Neuronal Activity Dynamics Underlying Epileptogenesis in a Genetic Mouse Model of Lafora Disease

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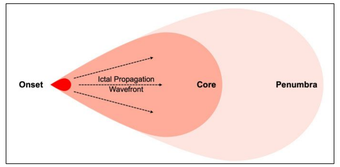
Introduction

- Lafora disease (LD) is a rare, lethal neurodegenerative disorder characterized by epileptic seizures, myoclonus, ataxia, and cognitive decline
- It is an autosomal recessive genetic disorder caused by the loss-of-function mutations in either *EPM2A* or *EPM2B* genes, encoding for laforin and malin, respectively
- Mechanisms of epileptogenesis in LD are not completely understood
- Here, we investigate the neuronal activity dynamics underlying epileptogenesis in laforin knockout mouse model of epilepsy using indigenously-designed polyimide-based flexible microelectrodes

Seizure-onset zone localization

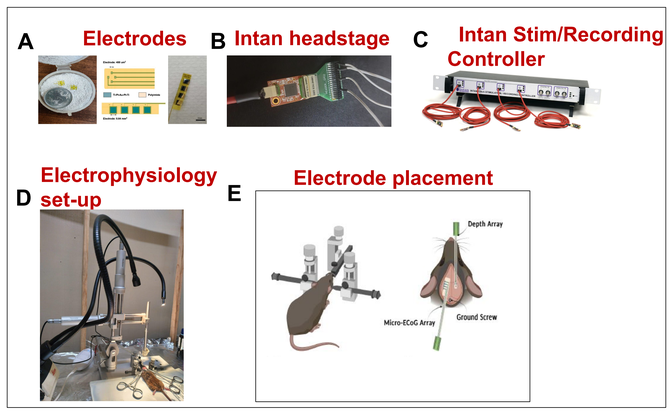


Methods

***In vivo* electrophysiology:**

- **Stereotaxic surgery for electrode implantation in mouse brain**
- **Video-EEG**
- **Surface ECoG**
- **Single unit recording using depth tetrodes**

Fig. 1: *In vivo* electrophysiology setup



Results

Fig. 2: PTZ-induced epileptiform activity in LD mice brain

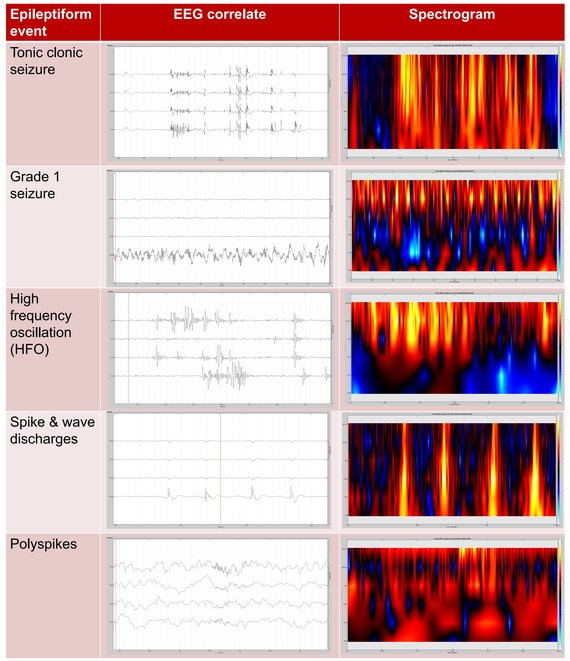


Fig. 3: EEG recording to characterize spontaneous epileptiform activity in LD mice brain

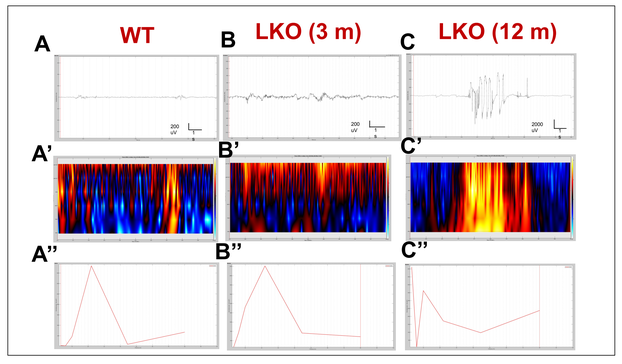
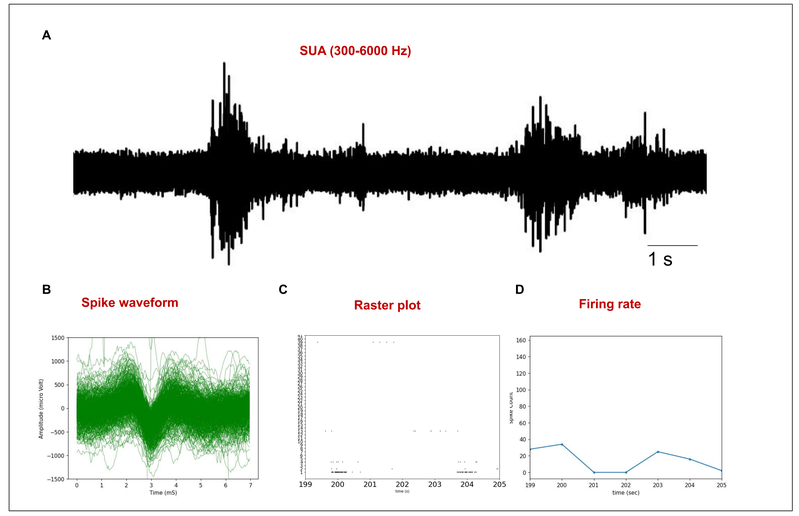


Fig. 4: Single unit neuronal recording using depth tetrodes in LD mice brain



A shows the single unit neuronal data (BP filter : 300-6000 Hz) recorded using depth tetrode implanted in temporal cortex of LD mouse brain, B shows the representative neuronal spike waveform obtained following spike sorting, C shows the raster plot for the spiking activity of the depth probe array, and D shows the neuronal firing rate across time. Note the heterogeneity in neuronal firing pattern during a given time epoch

Conclusions

- Proof-of-concept study to validate the efficacy of indigenously-designed microelectrodes
- Age-dependent progression of spontaneous epileptiform activity in LD mice brain
- Heterogeneity in neuronal spike firing rate at preictal, ictal and postictal phases
- Future studies involving chronic recording using 32-channel depth electrodes will give more insights into the seizure-onset zone in LD mice

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