Indian J Physiol Pharmacol 2006; 50 (4): 341–349

FUNCTIONAL STATUS OF AUDITORY PATHWAYS IN HYPOTHYROIDISM: EVOKED POTENTIAL STUDY

YUMNAM ANJANA*, NEELAM VANEY, O. P. TANDON AND S. V. MADHU**

*Departments of *Physiology and **Medicine,*
University College Of Medical Sciences and G.T.B. Hospital,
Dilshad Garden, Delhi – 110 095

(Received on July 25, 2006)

Abstract : Hypothyroidism is known to be associated with mental retardation, motor dysfunction, memory deficits and hearing impairment. In the present study, the functional integrity of the thalamocortical projections to the primary auditory cortex and association cortex has been assessed by using Auditory Evoked Responses i.e Auditory Brainstem (ABR), Mid Latency Response (MLR) and Slow Vertex Response (SVR). Thirty newly diagnosed hypothyroid patients and thirty healthy controls were taken for the study and ABR, MLR and SVR were recorded on computerized evoked potential recorder using 10–20 system of electrode placement. The second recordings for the hypothyroid patients were done 3 months after treatment with attainment of euthyroid states. The present study revealed a slight increase in absolute latency of wave III of ABR in hypothyroid patients and significant decrease in absolute latency of wave III and interpeak latency of I-III after treatment. There was a significant decrease in amplitude of wave V in hypothyroid patients and significant increase in amplitudes of ABR wave I and wave V after treatment. There was a significant increase in latency of wave Na of MLR and wave P2 of SVR in hypothyroid patients. The latencies of waves Na, Pa, Nb of MLR and waves PI and N2 of SVR showed significant improvement with thyroid hormone treatment. The results of the present study indicates that in hypothyroid state there might be slow conduction at the periphery and with treatment there is better recruitment of neuronal pool of the generators of the waves of ABR in the brainstem. We can also conclude that the thalamocortical projections of the auditory pathways are adversely affected in the hypothyroid state and this improves after treatment.

Key words : hypothyroidism, auditory brainstem response, mid latency response, slow vertex response

INTRODUCTION

Deafness is the most common otolaryngological manifestations associated with thyroid dysfunction. Hypothyroidism, both congenital and acquired has been associated with impaired hearing. It has been estimated that a significant hearing loss is

*Corresponding Author: Phone No.: 9871754571; E-mail: anjana_y@rediffmail.com

found in 25% of adult hypothyroid patients (1) and in 35% to 50% of children affected by cretinism (2, 3).

Kemp, 1907 was the first to document these symptoms in myxoedema, when he found hearing impairment in a severely hypothyroid female and this was reversed upon administering thyroid extract (4). Hilger was the first to audiometrically document the extent of hearing loss in acquired hypothyroidism (5). The hearing impairment may be conductive, sensorineural or mixed and benefit from thyroid therapy (6). It may be caused in part by a general diminution in cerebral activity; a myxoedematous infiltration of the middle ear has also been postulated to explain loss of conduction. In about half of the cases hearing improves when patient is treated with thyroid extract (7).

Auditory Brainstem Response (ABR) is one of the method used for assessing the effect of hypothyroidism on the auditory pathway in the brainstem. In hypothyroid state, there has not been any consistent findings in ABR among the available literature. Some workers reported prolongation of both peripheral and central conduction time in hypothyroidism while some studies showed that there were no statistically significant differences in ABR in hypothyroidism. The MLR and SVR represent the conduction in the central auditory pathways, from thalamus to auditory cortex. Thus integrity of the thalamocortical projections, the primary auditory cortex and association cortex can be assessed by using Mid Latency Response (MLR) and Slow Vertex Response (SVR). Very scant literature is available on the status of these auditory projections to the cortex.

Hence the present study aims to evaluate the auditory sensory process in the brainstem, thalamocortical and cortical areas in hypothyroid patients by using auditory evoked potentials (ABR, MLR, SVR) and the effect of treatment on these parameters.

METHODS

The study was conducted in the Electrophysiology Laboratory of Department of Physiology, University College of Medical Sciences, Delhi. The subjects were selected from the Thyroid Clinic, GTB Hospital, Delhi. Age and sex matched employees and post graduate students of UCMS & GTB Hospital were taken as controls for the study. The controls have no history of thyroid disease or any clinical evidence of thyroid dysfunction.

The clearance from the Ethical Committee of the College was obtained and an informed written consent was taken from all the subjects and healthy volunteers, after the recording procedure was explained to them.

The study was conducted on 30 newly diagnosed hypothyroid patients, of both sexes, with mean age of 32.63±8.59 years and in 30 controls with mean age of 29.73±6.87 years. The subjects were diagnosed based on general history, clinical examination and serum levels of fT_3, fT_4 and TSH.

The subjects were categorized into 3 groups :

Group I Healthy Controls

Group II Hypothyroid patients

Group III Hypothyroid patients becoming euthyroid following treatment.

Subjects suffering from any hearing impairment, systemic disease or any history of drug abuse (nicotine, alcohol, opium etc), pregnant females were excluded from the study group.

All subjects and controls were tested under similar laboratory conditions. They familiarized themselves to the experimental and environmental conditions of the laboratory. The recording for the controls was done once while that of the hypothyroid patients was done twice, before and after treatment for 3 months. The second recording was taken on attainment of euthyroid state.

Recording of auditory evoked potentials

The evoked potential (EP) recordings from the scalp of the subjects was done using Nihon Kohden Neuropack μMEB 9100. The EP were recorded with Silver-Silver Chloride disk electrodes from standard scalp locations of the 10–20 International System. The electrodes were placed at Cz (Active electrode), FPz (Grounding electrode), A1 and A2 (Reference electrode) after cleaning the scalp or skin site with alcohol followed by Skinpure Skin preparation gel and EEG paste Elefix™. The skin electrode contact impedance was kept at less than 5 KΩ. The subjects were instructed to close their eyes to avoid blink artifacts.

For recording ABR, 1000 click stimuli at the rate of 10 Hz with duration of 0.1 ms were delivered at 60 dB above hearing threshold through shielded headphones with –40 dB white noise masking the contralateral ear. Signals were filtered with bandpass 100 Hz and 3 KHz and averaged to 1000 stimuli. Peak latencies of all the waves, interpeak latencies of I-III, III-V and I-V and amplitudes of wave I and V was determined for each ear separately with the help of digital cursors. The amplitude was measured as the maximum height of the peak from the succeeding trough.

For recording MLR, 500 click stimuli at the rate of 5 Hz with duration of 0.1 ms and stimulus interval of 100 ms were delivered at 60 dB above hearing threshold through shielded headphones with –40 dB white noise masking the contralateral ear. Signals were filtered with bandpass 20 Hz and 1 KHz and averaged to 500 stimuli. The peak latencies of No, Po, Na, Pa, Nb, and Pb waves were recorded.

For recording SVR, 100 click stimuli at the rate of 0.5 Hz with duration of 0.1 ms and stimulus interval of 100 ms were delivered at 60 dB above hearing threshold through shielded headphones with –40 dB white noise masking the contralateral ear. Signals were filtered with bandpass 1 Hz and 50 Hz and averaged to 100 stimuli. The peak latencies of P1, N1, P2 and N2 were recorded.

Statistical analysis

The data obtained were analyzed using SPSS software. The average of left and right ear were taken and analyzed. The statistical analysis for the comparison between controls and hypothyroid patients was done using unpaired ‘t’ test. Paired ‘t’ test was used for

comparing the hypothyroid patients before and after treatment. All tests were two tailed. Results are expressed as Mean±SD.

RESULTS

There was no statistically significant difference in the absolute peak latencies, interpeak latencies of ABR in Group I (controls) and Group II (hypothyroid patients) as shown in Table I (Fig. 1). However, there was significant decrease in amplitude of wave V in hypothyroid patients. As seen from Table II a significant decrease in absolute peak latency of wave III (P<0.037) was observed in the cases after replacement therapy. In the remaining waves II, IV and V, a decrease in latencies was seen in the Group III though statistically insignificant. There was a significant decrease in absolute Inter-Peak Latency I-III (P<0.022) in hypothyroid patients after replacement therapy, though the remaining inter-peak latencies did not show significant changes (Table II). The amplitude of wave V was significantly (P=0.096) decreased in hypothyroid patients (Group II) (Table I). A significant increase in amplitudes of wave I (P<0.009) and wave V (P<0.009) were observed after treatment (Table II).

There was a significant increase (P<0.043) in latency of wave Na of MLR in hypothyroid patients as compared with controls, while the remaining waves Pa and Nb showed prolonged latencies though statistically insignificant (Table III) (Fig. 2). The latencies of waves Na (P<0.019), Pa (P<0.046) and Nb (P<0.000) showed significant reversibility with replacement therapy (Table IV). The remaining waves No, Po, Pb were not prominent in all the

TABLE I: ABR in Group I and Group II.

	No. of subjects	*Absolute peak latencies (msec)*					*Interpeak latencies (msec)*			*Amplitude (μV)*	
	n	*I*	*II*	*III*	*IV*	*V*	*I-III*	*III-V*	*I-V*	*I*	*V*
Group I	30	1.49±0.15	2.54±0.14	3.57±0.10	4.74±0.18	5.44±0.20	2.08±0.17	1.87±0.20	3.94±0.17	0.42±0.12	0.51±0.18
Group II	30	1.48±0.14	2.50±0.17	3.60±0.23	4.65±0.24	5.39±0.31	2.08±0.16	1.82±0.24	3.88±0.30	0.41±0.21	0.45±0.13*

*P<0.05

TABLE II: ABR in Group II and Group III.

	No. of subjects	*Absolute peak latencies (msec)*					*Interpeak latencies (msec)*			*Amplitude (μV)*	
	n	*I*	*II*	*III*	*IV*	*V*	*I-III*	*III-V*	*I-V*	*I*	*V*
Group II	30	1.48±0.14	2.51±0.17	3.60±0.23	4.65±0.24	5.39±0.31	2.08±0.16	1.82±0.24	3.88±0.30	0.41±0.21	0.45±0.13
Group III	30	1.49±0.14	2.48±0.18	3.50±0.18*	4.63±0.27	5.35±0.23	2.00±0.17*	1.85±0.17	3.86±0.19	0.48±0.26*	0.53±0.16*

*P<0.05

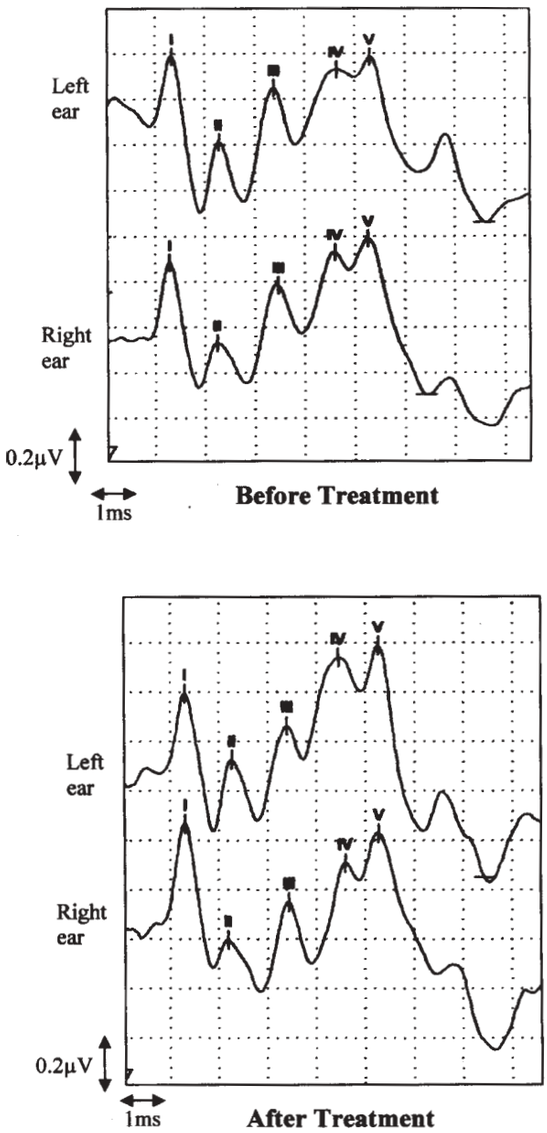

Fig. 1 : Representative waveform of auditory brainstem response in hypothyroid patient.

recordings. Hence the latencies of the above waves were not analyzed.

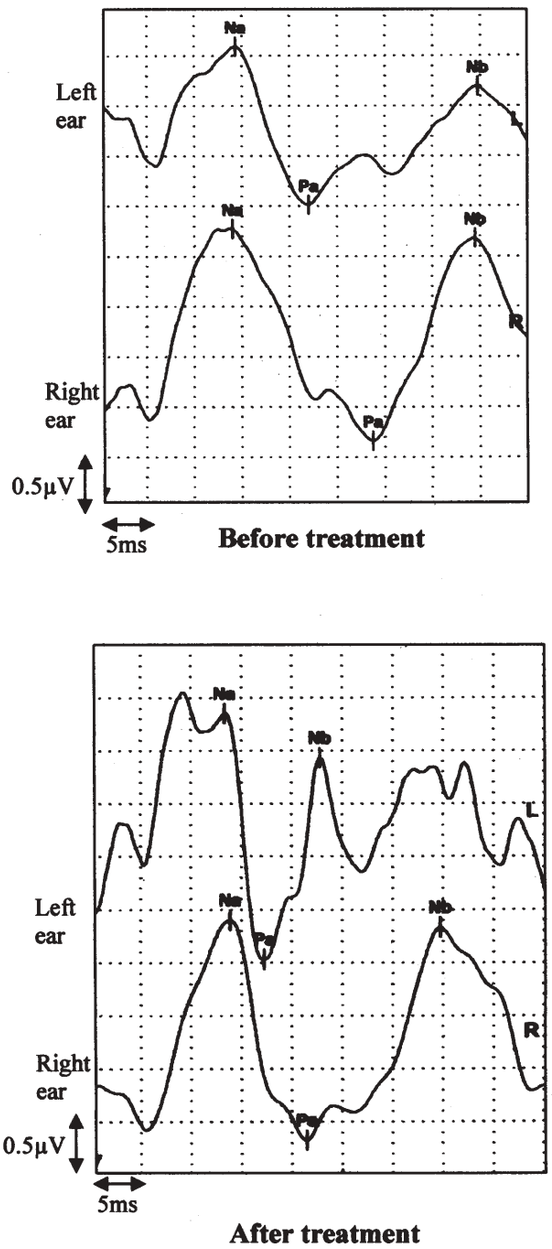

Fig. 2 : Representative waveform of mid latency response in hypothyroid patient.

TABLE III: MLR and AVR mean latencies in Group I and Group II.

	No. of subjects	*Mean latencies of MLR (msec)*			*Mean latencies of SVR (msec)*			
	n	*Na*	*Pa*	*Nb*	*P1*	*N1*	*P2*	*N2*
Group I	30	14.41±2.19	22.10±2.40	34.25±4.09	54.63±7.34	97.20±6.73	173.05±13.12	250.58±24.74
Group II	30	16.02±3.63*	23.47±4.18	35.93±3.60	56.68±8.26	99.78±8.10	180.40±13.65*	261.99±36.83

*P<0.05

TABLE IV: MLR and AVR mean latencies in Group II and Group III.

	No. of subjects	*Mean latencies of MLR (msec)*			*Mean latencies of SVR (msec)*			
	n	*Na*	*Pa*	*Nb*	*P1*	*N1*	*P2*	*N2*
Group I	30	16.02±3.63	23.47±4.18	35.93±3.60	56.68±8.26	99.78±8.10	180.4±13.65	261.99±36.83
Group II	30	14.45±2.94*	21.87±4.19*	30.17±6.71***	52.78±6.96***	99.61±9.51	181.98±18.66	241.78±23.50***

*P<0.05; ***P<0.001

The latency changes in waves P1, N1, P2 and N2 of SVR in Group I and Group II are shown in Table III (Fig. 3). A general trend of increase in latencies of waves P1, Nl and N2 was seen while a significant increase in latency of wave P2 (P<0.038) was observed. There was significant decrease in the latencies of wave P1 (P<0.000) and N2 (P<0.000) after treatment as shown in Table IV.

DISCUSSION

The functional integrity of the auditory pathway depends on the intact anatomical pathway, functional relay stations, myelination and thickness of the tract and absence of any compression or pressure from outside. Values of ABR (particularly the absolute and inter-peak latencies) represents the peripheral (from acoustic nerve and pontomedullary portion) and central (ponto-mesencephalic) conduction time.

Our findings of ABR as shown in Table I do not show any significant differences in absolute latencies and interpeak latencies of ABR though there is slight increase in wave III thereby indicating that in hypothyroid state there may be some slow conduction at the periphery, however after treatment with thyroid hormones, the latencies showed improvement while there is significant improvement in absolute latency of wave III (Table II) and lnterpeak latency of I-III (Table II). The baseline values obtained were similar to those obtained in our laboratory previously (8). The technical factors like stimulus rate, stimulus duration, filter settings etc were standardized and kept fixed as in the previous study from our laboratory.

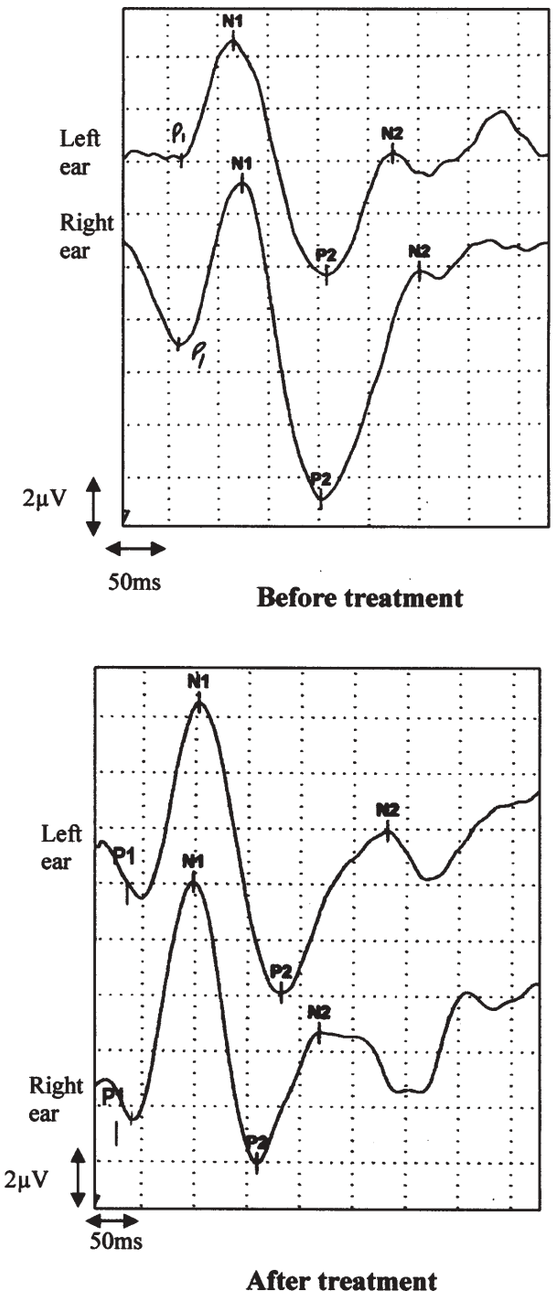

Fig. 3 : Representative waveform of slow vertex response in hypothyroid patient.

Our findings of ABR in are comparable with some of the other studies which have been done before. Anand et al demonstrated prolonged absolute latency of wave V and interpeak latencies I-III and I-V (9). These parameters did not show significant reversibility to normalcy following treatment. Vanasse et al found no significant difference in the brainstem evoked potentials when compared with that of the controls (10). Ozata et al in 1995 also found no abnormalities in BAEPs in patients with Subclinical hypothyroidism and concluded that BAEPs are not affected in subclinical hypothyroidism of short duration (11). But Huang et al, in 1989, observed prolonged latency and interpeak latency of BAEP in hypothyroidism (12). Recently in 2000 Khedr et al also found prolongation of all wave latencies and interpeak latencies in some of the hypothyroid patients in the brainstem auditory evoked potentials (13). Hohmann et al in 1990, recorded changes in conduction time of ABR in patient with hypothyroidism but no significant changes were found in the ABR following therapy (14). Di Lorenzo et al in 1995, also recorded abnormal ABR in overt hypothyroid patient and found that they remained abnormal even after treatment (15). These contradictory findings might be due to variations in recording procedures, sample size and extent of thyroid dysfunction.

In our study, it is seen that in hypothyroid patients there is decrease in amplitude of wave I while there is significant decrease in amplitude of wave V and there is significant improvement after treatment (Table I and II). This indicates that there is better recruitment of neuronal pool of the generators of these waves of ABR in the

brainstem which may further go in favor of subjective hearing improvement. In 1981, Mordechai et al found that the pattern of ABR was generally characterized by prolonged BSCT (Brainstem conduction tune), diminished amplitudes, flattened peaks and poor synchronization (16). Anand et al in 1989, demonstrated reduction of amplitudes of wave I, II and V, and these parameters did not show significant reversibility to normalcy following treatment (9). Thus our findings clearly indicate that presence of optimal thyroid hormones is required to improve excitability of neuronal pools (generators) in brainstem particularly for waves III and V.

In our study, there was significant prolongation of wave Na in the hypothyroid patients as compared with controls as shown in Table III and there was significant improvement in Na, Pa and Nb after treatment as observed in Table IV. As seen in Table III, there was significant prolongation of latency of wave P2 in hypothyroid patients while a prolongation is seen though statistically insignificant in all the other waves of SVR. There was significant improvement in the wave PI and N2 after treatment as shown in Table IV. The significant prolongation of latency of Na of MLR and P2 of SVR in hypothyroid subjects as well as other waves of MLR and SVR indicates that the thalamocortical projections of the auditory pathways are adversely affected in these patients. This finding is consistent with that of Crifo et al where they observed a longer latency of the SVR in the congenital hypothyroid group in comparison to the results obtained in normal subjects (17). Our findings suggest that thyroid hormone has profound influence on the auditory projections and are involved in their processing in the brain. That may be the reason why latencies of some waves of MLR and SVR decrease on treatment in hypothyroid patients. The findings of the present study suggest that normal levels of thyroid hormones are required for proper excitability of the thalamocortical projections and auditory processing at the cortical level. There has been no study, to the best of our knowledge, assessing the thalamocortical projections using MLR and SVR in adult hypothyroid patients.

The mechanism of improvement in sensory functions may be multifactorial as it has been shown that thyroid hormone do influence synthesis and release of neurotransmitter and sensitivity of receptors particularly H1 and H2 receptors in the brain. Thus in hypothyroid state, sensory functions might be deranged and they revert back to normal after treatment. The present study thus provides electrophysiological evidence to this effect. However the exact mechanism for such improvement remains to be further investigated.

ACKNOWLEDGEMENTS

We would like to thank Mr. B. Manjhi for his technical assistance during this study.

REFERENCES

1. Meyerhoff WL. Hypothyroidism and the ear: Electrophysiological, Morphological and Chemical Considerations. *Laryngoscope* 1979; 89 Suppl 19: 1–25.

2. Ritter FN. The effects of hypothyroidism upon the Ear, Nose and Throat: A Clinical and Experimental Study. *Laryngoscope* 1967; 77: 1427–1479.

3. De Long GR, Stanbury JB, Fierro Benitez R. Neurological signs in congenital iodine-deficiency disorders (Endemic Cretinism). *Dev Med Child Neurol* 1985; 27: 317–324.

4. Kemp WR. Deafness in Myxoedema. *Brit Med Jour* 1907; 1: 375.

5. Hilger JA. Otolaryngologic aspects of hypometabolism. *Ann Otol Rhinol Laryngol* 1956; 65: 395–413.

6. Parving A, Parving H, Lyngsoe J. Hearing sensitivity in patients with myxoedema before and after treatment with L-Thyroxine. *Acta Otolaryngol* 1983; 95: 315–321.

7. Howarth AE, Llyod HED. Perceptive Deafness in Hypothyroidism. *Brit Med Jour* 1956; 1: 431–433.

8. Tandon OP. Auditory brainstem evoked responses in healthy north Indians. *Indian J Med Res* 1990; 92: 252–256.

9. Anand VT, Mann SB, Dash RJ, Mehra YN. Auditory investigations in hypothyroidism. *Acta Otolaryngol (Stockh)* 1989; 108: 83–87.

10. Vanasse M, Fischer C, Berthezene F, Roux Y, Volman G, Mornex R. Normal brainstem auditory evoked potentials in adult hypothyroidism *Laryngoscope* 1989 Mar; 99(3): 302–306.

11. Ozata M, Ozkardes A, Corakei A, Beyhan Z, Gundogan MA. Subclinical hypothyroidism does not lead to alterations either in peripheral nerves or in brainstem auditory evoked potentials (BAEPs). *Thyroid* 1995 Jun; 5(3): 201–205.

12. Huang TS, Chang YC, Lee SH, Chen FW, Chopra JJ. Visual, brainstem auditory and somatosensory evoked potential abnormalities in thyroid disease. *Thyroidology* 1989 Dec; 1(3): 137–142.

13. Khedr EM, El Toony LF, Tarkhan MN, Abdella G. Peripheral and central nervous system alterations in hypothyroidism: electrophysiological findings. *Neuropsychobiology* 2000 Jan; 41(2): 88–94.

14. Hohmann D, Kahaly G, Warzelhan J. Effect of hyperlipidemia and hypothyroidism on auditory evoked brainstem responses. *HNO* 1990 Dec; 38(12): 446–450.

15. Di Lorenzo L, Foggia L, Panza N, Calabrese MR, Motta G, Tranchino G, et al. Auditory brainstem responses in thyroid diseases before and after therapy. *Horm Res* 1995; 43(5): 200–205.

16. Mordechai Z, Himelfarb MZ, Lakretz T, Gold S, Shanon E. Auditory Brainstem Responses in Thyroid Dysfunction. *J Laryngol Otol* 1981; 95: 679–686.

17. Crifo S, Lazzari R, Salabe GB, Amaldi D, Gagliardi M, Maragoni F. A retrospective study of audiology functions in a group of congenital hypothyroidism patients. *Int J Pediatr Otorhinolaryngol* 1980 Nov; 2(4): 347–355.