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RESEARCH ARTICLE

Early detection of auditory dysfunctions in patients with overt hypothyroidism

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ABSTRACT

Background: Widespread metabolic derangements in overt hypothyroidism have also been suggested to involve adult human brain with the involvement of cochlea and other inner ear structures. More interestingly, abnormal electrophysiological alterations in patients with normal hearing have also been documented. **Aims and Objectives:** This study is an attempt to detect auditory pathway dysfunctions by brainstem auditory evoked potential (BAEP) tests in overt hypothyroidism patients without clinical evidence of hearing defects. **Materials and Methods:** BAEP was performed in 25 female patients with overt hypothyroidism in the age-group of 30-50 years and 25 age-matched healthy females. BAEP absolute latencies I, II, III, IV and V, interpeak latencies (IPLs) I-III, III-V and I-V and BAEP amplitudes of wave I, wave V and amplitude ratios were compared and analyzed in the two groups by unpaired *t*-test. Statistical significance was considered at $P < 0.05$. **Results:** BAEP responses revealed statistically significant prolongation of mean absolute latencies (I, III and V) as compared to controls ($P < 0.05$) (both the ears) by unpaired *t*-test. IPLs prolonged too with statistical significance for I-V IPL prolongation ($P < 0.05$). Furthermore, wave V amplitude was found to be reduced in overt hypothyroidism with statistical significance ($P < 0.05$). **Conclusion:** BAEP documents abnormal alterations in patients with overt hypothyroidism with normal hearing with central as well as peripheral auditory pathway impairment. BAEP can be a useful objective tool to assess the patients for central nervous system involvement in overt hypothyroidism.

KEY WORDS: Brainstem Auditory Evoked Potentials; Absolute Latency; Interpeak Latency; Overt Hypothyroidism

INTRODUCTION

Hypothyroidism is the most common pathological hormone deficiency among the thyroid disorders.[1] Hypothyroidism describes a state with reduced thyroid functions resulting from intrinsic thyroid derangements which interfere with the adequate production of thyroid hormones (primary hypothyroidism). It may also be secondarily due to pituitary or hypothalamic failure.[2] The immense burden of the hypothyroidism is reflected in its higher prevalence rates in our country which is noticeably higher than in the developed nations. It barely reaches 5% in the United Kingdom and United States, while in India, it is reported to be far greater with about 11% subjects having diagnosed with the same.[3,4] Marked female preponderance is characteristically associated with the condition with 15.86% of females reported to be diagnosed as hypothyroidism in an Indian study as compared to the prevalence of 5.02% in males.[4] The middle-aged subjects form the most common age group affected, with the highest prevalence found in the age-group of 46-54 years (13.11%).[4]

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The progression of euthyroid (state with normal thyroid hormone levels) to hypothyroid state involves stages with subclinical hypothyroidism as the first stage, progressing to mild clinical hypothyroidism and finally presenting with overt hypothyroidism. The diagnoses of different stages require thyroid profile tests. In overt primary hypothyroidism, thyroid stimulating hormone (TSH) levels are high and T4 (tetraiodothyronine) and T3 (triiodothyronine) levels are low. A TSH concentration above the reference range combined with a free T4 (FT4) levels below the reference range indicates the presence of overt primary hypothyroidism in ambulant subjects.[5,6]

As a brunt of the metabolic derangement widespread in the body in hypothyroidism, adult human brain has also been suggested to be involved. Cerebral blood flow, oxygen consumption, and glucose consumption have been reported to be diminished.[7] Furthermore, studies involving recent brain imaging techniques provide insights into the association of the various neurologic and neurobehavioral symptoms with hypothyroidism.[8,9] There has been a characteristic association between thyroid diseases and otological symptoms. Role of certain mucopolysaccharides have been found in otitis media and also in sensorineural hearing loss.[10] Deposition of glycosaminoglycans in the cochlea has been suggested as the cause. Pendred's syndrome, a hearing disorder is also associated with hypothyroid state. In addition to the presence of hearing disorders in the hypothyroid, abnormal electrophysiological alterations in patients with normal hearing have also been documented.[11-14] Abnormal brainstem auditory evoked potentials (BAEPs) in overt hypothyroidism have been registered. BAEPs are electrophysiological investigations which represent electrical potentials recorded in response to a short auditory stimulation. BAEP waveform represents the conduction of sound waves through the auditory pathway up to the brainstem. Abnormal BAEP latencies in hypothyroids in various researches provide evidence regarding the involvement of the auditory pathways. Many researches, however, still provide contradictory findings with no significant alterations in BAEP latencies.[15-17] Furthermore, the pattern or site of the auditory pathway affections as central or peripheral needs to be investigated. This study hence has been undertaken to detect the alterations in BAEPs in overt hypothyroidism. Detection of functional alterations in the auditory pathways in the overt hypothyroidism, especially in those with no otological symptoms can prove to be more valuable. The study aims at an objective evaluation of the functional changes in the nervous system in the patients with hypothyroidism without clinical manifestations of hearing disorders.

MATERIALS AND METHODS

It was a case-control study which comprised 25 females diagnosed with overt hypothyroidism and 25 age-matched healthy females. Sample size calculation was done using mean ± standard deviation (SD) for absolute latency of wave V (as it was significantly delayed for both the ears in cases as compared to the controls) in a previous similar study.[12] Sample size was calculated at 95% confidence interval and power of 95%.

The recording of BAEP test was performed in the Electrophysiology Laboratory in the Department of Physiology, Maharishi Markandeshwar Institute of Medical Sciences, Mullana, Ambala, Haryana. The study group comprised the female patients from the outpatient and inpatient departments of surgery and medicine, and age-matched healthy females constituted the controls who were the inhabitants of the area of study. Approval from Institutional Ethical Committee was obtained to conduct the study. Informed consent was taken from all the subjects and a detailed clinical history obtained. Furthermore, detailed clinical examination including neuro-otological examination was performed, and the subjects were explained about the recording procedure before commencing the test. Anthropometric data were collected by measuring height, weight, and head sizes of the subjects. Head size was measured from nasion to inion. Body mass index (BMI) was calculated as: Weight (kg)/height (m^2). The study comprised two groups of subjects: Group I (cases) with 25 females diagnosed with overt hypothyroidism in the age group of 30-50 years and Group II (controls) with 25 age-matched, healthy female volunteers.

Inclusion Criteria

Patients diagnosed with overt hypothyroidism with TSH level >6 μIU/ml (laboratory serum reference ranges in adults: 0.28-6 μIU/ml) and FT4 <0.8 ng/dL (laboratory serum reference ranges in adults: 0.8-2.8 ng/dL) (by Chemiluminescence immunoassay method) were included in the study as cases and subjects with TSH and FT4 levels within the lab reference ranges (by Chemiluminescence immunoassay method) were selected as controls. All the subjects were in the age group of 30-50 years with normal hearing (normal audiograms).

Exclusion Criteria

All the conditions suggested to affect the BAEP responses (metabolic or other endocrine disorders, use of ototoxic drugs, history of drug abuse, hereditary and degenerative diseases, cigarette smoking, ear surgery, radiotherapy or chemotherapy) formed the exclusion criteria for the study.

Biochemical Analysis

Thyroid profile tests were performed by Chemiluminescence immunoassay method. The Laboratory reference ranges were TSH: 0.28-6 μIU/ml, FT3: 2.3-4.2 pg/ml and FT4: 0.8-2.8 ng/dL.

Duration between the diagnoses and the BAEP recordings ranged from <1 to 6 months.

BAEP Recording

BAEP test was recorded using Allengers Scorpio-EMG, EP, NCS equipment in a specially equipped room with quiet environment. Standard disc surface electrodes were placed after appropriate cleaning of the scalp skin. Electrode placement followed International 10/20 system. Active electrode was placed at Mi (ipsilateral mastoid process). Reference electrode and ground electrodes were placed at Cz and Fpz, respectively.[18] Monaural recording was done and auditory stimulus with rarefaction clicks of 0.1 ms pulse was provided. Click intensity was 80 dB nHL which was delivered through headphones at a rate of 11.1/s. A contralateral masking with white noise of 30 dB below the BAEP stimulus was done. The system band pass filter was set at 100-3000 Hz. Total number of clicks presented were 2000. Two responses were recorded and superimposed to ensure validity and replicability.

The parameters for the study were absolute latencies of waves I, II, III, IV and V and interpeak latencies (IPLs) I-III, III-V and I-V. Furthermore, amplitudes of wave I, wave V and amplitude ratio (V/I) were considered for the study. The data were expressed as mean ± SD. Unpaired Student's *t*-test was used for the comparison between the two groups using SPSS (Statistical Package for Social Science) version 20.0 statistical software. $P < 0.05$ was considered as significant.

RESULTS

Mean ages in the two groups (36.92 ± 6.2 and 38.76 ± 8.46 years) (among controls and overt hypothyroidism, respectively) differed with no statistically significant difference ($P = 0.38$; $P > 0.05$). Head size and BMI comparisons also revealed similar non-significant variations in the two groups ($P > 0.05$). Mean TSH level in controls was 1.99 ± 0.54 µIU/ml, while in cases, it was 107.24 ± 78.88 µIU/ml ($P < 0.0001$). FT4 measurements revealed that the mean values in the two groups varied (controls: 1.77 ± 0.4 ng/100 ml and cases: 0.32 ± 0.1 ng/100 ml) with a statistical significance of $P < 0.0001$ (Figure 1).

Mean BAEP wave V absolute latency increased in the hypothyroids when compared to the controls with $P < 0.001$ (both ears). Mean values of wave I and wave III absolute latencies also revealed prolongation with $P < 0.05$ (both ears) (unpaired *t*-test) (Table 1). IPL comparisons also demonstrated increase in mean values in the hypothyroids in both the ears but statistical significance ($P < 0.05$) could be found for IPL I-V (Table 2). We also observed decrease in the amplitudes studied (wave I, wave V and amplitude ratio V/I) among the hypothyroids. The statistical significance was

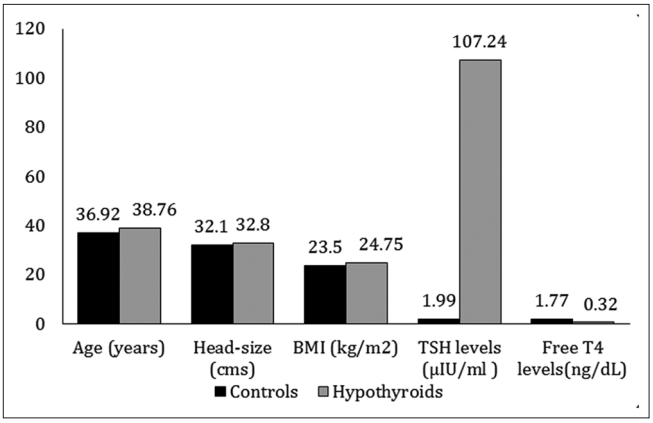

Figure 1: Mean values of demographic and anthropometric data and thyroid profiles compared in the two groups

obtained for wave V amplitude reduction among the hypothyroids ($P < 0.05$) (Table 3).

DISCUSSION

Involvement of thyroid hormones in various processes in the nervous system including a characteristic association with hearing impairment arise the need for the data evaluating the effect and extent of the involvement. This study has objectively assessed the auditory pathway involvement by BAEP tests in the patients with clinical hypothyroidism with no clinical manifestations of hearing defects. The results reveal abnormal BAEP changes in the hypothyroid patients as compared to the healthy controls which are in agreement with some previous similar researches.[11-14,16,19,20]

BAEP records in our study report statistically significant prolongation of absolute latencies (wave I, III and V) in the hypothyroid patients (Table 1). Similar absolute latency prolongation ($P < 0.001$) has been stated by Khedr et al.[13] Sharma et al., in a similar study which included 25 overt hypothyroidism, reported statistically significant ($P < 0.05$) prolongation of wave IV and V absolute latencies.[12] Kowsalya et al. also report absolute latency prolongation for wave III and wave V ($P < 0.05$).[19] Another study by Anjana et al. also described increase in the wave III absolute latency among the hypothyroids, though the delay was not significant statistically.[16] On the other hand, in a study by Vanasse et al., no statistically significant differences in BAEPs in adult hypothyroid patients were recorded.[15] Ozata et al. also supported the findings from the above study. The latter study, however, was conducted on the patients with subclinical hypothyroidism.[17]

IPLs in our study demonstrated a similar abnormal prolongation albeit only I-V IPLs delayed with statistical significance (Table 2). IPL prolongation has not been an infrequent finding in other researches. Sharma et al. report statistically significant prolongation of I-V IPL.[12] Khedr et al. and Jayanthi et al. report statistically significant

delay of all the three IPLs studied.[13,20] Kowsalya et al. also report increase in I-V IPL similar to our findings.[19]

The study also registered decrease in the amplitudes (wave I, wave V and V/I ratio) among the hypothyroids (Table 3). Statistically significant ($P < 0.05$) decrease was found for wave V amplitudes. Amplitude values in the evoked potentials indicate the extent of recruitment of nerve fibers and reduced BAEP amplitudes in our study suggest impaired recruitment of the neuronal pool in the brainstem. Our results are consistent with the study by Anjana et al. which reports a significant reduction in BAEP wave V amplitudes among the hypothyroids.[16] Another study which provides similar results with significant decrease in the BAEP amplitudes was that by Kowsalya et al. which documents decrease in both wave I and wave V amplitudes with statistical significance ($P < 0.05$).[19] Nevertheless, amplitude differences have been less consistent findings in various studies as compared to latency prolongations in the BAEP studies in hypothyroids, as majority of studies lack the inclusion of the parameter for study and others report no significant changes.[11-13,15,17,21] High variability of BAEP amplitudes with many subjective and technical factors can be attributed to it.

Various researches in the field of pathogenesis of the auditory derangements in thyroid disorders suggest the important role of thyroid hormones in peripheral as well as central conduction. Thyroid hormones were found to be involved in the gene expression for not only Schwann cells but also oligodendrocytes in the central nervous system (CNS). Furthermore, one of the thyroid hormone receptors was found to be necessary for cochlear myelinogenesis.[22] Diminished myelin synthesis is also supported by the studies by Delongs and Adams and Bhat et al.[23,24] Effect of low body temperature in overt hypothyroidism subjects has also been implicated in the prolongation of BAEP latencies. It causes an additional slowing of both peripheral and central conduction in overt hypothyroidism.[25] The effect of hypothermia on the brainstem evoked responses was first shown by Stockard et al. as increased I-V interval.[26] They reported an increase of approximately 0.18 ms/°C drop in temperature. The effect of hypothermia was supported by another study by Kusakari et al.[27]

Impairment of cerebral metabolism is another factor suggested to be involved in hypothyroidism. Reversible alterations in adult cerebral phosphate metabolism have been noticed in nuclear magnetic resonance spectroscopy in patients with acute hypothyroidism.[28]

Myxoedematous infiltration in the hypothyroids resulting in compressive neuropathy has also been attributed to

Table 1: Mean BAEP absolute latencies compared in hypothyroidism and controls

Groups	*N*	Absolute latency (ms±SD)									
		Wave I		Wave II		Wave III		Wave IV		Wave V	
		Right*	Left*	Right	Left	Right*	Left*	Right	Left	Right**	Left**
Group I (cases with overt hypothyroidism)	25	1.73±0.15	1.75±0.32	2.64±0.2	2.58±0.22	3.71±0.3	3.78±0.35	4.69±0.21	4.71±0.26	5.91±0.35	5.94±0.46
Group II (controls)	25	1.62±0.1	1.61±0.09	2.62±0.05	2.56±0.09	3.57±0.11	3.58±0.12	4.67±0.13	4.68±0.14	5.55±0.1	5.56±0.14

*P<0.05 for the comparisons between hypothyroidism and controls by unpaired *t*-test, **P<0.001 for the comparisons between hypothyroidism and controls by unpaired *t*-test. BAEP: Brainstem auditory evoked potential, ms: Milliseconds, SD: Standard deviation

Table 2: Mean BAEP IPLs compared in hypothyroidism and controls

Groups	*N*	Interpeak latency (ms±SD)					
		I-III		III-V		I-V	
		Right	Left	Right	Left	Right*	Left*
Group I (cases with overt hypothyroidism)	25	1.97±0.35	1.99±0.48	2.31±0.5	2.19±0.48	4.15±0.38	4.17±0.49
Group II (controls)	25	1.95±0.13	1.97±0.13	2.06±0.45	1.98±0.16	3.93±0.1	3.95±0.16

BAEP: Brainstem auditory evoked potential, ms: Milliseconds, SD: Standard deviation, IPLs: Interpeak latencies. *P<0.05 for the comparisons between hypothyroidism and controls by unpaired *t*-test

Table 3: Mean BAEP amplitudes and amplitude ratio compared in hypothyroidism and controls

Groups	*N*	Wave amplitude					
		Wave I (μv±SD)		Wave V (μv±SD)		V/I ratio (±SD)	
		Right	Left	Right*	Left*	Right	Left
Group I (cases with overt hypothyroidism)	25	0.43±0.59	0.45±0.65	0.44±0.33	0.47±0.41	2.15±1.75	2.18±1.45
Group II (controls)	25	0.44±0.38	0.46±0.32	0.69±0.39	0.76±0.52	2.35±1.67	2.11±1.67

BAEP: Brainstem auditory evoked potential, SD: Standard deviation, μv: Microvolts. *P<0.05 for the comparisons between hypothyroidism and controls by unpaired *t*-test

abnormal conduction. Cuddon suggested increased amounts of glycogen and glycosaminoglycans in the cytoplasm of Schwann cells and perineural cells. Vestibulocochlear and facial nerve might suffer from compressive nerve damage owing to these myxoedematous deposits.[29] Furthermore, transcription of some cochlear motor proteins, "prestin" and "otoferlin" which are thought to play important roles in sound transmission is also thought to be regulated by thyroxine.[30]

As both BAEP absolute as well as IPLs are affected in the present study, the involvement seems to be diffuse with both central as well as peripheral auditory pathway affection. Reduction of amplitudes was also noticed in the present study along with conduction time delays, suggesting reduced recruitment of neuronal pools in the auditory pathways. The underlying pathophysiology has been stated as multifactorial and various mechanisms including diminished myelin synthesis, low body temperature, cerebral metabolism impairment, involvement of cochlear motor proteins, and myxoedematous infiltration have been suggested to play roles.

LIMITATIONS

Correlation studies including the correlation of thyroid profile of the patients with their BAEP records which could not be included in the study would have contributed to the present findings. Furthermore, a follow-up of the study group could have been conducted to find out the changes in the BAEP records of the patients according to the progression or recovery of their hypothyroid status.

CONCLUSION

Overt hypothyroidism is associated with abnormal BAEP changes which are detectable before clinically evident hearing defects. Both central and peripheral auditory pathways are involved as evident by prolonged absolute as well as interpeak BAEP latencies. Patients can be monitored by BAEP tests for objective evaluation of auditory system in hypothyroidism. Further studies to provide evidence in favor of preventive measures for hearing disorders and CNS involvement are warranted which could contribute to a better prognosis of the condition.

REFERENCES

1. Roberts CG, Ladenson PW. Hypothyroidism. Lancet 2004;363:793-803.
2. Persani L. Clinical review: Central hypothyroidism: Pathogenic, diagnostic, and therapeutic challenges. J Clin Endocrinol Metab. 2012;97(9):3068-78.
3. Vanderpump MP. The epidemiology of thyroid disease. Br Med Bull. 2011;99:39-51.
4. Unnikrishnan AG, Kalra S, Sahay RK, Bantwal G, John M, Tewari N. Prevalence of hypothyroidism in adults: An epidemiological study in eight cities of India. Indian J Endocrinol Metab. 2013;17(4):647-52.
5. Caldwell G, Kellett HA, Gow SM, Beckett GJ, Sweeting VM, Seth J, et al. A new strategy for thyroid function testing. Lancet. 1985;1(8438):1117-9.
6. Klee GG, Hay ID. Biochemical testing of thyroid function. Endocrinol Metab Clin North Am. 1997;26(4):763-75.
7. Constant EL, de Volder AG, Ivanoiu A, Bol A, Labar D, Seghers A, et al. Cerebral blood flow and glucose metabolism in hypothyroidism: A positron emission tomography study. J Clin Endocrinol Metab. 2001;86(8):3864-70.
8. Koromilas C, Liapi C, Schulpis KH, Kalafatakis K, Zarros A, Tsakiris S. Structural and functional alterations in the hippocampus due to hypothyroidism. Metab Brain Dis. 2010;25(3):339-54.
9. Pilhatsch M, Marxen M, Winter C, Smolka MN, Bauer M. Hypothyroidism and mood disorders: Integrating novel insights from brain imaging techniques. Thyroid Res. 2011;4 Suppl 1:S3.
10. Simmons MA, Bruce IA, Penney S, Wraith E, Rothera MP. Otorhinolaryngological manifestations of the mucopolysaccharidoses. Int J Pediatr Otorhinolaryngol. 2005;69(5):589-95.
11. 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):200-5.
12. Sharma K, Kumar N, Behera JK, Sood S, Das S, Madan HS. Brainstem auditory evoked potential in clinical hypothyroidism. Avicenna J Med. 2015;5(3):79-82.
13. Khedr EM, El Toony LF, Tarkhan MN, Abdella G. Peripheral and central nervous system alterations in hypothyroidism: Electrophysiological findings. Neuropsychobiology. 2000;41(2):88-94.
14. Höhmann D, Kahaly G, Warzelhan J. Effect of hyperlipidemia and hypothyroidism on auditory evoked brain stem responses. HNO. 1990;38(12):446-50.
15. Vanasse M, Fischer C, Berthezène F, Roux Y, Volman G, Mornex R. Normal brainstem auditory evoked potentials in adult hypothyroidism. Laryngoscope. 1989;99(3):302-6.
16. Anjana Y, Vaney N, Tandon OP, Madhu SV. Functional status of auditory pathways in hypothyroidism: Evoked potential study. Indian J Physiol Pharmacol. 2006;50(4):341-9.
17. Ozata M, Ozkardes A, Corakci A, Gundogan MA. Subclinical hypothyroidism does not lead to alterations either in peripheral nerves or in brainstem auditory evoked potentials (BAEPs). Thyroid. 1995;5(3):201-5.
18. American Clinical Neurophysiology Society. Recommended standards for short-latency auditory evoked potentials guideline 9C: Guidelines on short-latency auditory evoked potentials. J Clin Neurophysiol. 2006;23(2):157-67.
19. Kowsalya V, Vijayakumar R, Chandrasekhar M. Electrophysiological changes on brainstem auditory evoked potentials in hypothyroid patients. Int J Basic Appl Med Sci. 2014;4:29-37.
20. Jayanthi M, Vinodha R. Prolongation of interpeak latency of brainstem auditory evoked potential in hypothyroidism. Int J Med Res Health Sci. 2016;5(3):22-7.
21. Santos KT, Dias NH, Mazeto GM, Carvalho LR, Lapate RL, Martins RH. Audiologic evaluation in patients with acquired hypothyroidism. Braz J Otorhinolaryngol. 2010;76(4):478-84.
22. Knipper M, Bandtlow C, Gestwa L, Köpschall I, Rohbock K, Wiechers B, et al. Thyroid hormone affects Schwann cell and

oligodendrocyte gene expression at the glial transition zone of the VIIIth nerve prior to cochlea function. Development. 1998;125(18):3709-18.
23. Delongs GR, Adams RD. The neuromuscular system and brain in hypothyroidism. In: Braverman LE, Utiger RD, editors. Werner and Ingbar's the Thyroid. 6th ed. Philadelphia, PA: Lippincott; 1991. p. 1027-39.
24. Bhat NR, Shanker G, Pieringer RA. Investigations on myelination *in vitro*: Regulation of 2,3'-cyclic nucleotide 3'-phosphohydrolase by thyroid hormone in cultures of dissociated brain cells from embryonic mice. J Neurochem. 1981;37(3):695-701.
25. Abbott RJ, O'Malley BP, Barnett DB, Timson L, Rosenthal FD. Central and peripheral nerve conduction in thyroid dysfunction: The influence of L-thyroxine therapy compared with warming upon the conduction abnormalities of primary hypothyroidism. Clin Sci (Lond). 1983;64(6):617-22.
26. Stockard JJ, Stockard JE, Sharbrough FW. Non-pathological factors influencing brainstem auditory evoked potentials. Am J EEG Technol. 1978;18:177-209.
27. Kusakari J, Inamura N, Sakurai T, Kawamoto K. Effect of hypothermia upon the electrocochleogram and auditory evoked brainstem response. Tohoku J Exp Med. 1984;143(3):351-9.
28. Smith CD, Ain KB. Brain metabolism in hypothyroidism studied with 31P magnetic-resonance spectroscopy. Lancet. 1995;345(8950):619-20.
29. Cuddon PA. Acquired canine peripheral neuropathies. Vet Clin North Am Small Anim Pract. 2002;32(1):207-49.
30. Weber T, Zimmermann U, Winter H, Mack A, Köpschall I, Rohbock K, et al. Thyroid hormone is a critical determinant for the regulation of the cochlear motor protein prestin. Proc Natl Acad Sci U S A. 2002;99(5):2901-6.

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