Epilepsy & Behavior 13 (2008) 256–259

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Case Report

Predicting epileptic seizures with a mental simulation task: A prospective study

Angela Alessia Bruzzo [a,b,*], Benno Gesierich [c], Guido Rubboli [b], Ram Lakhan Pandey Vimal [d,e,f,g]

[a] Department of Psychology, University of Bologna, V. Carlo Berti Pichat, 5-40127 Bologna, Italy
[b] Department of Neurosciences, Bellaria Hospital, University of Bologna, V. Altura, 3-40127 Bologna, Italy
[c] Center for Mind/Brain Sciences, University of Trento, Corso Bettini, 31-38068 Rovereto, Italy
[d] Vision Research Institute, Department of Neuroscience, 428 Great Road, Suite 11, Acton, MA 01720, USA
[e] Dristi Anusandhana Sansthana, A-60 Umed Park, Sola Road, Ahmedabad-61, Gujrat, India
[f] Dristi Anusandhana Sansthana, Sai Niwas, East of Hanuman Mandir, Betiahata, Gorakhpur U.P. 273001, India
[g] Dristi Anusandhana Sansthana, c/o NiceTech Computer Education Institute, Pendra, Bilaspur, C.G. 495119, India

ARTICLE INFO

Article history:
Received 9 February 2008
Accepted 20 February 2008
Available online 18 April 2008

Keywords:
Biological and nonbiological motion
Mental simulation
Motor imagery
Right temporal lobe epilepsy
Seizure prediction

ABSTRACT

The unpredictability of seizures is one of the most disabling aspects of epilepsy. We assessed the possibility of forecasting seizure onset by means of a behavioral task using mental simulation of biological and nonbiological movements. Four patients with epilepsy were included in a longitudinal study. In two patients with right temporal lobe epilepsy (RTLE), performance of the task changed depending on the epileptic cycle. In the preictal phase, timing precision decreased during simulation of biological movements and increased during simulation of nonbiological movements. In two other patients, the timing precision during simulation of biological movements was chronically decreased. The observed phase dependency of performance in patients with RTLE may indicate changes in brain states hours in advance of seizure onset. We suggest that our paradigm might be a simple and accurate method for the prediction of epileptic seizures. The validity of the approach for different types of epilepsy should be assessed in future studies.

1. Introduction

The ability to predict epileptic seizures well before clinical onset would enable the use of novel approaches to seizure control (e.g., on-demand delivery of antiepileptic drugs, electrical brain stimulation [1], behavioral strategies [2,3]) or simply allow patients to avoid dangerous or embarrassing situations. For at least two decades, the possibility of prospectively predicting an impending seizure from online EEG recordings has been studied intensively [4–15]. Nevertheless, the efficacy of these approaches remains to be assessed [13–15] and no clinical, applicable system has been described until now.

To our knowledge, there are no approaches using behavioral procedures for seizure prediction. For the first time, we have assessed the behavioral performance of four patients with epilepsy with a mental simulation task, which was previously used in schizophrenic patients [16]. We chose this task because the occurrence of psychotic episodes in epilepsy has frequently been described in the literature [17–22]. Hence, we hypothesized that performance of the mental simulation task in patients with epilepsy would change over the "epileptic cycle" (defined by the interictal, preictal, ictal and postictal phases), becoming more similar to the performance of schizophrenic patients in certain phases [23–27]. Within the scope of our study, a change in performance prior to seizure onset would have been of particular interest.

Briefly, in our previous study on schizophrenia [16], we investigated the mechanisms underlying mental simulation of biological and nonbiological movements. Biological motion, in contrast to nonbiological motion, refers to the active movements of living beings. Subjects had either to simulate mentally or to overtly reenact previously executed or observed movements of both types. The duration of each template movement was compared with the duration of the corresponding simulated or reenacted movement. Healthy controls exhibited very high timing precision when simulating biological movements and a strong distortion when simulating nonbiological movements. Paranoid schizophrenics, however, behaved in the opposite manner. Given this double dissociation, we [16] concluded that the mechanisms underlying mental simulation of biological and nonbiological movements are separate from each other. Performance of both subject groups was almost perfect for both movement types, when movements had to be reenacted. This second finding confirmed that perception, attention, and memory for movements were not the reason for the distorted timing during mental simulation.

The aim of the present study was to assess the performance of patients with epilepsy on the same task in different phases of the epileptic cycle. Patients were asked to perform the behavioral task

* Corresponding author. Fax: +39 (0)51 243086.
E-mail address: angela.bruzzo@libero.it (A.A. Bruzzo).

1525-5050/$ - see front matter © 2008 Elsevier Inc. All rights reserved.
doi:10.1016/j.yebeh.2008.02.013

daily during a longitudinal study. As temporal distance between seizure occurrence and test sessions changed randomly over the duration of the study, the correlation between this temporal distance and behavioral performance could be assessed.

2. Materials and methods

2.1. Patients

We recruited four patients from the Department of Neurological Sciences, Bellaria Hospital University of Bologna (Italy). All were women and right-handed [28], with an onset of epilepsy before 18 years of age (11 ± 1.41) and a mean duration of epilepsy of 15 years (±8.49). The level of education was, on average, 9.5 years (±2.12). Patients S1 (aged 32 years) and S2 (29 years) were affected by right temporal lobe epilepsy (RTLE). Patient S3 (31 years) was affected by left frontotemporal epilepsy, and patient S4 (38 years) was affected by idiopathic generalized epilepsy.

All patients were taking anticonvulsant drugs in polytherapy. Medication levels and types of drugs were maintained constant over the period of the study, and drugs were always taken at the same time. There is no information on possible effects of medications on our experiment. Before beginning the study, each patient underwent a neuropsychological assessment [28–35], outlined in Table 1, to ascertain that all patients were able to understand the task. No subject manifested psychogenic seizures. All patients were in good physical health, determined by a physical examination and laboratory evaluation including a complete blood count, glucose and hepatic enzyme levels, and renal and thyroid analyses.

2.2. Procedure

The local ethics committee at the University of Bologna, (Italy) approved the procedures in accordance with the ethical standards of the 1983 Declaration of Helsinki. All patients entered into the study after providing informed consent. Each subject was observed over a period of 29 days. The experimental task was undertaken every day at the same time (S1: 4 pm; S2: 7 pm; S3: 2 pm; S4: 1 pm), excluding weekends and holidays. This period included 18 recording days and 11 seizures for S1, 17 recording days and 6 seizures for S2, 18 recording days and 7 seizures for S3, and 18 recording days and 8 seizures for S4. The patients selected for this study were susceptible to several seizures per month. This permitted us to collect enough data; recruitment of more patients was difficult because such patients were not available to us. Subjects were required to mark on a calendar accurately the day, hour, and behavioral situation in which seizures occurred. Hence, subjects could not be kept totally naïve about the aim of the study. They were told that the aim was to investigate time estimation across epileptic phases. However, nothing was told about the working hypothesis (i.e., the expected difference among the experimental conditions and phases of the epileptic cycle were not discussed).

The behavioral task and procedure are described in detail elsewhere [16]. Each experimental trial consisted of two phases: (1) observation or execution of a movement, (2) followed by mental simulation of the very same movement. Briefly, in the first phase, patients had to observe (biological "other" or BO) or execute (biological "self" or BS) a parabolic arm/hand movement, or had to observe an analogous computer-generated movement (ball on computer screen: nonbiological movement, or NB). To initiate the parabolic arm/hand movements, the subject (in condition BS) or the experimenter (in condition BO) had to release a start key and move up and down in the vertical plane to press a stop key. Start and stop keys were positioned symmetrically with respect to the midsagittal plane in front of the subject. The screen for the presentation of the nonbiological movements was positioned about 15 cm behind the response keys, and the distance between the start and stop positions of the ball movements was identical to that between the start and stop keys. In the second phase of each trial, immediately following presentation of one of the three template movements (i.e., BO, BS, NB), subjects had to imagine the very same movement. In contrast to the previous study [16], participants were not asked to reenact the movements. This condition was omitted to avoid overloading the patients, who had to participate in the study every day in addition to their daily duties. Participants had to indicate the start and stop of the imagined movements by releasing and pressing the same start and stop keys as used during production of the biological template movements. But, to prevent the movements during mental simulation from being similar to the imagined movements, the subjects manipulated the keys with their left and right index fingers, while resting both hands statically on the table throughout the simulation. Duration of biological template movements and imagined movements was measured as the interval between key release and key press. Duration of nonbiological movements was defined as the time between onset and stop of the apparent motion of the ball on the screen. Durations of template and imagined movements were compared to measure timing precision during mental simulation. Each of the three conditions (i.e., NB, BS, BO) was repeated in 10 randomly ordered trials.

2.3. Statistical analysis

As patients were affected by different types of epilepsy, we analyzed data for each subject separately. The correspondence between the duration of each presented/executed template movement and that of the related imagined movement was measured by the proportional error. Subsequently, the mean proportional error (MPE) was calculated for each experimental condition and session. A regression analysis was performed to determine possible correlations between absolute MPE values and temporal distance of the test session from the preceding seizure and to the succeeding seizure.

Table 1
Neuropsychological assessment

Test	Scoring
Birmingham Object Recognition Battery [29]	25.14 ± 2.27
Global Assessment of Function (DSM-IV-TR) [30]	77.29 ± 4.60
Brief Psychiatric Rating Scale [31]	23.86 ± 1.07
Profile of Mood States [32]	17.43 ± 1.51
Beck Depression Inventory [33]	9.86 ± 1.07
Wisconsin Card Sorting Test: Perseverative Errors [34]	3.29 ± 0.76
Intelligence measures (Wechsler Adult Intelligence Scale—Revised) [35]	100.6 ± 4.60
Verbal IQ	
Performance IQ	102.6 ± 3.58
Full Scale IQ	102 ± 4

3. Results

The means of all MPE values resulting from all test sessions in the different experimental conditions for each patient are listed in Table 2. The range in time from the test session to the preceding/succeeding seizure is indicated as well. For patient S1, we found significant correlations between time from the test session to the succeeding seizure and MPEs in conditions NB ($F(1,16) = 33.74$, $P < 0.01$, $\beta = 0.82$) and BO ($F(1,16) = 5.18$, $P = 0.04$, $\beta = -0.49$). This correlation (between time from the test session to the succeeding seizure and MPE values) was also ob-

Table 2
Mean MPE values

Patient	Phase	MPE[a]			Time from preceding seizure[b] (h)	Time to next seizure[b] (h)
		NB	BS	BO		
S1	All	13.46 (3.92)	29.32 (5.95)	38.03 (7.13)	16–304.5 [18, 72.5 (17.1)]	3.8–264 [18, 55.5 (13.1)]
	Preictal	0.98 (0.19)	38.29 (8.63)	53.09 (9.02)	16.5304.5 [11, 59.3 (17.9)]	3.8–8 [11, 6.7 (2)]
	Inter-/postictal	33.08 (2.66)	15.21 (2.95)	14.37 (2.17)	16–208.5 [7, 98.8 (37.3)]	30–264 [7, 132.1 (49.9)]
S2	All	15.61 (2.39)	16.69 (4.21)	33.62 (3.61)	10–143 [17, 57.2 (13.9)]	0.5–104 [17, 39.7 (9.6)]
	Preictal	2.46 (0.74)	30.07 (10.13)	29.19 (4.96)	10–82 [5, 57.7 (25.8)]	0.5–3.25 [5, 1.4 (0.6)]
	Inter-/postictal	21.09 (1.55)	11.11 (3.38)	35.47 (4.70)	10–143 [12, 57 (16.4)]	23–104 [12, 55.7 (16.1)]
S3	All	22.35 (5.21)	44.07 (8.64)	47.55 (9.78)	18–209 [18, 71.5 (16.9)]	1.8–189.5 [18, 52.6 (12.4)]
S4	All	35.48 (4.80)	42.02 (13.88)	41.13 (12.18)	9–95 [18, 45.3 (10.7)]	1–100 [18, 44.4 (10.5)]

Note. MPE values from all test sessions (All) in the different experimental conditions (columns NB, BS, BO) were averaged for each patient (S1, S2, S3, S4). In addition, for patients S1 and S2, MPE values from test sessions within the preictal phase and interictal/postictal phases were calculated.

[a] Mean (SE).

[b] In brackets are the number of test sessions and mean (SE) time from the test session to the seizure.