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Seizures and the cardiorespiratory system

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Abstract

The cardio-respiratory aspects of seizures have been proposed as explanatory mechanisms for sudden unexpected death in epilepsy (SUDEP). Theories were proposed which considered seizures as a terminal event for SUDEP. Ictal asystole, ictal bradyarrhythmia and tachyarrhythmia are possible explanations which have been reported, although the relative occurrence of these phenomena remains low. Other observations from case reports and case series pointed towards apnoea and ictal hypoxaemia as a putative terminal event for SUDEP. Many theories also considered the modification of the cardio-respiratory system by the underlying chronic epilepsy and anti-epileptic agents. Preventive measures for SUDEP have yet to be established despite the growing understanding of the cardio-respiratory mechanisms of SUDEP.

INTRODUCTION

Clinicians are increasingly interested in, and involved with, the mechanisms of sudden unexpected death in epilepsy (SUDEP) as the phenomenon gains the attention of epileptologists, neurologists and physicians alike. There have been many popular theories about the cardiac and respiratory changes that accompany chronic epilepsy that may help us understand SUDEP. Very often the evidence pointing towards a causal linkage is fragmented and putting forward a unifying theory can prove to be a daunting task. It has been speculated that in some patients with SUDEP, seizure was a terminal event and that arrhythmia or apnoea can accompany the ultimate demise. Other evidence points towards a chronic condition being imparted by seizures with regards to the cardio-respiratory system, which then causes the sudden death. Among such circumstantial evidence exists the speculation upon the role of antiepileptic agents and some other conditions which might lead to both seizures and cardio-respiratory pathology, or where the cardio-respiratory condition being a mimicker of seizures.

CARIDAC ASPECTS

The cortical (higher) control of heart rate was studied by Jasper and Penfield extensively.[1] It was found that stimulating the anterior cingulate may produce variation in heart rates. In the study by Oppenheimer, stimulation of left insular cortex resulted in Bradycardia.[2] Case reports of patients undergoing intracranial monitoring for investigation of refractory epilepsy also showed that asystole may occur during recorded seizures. In one case report, electrical stimulation of left anterior cingulate using implanted electrodes produced asystole.[3] But just how common do we encounter ictal bradyarrhythmia in clinical practice? One hospital record review of 1,244 patients undergoing video monitoring yielded 5 cases of ictal asystole.[4] There has also been evidence suggesting enhanced QT shortening and persistent tachycardia after generalized seizures.[5] In a case control study comparing a SUDEP cohort with a matched epilepsy patient cohort, it was found that QTc was prolonged above pathological limits in 5/38 patients. However, neither pathological cardiac repolarization nor other ECG features were associated with SUDEP.[6] With regards to the effects of antiepileptic agents, it was known that carbamazepine and phenytoin may decrease QTc whereas sodium valproate may prolong it. It was also known that certain conditions such as congenital long QT syndromes may be a mimicker of seizures and yet causing sudden cardiac death.[7]

RESPIRATORY ASPECTS

The cortical control of respiratory efforts was known since the time of electrical stimulation studies[1] of the human brain. The cingulate, the rolandic and uncal regions were demonstrated to

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be apnoea-producing after electrical stimulation. There was neuronal input from higher centres to the brainstem region where the inspiratory and expiratory efforts were coordinated. Many aspects of the respiratory system were proposed to be causative of SUDEP, e.g. direct cortical influence, central apnoea and hypoxaemia, chronic obstructive apnoea, pulmonary oedema after seizures and aspiration. One case report cited the occurrence of persistent apnoea following a 56-second convulsive seizure.[8] But how common do we encounter ictal hypoxaemia? A study of 304 seizures in 56 patients with video monitoring and oxygen saturation data showed that desaturation to <90% occurred in 33% of all seizures and that desaturation correlated significantly with seizure localization, lateralization to right side, contralateral spread of seizures and female gender.[9] Two additional case reports also captured the death of patients with SUDEP while being video-monitored, and both pointed towards a respiratory mechanism being involved (apnoea).[10] Finally, one study cited a reduced percentage of seizures with desaturation in patients taking serotonin reuptake inhibitors (SSRI).[11] The significance of this remains unknown.

HAS UNDERSTANDING ABOUT CARDIO-RESPIRATORY MECHANISMS HELPED WITH PREVENTION?

Appropriate counseling at appropriate times is important for refractory epilepsy patients. At present, pacemaker or other cardiac devices are only indicated for patients with significant long pauses or pathological dysrhythmia. Apnoea detector and night supervision may be encouraged for patients with refractory epilepsy. The role of SSRI for ictal apnoea remains unknown. More clinical studies are needed to understand why SUDEP occurs in some but not others. Mechanistic theories may be multi-factorial rather than universal. The unexpected nature of demise in SUDEP will continue to pose a challenge for scientists.

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