

Apnoea and bradycardia during epileptic seizures: relation to sudden death in epilepsy

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Abstract

Objective—To record non-invasively ictal cardiorespiratory variables.

Methods—Techniques employed in polysomnography were used in patients with epilepsy undergoing EEG-video recording at a telemetry unit.

Results—Apnoea (> 10, range > 10–63, mean 24 s) was seen in 20 of 47 clinical seizures (three secondary generalised, 16 complex partial, and one tonic) and 10 of 17 patients. Apnoea was central in 10 patients, but obstructive apnoea was also recorded in three of 10. Oxyhaemoglobin saturation (SpO₂) dropped to less than 85% in 10 seizures (six patients). An increase in heart rate was common (91% of seizures). Bradycardia/sinus arrest was documented in four patients (mean maximum RR interval 5.36, range 2.8–8.6 s) but always in the context of a change in respiratory pattern.

Conclusion—Ictal apnoea was often seen. The occurrence of bradycardia in association with apnoea suggests the involvement of cardiorespiratory reflexes. Similar mechanisms may operate in cases of sudden death in epilepsy.

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It is well documented that otherwise well patients with epilepsy may die unexpectedly (sudden unexpected death in epilepsy (SUDEP)).^{1–17} Ictal autonomic mechanisms have been postulated with recent attention focused on changes in cardiac rhythm.^{16 18–22} Apnoea is known to occur during seizures,^{18 23–27} but systematic studies of ictal respiratory changes in adults are few. We set out to assess the yield and feasibility of routinely applying polysomnography techniques to seizure recordings in patients undergoing EEG/video-telemetry.²⁸

Patients and methods

The study, approved by the hospital ethics committee, was performed in the telemetry unit at the National Hospital for Neurology and Neurosurgery. Patients with a probable diagnosis of epilepsy admitted for EEG/video-telemetry were recruited. These were consecutive patients (two excluded) being monitored

using an in house assembled system that was adapted for the additional variables.

As well as routine video/audio recording time synchronised with 22 channels of EEG/ECG (± 5 EMG/EKG), the following were recorded: oxygen saturation and plethysmography using a pulse oximeter (Nellcor N200E, normal setting, disposable digital probes, Nellcor Adult Oxisensor D-25), mouth and nasal airflow (disposable Nellcor Adult Airflow Sensor, Model 971), and respiration (chest and abdominal Resptrace bands).

All physiological data, including oximetry, could be simultaneously displayed and epochs reviewed or plotted with an adjustable time scale of 10–40 seconds per page. Seizures were identified by review of video/EEG recordings. Baseline ECG rates were determined for epochs between 10 and 20 seconds and expressed as beats per minute (bpm). Ictal maximum and minimum rates were noted if the minimum rate differed by more than 10 bpm from baseline. The longest RR interval was measured. Respiratory changes associated with seizures were noted: ictal apnoea was defined as cessation of airflow of more than 10 seconds and characterised as central or obstructive.

Results

Of 33 patients approached, one declined and a further three withdrew. One other patient was being assessed for suspected apnoeic spells distinct from his epileptic seizures. Only the epileptic seizures were analysed. Seventeen patients (11 men, six women) had 47 clinical seizures recorded with additional cardiorespiratory variables. Mean age was 32 (range 18–43) years. The indication for recording was presurgical assessment in 13 and diagnostic in four. Only six of 17 patients had small reductions in their antiepileptic drugs. The epilepsy diagnosis was symptomatic generalised in two and localisation related in 15 (10 temporal, two frontal, three location uncertain).

The 47 clinical seizures included three secondary generalised tonic clonic seizures, 35 complex partial seizures, one spontaneous absence, and eight predominantly tonic seizures. Auras or pure electrographic seizures were not analysed.

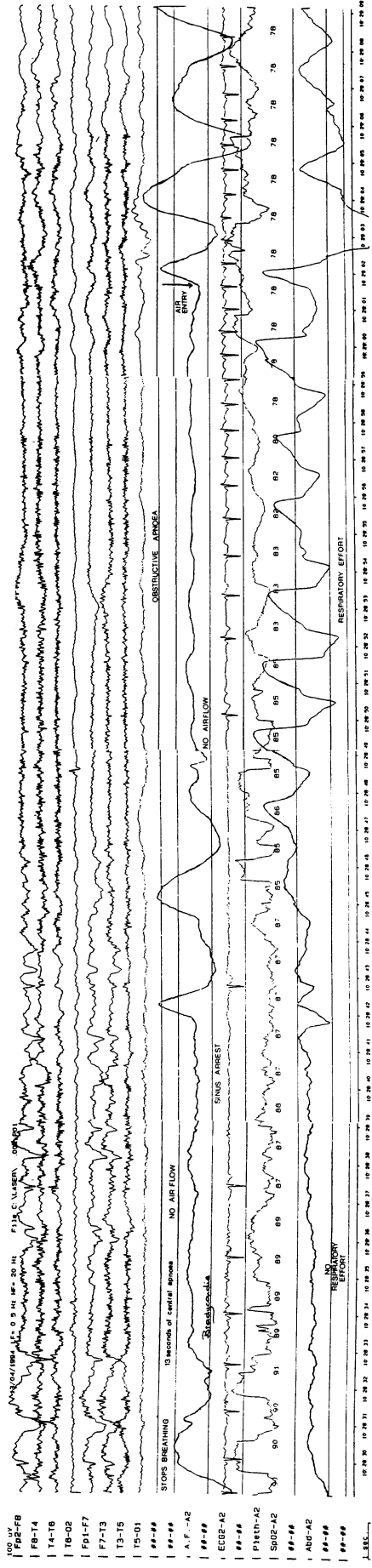
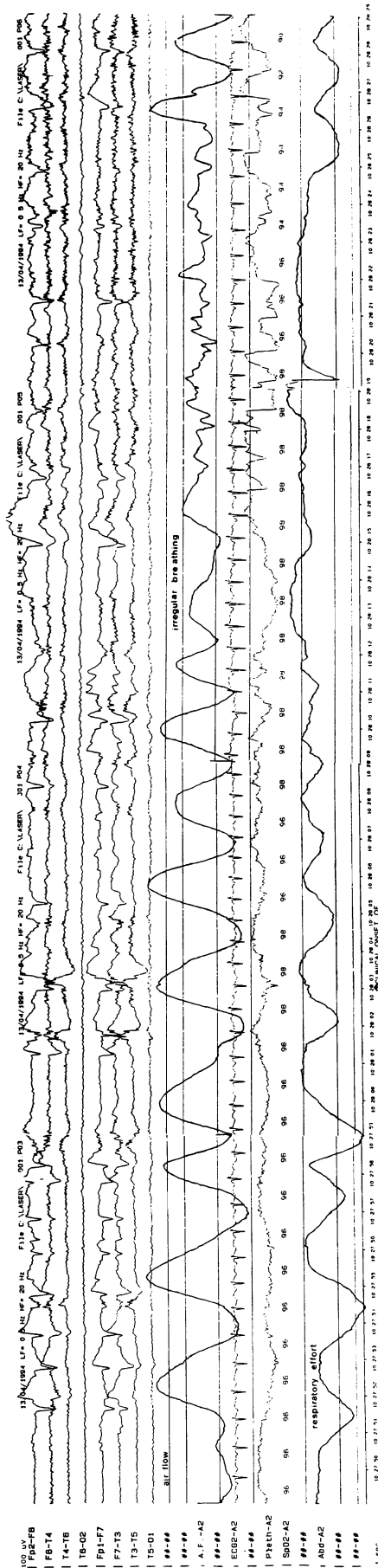
TECHNICAL CONSIDERATIONS

The recordings were informative in all but one case. Interpretation relied on integration of all data. Movement may result in an artefactual

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Central apnoea, bradycardia, and sinus arrest, followed by obstructive apnoea in a complex partial seizure in a patient with severe hippocampal sclerosis. AF = Air flow; Abd = abdominal trace; Pleth = plethysmography; LF = low frequency filter; HF = high frequency filter.

drop in oxyhaemoglobin saturation (SpO_2) readings towards 85%²⁹ and gross movements in readings cutting out altogether.³⁰ Preservation of plethysmography signal, gradual changes consistent with other physiological variables, and an appropriate lag³¹ in relation to occurrence of apnoea were all helpful in assessing validity of SpO_2 data. Only SpO_2 readings below 85% and supported by such concordant data are reported here; this probably underestimates ictal changes in oxygen saturation. Regarding other respiratory variables, even when the trace from one channel was unclear, the overall recording was informative in all but one case. The ECG traces were sometimes obscured by muscle artefact (see below). The least tolerated of the additional measurements by the patients was the airflow.

RESPIRATORY CHANGES

Apnoea associated with seizures

Apnoea (> 10 s) was documented in 10 of 17 patients (20 of 47 seizures) in three of three secondary generalised tonic clonic seizures, one of eight tonic seizures, and 16 of 35 complex partial seizures. Duration ranged from > 10 to 63 seconds with a mean of 24 seconds. The apnoea was central in all of the 20 seizures (10 patients), and, when it was possible to ascertain, occurred in expiration (14 of 20 seizures, eight of 10 patients). In addition, in three of 10 patients obstructive apnoea followed central apnoea. During one complex partial seizure infrequent and irregular breathing preceded a period of central apnoea (13 s) which was associated with sinus arrest (maximum RR interval 7.3 s; figure). This was followed by obstructive apnoea lasting 14 seconds during which the (seated) patient's head was slumped on to the chest. In two of the three generalised seizures, obstructive apnoea was also seen during the postictal phase.

SpO₂ during seizures

SpO_2 dropped to less than 85% in 10 seizures (six patients) in association with apnoea. The range was 55–83% (mean 71) and these changes were gradual and consistent with other events recorded and appropriate in timing to the occurrence of apnoea. Mean lag from the onset of the apnoeic spell to the start of a consistent decrease in SpO_2 from baseline was 25 (range 6–49) seconds (six seizures). Mean lag to the minimum SpO_2 recorded was 75 (range 39–108) seconds (seven seizures), and mean lag to the onset of a consistent rise in SpO_2 after return of effective ventilation was 23 (range 11–72) seconds (eight seizures). Quantification was not always possible as patients may have inadequate breathing before or after an episode of apnoea.

HEART RATE DURING SEIZURES

Decrease in heart rate

Transient bradycardia/sinus arrest (mean maximum RR interval 5.36, range 2.8–8.6 s) was documented in four patients (minimum five seizures). In three patients this occurred during apnoea. In the fourth patient bradycar-

dia occurred soon after seizure at a time of altered respiratory pattern. The patient characteristically emitted a forceful moan, lasting for 18 seconds and interrupted by some 10 very short inspirations. Lowest heart rates measured over 10 second epochs were equivalent to 6–42 bpm with a mean of 27 bpm in five seizures. These changes were brief, lasting less than 25 seconds.

Another patient with a baseline heart rate of 66 bpm, had an initial ictal tachycardia (102 bpm) during a period of hyperventilation. This was followed by an apnoeic spell and relative bradycardia (54 bpm) in one of eight tonic seizures.

In seven patients (including the two with tonic clonic seizures) the ECG tracing was obscured sufficiently at critical times during seizures such that transient bradycardia could not be excluded. In two patients bradycardia was recorded in other seizures.

Increase in heart rate during seizures

Increase in heart rate was frequently seen occurring in 91% of seizures (39 of 41), including patients with later ictal bradycardia. The increase in heart rate was usually early on in the seizure but could precede, coincide with, or follow scalp EEG or clinical onset and ranged from 15 to 99 bpm above baseline (mean 40). Maximum heart rates recorded ranged from 78 to 162 (mean 114) bpm.

Discussion

Theories suggested for the mechanism of sudden death in epilepsy have concentrated on autonomic instability during or soon after overt or subclinical seizures including cardiac arrhythmias. Yet, despite occasional case reports,^{32–34} systematic studies^{18–22} focusing on changes in heart rate in isolation have generally failed to support the hypothesis that malignant cardiac arrhythmias commonly occur during seizures. In this study of patients with telemetry, cardiorespiratory changes were often considerable, despite the fact that seizures recorded were mostly complex partial rather than secondarily generalised.

Tachycardias occurred very often, as previously reported.²⁰ This is considered a sympathetically mediated consequence of seizure discharge. Apnoea was seen in 10 of 17 patients and bradyarrhythmias in four of 17. Central apnoea was more common than obstructive apnoea. However, this may have been influenced by the presence of staff.

It is interesting that in a sheep seizure model of epileptic sudden death, striking hypoventilation was seen in the sudden death group but not in the surviving animals.³⁵ Some case reports refer to ictal bradycardia/sinus arrest.^{32–34} Interpretation of bradyarrhythmias is incomplete without simultaneous recording of respiration. In this study transient bradycardia/sinus arrest always occurred with a change in respiratory pattern. In three of four patients, bradyarrhythmias were not seen at or soon after the onset of the seizure but occurred later during an apnoeic spell. In the fourth patient,

this occurred soon after seizure onset, at a time of altered respiration when prolonged forceful moans were interrupted by very brief inspirations.

Regulation of the cardiac and respiratory systems are interrelated. One cardiorespiratory reflex of relevance is that of bradycardia in the presence of apnoea. Daly³⁶ has emphasised the risk of cardiac arrest in any clinical situation in which the patient's respiration is depressed either reflexly or centrally, a time of heightened vagal sensitivity. By contrast with the tachycardia seen in the presence of hyperventilation, carotid body stimulation secondary to and in the presence of apnoea results in bradycardia.³⁷ In this situation, ictal parasympathetic overactivity, usually overshadowed by sympathetic changes, may acquire greater importance. Although the seizure discharge could theoretically activate central regions, causing both bradycardia and apnoea, the evolution of the bradycardia in relation to the apnoea makes this less likely. Our results suggest that bradyarrhythmias may be potentiated by cardiorespiratory reflexes with apnoea playing a central part, and hypoxia providing an additional contributory factor. Of interest in this regard is the finding that sudden unexpected death in epilepsy is more common in young patients and that the magnitude of cardiorespiratory reflexes is known to diminish with age.³⁸

Whether patients consistently shown to have cardiorespiratory changes during seizures are more at risk of sudden death remains speculative. However, the finding of such ictal changes may influence clinical management during presurgical assessment, given an incidence of sudden unexpected death in epilepsy of the order of 1:200 per year in patients with chronic epilepsy.¹⁰ The potential influence of seizure focus on the type of changes found is of interest and requires a larger study, as does the influence of patient stimulation and positioning on apnoea. The second may be relevant to the finding, as yet unexplained, that most sudden unexpected deaths in epilepsy are unwitnessed.^{4,6,10,12,13} In the meantime, basic principles relating to both cardiac and respiratory resuscitation in seizures should be highlighted.

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