Neuroimaging in generalized seizure models: implications for epileptogenesis & behavior

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Disclosures
None

Talk outline
1. Why study absence epilepsy?
2. Interictal
   • Comorbidities: Anxiety, Depression, Inattention
   • Treatment: Neuroimaging and Phenotype
3. Ictal
   • Behavioral symptoms and neuroimaging
   • Underlying mechanisms

Why study absence?
Far from benign
Gold-standard drugs less effective than thought
Seizure suppression doesn’t cure all

Glauser et al., Epilepsia 2013

What to study in absence?
1. Interictal comorbidities
2. Ictal impairment

Caplan et al., Epilepsia 2008
Interictal Neuroimaging Abnormalities

Animal models of absence epilepsy

WAG/Rij and GAERS:
- Frequent seizures
- Arousal-dependent
- Similar electrographic waveform
- Different spike-wave frequency

Biological substrates of early treatment
- Reversed pathological expression of Na and HCN1 channels
  Blumenfeld et al., 2008
- Improves neuroimaging abnormalities e.g. fractional anisotropy
  Van Luijtelaar et al., 2013
- Alters epigenetics/DNA methylation
  Dezsi et al., 2013

Neuroimaging markers of epileptogenesis

Treating “resting” changes in rat models

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Translating to clinical improvements

Berg et al., Epilepsia 2014
Morse et al., unpublished

Years since initial diagnosis of epilepsy

Cumulative Probability of Complete Remission

VPA

ESM TIME vs ESM PROB

VPA

ESX

VPA

Part one summary

• fMRI supports validity of rodent model of absence seizures
• Epileptogenic changes are detectable with neuroimaging
• These changes, and epileptogenesis, can be treated

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Why use experimental neuroimaging?

Guo et al., Lancet Neurol 2016

Mishra et al., J Neurol 2016; Bai et al., J Neurol 2010
McCafferty et al., Nat Neuro in press

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What do we know from model imaging?

- Points of fixation
- Cemented to skull

McCafferty et al., unpublished

Experimental seizure behavior

- McCafferty et al., unpublished

Mechanisms of behavioral variation

Part Two Summary

- Behavioral impairment in absence varies
- A rodent model can uncover the causes of this variation

McCafferty et al., unpublished
Conclusions

Neuroimaging can:

1. Flag markers of epileptogenesis, which are treatable
2. Identify potential causes of behavioral arrest in seizure

Thanks!

- Hal Blumenfeld
- Ben Gruenbaum, Zachary Kratochwil, Isaac Freedman, Rashid Akbari
- Peter Herman, Josh Ryu, Basav Sanganahalli, Fahmeed Hyder
- Antoine Depaulis
- You all for listening!