Clinical Neurophysiology 119 (2008) 2201–2204

Contents lists available at ScienceDirect

Clinical Neurophysiology

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

K-complex-induced seizures in autosomal dominant nocturnal frontal lobe epilepsy

J. El Helou [a,b], V. Navarro [a,c,f], C. Depienne [d,e], E. Fedirko [e], E. LeGuern [d,e,f], M. Baulac [a,c,f], I. An-Gourfinkel [a,d,f], C. Adam [a,b,f,*]

[a] AP-HP, Epileptology Unit, Neurology 1 Department, La Pitié-Salpêtrière Hospital, Paris, France
[b] CNRS UPR640 'Neurosciences Cognitives et Imagerie Cérébrale', La Pitié-Salpêtrière Hospital, Paris, France
[c] INSERM U739 'Cortex et Epilepsie', La Pitié-Salpêtrière Hospital, Paris, France
[d] INSERM UMR-S679 'Neurologie et Thérapeutique Expérimentale', La Pitié-Salpêtrière Hospital, Paris, France
[e] Unité Fonctionnelle de Neurogénétique Moléculaire et Cellulaire, La Pitié-Salpêtrière Hospital, Paris, France
[f] UPMC Univ Paris 06, Paris, France

ARTICLE INFO

Article history:
Accepted 27 July 2008
Available online 31 August 2008

Keywords:
K-complex
ADNFLE
Frontal lobe epilepsy
Sleep
Microstructure
Cyclic alternating pattern

ABSTRACT

Objective: To examine in detail the relations between seizures and K-complexes in autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE).
Methods: Prolonged continuous video-EEG recording and analysis of 30 seizures in an 18-year-old woman suffering from ADNFLE with a CHRNA4 gene mutation.
Results: Twenty-seven of 30 recorded seizures started just after a K-complex. In nine cases a sound induced a K-complex that was immediately followed by the seizure. Most seizures preceded repetitive and brief ictal restarts.
Conclusions: Three new characteristics have been observed in this ADNFLE patient: a K-complex is almost invariably present at seizure onset; sounds trigger some seizures; ictal restarts occur often.
Significance: These new observations – the presence of K-complexes at seizure onset and occurrence of sound-triggered seizures – support the view that ADNFLE seizures may be initiated by K-complexes.

1. Introduction

Autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE) was first described in 1994 (Scheffer et al., 1994). Mutations associated with this hereditary epilepsy involve subunits of the neuronal nicotinic acetylcholine receptor (nAChR) (Steinlein et al., 1995). For many years nocturnal frontal lobe epilepsy (NFLE) seizures were not clearly differentiated from sleep disorders (Tinuper et al., 1990) and the relation between seizures and sleep is still not clear. EEG transients, rhythms or microstructural components of sleep have been suspected to facilitate or trigger NFLE seizures – the cyclic alternating pattern phase A (CAP-A) sequences (Terzano et al., 1991) in epilepsies with nocturnal partial motor seizures, a slow wave resembling a K-complex (KC) in NFLE (Tinuper et al., 1990), an atypical KC (Oldani et al., 1996) or spindles (Picard et al., 2006) in ADNFLE. Since these reports have not been documented in detail, we carried out a comprehensive video-EEG study of an ADNFLE case with a new mutation in which seizure onsets often coincided with KCs and were sometimes triggered by sound stimuli.

2. Patient and methods

An 18-year-old woman was monitored continuously over 8 days in our video-EEG unit for diagnosis. She had suffered from nocturnal seizures since the age of three: frequent nocturnal generalized clonic seizures initially, replaced later by seizures consisting of brief, stereotyped episodes, sometimes starting with an ascending heat sensation. The patient often remembered her ictal manifestations: right arm stretching, slow arm movements, mouth opening, chewing and breathing difficulties. Seizures were resistant to 10 anti-epileptic drugs: totally to topiramate, lamotrigine, valproate, carbamazepine, phenobarbital and partially to oxcarbazepine, gabapentine and diazepam (taken only occasionally) whereas levetiracetam and clobazam were not well tolerated. She also had mood disturbances and, during childhood, suffered from parasomnias, including sleep walking, sleep talking and night terrors. Her physical examination and brain MRI were normal. A genetic analysis revealed a novel mutation (Leu290Val) in the gene coding for the alpha 4 subunit (CHRNA4) of the neuronal nicotinic acetylcholine receptor (nAChR), located at the M2 domain. Her sister has manifested one isolated convulsive seizure and her mother has nocturnal frontal lobe seizures.

We (J.E. and C.A.) performed a clinical and EEG analysis of thirty seizures recorded on video-EEG.

* Corresponding author. Address: Unité d'Epileptologie, Service de Neurologie 1, Hôpital de La Pitié-Salpêtrière, 47–83 Boulevard de l'Hôpital, 75651 Paris Cedex 13, France. Tel.: +33 1 42161810; fax: +33 1 44245247.
E-mail address: claude.adam@psl.aphp.fr (C. Adam).

1388-2457/$34.00
doi:10.1016/j.clinph.2008.07.212

3. Results

Continuous video-EEG monitoring revealed clustered seizures consisting of 7–13 episodes per night which occurred on three nights. Nine of 30 recorded seizures were triggered by sudden noises such as door opening or shouting. Seizures started abruptly during sleep with an axial extension, then forced mouth opening, apnoea, dystonic posturing of the right then left arm followed by athetotic movements of right then both arms and ended with a snoring sound (see Supplementary Video). Some movements of the four limbs and a few oro-alimentary automatisms occurred just after a seizure. Episodes were stereotyped, of variable intensity and lasted 31 s on average (20–45 s). The patient woke during the seizure, and could often report events that had occurred during the episode; thus, consciousness was usually not lost. There was no neurological deficit post-ictally. Seizures occurred in sleep stage two (21 seizures) or three (9 seizures). Twelve seizures presented no major EEG artefacts. They consisted of (i) an initial, brief sequence of anterior bilateral rhythmic activity (1–3 s; 8.5–11 Hz), mingled with slower potentials, maximal from frontal regions, followed by (ii) transient slowing and disorganisation of rhythms then by (iii) renewal of the initial activity in a more sustained way, becoming slower and of larger amplitude, mainly over the midline fronto-central region (Figs. 1 and 2, Supplementary Figures S1–S3). Interestingly, 27/30 seizures began on the descending slope of a K-complex (Fig. 1, Supplementary Figures S1 and S2) or just after (Fig. 2 and Supplementary Figure S3). KCs were either spontaneous (18/27) or sound-evoked (9/27). For the sound-evoked seizures, the timing of clinical and EEG signs could be clearly defined with respect to the sound. In these cases they appeared immediately or very early during the seizure (Fig. 1). Most seizures (22/30) were followed by repetitive (1–10) brief restarts (Atalla et al., 1996) of an ictal rhythmic activity (6–12 Hz), clinically evident as chewing and athetotic hand movements. An ictal restart lasted on average 2.1 s (0.4–7 s) and only 18/88 restarts were associated with a KC. The mean duration of sequences of repeated restarts after a seizure was 61 s (15–140). Interictal EEG was normal.

4. Discussion

This analysis of 30 seizures from a genetically confirmed ADNFLE case shows that K-complexes were associated with the onset of 90% of seizures. Thirty per cent of these seizures were associated with a sudden sound, pointing to a likely causal relation. For these noise triggered seizures, the sound provoked the K-complex (Halász, 1993) and the seizure, and linked together these two latter events in such a way that the KC occurred just at the beginning of the seizure. Thanks to these noise triggered seizures, we also deduced that both EEG and clinical ictal signs occurred almost instantaneously at seizure onset. This information gave us significant clues to interpret the other seizures which presented with

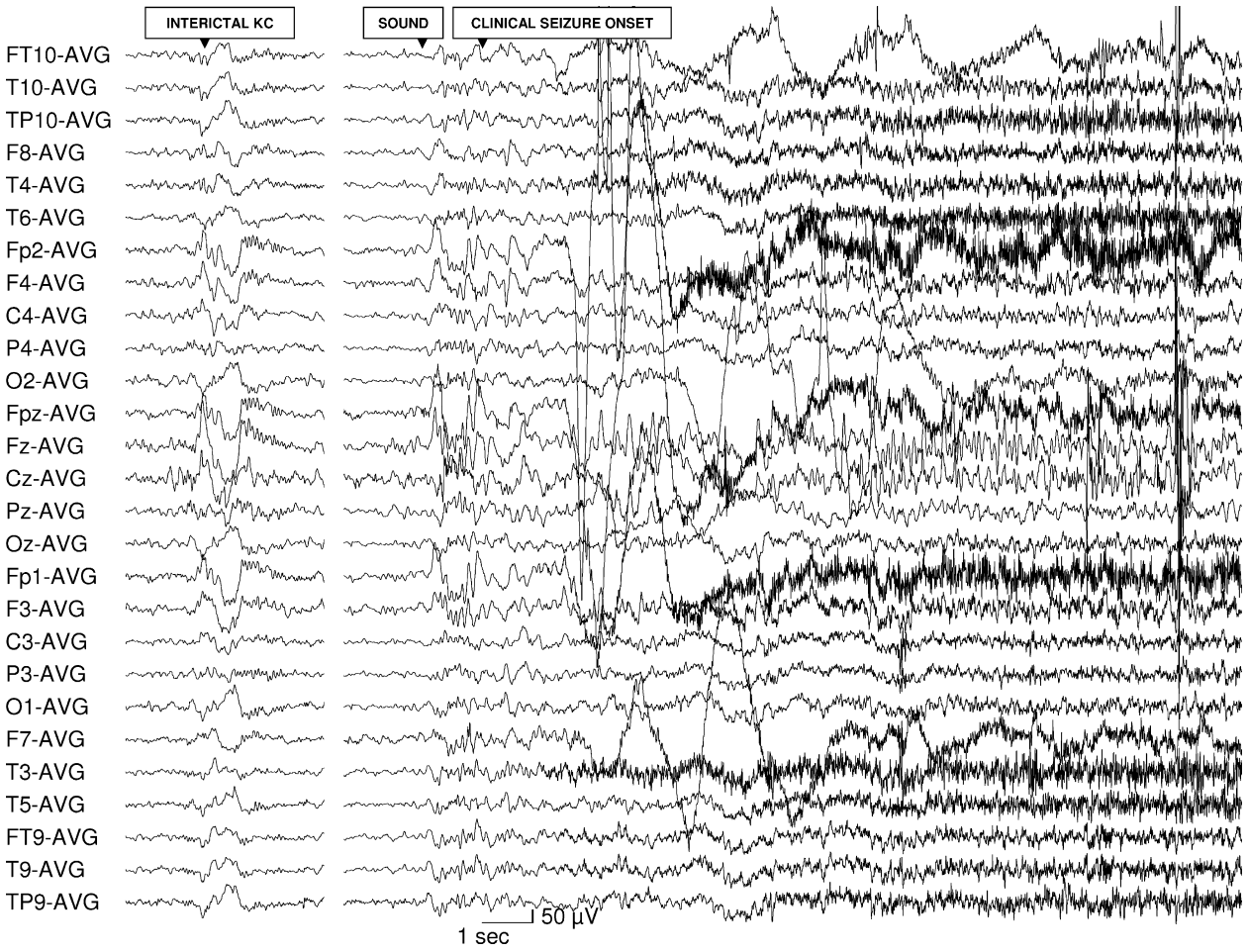

Fig. 1. This figure shows an Interictal KC (first part) and a seizure starting just after a sound induced KC (second part). The seizure starts, on the descending slope of the triggering KC, with a widely distributed rhythmic activity maximal over the frontal regions, which slows for a few seconds to resume clearly over the fronto-central midline. Note the resemblance between the Interictal KC and the KC at seizure onset. Clinical onset occurs very early. Averaged montage (Fp1, Fp2 and Fpz are excluded from average) with a 35 Hz low-pass filter.