

IN A HEARTBEAT: AUTONOMIC CHANGES DURING SEIZURES

Abnormalities in Cardiac and Respiratory Function Observed during Seizures in Childhood

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The aim of this study was to observe any changes in cardiac and respiratory function that occur during seizures. Thirty-seven children (20 boys, 17 girls; median age, 7 years 6 months; range, 1 year 6 months to 15 years 6 months) were studied. We recorded electroencephalograms, respiratory rate, heart rate, electrocardiograms, blood pressure, oxygen saturation, heart rate variability (time-domain analysis), and cardiac vagal tone. A respiratory pause was defined as an interruption in respiration lasting more than 3 seconds but less than 15 seconds. Apnea was defined as absence of respiration for more than 15 seconds. Tachypnea was defined as a 10% increase in respiratory rate from the preictal baseline. Bradypnea was defined as a 10% decrease in respiratory rate from the preictal baseline. Significant hypoxia was defined as a satu-

ration of less than 85%. A significant change in heart rate was taken as a 10% increase or decrease below the baseline rate. Data were obtained from 101 seizures: 40 focal seizures, 21 generalized seizures, and 40 absences. Focal seizures were frequently associated with significant respiratory abnormalities, tachypnea in 56%, apnea in 30%, frequent respiratory pauses in 70%, and significant hypoxemia in 40%. The changes seen in respiratory rate were statistically significant. Changes in cardiac parameters, an increase or decrease in heart rate, were observed in only 26% of focal seizures and 48% of generalized seizures. We conclude that seizure activity can disrupt normal physiologic regulation and control of respiratory and cardiac activity.

Cardiac Arrhythmias in Focal Epilepsy: A Prospective Long-term Study

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PURPOSE: Patients with epilepsy are at risk of sudden unexpected death. Neurogenic cardiac arrhythmias have been postulated as a cause. Electrocardiograms (ECGs) can be monitored by use of an implantable loop recorder for up to 18 months. We aimed to determine the frequency of cardiac arrhythmias in patients with refractory focal seizures over an extended period.

METHODS: Twenty patients received an implantable loop recorder at one hospital in the United Kingdom. Devices were programmed to record automatically if bradycardia (<40 beats/min) or tachycardia (>140 beats/min) was detected. Additionally, in the event of a seizure, patients and relatives could initiate ECG recording with an external activator device. Data were analyzed at regular intervals and correlated with seizure diaries.

RESULTS: More than 220,000 patient-hours were monitored over a 24-month period, during which ECGs were captured on implantable loop recorders in 377 seizures. One patient withdrew from the study. In 16 patients, median heart rate during habitual seizures exceeded 100 beats/min. Ictal bradycardia (<40 beats/min) was rare, occurring in eight (2.1%) recorded events, in seven patients. Four patients (21%) had bradycardia or periods of asystole with subsequent permanent pacemaker insertion. Three of these four (16% of total) had potentially fatal asystole.

CONCLUSIONS: Clinical characteristics of patients with periictal cardiac abnormalities are closely similar to those at greatest risk of sudden unexpected death in epilepsy. Asystole might underlie many of these deaths, which would have important implications for the investigation of similar patients and affect present cardiac-pacing policies.

COMMENTARY

Autonomic manifestations of seizures have been recognized for more than a 100 years. Changes in heart rate and respiration during the physical throes of a tonic-clonic seizure are predictable and are obvious to any onlooker. Autonomic phenomena during simple partial or complex partial seizures have long been observed as well, including piloerection, flushing, pallor, sweating, borborygmi, sexual sensations, and pupillary changes. Postictal autonomic occurrences, such as vomiting and an urge to urinate, also are common.

Not until 1986 did Blumhardt et al. systematically study heart rate during complex partial seizures and describe significant ictal changes (1). More than 92% of their patients had ictal tachycardia, with rates over 140 beats/min in one third of them. Other cardiac arrhythmias were also observed—most common was a sequence of sudden changes in rate, which led the authors to speculate on their relevance to sudden unexplained death in epilepsy (SUDEP).

Around the same time, more studies on SUDEP also were appearing, and its surprisingly high incidence rate (i.e., reaching 1 in 200 patient-years in some series) began to be appreciated. The growth of presurgical and diagnostic EEG monitoring, and the availability of inexpensive, automated electrocardiogram (ECG) analyzers, led to many more studies of ictal and postictal cardiorespiratory phenomena. Many of these studies were inspired by a desire to identify persons at particular risk for SUDEP, the cause of which is suspected by some to be ictal or postictal cardiac or respiratory arrest, or neurogenic pulmonary edema.

The most obvious link between ictal ECG changes and SUDEP has been the observation of ictal cardiac asystole. Cases of reversible asystole, lasting up to 30 seconds and occurring multiple times in the same patient, have been well documented. The phenomenon may be more common than is generally appreciated, because the only outward sign of asystole is loss of consciousness, with falling or slumping—symptoms that also may occur in complex partial seizures unassociated with any significant changes in cardiac rhythm. The suspicion that cardiac asystole may be associated with SUDEP is supported by results of the Rugg-Gunn et al. study.

Ictal respiratory changes have been less extensively studied than have cardiac changes. Subjective, early ictal respiratory symptoms are occasionally reported by patients as a catching of the breath or a vague change in the sensation of breathing that is difficult to describe. Such symptoms also may be more common than generally appreciated, because they might well be lost or missed among the more dramatic experiences of a seizure. Nashef et al. (2) reported frequent central apnea (60%) in a small study of 17 patients with mixed seizure types.

The cerebral cortex, particularly limbic structures such as the insula, amygdala, cingulate gyrus, and orbitofrontal cortex, modulates respiration, heart rate, and even intracardiac conduction. All of these structures are part of the central autonomic network that controls efferent visceral preganglionic sympathetic and parasympathetic activity (3). Penfield and Jasper (4) produced apnea with stimulation of the cingulate gyrus, uncus, and anterior insula and saw tachycardia with stimulation of the supplementary motor area.

Only a few animal models of ictal neurocardiogenic changes have been investigated. Studies in cats with pentylentetrazol-induced seizures showed ictal ECG changes and uncoupling of normal heart rate/blood pressure relations (5). Progressive alterations in postictal and interictal neurocardiac regulation were found in rats subjected to maximal electroshock seizures, predominantly suggestive of parasympathetic dysfunction (6). Postictal cardiac arrhythmias in this model could be prevented by pretreatment with atropine (7).

Investigators carrying out presurgical seizure monitoring have looked for consistent lateralizing value in the nature of ictal heart-rate changes. Differential changes in heart rate during intracarotid amytal injection seem to support such an approach. Zamrini et al. (8) found small but systematic differences in heart rate between left- and right-sided injections, with increases during left-hemisphere inactivation and decreases during right-hemisphere inactivation. Observations of partial seizures have generally supported the idea that right-sided cortical stimulation results more commonly in tachycardia and that left-sided stimulation causes bradycardia. Because of spread of ictal activity from one side to another or even intrahemispherically, ictal cardiac rhythm changes are neither sensitive nor specific enough to help localize or lateralize a seizure focus, a finding supported by Rugg-Gunn et al. (9,10).

One of the most important aspects of the two articles discussed here is the startlingly high incidence of significant periods of asystole observed when ECG monitoring is extended over long periods (median, 18 months), by using an ECG loop recorder implanted subcutaneously. Four (20%) of 20 patients with medically intractable epilepsy had asystole (≤ 18 seconds) or bradycardia so severe as to require cardiac pacemakers. All patients demonstrated tachycardia at some point, up to 175 beats/min.

O'Regan and Brown recorded both cardiac and respiratory rhythms in a small group of children with daily seizures; most of the patients had additional neurologic disorders, such as cerebral palsy, tuberous sclerosis, or autism. The smaller sample of seizures (40 focal seizures as compared with the 377 in the adult study) may explain the lower rate of significant ictal cardiac abnormalities found in these children. Ictal apnea (ranging from 15 to 30 seconds) was seen in 30% of partial seizures, with the number of secondary generalizations unspecified. Reductions in

oxygen saturation below 85% were seen only with tonic-clonic seizures and also were common (40%).

What is the clinician to do with such information? Today it remains impossible to identify patients at highest risk for SUDEP or even to select patients for detailed or prolonged cardiopulmonary evaluation. These studies serve as uncomfortable reminders that patients with uncontrolled epilepsy have a potentially fatal disorder, and the best therapeutic approach is still the often-elusive goal of complete seizure control.

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