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

Muna Yase
Neurological Surgery Summer Student Program
Kalume Lab
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 \textit{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 \textit{PIK3CA} mutation and this mouse model recapitulates several key features of MEG in humans.
PIK3CA mouse model develops epilepsy

Spontaneous seizure

Interictal spikes

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.

• 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).
Experimental procedure 2

SD & SHAM chamber

Recording chamber
Results

Example of spikes in MEG mouse

Spike
L. EEG
R. EEG
EMG

Spike
L. EEG
R. EEG
EMG

Number of spikes
0 100 200 300 400 500 600 700 800 900

Post SHAM
Post SD
Conclusion

- SD leads to an increase in the number of interictal spikes in MEG mice.
- This finding indicates that sleep deprivation exacerbates 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.
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.