Correlation Between the Changes in Ambulatory Electroencephalography Findings and Epilepsy Recurrence After Medication Withdrawal Among the Population in Southern China

Lian-hong YANG,1* Long-yuan JIANG,2* Rui-yan LU,1 Jian-qiang ZHONG,3 Shu-qiong LIU,1 En-xiang TAO,1 and Jian-hong YE1

Departments of 1Neurology and 2Emergency, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, PRC; 3Department of Neurology, Zeng Cheng People’s Hospital, Zeng Cheng, Guangdong, PRC

Abstract

Patients suffering from epilepsy need long-term medication. However, after the epilepsy is completely under control, the recurrence rate is high once the drug dose is reduced gradually. The present study investigated the possible correlation between the changes shown by ambulatory electroencephalography (EEG) and epilepsy recurrence after medication withdrawal, and assessed the value of ambulatory EEG findings in predicting the recurrence of epilepsy after medication withdrawal, in 265 patients from Southern China followed up for 5 years. Anticonvulsants were withdrawn until onset had been controlled thoroughly for over 3 years and ambulatory EEG detected no abnormalities. Ambulatory EEG was performed at least once per year, and findings at the first visit, during treatment, and before and after medication withdrawal were compared and analyzed. There were 47 patients with recurrent epilepsy in this study. Patients with normal ambulatory EEG findings at the first visit and during treatment had lower recurrence rate (about 8.1%) compared to patients with epileptic waves (25.0%), and patients with focal epileptic waves in the temporal, occipital, frontal, and parietal lobes, or in multiple areas was even higher. Patients with epileptic waves also showed higher clinical recurrence rate during the follow-up period. Abnormal ambulatory EEG findings are an important indicator of epileptic recurrence, and is of great value in predicting the recurrence of epilepsy after medication withdrawal.

Key words: ambulatory electroencephalography, epilepsy, recurrence

Introduction

Epilepsy is a chronic cerebral dysfunctional syndrome characterized by paroxysmal, sudden, and transient cerebral dysfunction evoked by super-synchronous discharge of neurons. Epilepsy patients need long-term medication, but after the onset of epilepsy has been completely controlled, the recurrence rate is high (19–27%) during reduction of the agent dose.7,9 The recurrence rate among patients with medication withdrawal after epileptic syndrome had been controlled thoroughly for 2 years was about 2.9 times high as that of patients without mediation withdrawal.30 Therefore, avoidance of the recurrence of seizures after anticonvulsant withdrawal has become important. Epileptic recurrence is related to such factors as the type and frequency of seizures, age at onset, psychological and neurological symptoms, timely treatment, constitution, and others,3,7,9 so these factors should be fully taken into consideration before the decision of medication withdrawal in patients with epilepsy.1,2,13

Electroencephalography (EEG) is the most important and basic examination method involved in the diagnosis and treatment of epilepsy, and is quite valuable for evaluating the development of the disease, and monitoring the therapeutic effect and determining the withdrawal of medication. However, whether the abnormal change detected by EEG before and after anticonvulsant withdrawal is one of
predictive risk factors for epileptic recurrence remains controversial. Moreover, routine EEG rather than ambulatory EEG has usually been used for clinical investigations.

The present study analyzed the follow up of 265 patients with epilepsy in the out-patient clinic of neurological department in our hospital for 5 years. The administration of anticonvulsants was stopped until epileptic onsets had been controlled thoroughly for over 3 years and normal ambulatory EEG findings were obtained. Ambulatory EEG findings at the first visit, during treatment, and before and after medication withdrawal were analyzed and the correlation between ambulatory EEG findings and the recurrence of epilepsy after medication withdrawal was further explored.

Subjects and Methods

This study included a total of 265 patients, 151 males and 114 females aged from 8 to 49 years (mean 21 ± 4.6 years), with epilepsy diagnosed by clinical manifestations and ambulatory EEG, persisting for 5 to 17 years (mean 7 ± 3.8 years). Patients presented with general tonic-clonic seizure in 98 cases, general tonic-clonic seizure in 35, partial seizure in 34, complicated partial seizure in 37, partial seizure with secondary generalized seizure in 40, muscular clonic seizure in 10, atonic seizure in 5, and unclassified epilepsy in 6. Ambulatory EEG was performed once a year during treatment in all patients. This study was conducted in accordance with the declaration of Helsinki, and with approval from the Ethics Committee of Sun Yat-sen Memorial Hospital, China. Written informed consent was obtained from all participants.

Ambulatory EEG was performed in all patients before medication withdrawal. Anticonvulsants were withdrawn gradually until epileptic onset had been controlled thoroughly for over 3 years and ambulatory EEG detected no abnormalities. The whole withdrawal process lasted about half a year among patients with absent seizure and one year among the others. After that, a 5-year follow-up was performed. Ambulatory EEG was performed once per year using the Galileo Halley32 Holter (EBNeuro S.p.A., Firenze, Italy) system. The scalp electrodes were located following the instructions of the international 10/20 system. Both mono-lead and double-lead EEG was continued for 24 hours. Records were then stored in small hard discs. We used a semi-automatic method to calculate a spike index, which was easily implemented in clinical settings. Spikes were detected by template matching, i.e. a typical spike in the EEG was manually selected as the template. Ambulatory EEGs at the first visit, during treatment, and before and after medication withdrawal were analyzed by two EEG operators. Abnormal waves were defined as regional spike-slow wave activity, consistently occurring over one location/region without spread to the contralateral hemisphere, or as focal with secondary bilateral synchrony, as defined by Larsson et al.10)

All data were statistically analyzed by SPSS® 10.0 software (SPSS Inc., Chicago, Illinois, USA). Categorical variables are represented as frequency and percentage. Comparisons of the numerical data and recurrence rate were carried out by χ² test. p < 0.05 was considered statistically significant.

Results

Clinical epilepsy recurred during treatment in 6 of 74 patients with no abnormalities on ambulatory EEG at the first visit (recurrence rate 8.1%). Clinical epilepsy recurred during treatment in 31 of 124
patients with abnormalities on ambulatory EEG (Fig. 1) at first visit, and recurrence rate was 25.0%, which was significantly different to the patients with no abnormalities ($\chi^2 = 8.70$, $p < 0.05$). Ten of 67 patients with nonspecific slow-waves (Fig. 2) developed recurrence, but with no significant difference in recurrence rate (14.9%) compared to the patients with no abnormalities ($\chi^2 = 1.62$, $p > 0.05$).

Patients with epileptic waves only in the central temporal area on ambulatory EEG (Fig. 3) had a lower recurrence rate (6.9%), whereas patients with focal epileptic waves in the temporal, occipital, frontal, and parietal areas (Fig. 4), or in multiple areas (Fig. 5) showed a higher recurrence rate (34.4% and 47.4%, respectively; Table 1).

After medication withdrawal, a total of 47 of 265 patients developed recurrent epilepsy during the follow-up period. Among these recurrent cases, epileptic waves reappeared in 17 of 47 patients (36.2%). Among other non-recurrent cases, epileptic waves were found in 22 of 218 patients (10.1%), showing a significant difference ($\chi^2 = 20.95$, $p < 0.05$).

Among the 124 patients with epileptic waves detected by ambulatory EEG, patients with epileptic waves that disappeared within one year after treatment had lower recurrence rate compared to patients with epileptic waves that disappeared by more than one year after treatment. Longer time period before the disappearance of epileptic waves was correlated with higher recurrence rate (Table 2).

**Discussion**

Abnormal EEG change as a risk factor for epileptic
recurrence has also attracted more and more attention. Experiments have suggested that if the disappearance of clinical onset is taken as the only standard for the decision of medication withdrawal, the recurrence rate of epilepsy could be as high as 21–40%, whereas if EEG improvement is also considered, the recurrence rate could drop to 4–27%.\(^{20}\)

This conclusion indicates that the EEG findings are very important for the decision of medication withdrawal in epilepsy treatment. Patients with abnormal EEGs showed low control rate but high recurrence rate, and even worse, always needed to be treated with multiple anticonvulsants.\(^{5,17}\) Many other laboratory studies have also supported an obvious correlation between epileptic recurrence and EEG abnormality before medication withdrawal.\(^{5,9,21}\)

Some children had primary epilepsy that could be controlled easily by valproate, and the recurrence rate was relatively higher among patients with paroxysmal discharge in EEG after medication withdrawal.\(^{15}\)

However, there is disagreement about the correlation between epileptic recurrence and abnormal EEG findings. The recurrence of epilepsy may be mainly related to the causes, age at the first onset, and the type of seizure rather than the changes in EEG.\(^{8,12,18}\)

Presumably, the controversy might be caused by various factors, such as different numbers of cases in different studies, different disease phases, and different methods adopted during follow up. Different standards involved in EEG detection may also partly contribute to this variance.\(^{4}\)

EEG acquired after sleepiness deprivation was found to be more valuable than routine EEG in predicting seizure recurrence.\(^{14}\)

In our study, 5-year follow up was carried out among 265 epilepsy patients whose onsets of epilepsy had been thoroughly controlled for over 3 years. To better and more accurately display the patient’s cerebral electronic activities, 24-hour ambulatory EEG was performed. Our results demonstrated that better prognosis and lower recurrence rate (8.1%) were found among patients with normal ambulatory EEG findings at the first visit and during treatment, whereas worse prognosis and higher recurrence rate (25.0%) were found among patients with epileptic waves detected by ambulatory EEG, especially focal epileptic waves in the temporal, occipital, frontal, and parietal areas, or in multiple areas. Our results also showed that patients with only paroxysmal focal epileptic waves in the central temporal area had good prognosis and low recurrence rate, which was consistent with previous findings.\(^{9,11,14}\)

Dynamic observation of patients with epileptic waves discovered that the earlier the epileptic waves disappeared after treatment, the better the prognosis and the lower the recurrence rate. The detection rate of epileptic waves in clinically recurrent cases was 36.2% during the follow up after medication withdrawal compared to only 10.1% in non-recurrent cases, showing a significant difference, in accordance with the previous result.\(^{19}\)

Since patients with reappearance of epileptic waves showed markedly higher recurrence rate, they need to be closely monitored and antiepileptic medication should be re-adopted when necessary.

In conclusion, ambulatory EEG is very useful for predicting the recurrence of epilepsy after anticonvulsant withdrawal. Generally speaking, epileptic recurrence is not only correlated with the different ambulatory EEG findings and abnormal wave types at the first visit, during the treatment, and before medication withdrawal, but is also correlated with the developmental trend of ambulatory EEG findings after medication withdrawal. To improve the life quality of epilepsy patients, it would be better to use a combined therapy and try to minimize all the possible factors that could lead to recurrence. In addition, ambulatory EEG should be performed periodically after anticonvulsant withdrawal. Compared with EEG, ambulatory EEG examination has several advantages. Ambulatory EEG can provide 24-hour non-stop monitoring without restricting daily life, display the cerebral activities in different situations, such as the awake, quiet, active, sleeping, and clinical onset stages. Ambulatory EEG can also detect abnormal waves more easily than EEG. Therefore, ambulatory EEG examination can absolutely improve the detection rate of abnormal waves and avoid the neglect of epileptic waves even in the sleeping phase.

**Conflicts of Interest Disclosure**

The authors have no personal financial or institutional interest in any of the drugs, materials, or devices in the article.

**References**


4) Gilbert DL, Sethuraman G, Kotagal U, Buncher CR:


9) Lamdhade SJ, Taori GM: Study of factors responsible for recurrence of seizures in controlled epileptics for more than 1 year after withdrawal of antiepileptic drugs. *Neurol India* 50: 295–300, 2002


11) Lin Q: [Children’s benign epilepsy with spike-waves in central temporal areas]. Zhonghua Shen Jing Ke Za Zhi 35: 190, 2002 (Chinese)


Address reprint requests to: Dr. Lian-hong Yang, Department of Neurology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou 510120, P.R. China. e-mail: lianhongyangcn163@163.com