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Detection of Paroxysms in Long-Term, Single Channel EEG-Monitoring of Patients with Typical Absence Seizures

Troels W. Kjaer, Helge B. D. Sorensen, Member, IEEE, Sabine Groenborg, Charlotte R. Pedersen and Jonas Duun-Henriksen

Abstract—Absence seizures are associated with generalized 2.5-5 Hz spike-wave discharges in the EEG. Rarely are patients, parents or physicians aware of duration or incidence of seizures. Six patients were monitored with a portable EEG-device over four times 24 hours to evaluate how easily outpatients are monitored and how well an automatic seizure detection algorithm can identify the absences. Based on patient-specific modeling, we achieved a sensitivity of 98.4% with only 0.23 false detections per hour. This yields a clinically satisfying performance with a positive predictive value of 87.1%. Portable EEG-recorders identifying paroxystic events in epilepsy outpatients are a promising tool for patients and physicians dealing with absence epilepsy. Albeit the small size of the EEG-device, some children still complained about the obtrusive nature of the device. We aim at developing less obtrusive though still very efficient devices e.g. hidden in the ear canal or below the skin.

Index Terms— Absence Seizures, Automatic Seizure Detection, Epilepsy, Single Channel EEG, SVM

I. INTRODUCTION

A dilemma when treating patients with epilepsy is that the attending physician does not know the number of seizures, and often the patient does not know it either [1]. The physician works with an otherwise normal patient with seizures happening elsewhere and the patient might be unaware of the episodes. Devices that record the seizures during normal everyday life conditions may reduce this problem.

Use of outpatient ambulatory electroencephalogram (EEG) began 50 years ago. At first the recording systems were large and heavy, the data quality poor and time to mount considerable. Since then the data quality has improved and the number of channels increased [2]. Now numerous portable recording systems of up to 36 channels with sampling rates of up to 400 Hz are commercially available. We currently work on unobtrusive solutions like a small earplug that communicates with a smartphone and is easily mounted by the patient in a few seconds [3]. This allows for access to real time registration as well as intervention and alarm systems.

Clinical investigations have documented that ambulatory EEG can record focal and generalized epileptiform activity [4], [5]. Several studies of long term (up to a few days) EEG recording has proven useful when validating a diagnosis of epilepsy, do seizure classification or when identifying seizure onset zone in patients undergoing epilepsy surgery workup [6]. Several studies have also found that ambulatory EEG monitoring is a useful tool in patients with generalized discharges [7], [8]. Furthermore, the number and location of electrodes is likely to be less important than in focal epilepsies [9]. When EEG is performed in the clinic in a short time slot at a specific time of day, much clinical important information is likely to be lost compared to repeated 24-h measures in the natural environment.

Especially within many idiopathic generalized epilepsies, there is a clear advantage of repeated EEG recordings. There exist a correlation between the amount of anti-epileptic drug intake and the number of seizures they have [10]. But the drugs entail considerable adverse effects [11] that should be minimized by optimization of treatment dosage.

In order to explore this central schism in epilepsy treatment we chose to investigate patients with typical Absence Seizures with repeated 24-h EEG recording at home. Typical Absence Seizures are seen in childhood absence epilepsy (CAE) and juvenile absence epilepsy (JAE) which are relatively common epileptic syndromes. Absences are characterized by rhythmic generalized 2.5-5 Hz spike-polyspike-wave paroxysms in the EEG [12]. Clinically, absences are characterized by sudden loss of awareness, a blank stare often with upward eye deviation and cessation of normal activities. On average the ictal duration is 9.4 ± 7 s and due to their subtle nature they are often overlooked by the surroundings [13]. In a study with ambulatory cassette EEG it was found that parents only
registered 6% of paroxysms lasting more than 3 s [14] which is the generally believed threshold for minimum length of a paroxysm with a clinical correlate [15], [16].

The generalized paroxysms of absence epilepsy are usually not truly generalized, i.e. the signal is present with certain topographic preferences especially in the frontal lobes [17]. This suggests that electrode placement for EEG-monitoring influence signal detection.

Multiple research groups have investigated the feasibility of ambulatory monitoring of absence epilepsy patients. Generally, the studies are small, aged and based on relatively short period (up to 12 hours) of EEG-recording. Early publication are based on combined analogue and digital analysis and demonstrate good agreement between visual inspection and the automated detection of sharp transients in one fronto-central EEG-channel [18], [19].

Later studies have used microcomputer based detectors of sharp transients with loose temporal coupling allowing for detection of spike-waves of varying frequencies [20]. It was found that automatic detection using a single channel did not perform as well as human specialists with the methods and signal quality available at that time. The authors state that multichannel EEG signal processing is required for comprehensive quantitative detection of clinical significant spike wave patterns. A similar microcomputer based study focused on the frequency of the wave component and found on the other hand acceptable level of detection with a single channel [21].

Recent studies have used comprehensive digital signal processing methods based on mixed spike and slow wave characteristics extracted by methods like wavelet analysis [9], [22]. However even the most recent of these studies have a limited amount of data with only few hours of recording in awake patients. Since delta activity during sleep shares some characteristics with the EEG during absences there is a pressing need for ultra-long term recording like the ones presented here.

Based on 20 standard-EEG recordings, we have previously found that the Fp1-F7 channel is the most sensitive channel for reliable detection of seizures in a group of patients with absence seizures [9]. That study showed it was possible to detect 97.2% of all seizures lasting more than 2 seconds without any false detections. However, it was limited to data recorded in the outpatient clinic of the hospital, thus not showing the type and extends of artifacts expected in ambulatory measurements of children. Furthermore, this location aligns well with an EEG monitoring application where parents can mount pre-gelled disposable electrodes themselves whenever there is indication for a prolonged ambulatory EEG. We thus set up an experiment with multiple day ambulatory EEG recordings with electrodes at Fp1 and F7.

II. METHODS

A. Participants

Children aged 5-18 years with suspected or diagnosed absence epilepsy were enrolled after informed consent by the custodian holder (approved by the local ethics committee, H-3-2011-054). Two pediatric outpatient clinics (Rigshospitalet and North Zealand Hospital) screened for participants by the attending physicians (SG, CRP). The selection of patients is probably biased towards cases that are more complicated since simple cases are handled out of hospital and the motivation for enrollment was based on suspicion of unrecognized epileptic episodes.

15 children aged 5-16 were monitored in this protocol. Six patients were suspected of having epilepsy based on teacher or parent observations but turned out not to have epilepsy. Two patients had epilepsy but not typical absences. One patient had previously had juvenile absence epilepsy and participated successfully to unmount the diagnosis. Therefore, we present data on six patients with absence seizures, see Table I. Five of the six patients were tapered up in antiepileptic drug (AED) during the trial. In only one patient (#5) the increase was partly founded in the EEG-monitoring-results during this study. The therapeutic approach to the rest of the patients did not consider the EEG-monitoring-results.

Data from the two first patients have previously been mentioned in [23] although without the extensive analysis done in this paper.

B. Study Protocol

The study protocol is schematized in Fig. 1. At the first experimental day, patients came sleep deprived to the department of clinical neurophysiology to have a standard-EEG performed as part of normal workup.

Three electrodes (Ambu® Neuroline 700, Ballerup, Denmark) were placed near Fp1 (Ref), F7 (Active 1) and TP7 (Active 2), see Fig. 2. Electrodes were connected to a tiny, portable EEG-recorder (Actiwave, CamNtech Ltd., Cambridge, UK) measuring only 3.7x2.7x8.5 cm and

![Fig. 1. Study protocol overview. Patients are monitored 24 hours on four independent days. At the first recording day, a standard scalp-EEG is performed at the hospital.](image-url)
weighing 8.5 g which was taped to their neck for the following 24 hours of recording. Then Ag/AgCl cup electrodes (Ambu® Neuroline Cup) for the standard-EEG were mounted with Ten20 conductive paste (Weaver and Company, Aurora, CO, USA) without interfering with the ambulatory electrodes. Patients were examined for 30 minutes in supine position with subdued light and eyes closed. Provocations with hyperventilation and photo-stimulation were performed. Half of the subjects dozed or fell asleep.

When the standard-EEG was completed, participants left the department with the portable EEG device still recording. They kept this device on for the following 24 hours until the parents dismounted it as the recording period was over. At approximately day 4, 8, and 30, JDH came to the patients’ home to mount the EEG device for another 24 hours of recording. To accommodate the plans for the families, we were very unrestricted on the exact timing of when to do the recordings.

If electrodes became loose, parents and children were instructed to simply push them back on, and perhaps apply extra tape over the electrodes if they found that necessary.

After each 24 hours recording the EEG was visually inspected and scored for paroxysms by an expert trained technician and the number was reported immediately to the treating physician, who could choose to include the inspected and scored for paroxysms by an expert trained technician and the number was reported immediately to the treating physician, who could choose to include the information in decision on medical action or not.

Parents were asked for some time during the four 24 hours recording sessions to be 100% attentive to whether their child had clinical episodes and note any of them on a report sheet. Before and after the experiments parents and children underwent a semi-structured interview regarding the effect of the absences on their child and how obtruded the children had felt wearing the portable EEG device.

C. Data Acquisition

The portable EEG device sampled with a frequency of 128 Hz. The hardware frequency band spans from 0.3 to 50 Hz and the dynamic range of the EEG-signal in the portable recorder was 400 µV peak to peak. Initial measurements showed this was inadequate so a voltage divider was constructed to double the dynamic range of 800 µVpp.

 impedances of approximately 5 kΩ [23]. The voltage division will thus only occur over the resistors. In [23] it was found that the thermal noise from the resistors only amounted to 0.30 µVrms which is well below the discrete voltage resolution of 0.78 µV meaning that the resistor noise contribution is small.

As the portable device was only able to store 14 hours and 33 minutes of EEG, the parents had to change devices after approximately 12 hours.

D. Feature Extraction and Transformation

Special attention has been paid towards development of features that were descriptive of the spike-wave pattern as well as using state-of-the-art digital signal processing methods. The signal processing diagram can be seen in Fig. 3.

The EEG signal was divided into 2 s windows with an overlap of 1 s. Each window was weighted with a Tukey tapered cosine window with a ratio of taper to constant sections of 1/3 [24]. Based on a previous study [9] multiple features were extracted for each window using MATLAB.

![Experimental setup. Three electrodes were attached to the skin at approximate location of Fp1 (Ref), F7 and TP7. VD is the voltage divider that doubles the dynamic input range to 800 µVpp.](image-url)

![Figure 2: Experimental setup. Three electrodes were attached to the skin at approximate location of Fp1 (Ref), F7 and TP7. VD is the voltage divider that doubles the dynamic input range to 800 µVpp.](image-url)

<table>
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<th>#</th>
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<th>Age [yr]</th>
<th>Body weight [kg]</th>
<th>Epileptic syndrome</th>
<th>AED at day 1</th>
<th>AED at day 30</th>
<th># of paroxysms</th>
<th>Paroxysm length [s]</th>
<th>Time analyzed [h]</th>
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<td>44</td>
<td>JAE</td>
<td>Nihil</td>
<td>VPA 600 mg</td>
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<td>11</td>
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<td>LTG 150 mg</td>
<td>VPA 900 mg</td>
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<td>Nihil</td>
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<td>LTG 75 mg</td>
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<td>CAE</td>
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<td>LTG 400 mg</td>
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<td>7</td>
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<td>CAE</td>
<td>LTG 25 mg</td>
<td>LTG 75 mg</td>
<td>171</td>
<td>8.7±6.7</td>
<td>93.2</td>
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</tbody>
</table>

M is male and F is female. JAE is Juvenile Absence Epilepsy and CAE is Childhood Absence Epilepsy. AED is Anti-Epileptic Drug. VPA is Valproate, LTG is Lamotrigine and ZNS is Zonisamide.

# of paroxysms are only those lasting more than three seconds and only included on days with at least five paroxysms recorded. Time analyzed is also based on days with at least five paroxysms.
R2011a. With use of the Mahalanobis distance criterion, the 10 most orthogonal features were selected for further analysis [25]. Only the method of extraction of these features will be presented here.

**Log-sum of Wavelet Transform**

The popular wavelet transform has previously proved to be a strong method for EEG characterization [26], [27] especially using the Daubechies 4 mother wavelet. With a sampling frequency of 128 Hz, the multilevel wavelet detail decompositions contain the following frequencies: $d_1$: 32-64 Hz, $d_2$: 16-32 Hz, $d_3$: 8-16 Hz, $d_4$: 4-8 Hz and $d_5$: 2-4 Hz. For each band the absolute sum was calculated for all windows [9]. The features were finally log-transformed to obtain normal distribution. Only $d_1$, $d_2$, $d_3$ and $d_5$ showed to be most valuable for the automatic seizure detection based on the feature selection criterion.

**Power Measures**

During an absence seizure, the EEG amplitude is greatly increased. From a background activity of ±15µV the amplitude can easily increase to ±200µV depending on the electrode positions [7]. The high amplitudes are especially pronounced in the frontal channels. Two power measures were thus used as features: One that computed the power in the signal in a frequency band of 1 to 30 Hz, representing most of the physiological EEG power in normal EEG, and one that computed the relative power between the 3 to 12 Hz band and 1 to 30 Hz, being close to 1 if signal is paroxysmal and lower if signal is due to wide band artifact. The pass-bands were computed by filtering with a FIR equiripple design of order 467.

The first feature was transformed by an exponentiation of 1/10 to ensure normal distribution. The latter needed no transformation.

**Cross-correlation Measures**

As a typical absence seizure is highly regular with its characteristic spike-wave pattern, two cross-correlation measures were developed. The first calculated the cross-correlation between two on each other following windows and the second was the cross-correlation between the same time signal filtered in the frequency band of 3-12 Hz and 1-30 Hz based on the same filtering as above. Both features were normalized to lag 0 and the features were extracted as the highest absolute value at any lag. To obtain normal distribution the exponentiation was set to $\frac{1}{2}$ and 2 respectively.

**Mean Phase Variance**

A typical absence seizure consists of a spike and a wave repeatedly. This might imply that the phase variation is higher than normal background EEG. To measure the phase variance we removed the offset from each window and calculated the imaginary part of the Hilbert transform. The relative phase between the signal window and the Hilbert transformed signal was then calculated and finally the variance constituted the mean phase variance and the feature. No transformation was needed to obtain normal distribution.

**Mahalanobis Variance**

Another way to compare the similarity of two signals is by the Mahalanobis distance. With the same filters as previously described, the signal was split into a 3-12 Hz frequency band and a 1-30 Hz band. The Mahalanobis distance was then calculated for each point in the 3-12 Hz band to the distribution of the 1-30 Hz band [25]. The variance of this result constituted the feature. To obtain normal distribution the exponentiation was set to $\frac{1}{4}$.

**E. Train/Test Data Split**

As new electrodes were mounted on every new recording day in the trial, data from different days had to be analyzed separately. This requires a stringent split of data into train and test sets. Only days with at least 5 recorded paroxysms were included to ensure a robust 5-fold cross-validation with 4/5 of data used for training and the last 1/5 for testing. As EEG is non-stationary, the non-paroxysmic EEG was split into 10 min epochs, each representing five 2min epochs that were either considered as training or test data. This ensured that data from all EEG states were included in the model without overfitting the model. To create a random stratified division, cvpartition was used in MATLAB for both the paroxysms and non-paroxysmic data.
F. Normalization, Subset Selection and Modelling

To ensure equal weight between the features in the classifier, they were normalized to zero mean, unit standard deviation based on the training data.

Data were strongly unbalanced with huge amounts of normal EEG even in patients with many paroxysms. There was typically up to 1,000 times more normal data than paroxystic. Therefore, before modelling the training set the amount of normal data had to be limited. It was chosen to do this by random under-sampling where the number of normal training windows is chosen as a factor of the number of paroxystic windows. This factor was set to 25 as a reasonable choice to ensure a broad representation of the heterogeneous background EEG without dismissing the rather homogeneous paroxystic windows. More advanced alternatives to under-sampling has been suggested [28] which would most likely lower the factor 25 and still represent the normal EEG satisfactorily, but this was not investigated in the present study.

Design of the classifier was based on modelling of data using a support vector machine (SVM) from the LibSVM package, vers. 3.18 [29] as a toolbox for MATLAB R2011a. SVM is a supervised, binary, quadratic minimization problem. It is applied in combination with a radial basis kernel to formulate nonlinear extensions of the linear algorithm whenever nonlinear trends in the data are present. By mapping of data into a high-dimensional kernel induced feature space, it is possible to obtain a global optimum with respect to classification performance.

To find the optimal settings of the SVM, gamma (the parameter deciding the width of the kernel) and C (the parameter deciding the cost of choosing normal samples over paroxystic) were varied. A radial basis kernel was used with a gamma varying between 0.005, 0.01, 0.02, 0.05, 0.1, and 0.2 and C was varied between 0.5, 1, 2, 4, and 8.

G. Performance Calculation

Four measures were found suitable for this study; sensitivity, $Se$, false detection rate, $FDR$, Specificity, $Sp$, and positive predictive ratio, $PPV$. All measures are based on the test data only. $Se$ was calculated as the number of truly detected paroxysms divided by the number of all registered paroxysms longer than 3 s. $FDR$ was calculated as the number of detected continuous windows in groups of at least two (corresponding to three seconds) divided by the number of hours of normal data tested upon. $Sp$ was calculated as the number of false positive windows divided by the total number of normal windows. $PPV$ was calculated as the number of truly detected paroxysms divided by the total number of detected windows in groups of at least two.

H. Model Selection

With gamma taking 6 different values and C taking 5, a total of 30 models were generated. To choose the optimal model a performance measure, $P$, weighting the tradeoff between false detections and sensitivity was developed. The optimization was treated as a minimization problem as the sensitivity was subtracted from 101. As the goal was to obtain a sensitivity of at least 90% and a $FDR$ below 1/h the (101-$Se$) would have a dynamic range of 11 while the $FDR$ would only have a dynamic range of 1. To obtain an approximate equal weight we added the value of five to the $FDR$ to reach equivalent means. This resulted in the following metric:

$$P = (FDR + 5) \cdot (101 - Se) \quad (1)$$

III. RESULTS

A. Patient Compliance

Six highly compliant subjects were identified for this study. They exhibited between 8 and 84 paroxysms on the first day of recording, but all were having fewer paroxysms on the last day of recording, most likely due to increase in AED during the experiment for five of the patients, see Fig. 4 and Table I. Two of the subjects experienced more than 40% of their maximum number of paroxysms at the final recording day. They could most likely have benefitted from continued monitoring to improve their treatment.

B. Automatic Paroxysm Detection

Based on the optimal setup we were able to detect 98.4% of all paroxysms with only 0.23 false detections per hour corresponding to 5.5 false detections per 24 hours, see Table II. The double inter-electrode distance TP7-Fp1 performed with a sensitivity of 96.0% and FDR of 0.33/h corresponding to 7.9 per 24 hours. Due to the large amount of data and only few windows being classified as false positives; the specificity was 100.0% for all patients on both channels.

An analysis of the false detection showed various artifacts primarily with low frequency contents. These were rather simple for a trained expert to distinguish from true paroxysms in a visual evaluation.
C. Patient and Parent Perception

For every hour of the four 24h-EEG-recording parents were asked to note the number of minutes they were attentive to a degree which would let them detect all seizures. According to these estimates parents should have observed a median of 8.75 seizures (range: 2-22) in each patient. The fraction they actually observed was only 4.7% of the possible (range: 0-100%). The patient in which all seizures were detected was only observed intensely for 30 minutes in which 2 out of 2 seizures were observed.

The semi structured interviews revealed a number of issues. One parent wanted to know if the child had seizures the parents did not see. Another parent reported that she was concerned about how seizures affected the brain. One family stated “Seizures are associated with many conflicts and emotions. Our child has lost all self-confidence due to the diagnosis”. A mother said "I lost my husband in a traffic accident 5 years ago. The fear of losing again is huge". Generally, patients and parents were happy that they chose to use it. On the other hand, if the system is made as a decision support system, it could be rejected manually. When the distance between two EEG-electrodes is less than 2 cm, the signal of these electrodes could be rejected manually. If the application is a system made for alarming relatives or health care personal, a system giving more false alarms than necessary is more to the patient when acquiring the device. However, the sensitivity and false detection rate are paramount. Parameters of 100% sensitivity and false detection rate of 0/h are difficult to obtain. What is acceptable depends on the clinical situation. If the application is a system made for alarming relatives or health care personal, a system giving more false alarms than necessary is more to the patient when acquiring the device. However, the sensitivity and false detection rate are paramount. Parameters of 100% sensitivity and false detection rate of 0/h are difficult to obtain. What is acceptable depends on the clinical situation.

IV. DISCUSSION

We have acquired a novel dataset of EEG from six children with typical absence epilepsy with four 24-h recordings over one month. Both the duration of the whole period of investigation and the duration of the individual recordings are much longer than what is normally used in the clinic.

When patients, relatives, and healthcare personnel choose a device for seizure detection a number of issues matter. Size, obtrusiveness, ease of use and price are what usually matters most to the patient when acquiring the device. However, the sensitivity and false detection rate are paramount. Parameters of 100% sensitivity and false detection rate of 0/h are difficult to obtain. What is acceptable depends on the clinical situation.

Data were analyzed retrospectively in a patient-specific setting. The latter would require the expert reviewer to score a certain amount of EEG and number of paroxysms before the algorithm fits the specific patient. For future work we will obtain a much larger dataset to investigate the possibility to train a generic algorithm as well as focus on the performance if only the first day is used for training in a patient-specific setting.

Clinically satisfying sensitivity and false detection rate could be obtained in 5 out of 6 patients. This implies that for the majority of patients the method could be useful as a clinical tool.

Thirty different models were constructed for each patient to find the optimal balance between sensitivity and FDR. A large proportion of the models showed similar performance levels. This makes us confident that the optimized model is robust. When comparing the performance to that of similar models in the literature our models seem quite promising [9], [22].

At first glance, 5.5 false detections per 24 hours might sound like a lot, but considering the high frequency of the absence; the positive predictive value is 87.1%. This means that the vast majority of detections are true. If a clinician should use the algorithm as a decision support system, it would be possible to present all the detected paroxysms while only 12.9% of displays would show false detections which could be rejected manually.

When the distance between two EEG-electrodes is increased, the amplitude of the recorded signal is generally increased; however, the noise level may also be affected. We therefore recorded two bipolar channels allowing for normal and double inter-electrode distance within the left fronto-temporal region based on the 10-20 system.

Sensitivity and FDR of the short inter-electrode distance channel, F7-Fp1, were superior to the long inter-electrode distance of TP7-Fp1. This might be due to multiple reasons: First of all, the TP7 electrode is placed near the temporalis patient group is in a confined age group, the inter-subject variability is expected to be relatively low. Before it can be used as a decision support system in the clinic a more generic method has to be developed. This can either be done by development of a one-fits-all algorithm, or by development of a patient-specific algorithm generic across time. The latter would require the expert reviewer to score a certain amount of EEG and number of paroxysms before the algorithm fits the specific patient. For future work we will obtain a much larger dataset to investigate the possibility to train a generic algorithm as well as focus on the performance if only the first day is used for training in a patient-specific setting.

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<th>Pt. #</th>
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Mean Sensitivity: 98.4%, FDR: 0.230, Specificity: 100.0%, PPV: 87.1%

Mean Sensitivity: 96.0%, FDR: 0.330, Specificity: 100.0%, PPV: 83.5%

FDR: False Detection Rate
PPV: Positive Predictive Value
muscle which generates EMG artifacts. Chewing artifacts are noticeable in the temporal region showing a high frequency burst followed by a slow frequency pattern resembling the spike-wave pattern of the absences. Furthermore, it was observed on channel TP7-Fp1 that some of the absence paroxysms actually showed amplitudes above the 800 μVpp dynamic range of the recording system. This resulted in signal cutting with a putative effect on the computed features.

The quality of single channel EEG-recordings has improved significantly in recent years. Several researchers have looked into the use of single channel EEG-devices for various clinical purposes. Generally there are positive results both in sleep monitoring with detection of sleep stages [30] and in seizure detection [9]. Thus development of less obtrusive single-channel EEG monitoring devices for clinical use seems realistic.

Clinical epileptologists often state “we treat the patient not the EEG”. However in some syndromes like CAE and JAE it probably does make sense to reduce the number and duration of paroxysms, i.e. treating the EEG. We have demonstrated a strong correlation between level of AED and the number of paroxysms, i.e. treating the EEG. We have demonstrated a method of quantification of generalized spike-wave EEG patterns by computer during prolonged recordings.,” in ISAM 1979; Proceedings of the Third International Symposium of Ambulatory Monitoring, 1980, pp. 383–392.


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