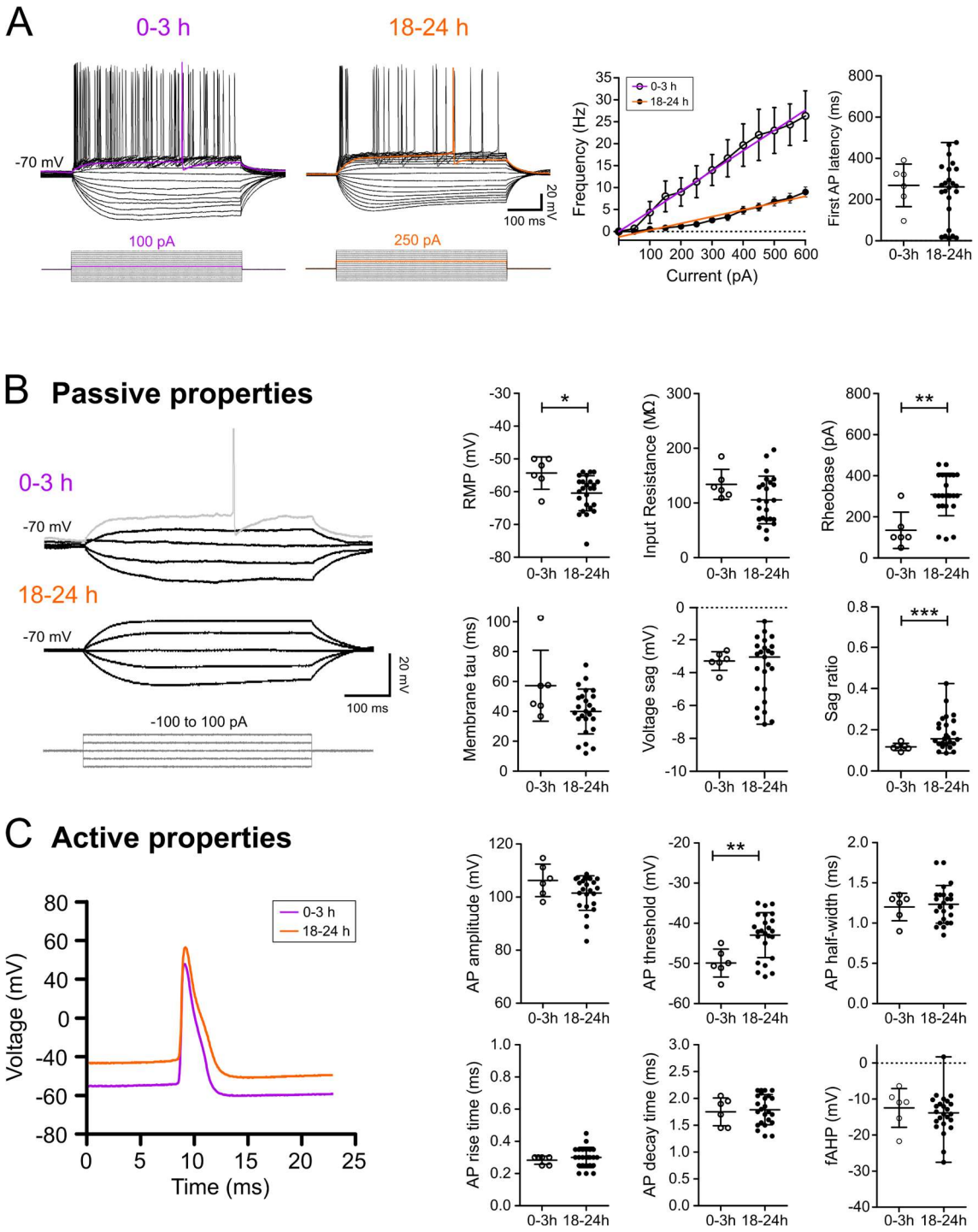
Supplementary information

Supplementary table 1: patients' information.

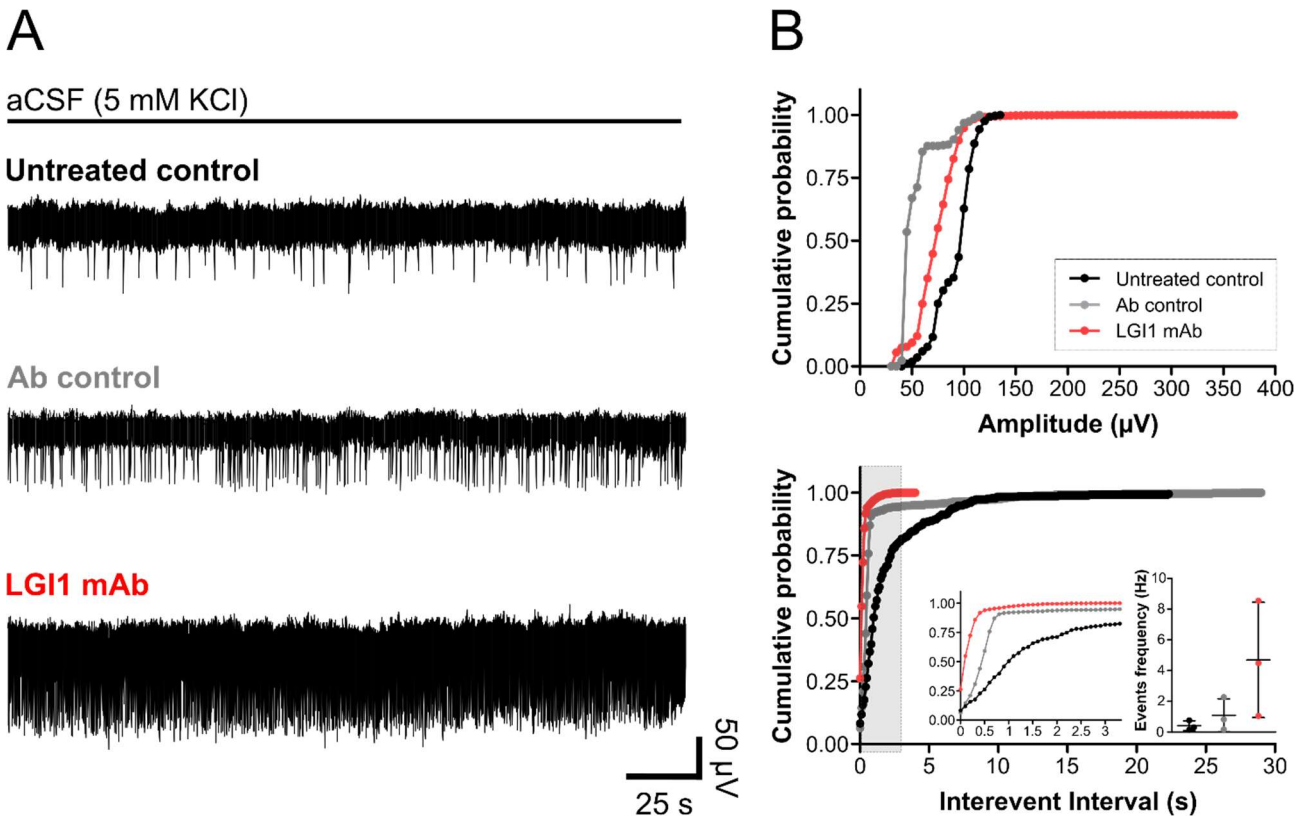
Sample ID	Diagnosis	Age	Biological sex	Medication 1 (mg)	Medication 2 (mg)	Medication 3 (mg)
#1	Temporal lobe epilepsy	27	Male	Lacosamide (400)	-	-
#2	Temporal lobe epilepsy	52	Male	Lamotrigine (300)	-	-
#3	Temporal lobe epilepsy	33	Male	Lamotrigine (800)	Brivaracetam (200)	-
#4	Temporal lobe epilepsy	52	Male	Levetiracetam (3000)	Primidone (750)	Carbamazepine (1200)
#5	Temporal lobe epilepsy	60	Male	Oxcarbazepine (1200)	Levetiracetam (3000)	-
#6	Temporal lobe epilepsy	22	Male	Oxcarbazepine (1500)	Valproic acid (1050)	Brivaracetam (225)
#7	Temporal lobe epilepsy	42	Female	Levetiracetam (2000)	Clobazam (3)	-
#8	Temporal lobe epilepsy	51	Female	Brivaracetam (200)	Lamotrigine (150)	Valproic acid (1500)
#9	Temporal lobe epilepsy	57	Male	Gabapentin (900)	Lamotrigine (600)	-
#10	Temporal lobe epilepsy	26	Male	Lacosamide (600)	Levetiracetam (1500)	-
#11	Temporal lobe epilepsy	13	Male	Lacosamide (250)	Brivaracetam (75)	Midazolam (if necessary)
#12	Temporal lobe epilepsy	22	Male	Lacosamide (250)	Oxcarbazepine (1575)	-
#13	Temporal lobe epilepsy	51	Female	-	-	-
#14	Temporal lobe epilepsy	40	Male	Lacosamide (100)	Brivaracetam (100)	

Supplementary Table 2: statistical results of firing frequency in the five different conditions. Two-way ANOVA interaction $F(4, 72) = 5.41$, p-value < 0.0001.

	Condition		Bonferroni *post hoc* test A vs B	
Injected current	**A**	**B**	**t-value**	**p-value**
200 pA	Control	Ab control	0.327	p>0.05
200 pA	Control	DTX-K	3.117	p>0.05
200 pA	Control	LGI1 mAb	1.418	p>0.05
200 pA	Control	LGI1 mAb + DTX-K	4.590	p<0.001
200 pA	Ab control	DTX-K	2.446	p>0.05
200 pA	Ab control	LGI1 mAb	0.908	p>0.05
200 pA	Ab control	LGI1 mAb + DTX-K	4.052	p<0.01
200 pA	DTX-K	LGI1 mAb	1.735	p>0.05
200 pA	DTX-K	LGI1 mAb + DTX-K	2.212	p>0.05
200 pA	LGI1 mAb	LGI1 mAb + DTX-K	3.568	p<0.01
300 pA	Control	Ab control	1.125	p>0.05
300 pA	Control	DTX-K	4.188	p<0.001
300 pA	Control	LGI1 mAb	3.312	p>0.05
300 pA	Control	LGI1 mAb + DTX-K	6.320	p<0.001
300 pA	Ab control	DTX-K	2.670	p>0.05
300 pA	Ab control	LGI1 mAb	1.774	p>0.05
300 pA	Ab control	LGI1 mAb + DTX-K	5.119	p<0.001
300 pA	DTX-K	LGI1 mAb	1.095	p>0.05
300 pA	DTX-K	LGI1 mAb + DTX-K	3.117	p>0.05
300 pA	LGI1 mAb	LGI1 mAb + DTX-K	4.038	p<0.01
400 pA	Control	Ab control	1.511	p>0.05
400 pA	Control	DTX-K	4.188	p<0.001
400 pA	Control	LGI1 mAb	4.964	p<0.001
400 pA	Control	LGI1 mAb + DTX-K	6.940	p<0.001
400 pA	Ab control	DTX-K	2.323	p>0.05
400 pA	Ab control	LGI1 mAb	2.825	p>0.05
400 pA	Ab control	LGI1 mAb + DTX-K	5.432	p<0.001
400 pA	DTX-K	LGI1 mAb	0.356	p>0.05
400 pA	DTX-K	LGI1 mAb + DTX-K	3.700	p<0.01
400 pA	LGI1 mAb	LGI1 mAb + DTX-K	3.579	p<0.01
500 pA	Control	Ab control	2.459	p>0.05
500 pA	Control	DTX-K	4.651	p<0.001
500 pA	Control	LGI1 mAb	6.440	p<0.001
500 pA	Control	LGI1 mAb + DTX-K	8.064	p<0.001
500 pA	Ab control	DTX-K	2.345	p>0.05
500 pA	Ab control	LGI1 mAb	3.685	p<0.01
500 pA	Ab control	LGI1 mAb + DTX-K	6.185	p<0.001
500 pA	DTX-K	LGI1 mAb	1.209	p>0.05
500 pA	DTX-K	LGI1 mAb + DTX-K	4.444	p<0.001
500 pA	LGI1 mAb	LGI1 mAb + DTX-K	3.725	p<0.01
600 pA	Control	Ab control	2.459	p>0.05
600 pA	Control	DTX-k	4.961	p<0.001
600 pA	Control	LGI1 mAb	7.829	p<0.001
600 pA	Control	LGI1 mAb + DTX-K	8.200	p<0.001
600 pA	Ab control	DTX-K	2.151	p>0.05
600 pA	Ab control	LGI1 mAb	4.384	p<0.001
600 pA	Ab control	LGI1 mAb + DTX-K	5.958	p<0.001
600 pA	DTX-K	LGI1 mAb	2.133	p>0.05
600 pA	DTX-K	LGI1 mAb + DTX-K	4.364	p<0.001
600 pA	LGI1 mAb	LGI1 mAb + DTX-K	2.963	p>0.05



Supplementary figure 1: **human CA3 pyramidal neurons show moderately decreased excitability after 18-24h slice incubation in control conditions compared to acute slices**. **A)** Left: representative traces of trains of action potentials, induced by increasing hyperpolarizing and depolarizing current injections (from -400 to 600 pA, 50 pA steps) obtained after 0-3h from recovery and 18-24h incubation, respectively. The first action potential (AP) evoked at the rheobase is highlighted in purple (0-3h) or red (18-24 h). In the middle, the plot shows the input-output linear relation between increasing depolarizing current injections and the neuronal firing frequency after 0-3h from recovery (empty points and purple line) and 18-24h incubation (black points and orange line) in control conditions (Data shown as mean ± SEM). On the right, a scatter plot showing the first AP latency after 0-3h and 18-24h. Data are shown as mean ± SD, 0-3h n = 6 from 2 patients; 18-24h n = 24 from 9 patients. Cells recorded acutely were more excitable than after 18-24 h (0-3h: r2 = 0.9896, 18-24h: r2 = 0.9494; ANCOVA F(1, 22) = 294.6, p-value < 0.0001). **B)** Left: the experimental steps used to determine the passive properties. Right: scatter plots comparing the main passive properties of neurons recorded after 0-3h (empty points) and 18-24h (black points). **C)** Left: representative action potentials recorded at the rheobase, which was employed to quantify the active properties. Right: scatter plots comparing the active properties of neurons recorded after 0-3h (empty points) and 18-24h (black points). **B)-C)** Each point indicates an individual cell and data are shown as mean ± SD (0-3h n = 6 from 2 patients, 18-24h n = 24 from 9 patients). Statistical comparison between the two groups was performed with unpaired t-test with Welch's correction. * p<0.05; **p<0.01; ***p<0.001.



Supplementary figure 2: **LGI1 mAb increased spontaneous network activity after 24 hours of incubation**. **A)** Example traces of spontaneous network activity recorded in aCSF 5 mM KCl after 24 h of incubation in untreated controls (upper), Ab control (middle), and LGI1 mAb (bottom). **B)** Cumulative distribution plots showing spike amplitude (upper) and inter-spike interval (lower), inset: on the left, grey-highlighted area of the cumulative plot is displayed at higher magnification; on the right, scatter plot depicting the spike frequency. Untreated control condition (black), Ab control (grey) and LGI1 mAb (red). Each dot of the cumulative distributions represents a bin, while the dots in the scatter plot of spike frequency represent 5 min recording from each patient's slices incubated in the three different color-coded conditions.