

The Correlation between Electroencephalography Amplitude and Interictal Abnormalities

Audit study

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العلاقة بين مدى التخطيط الدماغى والدلائل الكهربية غير الطبيعية للتشنجات دراسة مراجعة

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ABSTRACT: Objectives: The aim of this study was to establish the relationship between background amplitude and interictal abnormalities in routine electroencephalography (EEG). **Methods:** This retrospective audit was conducted between July 2006 and December 2009 at the Department of Clinical Physiology at Sultan Qaboos University Hospital (SQUH) in Muscat, Oman. A total of 1,718 electroencephalograms (EEGs) were reviewed. All EEGs were from patients who had been referred due to epilepsy, syncope or headaches. EEGs were divided into four groups based on their amplitude: group one $\leq 20 \mu V$; group two 21–35 μV ; group three 36–50 μV , and group four $> 50 \mu V$. Interictal abnormalities were defined as epileptiform discharges with or without associated slow waves. Abnormalities were identified during periods of resting, hyperventilation and photic stimulation in each group. **Results:** The mean age \pm standard deviation of the patients was 27 ± 12.5 years. Of the 1,718 EEGs, 542 (31.5%) were abnormal. Interictal abnormalities increased with amplitude in all four categories and demonstrated a significant association ($P < 0.05$). A total of 56 EEGs (3.3%) had amplitudes that were $\leq 20 \mu V$ and none of these showed interictal epileptiform abnormalities. **Conclusion:** EEG amplitude is an important factor in determining the presence of interictal epileptiform abnormalities in routine EEGs. This should be taken into account when investigating patients for epilepsy. A strong argument is made for considering long-term EEG monitoring in order to identify unexplained seizures which may be secondary to epilepsy. It is recommended that all tertiary institutions provide EEG telemetry services.

Keywords: Electroencephalography, abnormalities; Epilepsy.

المخلص: الهدف: تهدف هذه الدراسة إلى تقرير العلاقة بين مدى الجهد الكهربي في خلفية التخطيط الكهربي الروتينى للدماغ و الدلائل الكهربية غير الطبيعية بين التشنجات. الطريقة: تم إجراء هذه المراجعة البحثية في قسم علم وظائف الأعضاء السريري بمستشفى جامعة السلطان قابوس، مسقط، عمان. مجموع 1,718 تخطيطا لكهربية الدماغ في الفترة ما بين يوليو 2006 وديسمبر 2009 تم مراجعتها. جميع هذه التخطيطات كانت لمرضى محولين لأسباب تتعلق بمرض الصرع، الإغماء، أو الصداع. تم تقسيم التخطيطات الكهربية للدماغ إلى أربع مجموعات بناء على مدى الجهد الكهربي: المجموعة الأولى: $\leq 20 \mu V$ ، المجموعة الثانية: 20–35 μV ، المجموعة الثالثة: 36–50 μV ، المجموعة الرابعة: $> 50 \mu V$. تم تعريف الدلائل الكهربية غير الطبيعية بين التشنجات على أنها نبضات كهربية مصاحبة لمرض الصرع سواء كانت مترابطة مع أو بدون موجات كهربية بطيئة. الدلائل غير الطبيعية تم التعرف عليها خلال فترات الراحة، تنفس مع فرط التهوية، والتنبيه الضوئي في كل مجموعة. النتائج: معدل العمر \pm الانحراف المعياري للمرضى هو 27 ± 12.5 سنوات. من مجموع 1,718 تخطيطا لكهربية الدماغ كان هناك 542 (31.5%) تخطيطا غير طبيعي. أظهرت الدراسة أن الدلائل غير الطبيعية لتخطيط الدماغ تزداد مع مدى الجهد الكهربي للتخطيط في جميع المجموعات الأربع مع وجود علاقة معتدلة إحصائيا ($P < 0.05$). كذلك تبين أن هناك 56 (3.3%) تخطيطا دماغى مدى الجهد الكهربي فيها $\leq 20 \mu V$ وجميعها لم تظهر أي مؤشر على دلائل غير طبيعية في تخطيط الدماغ. الخلاصة: يعتبر مدى الجهد الكهربي لتخطيط الدماغ عاملا مهما في تحديد ظهور الدلائل غير الطبيعية في تخطيط الدماغ الروتينى. هذه النتيجة يجب أن تؤخذ في الاعتبار عند فحص مرضى الصرع. تؤكد الدراسة في مناقشة قوية على أهمية الأخذ في الاعتبار استخدام التخطيط الكهربي للدماغ طويل المدى للتوصل إلى تفسير للتشنجات التي يمكن أن تكون ثانوية لمرض الصرع. توصي هذه الدراسة بتوفير تخطيط الدماغ طويل المدى في كل المستشفيات المرجعية.

مفتاح الكلمات: تخطيط كهربية الدماغ، تشوهات؛ الصرع.

ADVANCES IN KNOWLEDGE

- This audit investigates and establishes electroencephalography (EEG) amplitude as an important factor that limits EEG outcomes.
- The data collected from this study sheds light on current EEG practices.

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APPLICATION TO PATIENT CARE

- The results of this audit will alert clinical neurophysiologists and neurologists to the impact of EEG amplitude on EEG interpretation.
- Furthermore, these results indicate the need to prolong EEG recordings and minimise the possibility of false-negative outcomes, particularly in patients with epilepsy.

ELECTROENCEPHALOGRAPHY (EEG) IS A well-established and essential investigation for evaluating cortical function. Abnormal waveforms such as epileptiform discharges seen on electroencephalograms (EEGs) may have a significant impact on the diagnosis of episodic disorders of consciousness such as epilepsy. Epilepsy affects 65 million people worldwide, with an incidence of 50/100,000 and a prevalence of 700/100,000 in developing countries.¹ EEG remains an essential laboratory investigation that can support clinical diagnoses.²

However, the sensitivity of EEG in demonstrating interictal epileptiform discharges is limited. The initial EEG may show epileptiform abnormalities in only 29–50% of cases.³ Therefore, the use of EEG during periods of hyperventilation, photic stimulation and sleep deprivation was introduced to increase the chance of finding abnormalities.⁴ Most EEGs are performed in an outpatient setting, utilising surface scalp electrodes which are positioned using the 10/20 international system or the modified Maudsley system.⁵

Rhythmic activity derived from the surface of the scalp is identified by its configuration, frequency, amplitude and location.^{2,4} These rhythms are not uniform and vary between and within individuals over time. For example, frequency is strongly influenced by the level of consciousness and underlying pathology. Slow activity (less than 3 hertz [Hz]) is commonly seen when individuals are in a deep sleep, as well as in those with organic disorders such as encephalopathies.⁶ The EEG amplitude represents the vector sum of the cortical potential differences at 90° to the surface in real time.^{7,8} These signals are recorded through the skull and can be influenced by the structures between the cortex and the recording electrodes,^{9,10} as well as age¹¹ and genetics.¹²

These EEG signals are modulated during periods of sleep¹³ and hyperventilation¹⁴ and also change with inter-electrode distance,^{14–16} variations in skull thickness^{17,18} and in the presence of underlying pathologies, such as a tumour or hydrocephalus. These pathologies can impede signals or affect conductivity, resulting in a reduction of the EEG voltage.^{9,10} When the EEG amplitude is less than 20 μ V, it becomes difficult to identify small abnormalities against a bland and relatively featureless background; this is defined as a low amplitude EEG.¹⁹ Such low amplitude EEGs

have been described in individuals from certain ethnic groups, such as African Americans,²⁰ and in those who have specific pathological conditions such as Huntington's disease²¹ or alcoholism.²⁰ They have also been reported in normal subjects during periods of increased attention and vigilance²² and when under general anaesthesia.²³

To the best of the authors' knowledge, no studies in the literature have thus far quantified the ability of low voltage EEG recordings to detect clinically relevant EEG abnormalities. This audit explored the relationship between EEG amplitude and the detection of interictal abnormalities by professionals in a busy clinical neurophysiology department.

Methods

This retrospective audit was conducted between July 2006 and December 2009 in the Department of Clinical Physiology at Sultan Qaboos University Hospital (SQUH) in Muscat, Oman. All of the EEGs reviewed were performed during the study period on non-homogenous patients over 13 years old. Participants of various ethnic groups were included in the audit, representing a composite of Omani society. The participants had attended the EEG laboratory for various reasons including epilepsy, syncope and headaches. The EEGs of patients in the intensive care unit or those with brain pathologies that could influence EEG amplitudes (such as a ventriculoperitoneal shunt, recent brain surgery or tumours) were excluded from the study.

The EEGs were recorded and analysed using the Comet series' model CMXLE-230 (Grass Technologies, Warwick, Rhode Island, USA) with 16 recording channels, using silver/silver chloride or gold-plated disc electrodes placed on the scalp according to the 10/20 international system. The high-pass filter was set to 1 Hz and the low-pass filter was set to 70 Hz. The notch filter was off in all cases.

After the application of the electrodes and impedance correction, each subject was requested to lie in a supine position. After 20–25 minutes in a relaxed wakeful state, an EEG recording was obtained. Activation procedures such as hyperventilation and photic stimulation were then carried out. If a subject felt drowsy, then a sleep recording was obtained after

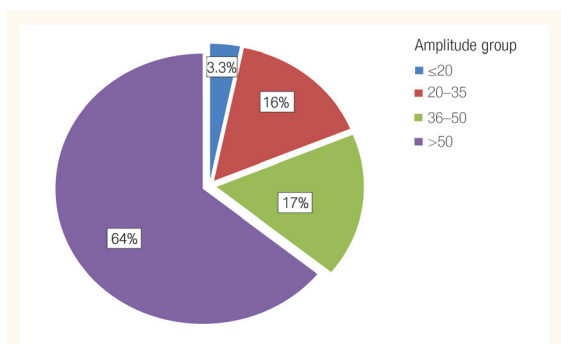


Figure 1: Distribution of all electroencephalograms by amplitude group (N = 1,718).

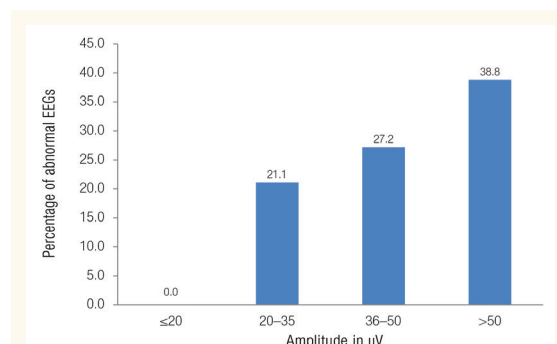


Figure 2: Percentage of all abnormal electroencephalograms (EEGs) by amplitude group (N = 542).

a further 10–20 minute interval. No sedatives were given at any time to any of the subjects included in this study. Each record was then interpreted by a qualified clinical neurophysiologist.

In order to determine the EEG amplitude, a standard approach was followed.²⁴ An area of not less than two seconds of maximum voltage, recorded over the occipital regions of the head with alpha activity during periods of quiet resting and with the patient's eyes closed, was determined visually and then highlighted. The amplitude was calculated as the peak-to-peak alpha activity in the bipolar double banana montage. Interictal epileptiform and slow wave abnormalities were identified in each EEG during periods of resting, hyperventilation and photic stimulation. The EEGs were subsequently labelled as normal or abnormal.

The amplitudes obtained were operationalised and classified into four categories with the following low voltages: group one $\leq 20 \mu\text{V}$;¹⁹ group two 20–35 μV ; group three 36–50 μV , and group four $> 50 \mu\text{V}$. The relationship between EEG amplitudes and reported abnormalities was analysed using the Statistical Package for the Social Sciences (SPSS), Version 18 (IBM, Corp., Chicago, Illinois, USA).

This study was approved by the Medical Research

& Ethics Committee at the Sultan Qaboos University College of Medicine & Health Sciences (MREC #297).

Results

A total of 1,718 EEGs were reviewed in this audit. Patients were aged 13–85 years old, with 75% of this patient population below 32 years of age (mean: 27 ± 12.5 years).

Figure 1 shows the distribution of the 1,718 EEGs according to amplitude categories, with 56 (3%) in group one, 266 (16%) in group two, 294 (17%) in group three and 1,102 (64%) in group four. The overall results of the abnormal EEGs are displayed in Figure 2. Of the 1,718 EEGs, a total of 542 (31.5%) were abnormal. The percentage of EEG abnormalities increased steadily with amplitude, as shown in Figure 2. To test whether this observed increase was significant (i.e. evidence of a trend in the population), Pearson's Chi-squared test was performed ($\chi^2 = 56.20$; $P < 0.001$). This demonstrated strong evidence of an association between amplitude and the detected abnormalities, particularly given that no abnormalities were detected in group one ($\leq 20 \mu\text{V}$).

All of the 1,718 patients underwent EEGs during periods of resting. While resting, a similar rise was observed in the percentage of abnormal EEGs with an increase in EEG amplitude [Figure 3]. These results are almost identical to those found overall [Figure 2]. There was also an association between amplitude and the frequency of abnormal EEGs during periods of resting ($\chi^2 = 49.366$; $P < 0.001$).

Hyperventilation was initiated in 1,310 patients [Figure 4]. The same steady increase in the percentage of abnormal EEGs with increasing amplitude was observed, although the percentages were lower than those seen while patients were resting. Pearson's Chi-squared test indicated a strong association between amplitude and the percentage of EEG-detected abnormalities during hyperventilation ($\chi^2 = 15.20$; $P = 0.002$).

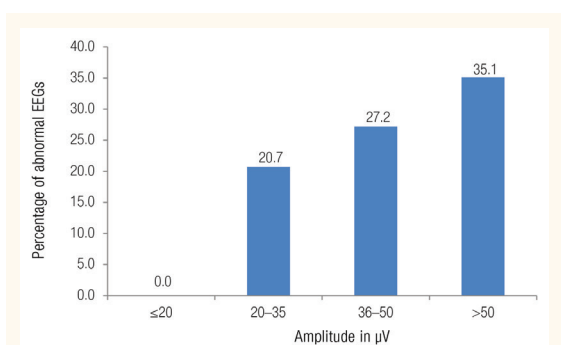


Figure 3: Percentage of abnormal electroencephalograms (EEGs) by amplitude group while resting (N = 1,718).

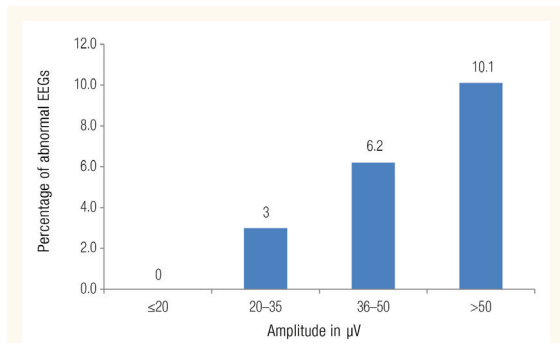


Figure 4: Percentage of abnormal electroencephalograms (EEGs) by amplitude group during a period of hyperventilation (N = 1,310).

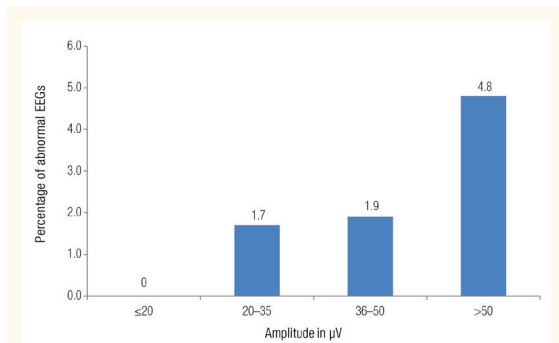


Figure 5: Percentage of abnormal electroencephalograms (EEGs) by amplitude group during a period of photic stimulation (N = 1,570).

Figure 5 shows the percentage of abnormal EEGs by amplitude range in those who underwent photic stimulation (n = 1,570). The same upward trend in the percentage of abnormalities was observed ($\chi^2 = 11.05$; P value = 0.011). This further indicates a highly significant association between amplitude and the percentage of abnormalities detected.

Discussion

The variability in EEG amplitudes among individuals has long been noted; however, this has never been correlated with the presence of interictal abnormalities. This audit identified EEG voltage/amplitude as an essential factor that influences the likelihood of finding an abnormality in EEGs carried out in a clinical service. To the best of the authors' knowledge, this is the first time that the importance of EEG amplitude has been demonstrated in both resting and activated EEG recordings (i.e. during periods of hyperventilation and photic stimulation).

This audit supports anecdotal observations related to the level of EEG amplitude and the sensitivity of recognising abnormal discharges. This was most marked in patients with very low voltage EEGs of ≤ 20 μV (3.3%), none of whom were found to have interictal abnormalities. Consequently, such an EEG is unlikely to demonstrate interictal abnormalities even if the patient were to have a significant disorder, such as epilepsy. For these patients, an alternative means of identifying abnormalities needs to be considered.

The significance of failing to find interictal abnormalities was illustrated by one of the authors' patients who had had a bland low amplitude recording (≤ 20 μV) and then suffered a seizure during the latter part of the recording. Upon review, the EEG showed only ictal discharges. This suggests that patients with low amplitude EEGs will require prolonged EEG video-telemetry recordings if epilepsy is still suspected,

despite an apparently normal interictal low-amplitude recording. The authors recommend that clinical neurophysiologists undertake a prospective study of all patients referred to them for testing. The patients' ultimate clinical diagnosis should be identified and subsequently correlated with their EEG amplitude and the observed abnormalities.

It is also worth noting that this audit provides information on the overall contribution of the provocative tests that are routinely performed as part of the standard EEG test, including hyperventilation and photic stimulation. In this audit, these tests showed a relatively modest contribution in identifying abnormalities, although the results could still be important clinically. Further studies are essential to identify the significance of these activation procedures in arriving at an ultimate diagnosis. Furthermore, while this audit may have limitations, it has highlighted some of the drawbacks of only using a standard EEG to identify potential abnormalities. In order to identify patients with clinically important syndromes such as epilepsy, prolonged EEG recordings with video-telemetry should be undertaken. This is particularly important for regional clinical neurophysiology departments, such as that of SQUH in Oman.

This study has a number of limitations. The study investigated the clinical practice of a single laboratory with an unselected patient population. As a result, only 56 records with mean voltages of ≤ 20 μV were obtained from the total population. Despite the low number of these records, the statistical analysis suggested that the association between amplitude and the detection of abnormalities was significant. The sample was also skewed towards a young population, with 75% under 32 years of age. Future studies are recommended to study the correlation between age, EEG amplitude and identified abnormalities.

Conclusion

A significant association was found between EEG amplitude and interictal abnormalities in this audit. This association may limit the likelihood of detecting abnormalities in EEG recordings, as was clearly seen among participants with low voltage EEGs. Such an effect would have ramifications on EEG reporting and could potentially impact patient care, particularly for those with epilepsy. Therefore, prolonged EEG recordings should be undertaken to minimise the risks of false-negative EEG outcomes.

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