ELECTROENCEPHALOGRAPHIC CHANGES DURING AND AFTER TREATMENT OF HYPERTHYROIDISM

By
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ABSTRACT

EEG and thyroid function tests have been studied in 32 hyperthyroid patients before, during and after antithyroid treatment. EEG abnormalities such as increase in alpha rhythm, slow rhythms, spikes and sharp waves and fast activity were found in 81% of the patients before treatment. A statistically significant correlation was found between the degree of EEG abnormalities and the severity of hyperthyroidism. During treatment and the period of observation which was extended to an average of 2½ year, a slight decrease in the occurrence of all abnormalities was observed, but even in the period 24-36 months after the start of the therapy, 65% of the patients still had abnormal EEG’s. These persistent abnormalities in EEG suggest that hyperthyroidism might cause irreversible damage to the brain cells. It should be realized that hyperthyroidism may be the cause of considerable EEG abnormalities however not only in the acute state of the disease but also several years after an otherwise successful antithyroid treatment.

It has been recognized for many years that abnormalities in the electroencephalogram (EEG) are very frequent findings in patients with hyperthyroidism. Thus an increase in the alpha rhythm frequency, slow rhythms, paroxysmal activity with diffuse spikes and sharp waves and an increased incidence of fast activity are the abnormalities most often described (Ross & Schwab 1939;
Condon et al. 1954; Skanse & Nyman 1956; Vague et al. 1957, 1961; Jackson & Renfrew 1966; Wilson & Johnson 1964). Previous investigators have described an almost complete regression of abnormalities in EEG following antithyroid treatment (Skanse & Nyman 1956; Vague et al. 1961; Wilson & Johnson 1964). Changes in EEG however have not been correlated to total thyroxine or free thyroxine in serum and studies of a larger group of hyperthyroid patients with frequent EEG recordings during antithyroid treatment have not been found in the literature.

**MATERIAL AND METHODS**

The group studied comprised 32 patients i.e. 29 women aged 14 to 77 years and 3 men aged 16 to 49 years. The diagnosis was based on the clinical picture and on several thyroid function tests. (BMR, PBI, serum thyroxine, normal range 4.5–13.5 μg/100 ml (Siersbæk-Nielsen 1967), resin-T3-test (Triosorb Abbott) normal range 22.2–34.4% (Hansen & Buhl-Jørgensen 1965), 131I uptake in the thyroid gland). The severity of the hyperthyroidism was estimated using a »free thyroxine index« (serum thyroxine in μg/100 ml × resin-T3-test in %). Patients with values below 700 were classified as mild, between 700 and 1100 as moderate and over 1100 as severe cases. The patients were treated with propylthiouracil (PTU) in conventional doses. Eleven of the patients were thyroidectomized after 3 to 6 months treatment with PTU. The remainder of the patients received long term treatment with PTU for a period of approximately 24 months. In 5 patients hyperthyroidism relapsed after withdrawal of PTU and in one patient shortly after thyroidectomy.

EEG’s were recorded with an 8-channel Kaiser electroencephalograph and the recordings were analyzed blindly by two of us (M. St. and P. Z. O.). The EEG parameters were quantitated: the dominant alpha activity was the mean of values measured with a ruler 6–10 places in the vertex occipital lead. The slow activity of 3–4 cps and 5–6 cps was recorded as present or not. Paroxysmal activity reflected diffuse sharp waves or spikes with or without high voltage slow waves and was graded from 0 to +++. Fast activity was measured as the activity above 14 cps in the fronto-central and parieto-occipital leads, and only an activity with a mean amplitude above 15 μV was considered. Finally the total abnormalities of a record was graded into 4 classes according to common usage and taking all the parameters into considerations.

The thyroid function tests and EEG’s were performed before and 2 weeks, 6 weeks, 3 months, 6 months, 9 months, 12 months, 18 months and between 24 and 36 months after beginning of antithyroid treatment. The average period of observation was 32 months.

**RESULTS**

The mean values of the thyroid function tests and the age and sex distribution were found to be typical for a large group of hyperthyroid patients studied previously (Siersbæk-Nielsen 1967). The incidence of EEG abnormalities before treatment was correlated to the grade of hyperthyroidism and the results are given in Table 1. The occurrence of slow activity as well as of paroxysmal
Table 1.
Correlation of severity of hyperthyroidism to occurrence of slow activity, paroxysmal activity, fast activity and total degree of abnormalities in EEG's from 32 patients before treatment.

<table>
<thead>
<tr>
<th>Severity of hyperthyroidism</th>
<th>mild</th>
<th>moderate</th>
<th>severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slow activity:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>6</td>
<td>11</td>
<td>2</td>
</tr>
<tr>
<td>5-6 cps</td>
<td>3</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>3-4 cps</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Paroxysmal activity:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>6</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>+</td>
<td>3</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>++</td>
<td>1</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Fast activity:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>9</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>+</td>
<td>1</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Degree of abnormalities:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Slightly abnormal</td>
<td>3</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Moderately abnormal</td>
<td>3</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Severely abnormal</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Activity increased with the severity of hyperthyroidism. Only 5 of 22 patients classified as mild or moderate cases of hyperthyroidism had slow activity as compared to 8 of 10 patients with severe hyperthyroidism. Statistical analyses using the chi square test showed a significant difference ($P < 0.001$). The increase in paroxysmal activity and fast activity was also found to be statistically significant ($P < 0.05$). When the abnormalities were expressed as the total degree of abnormalities, there was a significant correlation to the grade of hyperthyroidism ($P < 0.02$). The dominant frequency was also related to the grade of hyperthyroidism but no significant correlation was found. Nor was any significant correlation found between the degree of abnormalities in EEG, the age of the patients or the duration of the symptoms which varied between 1 and 24 months with an average of 6 months.

The results of the thyroid parameters and the EEG findings in the group of patients before, during and after antithyroid treatment are shown in Table 2. The data in Table 2 include only results from patients without any laboratory
Table 2.
Thyroid function tests and EEG findings before, during and after treatment of hyperthyroidism in 32 patients.

<table>
<thead>
<tr>
<th></th>
<th>Before treatment</th>
<th></th>
<th>During and after treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>2 weeks</td>
<td>6 weeks</td>
</tr>
<tr>
<td>Number of patients</td>
<td>32</td>
<td>15</td>
<td>30</td>
</tr>
<tr>
<td>Basal metabolic rate (%)</td>
<td>145 ± 19</td>
<td>127 ± 18</td>
<td>115 ± 20</td>
</tr>
<tr>
<td>Serum thyroxine (μg/100 ml)</td>
<td>21.7 ± 6.5</td>
<td>11.1 ± 6.2</td>
<td>6.8 ± 4.8</td>
</tr>
<tr>
<td>Resin T3-test (%)</td>
<td>43.8 ± 8.5</td>
<td>32.7 ± 6.8</td>
<td>26.7 ± 6.2</td>
</tr>
<tr>
<td>Dominant frequency</td>
<td>10.8 ± 1.20</td>
<td>10.1 ± 1.10</td>
<td>9.8 ± 1.00</td>
</tr>
</tbody>
</table>

**Mean ± SD**

**Slow activity:**
5-6 cps
11 34%o 7 47%o 9 30%o 7 25%o 6 22%o 4 17%o
3-4 cps
2 7%o 2 13%o 4 13%o 6 21%o 4 15%o 1 4%o

**Paroxysmal activity:**
(Spikes and sharp waves)
0
14 44%o 4 27%o 13 43%o 13 46%o 14 52%o 16 67%o
+
12 37%o 10 67%o 17 57%o 15 54%o 12 44%o 7 29%o
++
6 19%o 1 6%o 0 0%o 0 0%o 1 4%o 1 4%o

**Fast activity:**
> 14 cps and > 15 μV
8 25%o 2 14%o 5 17%o 4 14%o 4 15%o 4 17%o

**Degree of abnormality:**
Normal
6 19%o 1 7%o 8 27%o 7 25%o 11 41%o 9 38%o
Slightly abnormal
11 35%o 6 39%o 11 36%o 11 39%o 10 37%o 10 42%o
Moderately abnormal
13 39%o 8 54%o 11 37%o 10 36%o 6 22%o 5 21%o
Severely abnormal
2 7%o 0 0%o 0 0%o 0 0%o 0 0%o
or clinical signs of relapse of hyperthyroidism. During antithyroid treatment a rapid decrease in the mean values of all thyroid function tests was noted and normal values were reached between 2 and 6 weeks after treatment was started. The mean values of BMR failed to reach completely normal values due to cardio-pulmonary disease in some of the patients in whom an elevated BMR persisted in spite of normal thyroid function tests. During the following period of observation the mean values of the thyroid function tests remained almost unaltered.

The EEG recordings from the patients before treatment showed a mean value of the dominant frequency of 10.8 cps. Following only 2 weeks of therapy a significant decrease to 10.1 cps was found ($P < 0.05$). From 2 to 6 weeks a further slight decrease was noted and during the remainder of the period of observation, no significant alterations were observed.

Slow activity below 7 cps was demonstrated in 41% of the patients before treatment. A reduction in slow activity was noted about 32 months after the start of antithyroid therapy. At this time 3–6 cps activity was present in 21% of the patients but the reduction was not statistically significant as compared to the incidence before treatment (sign test).

The paroxysmal activity before treatment was present in 65% of the patients. After only 2 weeks of treatment the degree of paroxysmal activity was found to be altered with almost complete disappearance of the most marked abnormalities. After a euthyroid state for about 2½ year paroxysmal activity was still present in 34% of the patients. The total incidence of paroxysmal activity at this time was found to be significantly decreased compared to the incidence before treatment ($P < 0.01$).

Fast activity was only registered if frequencies over 14 cps with a voltage over 15 µV were found. Only 25% of the patients had this abnormality in the EEG before treatment. During treatment a slight though not significant decrease, was noted.

In summary a total degree of abnormality in the EEG was found in 81% of the patients before treatment. After 3 months of therapy however, there was a general tendency to a decrease in the number of abnormalities with an increase in the occurrence of normal EEG's. But even during the period 24–36 months after the beginning of therapy 65% of the patients had abnormal EEG recordings. This incidence was statistically significantly lower than the incidence found before treatment ($P < 0.05$).

DISCUSSION

Our findings of a high incidence of EEG abnormalities as manifested by the slow activity, paroxysmal activity and fast activity which are characteristic, but not specific for patients with hyperthyroidism are in agreement with
previous studies (Ross & Schwab 1939; Condon et al. 1954; Skanse & Nyman 1956; Vague et al. 1957, 1961; Wilson & Johnson 1964). The use of a free thyroxine index is generally accepted at present in clinical work as a valuable aid to an evaluation of the thyroid function. Several other thyroid function tests have also been used in the present study to make sure the diagnosis and to evaluate the severity of the hyperthyroidism and later on in the follow up to ensure that the patients had become and remained euthyroid. We have found a statistically significant increase in the degree of EEG abnormalities in patients with severe hyperthyroidism as compared to patients suffering from mild hyperthyroidism. Skanse & Nyman (1956) were unable to demonstrate a relation between EEG abnormalities and the severity of thyrotoxicosis as assessed by the BMR.

A more thorough comparison between our findings and previous studies is difficult, mainly because of different recording techniques and various criteria for evaluating the different types of EEG abnormalities. However, when evaluating the total degree of EEG abnormalities, our results are in good agreement with the findings of Condon et al. (1954) and Skanse & Nyman (1956). A more detailed description of the electroencephalographic findings in the present material will be published elsewhere Zander Olsen et al. (1972).

During antithyroid treatment a significant decrease in the dominant frequency was noted within 2 weeks. It has not been recognized previously that the normalization of the dominant frequency occurs so shortly after the initiation of therapy. Also the most marked occurrence of spikes and sharp waves disappeared after a few weeks of antithyroid therapy. These EEG abnormalities are typical of that seen in epileptic patients and Skanse & Nyman (1956) described convulsive seizures in a patient with thyrotoxicosis. In the present study, none of the patients had epileptic attacks. During the whole period of observation, which was extended to an average of 2½ year a slight, though with the exception of slow activity, statistically significant decrease in the occurrence of all abnormalities was observed. Contrary to previous investigators (Vague et al. 1961; Wilson & Johnson 1964) who described the disappearance of slow activity following antithyroid therapy, we have found a considerable incidence of this abnormality more than 2 years after the start of antithyroid therapy. These persisting changes in EEG's suggest that hyperthyroidism may cause irreversible damage to the brain cells. We find it important to emphasize that hyperthyroidism may cause severe EEG abnormalities in the acute state of the disease as well as in the years following what appears to be an otherwise successful antithyroid therapy.
REFERENCES


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