Informing patients about the impact of provocation methods increases the rate of psychogenic nonepileptic seizures during EEG recording

Robert Hoepner a,d,1, Kirsten Labutta b,c,1,2, Martin Schoendienst a,3, Theodor W. May c,4, Christian G. Bien a,5, Christian Brandt a,c,6

a Bethel Epilepsy Centre, Mara Hospital, Bielefeld, Germany
b Department of Clinical Psychology and Psychotherapy, University of Bielefeld, Germany
c Society for Epilepsy Research, Bielefeld, Germany
d Department of Neurology, St. Josef Hospital, Ruhr University, Bochum, Germany

Abstract

Observation of psychogenic nonepileptic seizures (PNESs) during video-EEG represents the diagnostic gold standard for PNESs. Different provocative techniques have been used to increase PNES frequency during EEG. These techniques include placebo administration, suggestion strategies, or both. In order to avoid the appearance of deception, we investigated the following hypothesis: If patients with PNESs were informed about the possible reduction of seizure threshold caused by hyperventilation and photic stimulation prior to EEG without any other suggestive strategies, PNESs would occur more frequently. In total, 34 inpatients with a diagnosis of PNESs, who had been informed prior to EEG about the increased seizure risk during hyperventilation and photic stimulation (study group), and 80 “noninformed” patients (control group) were enrolled. Psychogenic nonepileptic seizures occurred significantly more often in the study group compared to controls (38% vs. 10.0%, p = 0.001). Our results imply that simply providing correct and explicit information about provocation techniques substantially increased the PNES rate.

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1. Introduction

Psychogenic nonepileptic seizures (PNESs) are episodes of altered movement, sensation, or experience resembling epileptic seizures but not associated with ictal epileptiform discharges in the brain but which, instead, have a psychological origin [1,2]. Psychogenic nonepileptic seizures are frequently associated with further psychiatric disorders, such as affective and anxiety disorders [1]. The prevalence of PNESs is 2–33/100,000 in the general population [3]. About 20% of the patients initially diagnosed with intractable epileptic seizures actually suffer from PNESs [4]. To prove a PNES diagnosis, EEG recording during a PNES must demonstrate physiological brain activity and the absence of epileptic discharges [1]. It is, however, often laborious to wait for the spontaneous occurrence of PNESs. Therefore, protocols to induce PNESs during EEG are used by nearly 40% of the American Epilepsy Society members [5]. Common induction procedures are based on placebo effects (e.g., sodium chloride administration or application of a colored patch placed on the skin) [6,7] and suggestion strategies (verbal reinforcement of clinical symptoms) [8]. The use of placebo and suggestion in order to induce PNESs has been controversial [9,10]. In the current study, we aimed to investigate whether giving correct information about seizure-provoking methods is sufficient to increase the frequency of PNESs. We hypothesized that PNESs would occur more frequently during EEG with hyperventilation and photic stimulation if patients with PNESs were explicitly informed about the possible reduction of seizure threshold caused by these methods prior to EEG.

2. Methods

Because of a change in clinical procedure since the 15th of June 2011, prior to EEG, all inpatients of Bethel Epilepsy Centre, a tertiary referral center for epilepsy, were routinely informed about the effect of seizure threshold reduction caused by hyperventilation and photic stimulation in some patients with epilepsies. Detailed written information about the potential consequence of hyperventilation and photic stimulation was given to the patients by the attending physician.
during the first inpatient visit. The attending physician usually gave some additional verbal information about the procedure and the physiological effect of hyperventilation and photic stimulation. The written patient information contained correct information about the frequency of epileptic discharges and seizures triggered by both methods in patients with focal epilepsies and generalized epilepsies. It also said that PNESs may occur during hyperventilation or photic stimulation (see Supplemental material 1 and Table 1). The reason for this information was that we do not think that PNESs are inducible by hyperventilation and photic stimulation via physiological or pathophysiologial reactions of the brain, but their occurrence during administration of these techniques, especially in combination with psychological strategies like suggestion or verbal reinforcing, as previously reported in the literature, is possible [7,8,11,12]. An EEG recording was performed after a 24-hour reflection period and only if the patient information was signed before the EEG occurred.

Before June 15, 2011, routine clinical procedure did not include explicit patient information about reduction of seizure threshold by hyperventilation and photic stimulation given prior to EEG recording. Patients who attend a tertiary reference center for epilepsy are usually used to undergoing an EEG, so no specific information was given. In both groups, EEG was performed by an EEG-technician, in the absence of a physician, without any reinforcing strategies or unnecessary medical instruments. At the beginning of a 15- to 20-minute EEG recording, photic stimulation was presented for 3 min with a defined set of frequencies between 1 and 50 Hz. Each frequency was tested under two conditions: immediately after eye closure and with closed eyes. Afterwards, patients were instructed to hyperventilate for 5 min. Psychogenic nonepileptic seizures during EEG was defined as a seizure without a corresponding EEG seizure pattern and a normal background activity during the attack. If a PNES occurred, patients were asked afterwards to score the event on a scale between 1 (totally atypical) and 10 (absolutely typical). A cutoff score ≥7 points was used for identifying a typical PNES.

The diagnosis of PNES disorder was not exclusively based on the above-mentioned EEG procedure as it also relied on an extensive and multidisciplinary diagnostic procedure at Bethel Epilepsy Centre which includes long-term EEG, MRI, seizure semiology, and psychiatric evaluation, among others. Thirty-four patients (27 having pure PNESs and 7 having both PNESs and epileptic seizures) were previously informed in the way described above. Eighty patients (46 having pure PNESs and 34 having both PNESs and epileptic seizures) underwent EEG between January 2010 and June 2011 and were, therefore, not informed. We compared the frequency of PNESs during EEG in the two groups. Data resulted from a change of routine clinical practice and were collected retrospectively. Furthermore, all patients gave written informed consent that the data collected – including video-EEG recording – during their inpatient treatment could be used for scientific purposes.

For statistical analysis, we performed Fisher’s exact test, Mann–Whitney test, and Mantel–Haenszel test using SPSS 18.

3. Results

We investigated 114 patients with PNESs. Table 2 illustrates the patients’ characteristics, demonstrating that the only significant difference between the groups is the rate of patients having pure PNESs diagnosis. Of the study group patients, 38.2% had a PNES during the EEG. Psychogenic nonepileptic seizures occurred in 4 patients during hyperventilation, in 4 patients during photic stimulation, in 2 patients during both provocative techniques, and in 3 patients during the EEG recording after the provocative techniques had been performed. Psychogenic nonepileptic seizure events were characterized afterwards by all of the 13 patients (mean: 9.31, SD: 1.03, min.: 7, max.: 10), and everyone scored his/her PNES as typical (≥7 points). Psychogenic nonepileptic seizures occurred significantly less frequently in the control group patients (10.0%; p = 0.001). The rate of patients having pure PNESs diagnosis was significantly higher within the study group (p = 0.03) (Table 2). The Mantel–Haenszel test showed that the higher rate of PNESs was still significant when groups were stratified according to diagnosis (PNESs plus epilepsy vs. pure PNESs diagnosis) (Table 3). Excluding patients with additional epileptic seizures, the informed patients had a significantly higher rate of PNESs occurrence during EEG compared to the controls (p = 0.02) (see Table 3).

4. Discussion

We demonstrated a significantly increased rate of PNESs during EEG if patients with PNESs were informed previously about the potential reduction of seizure threshold caused by hyperventilation and photic stimulation in some patients with epilepsy. Our study population
consisted of patients with pure PNESs and patients with PNESs and epileptic seizures. We included patients with both seizure types as patients with double diagnosis are quite common in epilepsy centers [4]. We did not find an effect of the additional diagnoses of epilepsy on the increased PNES rate of the informed patients as shown by the Mantel–Haenszel test. Furthermore, the PNES rate was also significantly higher in the informed patients compared to the noninformed patients when patients with epilepsy were excluded from the analysis. In comparison to other studies inducing PNESs with placebo or with hyperventilation and suggestion strategies [6–8], the occurrence of PNESs was lower in our study. Using placebo and suggestion methods in order to induce PNESs is controversial because the element of deception inherent in such strategies might irritate patients and might have a negative effect on the doctor–patient relationship. Further, there are, however, other differences to our approach. Devinsky and Fisher – in contrast to our study – did not mention the rate of successfully induced PNESs by their procedure [13]. In addition to hyperventilation and photic stimulation, Benbadis et al. also applied suggestive strategies: “The technologist gradually increased photic frequency and asked key questions about the occurrence of the habitual symptoms while testing responsiveness and reinforcing any clinical change (e.g., “tremor is beginning”)” [8,11]. We only gave information but did not use any reinforcing strategies during the EEG recording. Benbadis et al. did not – in contrast to our study – include a control group [8,11]. McGonigal et al. also used verbal reinforcing strategies as a supporting suggestive tool (“Any clinical change occurring during recording (for example, shaking of a limb, apparent unresponsiveness) was commented on by AMcG, for reinforcement”) [12]. So, we used a different approach. There is also a difference in the results. According to our knowledge, our study is the first study to analyze exclusively the effect of patient information on PNES frequency because we had excluded any other verbal reinforcing or suggestion strategies during EEG recording. The fact that three out of 13 recorded PNESs did not occur during hyperventilation and photic stimulation but after administration of hyperventilation and photic stimulation does not contradict our findings. An elicitation of those spells by the information procedure is still possible.

Nevertheless, correct diagnosis of PNESs is very important to initiate appropriate treatment [9,10]. Our results indicate that providing explicit information about the seizure threshold reduction caused by hyperventilation and photic stimulation is sufficient to increase the PNES frequency substantially without misinformation.

Because of our findings, we propose, even from an economic point of view, a step-by-step approach for diagnosing PNESs. As a first step, an outpatient EEG recording with our information procedure might be performed. When no seizure occurs, it might be useful to conduct an inpatient EEG using suggestion strategies in a protected environment [8].

Our study and especially the study design had some limitations, which should be discussed. First, we present data of a retrospective study. Especially, the information procedure of the control group was, because of the retrospective design, not standardized, which is, however, not unusual as patients of a tertiary referral center like ours are regularly acquainted with this examination. Our findings should be reevaluated in a prospective manner. Second, it is a study with inpatients of a specialized epilepsy center. So, the idea that the patients included form a selected population cannot be excluded, although we do not have any indication for this. Third, the control group was included chronologically before the study group. Baseline seizure frequency did not differ significantly between the study and control groups, but there are many missing values in the control group. This is also due to the study’s retrospective nature and may be regarded as a limitation of our study. Generally, possible confounders due to this chronological difference should be considered. We think, however, that this is unlikely because diagnostic pathways and treating physicians as well as nurses and EEG technicians have remained significantly unchanged since January 2010, the beginning of our retrospective data analysis.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.yebeh.2013.06.009.

**Study sponsorship or funding**

None.

**Disclosures of all authors**

Robert Hoepner, Kirsten Labudda, Theodor W. May, and Martin Schoendienst have no disclosures.

Christian G. Bien served on the scientific advisory boards of UCB and Eisai, Germany, undertook industry-funded travel with the support of Eisai, UCB, Desitin, and Grifols (all in Germany), and obtained honoraria for speaking engagements from Eisai, UCB, GlaxoSmithKline, and Desitin (all in Germany).

Christian Brandt served on the scientific advisory boards for UCB and Pfizer, received funding for trips from UCB and Pfizer, received honoraria for serving on steering committees for Pfizer and Desitin and for being a speaker for Pfizer, Desitin, Eisai, UCB, and GSK, and received research support from Pfizer.

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