Clinical commentary

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Bradycardia and asystole during generalised interictal EEG discharges

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ABSTRACT – Few studies have investigated the effects of interictal epileptic discharges on the cardiac autonomic system. This study reports the case of a 37-year-old man with refractory generalised epilepsy, who recently reported an increase in frequency of nocturnal tonic-clonic seizures, not responding to treatment. During the nocturnal video study, in non-rapid eye movements sleep, we recorded 106 generalised sharp- and polyspike-waves lasting for 3 to 7 seconds, associated with bradycardia and asystole, without behavioural changes and without increase in deltoid muscle activity. The asystole had a duration of between 3 and 8 seconds. In one case, a 7 second asystole was associated with a tonic-clonic generalised seizure. A 24-hour electrocardiographic study revealed a bradycardia and a Wenckebach atrioventricular block. Heart rate analysis at the time of the interictal epileptic discharges revealed an abrupt increase in the RR interval, occurring simultaneously with the onset of interictal epileptic discharges and followed by a return to values below baseline value. A cardiac pacemaker was installed with a reduction of asystole length during the interictal epileptic discharges. Our findings indicate, for the first time, the role of interictal generalised discharges in EEG-related asystole and bradycardia. These data support the hypothesis that some patients with epilepsy may be predisposed to disturbances of the autonomic cardiac system.

Key words: epilepsy, interictal generalized discharges, asystole, bradycardia, autonomic nervous system

There is general agreement that interictal epileptic discharges (IED), like seizures, may result in cardiac arrhythmias, as suggested by the fact that cortical pathways regulate the cardiovascular system (Oppenheimer, 2007) and the appearance of cardiovascular dysfunction in patients with cerebral lesions (Surges and Sander, 2012). Severe bradycardia and asystole occur in 0.3-0.5% of patients with focal seizures involving the insular, frontal, and anterior temporal areas (Strzelczyk et al., 2008), as well as during IED (Nei et al., 2011). All aforementioned authors stress the link between these signs of cardiac
Autonomic nervous system and interictal generalised EEG discharges

Figure 1. Representative sleep EEG recording during stage 2 of NREM sleep showing the appearance of an interictal generalised epileptic discharge associated with bradycardia and asystole.

dysfunction and the increased risk of sudden unexpected death in epilepsy (SUDEP). Since the occurrence of SUDEP is over-represented during sleep (40%) (Surges and Sander, 2012) when cardiac arrhythmias related to seizures or IED are more frequent, the current hypothesis stresses the role of a cardiac dysfunction of the autonomic nervous system (ANS) (Sevcencu and Struijk, 2010). Although the literature on ictal asystole and bradycardia is sparse, there is general agreement on the key role of an ANS dysfunction, inducing an imbalance between sympathetic and parasympathetic tone, as assessed by the Heart Rate Variability (HRV). These changes may depend on the duration of the epilepsy, the frequency of nocturnal IED, and possible medication.

In the present report, we describe, for the first time, a sleep EEG study and heart rate (HR) analysis in one case showing arrhythmia during generalised IED.

Case study

The clinical history of the patient (a 37-year-old male) revealed at the age of 3 years, during infancy, the development of several nocturnal focal and generalised seizures with accompanying falls. The proposed diagnosis was Lennox-Gastaut syndrome as defined by the presence of atypical absences and atonic and generalised tonic-clonic seizures. Treatment consisted of phenobarbital, valproate, and clonazepam. At the age of 19 years, the patient developed several types of seizures, either focal or generalised tonic-clonic, all occurring during sleep and not responding to treatment with carbamazepine, gabapentin, or lacosamide. A brain MRI and an awake EEG study were found to be normal. In the first nocturnal recording, spikes and sharp waves, more pronounced in the frontal anterior left areas, were
Figure 2. Averaged changes of the RR interval around the interictal generalised discharges examined from 40 seconds before to 40 seconds after the events. The line indicates the onset of the events. Simultaneously with the discharges, an ictal increase of the RR interval occurred (bradycardia), followed by a slow progressive rise of the heart rate after the events, however, without reaching the values recorded prior to the onset of the EEG event.

detected without corresponding clinical events. A second sleep EEG study was performed at age 37 years when the patient reported an increased frequency of generalised tonic nocturnal seizures without an effect of antiepileptic treatment (gabapentin, lacosamide, or clonazepam). The EEG during wakefulness was normal but during sleep, several IED (n=106; mean duration: 16.3 seconds) occurring during non-rapid eye movement (NREM) sleep were detected and associated with bradycardia (i.e. slowing of HR below 40 beats) and asystole (i.e. heart stops beating) (figure 1). Since the arrhythmias could possibly be aggravated by medication, lacosamide was replaced by rufinamide.

The 24-hour EEG monitoring performed one month after the above finding confirmed the persistence of bradycardia and asystoles, with one of these episodes lasting for 7 seconds and inducing the appearance of a generalised tonic seizure. After the application of a pace-makers, the arrhythmias disappeared.

In the first recording showing arrhythmias, we performed an analysis of the RR intervals around the IED for a time span of 80 seconds, with 40 seconds before, and 40 seconds after the event in NREM sleep. As indicated in figure 2, an abrupt change of the RR interval occurred simultaneously with the onset of the generalised IED and was followed by a slow return to values below the baseline that might indicate either an increased parasympathetic activity or a decreased sympathetic activity, or both.

Discussion

The most interesting finding in this report is the presence during NREM sleep of generalised IED associated with bradycardia and asystole which induced, in one recording, a tonic-clonic seizure. The asystoles and bradycardia were not preceded by HR changes before the event and occurred simultaneously with the EEG discharges (figures 1 and 2).

Events of cardiac alterations are more frequently described in focal epilepsy either at the temporal level (Britton et al., 2006; Strzelczyk et al., 2008) or frontal level (Leung et al., 2007). During the seizures, the HRV analysis showed subtle cardiac dysfunctions with an increase in high frequency (HF) power and a decrease of low frequency (LF) power reflecting an increase of parasympathetic tone and a fall of sympathetic activity, respectively.

To the best of our knowledge, few studies have examined the cardiac autonomic instability during generalised IED. According to previous research (Brotherstone and McLellan, 2012), during IED, an abrupt autonomic alteration takes place with an abrupt occurrence of bradycardia and asystole in association with the onset of the generalised IED. The simultaneous association between the cardiac arrhythmia and the onset of the IED support the hypothesis that IED may activate the insula, cingulate cortex, amygdala, and hypothalamus which regulate cardiac function via connection to the brainstem (Britton et al., 2006; Leung et al., 2007; Oppenheimer, 2007).

In line with previous data (Moseley et al., 2011; Strzelczyk et al., 2011), the implantation of a cardiac pacemaker reduced the arrhythmias and the consequent seizures.

In conclusion, our observation confirms that even during generalised IED, cardiac arrhythmias may occur simultaneously and be associated with the onset and the length of the IED. This finding suggests that, independent of medication profiles, some types of epilepsy may be predisposed to disturbances of the autonomic cardiac system. Assessment of HR analysis might be useful for therapeutic purposes, as some epileptic drugs may act on cardiac excitability and potentially lead to cardiac arrhythmias.

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None of the authors have any conflict of interest to declare.

References


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**TEST YOURSELF**

(1) In the monitoring of epileptic patients, the recording of autonomic parameters such as ECG and respiration is:
A. Not useful
B. Useful in specific cases
C. Necessary in all cases

(2) Cardiac arrhythmias are described during:
A. Partial seizures
B. Generalised seizures
C. Intertical discharges
D. All conditions

(3) Occurrence of bradycardia and/or asystole during the EEG recording may indicate the effect of medication and their risk of SUDEP:
A. Yes
B. No

*Note: Reading the manuscript provides an answer to all questions. You can check for the correct answer by visiting the Educational Centre section of www.epilepticdisorders.com*