diagnosed subclinical hypothyroid patients (Group II)

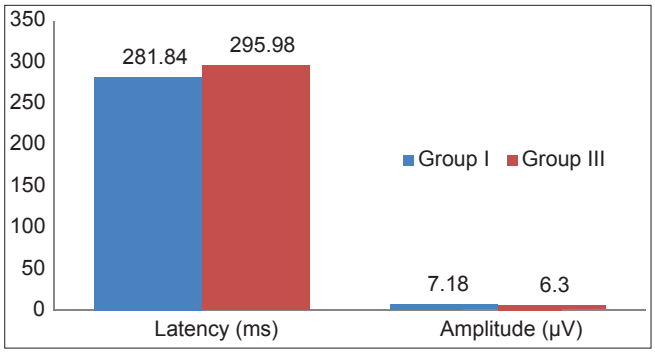

Figure 2: Comparison of P300 latency and amplitude between control (Group I) and newly diagnosed clinical hypothyroid patients (Group III)

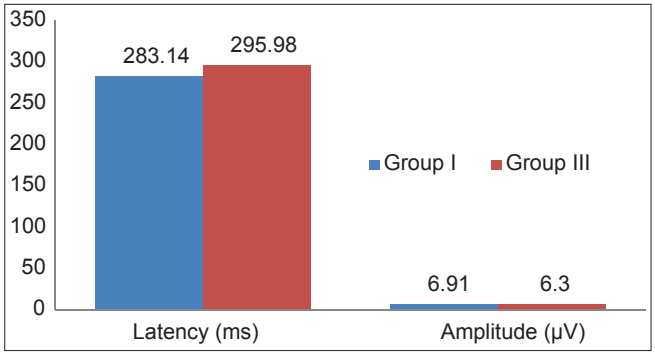

Figure 3: Comparison of P300 latency and amplitude between newly diagnosed subclinical (Group II) and clinical (Group III) hypothyroid patients

and with TSH, it was also positive (0.159), but none was statistically significant.

Table 4 shows that the correlation coefficient between P300 latency and TSH was positively correlated (0.414) and statistically significant, while with T4, it was negatively correlated (−0.072) and non-significant. The correlation coefficient between P300 amplitude and T4 was positive (0.196), while with TSH, it was negative (−0.013), though both were statistically non-significant.

Table 3: Correlation of hormone level with P300 latency and amplitude in group II

Parameters	P300 latency	P300 amplitude
T4	–0.546	0.042
TSH	0.267	0.159

TSH: Thyroid stimulating hormone

Table 4: Correlation of hormone level with P300 latency and amplitude in group III

Parameters	P300 latency	P300 amplitude
T4	–0.072	0.196
TSH	0.414	0.013

TSH: Thyroid stimulating hormone

DISCUSSION

Normal brain function requires thyroid hormones. Thyroid dysfunction is related to nervous system disorder involving GABA as reported by clinical studies.[8] The role of thyroid with regard to cognition is not yet clear.[9] Studies done recently shows that the cases previously considered asymptomatic may be having many non specific subjective features. In these patients there may be fine but subtle difference from euthyroid. The transition from normal euthyroid to hypothyroid is continuous and hence while assessing a case both the degree and duration of the case has to be considered. Subclinical hypothyroidism is marked by increase in serum TSH level while thyroid hormone level in serum is normal. One result of this which is postulated is there is an alteration on cognitive function and mood. Our result in Table 2 shows that there is significant difference in P300 latency between clinical and subclinical cases while there is highly significant difference between clinical and controls.

Our finding is supported by studies made by Tutuncu *et al.* who reported that there is delay of P300 latency in both mild and severe case of hypothyroidism.[10] Hala *et al.* and Jensovsky *et al.* also derived the same finding when studying the effect of hyper and hypo thyroidism on P300 latency.[11] On the contrary studies by Osterweil *et al.* showed no difference in P300 latency.[12] Studies by Mahmoud *et al.* also showed no difference.[13]

We further went ahead to find out a correlation between T4, TSH and P300 latency and amplitude which showed significant negative correlation in clinical cases when T4 was compared with *P* 300 latency while the rest have been non significant as shown in Tables 3 and 4.

CONCLUSION

P300 latency in case of newly diagnosed clinical hypothyroid patients was significantly increased in comparison to newly diagnosed subclinical cases and control groups.

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