A Case Study on Circadian, Ultradian and Homeostatic Processes of Sleep Regulation in a Pubescent Child with Epilepsy

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Key words: pubescent child, epilepsy, sleep regulation, EEG delta activity.

Abstract

To examine three separate processes (homeostatic, circadian and ultradian processes) of sleep regulation in a school-going pubescent girl with epilepsy, the consecutive 7-day motility and two-night polysomnographic sleep were monitored and analyzed. The motility showed a circadian rest / activity rhythm with a nearly 24-hour interval. Ultradian alternation of NREM sleep and REM sleep (sleep cycle) was observed with an interval of about 102 min. EEG delta power during NREM sleep was found to significantly decline as a function of sleep cycle, independent of EEG epileptic discharges which were activated during NREM sleep. Homeostatic sleep regulation is not likely to be disturbed by epilepsy. These results suggest that three major processes of human sleep regulation may work fairly in the present child who took anti-epileptic medication chronically.

Introduction

Human sleep is assumed to be regulated by three separate processes; homeostatic, circadian, and ultradian processes (1). A homeostatic process is a sleep / wake dependent process (Process S) which underlies the rise in sleep pressure during waking and its decay during sleep. The time course of this process is estimated from EEG delta activity which is used as an indicator of NREM sleep intensity. A circadian process is a nearly 24-hour rhythm, controlled by multimodal oscillators, of the sleep / wake cycle or body temperature. An ultradian process regulates the cyclic alternation of NREM (nonREM) sleep and REM sleep with a short interval of about 100 minutes.

"Does my child really sleep at night?" This is one of the worries that parents often have about their epilepsy-affected child. It seems likely that anti-epileptic medication, which suppresses seizures and produces profound behavioral inhibition, will induce an apparent sleep-like state during the night. This study aimed at finding objective evidence of the above-mentioned three separate processes of sleep regulation in a school-going pupil with epilepsy. The first approach employed in this study was an activity-based monitoring of sleep / wake cycle. Actigraphy is a useful tool to examine a circadian sleep / wake cycle or rest / activity rhythm not only for adults but also for children (2). The second step was all-night polysomnographic (PSG) recording to examine an ultradian alternation of NREM sleep and REM sleep. Finally a spectral analysis of sleep EEG

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was performed for EEG delta activity which is known as a useful indicator of NREM sleep and a good marker of homeostatically regulated sleep processes in adults (1). The computer-based automatic detection of EEG epileptic activities was attempted to assist reading and not for diagnosis.

Method

A 15-year-old school-going girl participated in this study as a volunteer. She was first affected by convulsions about 4 months after birth and taken to hospital at 7 and 9 months of age. Anti-epileptic drugs (carbamazepine and sodium valproic acid) were regularly taken in the morning and in the evening. Informed consent was obtained from her mother concerning the present study.

Daytime and night motility was recorded on seven consecutive days by using a wrist actigraph (Ambulatory Monitoring Inc.) worn on the non-dominant hand. The volunteer was willing to wear the wrist-watch-type motion sensor. The actigraphic data, consisting of the number of zero crossings with a resolution of 0.01 G / rad / sec, were registered every minute. Scoring of sleep and wake conditions was automatically performed (application program: Action-W, ver 2). The volunteer slept two nights with her usual bed-time routines in the sleep laboratory during the actigraph- monitoring periods. Standard PSG recordings (3) were made using a digital polygraphic amplifier system with a sampling frequency of 100 Hz: central electroencephalograms (EEGs) with referential derivation from regions C3 and C4, electrooculograms (EOGs) with referential derivation from outer canthi of right and left eyes, electromyogram (EMG) and electrocardiogram were recorded. The first night was used for adaptation to the recording environment because the volunteer was a novice to all-night sleep recording. After the volunteer was awakened at the scheduled time in the morning, the subjective sleep perception was interrogated.

Data on the second night were analyzed. The standard scoring system of sleep stages (3) was partially employed here, because the system was designed for normal, usual sleep patterns of adult humans, not for abnormal or deviant normal EEG patterns (4). One major interest of this study concerned confirmation of a cyclic alternation of NREM sleep and REM sleep. PSG records were visually classified for each 10-sec epoch into five states: waking, NREM sleep (roughly corresponding to stages 1, 2, 3, and 4 of standard scoring system (3)), REM sleep, ambiguous state with lowered muscle tone and no rapid eye movements against the background of low-voltage EEG, and epilepsy dominant state in which the percentage of time occupied by EEG spikes and sharp waves was more than 50 %. EEG power spectra were computed for each epoch using a maximum entropy method, and summed powers were obtained for five bands: delta (1-4 Hz), theta (4-8 Hz), alpha (8-13 Hz), sigma (13-15 Hz) and beta (15-20 Hz). Artifact elimination was visually performed for epochs which were scored as movement time (MT).

EEG epileptic patterns, which were observed on two-night PSG recordings of the volunteer, mainly consisted of spikes and sharp waves. Epilepsy-related spikes and sharp waves are known as a transient, clearly distinguished from the background EEG activity, with a negative amplitude and a short duration from 20 msec to 200 msec (5). Automatic detection of the spikes and sharp waves was made by applying the method of a moving linear regression analysis which had been originally developed for slow and rapid eye movements during hypnagogic state and during sleep (6, 7). The main algorithm was that the arctangent to a slope of a regression line, i.e. an absolute value of angle (degree/Δt), was computed in each 30-msec window which moved with a

step of 10 msec because the angle was considered as the velocity index of EEG. In this study spikes and sharp waves were identified as a triphasic waveform (P1-N1-P2) with a high-amplitude negative peak. Detection criteria of the waveform included (a) N1-P2 peak (a large negative peak) amplitude of more than 160 μV; (b) P1-P2 peak time of more than 50 msec and less than 150 msec; (c) angle of more than 75 degree/Δt.

Results

Examples of outcomes of automatic detection of EEG epileptic activities are given in Fig. 1. Eleven outputs of detection were signaled coincidently with original spikes and sharp waves, and three kinds of parameters of the triphasic wave forms were precisely measured: peak amplitude (PA), peak time (PT) and angle. The total number of detected spikes and shape waves was 17,136 on the one-night PSG record. The average values of waveform parameters were 343.4±123.2 μV for PA, 94.4±14.3 msec for PT, and 81.1±2.8 degree/Δt for angle.

Actigraphic data, as illustrated in Fig. 2, revealed a circadian rest / activity rhythm (sleep / wake cycle) with an averaged bed-time interval of 24.1 hrs±51.3 min. Daytime activity increased high but began to vary irregularly after school and toward the evening. Night motility remained low and any epilepsy-related behaviors (seizures) were not recorded during the rest phase (sleep). On Saturday the volunteer had a 2-hour daytime nap and the timing of sleep became later by about 60 min than weekdays, but on Sunday a readjustment of the rhythm was made to her usual bed-time routine. Amounts of sleep seemed constant through seven days. The parameters of behavioral sleep were computed and the outcomes were as follows: sleep time 494.6±19.3 min, sleep efficiency 9.6±0.6 %, sleep latency 7.3±1.9 min, and waking minutes after sleep onset (WASO) 2.1 ±2.7 min. Taken together, the volunteer seemed to be a good sleeper in terms of motility.

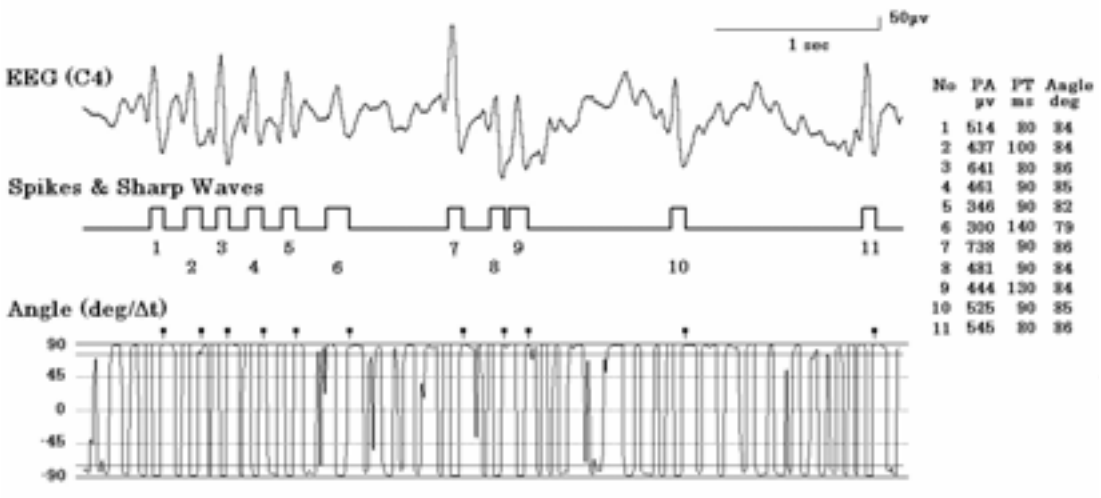

Fig. 1 Examples of automatic detection of EEG spikes and sharp waves.

Outcomes of automatic detection of epilepsy-related spikes and sharp waves are numbered from 1 to 11 on the second trace. The processing of angles within a 30-msec moving window is drawn on the third trace. Measurements of waveform parameters (peak amplitude, peak time and angle) are listed on the right columns.

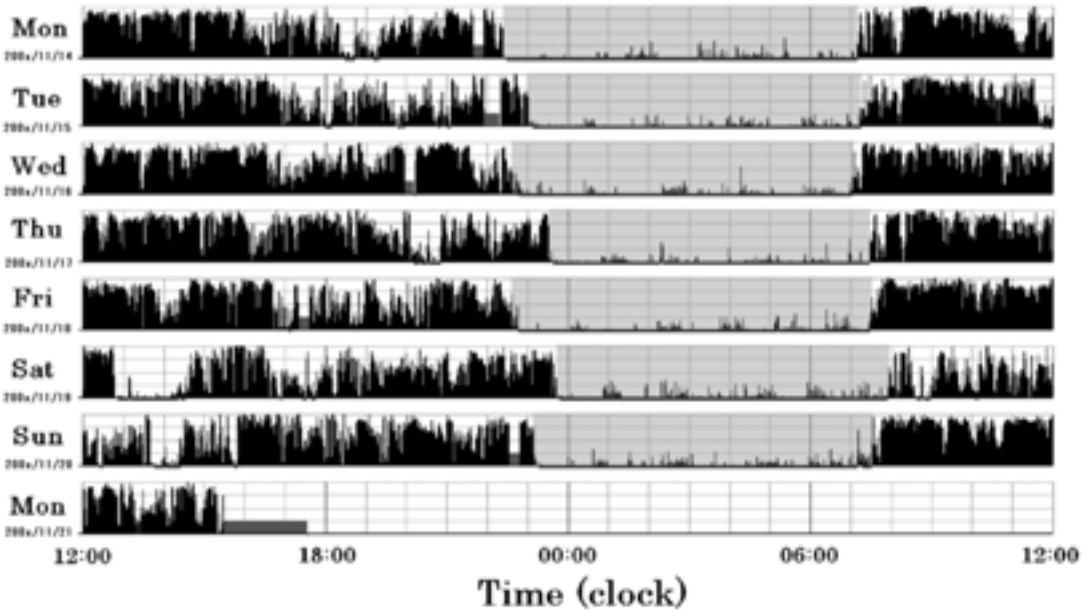

Fig. 2 Actigrams obtained by recording on seven consecutive days.
Activity is plotted every minute with a vertical solid line. Seven time zones with lowered activity are gray-colored, indicating rest phases (sleep).

The time course of all-night PSG and EEG band powers is drawn in Fig. 3. EEG power was normalized every epoch with respect to over-night summed power (100 %) for each EEG band, because it seemed best to use the same scale for all five EEG bands when comparisons between bands were to be made. At the top of the figure, sleep states indicate that the child fell into sleep quickly with sleep latency of 8.2 min, the elapsed time from the lights-out till the first epoch of NREM sleep. Sleep efficiency, the ratio of total sleep time to time in bed (480 min), was 88.8 % which was near to the lowest value (85 %) of normal sleep efficiency. The reduced efficiency may be explained by the following two facts: one is low percentages of REM sleep (2.2 %) and NREM sleep (58.6 %) and the other a higher percentage of miscellanea, comprising an ambiguous state (25.4 %), epilepsy dominant state (2.5 %) and WASO (7.9 %, 37.8 min). Ambiguous states were common around the beginning and the ending of REM sleep episodes. REM sleep episodes were often interrupted, except for the last episode which began 6.5 hours after the lights-out and lasted about 15 min. The appearance of MT (13.5 min, 2.8 %) was often coincident with the ambiguous state. After the time-consuming and laborious classification of PSG records into five sleep states, sleep cycles were defined as periods from the beginning of one NREM sleep episode, followed by REM sleep episode, to the beginning of another one. The volunteer alternated NREM / REM sleep cycles four times a night, lasting an average of 102.3 ± 16.7 min. Correspondingly each of five EEG band powers showed the cyclic change in intensity which was characterized as increasing during NREM sleep episodes and as decreasing during REM sleep episodes.

Furthermore, EEG powers significantly declined as a function of sleep cycle only in delta activity ($\tau = -1$, $p<0.05$). Note that EEG epileptic activities were activated during NREM sleep episodes and silent

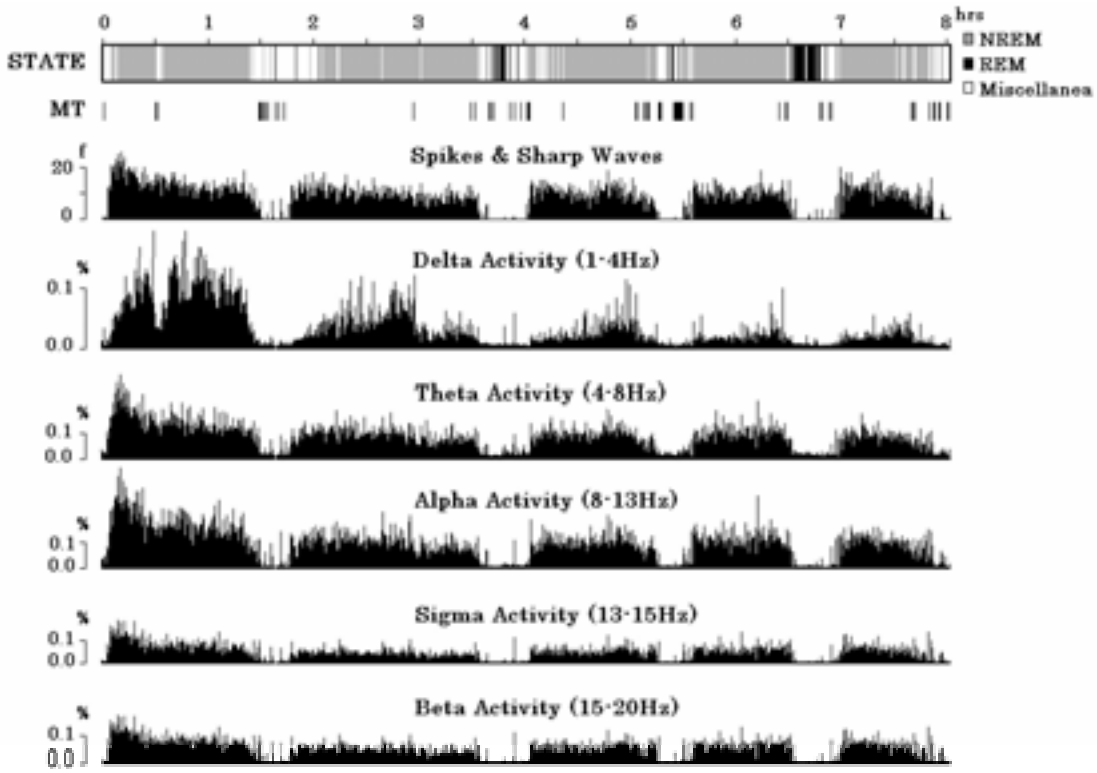

Fig. 3 Cyclic changes in EEG powers and epileptic activities during night sleep.
States: NREM sleep, REM sleep and Miscellanea comprising ambiguous state, epilepsy-dominant state and waking. MT: movement time. f: the number of detected EEG spikes and sharp waves. Normalized powers (%) of five EEG bands were plotted, respectively.

during REM sleep episodes and waking. Then it was examined whether the decay of EEG delta power along sleep cycles might be related to changes in appearance of EEG spikes and sharp waves. Pearson's product-moment correlation coefficients between EEG powers and the number of spikes and sharp waves were computed for each epoch for each of five EEG bands, and the coefficients were averaged for each sleep cycle. The outcomes were plotted in Fig. 4. Powers of delta band (mean r = 0.12±0.10) and of beta band (r = 0.16±0.12) yielded consistent lower correlations with epileptic activities from the second cycle through the fourth cycle, except for the first sleep cycle. The remaining EEG band powers kept higher correlations for all sleep cycles (theat: 0.38±0.09, alpha: 0.39±0.07 and sigma:0.32±0.08). The result suggested the likelihood that the decay of EEG delta power during NREM sleep may take place independent of epilepsy.

Discussion

The findings in this study provide evidence of three separate processes of sleep regulation (1) in the present epilepsy-affected child. The results of actigraphic analyses of motility demonstrated the circadian rest /

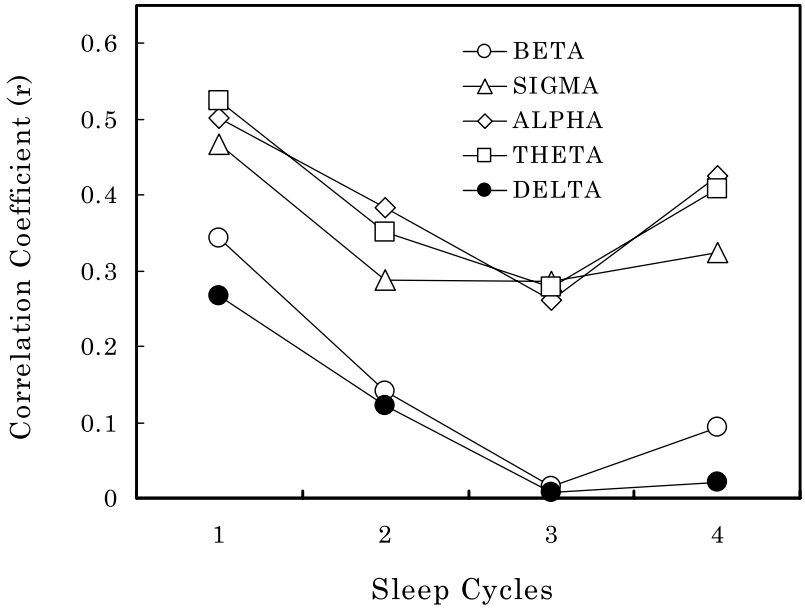

Fig. 4 Correlation of EEG powers and epileptic activities during night sleep.
Pearson's product-moment correlation coefficients were computed between EEG band-powers and the number of epileptic spikes and sharp waves.

activity rhythm which was fairly entrained to a day and night cycle. The ultradian alternations of NREM sleep and REM sleep were confirmed on the time course of sleep states and of EEG powers. The significant decay of EEG delta power, which took place as a function of sleep cycles and independent of EEG epileptic discharges, suggest that homeostatic sleep regulation (2) might not be disturbed.

Cyclic alternations of NREM sleep and REM sleep seen in the present child may be explained by the fact that the chronic administration of an anti-epileptic drug (carbamazepine) does not disrupt REM sleep (8). REM sleep episodes were often interrupted, however. The percentage of appearance of ambiguous states, characterized by the lowered muscle tone and no rapid eye movements against the low-voltage EEG background, seemed to be highly similar to the percentage of REM sleep known in normal sleeper. This study can provide no direct evidence to prove whether the ambiguous state might be parts of REM sleep episode or not.

Finally, the automatic detection of EEG epileptic activities in this study exhibited differences in occurrence of spikes and sharp waves between periods during NREM sleep and REM sleep; they were common and frequent during NREM sleep while seldom seen during REM sleep. This result seemed to be in line with the finding of activated epilepsy during NREM sleep (9). It should be considered with caution regarding automatic detection of epileptic spikes that the precise definitions of spikes are still difficult and vary from researcher to researcher (5).

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