



Bonn Lecture Series in Neuroscience



Mapping local seizure progression at cellular resolution in vivo

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Understanding the fine-scale neural activity that underlies epilepsy is key to identify potential breaking points of this frequently intractable disease. Yet, the detailed in vivo dynamics of seizure progression in cortical microcircuits remain largely unknown. We combine fast twophoton calcium imaging (30-Hz) with field potential recordings to map the spread of locally induced (4-AP or picrotoxin) seizures in anesthetized and awake mice with unprecedented spatiotemporal precision. Using single-layer and microprism-assisted multi-layer imaging in two different cortical areas we uncover reliable recruitment of local neural populations within and across cortical layers, and find layer-specific temporal delays, suggesting an initial supra-granular invasion followed by deep-layer recruitment during lateral seizure spread. Intriguingly, despite consistent progression pathways, successive seizures show pronounced temporal variability that critically depends on GABAergic inhibition. We propose an epilepsy circuit model resembling an elastic meshwork wherein ictal progression faithfully follows preexistent pathways but varies flexibly in time, depending on the local inhibitory restraint.