Supporting Information

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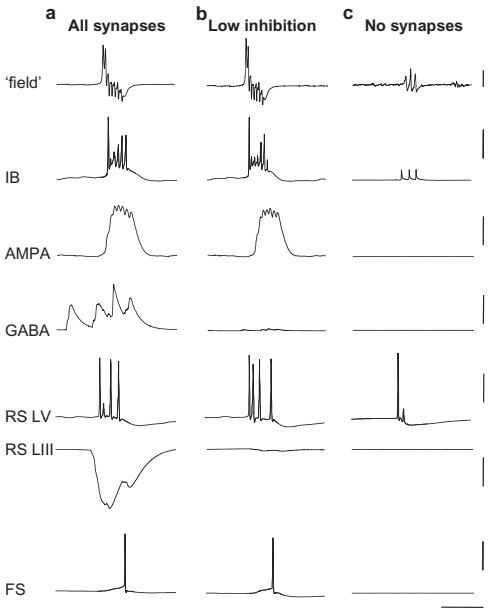

Fig. S1. Axo-axonic gap junctions between pyramidal neurons drive interictal discharges in a computational cortical column model. In each case illustrated the interictal discharge was generated by a transient, 50 ms increase in gap junction conductance between IB cell axons from 0 nS to 8 nS. (*A*) Example interictal events from the cortical column model with both excitatory and inhibitory synapses intact. The period of field potential VFO corresponds to high levels of action potential generation in layer 5 principal cells (IB, RS LV). In contrast, fast spiking, perisomatic targeting interneurons (FS) fired only a single action potential during each interictal discharge, and superficial layer pyramid responses were dominated by strong inhibition (RS LIII). The conductance changes caused by AMPA and $GABA_A$ receptor-mediated synaptic activity in IB cells are plotted for comparison between each of the three conditions. (*B*) Almost identical interictal field discharges are generated in the cortical column model when network inhibition is reduced to 5% of values used in (*A*). Note the near absence of inhibition to both IB cells (GABA) and superficial pyramids (RS LIII), but similar patterns of discharge for the gap-junctionally and chemical-synaptically connected neurons (IB, RS LV) and consequently similar pattern of synaptic activation of interneurons (FS). (*C*) Complete removal of chemical synaptic transmission alters the size and shape of the interictal discharge, but VFO remains, cf Fig. 3*A* showing a very poor correlation between synaptic excitation, inhibition, and VFO power. As the strength of deep layer recurrent synaptic excitation is reduced, the intensity of bursting diminishes, and more spikelets than spikes appear, as in Fig. 5*B*. [Scale bars, "field," arbitrary; IB, RS LV, FS, 40 mV; RS LIII, 2 mV; AMPA, 70 nS; GABA, 20 nS, 50 ms.]

Table S1. Summary of clinical data

Patient no.	Age/gender	Seizure semiology	MRI/pathology	Drugs	Surgical outcome
1	44/M	Complex partial	Mesial temporal sclerosis (CA1 sclerosis)	PreGAB/OX	Seizure-free*
2	20/M	Complex partial	Mesial temporal sclerosis (loss of CA1 neurons)	CBZ	Reduction in seizure frequency
3	25/F	Complex partial with secondary generalization	Oligodendroglioma	LEV	Reduction in seizure frequency
4	36/M	Partial with secondary generalization	Dysembryoplastic neuroepithelial tumor	CBZ	No change
5	11/M	Complex partial with secondary generalization	Hippocampal sclerosis (CA1 sclerosis)	LEV/LAM	Seizure-free
6	54/M	Complex partial with secondary generalization	Mild nonspecific reactive changes	CBZ	Reduction in seizure frequency
7	28/F	Complex partial	Mesial temporal sclerosis (CA1 sclerosis)	GABA/CBZ/LEV	Seizure-free
8	21/F	Complex partial	Astrocytoma	CBZ/VAL	Seizure-free
9	37/F	Complex partial	Mesial temporal sclerosis (CA1 sclerosis)	ZOM/LEV/CLB	Seizure-free
10	40/F	Complex partial with secondary generalization	Hippocampal sclerosis (loss of CA1 neurons)	ZOM/PHE	Reduction in seizure frequency
11	17/M	Partial motor/complex partial seizures	Hippocampal sclerosis (CA1 sclerosis)	LEV/VAL	Seizure-free

Verified pathology is shown in parentheses. Drug abbreviations: CBZ, Carbamazepine; CLB, Clobazam; GABA, Gabapentin; LAM, Lamotrigine; LEV, Levetiracetam; Ox, Oxcarbamazepine; PHE, Phenytoin; PreGAB, Pregabalin; VAL, Valproate; ZOM, Zonisamide.
*Surgical outcome after 1 month.