Cardiac and Autonomic Functions in Epilepsy

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Partners Against Mortality in Epilepsy Conference - June 21-24, 2012
<table>
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<tr>
<th>Name of Commercial Interest</th>
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<td>Lundbeck</td>
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Learning Objectives

• To understand potential cardiac autonomic risk factors and mechanisms of SUDEP

• To appreciate the limitations of our existing knowledge and the need for systematic studies
Sudden cardiac death

• Risk factors: Predisposition for Arrhythmia
  • Autonomic dysfunction
  • Structural
  • Genetic

• Mechanisms: Arrhythmia
  • Primary or secondary Ischemia
  • Ventricular fibrillation
  • Fulminant heart failure
  Takotsubo Syndrome
SCD: mechanisms can be readily observed, the outcome is common and cardiac autonomic measures routinely obtained.

How to look for a mechanism which is not clear and for autonomic risk factors which have not been routinely obtained in an outcome which is rare?
## Substitute population

### Interictal
- Epilepsy
- TL epilepsy
- Dravet syndrome
- Uncontrolled epilepsy
- Surgical failure
- (SUDEP) patients

### Ictal
- Seizures
- GTC
- GTC with PGES
- (SUDEP)

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Schuele S. J Clin Neurophysiol 2009. Effects of seizures on cardiac function
Sevcencu C, Struijk JJ. Autonomic alterations and cardiac changes in epilepsy
Cardiac Autonomic Function

• **Interictal:** Heart rate
  Heart rate variability
  Baroreflex

• **Peri-Ictal:** Heart rate
  Electrodermal activity
  Heart rate variability
  Repolarization
Interictal Cardiac Effects

Asymptomatic cardiac arrhythmia: not more frequent than in controls

Autonomic function testing: abnormal blood pressure variability decreased baroreflex sensitivity

Heart Rate Variability

- **Time Domain**
  - Directly calculated from N-N intervals
  - SDNN, SDANN
  - RMSSD

- **Frequency Domain**
  - Power in defined frequency bands
  - HF: 0.15-0.4 Hz  vagal
  - LF: 0.04-0.15 Hz  sympathovagal modulation
  - HF/LF ratio:  sympathovagal balance

HRV in Chronic Epilepsy

Lotufo PA et al. Epilepsia 2012. Meta-analysis HRV

A  HF – epilepsy vs. healthy

B  LF – epilepsy vs. healthy
Cardiac Autonomic Function

- Interictal: Heart rate, Heart rate variability, Baroreflex

- **Peri-Ictal:** Heart rate, Electrodermal activity, Heart rate variability, Repolarization
Ictal Bradycardia syndrome

Asystole (> 4 sec) (2%)

Video EEG monitoring: 5 out 1244 patients with IA (0.4%)

Implantable Loop recorder:
- 20 patients with refractory focal epilepsy
- Implantable ECG loop recorder for 18 months
- 220 000 patient-hours recorded
- 3/20 (16%) potentially fatal asystole
- Asystole: 5 sec; 4.6sec/18 sec; 14 sec

Rocamora 2003; Rugg-Gunn 2004; Britton 2006
The upper row shows two patients with IA with an asystole of 5.3 s (left) and 22.0 s (right). The lower row shows two patients with VVA with an asystole of 8.1 s (left) and 28.4 s (right).

EDA in GTC

Figure 1
Long-term electrodermal activity (EDA) recordings obtained from a wearable biosensor

Poh M-Z et al. Autonomic changes with seizures correlate with postictal EEG suppression
Poh M-Z et al. Autonomic changes with seizures correlate with postictal EEG suppression
Poh M-Z et al. Autonomic changes with seizures correlate with postictal EEG suppression
EDA in GTC with PGES

Poh M-Z et al. Autonomic changes with seizures correlate with postictal EEG suppression
Ictal Tachycardia with GTC

Risk for VT/Fib: QTc and QTd

**Figure 3.**
Summary of interictal and peri-ictal alterations of cardiac repolarization in people with chronic epilepsy. Coexistence of increased QTd and abnormal QT shortening facilitates onset of ventricular tachycardia/fibrillation. Premature ventricular contraction, PVC. Question marks indicate limited or inconclusive clinical evidence.

_Epilepsia © ILAE_

11 seizures (9 patients) transiently increased their corrected QT beyond normal limits.

Increased TWA after GTC

Ictal TA and QTc in SUDEP

Ictal Tachycardia: > 90% of seizures, 20-25% preceding onset

Population
21 patients with SUDEP
VEEG results
Control: 43 pts focal epilepsy

Results
Maximal ictal HR:
149 bpm vs. 126 bpm, p < 0.001

Greater increase in Sz from sleep:
78 bpm vs. 47 bpm increase (p= 0.27)

No difference in ictal repolarization
and rhythm abnormalities

Ictal TA and QTc in SUDEP

Higher ictal heart rates preferentially occurred during SGTCS

No difference in absolute changes of HRV or QTc during and after seizures

Sudden cardiac death

- **Risk factors:**
  - Predisposition for Arrhythmia
    - Autonomic dysfunction
    - Structural
    - Genetic

- **Mechanisms:**
  - Arrhythmia
    - Primary or secondary Ischemia
    - Ventricular fibrillation
    - Fulminant heart failure
  - Takotsubo Syndrome
Cardiac Near-SUDEP

Malignant arrhythmia:
51 year old RHW
Refractory epilepsy since age 3 years
4 AEDs (CBZ, PHT, ZNS, TPM)
PMHx: HTN, DVT
MRI: R MTS
EKG: 1st AVB

Cardiac Near-SUDEP

**Takotsubo Syndrome:**
- Stressful condition, including seizures (59 cases reported)
- Reaction to catecholamine surge
- Clinical picture:
  - Female, > 60 yrs, absence of chest pain
  - Reversible akinesis, “ballooning”
  - ST segment or T wave abnormalities, high troponin
  - Normal coronary angiography
- Outcome: 8% lethal
  - Complications: cardiogenic shock, arrhythmia, sudden death

Dupuis M et al. Seizure 2012. TKS: A possible mechanism of SUDEP.
Impact on Clinical Care and Practice

- Epilepsy is associated with frequent interictal and ictal cardiac autonomic changes
- Modern cEEG monitoring should include recording of at least ECG and oxygen saturation.
- Systematic prospective data are necessary to obtain class I evidence of cardiac risk factors and mechanisms involved in SUDEP.