NEUROIMAGING IN EPILEPSY: WHY IS IT NECESSARY?

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EPILEPSY

- AFFECTS 0.5%-1% OF POPULATION
- 70% OF EPILEPTICS CAN BE CONTROLLED WITH MEDICATION (USUALLY BY THE 3rd ‘REASONABLE’ MEDICATION ATTEMPTED)
- OF THE REMAINING 30%, ABOUT HALF (15%) ARE SURGICAL CANDIDATES
- THE OTHER 15% ARE NEITHER CONTROLLED NOR CAN BE HELPED WITH RESECTIVE SURGERY
- NEW MEDICATIONS, KETOGENIC DIET, VAGAL NERVE STIMULATOR
PRIMARY GENERALIZED VERSUS PARTIAL SEIZURES

- PRIMARY GENERALIZED SEIZURES HAVE A GENERALIZED ONSET ON EEG, i.e., NO FOCUS
  - CAN BE CONVULSIVE (e.g., tonic, tonic-clonic) OR NONCONVULSIVE (e.g., petit mal absence)
- PARTIAL SEIZURES HAVE A FOCAL ONSET.
  - CAN BE SIMPLE PARTIAL (no LOA) OR COMPLEX PARTIAL (with LOA)
  - CAN GENERALIZE INTO CONVULSION (i.e., secondary generalization)
- MYOCLONIC SEIZURES AND ATONIC SEIZURES CAN BE EITHER PARTIAL OR PRIMARY GENERALIZED
EPILEPSY: Diagnostic tests

- EEG
- SLEEP-DEPRIVED EEG
- MRI (except in typical absence 3 Hz s/w)
- VIDEO-EEG MONITORING (localization of seizure onset for surgical evaluation; differential diagnosis to determine if episodes are seizures; to determine if patient’s seizures are really controlled)
- PET SCAN OR ICTAL SPECT SCAN (surgical evaluation)
NEUROIMAGING IN EPILEPSY

• PRIMARY IMAGING MODALITY IS MRI
• CT/MRI TYPICALLY UNDERESTIMATE THE EPILEPTOGENIC REGION
• WHEN MALFORMATION IS PRESENT, IT MAY NOT BE ENTIRELY SEEN ON MRI
• SEIZURES OFTEN DO NOT ARISE FROM THE LESION ITSELF, BUT FROM SOME PERIPHERAL LOCATION
NEUROIMAGING IN EPILEPSY

• FUNCTIONAL IMAGING SHOWS BETTER CORRELATION WITH EPILEPTOGENIC ZONE
• PET: GLUCOSE METABOLISM, NEUROTRANSMITTERS & RECEPTORS
• SPECT: SISCOM SHOWS SEIZURE FOCUS FOR A SINGLE SEIZURE, DOES NOT MAP OUT THE EPILEPTOGENIC ZONE
VALUE OF NEUROIMAGING IN EPILEPSY

• GENERAL LOCALIZATION OF EPILEPTOGENIC REGION (MRI, PET, SPECT)
  – Beware of false positives, need EEG correlation

• ASSESS FUNCTIONAL INTEGRITY OF REGIONS OUTSIDE THE EPILEPTIC FOCUS, INCLUDING CONTRALATERAL HEMISPHERE (PET, SPECT)
  – Rule out surgical candidates (PET, SPECT)

• DIFFERENTIATE BETWEEN PRIMARY AND SECONDARY GENERALIZED EPILEPSY (PET)

• DEFINE MOTOR, LANGUAGE CORTEX, ALSO MEMORY TESTING (fMRI, PET)

• EVALUATE PROGRESSION OF DISEASE (PET, SPECT)
NONLESIONAL EXTRA-TEMPORAL LOBE EPILEPSY

• SEIZURE-FREE OUTCOME IN ONLY 50%-55% WITH 2-STAGE SURGERY: NO APPRECIABLE CHANGE IN PAST TWO DECADES. WHY??

• GRID PLACEMENT GUIDED BY SCALP EEG FINDINGS AND SEIZURE SEMIOLOGY

• PET FURTHER GUIDES GRID PLACEMENT ---> CLASS 1 OUTCOME IN AT LEAST 80%
FDG PET in Neocortical Epilepsy
Focal hypometabolism with normal high-resolution MRI

8 year old girl, with uncontrolled seizures
Ictal onset in right central region (C4-F4)    Pathology: Cortical dysplasia
FDG PET in Neocortical Epilepsy: Multilobar Hypometabolism

Intracranial EEG: R frontal onset, R temporal spread
SEIZURE ONSET AT BORDERZONE OF GLUCOSE HYPOMETABOLISM

- seizure onset
- early spread
- inactive electrodes

hypometabolism

Children's Hospital of Michigan, Wayne State University, Detroit

Juhász et al.: Ann Neurol 2000
Expansion of glucose hypometabolism with persistent epilepsy

1st FDG PET scan
4.8 years
3 seizures/week

2nd FDG PET scan
6.5 years
2-3 seizures/day
SURGERY FOR INFANTILE SPASMS & WEST SYNDROME

• PET IDENTIFIES FOCAL CORTICAL DYSGENESIS IN CRYPTOGENIC CASES FOR SURGICAL TREATMENT (Chugani et al., Ann Neurol 1990): 5 patients with normal MRI, focal PET lesions

• SURGERY FOR INTRACTABLE INFANTILE SPASMS (Chugani et al., Epilepsia 34:764-71, 1993): 23 patients (17 with active infantile spasms, 6 with recent spasms): 15 became seizure-free, 3 had 90% seizure reduction, 1 had 75% reduction, 4 showed no benefit from surgery
Infantile Spasms

Children’s Hospital of Michigan
Wayne State University, Detroit

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SURGERY FOR INFANTILE SPASMS & WEST SYNDROME

- Metabolic lesions not always shown early on MRI
- Best surgical candidates have unilateral MRI or PET lesion
- Structural or functional localization should be concordant with EEG focus
- Extent of lesion (‘nociferoius’ cortex) must be defined
- Contralateral hemisphere should be normal
Infantile Spasms: Metabolic Patterns

Surgical Candidate - 20%

Multifocal - 65%

Bitemporal/Autism - 10%

Metabolic/Neurogenetic - 5%
TIMING OF MRI IS IMPORTANT

At 6 months of age

At 3 years of age

Sankar R, AJNR, 1995
Increased cortical glucose metabolism due to frequent interictal spiking: false lateralization!!!
PET SCANNING IN EPILEPSY

- $[^{11}C]C$ARFENTANIL: binds to mu-opiate receptors
- $[^{11}C]D$OXEPINE: binds to histamine H1 receptors
- $[^{11}C]F$LUMAZENIL: binds to benzodiazepine site on GABA-A receptor
- ALPHA$[^{11}C]M$ETHYL-L-TRYPTOPHAN: measures tryptophan metabolism by serotonin and kynurenine pathways
Area of decreased flumazenil binding is smaller than glucose hypometabolism

EEG: left temporal-parietal focus

FDG

FMZ
AMT PET in Tuberous Sclerosis Identifies Epileptogenic Lesion(s)

FDG PET

Multiple areas of hypometabolism indicate multiple tubers

AMT PET

Epileptogenic tuber with increased uptake
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Involvement of Extratemporal Areas In Temporal Lobe Epilepsy

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4 YR 4M OLD BOY WITH SEVERE EPILEPSY AND AUTISM
4 YR OLD BOY, LANDAU-KLEFFNER SYNDROME

FDG PET
HEMIMEGALENCEPHALY

Unilateral

11 y.o., M

Mild contralateral involvement

7 m.o., M

Severe bilateral

22 y.o., M
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PARTIAL EPILEPSY vs. PRIMARY GENERALIZED EPILEPSY

- EEG: GENERALIZED EPILEPTIFORM DISCHARGES

- ANTICOVULSANTS FOR PRIMARY GENERALIZED EPILEPSY NOT HELPFUL

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STURGE-WEBER SYNDROME:
Rapid Progression of Severe
Hypometabolism is Associated with Good
Cognitive Outcome

5 months    38 months    5 years
Extent of Hypometabolism vs. Cognitive Functions

T-P-O Hypometabolism
IQ = 55

Hemispheric Hypometabolism
IQ = 79
Early, rapid hemispheric progression in SWS

- “autohemispherectomy”
- often well controlled seizures
- relatively preserved cognitive functions
- functional reorganization, likely in the contralateral hemisphere

40 months old boy
Verbal IQ: 93
FDG PET in children with SWS and recent onset seizures: transient (interictal) hypermetabolism

Chugani et al., 1989

- Increased glucose metabolism (interictal!) in some infants
- Switched to decreased metabolism on follow-up PET

FDG PET (baseline)

FDG PET (follow-up)

4 months old

1 year old
Increased cortical glucose metabolism in contralateral visual cortex

Patients with severe ipsilateral occipital hypometabolism

Control
CONCLUSION

• VARIOUS NEUROIMAGING MODALITIES PLAY COMPLEMENTARY ROLES IN THE EVALUATION AND TREATMENT OF EPILEPTIC DISORDERS
• NEUROIMAGING MUST NOT BE USED AS AN INDEPENDENT TOOL FOR EPILEPSY
• RATHER, NEUROIMAGING FINDINGS SHOULD BE CORRELATED WITH SEIZURE SEMIOLOGY AND EEG FINDINGS FOR CONCORDANCE
• REFINEMENT OF THE NEUROIMAGING APPROACH WILL ALLOW PRECISE DEFINITION OF EPILEPTOGENIC BRAIN REGIONS TO BE RESECTED AND THOSE TO BE SPARED