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# Electroencephalographic Studies in Perimenarchial Girls

By

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EEG examinations were made in 88 healthy girls between 10 and 14 years in pre- or postmenarche, further in two groups of neurologically healthy girls of similar age, both including 25 cases, suffering from juvenile metropathy or intermittent amenorrhoea. The findings were compared with the gynaecological diagnosis and the results were analyzed statistically.

Seventy per cent of the cases showed EEG changes before the menarche and this proportion improved to 50% after the menarche. The greatest number of normal records was obtained during menstruation.

Particularly many paroxystic signs could be observed in the patients suffering from metropathy. This fact calls attention to the increase of the general convulsive disposition on the basis of hormonal disturbances. In the cases of juvenile metropathy, the EEG approached the physiological condition during ovulation, but the difference was not significant statistically. In intermittent amenorrhoea, the EEG curve was normal during menstruation, and always pathological during ovulation; this difference was significant statistically.

Brain activity recorded by electroencephalography seems to change in an irregular manner during childhood. Therefore, interpretation of the EEG is more difficult in children than in adults. In children, the initial slow rhythm becomes regular and by 6 years of age the pattern is mainly made up of theta waves, whereas by 10 years alpha waves predominate. At the onset of adolescence this continuous maturation in EEG may serve as a guideline for studying the neuroendocrine status. The prepubertal-pubertal period, especially in girls, is well signalized by different hormone productions and by changes in the secondary sex character. The present investigation has been aimed to study whether the EEG of pre- and postmenarchial girls was representing these hormonal influences as well as the events preceding the menarche, in order to forecast imbalances in the function of the subcortical neuroendocrine centre. The results then were compared to those gained in postmenarchial menstruation disorders.

## Material and Methods

The physiologic material included 88 girls, aged between 10 and 14 years. They formed two groups:

*Group A* contained 45 healthy girls not yet menstruating but already showing significant pubertal features;

*Group B* was composed of 43 healthy girls with normal menstruation.

As for the pathologic group, having selected two opposite extremes of juvenile menstruation trouble, we have examined 25 girls suffering from juvenile metropathy, and 25 who had raromenorrhoea. The upper age limit of these patients was 14 years. All of them were completely free from diseases of the nervous system.

Routine observations were made on each girl concerning the following data.

1. Stage of maturation, as judged from secondary sex character, rated from 1 to 3 for axillary and pubic hair, as well as for breast development (19, and 11 respectively).

2. Development of hymen and uterus, rated from 1 to 3 [15].

3. Demonstration of pathogens by culture, for Trichomonas vaginalis on Szeness's transport medium [18], for yeast-like fungi on Sabouraud-medium, for pyogens on blood agar, for Enterobacteriaceae on eosinmethylene blue plates. Detection of Enterobius vermicularis was done by Makara's method [12].

4. Cytohormonologic examination was done by staining according to Shorr.

5. Basal temperature curve.

Brain activity was recorded by an 8-channel EEG. The examining neurologist had no information about the patient. In the physiologic groups A and B, only one encephalogram was made of each girl, whereas three were made of those who suffered from menstruation troubles: one during menses, one at the time of supposed ovulation (14—15th day of cycle), and one immediately before menstruation (26—27th day of cycle), possibly in conformity with the phases of a normal cycle. In this way 219 encephalograms from 138 girls were evaluated in such a manner that, besides the classical and normal electric signs, the following variants were taken into consideration as demonstrative marks of more refined phenomena.

1. Lability of frequency and of amplitude (Fig. 1a).

2. Slowing of basic activity (Fig. 2).

3. Increased reaction to hyperventilation (Fig. 3).

4. Paroxysmal electric manifestations (Fig. 4).

5. Accidental focal signs.

None of these signs can be regarded as doubtlessly pathologic, whether they appear pathologic, separately or in combination, except when the deviations are accompanied by adequate neurologic signs. As such, clinical symptoms did not occur in the material examined and this is why we have judged the electrical activity as "normal" (Fig. 1) or "variation".

## Results

### *Group A Premenarche, 45 cases*

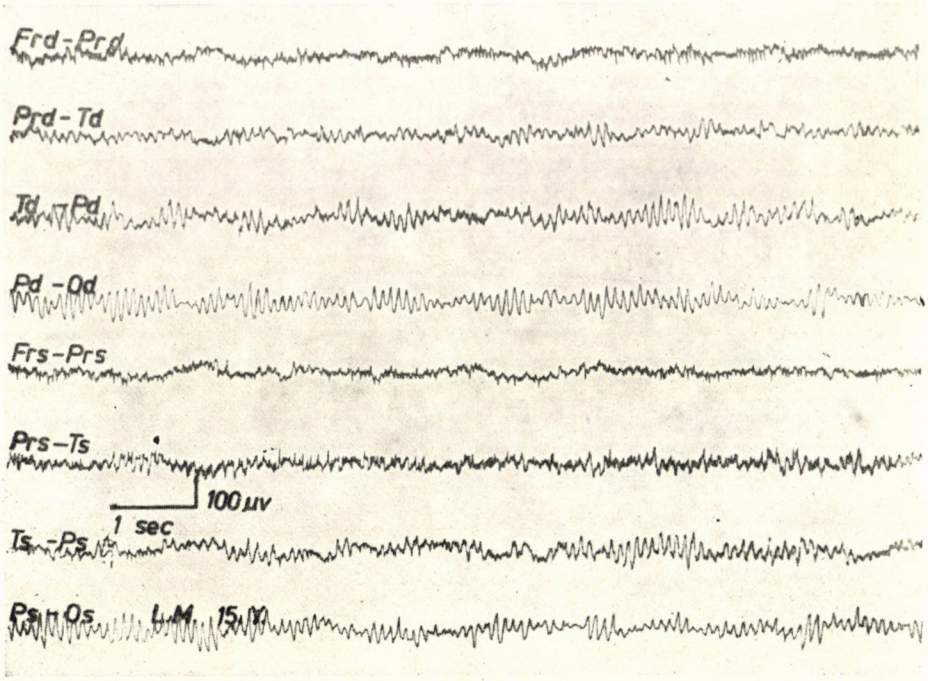
Of these, 29 girls had a vaginal discharge; besides,

| | |
|---|---|
| vaginal candidiasis | 11 |
| enterobiasis | 11 |
| trichomoniasis | 1 |
| obesity | 5 |
| nocturnal enuresis | 1 |

Development of the sex organs was recorded in order to determine whether they might have an influence on the EEG. In this respect a statistical analysis was made comparing the data of sexual development with the EEG but no statistical significance could be detected.

Regular rhythmic electrical activity was observed in 13 cases only. Nine girls showed a lability of frequency and one (who began to menstruate ten months later) showed a 5—7 c/s theta dominance.

Next, we established exact data of the menarche in the girls studied. It occurred at various intervals after the examination, from one day to 14 months, but mostly between


Frd-Prd
Prd-Td
Td-Pd
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Frs-Prs
Prs-Ts
100 µv
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L.M. 15 Y.

*Fig. 1*

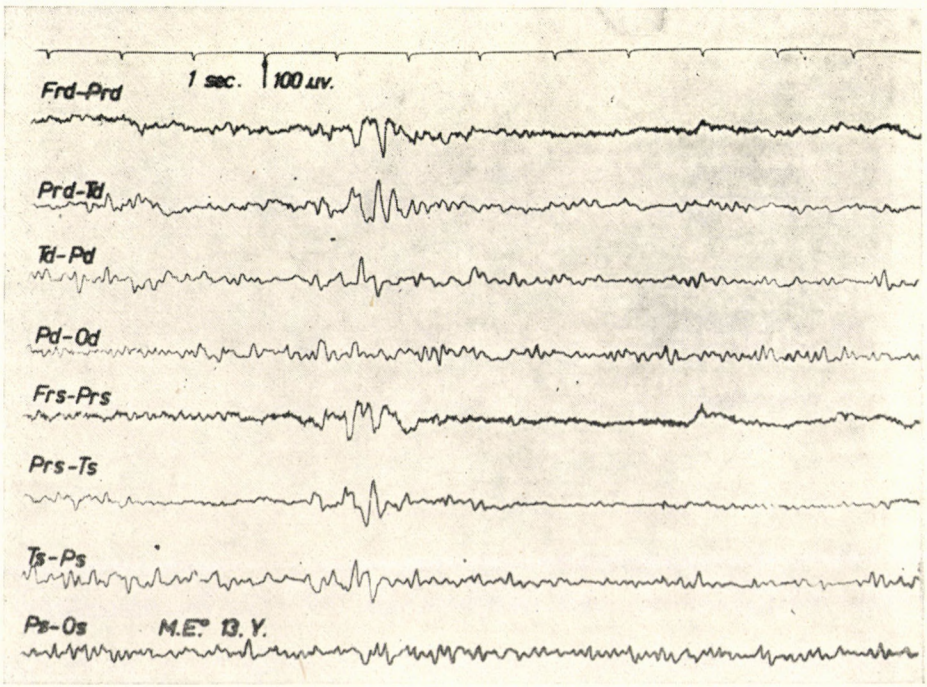
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*Fig. 1a*

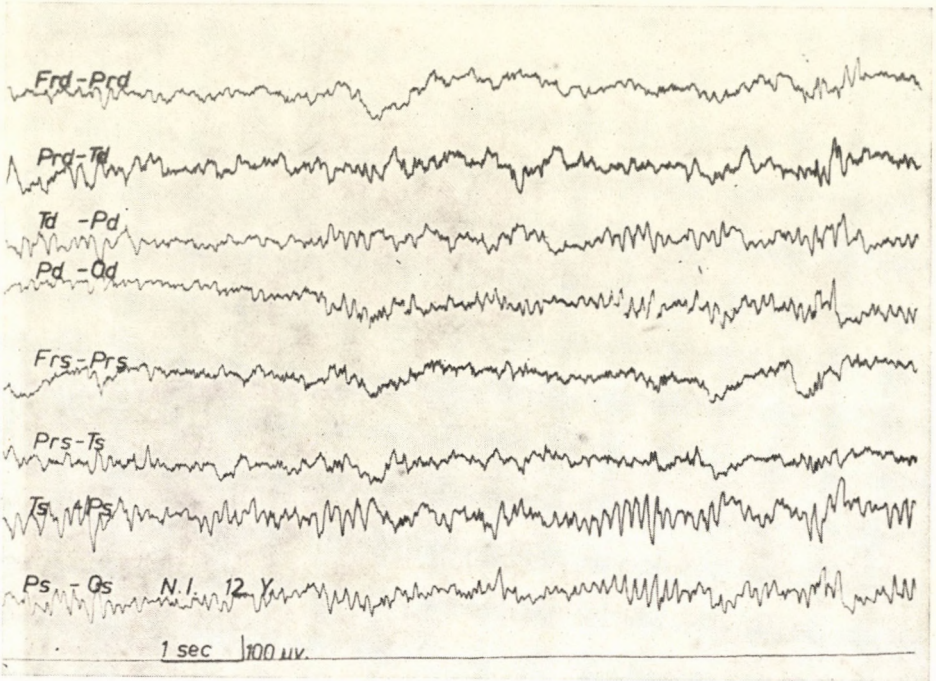
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*Fig. 2*

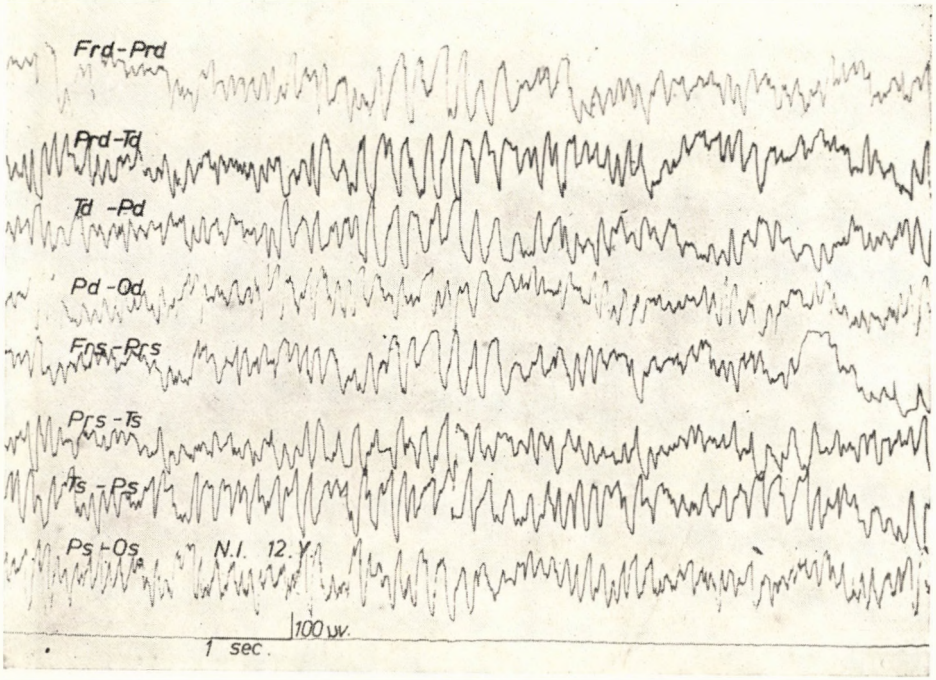
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*Fig. 3*

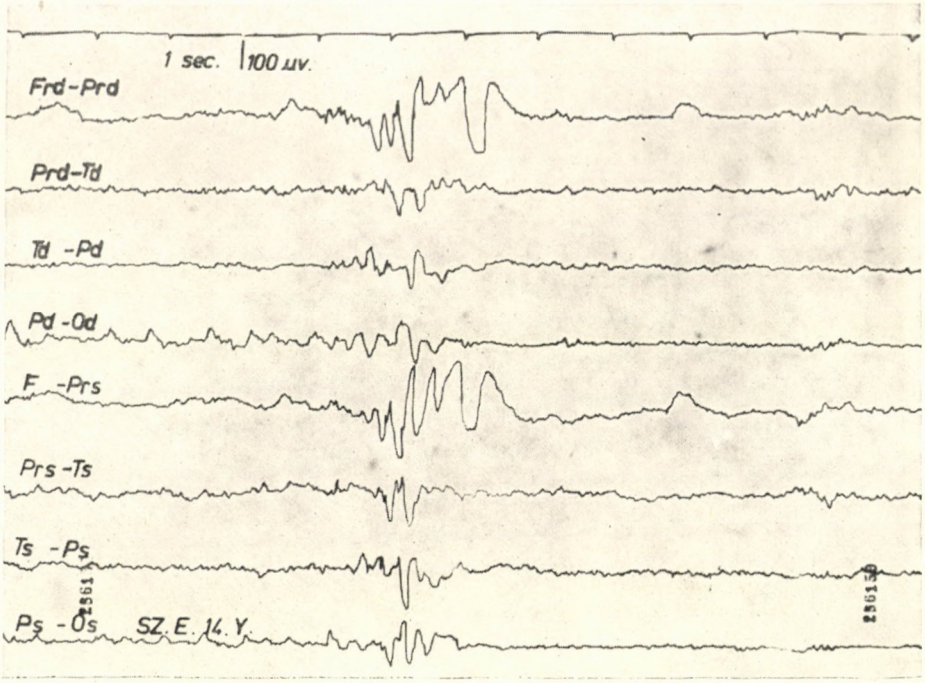


*Fig. 4*

8 and 12 months. In comparing retrospectively the time factor of each girl's menarche with the EEG variations, no significant interrelation was found, although it was clear that only about one third of the records showed rhythmic regular basic activity, the others seemed to be immature.

TABLE I

Interrelation of EEG and of menarche

| Time | EEG curves | | |
|---|---|---|---|
| | normal | variation | Total |
| 0— 6 months | 5 | 14 | 19 |
| 6—14 months | 3 | 11 | 14 |
| | 8 | 25 | 33 |

*Group B Postmenarche, 43 cases*

A distinction was made according to the menarchial history of the girls, classifying them on the basis of the duration of the menarche, but no significant association between menarchial age and EEG type could be demonstrated. At the time of the study, 22 girls had their menses since less than one year, 17 since 2 years and 4 since 3 years. The EEG of group A was constantly improving toward regular, rhythmic electrical activity, although this was not significant statistically. In group B, nearly half of the girls had curves with variations, independently of menarchial age.

TABLE II

Interrelation of EEG and phases of the cycle

| EEG | Phase I (sub mensem) | Phase II (ovulation) | Phase III (premenstrual) | Total |
|---|---|---|---|---|
| normal | 22 | Ø | 1 | 23 |
| variation | 17 | 2 | 1 | 20 |
| | 39 | 2 | 2 | 43 |

The following diseases could be demonstrated in group B:

| | |
|---|---|
| enterobiasis | 9 |
| vaginal candidiasis | 7 |
| trichomoniasis | 3 |
| obesity | 5 |

The data obtained were grouped according to the different phases of the menstrual cycle, taking into account the day of the cycle on which the EEG examination was carried out. In this group, a relatively higher frequency of rhythmic, regular curves was observed for 1—5 days during the menstrual flow, whereas the distribution in the other three phases seemed to be equal. Statistically, this was not significant.

In two records, a moderate increase of low frequency has been observed; in 8 records, the amplitude was very low.

*Group C = Juenile metropathy, 25 cases*

Appearance of irregular abundant bleedings outside the cycle soon compels the patient to visit the doctor. Thus ten girls were seen at the paediatric gynaecology clinic during the first six months following menarche and the others were in their first menarchial year. When hormonal treatment was given to these girls, we have always taken into consideration the drugs administered, in view of their influencing our results. Thus, oestrogen was administered to four girls in the ovulation period, progesteron once sub mensem, and two times in premenstruum. Lynoestrenol was prescribed to three girls in the premenstrual period.

Independently of the time since the menstrual onset, two-thirds of the curves showed an alteration in the slow wave pattern of group C. A biphasic flat basal temperature curve was observed in half of the girls, while the other half had monophasic curves. A comparison of these two types revealed that the basal temperature had no influence on the EEG.

Fourteen girls were treated exclusively with vitamin E during the whole period of investigation, and ten girls received alternately hormone substitution and vitamin E. Two girls were treated by hormone alone. One girl was subjected to two serial EEG examinations, and was thus investigated 6 times during two consecutive men-

strual cycles. Alterations of different types have been detected in 36 girls who obtained vitamin E, in 10 girls who were treated with hormones, and in 2 girls without treatment. The differences were not significant statistically.

The EEG-s showing a marked slowing of the background activity and some paroxysmal phenomena in the various phases of the cycle were found to display alterations during the menstruation in 80% and in the two other phases in 50%. These changes were, however, not significant statistically. When considering the EEG records of all the girls, i.e. calculating also stable unchanged curves during the whole cycle, the difference disappeared completely.

In group C, we observed remarkably more EEG curves with paroxysmal tendencies. This suggests the possibility that the metropathic hormonal dysfunction may contribute to the convulsive disposition, and it supports the experience according to which even treated and compensated epileptic girls have seizures at the onset of menstruation. The examined EEG-s leave the impression that the hormonal activity of the patients suffering from menstruation troubles of this type approaches physiological conditions at the time of ovulation; it is in this period that electrical activity is most balanced, while it has a distinctly altered aspect during menses. The small number of our cases (25 subjects, 73 EEG records) did not allow to draw a final conclusion.

*Group D Raromenorrhoea, 25 cases*

The girls examined because of this type of disease were mostly in their second or third menarchial year and the absence or an irregular delay of menstruation lasted since 6—12 months. The majority of the patients (19 cases) were treated with vitamin E; no other drugs were employed.

About two-thirds of the EEG curves in this group had altered patterns during the cycle examined. Similarly, about two-thirds of those who had their menarche more than one year also showed a slight or moderate

TABLE III

Juvenile metropathy
Interrelation of EEG and phases of the cycle

| EEG | Phase I (sub menses) | Phase II (ovulation) | Phase III (premenstruum) | Total |
|---|---|---|---|---|
| normal | 2 | 4 | 4 | 10 |
| variation | 8 | 3 | 4 | 15 |
| | 10 | 7 | 8 | 25 |
| | $\chi^2 = 2.85$ [2] | $P < 0.1$ | | |

TABLE IV

Raromenorrhoea
Interrelations of EEG and phases of the cycle

| EEG | Phase I (sub mensem) | Phase II (ovulation) | Phase III (premenstrual) | Total |
|---|---|---|---|---|
| normal | 5 | Ø | 2 | 7 |
| variation | 2 | 8 | 6 | 16 |
| | 7 | 8 | 8 | 23 |
| | $\chi^2 = 9.13$ [2] | $P < 0.05$ | | |

increase of low frequency activity, at least once in the course of the cycle. Among the 8 girls menstruating since less than one year, there was only one whose EEG was regular, rhythmic in all three examinations. Furthermore, we have not observed interrelations with the basal temperature; in the case of both biphasic and monophasic curves, the alteration of the slow wave EEG pattern showed a proportion of about 2/3.

As for the treatment consisting exclusively of vitamin E, 27 of the treated and 10 of the untreated patients showed some alteration of the EEG pattern. The difference was not significant statistically.

As in the metropathic patients, in girls whose EEG curves showed various electrical patterns during the various phases of the cycle, there was a pronounced lability of frequency and amplitude in 30% of the cases during menstruation, in 100% during the ovulation period, and in 75% during the premenstrual phase. This difference was significant statistically ($P < 0.05$). Taking into consideration the EEG records of all girls, the difference in distribution persisted. Thus, the EEG was the most regular during menstruation, like in the cases with normal menses; it was then that the hormonal activity approached the physiologic state. At the time of ovulation, however, electric activity was always dysrhythmic.

## DISCUSSION

The first part of our investigation, involving 88 healthy perimenarchial girls with single EEG records, only tended to reflect a poorly studied area in the pubertal period. We could not gather more data, but literature is equally scarce in this field. TANNER [19] already pointed at the discrepancy appearing in the pertinent papers and emphasized the need for further investigations of this kind. HENRY [10], ELLIS and LAST [2], SMITH [17] observed in the pubertal period a significant sexual difference in alpha rhythm, with a higher frequency in girls as compared to boys. Recently, PETERSÉN and EEG-OLOFSSON [16]

have carried out investigations in 743 selected children, 389 girls and 354 boys concerning the EEG development in relation to age and sex. They found that girls responded significantly more intensely than boys to hyperventilation and intermittent photic stimulation. They stressed the importance of maturational factors in the differences. Although we had no male control cases, in the girls we observed a relative lack of faster waves, and a lower than usual amplitude of alpha activity.

In the premenarchial state, 70% of the curves displayed a slight or moderate increase in low frequency activity. After menarche, independently of age, secondary sex character and menstrual history, the incidence of this alteration decreased to 50%. To investigate the cause of the improvement, a comparison was made between the EEG and the basal temperature. Although in the postmenarchial group 27 girls showed biphasic basal temperature curves, these were independent of the EEG change. In any case, a regular, rhythmic electrical activity was observed by us mostly during the 1st to 5th menstrual days, while the ovulation periods and the secretion phases showed some reduction in alpha activity. It is therefore suggested that the hormonal steady state is appearing in well pronounced rhythmic EEG records sub mensem and perhaps it is the hormonal imbalance which might be taken into consideration in the interpretation of the lability of cerebral electric activity.

Since the EEG had become a routine diagnostic procedure, several authors have studied the manifestation in electric brain activity of menstrual disturbances. Dusser de Barenne and Gibbs [1] examined daily electroencephalograms of 11 healthy young women during at least one menstrual cycle and noted day-to-day variations in the electrical activity in all cases. This study revealed no rigid relation between cortical activity and the menstrual cycle, but in the majority of women the activity became slower after the beginning of menstrual flow and in some a disturbance in frequency regulation occurred at the midmenstrual period. Heiss and Lechner [9] observed in 17 women between 20 and 30 years of age suffering from serious dysmenorrhoea an accumulation of alpha rhythm during menstruation simultaneously with slower potentials, as well as with a mild dysrhythmia and slight alterations. Faure and Guérin [4], further Faure et al. [5] examined 250 adult women, searching for a relation between the EEG curve and the hormonal changes occurring during the cycle. They succeeded in separating several groups on the basis of clinical and laboratory results, which seemed to be reflected in the EEG, e.g. hyperfolliculinuria, hyperluteinism, lutein insufficiency. Then, Faure and Loiseau [3] repeated the examination in 40 cases with hormonal disturbances and confirmed that the EEG alterations were related to the 17-ketosteroids, 17-hydrocorticosteroids, 11-oxysteroids and to the increase of pregnanediol. No studies

are, however, known concerning girls with postmenarchial bleeding disorders during maturation.

The effect of sexual hormones on the EEG is well known from animal experiments. MALYSHENKO [13] induced hypersynchronization in female rats by administering oestrogens, while progesterone caused a rapid decrease of amplitude and a slowing of rhythm. Hormonal anticonception opened new possibilities in research. GRAUDENZ and HELLER-FICHTNER [8] examined 33 epileptic and 40 non-epileptic women taking the pill and confirmed the increased disposition to convulsions of the epileptics, having observed seizures. FERRONI et al. [6] examined 36 non-epileptic women treated with synthetic oestroprogestogens and found a small number of pathological curves. ZAICHKINA [20] observed 60 women suffering from menstruation epilepsy during several cycles, and stated that the seizures were caused less by the absolute or relative lack or abundance of sexual hormones than by disturbances in their balance which involved changes in diencephalic activity. This may explain our own pubertal and hormonologically instable cases, in which we could not demonstrate direct connections between the hormonal level and the EEG picture, but the curve exhibited different alterations during the cycle.

Finally, we wish to mention the data published by GAUTRAY et al. [7] who charted by computer 2 healthy and 4 anovulatory cycles; the latter were treated with clomifene. These authors showed that the theta waves reached their maximum before ovulation, whereas the alpha waves were at the minimum in this phase. In the lack of similar possibilities of evaluation, we can only state that in our cases physiological EEG records occurred in a significant number during menstruation in patients with raromenorrhoea. In contrast, in the patients with juvenile metropathy, a pattern approaching the physiologic type occurred at the time of ovulation.

MATSUMOTO et al. [14] reported their EEG observations in patients on prolonged combined oestrone-progesterone treatment. A slow spindle was observed in all the patients with amenorrhoea and anovulatory cycles, regardless of the kind of drug administered, whereas it did not appear in the controls displaying a normal menstrual cycle. It has been concluded that the wave patterns are in some way related to ovulation.

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