Imaging with MRI, PET & SPECT in Evaluation of Epilepsy Surgery

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- Identify potential candidates who may benefit from epilepsy surgery
- Confirmation of focus (critical for epilepsy surgery)
- Identify areas to be spared during epilepsy surgery (cortex and white matter)

Gaillard WD et al *Epilepsia* 2009
Imaging

- Structural high resolution MRI, epilepsy protocol
- PET
- SPECT
- MEG/3D EEG/fMRI-EEG
- Functional Mapping Cortex (fMRI, MEG, TMS)
- DTI: Tractography for White Matter Tracts

- DTI focus localization: Not yet fully evaluated
- Connectivity analysis: Not yet stable/reliable

MRI Epilepsy Protocol (>2 yrs): To optimize detection of structural lesions

- High Resolution 3D T1 weighted (SPGR) 1 mm
  - Preferably acquired in sagittal plane (for motion)
- Axial & Coronal T2
- Axial & Coronal FLAIR
- Oblique Coronal High resolution (≤3mm) FSE ⊥ to the long axis of the hippocampal formation
- Gadolinium contrast not necessary unless tumor or inflammation suspected

Gaillard WD et al., *Epilepsia* 2009
Epilepsy: Protocol continued

- Standard sequences with increased resolution
  - 3 Tesla MRI units better than 1.5 Tesla (or lower)
  - Decrease slice thickness
    - From 4-5 mm to 1-2 mm
    - Normal cortex is about 2 mm in thickness
    - Thicker images may not reveal focal lesions
- Pulse sequences not used in common practice
  - magnetization transfer, MR spectroscopy, susceptibility imaging, DTI, ASL
- Infants (< 2yr)
  - T2 Axial, coronal, sagittal (or 3D)
  - 3D T1 & FLAIR less useful
ILAE 2004 Pediatric Epilepsy Surgery Survey

- MCD/FCD 42%
- Tumor 20%
- Stroke 10%
- MTS 7%
- Gliosis/No clear pathology 6%
- TS 5%
- Hypothalamic Hamartoma 3%
- Rasmussen 3%
- Vascular (include Sturge Weber) 4%

Harvey AS et al., *Epilepsia* 2008
Class 1A Seizure Outcome
2004 ILAE Pediatric Outcome Survey

- If clear MRI abnormality completely resected seizure free in ~85%
- If clear MRI abnormality incompletely resected seizure free in <20%
- If MRI normal; PET/SPECT/MEG focal and resected seizure free in ~40-60%
- If image normal (MRI and PET/SPECT/MEG then seizure free in <10%

Courtesy G Mathern
Cavernoma  AVM  Stroke
Mesial Temporal Sclerosis
Focal Cortical Dysplasia

Bright
Thick
Blurred Gray-White matter junction
Unilateral Lt TE WM Hypomyelination (associated with FCD)
2 y.o., severe (catastrophic) focal right sided seizures, left hemiparesis

Bottom Of the Sulcus FCD

FSE T2, 5/1.5, 192x256

2/0, 192x320, 8 Channel
1.5T
3D SPGR T1WI
1.3 mm slices, 0mm spacing

2D T2 FLAIR
5 mm slices, 0mm spacing

3T
3D SPGR T1WI
1 mm slices, 0.5 mm spacing

3D T2 FLAIR CUBE
2 mm slices, 0 mm spacing
Pulse sequences not used in common practice
Magnetization transfer (better at 1.5T than 3T!)

7 y.o., right parietal sz
Structural MRI

- Special sequences/imaging infants
- Timing imaging dysplasia in infants: They come and go: Best <4mo; > 24mo
- .....and Repeat if normal and seizing q 3-6 mo
• FCD IIIA. Not seen 18 mo, apparent 4 yrs
Imaging: FDG-PET

- Measure of metabolic rate (synapse): Glucose uptake and consumption
- Ictal FDG-PET uncommon and unreliable
- Interictal: Regional hypometabolism lateralizes the seizure focus; less reliable localizing focus
- Regional hypometabolism more widespread than epileptogenic zone
- Regional hypometabolism: Good surgical outcome adults with childhood onset epilepsy (class 2)
- Reduces need for invasive (less extensive) recording
18FDG-PET

- Greater hypometabolism, better outcomes
- Remote and/or Bilateral PET abnormality associated w/ poor outcomes
- May be helpful in young, < 2 years, when MRI less sensitive to identifying dysplasia (Class 4)
- Re-review of MRI may find FCD (Class 4)

Wong et al 2012; Theodore et al 2012
Multilobar FCD I and normal MRI

Truly sharply demarcated and focal PET
More likely to have clear FCD

FDG Meta-analysis
46 Studies 1992-2006

- Ipsilateral PET hypometabolism:
  - 86% predictive value for good outcome
    - Does it add anything to lesional MRI?
- 80% with normal MRI
  - Predicts outcome
- 72% in patients with non-localized ictal scalp EEG

Willmann et al 2007
[11C] α-methyl tryptophan Serotonin Precursor
Increased Uptake in Epileptic Foci

- TS: AMT uptake ~ spiking tubers
- ↑ AMT uptake in neocortical foci, MCDs
- May help predict outcome from tuber resection
- Diversion from 5HT synthesis to excitatory quinolinic or kynureninic acid?
- ↑ serotonergic innervation ~ neurogenesis
- FDG tubers “Cold”, AMT epileptogenic tuber “Hot” Helpful in one third children with TS (n=191)
SPECT

- HMPAO, ECD (99-Technetium)
- Markers of CBF
- Long half life (6 hours)
- Can scan several hours after injection
- Can not quantify
- Always perform with EEG
- Timing of injection in relation to seizure critical
SPECT

- Interictal, SuSPECT: False lateralizing 10%
- Ictal Superior
- Subtraction Inter-Ictal from Ictal (or SPM)
  - Co-registration with structural MRI
  - Increases inter and intra rater agreement from 70 to 85% & localization value 31-74% to 74-93%
  - 80-90% when lesion present (Class 3 adults)
  - 59-76% non lesional (Class 4)
- Reliability depends on timing/delay injection in relation to seizure onset (later injection increases false localization/lateralization)
- Propagation effects

O’Brien et al, 98, 99; Vera et al, 99
Temporal lobe Focus: ECD SPECT CBF

Injection 12 seconds
After seizure onset

O’ Brien et al Neurology 1999
PET-SPECT COMPARISONS

- Depend on methodsy, experience
- Generally show similar results
- FDG-PET may be superior for TLE
- SPECT may be superior for ETLE
- Value of concordance debated
  - Is it worth doing both?
- Neither adds much if MRI, EEG localizing.

Functional Imaging Pitfalls

- **Ictal SPECT**
  - Very sensitive to injection time
  - Sensitive to seizure spread
  - Reflects only one seizure

- **FDG PET**
  - Averages activity over 30-40 minutes
  - May be sensitive to time since last seizure (< 2 days)
  - May be sensitive to most recent seizure type?

- A lot may depend on how scans are analyzed
  - Visual?
  - Quantitative?

- Can you trust the radiologists?
N=160; 77 iEEG; 72 Seizures; 62 resection; 38 (61%) Engle I MRI negative (43%), unclear, small FCD

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MRI Negative & Image Negative

- 1.5 T MRI epilepsy protocol reviewed & negative
- 3T MRI epilepsy protocol reviewed & negative
- Then if MRI- perform PET, SPECT, or source localization
- 3T epilepsy protocol reviewed after vEEG, PET, SPECT, &/or source localization (MEG, 3D EEG) = MRI negative
- Image negative: MRI, PET, SPECT, MEG all Negative
- If MRI positive: Excellent likelihood of seizure control (80-85%)
- If MRI Negative but Image Positive: Good likelihood of seizure control (40-60%)
- If Image negative: Outcome poor <20%

Salamon et al, Neurology, 2008

32/229 discordant
86% concordant
14% discordant

fMRI > IAT for Predicting Naming outcome
fMRI Language Group Maps for Children
Ages 4-12 years (n=68, p<0.05 corrected)

Auditory Category Decision
Listening to Stories

Auditory Description Decision Task
Reading Stories
(6-12, n=48)
30% MRI negative patients will have atypical language dominance.
fMRI Semantic Decision Task Predicts Post-Op Naming

AI > 0.4 risk of language measure decline

Failed fMRI

- Disruption **BOLD** Signal
  - Glioma, Edema & Mass Effect (Bookheimer et al, 1997)
  - AVM and Vascular Steal (Lehericy et al, 2002)
  - Post-Ictal state (Jayakar et al, 2002)
  - Arterial Stenosis (Rother et al, 2002)

Listen Repeat Sem Flu Phon Flu

2 Weeks Later
9 children presented at Epilepsy Conference
With normal MRI

Seemingly focal vEEG, Seizure (w/ time multi-focal)

One focal PET

All 9 had significant genetic causes for their epilepsy
6 SCN1A; 2 SCN2A; (1 CHRNA2)
relative contraindications to surgery (unless
clear structural abnormality present that may)
Genome-wide association study
1,018 people with mTLE & MTS;
7,552 control subjects,
Validation independent sample
959 people with mTLE & MTS;
3,591 control subjects.
Cases with mTLE with MTS
w/ (n = 757) & w/o (n = 803)
febrile seizures

Significant association for
mTLE, MTS, & febrile seizures
w/ SCN1A gene, P:3.36 ×10(-9),
odds ratio (A) = 1.42,
95% confidence interval: 1.26-1.59

Kasperaviciute D et al., Brain, 2013
Epilepsy Surgery Evaluation Protocol

ILAE

Epilepsy Conference

Non-resective or No Surgery
- Multi-focal Generalized Eloquent cortex
  - No ECoG
  - Hemispherectomy
  - HT/Harmatoma

One Stage
- Non-focal lesions with a clear penumbra
  - FCD
  - Non-focal lesions without a clear penumbra
  - Inconclusive Localization
  - Divergent Data

Two Stage
- Extra-Operative
- Intra-Operative

Mapping

Jayakar P. Epilepsia 2014
Summary I

• There is no substitute for a high quality, high resolution, MRI epilepsy protocol (preferably at 3T) reviewed at initial evaluation and after non invasive evaluation (neurophysiological and functional imaging) by skilled readers of MRI.
Summary II

- Clear MRI Lesion: PET, SPECT, MEG add little
- FDG-PET: Non-lesional MRI helpful 60-80%
- SPECT/MEG when PET negative or unavailable
- FDG-PET, iSPECT, MEG about 60-70% helpful
- FDG-PET lateralizes, iSPECT, MEG better localization but more propagation effects
- Use modality with greatest access and skill as comparable, may be complementary, all limitations
- Negative or discordant results, DO genetic & inflammatory testing then consider invasive monitoring & higher risk of poor outcome
Summary III

- fMRI provides reliable data to identify eloquent cortex, and to guide localization of critical cortical functions: motor, sensory, language, (and memory)
- Outcome related to resection of MRI abnormality, not PET, SPECT, or MEG abnormality