Pyridoxine Dependent Convulsion: Effect of Pyridoxine Therapy on Electroencephalograms

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IINUMA, K., NARISAWA, K., YAMAUCHI, N., YOSHIDA, T. and MIZUNO, T. Pyridoxine Dependent Convulsion: Effect of Pyridoxine Therapy on Electroencephalograms. Tohoku J. exp. Med., 1971, 105 (1), 19-26 — In a 7-month-old boy with vitamin B₆ dependent convulsion it was found that distribution of energy % of the EEG basic waves as well as an auto-correlogram of EEG remained abnormal 24 hours after an intramuscular injection of 20 mg of pyridoxal phosphate, but both were changed to normal patterns after a long term B₆ therapy.

vitamin B₆ dependent convulsion; EEG basic waves and auto-correlogram of EEG


The present report deals with a 7-month-old boy of this disorder with special reference to EEG findings including a frequency analysis of basic waves and an auto-correlogram of them before and after the vitamin B₆ administration.

CASE REPORT

Y.T., an 8-day-old boy, was admitted to our hospital on July 21, 1969, because of frequent vomiting and convulsion. The patient was born on July 13, 1969, after an uneventful pregnancy, weighing 3.4 kg. The delivery was done by vacuum extraction. At birth there was no asphyxia. He was the first child of healthy unrelated parents. His mother had taken a vitamin B₆ preparation, 12 mg per day, from the 5th month of pregnancy through the delivery. Family history revealed that there was none having a disorder of central nervous system.

When 2 days old, convulsion and vomiting developed, and persisted until 7 days of life, when convulsive seizures and vomiting became more frequent and

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severe. On admission, on July 21, 1969, physical examination revealed a slightly poorly nourished boy with cephalohematoma on the right temporo-occipital region. Auscultation of the heart and lungs revealed no abnormalities. The abdomen was distended. The liver was palpable one finger breadth below the right costal margin and the spleen was not palpable. Neither rigidity nor spasticity of the extremities was found. Knee jerks were not exaggerated on both sides, but Babinski's sign was bilaterally positive.

After admission, frequent convulsions, consisting of general convulsions of tonic type associated with rolling up of the eyes, and of sometimes massive myoclonic jerks, occurred almost everyday. The seizures did not respond to the treatment with calcium gluconate or with anticonvulsive drugs such as phenobarbital, diphenylhydantoin, methohexital, ethosuximide, nitrazepam and acetazolamide.

On November 13, 1969, when 4 months old, status epilepticus of massive myoclonic jerks occurred. The convulsive state could not be controlled by an intravenous injection of thiopentothal. About 2 minutes after an intravenous injection of 20 mg of pyridoxal phosphate, the seizures were abolished completely.

Three or 5 days after interruption of the pyridoxine therapy, he became irritable, then being followed by massive myoclonic jerks.

The patient, at the age of 15 months, has been given orally 30 mg of pyridoxine hydrochloride per day. At the present time he has no convulsions but is mentally retarded.

Laboratory findings: Hemoglobin concentration was 15.5 g/100 ml. The white blood cell count and differential count were normal. Urinalysis was negative for sugar, protein, urobilinogen and sediments showed no abnormal findings. Normal values were recorded for the serum concentration of sodium, potassium and chloride. At the time of his admission, the serum concentration of calcium was 7.8 mg/100 ml and that of phosphorus being 8.9 mg/100 ml, but returned to normal values 2 days thereafter. The blood glucose level was found normal. A normal pattern of urinary amino acids was found by the two dimensional thin-layer-chromatography. The activities of glutamic oxaloacetic acid (GOT) and glutamic pyruvic acid (GPT) transaminases in the serum and the red cells were found to be normal. Urinary excretion of xanthurenic acid after an oral administration of 100 mg of L-tryptophan per kg of body weight (Glazer et al. 1951) was found to be within the normal limits. No urinary excretion of cystathionine was detected by an autoanalyzer of amino acids after an oral administration of 100 mg of L-methionine per kg of body weight. The activity of serine-hydroxymethylase in the leukocytes, determined by Bertino et al.'s method (1962), was found to be normal.

Electroencephalographic Study

The EEGs were recorded using a 13-channel electroencephalograph (Toshiba model DSH-013B).

The basic wave of EEG derived from the monopolar left occipital lead according to the 10-20 International System was recorded in an awake state.
For the measurement of integrated voltages of frequency bands, a two-channel frequency analyzer (Toshiba model DDA-002A) was used. The time of the integration was 10 sec. The basic waves of EEG were divided into 5 bands: δ, 2-4 C/S; θ, 4-8 C/S; α, 8-13 C/S; β₁, 13-20 C/S; and β₂, 20-30 C/S. The integrated voltages at each of the frequency bands were averaged over 6 epochs consisting of 10 sec of data. Energy % was calculated according to the following formula:

\[
\text{Energy } \% \text{ of the } \delta \text{ band} = \frac{V_\delta^2}{V_\delta^2 + V_\theta^2 + V_\alpha^2 + V_\beta_1^2 + V_\beta_2^2} \times 100
\]

The auto-correlation functions of basic waves of 60 sec of EEG were calculated according to the following formula:

\[
R_{xx}(\tau) = \frac{1}{T} \int_0^T \left[ x(t-\tau) - \bar{x} \right] \left[ x(t) - \bar{x} \right] dt.
\]

Rxx is an auto-correlation function, T is 60 sec, and τ is measured at n, where \( \tau = 16 \) msec, \( n = 0, 1, 2, \ldots \). For this estimation, an automatic analog correlator (TEAC model C-10) was used.

**RESULTS**

In order to examine an effect, if any, of the B₆ administration upon EEG findings, the oral dose of pyridoxine hydrochloride which had been continued until...

![Fig. 1. The EEG tracing 3 days after withdrawal of the B₆ therapy: High voltage irregular slow activity with spike discharges appearing independently in all areas.](image-url)
TABLE 1. Distribution of energy % of each bands of the EEG basic waves before and after an intramuscular administration of 20 mg of pyridoxal phosphate (PALP) in our patient (at the age of 7 months)

<table>
<thead>
<tr>
<th>Energy %</th>
<th>Our patient (7 months old)</th>
<th>Intramuscular administration of 20 mg of PALP</th>
<th>Controls* (7 months old)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before 8 min 3 hr 24 hr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>δ</td>
<td>69,5 92,0 83,6 61,3</td>
<td>41,3</td>
<td></td>
</tr>
<tr>
<td>θ</td>
<td>22,3 6,9 15,1 32,4</td>
<td>48,0</td>
<td></td>
</tr>
<tr>
<td>α</td>
<td>4,4 0 0,7 2,4</td>
<td>7,1</td>
<td></td>
</tr>
<tr>
<td>β₁</td>
<td>2,7 0 0,1 0,9</td>
<td>3,5</td>
<td></td>
</tr>
<tr>
<td>β₂</td>
<td>1,1 1,1 0,5 3,0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Values for controls were obtained by N. Yamauchi of our department.

TABLE 2. Distribution of energy % of each bands of the EEG basic waves after long-term treatment with vitamin B₆ (30 mg per day) in our patient

<table>
<thead>
<tr>
<th>Energy %</th>
<th>Our patient (7 months old)</th>
<th>Controls* (7 months old)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>δ</td>
<td>46,8</td>
<td>41,3</td>
</tr>
<tr>
<td>θ</td>
<td>45,0</td>
<td>48,0</td>
</tr>
<tr>
<td>α</td>
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<td>1,5</td>
<td>3,5</td>
</tr>
<tr>
<td>β₂</td>
<td>4,6</td>
<td></td>
</tr>
</tbody>
</table>

* Values for controls were obtained by N. Yamauchi of our department.

Fig. 2. An auto-correlogram of the EEG basic waves 3 days after withdrawal of the B₆ therapy.

The time of the EEG examination, was stopped, when the patient was 7 months old.

The EEG was taken 3 days after withdrawal of the B₆ preparation (Fig. 1), then examined 8 minutes, 3 and 24 hours after an intramuscular injection of 20 mg of pyridoxal phosphate (PALP).
Fig. 3. An auto-correlogram of the EEG basic waves 3 hours after an intramuscular administration of 20 mg of pyridoxal phosphate (PALP).

Fig. 4. An auto-correlogram of the EEG basic waves 24 hours after an intramuscular administration of 20 mg of PALP.

Fig. 1 shows hypsarhythmia; high voltage irregular slow activity with spike seizure discharges appearing independently in all areas.

An increase in energy % of the $\delta$ band associated with a decrease in energy % of the $\theta$ band was observed before, 8 minutes, 3 hours and 24 hours after the intramuscular injection of 20 mg of PALP in our patient (cf. Table 1).

The energy % of the $\delta$ and $\theta$ bands was normalized in our patient at the age of 7 months, who had been treated with oral dose of 30 mg of pyridoxine hydrochloride for a 3-month period (cf. Table 2 and Fig. 5).

Auto-correlograms of the EEG basic waves were examined 3 days after withdrawal of the $B_6$ therapy (cf. Fig. 2), 3 hours (cf. Fig. 3), and 24 hours (cf. Fig. 4) after an intramuscular injection of 20 mg of PALP, showing that the irregularity of the EEG basic waves was not corrected even 24 hours after the PALP injection. An auto-correlogram, taken after the long-term $B_6$ therapy consisting of oral administration of 30 mg of pyridoxine hydrochloride per day for a 3-month period, shows the EEG basic waves of the normal regularity (cf. Fig. 6).
Fig. 5. The EEG tracing after long-term treatment with vitamin B₆ (30 mg per day): Moderate or high voltage 4 per second activity without seizure discharges.

Fig. 6. An auto-correlogram of the EEG basic waves after a treatment with 30 mg of vitamin B₆ per day orally for a 3-month period.
DISCUSSION

As for EEG findings of pyridoxine dependent convulsion, it has been mentioned that the EEG reverted to the normal pattern 2-5 minutes after a parenteral administration of pyridoxine (Scriver 1960, French et al. 1965, and Swaiman and Milstein 1970), or that the EEG did not become normal soon after administration of pyridoxine but was changed to a slow wave pattern (Marie et al. 1961, Waldinger and Berg 1963, and Arima et al. 1966).

In our case, it was found that the EEG was free from spike discharges but showed an increase in slow wave activity, soon after an intramuscular injection of PALP. The EEG is still delta dominant even 24 hours after the injection. Gentz et al. (1967) reported that the convulsions disappeared soon after an institution of the treatment with 40 mg of pyridoxine per day, but the EEG pattern did not show a definite improvement until pyridoxine had been given in large doses over a period of time.

Waldinger and Berg (1963) reported that EEG tracing of a B₆-dependent convulsion at the age of 3 years who had been on a diphenylhydantoin and pyridoxine therapy, showed fairly regular activity somewhat slower than normal for age. In our case, after a long-term therapy with pyridoxine hydrochloride, the EEG pattern, its frequency spectrum and its auto-correlogram became normal.

References

11) Inuma, K., Narisawa, K., Yamauchi, N., Yoshida, T. & Mizuno, T. A case of vitamin


