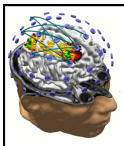

How do we evaluate patient before Epilepsy surgery:

Imaging and New EEG techniques

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Outline

- Neuroimaging tools
  - MRI, , techniques, high resolution MRI 7T
  - Ictal SPECT
  - PET
- EEG
  - EEG source localization
  - High density EEG
  - EEG-fMRI
  - High frequency Oscillation (HFO)

MRI brain

- Neuroimaging plays a crucial role in identifying anatomic lesions responsible for epilepsy
- Assist in localizing eloquent cortex and white matter tracts for presurgical planning
- MRI epilepsy protocol should include
  - Volumetric T1-weighted imaging with 1- to 1.5-mm section thickness
  - T2-weighted imaging
  - Fluid attenuated inversion recovery (FLAIR)
  - Proton density
  - Inversion recovery sequences in at least two orthogonal planes, covering the entire brain

High resolution MRI 7T

- With its higher signal-to-noise (SNR) and contrast-to-noise ratio (CNR) compared to lower field strengths, high resolution, contrast-rich images can be obtained of diverse pathologies,
- Additional pathophysiological information can be gained compared to lower field strengths
- Because of clear depiction of small anatomical details, and higher lesion conspicuousness, earlier diagnosis and start of treatment

SPECT in Epilepsy

- The localizing value of ictal SPECT based on cerebral metabolic and perfusion coupling
- Ictal hyperperfusion used to localize the epileptogenic zone noninvasively, and particularly useful in MRI-negative partial epilepsy and focal cortical dysplasias
- Subtraction ictal SPECT coregistered with MRI (SISCOM) improves localization area of hyperperfusion
- Ictal SPECT should be interpreted in context of full presurgical evaluation

SPECT in Epilepsy

- Early ictal SPECT injections minimize problem of
  - Seizure propagation
  - Nonlocalization due to early switch from ictal hyperperfusion to postictal hypoperfusion during brief extratemporal seizures
- Ictal hypoperfusion may reflect ictal inhibition or deactivation
- Postictal and interictal SPECT studies less useful to localize ictal-onset zone
- The area of highest ictal hyperperfusion usually ictal-onset zone, unless seizure propagated.

SPECT in Epilepsy

- Several propagation patterns have been described.
  - Often from posterior brain regions (parietooccipital lobes) to anterior brain regions (temporal and frontal lobe)
    - Noachtar et. al reported propagation in 85% of parietooccipital epilepsy
  - Another propagation pattern is from the temporal to frontal lobe
  - Propagation from one temporal lobe to contralateral temporal lobe reported in ~1% of cases

SPECT in Epilepsy

- Ictal SPECT injected during SPS gave no information in ~40% of cases
- CPS give best results, and secondarily generalized seizures may give multiple regions of hyperperfusion
- Duration of injected seizure important in interpretation of ictal SPECT
  - After injection in vein, tracer takes ~30 s to reach the brain
  - Postictal switch (i.e., switch from ictal hyperperfusion to postictal hypoperfusion) ~1–2 min in TLE
  - Extratemporal seizures should last ≥10–15 sec after ictal SPECT injection to give localizing information

SPECT in Epilepsy

- MR-negative partial epilepsy remains a difficult of presurgical evaluation, invasive EEG studies usually indicated
  - With ictal SPECT and invasive EEG
    - Siegel and colleagues (2001) reported a good seizure outcome in 83% of patients with refractory MR-negative partial epilepsy
- Ictal SPECT in combination with 3-T MRI scanning appears particularly promising for detection of subtle FCD

PET and Epilepsy

- PET is valuable clinical tools in the management of patients with medically resistant, partial epilepsy who are under evaluation for surgical treatment.
- The value of PET for localization has been firmly established for patients with
  - Temporal lobe epilepsy (TLE)
  - Extratemporal lobe epilepsy (ETE)
- Very useful test to identifying the source of seizure activity in the brain because it is non-invasively identify metabolic focus

PET and Epilepsy

- PET-FDG imaging especially when performed concurrently with surface EEG, may be useful for localizing all of the seizure focus for surgical resection
- It has invaluable role in research into the epileptogenesis or to identify underlying cause
- PET has been applied for presurgical evaluation since 1970
- The sensitivity of FDG-PET in
  - Temporal lobe epilepsy is high up to 80-90% to identify foci of seizure onset
  - In TLE with hippocampal sclerosis, interictal FDG-PET showed up to 100% sensitivity

PET isotopes and tracers used in epilepsy

Isotope/half-life	Tracer	Target function	Clinical application
F18/ 109 min	18FDG	Glucose metabolism	Focus localization Brain fn, Integrity
11C/ 20 min	(11C)-flumazenil	$GABA_A$-receptors	Focus localization
	a[11C]-methyl-L tryptophan	Brain serotonin synthesis	Focus localization
	(S)-[N-methyl-[11C]ketamine	NMDA-receptors	Focus localization
	[11C]doxepin	Histamine H, receptors	Focus localization
	[11C]carfentanil	Mu-opiate receptors	Focus localization
	[11C]WAY	$5\text{-}HT_{1A}$ receptors	Focus localization

Evaluation of PET in epilepsy

- Focal epilepsy: refractory
  - Temporal lobe epilepsy
  - Extratemporal lobe epilepsy
- Childhood epilepsy
  - Intractable, non-lesional partial epilepsy
  - Intractable partial epilepsy in whom clinical, discordant EEG data
  - Inadequately define the boundaries
  - Infants with unilateral hemispheric epilepsy syndromes

PET studies of focal epilepsy

- Interictal PET
  - Demonstrate areas of reduced glucose metabolism that correspond to epileptogenic zone in partial seizures
  - However, hypometabolic changes usually larger than pathological abnormalities

PET in temporal lobe epilepsy

- 18FDG-PET in TLE is a reliable localizing technique with true positive results in approximately 70% of patients
- Mechanism of interictal hypometabolism on FDG-PET remains unclear
  - Possibly TLE with MTS; hypometabolism caused by neuronal loss, deafferentation or partial volume effect
- Hypometabolism usually diffuse, involving entire temporal lobe of epileptogenic side, including polar and lateral regions as well as mesial structures

Mesial temporal lobe epilepsy

- Neuropsychological test: verbal memory deficit
- The patient did not want an operation, but chose Gamma knife
- After Gamma knife first 2-3 months had dyscognitive seizure 0-1 per month, but had only a few seizure since then (3 years after Gamma knife)

PET in Extratemporal lobe epilepsy

- Localization of seizure foci in extratemporal lobe epilepsy, more difficult than with TLE
- Hypometabolism concordant with EEG focus
  - 32% in FLE
  - 77% of TLE
- Hypometabolic region is not necessarily congruent with location and extent of epileptogenic lesion
- Hypometabolic region usually includes structural lesion, but often extends to involve >one lobe or whole hemisphere
- Bilateral temporal hypometabolism commonly found

Usefulness of PET

- It is very useful in particularly cases that have a MRI negative or localization discordant cases
- In Extratemporal lobe epilepsy, success rate of surgery is only 50% despite an extensive usage of PET and MRI imaging modalities
- Area of abnormal glucose metabolism commonly larger than epileptogenic zone.
- FDG-PET might be regionalizes the epileptic focus, but have a poor localization in ETE

Usefulness of PET

- In frontal lobe epilepsy, PET provides a correct localization only 50% in cases with a normal MRI
- However, PET and Ictal SPECT localizing information usually used as a guide for intracranial grid placement

Ictal PET

- Ictal PET
  - Usually achieved by chance or can be done when patient had prolonged seizure i.e. status epilepticus
  - 18FDG uptake occurs >40-minute period after injection, therefore data will reflect an amalgam of ictal, postictal and interictal conditions
  - PET cannot be done in VEM

EEG source imaging in epilepsy

- Model-based imaging technique that integrates temporal and spatial components of EEG to identify the generating source of electrical potentials recorded on the scalp
- Recent advances in computer technologies made analysis of ESI data less time-consuming, and have rekindled interest in this technique as clinical diagnostic tool
- ESI seems to be a promising tool for epilepsy evaluation; however, the precise clinical value of ESI in presurgical evaluation of epilepsy and in localization of eloquent cortex remains to be investigated

Utility of EEG source imaging

- Identification of the irritative zone (spikes and/or sharp waves)
  - Presurgical assessment of patients with refractory focal epilepsy
  - Accurate definition of focal epilepsies
  - Identification of the ictal onset zone (EEG seizure onset)
  - Identification of seizure networks (seizure propagation)
  - Identification of eloquent cortex (visual, auditory and somatosensory regions)

EEG-fMRI

- EEG/fMRI promising additional tool for presurgical epilepsy evaluation
- Allowing a precise non-invasive identification of epileptic foci
- Use to localize eloquent cortex

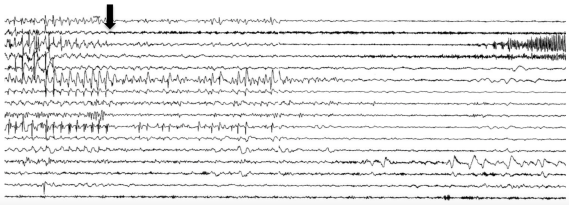
High frequency oscillations (HFOs)

- High frequency oscillations (HFOs) have recently been recorded in epilepsy patients and proposed as possible novel biomarkers of epileptogenicity
- HFO characteristics correlate with the clinical manifestation of seizures may yield additional insights for delineating epileptogenic regions

Seizure onset zone

The area of cortex that initiates seizures (Lüders et al. 2006)

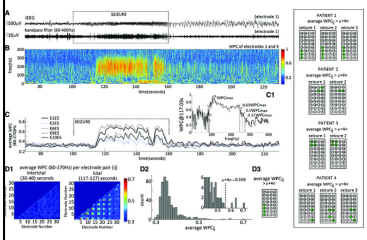
➡ Visual analysis of the 'low voltage fast activity'



Epilepsia
Official Journal of the International League Against Epilepsy

Mapping the coherence of ictal high frequency oscillations in human extratemporal lobe epilepsy

Marija Cotic, Osbert C. Zalay, Yotin Chinvarun, Martin del Campo, Peter L. Carlen, Berj L. Bardakjian



March 2015

HFOs shown to localize to epileptogenic zone

Correlation between ictal HFO intensity and coherence, ictal HFO coherence can act as an epilepsy biomarker

Ictal HFO coherence and intensity in the 80–270 Hz frequency range, this band may be targeted when defining seizure-related regions of interest for characterizing ETLE

Spatial Coherence Profiles of Ictal High Frequency Oscillations Correspond to those of Interictal Low Frequency Oscillations in the ECoG of Epileptic Patients.

Marija Cotic Yotin Chinvarun Martin delCampo
Peter Carlen Berj Bardakjian

IEEE transactions on bio-medical engineering (Impact Factor: 2.23). 12/2014;

- Relationship between cohered HFO intracranial EEG (iEEG) activity with that of slower low frequency oscillations (LFOs; <80 Hz)
- LFOs (in the 8-12 Hz frequency range) play an important role in controlling cortical excitability, by exerting an inhibitory effect on cortical processing,
- The presence of strong theta activity (4-8 Hz) in awake adults suggestive of abnormal and/or pathological activity
- Overlapping spatial regions exhibiting increased coherence in both ictal HFOs and interictal LFOs identified local abnormalities that underlie epileptogenic networks

Journal of Neural Engineering

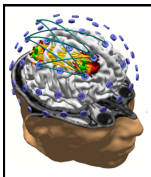
Journal of Neural Engineering > Volume 12 > Number 2

Defining regions of interest using cross-frequency coupling in extratemporal lobe epilepsy patients

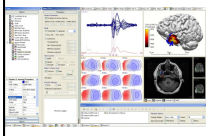
Mirna Guirgis[1], Yotin Chinvarun[2], Martin del Campo[3], Peter L Carlen[1,3,4] and Berj L Bardakjian[1,5]

- An automated system is proposed to objectively localize this EZ by identifying regions of interest (ROIs)
- LFO-modulated HFOs can be used to identify ROIs in extratemporal lobe patients
- Delta-modulated HFOs may provide more accurate localization of the EZ. result in better surgical outcomes when used to compliment the SOZs identified by clinicians for resection

March 2015

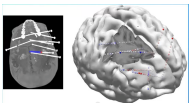


International Clinical workshop: Curry software



Monday 5 October to Wednesday 7 October 2015
Pramongkutklao Hospital

- This hands-on workshop, which is intended for physicians and EEG/MEG technologists, is specifically focused on the evaluation of epilepsy EEG and MEG data
- Course duration is 2 ¼ days
  - Introduction to basic EEG/MEG review
  - Evoked response data analysis.
  - Inter-ictal and ictal data review, spike/seizure mark-ing, event segregation by field analysis, and averaging
  - Source analysis methods for the above data types, includ-ing the use of indi-vidual MRI and realistic head models
  - Intracra-nial EEG review, including integration with MRI and CT to localize electrodes and co-registration with other func-tional imag-ing data, such as PET



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