



Research Article

Relationship Between EEG Recordings and Early Prediction of Epilepsy Progression: a 13 Years Follow-up Study

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Summary

The application of the electroencephalography (EEG) to predict and diagnose the epilepsy has been established for many years. But the clinical value of EEG prognostication for the epilepsy progression is also contradictory. The purpose of the present study is to explore the relationship between EEG recordings and early prediction of epilepsy progression in a cohort of epilepsy patients. Ninety-eight epileptic patients were followed up clinically and with the routine EEG recordings for at least 13 years. All of the patients (26 patients) initially performed the epileptiform discharges ended up with poor or moderate seizure symptoms, while 58.8% patients with normal initial EEG recordings had satisfactory clinical outcomes. Deterioration of the recordings over time was related with un-favourable results in a significant proportion of patients (85%). Meantime, about half (49%) of the patients with normal initial recordings performed satisfactory clinical outcomes. A small percentage (4.5%) of the improved EEG evolution performed the un-satisfactory clinical outcomes, while 70.4% of the deteriorated EEG evolution. The preliminary findings suggest that the EEG analysis technology holds considerable promise and early predictive value for identifying seizure intractability, which could provide the guidance for treatment in the early period.

Key words: Electroencephalography; early prediction; epilepsy; seizure

EEG Kayıtlama ve Epilepsi Progresyonunun Erken Tahmini Arasındaki İlişki: 13 Yıllık İzleme Çalışması

Özet

Amaç: Epilepsinin tahmin ve tanısında Elektroensefalografinin (EEG) uygulanması yıllardan beri yapılmaktadır. Ancak epilepsi ilerlemesinde EEG'nin klinik değeri ve prognostikasyonu hala tartışmalıdır.

Bu çalışmanın amacı bir grup epilepsi hastasında EEG kayıtlama ile epilepsi progresyonunun erken tahmini arasındaki ilişkiyi araştırmaktır.

Yöntem: Doksansekiz epileptik hasta en az 13 yıldan beri rutin EEG kayıtlaması ile izlendi.

Sonuç: Başlangıçta epileptiform bozukluk ile sonlanan tüm hastalar zayıf ya da ılımlı nöbet semptomları gösterdiler (26 hasta). Buna karşılık normal başlangıç EEG kayıtlaması olanlar tatminkar klinik sonuç Verdi (%58,8). Zaman içerisinde kayıtlarda bozukluk gösterenler arasında önemli bir bölüm hasta grubu kötü sonuçlandı (%85). Aynı zamanda başlangıç kayıtlamaları normal olan hastaların yaklaşık yarısı (%49) tatminkar klinik iyileşme gösterdi. İlerleyen EEG gelişimi gösteren küçük orandaki bir hasta grubu (%4,5) kötü klinik sonuç verirken, EEGleri %70,4 oranında bozulma gösterdi.

Yargı: Bu ilk sonuçlar EEG analiz teknolojisinin, erken evrede tedavi kılavuzu olabilecek tarzda inatçı nöbetleri tanımada önemli ölçüde erken tahmin değeri olabileceğini göstermektedir.

Anahtar Kelimeler: Elektroensefalografi; erken tahmin; epilepsi; nöbet

INTRODUCTION

Significance outcomes:

1. Ninety-eight epileptic patients were followed up clinically and with the routine EEG recordings for at least 13 years.
2. Recordings deterioration was related with un-favourable results, and normal initial EEG recordings had satisfactory outcomes.
3. EEG analysis technology holds considerable promise and early predictive value for identifying seizure intractability

Limitations:

Ninety-eight epileptic patients included in this study might be a little small sample.

The application of the electroencephalography (EEG) to classify and diagnose the epilepsy has been established successfully. But the prognostic value or significance of EEG in the epilepsy clinics is also elusive, just because many more contradictory data for the application of EEG in clinics. There are two contrary aspects for the prognostic value of EEG, some hold the view that the EEG patterns were unpredictable usefulness^(8,12,15), others provide the opposite viewpoints. Hghes et al.⁽⁹⁾ found that the EEG, especially for the early recordings, can predict the recurrence of the poorly controlled patients, which study is based on 1478 EEG records from 300 epilepsy patients. In case of seizure disorders that become evident at a large age, it has been reported that an epileptiform pattern in the initial recording has predictive value with regard to the future recurrence of seizures and the severity of the patient's clinical condition^(1,7). Kanemura et al.⁽¹¹⁾ discovered that the presence of frontal EEG paroxysms may indicate a higher risk of epilepsy in autism spectrum disorders.

Kanemura et al.⁽¹⁰⁾ also found that the combination of spike rate and extended periods of high-frequency paroxysmal EEG abnormalities may predict the evolution of atypical rolandic epilepsy. The present study analyzed a serial of EEG recordings which performed from January 1996 to January 2011. The correlation between EEG recordings and long-term clinical or social outcomes of the epilepsy patients was investigated to predict the ongoing tendency in this study.

MATERIAL AND METHODS

Subjects

In this study, 98 epileptic patients (53 males and 45 females) were recruited followed up from January 1995 to January 2011 at the department of Neurology. The above patients were closely monitored clinically and electrophysiologically for at least 13 years and completed the monitoring period between 2008 and 2011 years. The age (at the end of this study), follow-up duration, epilepsy duration, seizure types were listed in the Table 1. Furthermore, the epilepsy was classified into two types, including generalized epilepsy and focal (partial) epilepsy. The present study has been approved by the ethical committee of Beijing Tiantan Hospital. All of recruited patients have been gave their informed consent.

Follow-up procedure

All of the patients were diagnosed and evaluated for their epilepsy in our neurological department. We defined two regular check appointments, excluding the extra visits for other reasons. At least one time check could be guaranteed, performing the EEG in one year. During the past 13 years, all of the recruited patients performed better compliance regularly presenting the appointments.

Table 1 Baseline demographic, clinics of subjects with Epilepsy (n=98)

	Mean (SD)	Median (range)
Age, year	48.7 (5.6)	51(39 to 61)
Follow-up duration, year	15.8 (2.4)	15 (13 to 16)
Epilepsy duration, year	18.9 (3.7)	17 (13 to 32)
Gender		
Males		53
Females		45
Epilepsy type		
Generalized seizures		37
Partial seizures		61

Exclusion criteria for the follow-up patients: ①sleep deprivation; ②seizure-provoking medications; ③alcohol consumption; ④prolonged exposure to intermittent light stimulation; ⑤prolonged occupation with videogames or computers; ⑥other neurological disorders of central nervous system. The patients who performed the above criteria were excluded from the present study and prevented from the continual follow-up.

EEG recording

During the morning sessions, all patients' EEGs were recorded in the outpatient clinic. There were three EEG recorders were detected, including a 12-channel Alver Reega 2000, a 16-channel Era (Ote Biomedica), and an Elema-Schonander 16-channel Mingograf. We placed 21 electrodes according to the 10-20 system. With the 16-channel machines, a monopolar and two dipolar montages, including one longitudinal and one transverse, were recorded on paper. With the 16-channel machine, two longitudinal

two transverse, and the monopolar montage were used. Each session lasted 45 min. No sleep deprivation or sleep-induced recordings were included in the study. In order to avoid the deviations, two investigators were employed at the same time to evaluate the EEG recordings.

EEG evolution

In the present study, the evolution of EEG recording includes deterioration and improvement. The EEG recording improvement criteria: ①The epileptiform patterns were detected in the initial recordings, but not in discovered in the subsequent EEG recordings; ②The specific findings were detected in the initial recordings, but not in 2 or fewer of the subsequent 14 recordings. The EEG recording deterioration: ①The non-specific abnormalities appeared in more than half of the subsequent recordings in those patients in whom no such abnormalities had been detected in the initial recordings; ② Epileptiform patterns appeared in two or more of the subsequent

recordings in those patients in whom no such patterns had been detected in the initial recordings.

EEG recording classification

For all the patients, the initial EEG recordings were recorded before the first drug using, while the subsequent EEG recordings were performed under the anti-epileptic therapy. The initial EEG recordings were classified into three types at the epilepsy onset, including: ①Normal EEG: normal status of EEG recordings in epilepsy patients; ②Epileptiform EEG: abnormal EEG recordings with the specific epileptiform patterns, such as spikes, spike-wave and polyspike-wave complexes, or sharp waves clearly distinguished from the background; ③ Non-specific EEG: abnormal with non-specific EEG recordings, such as attenuation or unilateral asymmetry of amplitude, diffuse or focal slowing, reactivity of rhythm.

Clinical outcomes

According to the occurrence frequency of the seizures, the clinical outcomes were classified into three categories, such satisfactory, moderate, and unsatisfactory. The seizure frequency less than one time per 6 months represents the satisfactory outcome, one or more than one time per 6 months but less than one time per month represents the moderate outcome, more than one time per month represents the unsatisfactory outcome.

Statistical analyses

SPSS 11.0 for windows was used for statistical analysis. Statistical analysis was performed using the T test, and Spearman rank correlation was used in correlation analysis. The level of significance is set to 0.05.

RESULTS

EEG initial recordings and evolution

At the first time seizure appeared, the initial recordings were detected. For the

initial normal EEG, there were 34 patients, and account for 34.7%. In ten patients, EEG recordings become abnormal subsequently, disclosing specific epileptiform patterns in four patients and non-specific abnormal findings in the other six, while in the remaining 24 patients the EEG recordings remained constantly normal. For the initial non-specific EEG, there were 38 patients, and account for 38.8%. In 17 patients, specific epileptiform patterns appeared in the course of the serial EEGs that followed. In another 10 patients, the initially non-specific abnormal findings gradually disappeared in the course of the 13 years. The EEG findings of the remaining 11 patients remained unchanged. For the initial EEG, specific epileptiform patterns accounted for 26.5% (26 patients). In 12 of them, the EEG recordings were improved (the epileptiform patterns were no longer detectable, but were replaced by non-specific recordings). While in the other 14 patients, the EEG recordings consistently performed the specific epileptiform patterns (Table 2).

Correlations between EEG recordings and clinical outcomes

The group of patients that presented with satisfactory, moderate and un-satisfactory outcome at the initial stage with normal and non-specific abnormal EEG had statistically significantly better clinical outcome compare with the initial stage of abnormal epileptiform EEG patterns (The X^2 test indicated that all of the three outcome groups with $P < 0.05$). The satisfactory outcome patient amounts in the normal and non-specific EEG group were higher significantly compared with the epileptiform EEG (Table 3) (both $P < 0.01$), and there were no significant different between normal and non-specific EEG group ($P > 0.05$). For the moderate outcome, the amounts in the normal EEG group were significant higher the non-specific EEG group ($P < 0.05$), but no difference was found between normal and epileptiform

EEG group ($P>0.05$). The normal group showed the lowest un-satisfactory amounts in the three initial EEG group, and significant lower than the non-specific and epileptiform EEG group ($P<0.01$ and $P<0.001$, respectively). Furthermore, the un-satisfactory amounts in the non-specific EEG group were significantly lower than the epileptiform EEG group ($P<0.01$).

In this study, we analyzed the correlations between EEG recordings and clinical outcomes. The results indicated an obvious positive correlation between the EEG recordings and clinical outcomes ($r=0.84989$, $P<0.05$), showing a statistical significance. The regression equation was meaningful ($Y=0.4522X + 1.1121$) (Figure 1).

Correlations between EEG recordings and clinical outcomes

From the Table 4, we could found that the satisfactory outcomes amounts in the improved EEG evolution group were significantly higher than in the unchanged ($P<0.05$) and deteriorated EEG evolution group ($P<0.001$). The moderate outcomes performed the same tendency that the amounts were higher significantly than the

unchanged ($P<0.05$) and deteriorated EEG evolution group ($P<0.001$). Oppositely, in the un-satisfactory outcome group, the unsatisfactory amounts were lower significantly than the unchanged ($P<0.01$) and deteriorated EEG evolution group ($P<0.001$). In all of the three clinical outcome groups, there were significant different amounts between the unchanged group and deteriorated group (all of the $P<0.01$).

By analyzing the results relationship between EEG evolution and clinical outcomes, we found that there was a significant correlation ($r=0.78653$, $P<0.05$). The regression equation was meaningful ($Y=0.3361X + 1.4132$) (Figure 2).

Gender's effect on the severity of epilepsy
In this section, we deduced the severity of epilepsy of the patients from the number of the antiepileptic drug (AED). Based on the results summarized in the Table 5, we could conclude that there were no significant correlation between the severity of epilepsy and the gender of the patients.

Table 2 Electroencephalography evolution

Initial EEG	EEG evolution			Total
	Improved	Unchanged	Deteriorated	
Normal	0	24	10	34
Non-specific	10	11	17	38
Epileptiform	12	14	0	26
Total	53	49	27	98

Table 3. Comparison of clinical outcomes in three initial EEG recordings groups

Initial EEG	Clinical outcomes		
	Satisfactory (n)	Moderate (n)	Un-satisfactory (n)
Normal EEG	58.8% (20)**	35.3% (12) ^{##}	5.9% (2) ^{*,##}
Non-specific EEG	50% (19)**	23.7 (9)**	26.3 (10)**
Epileptiform EEG	0	34.6% (9)	65.4% (17)
X^2	14.36	12.81	8.84
P	0.007	0.013	0.038

Table 4. Comparison of clinical outcomes and EEG evolution recordings

EEG evolution	Clinical outcomes		
	Satisfactory (n)	Moderate (n)	Un-satisfactory (n)
Improved	54.5% (12) ^{**,#}	40.9% (9) ^{**,#}	4.5% (1) ^{**,##}
Unchanged	46.9% (23)**	34.7 (17)**	18.4% (9)**
Deteriorated	14.8%(4)	14.8% (4)	70.4% (19)
X^2	17.53	9.17	20.48
P	0.0024	0.046	0.009

Table 5. Epilepsy type relative severity of epilepsy in relation to gender

Epilepsy and drugs	Gender		Total
	Males (n)	Females (n)	
Generalized/one AED	16	13	29
Generalized/two or more AEDs	3	4	7
Partial/one AED	14	12	26
Partial/two or more AEDs	20	16	36
Total	53	45	98

AED, antiepileptic drug. Generalized epilepsy represents patient take one type antiepileptic drug;

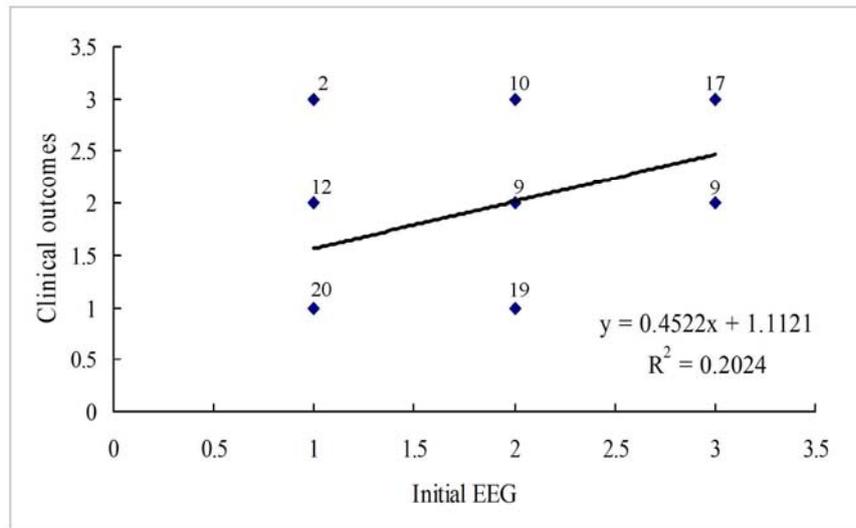


Figure 1: Correlations between EEG recordings and clinical outcomes. In the X axis, 1 represents normal initial EEG, 2 represents non-specific abnormal EEG, and 3 represents abnormal epileptiform EEG. In the Y axis, 1 represents satisfactory outcome, 2 represents moderate outcomes, and 3 represents un-satisfactory outcome. The number upper the coordinate points represent the number of patients.

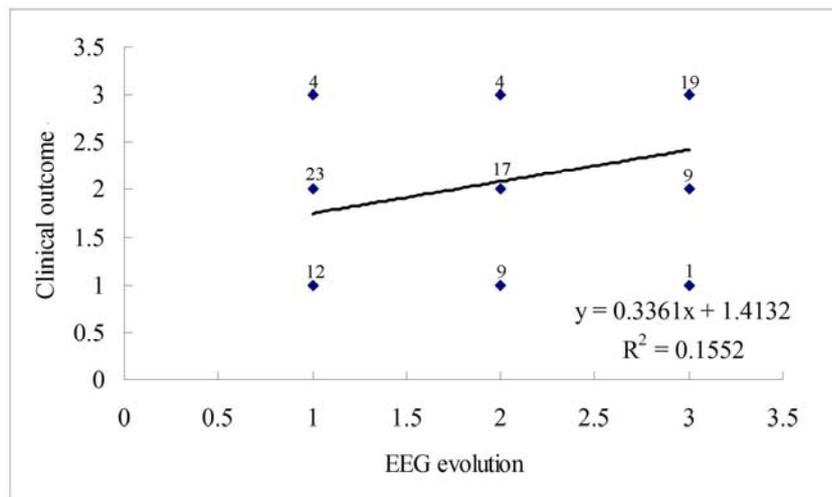


Figure 2: Correlations between EEG recordings and EEG evolution. In the X axis, 1 represents the improved EEG evolution, 2 represents unchanged EEG evolution, and 3 represents deteriorated EEG evolution. In the Y axis, 1 represents satisfactory outcome, 2 represents moderate outcomes, and 3 represents un-satisfactory outcome. The number upper the coordinate points represent the number of patients.

DISCUSSION

A better prediction of the long-term evolution of epilepsy plays a significant role for the patients, care-givers and treating physicians alike. The early identification of patients who destined to develop intractable epilepsy has practical importance for clinics. The prediction may critically influence decision-making regarding the patients' treatment. Nowadays, there is a continuing interest for the development of reliable prognostic factors in epilepsy. Till now, there are a lots number of clinical and laboratory variables of prognostic value in clinics^(2,12,17), such as EEG. We discussed this topic by exploring the association or correlation between serial EEG recordings and long-term clinical outcome in 98 epileptic patients who were followed up for at least 13 years.

Our data indicated that both the initial EEG recordings and the following repeat EEG recordings carried very useful information which could be reflect the long-term prognosis of the epileptic patients. Interestingly, all of the patients with the epileptiform discharges (26 patients' EEG recordings) in their initial EEG recordings ended up with poor (17 patients' EEG recordings) or moderate (9 patients' EEG recordings) seizure control. In contrast, 58.8% (20/34) patients with normal initial EEG recordings had satisfactory clinical outcomes, 35.3% (12/34) patients had moderate outcomes, and only 5.9% (2/34) patients had the un-satisfactory clinical outcomes. We found that the deterioration of the recordings over time was related to the unfavourable results in the majority of patients (23/27, 85%), while stable or improved EEG recordings could predicted a favourable clinical outcome (35/72, 49%). The correlation analysis also indicated that there were a significant correlation between the initial EEG and the clinical outcomes. So we could conclude that the changes of the initial EEG could

reflect the tendency of the clinical outcomes. The relationship of EEG evolution recordings and clinical outcomes was also investigated in the present study. The EEG evolution recordings could predict the clinical outcomes in a partially accuracy.

Only a small percentage (1/22, 4.5%) of the improved EEG evolution performed the un-satisfactory clinical outcomes. Eighteen points for percentage of the unchanged EEG evolution performed the un-satisfactory clinical outcomes. However, the percentage of the deteriorated has enhanced the un-satisfactory rat to 70.4% (19/27). Conversely, the satisfactory rates of the EEG evolution were decreased accordingly to priority of improved, unchanged, and deteriorated EEG sequence. So our results indicated that the clinical outcomes related significantly to the EEG evolution.

The previous studies exploring the prognostic factors in epilepsy have provided limited information regarding EEG as most of them focus on clinical parameters. Erdal et al.⁽⁶⁾ established a Semi-reversible cranial magnetic resonance imaging method for the epilepsy clinics outcomes, but not for the EEG detection. Pinheiro-Martins et al.⁽¹⁴⁾ found a prognostic model for the surgical outcome of the lobe epilepsy, and which performs a significant effects for the prediction of epilepsy. In addition, those studies that considered EEG as a prognostic factor provided controversial results. Elwes et al.⁽⁵⁾ and the Collaborative Group for the study of Epilepsy⁽³⁾ concluded that the presence of epileptic, focal, slow-wave or background abnormalities in the pre-treatment EEG of patients with newly diagnosed epilepsy was devoid of prognostic value.

Recently, many studies have discovered the usefulness of EEG as a prognostic factor in epilepsy. Gatzonis, et al.⁽⁷⁾ have concluded that the serial EEG findings can

be utilized for the epilepsy prognostic evaluation. Schreiner and Pohlmann-Eden⁽¹⁶⁾ found that the presence of focal epileptiform activity in the initial EEG after a first unprovoked seizure was a significant predictor of seizure recurrence. Di Gennaro et al.⁽⁴⁾ found that the postoperative interictal epileptiform discharges in postoperative EEG may predict long-term outcome in patients undergoing resective surgery for ET epilepsy. Ko et al.⁽¹⁾ concluded that diffuse slowing and focal spike and wave activity were independent predictors of seizure intractability in epilepsy patients. The present study is consistent with the above studies, and proved that the EEG analysis is an effective method to predict the seizure occurrence. The results indicated that patients with abnormal initial EEG findings or with the deteriorating recordings are correlated with the intractable seizures.

In conclusion, the preliminary findings suggest that the EEG analysis technology holds considerable promise and early predictive value for identifying seizure intractability, which could provide the guidance for treatment in the early period.

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