

The Effects of Sleep Deprivation on Epilepsy in a Mouse Model of Megalencephaly

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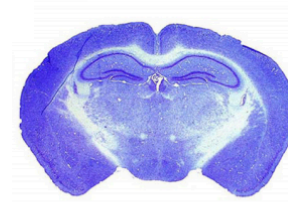
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Introduction

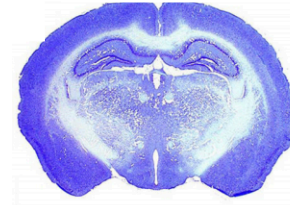
- Megalencephaly (MEG) is a developmental disorder associated with brain overgrowth, frequent cortical malformations, variable intellectual disability, and epilepsy.
- The Dobyns lab at SCRI has recently identified that gain-of-function mutations in *PIK3CA* gene constitute an important cause for MEG.
- The Kalume, Dobyns, and Millen labs at SCRI have developed a mouse model of MEG carrying a *PIK3CA* mutation and this mouse model recapitulates several key features of MEG in humans.



Control

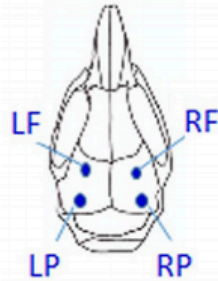
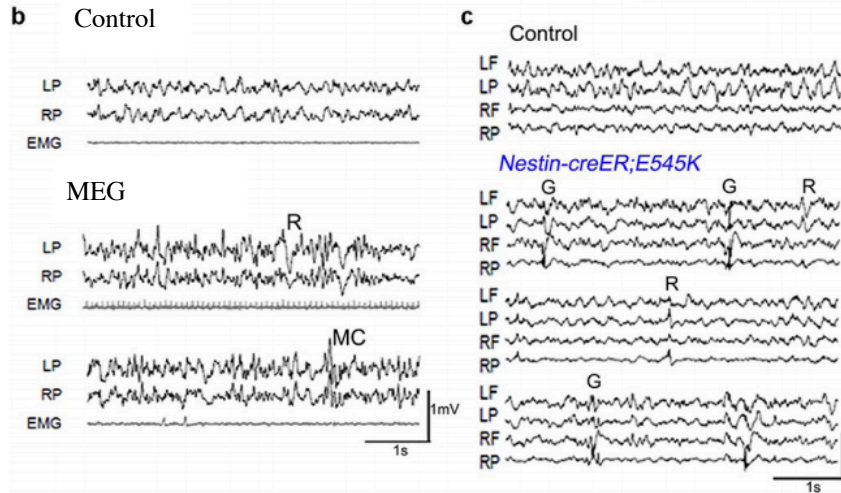


MEG

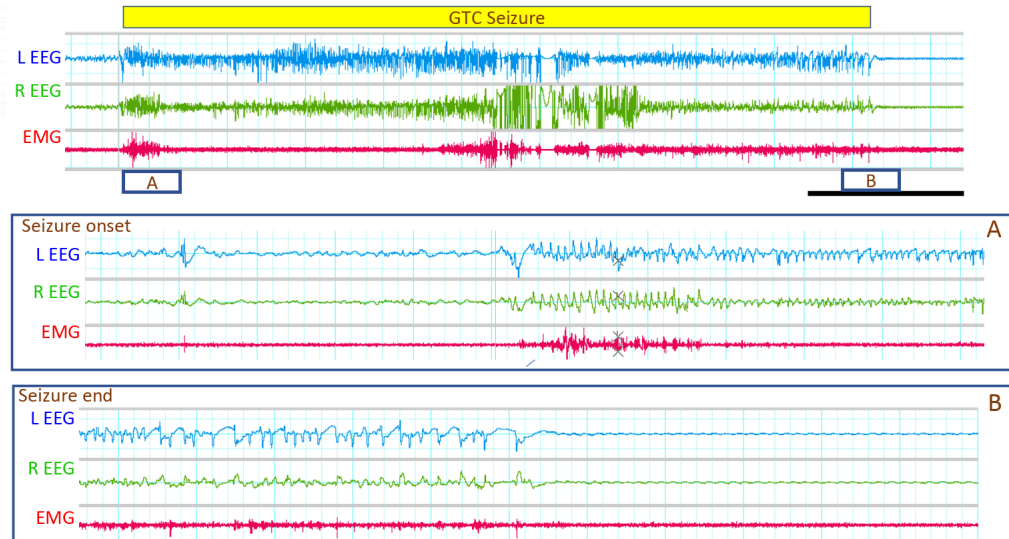


PIK3CA mouse model develops epilepsy

Interictal spikes



Spontaneous seizure



Roy, Achira, et al., *Elife* 4 (2015)



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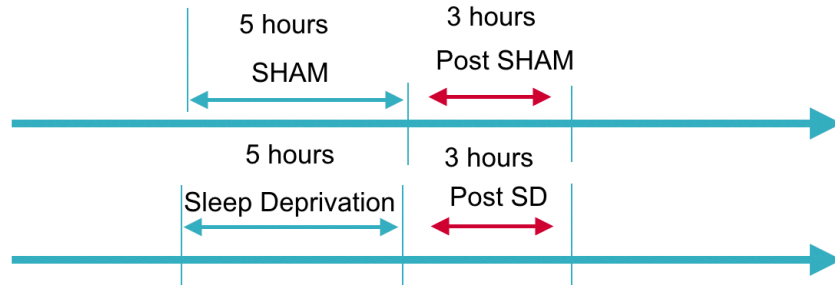
Aim: What is the impact of sleep deprivation on epilepsy in MEG?

- Sleep disturbances are common in people with epilepsy
 - Associated with poor seizure control
 - Poor quality of life of the patients
 - Poor sleep can lead to behavioral and attentional problems.

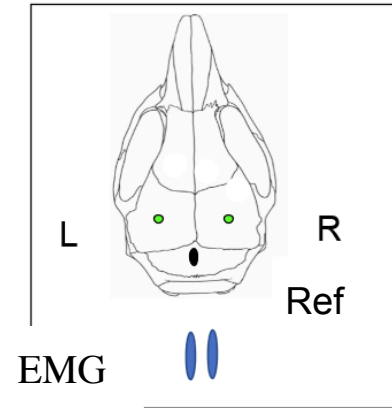


Experimental procedure

- Mice used in these experiments were held under a 12-hr light and dark cycle.
- EEG electrodes were placed bilaterally through small cranial burr holes over frontal and posterior cortices and were fixed in place.
- There were two groups: SHAM and Sleep deprivation (SD).

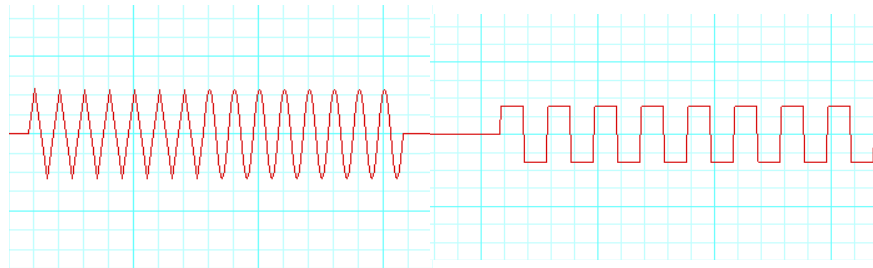


Electrode placement

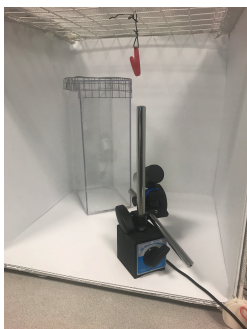


Experimental procedure 2

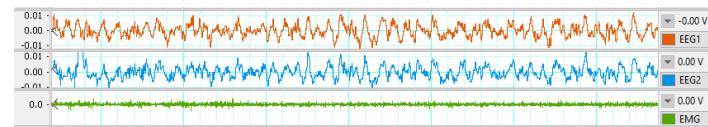
SD & SHAM chamber



Recording chamber



A
B
C

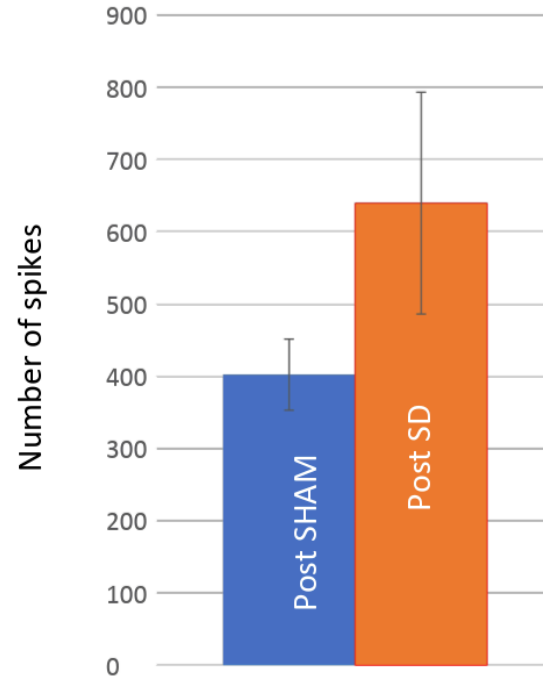
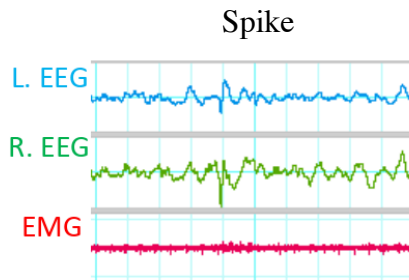
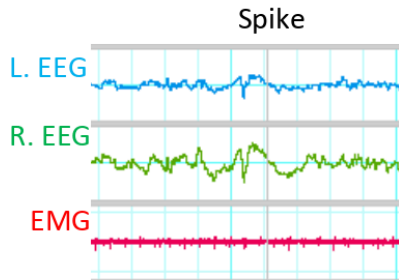


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Results

Example of spikes in MEG mouse



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Conclusion

- SD leads to an increase in the number of interictal spikes in MEG mice.
- This finding indicates that sleep deprivation exacerbate the severity of epilepsy.
- Interictal spikes are hallmarks of the epileptic brain, and in clinics they help to confirm the diagnosis of epilepsy and to characterize generalized vs. partial epilepsies.



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Future directions

- Increase the sample size of this experiment.
- Further characterize the impact of sleep deprivation on other markers of epilepsy.
 - Such as myoclonic seizures, generalized tonic clonic seizures, fast EEG activity, and focal spiking.
- Examine changes in epileptic events in relation with Non-REM sleep and REM sleep.



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