Heart rate increase in otherwise subclinical seizures is different in temporal versus extratemporal seizure onset: support for temporal lobe autonomic influence

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ABSTRACT – Ictal heart rate was investigated in otherwise subclinical epileptic seizures to test the hypothesis as to whether ictal tachycardia is physiological and not a physical or psychological stress response. In addition, we aimed to evaluate the localizing significance of pure ictal tachycardia. We included 21 epilepsy patients, who showed an ictal EEG seizure pattern during 22, otherwise subclinical seizures. All patients underwent ictal video-EEG recordings to evaluate the possibility of resective epilepsy surgery. The changes in heart rate in these patients were investigated in order to determine their relationship to localization and duration of EEG seizure patterns. Ictal tachycardia was observed in 41% of the otherwise subclinical seizures (nine out of 22), and significantly more often in seizures arising from the temporal lobe than from extratemporal regions (62% versus 11%, p < 0.0018). The seizure duration as defined by EEG was significantly positively correlated with an increase of heart rate (p = 0.043). Ictal heart rate can increase as a result of epileptic activation of autonomic cortex, reflecting a temporal lobe autonomic influence. Thus, measurement of heart rate should be included in the evaluation of otherwise subclinical epileptic seizures, because of its localizing value.

Key words: vegetative seizures, autonomic seizures, subclinical, EEG-video monitoring, autonomic cortex

Epileptic seizures are often accompanied by tachycardia (Zijlmans et al. 2002). Mesiotemporal structures, particularly the amygdala, which play a role in both autonomic control and epileptogenesis have been identified in animal models (Oppenheimer et al. 1991). Moreover, a growing number of studies also indicate that the insular cortex and temporal lobe are influential in the control of cardiovascular function in humans (Oppenheimer et
Ictal tachycardia seems to help discriminate between seizures arising from temporal or extratemporal regions (Garcia et al. 2001). It has not yet been clarified, whether tachycardia develops because of physical or psychic stress during the seizures or whether it reflects epileptic activation of the autonomic cortex. We therefore investigated changes in heart rate during otherwise subclinical seizures to identify autonomic seizures and to determine their relationship to the localization and duration of EEG seizure patterns.

**Patients and methods**

A review of the database of the University of Munich Epilepsy Monitoring Unit (552 patients), identified 27 patients who had had subclinical seizures documented by EEG and video. Subclinical seizures were defined as EEG seizure patterns that were not associated with any disturbances of sensory phenomena, motor functions, or consciousness in the awake patient, with any movements during sleep or arousals on EEG. Twenty-one patients with a total of 22 subclinical seizures, in whom ictal EEG files and high-quality video could be retrieved for analysis, were selected. Heart rate before and during the EEG seizure patterns was analyzed in these patients and correlated with the localization and duration of their EEG seizure patterns.

**Patients**

Twenty-one patients participated in the study (11 men, 10 women; median age = 33 years, range 17-76 years). Ten patients had temporal lobe epilepsy, four patients had frontal lobe, and one patient parieto-occipital lobe epilepsy. Another two patients had left hemispheric epilepsy, two had right hemisphere focal epilepsy, and two had focal epilepsy which could not be lateralized. All patients were considered candidates for epilepsy surgery and were off anti-epileptic medication during EEG-video monitoring to record seizures.

**EEG-video monitoring**

All patients underwent continuous EEG-video monitoring with 32-64 channel EEG machines (Vangard, Cleveland, OH, USA). The patients were observed for 24 hours, day and night, by technicians specially trained in EEG video monitoring. The EEG was digitized at a sampling rate of 200 Hz (12 bit), amplified, and stored on hard discs and magneto-optical discs for off-line analysis. All seizures were analyzed off-line on EEG and time-synchronized video. Recordings were performed with surface electrodes in 13 patients and with subdural electrodes in another 8 patients. The localization or lateralization of seizure origin in these eight patients had been previously hypothesized on the basis of non-invasive EEG-video recordings. Responsiveness was tested systematically during the EEG seizure patterns in 13 patients. EEG seizure patterns occurred in nine patients during non-REMsleep. As direct observation and video recordings of these sleeping patients did not reveal any clinical change in behavior, they were not awakened and tested formally. Electroencephalography revealed no arousal.

**Heart rate analysis**

Heart rate was calculated from RR distances in the ECG. Measurements started 10 seconds prior to the onset of EEG seizure patterns and were calculated until heart rate remained constant after the seizure had ceased. An increase in heart rate was calculated by dividing the maximum frequency by the minimum frequency. In 12, non-epileptic controls with pseudoseizures and parasomnias (age 4-83 years, median 29 years) the mean increase in heart rate during long-term EEG-video monitoring was 1.6 (+ 0.2 SD). On the basis of this calculation, an increase of 1.8 was considered significant. Heart rate was plotted against time to exclude the impact of extrasystoles on the calculation. The resulting curves were fitted with a third grade polynomial fitting curve to calculate the point of maximum heart rate increase. The slopes of the fitting curves were calculated at this point (figure 1). Mean maximum slopes of heart rate were 30% with a standard deviation of 50% in our controls (figure 1, slope line). A maximum increase in slope of at least 100% was considered significant (figures 2a, b).

**Results**

Thirteen EEG seizure patterns were localized to the temporal region (right n = 8, left n = 5), eight seizure patterns were localized to the frontal area (right n = 4, left n = 4), and one to the right occipital region. The median duration of the EEG seizure patterns was 57.1 s (range 16.1 s - 178.9 s). Patient data and results of heart rate analyses are summarized in table 1.

Median increase of heart rate in all patients was 1.5 fold compared to the heart rate before seizure onset (range 1.1-3.7). Median increase of heart rate was higher in patients with seizures of temporal origin than in those with seizures from an extratemporal origin (1.8 versus 1.3, range 1.2-3.7 versus 1.2-1.8). A significant ictal increase in heart rate was observed in 9 out of 22 seizures (8 out of 21 patients). Significant ictal tachycardia was seen more often in patients with regional temporal EEG seizure patterns (62%, 8 out of 13) than in those with regional extratemporal seizure patterns (11%, 1 out of 9; p < 0.0018). Families of slope lines at the point of maximum increase in heart rate set at zero are shown in figure 2.
There was a correlation between duration of seizure patterns and tachycardia (Mann-Whitney test, $p = 0.043$). There was no significant decrease in the heart rate during seizures. Furthermore, there was no correlation between lateralization of the EEG seizure pattern and changes in heart rate (Chi square, $p = 0.548$).

**Discussion**

Our study investigated whether ictal tachycardia could be (i) a secondary to psychic or physical stress, or (ii) a result of an epileptic activation of cortical areas responsible for autonomic functions. We found that a significant increase in heart rate in 9 out of 22 seizures was not associated with any subjective (aura) or clinical seizure manifestations other than tachycardia. This makes it extremely unlikely that the ictal tachycardia in our patients was secondary to physical or psychological stress. Sinus tachycardia frequently occurs in various types of epileptic seizure (Nei et al. 2000), but it predominates in seizures originating in the temporal lobe (Epstein et al. 1992, Galimberti et al. 1996, Baumgartner et al. 2001, Garcia et al. 2001, Zijlmans et al. 2002). Our findings in otherwise subclinical seizures support this view: significant tachycardia was seen in 8 out of 13 temporal seizure patterns, but in only 1 out of 9 extratemporal seizure patterns.

Several clinical and experimental studies support the hypothesis that autonomic heart functions are represented in the insular cortex (Zamrini et al. 1990, Oppenheimer et al. 1991, Epstein et al. 1992). Electrical stimulation of the insular cortex in humans is associated with cardiovascular changes (Oppenheimer et al. 1992). In a study of six patients, bradycardia was more often elicited during left insular stimulation, whereas tachycardia occurred more often during right insular stimulation (Oppenheimer et al. 1992). Twenty six out of 45 patients with ictal bradycardia reported in the literature had seizure localized to the left hemisphere. Nineteen were localized on the right side (Tinuper et al. 2001). Tachycardia preceded EEG seizure onset in 75.9% of the seizures in a recent study on focal epilepsies (Leutmezer et al. 2003). Heart rate changes preceded EEG onset significantly more often in mesial TLE as compared with extratemporal epilepsy. In this study, it is not mentioned whether the patients were tested at the onset of the tachycardia (Leutmezer et al. 2003). Thus, the relation of the ictal tachycardia to clinical seizure onset is not clear. It cannot be excluded that at least some patients had an aura at this time. Auras are frequently not associated with EEG seizure patterns on surface EEG recordings and typically, clinical aura onset precedes the EEG onset.
It was concluded that the ictal EEG discharges directly influence areas of the central autonomic network, thus regulating heart rate and rhythm (Leutmezer et al. 2003). However, from the data presented in this study it cannot be exclude that tachycardia was secondary to the experience of aura and associated psychological stress in their patients (Leutmezer et al. 2003). To overcome this problem it was crucial in our study to exclude patients who did experience auras during ictal tachycardia.

The development of tachycardia usually requires widespread unilateral limbic involvement of the ictal discharges, irrespective of the side of origin (Epstein et al. 1992). Our finding of a positive correlation between duration of seizure patterns and significant tachycardia emphasizes this importance of widespread epileptic activity. The subclinical seizure became symptomatic and thereby constituted an autonomic seizure only if it spread to enough of the cortex.

The mechanism by which partial seizures cause autonomic symptoms and signs is thought to involve the spread of ictal epileptic discharges from the cortex to the hypothalamus. The large number of limbic-hypothalamic
connections probably accounts for the prominence of autonomic symptoms in seizures originating from the temporal lobe (Liporace and Sperling 1997, Cerullo et al. 1998).

A subclinical or purely electrographic seizure pattern is defined as an ictal pattern that is identical to EEG patterns during epileptic seizures lacking behavioral symptoms. The documentation of symptoms requires adequate monitoring. Direct observation and video recordings in our study did not show any ictal symptoms during EEG seizure patterns that were defined as subclinical. However, we cannot exclude the possibility that our testing procedure failed to detect subtle motor or neuropsychological symptoms. Autonomic symptoms and signs occurring during epileptic seizures are often missed because of inadequate testing and observation. Ictal tachycardia also occurred during sleep. A retrospective review revealed that ictal tachycardia had not been initially detected in 41% of our patients with “subclinical seizures”.

We conclude that purely ictal tachycardia indicates epileptic activity in or close to the temporal cortex. It is not exclusively a phenomenon secondary to physical or psychological stress during seizures. In view of its localizing value, the analysis of heart rate should be included in the evaluation of otherwise subclinical epileptic seizures.

### References


