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Incidental epileptiform discharges in patients of a tertiary centre

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HIGHLIGHTS

- Non-epileptic patients with incidental epileptiform discharges (ED) during routine EEG at a tertiary centre were identified for this study.
- Group matching of patients with incidental ED and disease controls with respect to gender and neuroimaging findings was performed.
- The presence of incidental ED increased the likelihood of epilepsy during follow-up more than 8-fold.

ABSTRACT

Objective: This controlled study set out to assess the rate of incidental epileptiform discharges (ED) during routine EEG and the incidence of epilepsy within a 4-year follow-up period in patients without a history of epilepsy.
Methods: We retrospectively analyzed electroencephalography (EEG) recordings of 1750 consecutive patients referred to the Department of Neurology at the Vienna General Hospital between January 1 and December 31, 2009. The incidence of epilepsy in patients with ED and no prior history of epilepsy was compared with a disease control group matched for gender and neuroimaging findings.
Results: ED were identified in 26 (4%) of 629 patients without a history of epilepsy. Sixteen (62%) of these patients developed epilepsy during follow-up compared with five (19%) of the disease controls ($p = 0.01$), yielding an adjusted odds ratio of 8.8 (95% CI 2.1–37.7) for developing epilepsy in patients with ED and no prior history of epilepsy.
Conclusions: Incidental ED during routine EEG significantly increase the likelihood of developing epilepsy.
Significance: Patients with incidental ED should be specifically asked for any signs and symptoms suggestive of seizures, since they appear more prone to develop epilepsy.

1. Introduction

Routine electroencephalography (EEG) may reveal incidental epileptiform discharges (ED) in healthy individuals (Gregory et al., 1993; Jabbari et al., 2000) and patients without a history of seizures (Bozorg et al., 2010; Goodin and Aminoff, 1984; Sam and So, 2001; Zivin and Marsan, 1968). The incidence of ED found in these studies ranges between 0.5% (Gregory et al., 1993) and 12% (Goodin and Aminoff, 1984).

In the only study to date that differentiated between unprovoked and provoked seizures ED were found in 12% of patients without a history of unprovoked seizures (Sam and So, 2001). Three fourths of these patients suffered from an underlying acute or progressive cerebral disorder. During follow-up 6% of these patients suffered seizures that were acutely provoked by the underlying disorder and none developed epilepsy (Sam and So, 2001). The interpretation of these findings is hindered by the lack of a sufficiently matched disease control group.

Thus, the aims of our study were (1) to assess the prevalence of ED in patients without a history of epilepsy, (2) to assess the incidence of epilepsy in this population during a 4-year follow-up and (3) to compare it with the incidence of epilepsy in a disease control group matched for neuroimaging results.

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2. Methods

Between January 1 and December 31, 2009 routine EEGs of all consecutive in and outpatients referred to the Department of Neurology at the Vienna General Hospital were reviewed by two EEG-board certified authors (E.P. and S.A.-W.).

EEGs were either ordered by neurologists working in the Vienna metropolitan area or after consultation of a neurologist on call at the Vienna General Hospital.

The EEGs were performed with a commercially available digital EEG system (alpha-trace 32-channel digital EEG record, B.E.S.T. Medical Systems, Vienna) for 30 min and included activation methods. The latter included 3 min of vigorous hyperventilation and photic stimulation at the following rates: 1, 3, 8, 10, 12, 15, 20 and 30 Hz. The EEG electrodes were placed according to the extended International 10-20 System with additional fronto-temporal electrodes (FT9/FT10).

Patients in this study were identified from our database of EEG procedures. For the purpose of this study we divided the reason for referral into the following categories: (A) follow-up in an epilepsy patient, (B) status epilepticus, (C) history of symptoms strongly suggestive of a seizure, (D) nonspecific symptoms not suggestive of a seizure (e.g. somnolence, headache, dizziness or visual disturbance) and (E) intensive care patient regardless of etiology.

We used the following inclusion criteria for this study: (1) the EEG was performed between January 1, 2009 and December 31, 2009. (2) The patient resided in the Vienna metropolitan area when the EEG was recorded. (3) The patient had no history of epilepsy. (4) The patient had no acute symptomatic or provoked seizures for which the index EEG was done.

Consequently, patients from referral category A–C and E were excluded from the final analysis. Patients from category D with a history of febrile seizures during childhood or prior acute symptomatic seizures due to hypoglycaemia or dehydration that were unrelated to the index EEG were explicitly included. Seizures were considered unrelated to the referral for the index EEG if it had been documented that the provoking condition had been sufficiently treated and the patients had fully recovered by the time they were referred for the index EEG.

Neuroimaging results of patients from referral category D with ED were obtained and further divided into the following categories: unremarkable, neoplasm, vascular pathology, inflammation, miscellaneous. Only patients whose neuroimaging procedures were performed within 2 weeks prior to or after the EEG procedure were included in this study. Disease controls were selected from the remaining patients of referral category D according to the following and pre-defined criteria: (1) their neuroimaging results had to fit into one of the above mentioned groups and resemble the neuroimaging result of each patient with ED of each subgroup as closely as possible and (2) the gender distribution in each subgroup of patients with ED had to be mirrored by each disease control subgroup. At the time of disease control selection the author (S.S.) who performed the search was blinded to their outcome regarding epilepsy during the follow-up, thus, ensuring to avoid any selection bias with respect to our controlled study design.

The medical records of patients in referral category D with ED and the disease controls were reviewed to determine whether they had suffered from unprovoked seizures, acutely provoked seizures or developed epilepsy after the index EEG. The patients were followed up until death, last contact or December 31. 2013, whichever came first. The medical record information system available at the Vienna General Hospital contains all entries made by hospital doctors in the Vienna metropolitan area. The medical records of each patient following the index EEG were available and reviewed thoroughly for the purpose of this study. We did not perform follow-up via telephone interviews and strictly relied on information entered by medical staff in the Vienna metropolitan area.

Seizures and epilepsy were defined according to the Classification and Terminology of the International League Against Epilepsy (ILAE) (Berg et al., 2010). To avoid selection bias, the determination of seizure occurrence was independent of the clinical diagnoses or impression provided in the medical records by the patients' physicians.

The statistical analysis of the data was performed using commercially available statistical software (SPSS 20.0; Chicago, IL). Continuous data are presented as means ± standard deviation (SD), nominal data as total numbers and percentages. Demographic and clinical characteristics of the patient groups A–E were compared using ANOVA with a post hoc Bonferroni test (corrected p-level set at <0.001). Patients with ED and the disease controls were compared using chi squares. We performed a logistic regression analysis to assess the risk of developing epilepsy if ED had been detected. We adjusted the model for age, gender, neuroimaging results (groups: unremarkable, neoplasm, vascular pathology, inflammation, miscellaneous) and cortical involvement of brain lesions (adjusted odds ratios (ORs) with 95% confidence intervals (95% CIs)). The level of significance was set at $p < 0.05$.

The study protocol was approved by the Ethics Committee of the Medical University of Vienna.

3. Results

One thousand seven hundred and eighty-one EEG recordings were performed between January 1 and December 31, 2009 at the Department of Neurology, Vienna General Hospital. Thirty-one (2%) EEG recordings were excluded due to missing clinical data. One thousand seven hundred and fifty patients and their EEG recordings (860 (49%) female), aged 52 ± 20 years (range 15–97 years), met the inclusion criteria.

The patients were distributed among the referral categories as follows: (A) follow-up in epilepsy patient ($n = 428$, age 43 ± 17 years), (B) status epilepticus ($n = 4$, age 52 ± 21 years), (C) symptoms strongly suggestive of a seizure ($n = 455$, age 60 ± 16 years), (D) unspecific symptoms not suggestive of a seizure ($n = 629$, age 55 ± 19 years) and (E) intensive care patient ($n = 234$, age 59 ± 16 years). The number of patients with ED was 65 (15%), 0, 51 (11%), 26 (4%) and 29 (12%) in referral category A–E. respectively. The five groups differed significantly regarding their age ($p < 0.001$) and the incidence of ED ($p < 0.001$).

3.1. Patients with incidental ED

Twenty-six (4%) patients in the referral category D showed ED. Of these, 7 were somnolent during the EEG recording, 19 patients maintained wakefulness, in one patient ED (temporal spikes) were induced by hyperventilation, and none by photic stimulation. Three disease controls were somnolent during the EEG recording. 23 disease controls maintained wakefulness. None of the patients or disease controls had a history of seizures of any type prior to the routine EEG.

The types of ED in these patients comprised (multi-)regional spikes ($n = 21$ (80%)), EEG seizure pattern ($n = 3$ (12%)) and periodic lateralized epileptiform discharges (PLED) ($n = 2$ (8%)) (Table 1) (Hirsch et al., 2013). Sample figures of these ED can be seen in Fig. 1. Eleven (42%) patients showed multiregional spikes (Table 1). Twenty-two (85%) of the patients with incidental ED had abnormal neuroimaging results (Table 1). In 11 (42%) patients the localization of the ED was concordant to the site of the brain

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