Asynchronous suppression of visual cortex during absence seizures in *stargazer* mice

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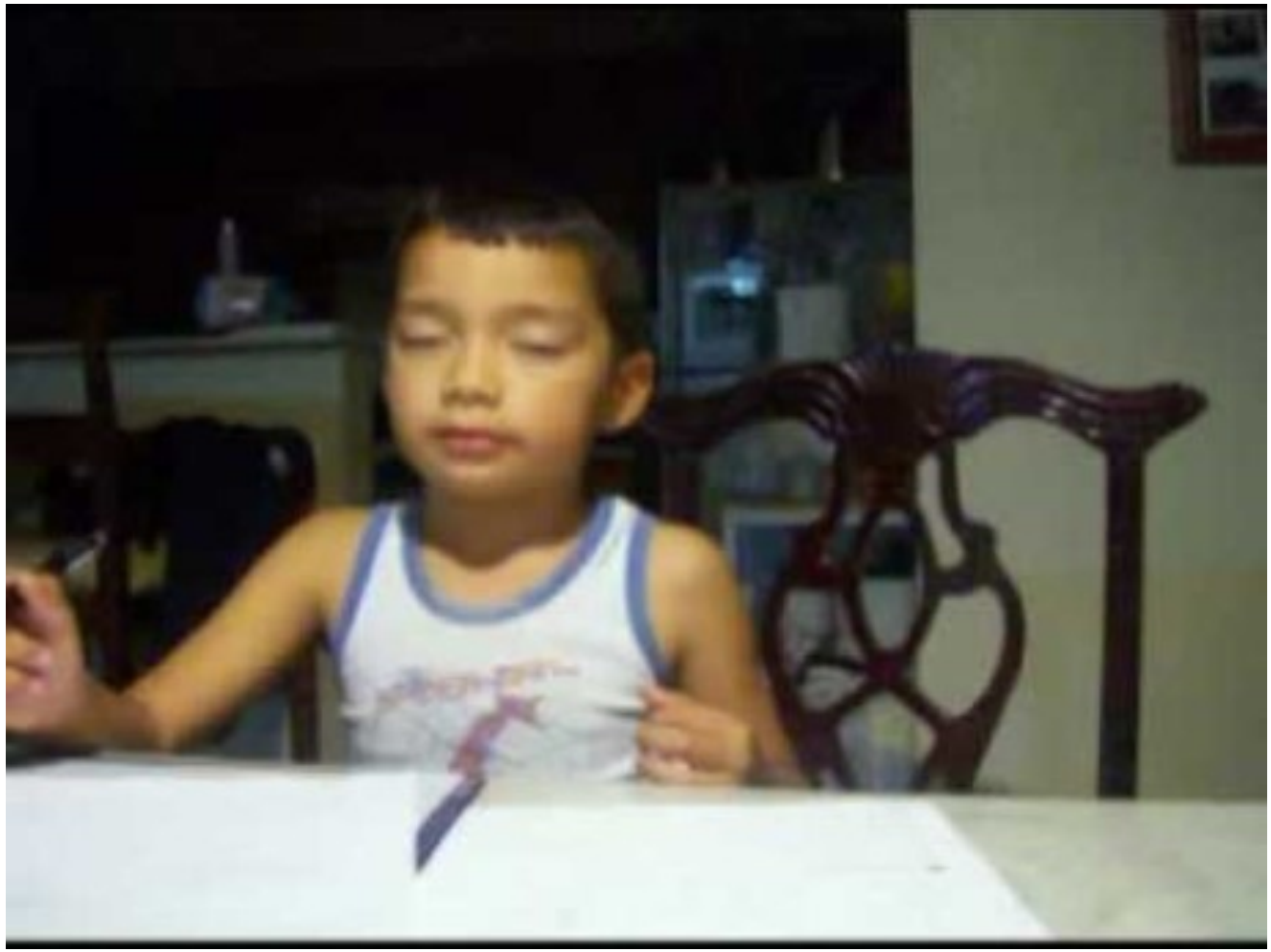


Absence seizures

- brief, sudden lapses of consciousness
- no confusion or recovery period
- duration: <30 sec
- no memory of the episode
- common in children between 4-14 years old

3Hz Spike-wave discharges in absence seizures

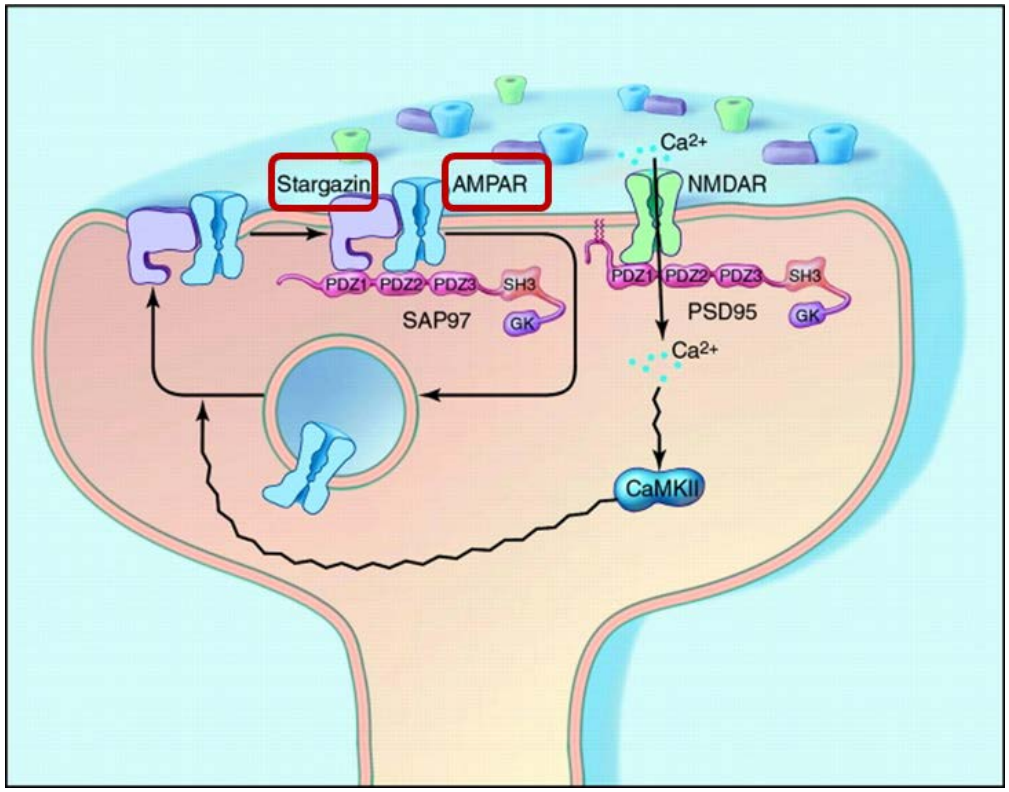
EEG

Stargazer mouse: A model for absence epilepsy

Dysfunctional stargazin

Mistrafficking of AMPA receptors

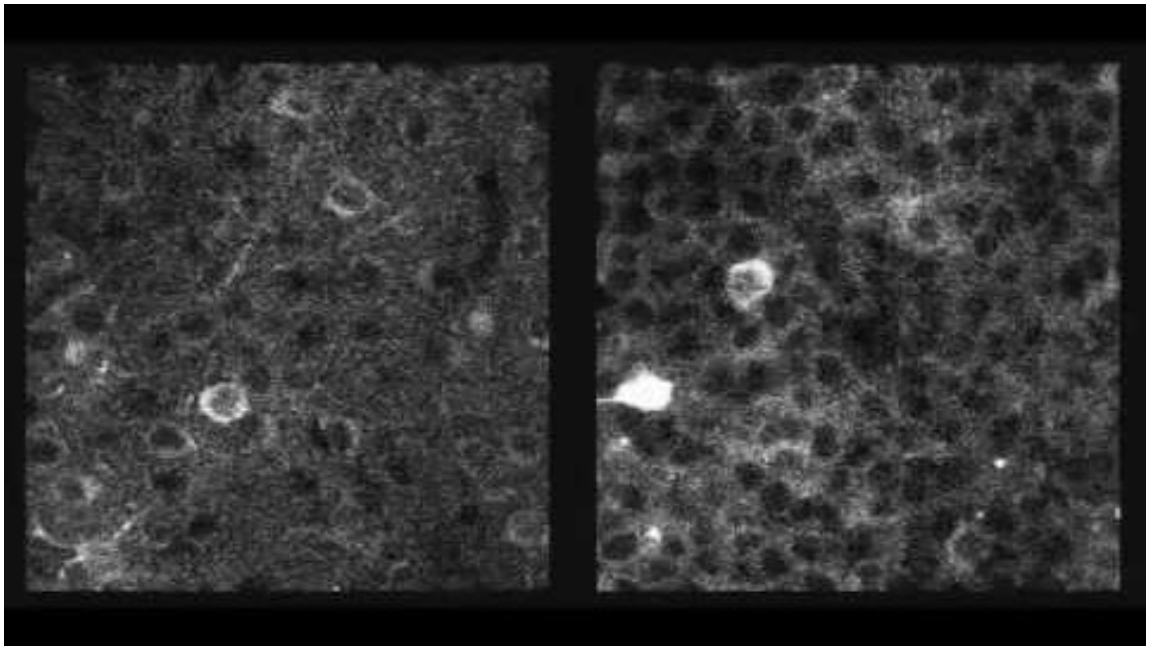
Seizures



What about the brain cells ?

In vivo imaging of calcium activity

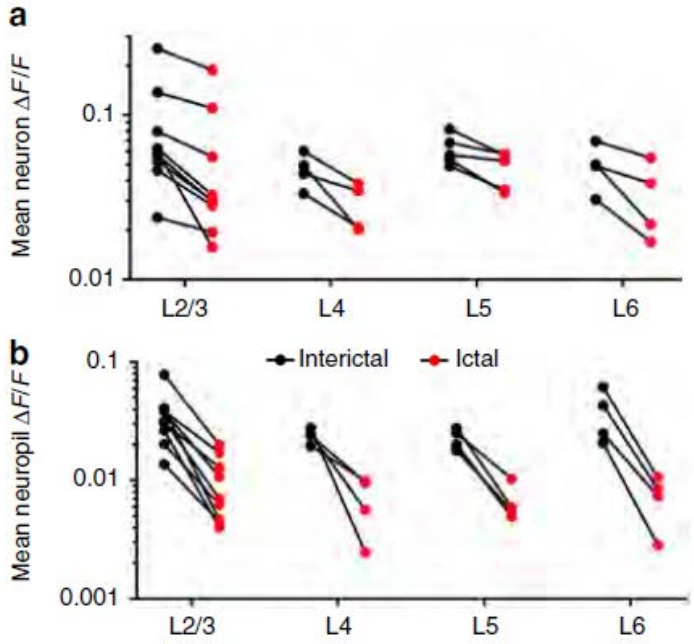
Calcium indicator GcaMP6 with in vivo 2- photon cellular microscopy



Experimental approach

- Functional activity within GCaMP6-labeled neurons and neuropils were visualised

Visual cortex is suppressed during absence seizures

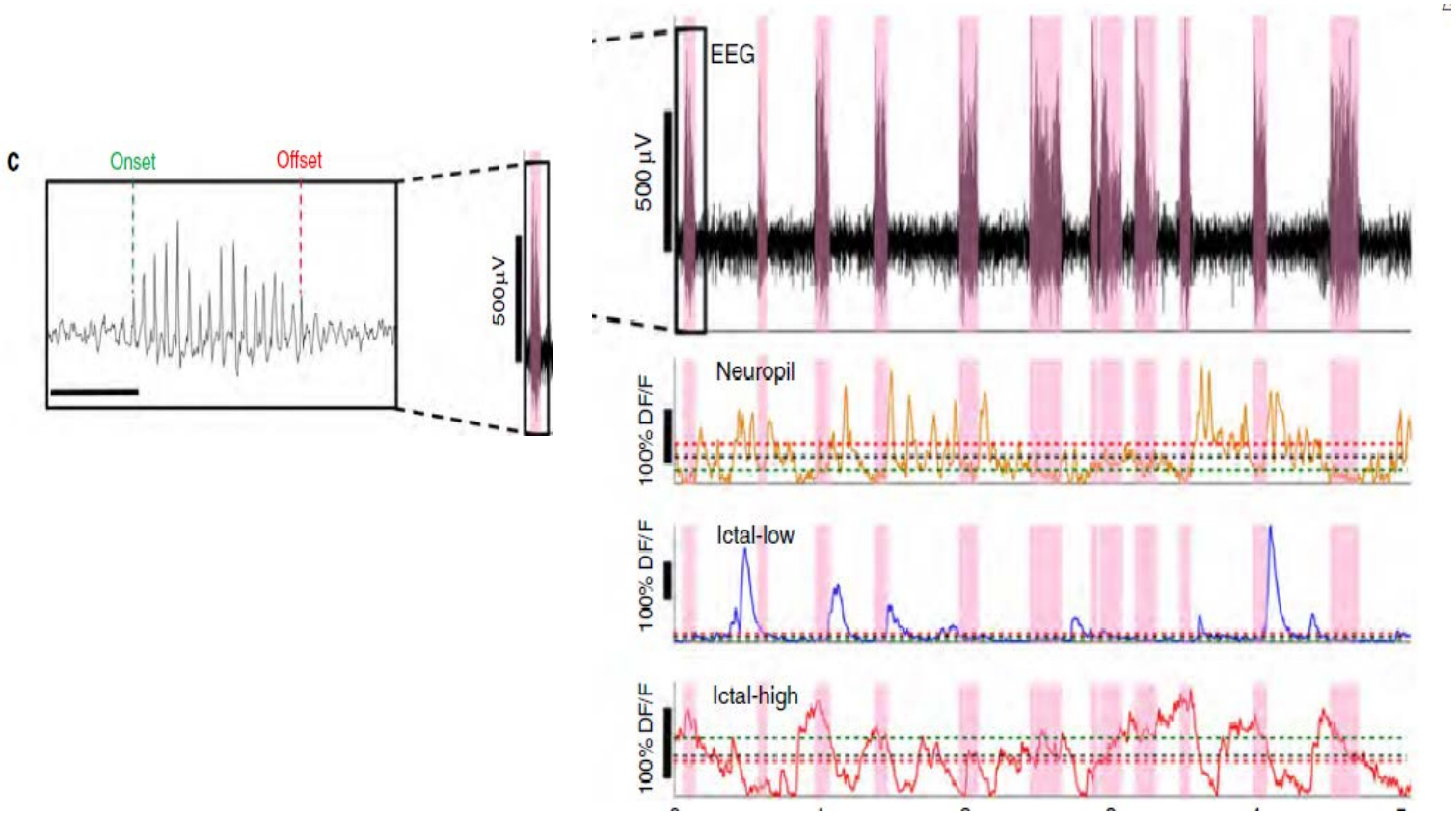


Experimental approach

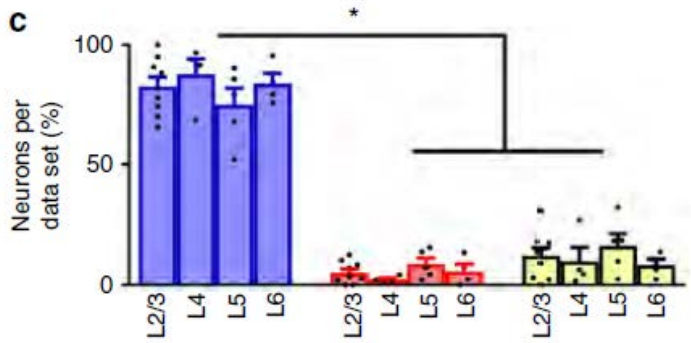
- Ca activity of individual neurons was aligned to EEG seizure onset or offset
- Ca activity were compared between ictal and interictal states

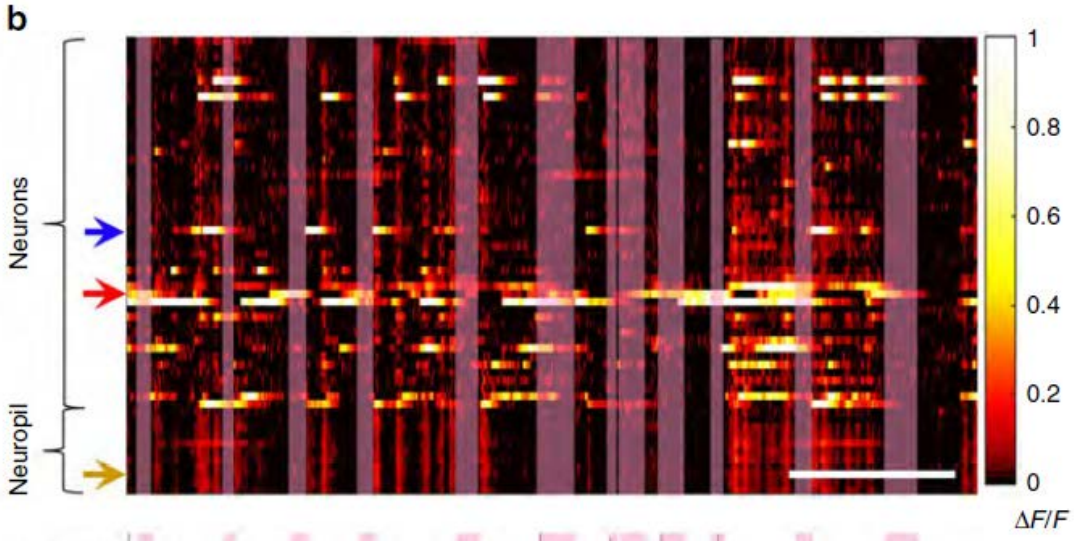
Patterns emerged

- Ictal low neurons
- Ictal high neurons
- Neutral

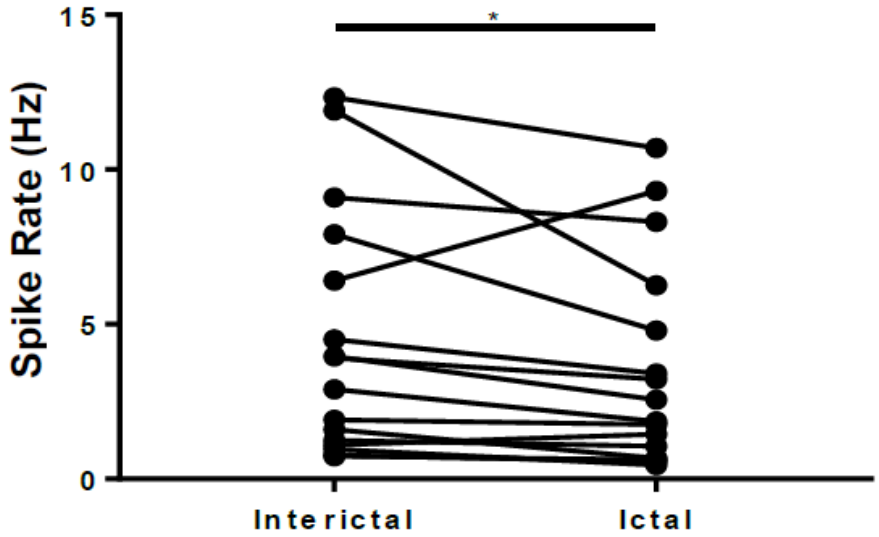

C
Onset
Offset
500µV
EEG
500 µV
Neuropil
100% DF/F
Ictal-low
100% DF/F
Ictal-high
100% DF/F

Visual cortex is suppressed during absence seizures




b
Neurons
Neuropil
1
0.8
0.6
0.4
0.2
0
ΔF/F

Visual cortex is suppressed during absence seizures

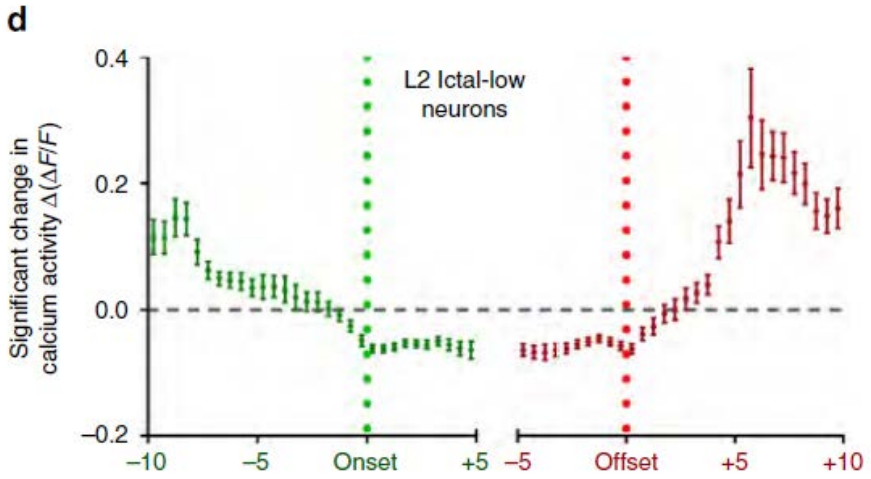


Activity and Time of seizure

Compared Ca activity in half-second windows to a Ca activity baseline

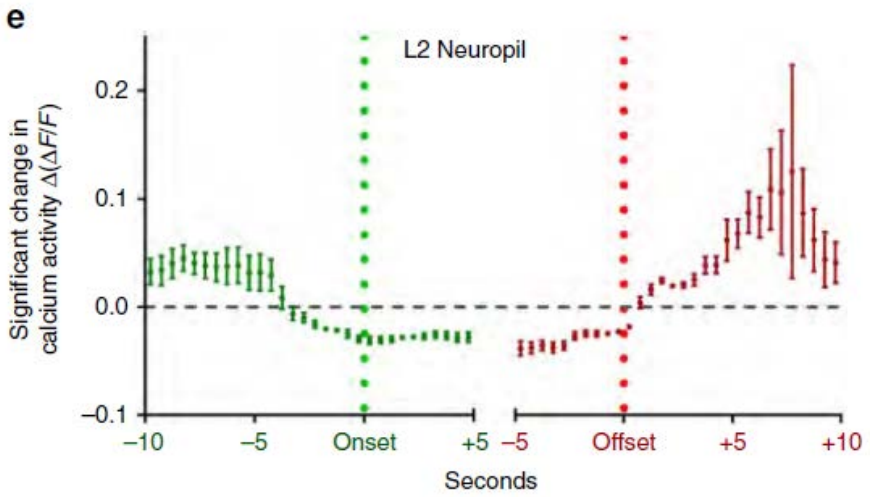
- Starting 10 sec before and up to 5 sec after seizure onset -> 33,1% neurons changed activity
- Starting 5 sec prior to until 10 sec after seizure offset -> 41,1% neurons changed activity

Hypoactivity starts several seconds before seizure onset



L4, L5, L6 showed similar reductions

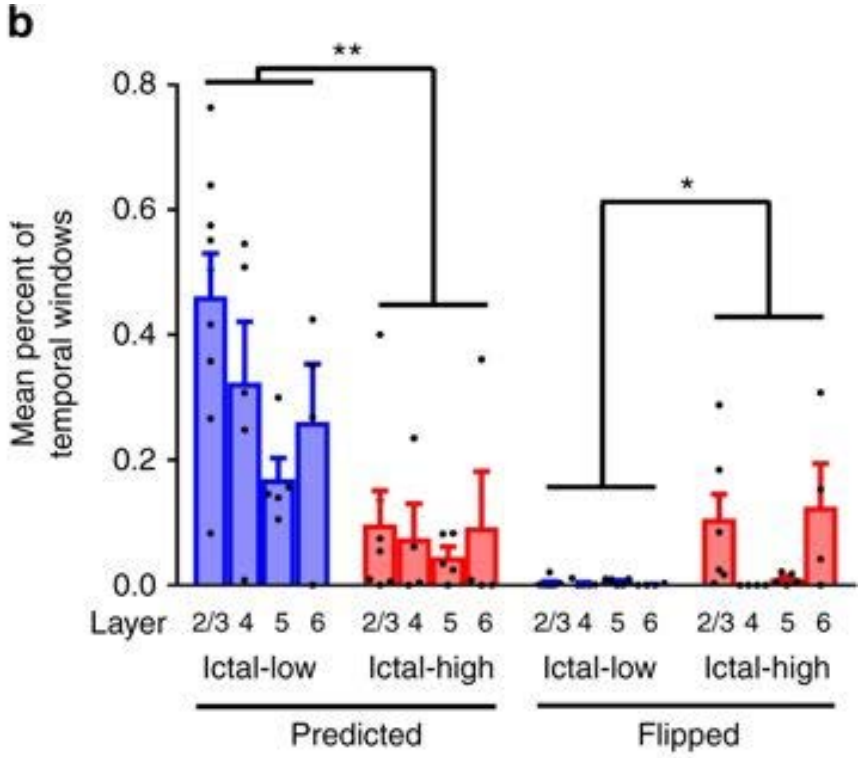
Hypoactivity starts several seconds before seizure onset



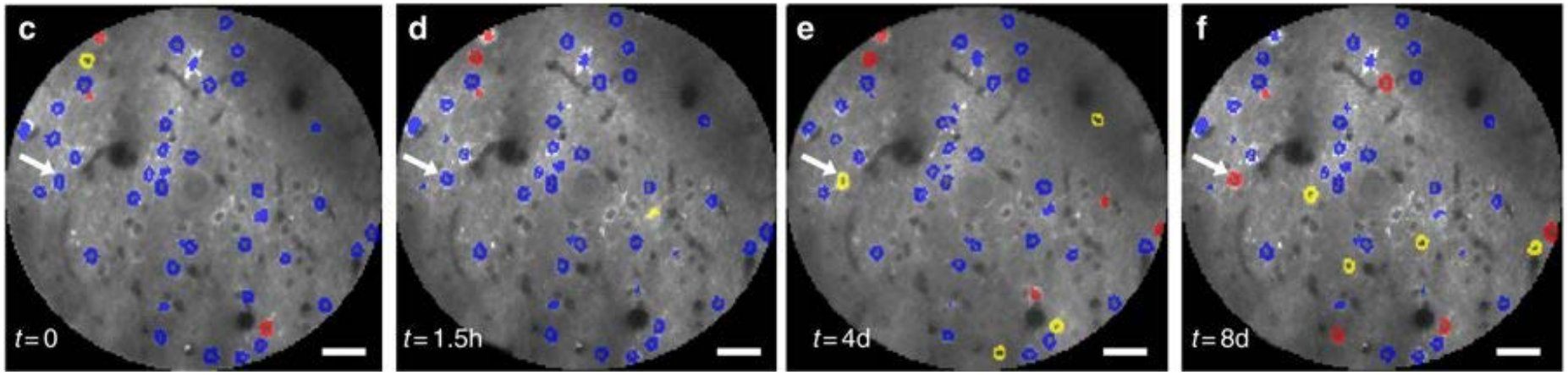
Activity and Time of seizures

- Ictal high neurons: 21,7% changed activity
- Neutral neurons: 31,6% changed activity

Can an ictal high neuron become ictal low and vice versa?

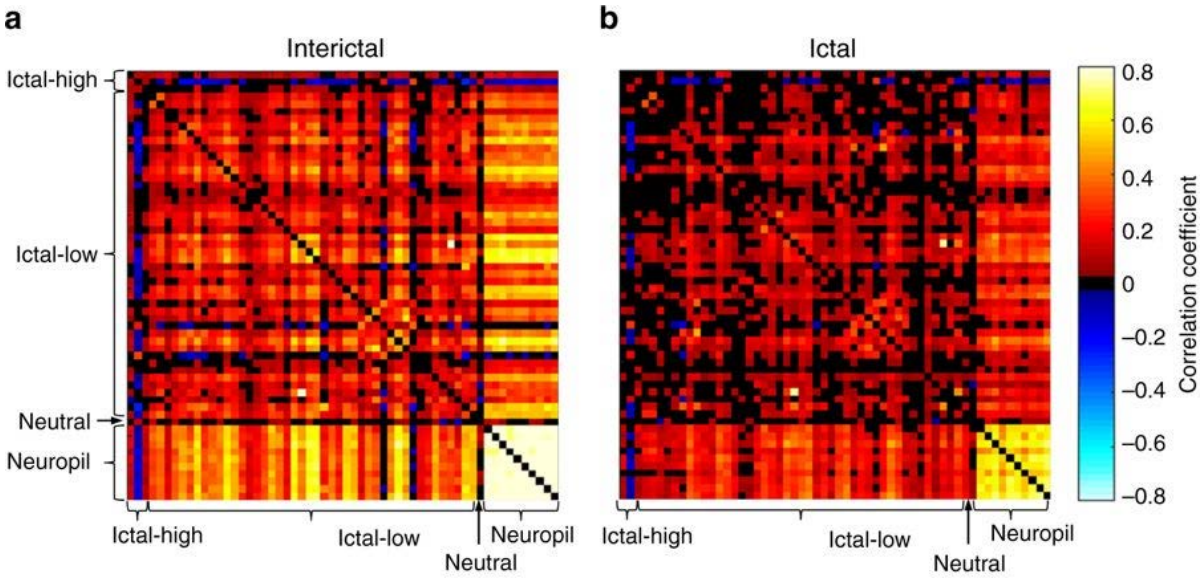


What about long term changes?



Blue = Ictal-low ,red = Ictal-high, yellow = neutral, uncolored = quiet

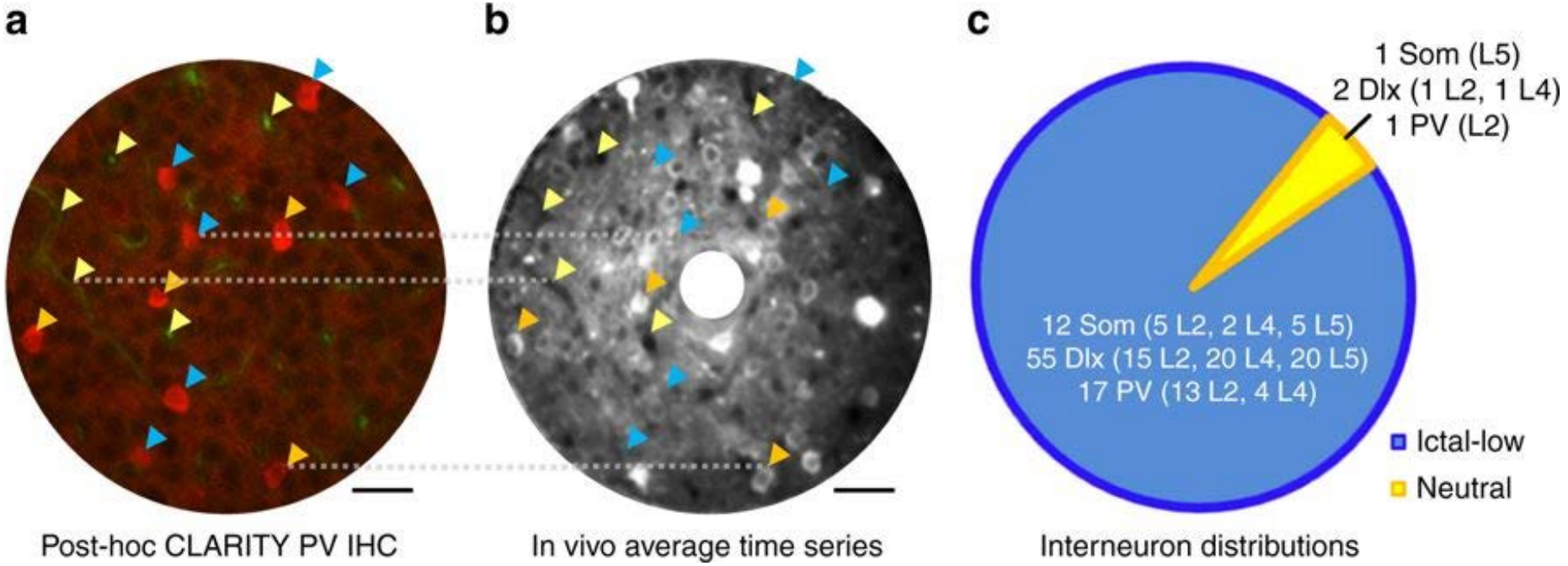
Are neurons synchronized?



red = correlated

black = not correlated

Are inhibitory inter-neurons the ictal high ones?



Conclusions

- Most of the neurons present with low activity during seizures
- Hypoactivity starts several seconds before seizure onset
- Activity is not synchronized among neurons
- Neurons change their state between ictal high and low-instability
- PV and ST inhibitory interneurons have also low activity

Future Directions?