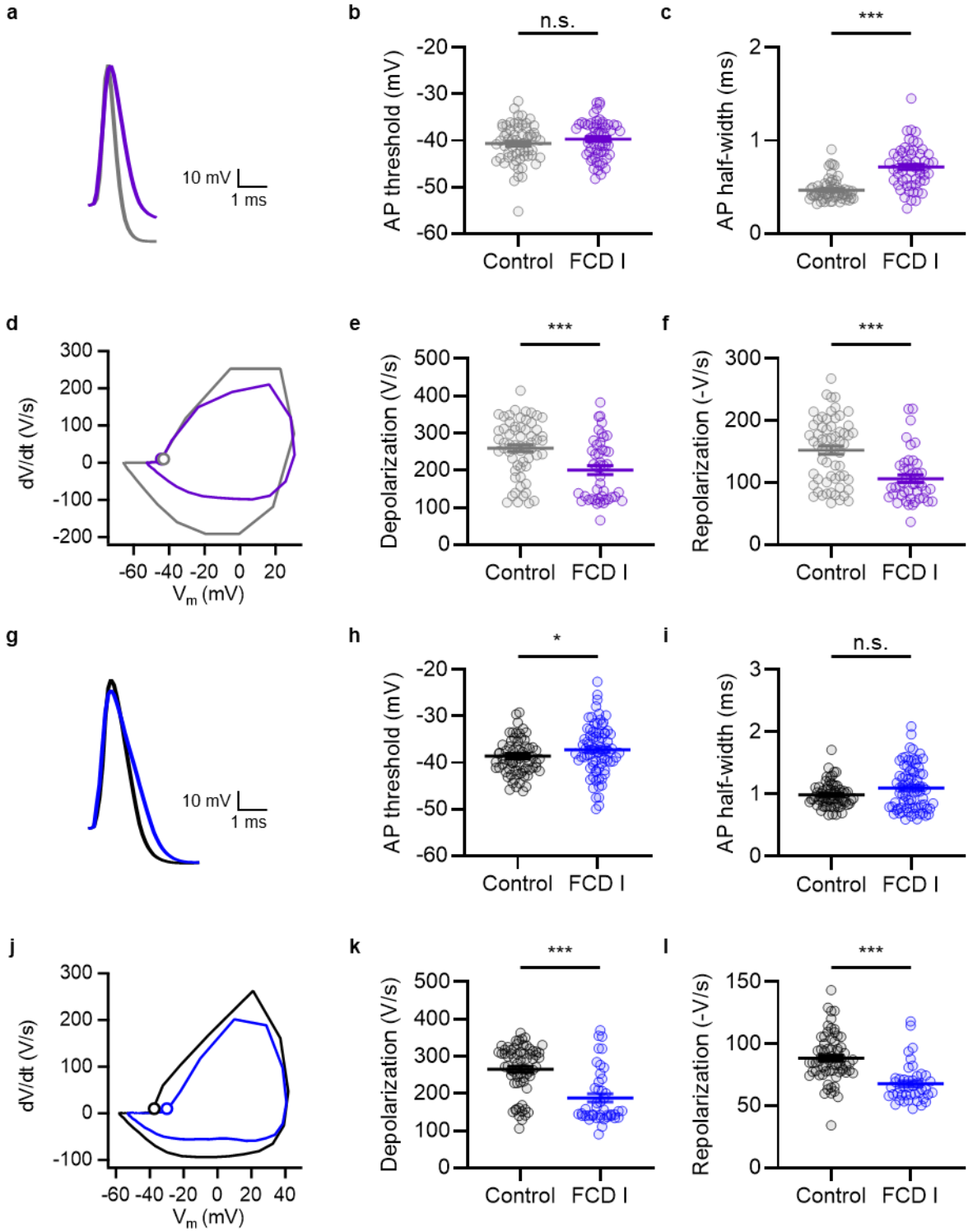
Net synaptic drive of fast-spiking interneurons is inverted towards inhibition in human FCD I epilepsy

Supplementary Information
(Supplementary Table 1 & Supplementary Figures S1-S9)

Patient	Age	Sex	Diagnosis	pHFO	Brain region	Recorded cells	
SN-P03	29	F	FCD I	+	Temporal cortex	PN 12	FSIN 2
SN-P05	49	M	FCD III	+	Temporal cortex	PN 5	FSIN 1
SN-P06	36	M	FCD III	+	Temporal cortex	PN 9	FSIN 2
SN-P07	44	M	FCD III	+	Temporal cortex	PN 7	FSIN 7
SN-P08	31	F	FCD I	+	Temporal cortex	PN 11	FSIN 1
SN-P09	48	M	FCD III	+	Frontal cortex	PN 6	FSIN 4
SN-P10	27	M	FCD I	+	Temporal cortex	PN 4	FSIN 5
SN-P11	20	M	FCD I	+	Temporal cortex	PN 10	FSIN 5
SN-P12	20	F	FCD III	+	Temporal cortex	PN 5	FSIN 4
SN-P13	39	M	FCD III	+	Temporal cortex	PN 4	FSIN 7
SN-P16	18	F	FCD I	-	Temporal cortex	PN 3	FSIN 12
SN-P19	23	M	FCD I	+	Temporal cortex	PN 1	FSIN 8
SN-P29	39	F	FCD I	+	Occipital cortex	PN 6	FSIN 2
SN-P30	38	M	FCD III	-	Temporal cortex	PN 1	FSIN 5
SN-P31	30	F	FCD III	+	Temporal cortex	PN 1	FSIN 4
SN-P15	19	F	Tumor	N/A	Frontal cortex	PN 5	FSIN 13
SN-P18	47	F	Tumor	N/A	Parietal cortex	PN 9	FSIN 6
SN-P20	50	F	Tumor	N/A	Frontal cortex	PN 0	FSIN 1
SN-P21	76	M	Tumor	N/A	Frontal cortex	PN 5	FSIN 1
SN-P22	45	F	Tumor	N/A	Frontal cortex	PN 9	FSIN 6
SN-P23	35	M	Tumor	N/A	Frontal cortex	PN 3	FSIN 9
SN-P24	23	M	Tumor	N/A	Frontal cortex	PN 16	FSIN 9
SN-P25	33	F	Tumor	N/A	Parietal cortex	PN 4	FSIN 5
SN-P27	44	M	Tumor	N/A	Frontal cortex	PN 7	FSIN 8
SN-P28	52	M	Tumor	N/A	Frontal cortex	PN 10	FSIN 3

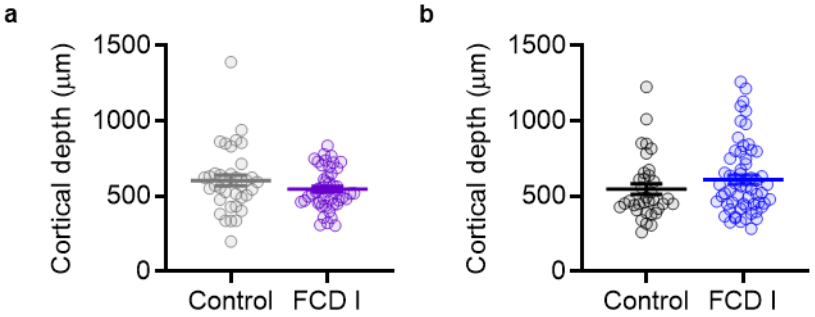
Supplementary Table 1. Demographic information of patients included in the present study. Patients diagnosed with FCD I or FCD III (FCD I associated with heterogeneous lesions) were included in the FCD I epilepsy group. Patients diagnosed with tumor without seizure history were included in the control group.

Supplementary Fig. S1



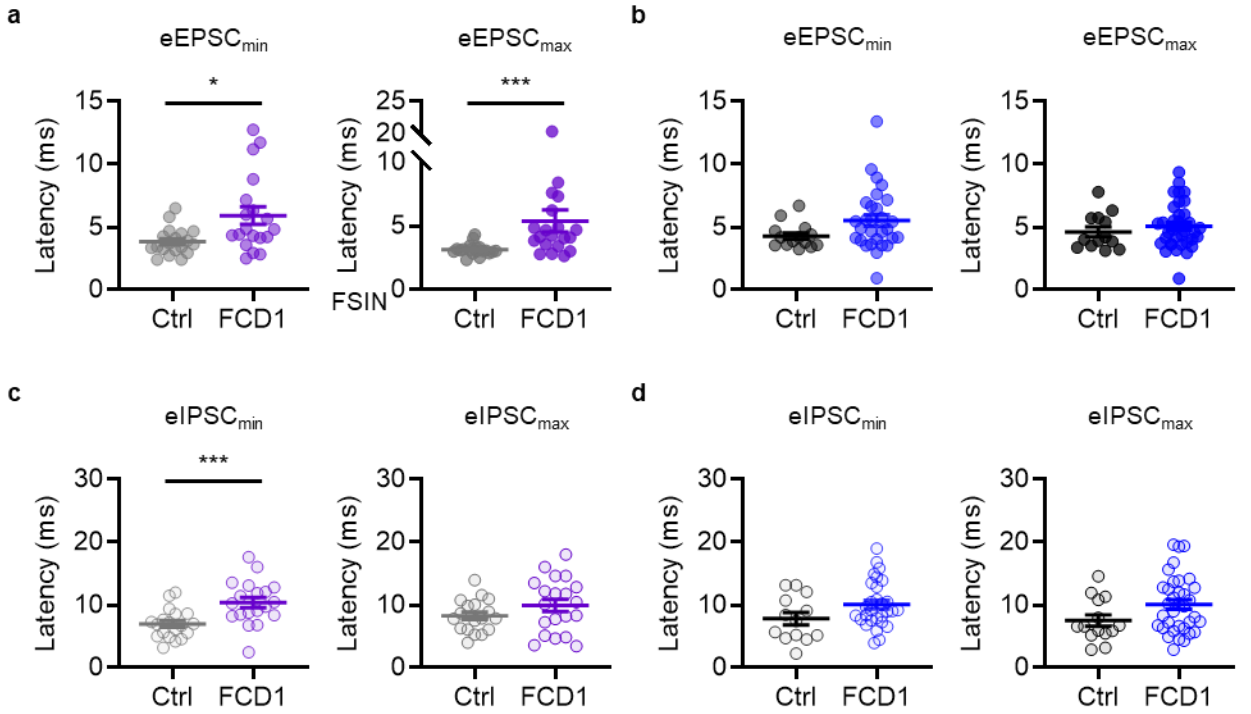
Supplementary Fig. S1 (related to Fig. 1)**.** Single AP kinetics of L2/3 neurons. (**a**) Representative traces of AP from an FSIN in the control (gray) and FCD I (purple) group. (**b**) AP threshold. (**c**) AP half-width. (**d**) Representative examples of dV/dt plotted against V_m, taken from the same spikes shown in panel **a**. (**e**) Maximum rate of depolarization. (**f**) Maximum rate of repolarization. (**g-l**) Same as in panels **a-f**, but from PNs in the control (black) and FCD I (blue) group.

Supplementary Fig. S2



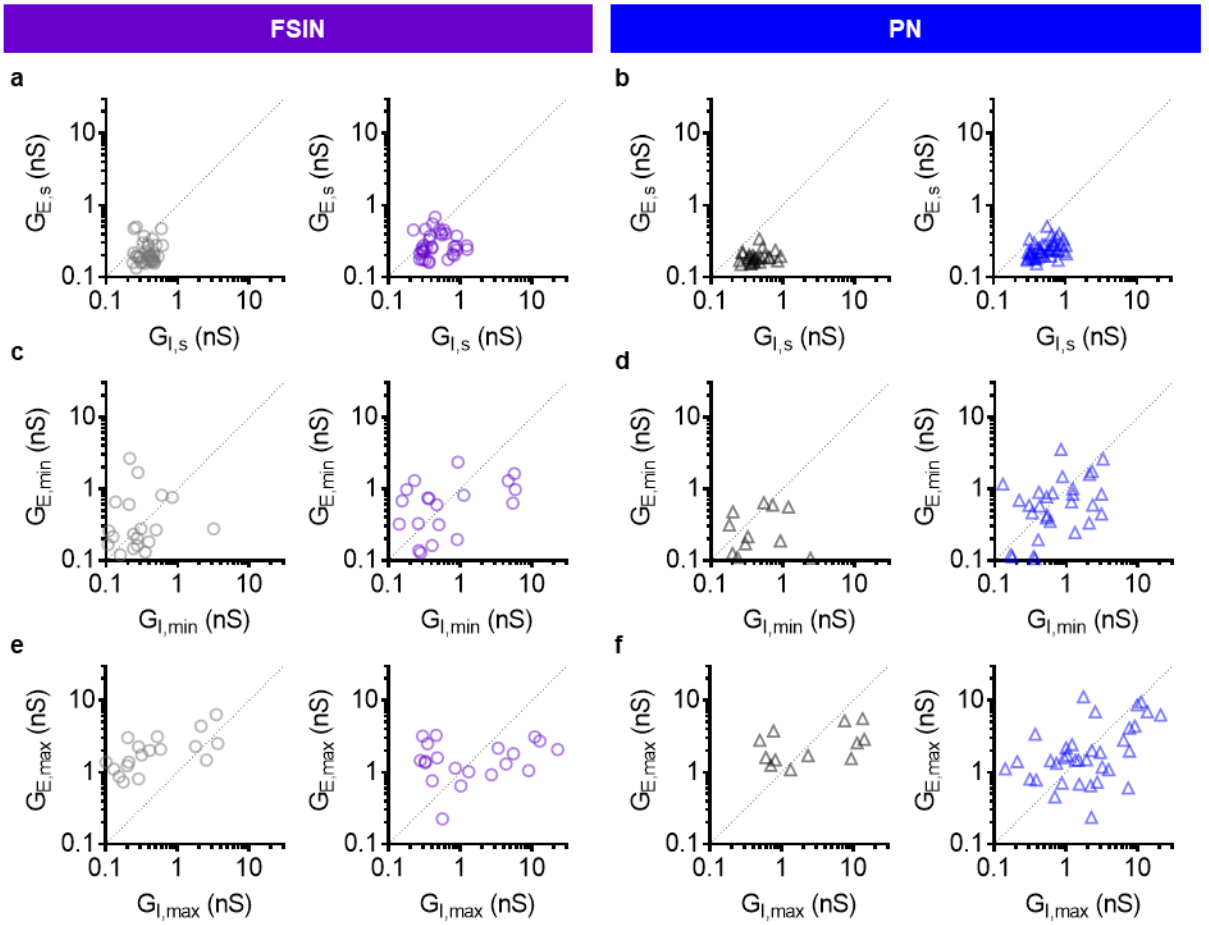
Supplementary Fig. S2 (related to Fig. 1)**.** Cortical depths of L2/3 neurons included in the present study, measured as the distance between the pia and the soma. **(a)** FSIN. **(b)** PN.

Supplementary Fig. S3



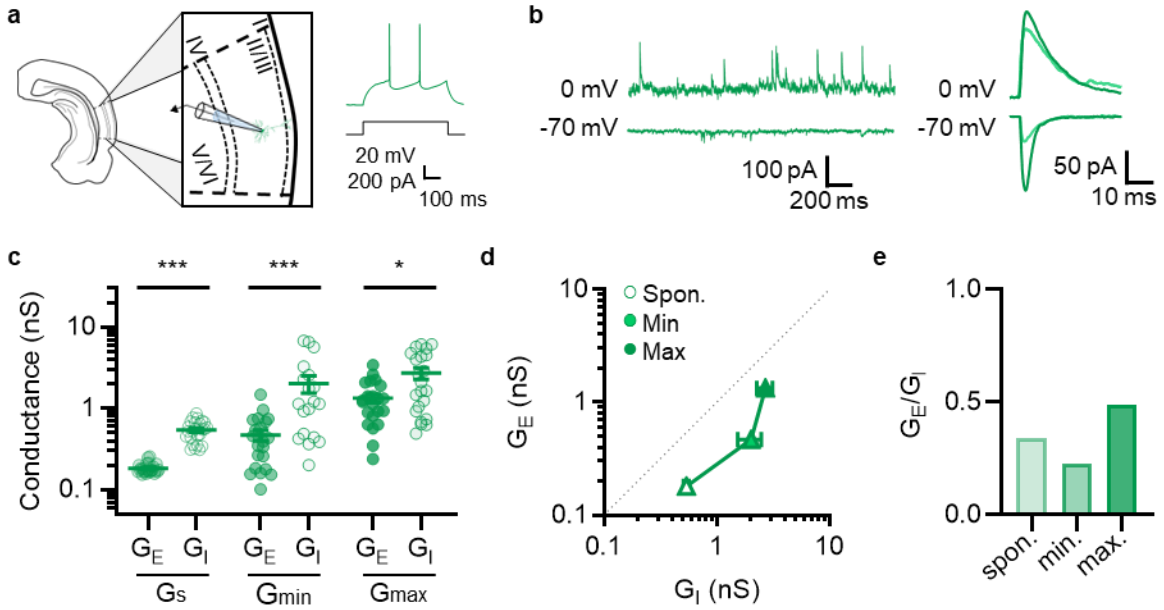
Supplementary Fig. S3 (related to Fig. 3, 4)**.** Latency of postsynaptic responses at FSINs and PNs evoked by local electric stimulation in L2/3. Latencies of minimally or maximally evoked PSCs were not significantly different from each other regardless of the postsynaptic cell type or association with FCD I epilepsy, although synaptic latencies at postsynaptic FSINs tended to be slower in FCD I epilepsy compared to control. **(a)** EPSC at FSINs. **(b)** EPSC at PNs. **(c)** IPSC at FSINs. **(d)** IPSC at PNs.

Supplementary Fig. S4



Supplementary Fig. S4 (related to Fig. 3, 4)**.** Distribution of individual G_E and G_I values represented in the G_E *vs.* G_I plots in Fig. 3F, 4F. (**a**) $G_{E,s}$ and $G_{I,s}$ at FSINs (gray, control; purple, FCD I). (**b**) $G_{E,s}$ and $G_{I,s}$ at PNs (black, control; blue, FCD I). (**c**) $G_{E,min}$ and $G_{I,min}$ at FSINs. (**d**) $G_{E,min}$ and $G_{I,min}$ at PNs. (**e**) $G_{E,max}$ and $G_{I,max}$ at FSINs. (**f**) $G_{E,max}$ and $G_{I,max}$ at PNs.

Supplementary Fig. S5



Supplementary Fig. S5 (related to Fig. 3, 4)**.** Synaptic E-I balance at PNs in the rat cortex. **(a)** Rat L2/3 PN from TeA. **(b)** Representative traces of spontaneous or evoked EPSC and IPSC at rat PNs. **(c)** G_E and G_I at rat PNs, calculated from respective current amplitudes. **(d)** G_E *vs.* G_I at rat PNs. **(e)** G_E/G_I at rat PNs.

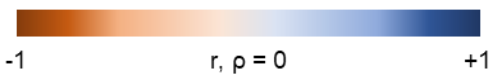
Supplementary Fig. S6

a

		sEPSC freq	sIPSC freq	sEPSC amp	sIPSC amp	$eEPSC_{min}$	$eIPSC_{min}$	$eEPSC_{max}$	$eIPSC_{max}$
Ictal / pHFO area	FSIN	0.55	0.65	0.59	-0.15	-0.22	0.09	-0.15	-0.23
		0.04 (*)	0.02 (*)	0.03 (*)	0.63	0.50	0.78	0.63	0.44
	PN	0.49	0.73	0.08	-0.13	-0.10	-0.33	-0.37	-0.14
		0.09	0.005 (**)	0.80	0.68	0.77	0.33	0.24	0.65
pHFOs (Ripple)	FSIN	-0.30	0.26	-0.27	-0.08	0.43	-0.04	-0.28	-0.05
		0.30	0.40	0.35	0.80	0.17	0.90	0.36	0.87
	PN	0.04	0.14	-0.34	-0.53	-0.46	0.25	-0.30	0.30
		0.89	0.65	0.26	0.06	0.15	0.45	0.34	0.35
pHFOs (Fast Ripple)	FSIN	-0.44	-0.06	-0.64	0.06	0.29	-0.06	-0.19	0.18
		0.12	0.83	0.01 (*)	0.86	0.36	0.85	0.53	0.55
	PN	-0.18	0.06	-0.52	-0.40	-0.37	0.59	-0.11	0.65
		0.57	0.84	0.07	0.17	0.26	0.05	0.73	0.02 (*)

b

		sEPSC freq	sIPSC freq	sEPSC amp	sIPSC amp	$eEPSC_{min}$	$eIPSC_{min}$	$eEPSC_{max}$	$eIPSC_{max}$
Ictal / pHFO area	FSIN	0.69	0.70	0.65	-0.04	-0.25	0.21	-0.07	-0.18
		0.008 (**)	0.009 (**)	0.01 (*)	0.91	0.43	0.51	0.81	0.56
	PN	0.53	0.57	0.23	-0.31	0.05	-0.50	-0.52	-0.17
		0.06	0.04 (*)	0.45	0.30	0.88	0.12	0.08	0.60
pHFOs (Ripple)	FSIN	-0.25	0.07	-0.17	0.01	0.43	-0.03	-0.13	0.08
		0.38	0.83	0.55	0.98	0.17	0.92	0.68	0.81
	PN	-0.23	-0.05	-0.34	-0.33	-0.28	0.10	-0.47	0.34
		0.46	0.88	0.26	0.27	0.40	0.78	0.13	0.28
pHFOs (Fast Ripple)	FSIN	-0.40	-0.12	-0.53	0.06	0.05	-0.16	-0.20	0.34
		0.16	0.70	0.05	0.85	0.89	0.62	0.52	0.26
	PN	-0.32	0.05	-0.64	-0.31	-0.41	0.21	-0.38	0.55
		0.28	0.86	0.02 (*)	0.30	0.21	0.54	0.22	0.07



Supplementary Fig. S6 (related to Fig. 5, 6)**.** Correlative analysis between clinical significance and single-cell synaptic properties, respectively represented by the spatial extent of cortical areas displaying either ictal discharges or pHFOs and the number of ripple or fast ripple pHFO events per hour (measured from iEEG), and PSC frequency and amplitudes (measured from slice electrophysiology). **(a)** Pearson correlation coefficient (r) and P-values. **(b)** Spearman correlation coefficient (ρ) and P-values.

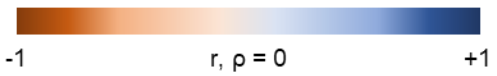
Supplementary Fig. S7

a

		AP frequency	AP threshold	AP half-width	Max depol.	Max repol.
Ictal / pHFO area	FSIN	0.55 0.04 (*)	-0.25 0.40	-0.12 0.67	-0.29 0.35	-0.09 0.77
	PN	0.26 0.36	-0.03 0.93	0.30 0.30	-0.38 0.21	-0.10 0.75
pHFOs (Ripple)	FSIN	-0.13 0.65	-0.28 0.33	0.10 0.74	-0.16 0.60	-0.20 0.52
	PN	0.62 0.02 (*)	-0.19 0.51	-0.06 0.85	-0.23 0.44	0.12 0.69
pHFOs (Fast Ripple)	FSIN	-0.04 0.90	-0.09 0.75	-0.05 0.87	0.15 0.64	0.16 0.61
	PN	0.53 0.05 (*)	-0.16 0.59	-0.35 0.22	0.08 0.80	0.40 0.18

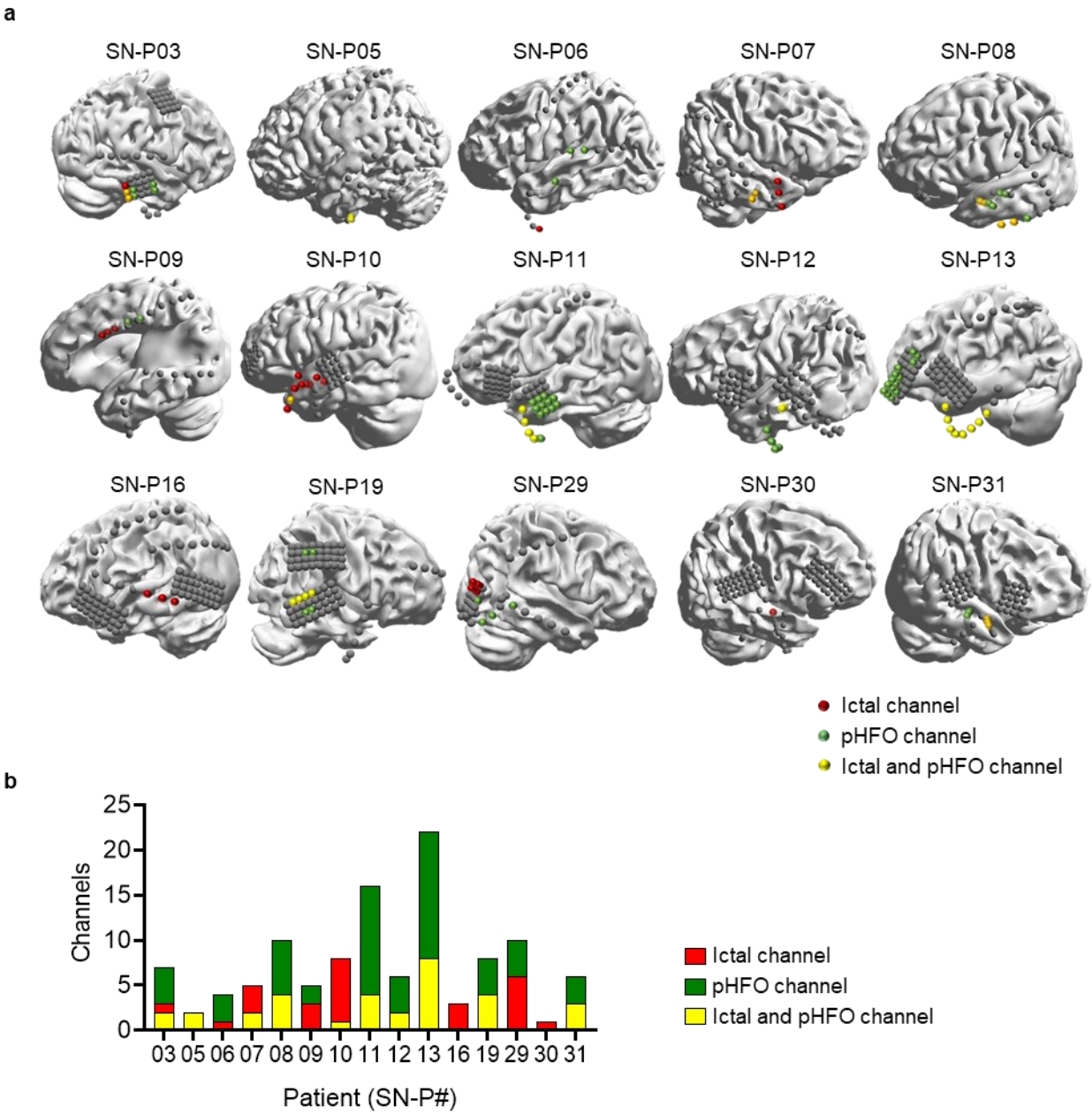
b

		AP frequency	AP threshold	AP half-width	Max depol.	Max repol.
Ictal / pHFO area	FSIN	0.50 0.07	-0.22 0.45	-0.20 0.48	-0.14 0.66	-0.02 0.95
	PN	0.25 0.38	-0.09 0.75	0.38 0.18	-0.33 0.27	-0.13 0.66
pHFOs (Ripple)	FSIN	-0.19 0.51	-0.29 0.32	0.04 0.90	0.07 0.82	-0.17 0.58
	PN	0.68 0.01 (**)	-0.06 0.83	-0.11 0.70	-0.07 0.82	0.26 0.39
pHFOs (Fast Ripple)	FSIN	-0.09 0.76	-0.16 0.57	-0.02 0.94	0.18 0.57	0.15 0.62
	PN	0.62 0.02 (*)	-0.16 0.57	-0.32 0.27	0.22 0.47	0.52 0.07



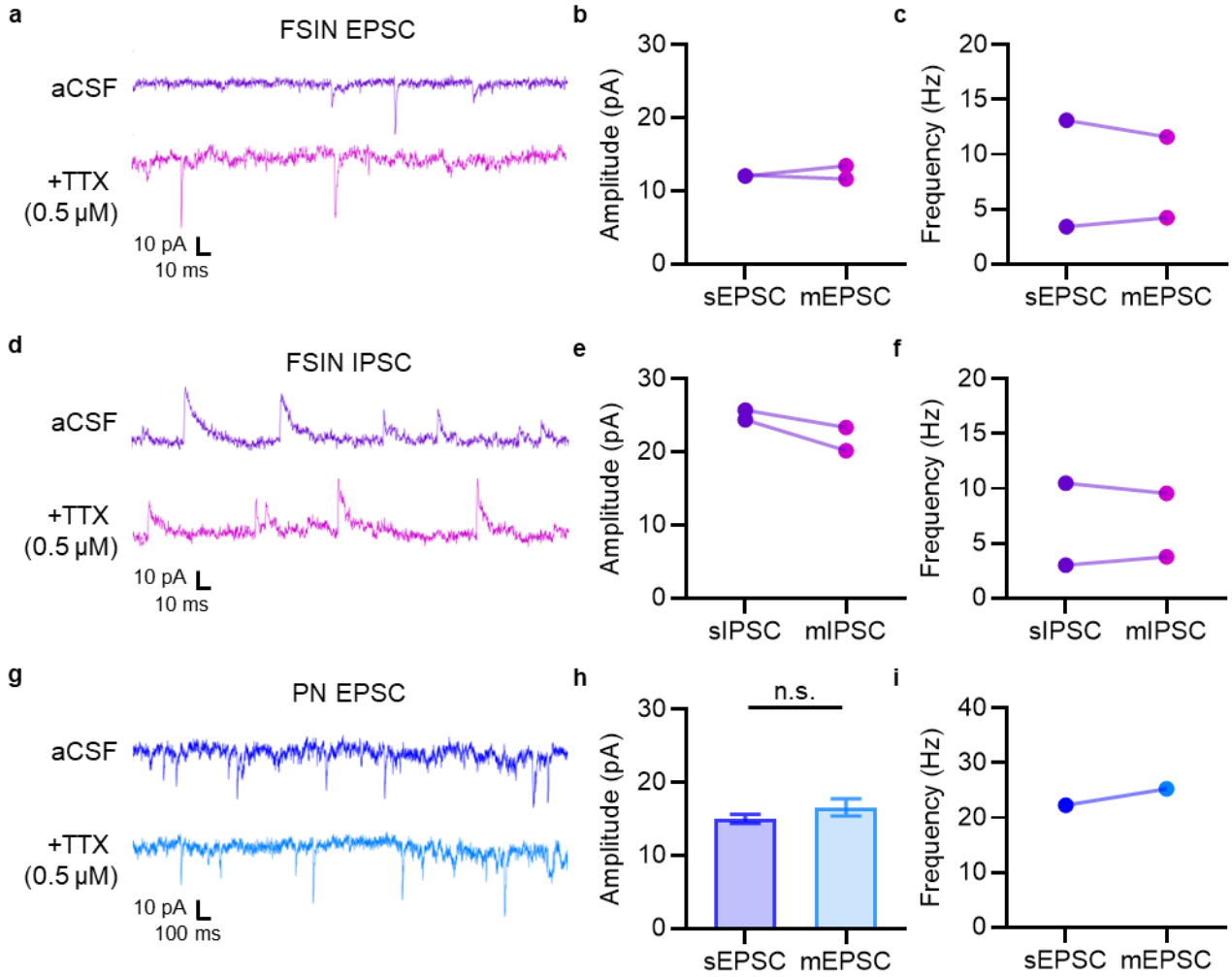
Supplementary Fig. S7 (related to Fig. 5, 6)**.** Correlative analysis between clinical significance and single-cell synaptic properties, respectively represented by the spatial extent of cortical areas displaying either ictal discharges or pHFOs and the number of ripple or fast ripple pHFO events per hour (measured from iEEG), and AP characteristics (measured from slice electrophysiology). **(a)** Pearson correlation coefficient (r) and P-values. **(b)** Spearman correlation coefficient (ρ) and P-values.

Supplementary Fig. S8



Supplementary Fig. S8 (related to Fig. 5, 6)**.** Electrode locations for the iEEG data included in the present study. Channels displaying ictal activity are labeled in red, and those displaying pHFOs are labeled in green; channels exhibiting both ictal activity and pHFOs are labeled in yellow. For patient information, refer to **Supplementary Table 1**. **(a)** Channel distribution in each patient. **(b)** Number of channels displaying ictal discharges and/or pHFOs from each patient.

Supplementary Fig. S9



Supplementary Fig. S9 (related to Fig. 2, Supplementary Fig. S5)**.** Comparison between spontaneous and miniature PSCs, measured in series with bath application of TTX from two human L2/3 FSINs and one PN in the FCD I group. **(a)** Representative traces of sEPSC and mEPSC at FSINs. **(b)** sEPSC and mEPSC amplitude. **(c)** sEPSC and mEPSC frequency. **(d)** Representative traces of sIPSC and mIPSC at FSINs. **(e)** sIPSC and mIPSC amplitude. **(f)** sIPSC and mIPSC frequency. **(g)** Representative traces of sEPSC and mEPSC at the PN. **(h)** sEPSC and mEPSC amplitude. **(i)** sEPSC and mEPSC frequency.