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Review

Ictal tachycardia: The head–heart connection

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ABSTRACT

Epileptic seizures can lead to changes in autonomic function affecting the sympathetic, parasympathetic, and enteric nervous systems. Changes in cardiac signals are potential biomarkers that may provide an extra-cerebral indicator of ictal onset in some patients. Heart rate can be measured easily when compared to other biomarkers that are commonly associated with seizures (e.g., long-term EEG), and therefore it has become an interesting parameter to explore for detecting seizures. Understanding the prevalence and magnitude of heart rate changes associated with seizures, as well as the timing of such changes relative to seizure onset, is fundamental to the development and use of cardiac based algorithms for seizure detection. We reviewed 34 articles that reported the prevalence of ictal tachycardia in patients with epilepsy. Scientific literature supports the occurrence of significant increases in heart rate associated with ictal events in a large proportion of patients with epilepsy (82%) using concurrent electroencephalogram (EEG) and electrocardiogram (ECG). The average percentage of seizures associated with significant heart rate changes was similar for generalized (64%) and partial onset seizures (71%). Intra-individual variability was noted in several articles, with the majority of studies reporting significant increase in heart rate during seizures originating from the temporal lobe. Accurate detection of seizures is likely to require an adjustable threshold given the variability in the magnitude of heart rate changes associated with seizures within and across patients.

1. Introduction

Epilepsy affects 65 million people worldwide. Despite available treatments, more than 1 million people still suffer from seizures that severely limit their daily activities and quality of life. Most medical therapies for epilepsy consist of daily regimens of anti-epileptic drugs and/or electrical stimulation provided by medical devices such as VNS Therapy®. Once a clinical seizure starts, rescue medications can be administered in an attempt to disrupt progression of a given seizure and manage seizure emergencies, such as prolonged, repetitive seizures, or status epilepticus. However, rescue medications, for example rectal diazepam, are not appropriate for all patients, require caregiver administration, and may have undesirable side effects. Automatic and non-invasive delivery of treatment prior to or at the onset of a clinical seizure may provide patients with epilepsy peace of mind and increased control over their seizures.

Heart rate can be measured easily when compared to other biomarkers that are commonly associated with seizures (i.e., long-term EEG), and therefore it has become an interesting parameter to explore for detecting seizures. Cardiac signals are robust, easy to record, and algorithms can be adapted to individual patients based on predetermined heart rate changes in response to epileptic seizures. Understanding the prevalence and magnitude of heart rate changes associated with seizures, as well as the timing of such changes relative to seizure onset, is fundamental to the development and use of cardiac based algorithms for seizure detection.

Epileptic seizures can lead to changes in autonomic function affecting the sympathetic, parasympathetic, and enteric nervous systems. Changes in cardiac signals are potential biomarkers that may provide an extra-cerebral indicator of ictal onset in some patients.

The parasympathetic and sympathetic systems act in concert to maintain homeostasis and regulate key visceral functions such as heart rate. In particular, the anterior cingulate, insular, posterior orbito-frontal, and the pre-frontal cortices play key roles in influencing the autonomic nervous system at the cortical level

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along with the amygdala and hypothalamus.[1,2] In patients with epilepsy, ictal discharges that occur in or propagate to these structures can lead to increased sympathetic outflows, impacting autonomic function. Research involving experimental stimulation of various neural structures suggests that the propagation of epileptic discharges to the right insular cortex is a primary driver of sympathetic-parasympathetic changes that influence heart rate.[3] Although sympathetic responses such as sinus tachycardia are the most common changes that occur during seizures, parasympathetic responses such as bradycardia can also occur if the ictal discharges propagate to cortical regions governing depressor responses.[1]

Sinus tachycardia characteristically refers to a heart rate that exceeds the normal range for a resting heart rate. The upper threshold of a normal heart rate depends on and decreases with age, however no standard definition exists. The upper threshold of heart rate for people >15 years of age is commonly considered to be 100 beats per minute (bpm) while the upper threshold for children 6–11 months of age is >169 bpm.[4] Ictal tachycardia can be defined as the occurrence of sinus tachycardia either prior to, during, or shortly after the onset of ictal discharges.[2] This review describes the prevalence and characteristics of ictal tachycardia in patients with epilepsy as reported in the literature.

2. Methods

A review of the literature was conducted per MEDDEV 2.7.1[5] to summarize the prevalence of ictal tachycardia in patients with epilepsy as reported in the literature. Only full original peer-reviewed research (no meeting abstracts or review articles) related to the research objective were included. The reference lists of key relevant articles were also searched and additional articles were identified. Known references that were not found in the literature search were also included for completeness. The literature search for this topic was conducted in April 2013 using PubMed (Fig. 1). Three independent searches were conducted using the following keywords: (1) ictal tachycardia (46 primary citations), (2) heart rate variability seizure (79 primary citations) and (3) ictal bradycardia (63 primary citations). The combination of the results of these three searches provided 165 unique citations. Upon review of the abstracts, 19 were review articles (17 were unrelated to ictal tachycardia, 2 were used to identify additional primary articles), 7 were case reports, and 105 were not directly related to ictal tachycardia; the remaining 34 articles were obtained and reviewed. Upon review of the full publications, an additional 10 papers were excluded as they were not directly related to ictal tachycardia. Articles were included if they reported the proportion of patients or seizures that exhibited an increased heart rate or ictal tachycardia. An evaluation of the study design and measures to reduce bias was also performed. For the primary search, 24 clinical articles were identified that reported changes in heart rate associated with epileptic events.[6–29] An additional 10 articles that were not identified in the primary search were also included that were either known to the authors or identified as additional references from the primary articles.[30–39]

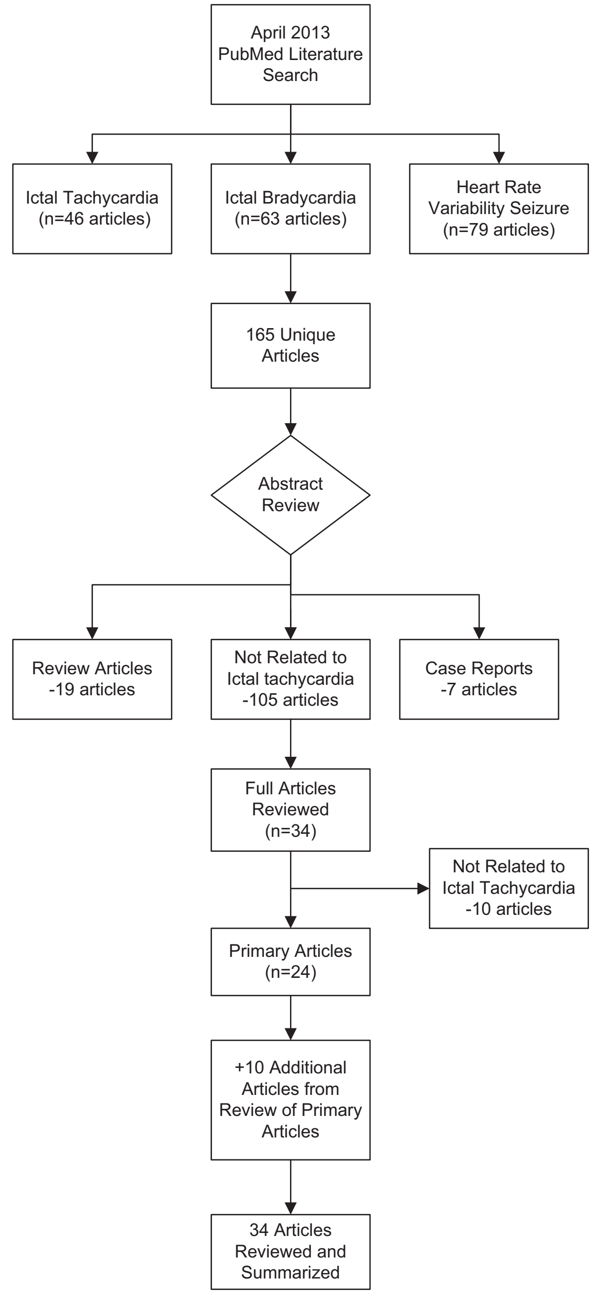

Fig. 1. Literature review of ictal tachycardia.

3. Results

The 34 articles identified were reviewed and are summarized alphabetically by author's last name in Table 1. The literature was assessed based on several key characteristics that define this clinical phenomenon including the overall prevalence of ictal tachycardia in the patient population, the prevalence of ictal tachycardia by seizure type, as well as potential differential indicators of ictal tachycardia including lobe of seizure onset and lateralization. Consistent with the diverse nature of the epilepsies, the results presented here include a range of etiologies, seizure types, patient characteristics, and definitions of ictal tachycardia. The occurrence and magnitude of ictal tachycardia may be influenced by patient and/or disease state characteristics. Thus, in addition to overall summary data, we present results by seizure type, lobe of onset, lateralization, and degree of tachycardia. Finally, the magnitude and timing of the respective changes in heart rate associated with seizure onset are discussed. Defining these characteristics promotes understanding of potential mechanisms of action for ictal tachycardia and also provides insight on patient selection for use and programming of cardiac based seizure detection algorithms.

3.1. Study design

The study designs utilized by the articles reviewed were primarily prospective or retrospective case series of observational