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Auditory brain stem responses in thyroid dysfunction

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HYPOTHYROIDISM, both congenital and acquired, may be associated with impaired hearing. The hearing loss, affecting about 25 per cent of subjects with acquired hypothyroidism, is reversible upon proper substitution therapy (Howarth and Lloyd, 1956). However, we are not aware of reports on hearing disorders in hyperfunction of the thyroid gland.

Several investigators have studied the auditory electrical responses in hypothyroidism. In hypothyroid guinea-pigs Rubinstein *et al.* (1975) described changes in amplitude and latency of the auditory nerve action potential, which reversed on treatment with thyroid hormone. Kohonen *et al.* (1971) observed diminished voltage of the cochlear microphonic in guinea-pigs rendered hypothyroid with radioiodine. Rubinstein *et al.* (1974) recorded a prolonged latency period of cortical auditory evoked responses in four patients with congenital, sporadic hypothyroidism who were treated with thyroxine. In a recent study Mendel and Robinson (1978) examined auditory brainstem responses in a two-year-old child with congenital hypothyroidism. Wave I and II only were recognizable but following treatment with thyroxine the auditory brain stem responses (ABR) returned to normal. Lolas *et al.* (1977) found low amplitudes of the slow brain potentials evoked by visual stimuli in hypothyroid subjects and high amplitudes in hyperthyroid ones.

The relationship between hearing loss and thyroid dysfunction, and the mechanism by which thyroid hormones affect hearing, is not well understood. However, it is known that both deficiency and excess of the thyroid hormones may induce biochemical and morphological changes in the nervous system. Thyroid hormone is known to influence the synthesis of proteins (Sokoloff, 1977), production of enzymes and myelin, as well as to determine the level of brain lipids (Bass *et al.,* 1977). The growing nervous system is especially prone to be affected by thyroid deficiency. Sterling (1975) postulated that thyroxine acts as a neurotransmitter.

The purpose of this study is to investigate auditory brainstem responses (ABR) both in hypo- and hyper-thyroid states, as well as to

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describe the dynamic changes of these responses associated with a fluctuating level of serum thyroxine.

Material and Methods

ABR were recorded in 32 subjects, 26 women and 6 men. The age of the women ranged from 13–88 years (mean 45·4 years) and that of the men from 35–74 years (mean 58·5 years). Six patients presented with untreated hyperthyroidism and six others with untreated hypothyroidism. The remaining 20 subjects were being evaluated for suspected dysfunction of the thyroid gland, or were under active treatment for various grades of hyper- or hypo-activity of the gland. The diagnosis of thyroid dysfunction was based on clinical signs and symptoms as well as on a radioimmunoassay of serum T_4 (normal range 4–11 μg. per cent). Serum T_3 and TSH were assessed in a limited number of patients.

The patients were examined in a reclining position, without sedation, in an ordinary unscreened hospital room. The recordings were made with a Medelec-Amplaid MK III electrical evoked response system. The potentials were measured between an earlobe electrode and a vertex surface electrode (ground to nose). Click stimuli were presented at a repetition rate of 10/second and at an intensity of 80 dbHL. Fig. 1 shows an ABR recording from a normal subject. The nomenclature proposed by Sohmer and Feinmmesser (1977) was used. Wave N_1 was referred to the auditory nerve action potential, N_2 to the cochlear nucleus, N_3 to the olivary complex, N_{4a} to the lateral lemniscal nuclei, N_{4b} and N_5 to the inferior colliculus. Brainstem conduction time (BSCT) was defined as the N_1–P_4 interval and its normal value, as determined in 15 young and healthy subjects, was 4·68 ms. (SD 0·10 ms.). Test/re-test were performed

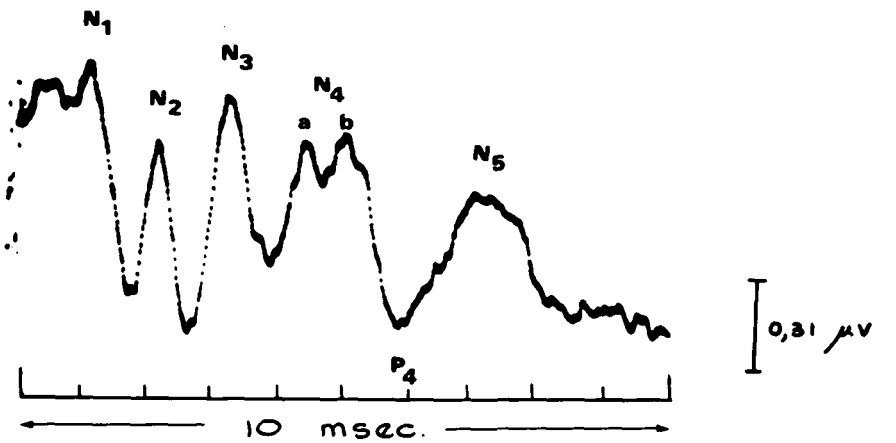


FIG. 1
An ABR recording of a normal subject.

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in each subject. Tonal and speech audiometry was completed in all subjects, except in one with myxedematous coma.

Results

Untreated hyperthyroidism was studied in six patients, five women and one man, whose ages ranged from 27–55 years (mean 35·2 years). Grave's disease was diagnosed in five subjects and autonomous toxic adenoma—in one. The serum level of T_4 was 14–15 μg. per cent or higher in all the patients; T_3 was tested in three patients and its value ranged from 320 to more than 400 ng. per cent. Hearing acuity was within normal limits in all the subjects. BSCT was decreased and it ranged from 4·30–4·55 ms. (mean 4·42 ms., SD 0·09). In some patients the pattern of ABR was characterized by high amplitude of waves, sharp peaks and jittery contours.

The dynamics of BSCT and the correlation between the BSCT shift and the level of serum thyroxine are demonstrated in a woman aged 55 with hyperthyroidism due to a toxic autonomous adenoma (Fig. 2). ABR recorded prior to the onset of therapy are shown in the top trace. Serum T_4 was more than 15 μg. per cent and T_3—320 ng. per cent. The peaks of the waves are sharp and high in amplitude. The pattern of the responses appears to be jittery and BSCT is shortened (4·40 ms.). The patient was given propylthiouracil and propanolol; five weeks later her serum T_4 fell to 12 μg. per cent and T_3 to 288 ng. per cent. ABR (Fig. 2, middle trace) appeared smooth in pattern and well defined; BSCT increased to 4·63 ms. The bottom trace of Fig. 2 shows normal responses six weeks following a hemithyroidectomy. Serum T_4 was 5 μg. per cent, T_3—157 ng. per cent and BSCT—4·69 ms.

Untreated hypothyroidism was observed in six patients, three men and three women. The age of the men ranged from 47–74 years (mean 63 years) and of the women from 13–49 years (mean 32 years). Four patients underwent total thyroidectomy for thyroid carcinoma; one, a girl of 13 years, suffered from Hashimoto's thyroiditis and one patient had panhypopituitarism. Serum T_4 was less than 4 μg. per cent in all the patients, T_3 was less than 70 ng. per cent in four, 133 ng. per cent in one (Hashimoto's disease) and was not examined in one. Hearing acuity was unimpaired in three patients, moderately diminished in a 47-year-old man and markedly diminished in two men aged 68 and 74.

The pattern of ABR was generally characterized by prolonged BSCT, diminished amplitudes, flattened peaks and poor synchronization. BSCT ranged from 4·85–5·40 ms. (mean 5·06 ms., SD 0·16).

The dynamic changes of BSCT and of serum T_4 are demonstrated in two patients. The first one was a girl of 13 with Hashimoto's thyroiditis (Fig. 3). The upper trace of Fig. 3 shows a normal ABR pattern with prolonged BSCT (4·87 ms.). This recording was done when the serum T_4 was 4 μg. per cent. No therapy was given for six weeks and serum T_4 fell to

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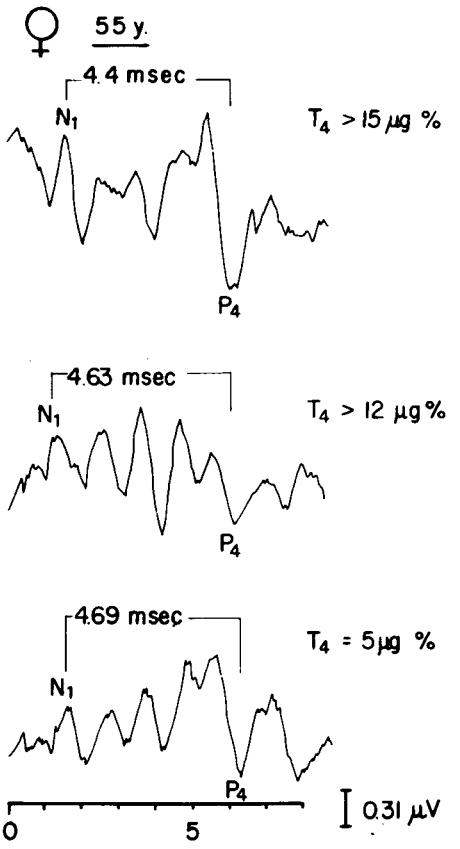


FIG. 2
ABR in a patient with hyperthyroidism.

less than 4 μg. per cent. Mild symptoms of hypothyroidism supervened. Additional prolongation of the BSCT (5·26 ms.) was observed (lower trace). The response pattern appeared to be well preserved. It should be stressed that in older hypothyroid subjects the changes in the wave pattern (amplitudes and synchronization of responses) were more pronounced.

The second case (Fig. 4) was a man 47 years of age who suffered from papillary carcinoma of the thyroid gland and squamous cell carcinoma of the larynx. His neck was irradiated in childhood for enlarged cervical lymph nodes. Fig. 4a shows normal ABR recorded prior to surgery. Serum T_4 was 8 μg. per cent and BSCT 4·75 ms. Seventeen days following total thyroidectomy and laryngectomy serum T_4 fell to less than 4 μg. per cent and BSCT increased to 5·0 ms. The amplitude of the waves appeared low and the peaks of N_4 and N_5 were flattened and poorly synchronized (Fig. 4b). Three weeks after the onset of therapy with synthetic L-thyroxine (Fig. 4c), serum T_4 increased to 8 μg. per cent and BSCT

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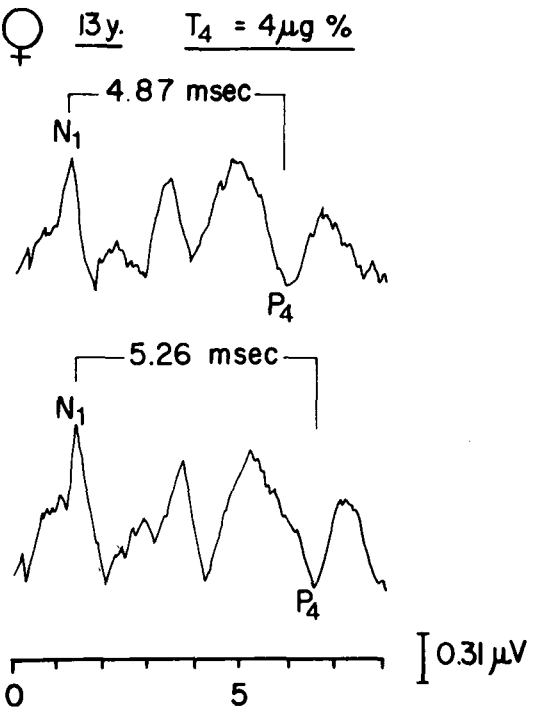


FIG. 3

ABR in a patient with Hashimoto's thyroiditis.

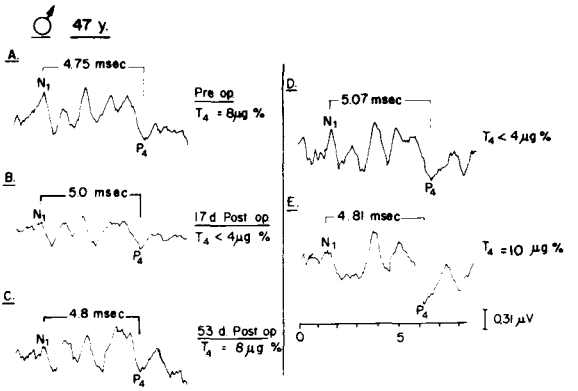


FIG. 4

Dynamic changes of ABR in a patient with fluctuating thyroid function.

returned to a normal value (4·8 ms.). The patient stopped taking thyroxine and did not return for follow-up examination. After a period of one year he appeared clinically myxedematous, his serum T_4 fell to less than 4 μg. per cent and BSCT increased to 5·07 ms. (Fig. 4d). Synthetic L-thyroxine was readministered and two months later his serum T_4 increased to a normal level (10 μg. per cent) and BSCT shortened to 4·81 ms. (Fig. 4e).

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A good correlation was observed between BSCT and the level of serum T_4. In Fig. 5 BSCT is plotted as a function of the level of serum T_4. The normal ranges of BSCT and of serum T_4 are delineated by horizontal and vertical lines respectively. The area between the intersecting lines represents the normal range of BSCT and serum T_4. Some of the patients were tested on several occasions at different stages of their disease. It is apparent that hypothyroid patients (open circles) concentrate above and to the left of the normal range area (i.e. they exhibit prolonged BSCT and low level of serum T_4), whereas hyperthyroid patients (filled circles) concentrate below and to the right of the normal range (i.e. they exhibit shortened BSCT and high level of serum T_4).

Discussion

This study attempts to correlate the clinical thyroid status and the level of serum thyroxine with the features of auditory brainstem responses. A characteristic pattern of ABR was observed both in hyper- and hypofunction of the thyroid gland. This pattern fluctuated in relation to the thyroid status of the patient. The most conspicuous change took place in the brainstem conduction time; however, amplitude of responses and synchronization varied too. In general, a good correlation was observed between the value of BSCT and the level of serum T_4 (Fig. 5). However, in

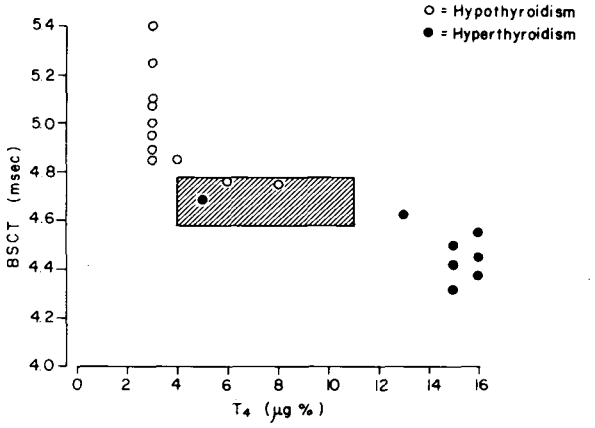


FIG. 5

BSCT in patients with thyroid dysfunction as a function of the level of serum T_4 (hypothyroid patients—open circles, hyperthyroid patients—filled circles, normal range of BSCT and serum T_4—shaded area).

patients maintained on synthetic L-thyroxine after total thyroidectomy, the value of serum T_4 was elevated, even though the patient appeared to be euthyroid and his BSCT was normal. This apparent discrepancy is due to the relatively long biologic half time of T_4 (Sterling, 1975). The dynamic alterations of ABR were studied as myxedema supervened following total thyroidectomy or cessation of thyroxine therapy in an athyreotic subject,

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and during the course of a therapeutic attempt to restore an euthyroid state in patients suffering from thyrotoxicosis or from a hypothyroid state. In some subjects BSCT reflected a change in the thyroid status earlier than the value of serum T_4 and it helped to avoid confusion evoked by elevated levels of serum T_4 in athyreotic patients maintained on synthetic L-thyroxine.

Serial ABR tests may be easily performed during the course of therapy and the results are available immediately. BSCT appears to be a sensitive index of the thyroxine-dependent cellular status in the neural pathways of the brainstem, and it may thus serve as an important tool in the overall assessment of the thyroid status.

In the present series of patients suffering from thyroid dysfunction conventional audiometry detected hearing loss in three elderly patients only. However, the ABR recording showed dynamic changes in the auditory BSCT related to the thyroid functional state in all the patients. To date we do not understand the mechanism by which thyroid dysfunction affects the auditory system. However, it has been shown that deficiency or excess of the thyroid hormone may induce biochemical, metabolic and morphological changes in the nervous system (Bass *et al.*, 1977; Sterling, 1975). Thus, it is possible that the dynamic changes in BSCT in patients with fluctuating thyroid function may reflect the activity of the thyroid hormone in the nervous system.

The results of this preliminary study suggest that further investigation is needed to understand the role of thyroid hormone in audition. Also, further research is required to explore the possibility of using the ABR technique as a tool in assessing thyroid function.

Summary

A characteristic pattern of ABR was observed in hyper- and hypofunction of the thyroid gland. The most conspicuous change took place in the BSCT. Its value correlated well with the level of serum T_4. Dynamic changes of ABR pattern were recorded during the development of myxedema and on return to an euthyroid state.

This preliminary study suggests that examinations of ABR may serve as a tool in the overall assessment of thyroid status.

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