Intracranially recorded ictal direct current shifts may precede high frequency oscillations in human epilepsy

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Hypothesis

- Ictal DC shifts are generated by glias.

Big Questions

- What is the occurrence rate of intractable partial epilepsy in ictal DC shifts, HFOs, and conventional recorded ictal pattern?
- What is the relative onset of ictal DC shifts, HFOs, and conventional recorded ictal pattern?
- What is the correlation of pathology among DC shifts, HFOs, and conventional recorded ictal pattern?

Background

- Epileptogenic markers
  - Ictal DC shifts - activity of glias and pyramidal neurons
  - High frequency oscillations
  - Both located in same area - predict onset
- Seizure onset - beta, alpha, theta, and delta activity
- Epileptic HFOs - come from APs of pyramidal cells and interneurons
- HFO ripples
  - Ripples - 80–200 Hz
  - Fast ripples - 250–500 Hz
    - Ictal epileptogenicity
- Digital EEG - records and analyzes patterns
- Ictal DC shifts precede HFOs

Methods

- 16 patients
  - 6 females, 10 males
- Define seizure onset zone with chronic intracranial electrode implantation
- Age at seizure onset - 13.2 ± 10.5 years
- Age at epilepsy surgery - 28.9 ± 7.6 years
- Pathological diagnoses of patients:
  - focal cortical dysplasia (FCD) n=9
  - glioma with or without FCD n=4
  - hippocampal sclerosis (HS) n= 2
  - low-grade neuroepithelial tumor n= 1

Methods

Patients:

- 1 & 2 -- MRI shows destructive feature in glioma lesion (necrosis, edema)
- 3 & 4 -- 8-33 years history of epilepsy
- 15 patients had 18F-fluorodeoxyglucose PET
- 3 patients had ictal single-photon emission computed tomography imaging
- Subdural and depth electrodes used
- Magnetization-prepared rapid gradient echo volumetric scan
    - Before and after surgery, implantation
- Electrocorticogram recorded with EEG1100
- Simultaneously record ictal DC shifts, HFOs, and conventional recorded ictal pattern
- Seizures analyzed - 2.9 ± 2.3 days

Methods

- High frequency filter - 1 Hz
- Conventional ictal EEG onset recordings - 30s before and after, total 60s
- Duration - From onset to end
- Amplitude - Absolute value of greatest difference between onset and peak

Results

- 12 of 16 - ictal DC shifts
- Glioma Patients - Ictal DC shift in 3 / 4
  - HFOs in 50%
  - Two patients with FCD showed ictal DC shifts and HFOs
- FDC patients - 7 / 9
  - HFOs in 44.4%
- HFOs - 8 / 16
  - 46.3% of all seizures analyzed of 108 total
  - 3 / 8 = fast ripples
  - 5 / 8 = slow ripples
- HS patients - 1 / 2 showed HFOs
- Ictal DC shifts preceded HFOs by 3.4 ± 2.9 s

Results

- 7/16 showed ictal DC shifts and HFOs in each seizure
- 6 patients w/ conventional ictal pattern- earlier onset time of ictal DC shifts than HFOs
- Within subjects - statistically significant difference in 5 patients
- 12 patients - no statistical difference of onset time between ictal DC shifts and HFOs

Results

- |Time difference| of ictal DC shifts and HFOs - varies among patients compared to conventional onset
- 1 subject showed ictal DC shifts in white matter w/ delayed onset from conventional ictal pattern (via 3D MRI)
- HFOs not appreciated at depth electrode
- 3/15 patients - No ictal DC shifts or HFOs
- 11 patients - showed ictal DC shifts
- 7 patients - showed HFOs
- No significant difference in location of electrodes in terms of ictal DC shifts, HFOs and conventional ictal change
- No statistical difference in patients with complete and incomplete resections

Discussion

- Glias - actively involved in birth of ictal DC shifts
  - Resulting in seizure ignition
  - Dysfunctional gap junctions
- Ictal DC shifts were recorded from white matter, but not HFOs
- Ictal DC shift were generated by glias
- Ictal DC shifts precede HFOs
- AC amplifiers provide useful information to supplement EEG findings
  - Wide band EEG facilitates localization of the epileptogenic zone in refractory partial epilepsy.
- Microwire superior to clinical macroelectrode for recordings
- Seizure outcome after resection surgery - Good
  - Most became seizure free
- Epileptogenic zones must be located at or very close to the areas with the ictal DC shifts and HFOs.

Conclusion

- Ictal DC shifts and HFOs indicate the exact position of the core of tissue giving rise to epileptic seizures in human intractable epilepsy.
- DC shift preceding HFOs largely suggests an active role of glia in the birth of seizures