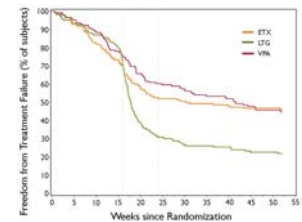


Neuroimaging in generalized seizure models: implications for epileptogenesis & behavior

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Why study absence?

Far from benign
Gold-standard drugs
less effective than
thought
Seizure suppression
doesn't cure all



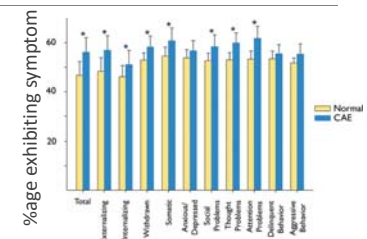
Glauser et al., Epilepsia 2013

Disclosures

None

What to study in absence?

1. Interictal comorbidities
2. Ictal impairment



Caplan et al., Epilepsia 2008

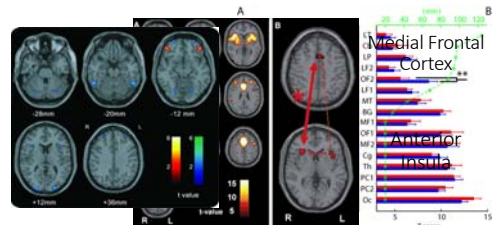
Talk outline

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

Talk outline

1. Why study absence epilepsy?
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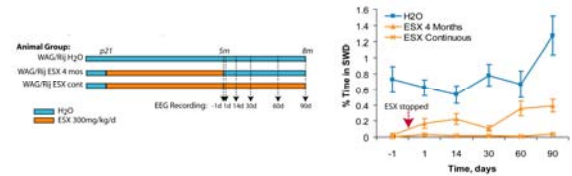
Interictal Neuroimaging Abnormalities



** one-way ANOVA A) $P = 0.006$ (for OF2); B) $P = 0.025$ (for OF2).

Killorain et al., Neurology 2011

Treating “resting” changes in rat models



Blumenfeld et al., Epilepsia 2008

Animal models of absence epilepsy

WAG/Rij and GAERS:

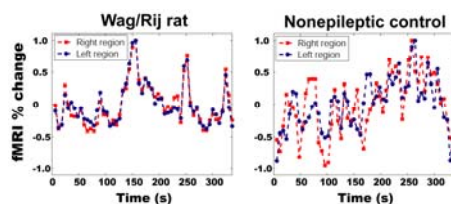
- Frequent seizures
- Arousal-dependent
- Similar electrographic waveform
- Different spike-wave frequency



Biological substrates of early treatment

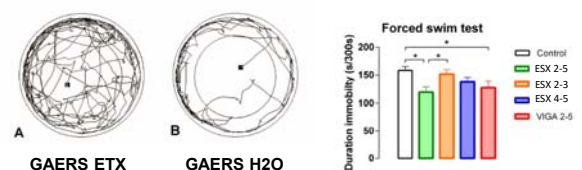
- Reversed pathological expression of Na and HCN1 channels
Blumenfeld et al., 2008
- Improves neuroimaging abnormalities e.g. fractional anisotropy
Van Luijtelaar et al., 2013
- Alters epigenetics/DNA methylation
Dezsi et al., 2013

Neuroimaging markers of epileptogenesis



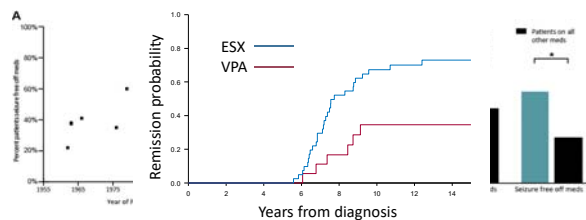
Chahbouh et al., Neurology 2009

Treating “resting” changes in rat models



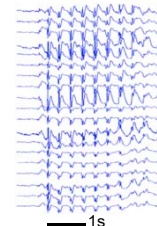
Dezsi et al., Epilepsia 2013, van Luijtelaar et al., Neurobiol Dis 2013

Translating to clinical improvements



Reget et al., *Epilepsia* 2014

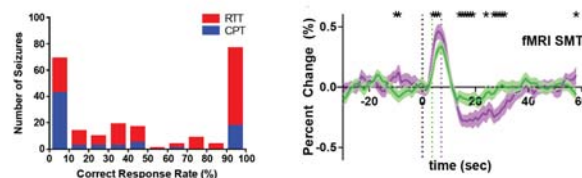
Absence seizures and behavior



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

Absence seizures and behavior

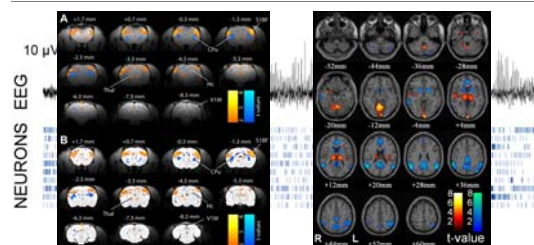


Guo et al., *Lancet Neurol* 2016

Talk outline

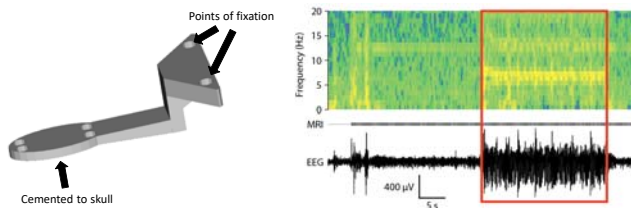
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Why use experimental neuroimaging?

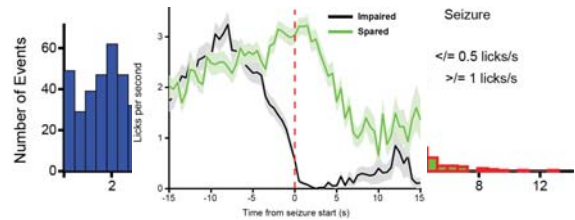


Mishra et al., *J Neurosci* 2014; Bhat et al., *J Neurosci* 2015

What do we know from model imaging?

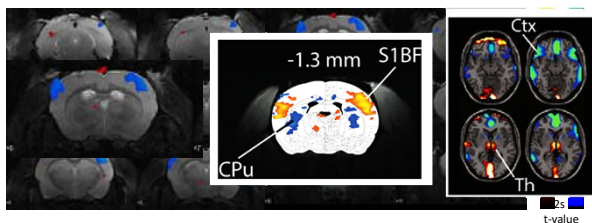


Experimental seizure behavior



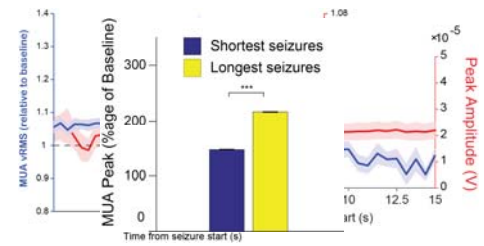
McCafferty et al., unpublished

What do we know from model imaging?



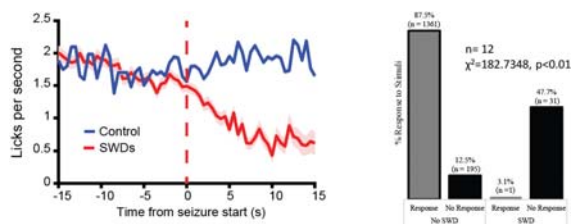
McCafferty et al., unpublished

Mechanisms of behavioral variation



McCafferty et al., unpublished

Experimental seizure behavior



McCafferty et al., unpublished

Part Two Summary

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

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Conclusions

Neuroimaging can:

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

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- Antoine Depaulis
- You all for listening!