CIRCADIAN DYSRHYTHMIAS IN THE EEG OF CHILDREN WITH CLONAZEPAM TREATMENT

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ABSTRACT

The effects of different anticonvulsants on the system of circadian and ultradian rhythms in the EEG of children was investigated in ten 24-h recordings of children with different forms of epilepsy. Circadian dysrhythmias could be found in children with Clonazepam treatment.

KEYWORDS

Circadian dysrhythmia, EEG, Anticonvulsants, Chronobiologic Frequency profile, Clonazepam

INTRODUCTION

It is a generally accepted fact that medication with anticonvulsants is connected with numerous physiologic and psychologic side effects which depend on the choice of medicaments (Kutt and Louis, 1972), and changes of behavioral schedules (sleep, activity, etc.) can often be observed. The purpose of this study is the detection of eventual changes in the EEG rhythm spectrum due to different anticonvulsants.

METHOD

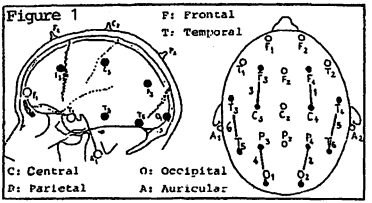
Ten 24-h-EEGs were recorded for children suffering from different forms of epilepsy. There were four medication groups which are shown in table 1.

Table 1: Different medication groups (classification of subjects)

Ø	No medication (2 subj.,average age 15.5 months)
P	Phenobarbital (2 subj.,average age 11.5 months)
CP	Clonazepam and Phenobarbital (4 s.,av.age 13.8 m
C	Clonazepam (2 subj., average age 9.5 months)

The EEG was recorded using small-surface chlorinated silver electrodes which were pasted to the child's head according to a reduced Ten-Twenty-system (Figure 1). On-line computations of 5-minutely "frequency histograms" (see Meier-Koll, 1978, Arbogast et al., in press) to obtain EEG characteristics to be used for for further analyses. Spectral analyses of variance were computed,using the data of the temporal and parieto-occipital channels of the left hemisphere, within eight chronobiologic period ranges from 24 hours to 45 minutes (see Arbogast, 1984). Multiple classification analysis based on spectral analysis of variance was applied to quantify the effects due to medication. Chronobiologic frequency profiles (see Arbogast, 1984, Arbogast et al., in press) were used to summarize results.

Figure 1



RESULTS

The impact of medication on the spectrum of chronobiologic rhythms in the EEG was found to be highly dependent on the choice of anticonvulsants. In terms of percentual contributions of different chronobiologic periodicities to the total variability in the EEG, the following statistically significant effects could be detected ($p < .05$):
Circadian variation is slightly increased in case of Phenobarbital treatment, while Clonazepam seems to cause a strong reduction. The semidian component is reduced in case of Phenobarbital or Clonazepam treatment (groups P and C, see table 1). A prominent 8-hour component can be found in EEG variation of children treated with Clonazepam (group C in Table 1). Circaduohoran rhythms are more prominent for all kinds of medication, especially for Clonazepam alone (group C in table 1). Figure 2 displays all significant medication effects graphically

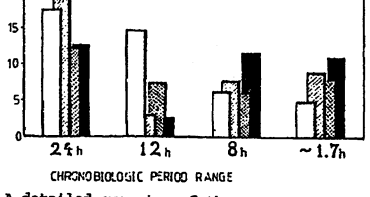


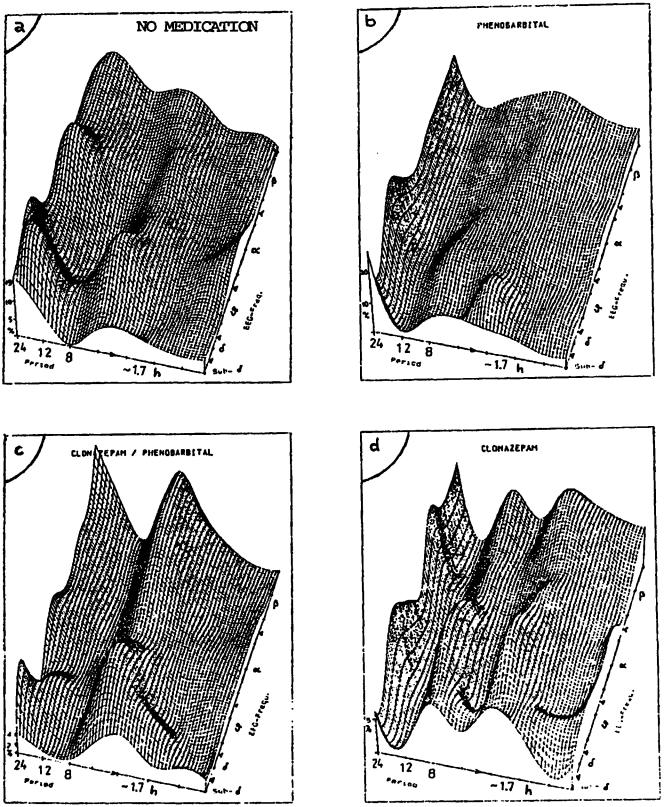
Figure 2:

Bar Diagram of rhythm percentages of different chronobiologic periods in the EEG within different medication groups (total of 10 children with ages ranging from 8 to 20 months. Results of spectral analyses of variance including multiple classification analysis.

□ : No medication
▨ : Phenobarbital
▩ : Phenobarbital and Clonazepam
■ : Clonazepam

A detailed overview of the average structure of chronobiologic rhythmicity within the four medication groups is given by the chronobiologic frequency profiles in figure 3. The strong effects of Clonazepam treatment can be seen by comparing c), d) to a), b).

Figure 3



Chronobiologic frequency profiles for children with different forms of therapy: Percentual contribution (z-axis) of different chronobiologic periodicities (x-axis) within different EEG frequency ranges (y axis). a) 2 individuals, 11 resp. 20 months; b) 2 individuals, 11 resp. 12 months c) 4 ind., 11,12,12, resp. 23 months; d) 2 ind., 8 resp. 11 months of age.

DISCUSSION

Up to now, only time-unspecified side effects of anticonvulsants were considered and described : sleepiness, general tiredness, reduced mental ability and specific physiologic changes (compare Kutt and Louis, 1972).
In this study, it could be shown that medication with anticonvulsants can also cause circadian dysrhythmias in the EEG. Especially if the medicament of choice is Clonazepam, the circadian component is strongly reduced while ultradians become predominant, corresponding to behavioral observations which can often be made in clinical routine. Dyschronisms of this kind can eventually be avoided if therapy is oriented towards chronopharmacological aspects, which is postulated by Halberg (1978) because of evident circadian receptor rhythms in the CNS.

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