Supplementary Tables – General Parameters

Parameter	Value	Application
Reference temperature	37 °C	Nernst / GHK equations
Patch-clamp temperature	34 – 35 °C (measurements of V_{rest} and V_{thr})	Difference < 2 mV relative to 37 °C – negligible
$[Cl^-]_o$ (control)	130 mM	Standard ACSF
$[K^+]_o$ (control)	3 mM	Standard ACSF
Nernst constants (log10; 37 °C)	K^+ = +61.54 mV Cl^- = −61.54 mV	*RT/F × 2.303*

A Nernst constant of 61.54 mV (R = 8.314 J mol^{-1} K^{-1}, T = 310 K, F = 96 485 C mol^{-1}) was assumed for 37 °C.

Reducing the temperature to 35 °C lowers this constant to 61.12 mV, shifting all calculated equilibrium potentials by ≈ 0.68 % (≈ 0.57 mV) when Cl^-_i = 5.8 mM.

Throughout this supplement we use f_K = 0.15–0.25 and g_{Cl} = 0.15 (g_{Cl} calibrated to (Doyon et al. 2011) consistent with (Booth and Rinzel 1995)). We define f_K as the fractional contribution of K^+ leak to $\sum g_{leak}$.

Supplementary Table S1. Calculated equilibrium potentials (E_{GABA}) and relative shifts (ΔE_{GABA}) for intracellular chloride concentrations between 5.0 mM and 8.0 mM at 37 °C

$[Cl^-]_i$ (mM)	E_{GABA} (mV)	ΔE_{GABA} (mV)
5.0	−87.02	−3.96
5.5	−84.48	−1.42
5.8 (control)	−83.06	0.00
6.0	−82.15	+0.91
6.5	−80.01	+3.04
7.0	−78.03	+5.02
7.5	−76.19	+6.87
7.9 (CRS)	**−74.80**	**+8.25**
8.0	−74.47	+8.59

Equation:

$$E_{GABA} = -61.54\ \text{mV} \times log_{10}\left(\frac{[Cl^-]_o}{[Cl^-]_i}\right)$$

Note: Values in this table were calculated using a Nernst constant of 61.50 mV (rounded) to match source conventions. This differs by ≤ 0.06 mV from the 61.54 mV constant given in the General Parameters and has no material impact on ΔE_{GABA}.

Supplementary Table S2. Predicted shift of the resting membrane potential (ΔV_{rest}) produced by transient increases in extracellular potassium concentration ($\Delta[K^+]_o$) for three values of f_K (fractional K^+ conductance)

$\Delta[K^+]_o$ (mM)	ΔV_{rest} (mV) f_K=0.15	f_K=0.20	f_K=0.25
0.2	0.26	0.34	0.43
0.4	0.50	0.67	0.84
1.0	1.15	1.54	1.92
2.0	2.05	2.73	3.41
3.0	2.78	3.70	4.63
3.5	3.10	4.13	5.16

Equation:

$$\Delta E_K = 61.54\ \text{mV} \times log_{10}\left(\frac{3 + \Delta[K^+]_o}{3}\right)$$

For the cumulative depolarisation budget we used:

$$\Delta V_{rest} = f_K \times \Delta E_K$$

Note: Values in this table were calculated using a Nernst constant of 61.50 mV (rounded) to match source conventions. This differs by ≤ 0.06 mV from the 61.54 mV constant given in the General Parameters and has no material impact on ΔE_{GABA}.

Supplementary Table S3. Sensitivity of the resting-potential shift (ΔV_{rest}) to graded reductions in membrane KCC2 triggered by interleukin-6

KCC2 loss (%)	ΔE_{GABA} (mV)	ΔV_{rest} (mV) (g_{Cl}=0.15)
20	+5.1	+0.8
30	+7.6	+1.1
40	**+10.1**	**+1.5**
50	+12.6	+1.9

Equation:

$$\Delta V_{rest} = 0.15 \Delta E_{GABA}$$

ΔE_{GABA} values were obtained as in Supplementary Methods 2.1.

Supplementary Table S4. Resting-potential shift (ΔV_{rest}) for different ventral-to-dorsal ratios of GIRK conductance ($g_{GIRK\ v/d}$) and input resistance ($R_{in\ v/d}$)

$g_{GIRK\ v/d}$	$R_{in\ v/d}$	ΔV_{rest} (mV)
0.30	1.30	0.44
0.30	1.50	0.51
0.30	1.70	0.57
0.35	1.30	0.51
0.35	**1.50**	**0.59**
0.35	1.70	0.67
0.40	1.30	0.59
0.40	1.50	0.68
0.40	1.70	0.77

Equation:

$$\Delta V_{rest} = 0.90\ \text{mV} \times \left(\frac{R_{\text{in,v}}}{R_{\text{in,d}}}\right) \times \left(\frac{g_{\text{GIRK,v}}}{g_{\text{GIRK,d}}}\right) \times (1 + 0.25)$$

where 0.25 represents the TASK-channel contribution to the total leak current.

Supplementary Table S5. Predicted change in resting-membrane potential (ΔV_{rest}) produced by a chronic increase of extracellular potassium ($\Delta[K^+]_o$) under three values of the potassium-leak fraction (f_K)

$\Delta[K^+]_o$ (mM)	f_k = 0.15	f_k = 0.20	f_k = 0.25
0.25	0.321	0.428	0.534
0.30	0.382	0.509	0.636
0.35	0.442	0.589	0.737

0.40	0.501	0.669	0.836
0.45	0.560	0.747	0.933

Equation:

$$\Delta V_{rest} = f_K \times 61.54\ \text{mV} \times \log_{10}\left(\frac{3 + \Delta[K^+]_o}{3}\right)$$

Note: Values in this table were calculated using a Nernst constant of 61.50 mV (rounded) to match source conventions. This differs by ≤ 0.06 mV from the 61.54 mV constant given in the General Parameters and has no material impact on ΔE_{GABA}.

Supplementary Table S6. Attenuation of local depolarisation at the soma (Att %) reported by multi-compartment models of CA1 pyramidal neurones

Publication	Model / figure	Att %
(Booth and Rinzel 1995)	Fig. 6B	11
(Doyon et al. 2011)	Fig. 4C	14
(Migliore et al. 2018)	Fig. 3A	12
(Currin and Raimondo 2022)	Suppl. Fig. S3	13

Supplementary Table S7. Supra-additive synergy (Synergy %) when two inhibitory-Cl^- manipulations are applied simultaneously

Publication	Experimental combination	Synergy %
(Doyon et al. 2011)	KCC2 ↓ 60 % **plus** $GABA_A$ frequency ↑ 200 % (Fig. 4C)	15
(Currin and Raimondo 2022)	Cl^- plus distal inhibition (Suppl. Fig. S3)	19

Supplementary Table S8. Summary statistics (mean ± SD) for the data in Supplementary Tables 6 & 7.

Metric	Mean	SD
Att %	12.5	1.29
Synergy %	17.0	2.83

(Att % = 100 × [1 − $\Delta V_{soma}/\Delta V_{injected}$]; Synergy % = 100 × [($\Delta V_{combo} - \Sigma\,\Delta V_{single}$)/$\Sigma\,\Delta V_{single}$]).

Supplementary Table S9. *GRM3* risk haplotype – prolongation of τ_{EPSP} via glutamate spill-over

Parameter	Value	Source / note
↓ mGlu3 mRNA	10–15 %	(Ghose et al. 2009)
↓ EAAT2 protein	−30 %	(Abdul et al. 2009) Fig. 2D AD hippocampus – used as upper bound
ΔGlu_{extra}	+35 %	−(ΔEAAT2 + 0.4 × ΔmGlu3)
Slope $\Delta\tau/\Delta Glu$	0.7	(Wild et al. 2015)
Modelled $\Delta\tau_{EPSP}$	+25 %	Table 2.13 (Methods)

35 % = 30 % (EAAT2) + 0.4 × 12.5 % (mGlu3)

Δ values denote relative changes; decreases are negative. Formula ΔGlu_{extra} = −(ΔEAAT2 + 0.4·ΔmGlu3) with ΔEAAT2 < 0, ΔmGlu3 < 0 yields a positive increase in Glu_{extra}.

Coefficient 0.4 was chosen to keep presynaptic mGlu3 below transporter-driven effects; sensitivity 0.3–0.5 changes $\Delta\tau_{EPSP}$ by ±3–4 pp (EAAT2 −30% case) without altering conclusions.

Supplementary Table S9a. GRIN1 mRNA reduction — mapping to g_{NMDA} (lower-bound proxy)

Parameter	GRIN1 (NR1) mRNA reduction
Value:	18 % (mid-point of probe range)
Source / note:	(Weickert et al. 2013) (DLPFC qPCR; mid-range value used as lower-bound proxy).

Mapping mRNA→conductance (small-signal):	Assumption: linear, $g_{NMDA} = g_{NMDA,ctrl}$ (1 − ΔmRNA) Source / note: modelling convention for small fractional changes; KO data (South et al. 2003) used only as mechanistic ceiling (−86 %), not for scaling.
Target cell class:	PV-like / FS interneurons receive a substantial NMDA drive Source / note: (Povysheva and Johnson 2012) (supports relevance of NMDA drive on PFC INs).
Region transfer:	DLPFC → mPFC (1:1) Source / note: lower-bound transfer, flagged as model assumption (∗).
Model outcome (used in Table 2.12):	$\Delta g_{NMDA} \approx -18$ % (mPFC). Not converted to mV; used qualitatively as E/I shift → τ_{EPSP} ↑.
Equation used:	$\Delta g_{NMDA} = k\ \Delta$mRNA, with k = 1 (small-signal, lower bound). No direct τ_{EPSP} % is claimed from this line; direction only.

Supplementary Table S10. *GABRA1* mRNA ↓ 40 % – effect on τ_{IPSC} and R_{in}

Parameter	Value	Source / note
GABRA1 mRNA (PFC, BA9)	−40 %	(Glausier and Lewis 2011) Fig 2B
$\Delta\tau_{mIPSC}$ w α1 KO	+55 %	(Bosman et al. 2005) Table 1
Scaling factor for partial loss	×0.45	Linear interpolation: 40 / 90 (conservative)
mIPSC amplitude (A/A_{ctrl})	0.74	Chosen so that $Q/Q_{ctrl} \approx 0.93$ (see text)
mIPSC time constant (τ/τ_{ctrl})	1.25	1 + 0.55 × 0.45
IPSC charge (Q/Q_{ctrl})	0.93 (−7 %)	0.74 × 1.25
Modelled $\Delta\tau_{IPSC}$	+25 %	Table 2.13 (Methods)
Modelled g_{inh}	−7 %	$g_{inh} \propto Q$
ΔR_{in} (from Σg_{tot})	+1.4 %	$g_{inh} \approx 20$ % Σg_{tot}; 0.20 × 7 % ≈ 1.4 %

Supplementary Table S11. *COMT* Val158Met – increase in F–I gain

Parameter	Value	Source / note
CSF ΔHVA (meta-analysis)	−16 %	(Saloner et al. 2020) (n = 132)
ΔDA ≈ −ΔHVA (sign and lower-bound magnitude). Used only to set order-of-magnitude for gain.	0.9	(Vijayraghavan et al. 2007)
Modelled Δgain F–I	+14 %	Table 2.13 (Methods)

Supplementary Table S12. *CACNA1C* rs1006737 A – increase of τ_{EPSP} and rheobase shift

Parameter	Value	Source / note
$\Delta I_{Ca,L}$	+30 %	(Mertens et al. 2015) Fig 3C (hiPSC neurons)
Slope $\Delta\tau$ / ΔCa_{post}	0.5	(Wild et al. 2015)
Modelled $\Delta\tau_{EPSP}$	+15 %	—
Ratio $\alpha = \tau_m/(\tau_m + T)$	0.4	(Tuckwell 1988); CA1
Lapicque/Tuckwell formula	Δrheo = $-\alpha \cdot \Delta\tau_{EPSP}$	—
Modelled Δrheobase	−6 %	Exported to Table 3.3

For a representative rheobase of 150 pA (CA1 pyramidal, T = 5 ms) a 6 % decrease corresponds to ≈ 9 pA, well below the 10–20 pA step size used in typical current-step protocols.

Supplementary Table S13. *NRG1* HapICE – reduction of g_{inh}

Parameter	Value	Source / note
Loss of PV interneurons	30 %	(Fazzari et al. 2010)

N_{PV} / $N_{PV,ctrl}$	0.70	—
Booth–Rinzel rule (power 0.3)	—	(Booth and Rinzel 1995)
Modelled g_{inh}	−10 %	Table 2.13 (Methods)
IPSC measurement	−25 %	(Yin et al. 2013)

In the allelic block we adopt α = 0.3 as the lower-bound variant, consistent with the sensitivity range defined in Supplementary Methods 2.6.3.

Supplementary Table S14. C4A over-expression – synaptic connectivity loss

Parameter	Value	Source / note
Synapse pruning (microglia engulfment, PSD-95^{+})	↑ ≈ 35 %	(Yilmaz et al. 2021) Fig 4C–E
Spine density (apical dendrites, L2/3)	↓ 25 %	(Yilmaz et al. 2021) Fig 5B
mEPSC frequency	↓ 20 %	(Yilmaz et al. 2021) Fig 6B
mEPSC amplitude	↓ 15 %	(Yilmaz et al. 2021) Fig 6C

We summarize a −20% g_{exc} as the mean of mEPSC frequency and amplitude decrements; spine loss supports the same direction but is not double-counted.

Supplementary Table S15. *SCN2A* R1882Q – reduced rheobase

Parameter	Value	Source / note
$\Delta I_{Na,pers}$	+40 %	(Ben-Shalom et al. 2017)
ΔV_{thr}	−3 mV	(Ben-Shalom et al. 2017) Fig. 1E
Modelled Δrheobase	−15 %	Table 3.3

V_{thr} from HEK293/Nav1.2 is used only as a shift parameter; kinetics are not transferred.

$$I_{rheo} \propto (V_{thr} - V_{rest})/(R_{in} \cdot T)$$

Supplementary Table S16. Amphetamine (2 mg kg^{-1} i.p.) – reduction of rheobase

Parameter	Value	Source / note
WT rheobase (threshold current)	120 ± 5 pA	(Rosenkranz and Grace 2002) Fig. 3D
Post-AMPH rheobase	105 ± 5 pA	(Rosenkranz and Grace 2002) Fig. 3D
Modelled Δrheobase = (105 − 120) / 120 = −12.5 % → reported as −12 % (rounded conservatively).		
Directional support	DA ↑ (microdialysis)	(Di Chiara and Imperato 1988)
Δrheobase	−12 %	Exported to Table 2.15 (Methods)

Supplementary Table S17. Chronic-intermittent ethanol (CIE, 5 weeks) – changes in NMDA/AMPA ratio and mIPSC frequency

Parameter	Value	Source / note
Δ(NMDA / AMPA)	+30 %	(Kroener et al. 2012) Fig. 4B
$\Delta mIPSC_{freq}$	−15 % (trend, p = 0.08)	(Kroener et al. 2012) Fig. 4C
Export: NMDA/AMPA	**+30 %**; $mIPSC_{GABA}$	−15 % (flagged as trend).

Supplementary Table S18. Alcohol withdrawal (72 h) – change in R_{in} and IPSC frequency

Parameter	Control	72 h WD	Δ (%) / Source
R_{in} PV interneurons (MΩ)	155	186	+20 % —(Quadir et al. 2024) bioRxiv preprint Fig. 2B
$IPSC_{freq}$ (Hz)	7.8	5.9	−24 % —(Quadir et al. 2024) bioRxiv preprint Fig. 2D
Export: R_{in} PV-IN = +20 %; $IPSC_{GABA\ freq}$ ↓ (~−24 %)			

Supplementary Table S19. IL-6 ↑ → KCC2 ↓ → ΔE_{GABA} → ΔV_{soma}

Parameter	Value	Source / note
↓ $g_{KCC2,surf}$	−40 %	(Jin et al. 2022) Fig. 5C
↑ $[Cl^-]_i$	5.8 → 8.6 mM	At 40 % KCC2 loss the model of (Doyon et al. 2011) predicts an increase of ~48 %; we model this as a rise from 5.8 to 8.6 mM. 8.6

		mM is chosen conservatively below this upper limit
E_{GABA}	−72.6 mV	ΔE_{GABA} = 61.54 mV × [$\log_{10}$(130/8.6) − $\log_{10}$(130/5.8)] ≈ +10.5 mV.
ΔE_{GABA}	+10.5 mV	(Rivera et al. 2004) (40 % KCC2 loss)
g_{Cl} fraction in V_{rest}	0.15	(Booth and Rinzel 1995)
ΔV_{soma}	+1.6 mV	0.15 × 10.5 mV
Baseline E_{GABA}	−83 mV	Calculated for $[Cl^-]_i$ = 5.8 mM (see Suppl. Table 1)

Minimal scenario 5.8 → 7.9 mM

Supplementary Table S20. P2X7R ↑ + slowed $[K^+]_o$ clearance

Parameter	Value	Source / note
Extracellular ATP (microglia)	+210 %	(Shan et al. 2022) Fig. 4B
$t_{½}$ of $[K^+]_o$ clearance	× 1.7	(Shan et al. 2022) Fig. 4D
Excess $[K^+]_o$	+0.12 mM	Diffusion model (conservative)
$[K^+]_o$ absolute	3 → 3.12 mM	—
ΔE_K	+1.05 mV	61.54 mV × $\log_{10}$(3.12/3)
g_K fraction in V_{rest}	0.15	(Booth and Rinzel 1995)
ΔV_{soma}	≈ 0.16 mV	0.15 × 1.05 mV

Supplementary Table S21. ROS → 40 % Kir2.1 block

Parameter	Value	Source / note
↓ $g_{Kir2.1}$	−40 %	(Wang et al. 2022) Fig 3D
g_{Kir} / g_K	0.30	(Ding et al. 2016)
g_K / g_{total}	0.15	(Booth and Rinzel 1995)
Net Δg_{Kir} / g_{total}	0.018 (= 0.40 × 0.30 × 0.15)	—
Baseline V_{rest}	−71 mV	(Cembrowski et al. 2016)
Baseline E_K	−90 mV (3 mM $[K^+]_o$)	Nernst
ΔV_{soma} (Kir block)	+0.34 mV	0.018 × $\lvert V_{soma} - E_K \rvert$
Time window	24 – 72 h	(Wang et al. 2022)

† The TRPM2 effect (+5–10 pA inward current, (Wang et al. 2022)) is negligible relative to Kir2.1 and was not included in ΔV.

Supplementary Table S22. ECS shrinkage (Δf_K = −0.03)

Parameter	Value	Source / note
↓ f_K	−0.03	(Syková and Nicholson 2008) Fig. 5A–B
Burst $[K^+]_o$	6 mM (CRS)	—
ΔE_K (burst)	≈ 18.53 mV	61.5 mV × $\log_{10}$(6/3)
ΔV_{soma}	≈ $\lvert \Delta f_K \rvert$ × ΔE_K(6 mM) = 0.03 × 61.54 × $\log_{10}$(6/3)	≈ 0.56 mV

Δf_K adapted from (Syková and Nicholson 2008) Fig. 5A–B (chronic astrocytic swelling).

The depolarisation is calculated as the additional gain during a K^+ burst due to reduced fractional K^+ conductance (Δf_K), i.e. $\Delta V_{soma} \approx \lvert \Delta f_K \rvert \times \Delta E_K$(burst).

Supplementary Table S23. Caffeine – GIRK block

Dose (p.o.)	$[Caf]_{CSF}$ (µM)	GIRK block (%)	ΔV_{raw} (mV)	ΔV_{soma} (mV)	Source / note
100 mg	4 – 6	10 – 15	0.67 – 1.00	0.8 – 1.2	(Blanchard and Sawers 1983; Nehlig 2018) slope 2.5 % μM^{-1}; (Lopes et al. 2019) slice, Fig. 2C-D

400 mg	12 – 16	25 – 35	1.7 – 2.4	2.1 – 2.9	GIRK saturation above 10 µM
10 µM slice	—	25	1.66	1.9	Acute hippocampal slice; (Lopes et al. 2019)

$\Delta V_{raw} = 0.35 \times \text{block} \times |E_K - V_{rest}|$, with $|E_K - V_{rest}| \approx 19$ mV.

$\Delta V_{soma} = \Delta V_{raw} \times k_{R(\theta)} \times k_{PV} = \Delta V_{raw} \times 1.10 \times 1.10$.

The block-versus-concentration slope flattens above 10 µM; we therefore used 25–35 %.

The slope of 2.5 % μM^{-1} was obtained by linear regression of the 0–10 µM data in (Lopes et al. 2019) ($R^2 = 0.94$); own calculations.

Conversion from dose to CSF concentration was based on (Blanchard and Sawers 1983; Nehlig 2018).

Supplementary Table S24. "Low-PV" window (25 % drop in g_{inh})

Parameter	Value	Source / note
↓ g_{inh} (PV)	−25 %	(Donato et al. 2013), Fig. 3E
g_{inh} / g_{total}	0.20	(Booth and Rinzel 1995)
ΔE ($V_{rest} - E_{GABA}$)	12 mV	−71 − (−83)
ΔV_{soma}	+0.6 mV	0.20 × 0.25 × 12 mV

† PV → pyramidal IPSPs act perisomatically; there is no dendritic attenuation, hence the attenuation coefficient (*Att*) = 1.

$\Delta E = V_{rest} - E_{GABA} = 12$ mV in CA1.

Supplementary Table S25. Nicotine – somatic depolarisation in vCA1

Scenario	$[Nic]_{CSF}$ (µM)	ΔV_{raw} (mV)	ΔV_{soma} (mV)	Source / note
4 cigarettes h^{-1}	0.20 – 0.30	0.076 – 0.114	0.09 – 0.13	(Ji and Dani 2000; Rose et al. 2010), Fig. 2B (0.38 mV μM^{-1})
2 cigarettes h^{-1}	0.10 – 0.15	0.038 – 0.057	0.04 – 0.07	same as above
Peak after 1 cigarette	0.25	0.095	0.12	$t_{½} \approx 45$ min (Picciotto et al. 2008)
10 µM slice	—	3.8	3.8	Acute hippocampal slice; (Ji and Dani 2000), Fig. 2C

† $\Delta V_{raw} = 0.38$ mV $\mu M^{-1} \times [Nic]_{CSF}$

‡ $\Delta V_{soma} = \Delta V_{raw} \times k_{R(\gamma)} \times k_{PV} = \Delta V_{raw} \times 1.15 \times 1.10$

For the slice row, ΔV_{soma} is taken directly from the recorded ΔV (kR = kPV = 1), as this is a local measurement without network-level scaling.

Supplementary Table S26. Baseline equation and input parameters for a magnetite nanocrystal chain

Parameter	Nominal value	Tested range	Source
α_{ds}	0.50	0.45 – 0.55	(Golding et al. 2005) Fig. 3

κ	8.27 μV × μT⁻¹	± 7 % †	(Kirschvink 1996)
Φ (16.7 Hz)	1.0 × 10²	80 – 120	(Kirschvink et al. 1992); see Supplementary Methods 2.11.2
Φ (7.83 Hz)	40	30 – 60 (± 25 %)	(Kirschvink et al. 1992); see Supplementary Methods 2.11.2
$B_{rms-city}$	0.15 μT	0.10 – 0.20 μT	(Schüz et al. 2000; Brix et al. 2001; Bundesamt für Strahlenschutz (BfS) 2023 Fig 3.2; Loizeau et al. 2024)
$B_{rms-countryside}$	1 pT	0.5 – 2 pT	(Nickolaenko and Hayakawa 2014; Han et al. 2023)
Q_θ	10	5 – 10	(Buzsáki and Draguhn 2004; Zemankovics et al. 2010), Fig. 2

Baseline equation – see Supplementary Methods 2.11.3.

Φ_{nom} are fitted parameters consistent with Kirschvink-style chain models; |H(f)| from a Lorentzian with Q ≈ 12 (see Supplementary Methods S2.11.2).

Supplementary Table S27. Sensitivity matrix – urban environment (16.7 Hz)

Φ \ α	**0.45**	**0.50**	**0.55**
80	45 μV	50 μV	55 μV
100	56 μV	62 μV	68 μV
120	67 μV	74 μV	82 μV

Nominal prediction: ΔV_{soma} = 62 μV (0.062 mV)

Extreme scenario (0.55; 120) → 0.082 mV.

Supplementary Table S28. Sensitivity matrix – rural environment (7.83 Hz)

Φ \ α	**0.45**	**0.50**	**0.55**
30	0.11 nV	0.12 nV	0.14 nV
40	0.15 nV	0.17 nV	0.19 nV
60	0.22 nV	0.25 nV	0.28 nV

All ΔV_{soma} values are rounded to two significant figures.

Note that Φ is a dimensionless effective gain factor ($|H(f)|\cdot\Phi_{nom}$) of the magnetite chain and should not be confused with the mechanical quality factor Q.

Nominal prediction: ΔV_{soma} = 0.17 nV

Supplementary Table S29. ΔV_{soma} versus Johnson noise (band 0 – 5 kHz)

Compartment	**Parameter (R or C)**	**Value**	**Formula**	**V_{rms} [μV]**	**ΔV_{soma} / V_{rms} (reference specified)**
Dendritic branch	R	200 MΩ	√(4 kB T R Δf), Δf=5 kHz	≈ 130	62 μV / 130 μV ≈ 0.48
Whole cell (soma)	C	150 pF	√(kB T / C)	≈ 5.3	62 μV / 5.3 μV ≈ 12×
Small compartment (note)	C	15–20 pF	√(kB T / C)	≈ 15–17	–

Dendrite: V_{rms} via √(4kTRΔf), Δf=5 kHz. Whole-cell: V_{rms} via √(kT/C). Ratios compare ΔV_{soma} either to dendritic V_{rms} (conservative cross-compartment) or to whole-cell V_{rms} as indicated in text.

Supplementary Table S30. One-second traction-field bursts (16.7 Hz)

Scenario	B_{rms}	ΔV_{soma}	ΔVsoma (after RC filter, τ = 20–50 ms)
City – 24 h median	0.15 µT	0.062 mV	0.027–0.011 mV (~40–80 % attenuation)
City – peak × 3	0.45 µT	0.19 mV	0.083–0.036 mV (~40–80 % attenuation)
Countryside – median	1 pT	0.17 nV	0.07–0.03 nV
Countryside – peak × 3	3 pT	0.50 nV	0.22–0.09 nV

$$|H_{RC}(f)| = \frac{1}{\sqrt{1+(2\pi f\tau)^2}}, \quad f = 16.7\text{Hz},\ \tau = 20-50\text{ms} \Rightarrow |H_{RC}| \approx 0.44-0.19.$$

Supplementary Table S31. Matrix of percentage changes (layer × axis) – CRS + CACNA1C A + hot spot variant

Axis / Layer	Layer 1 (CRS ≥ 14 d)	Layer 2 (allele / drug)	Layer 3 (CREB hot spot)	Layer 4 (minute–hour bias)
Rheobase	−44 %	−6 %	−15 %	—
R_{in}	+29 %	—	—	—
τ_{EPSP}	+15 %	+15 %	+25 %	—
$IPSC_{PV\rightarrow pyr}$	−16 %	—	—	—
ΔV_{margin}	+11.3 mV	0 mV	+3.2 mV	+0.5–3 mV

Layer 4 acts purely additively on V_{margin}; it does not modify passive parameters.

Combination rule (Fricker and Miles 2000; Magee and Cook 2000):

$$Overall\ factor = \prod_{i=1}^{n}\left(1+\frac{\Delta_i}{100}\right).$$

(Spruston and Johnston 1992; Dougherty et al. 2012; Kim and Johnston 2015; MacKenzie and Maguire 2015; Pignatelli et al. 2019; Zhang et al. 2021).

Supplementary Table S32A. Propagation of uncertainty – *CACNA1C* A variant

Axis	Final value	σ_{base}	σ_{mult} (RSS)	σ_{tot}
Rheobase	63 pA (140 × 0.447)	10 pA	19 pA	≈ 21.5 pA
R_{in}	142 MΩ (110 × 1.29)	8 MΩ	9.2 MΩ	≈ 12.1 MΩ
τ_{EPSP}	24.8 ms (15 × 1.652)	1.0 ms	2.6 ms	≈ 2.8 ms
$IPSC_{PV\rightarrow pyr}$	0.84	—*	0.05	0.05

* For the normalised quantity (= 1.0) no published standard deviation is available; we therefore applied a conservative ±5% multiplicative uncertainty.

$$\sigma_{tot} = \sqrt{\sigma_{base}^2 + \sigma_{mult}^2}$$

For all other parameters, σ_{mult} reflects a parameter-specific multiplicative uncertainty derived from the variability of the underlying experimental sources (typically 5–30%; see Supplementary Methods 2.6). These uncertainties are applied as relative multipliers to the final values.

Supplementary Table S32B. Combined factors (*SCN2A* R1882Q variant)

Axis	Overall factor	Change %
Rheobase	0.56 × 0.85 × 0.85 = 0.404	− 59.6 % (Rounded) − 60 %
R_{in}	1.29	+ 29 %
τ_{EPSP}	1.44	+ 44 %
$IPSC_{PV\rightarrow pyr}$	0.84	− 16 %

Layers 1 and 3 are identical to Supplementary Table S31; in Layer 2 a −15 % rheobase shift was assumed, all other axes 0 %.

Supplementary Table S33. Scaling constants used in transient-gain mode

Parameter	Value	Source / note
ΔR_{in}	+29 %	(electrotonic cascade)
k_R (θ)	1.10 (after correction)	corrected from 1.29 by filtering
k_R (SWR)	1.00	($\omega\tau \gg 1$; R_{in} increase negligible at 150 Hz)
PV-shunt	−16 %	Hot spot + *CACNA1C* A
k_{PV}	1.10	(Booth and Rinzel 1995), leak-divisive model

$k_R(\theta)$ was reduced from 1.29 to 1.10 after accounting for frequency filtering and increased R_{in} in the combined CRS + hotspot + *CACNA1C* scenario.

k_R (γ) — 1.15 — high-γ envelope; mild R_{in} effect

Supplementary Table S34. Sensitivity of ΔV_{soma} to ± 10 % changes in k_R (electrotonic gain) and k_{PV} (PV shunt)

Transient	k_R variation (± 10 %)	k_{PV} variation (± 10 %)	ΔV_{soma} range [mV]
θ	1.0 – 1.2	1.0 – 1.2	0.99 – 1.44
SWR	0.9 – 1.1	1.00 – 1.00	0.36 – 0.44

With the largest deviations (± 10 %), ΔV_{soma} changes by ≤ 20 %. This does not alter the qualitative conclusion that θ and SWR remain the leading candidates for ELF phase-locking.

Supplementary Table S35. Input parameters of the phase-coincidence model

Band	Fraction of sites f_i	Period T_i [ms]	Hit probability $p_i(\Delta t)$	Sources
7.83 Hz	1.00	128	$p_1 = \Delta t/T_1$	(Nickolaenko and Hayakawa 2014)
16 – 18 Hz	0.62	60	$p_{16} = \Delta t/T_{16}$	(Kirschvink 1996; Brix et al. 2001; Loizeau et al. 2024)
20 – 28 Hz	0.18	42.5 ± 7.5 (≈ 35–50 ms)	$p_{20} = \Delta t/T_{20}$	(Paniagua et al. 2007; Gajšek et al. 2016)

For any specific Δt we use

$$p_i = \begin{cases} \dfrac{\Delta t}{T_i}, \Delta t < T_i \\ 1, \Delta t \geq T_i \end{cases}$$

Supplementary Table S36. Calculation of P_{phase} in an urban environment (Δt = 20–30 ms)

Δt	p_1	p_{16}	p_{20}	$1 - f_1p_1$	$1 - f_{16}p_{16}$	$1 - f_{20}p_{20}$	$P_{phase,city}$	± 10 % CI
20 ms	0.156	0.333	0.471	0.844	0.794	0.915	0.387	0.31 – 0.46
25 ms	0.195	0.417	0.588	0.805	0.741	0.894	0.467	0.39 – 0.54
30 ms	0.234	0.500	0.706	0.766	0.690	0.872	0.539	0.45 – 0.61

$$P_{\text{phase,city}} = 1 - (1 - f_1p_1)(1 - f_{16}p_{16})(1 - f_{20}p_{20})$$

Supplementary Table S37. Calculation of P_{phase} in a rural environment

Δt	p_1	$P_{phase,village}$	± 10 % CI
20 ms	0.156	0.156	0.14 – 0.17
25 ms	0.195	0.195	0.18 – 0.21
30 ms	0.234	0.234	0.21 – 0.26

Because only the 7.83 Hz band contributes in the rural scenario:

$$P_{\text{phase,village}} = f_1 p_1 = 1.00 \times p_1$$

Supplementary Table S38. Urban gradient ($G = P_{city} / P_{village}$)

Δt	Gradient	95 % CI (± 10 %)
20 ms	2.48	2.0 – 3.0
25 ms	2.40	1.9 – 3.0
30 ms	2.30	1.9 – 2.8

Shift in the correlation threshold r

If the frequency bands are partially correlated we introduce a reduction factor

$$\rho = 1 - r$$

For $r = 0.02 \ldots 0.10$;

Supplementary Table S39. Sensitivity to inter-band correlation ($\Delta t = 25$ ms)

r	ρ	$P_{phase,city}$ ($\Delta t = 25$ ms)	G
0.02	0.98	0.460	2.31
0.05	0.95	0.444	2.22
0.10	0.90	0.420	2.15

Conclusion: even at r = 0.10 the gradient remains > 2.1.

Supplementary Table S40. Variation of the 16–18 Hz band fraction (± 15 %)

f_{16}	P_{city}	Gradient
0.53 (−15 %)	0.441	2.26
0.62 (nominal)	0.467	2.40
0.71 (+15 %)	0.496	2.44

Supplementary Table S41. Theta + SWR coincidences in mice (RUN state, vCA1)

Variable	Nominal value	Unit	± 10 % range	Source / comment
f_θ	10	Hz	9 – 11	(Fernández-Ruiz et al. 2017; Fig. 2B)
$\lambda_{\theta\text{-window}} = 4 f_\theta \times 60$	2 400	min^{-1}	2 160 – 2 640	calculated
$\Delta t_\theta = 1 / (4 f_\theta)$	25.0	ms	22.7 – 27.8	calculated
λ_{SWR}	1.90	min^{-1}	1.71 – 2.09	(conservative value from the lower quantile of waking-ripple distributions; waking SWR rates vary widely — see consensus and reviews) (Liu et al. 2022a — consensus statement)
t_{SWR}	100	ms	90 – 110	(Ylinen et al. 1995; Jiang et al. 2020)

$t_{eff,SWR}$	109.8	ms	99.8 – 119.8	+9.8 ms ($\tau_{EPSP,eff}$ − 15 ms)
$t_{sum} = t_{eff,SWR} + \Delta t_{\theta}$	135	ms	124.8 – 144.8	calculated
p_{hit}	0.00428	–	0.00356 – 0.00505	$\lambda_{SWR} \times t_{sum}$ / 60
$N_{hit,raw} = p_{hit} \times \lambda_{\theta\text{-window}}$	10.26	min^{-1}	7.68 – 13.32	–
$N_{hit,city}$	4.79	min^{-1}	3.59 – 6.24	$\times P_{phase,city} = 0.467$
$N_{hit,village}$	2.00	min^{-1}	1.50 – 2.60	$\times P_{phase,village} = 0.195$

Supplementary Table S42. Theta + SWR coincidences in humans (vCA1)

Wake state	f_{θ} [Hz]	$\lambda_{\theta\text{-window}}$ [min^{-1}]	λ_{SWR} [min^{-1}]	t_{sum} [ms]	p_{hit}	$N_{hit,raw}$ [min^{-1}]	$N_{hit,city}$	$N_{hit,village}$	± 10 % CI (city / village)
Rest	7.0	1 680	1.2	146	0.00291	4.90	2.29	0.96	1.68 – 3.03 / 0.70 – 1.27
Slow walk	8.8	2 112	0.9	138	0.00207	4.38	2.05	0.85	1.51 – 2.72 / 0.63 – 1.13
β-arousal	16.0	3 840	0.8	126	0.00168	6.44	3.01	1.26	2.21 – 3.98 / 0.92 – 1.66

±10% sensitivity band (simultaneous ±10% perturbation of all input parameters; see Supplementary Methods S2.15.4).

Supplementary Table S43. Sensitivity analysis (± 10 %) – extreme values of N_{hit}

Species / state	$N_{hit,\ city}$ [min^{-1}]	$N_{hit,\ village}$ [min^{-1}]
Mouse (RUN)	3.59 – 6.24	1.50 – 2.60
Rest	1.68 – 3.03	0.70 – 1.27
Slow walk	1.51 – 2.72	0.63 – 1.13
β-arousal	2.21 – 3.98	0.92 – 1.66

Ranges span the minimum and maximum N_{hit} values observed across the ±10% parameter grid (f_{θ}, λ_{SWR}, t_{SWR}).

Supplementary Table S44. Physical parameters for amplification of the 7.83 Hz signal

Parameter	Calm	Geomagnetic storm Kp ≥ 6	Unit	Source / formula
B_{rms}	0.3 pT	3 pT	pT	(Sátori et al. 2007)
κ	8.27	—	$\mu V\ \mu T^{-1}$	(Kirschvink 1996) chap. 12, tab. 2, p. 242
Φ (chain, 7–20 Hz)	40 (30–60)	40 (30–60)	–	(Kirschvink et al. 1992; Winklhofer and Kirschvink 2010) see Supplementary Methods S2.11.2
α_{ds}	0.50	0.50	–	(Golding et al. 2005)
ΔV_{soma}	5×10^{-8}	5×10^{-7}	mV	$\kappa \cdot B \cdot \Phi \cdot \alpha_{ds}$

Supplementary Table S45A. Calculation steps for P_{phase} (city / village) (g = 0.13)

Band	f_i	p_i (calm)	p_i (storm)	$1 - f_i p_i$ (calm)	$1 - f_i p_i$ (storm)

7.83 Hz	1.00	0.195	0.325	0.805	0.675
16–18 Hz	0.62	0.417	0.417	0.740	0.740
20–28 Hz	0.18	0.588	0.588	0.894	0.894
Product of the three	–	0.534	0.447	–	–
$P_{\text{phase,city}}$	–	0.467	0.553	–	–
$P_{\text{phase,village}}$	–	0.195	0.325	–	–

$$\boldsymbol{P_{phase} = 1 - \prod_{i} (1 - f_i p_i)}$$

In the village scenario only the 7.83 Hz band contributes; therefore $P_{phase,village} = f_1\, p_1 = 1.00 \times p_1$

Supplementary Table S45B. Calculation steps for P_{phase} (city / village) (g = 0.22) full

Band	f_i	p_i (calm)	p_i (storm)	$1 - f_i p_i$ (calm)	$1 - f_i p_i$ (storm)
7.83 Hz	1.00	0.195	0.415	0.805	0.585
16–18 Hz	0.62	0.417	0.417	0.740	0.740
20–28 Hz	0.18	0.588	0.588	0.894	0.894
Product of the three	–	0.534	0.388	–	–
$P_{\text{phase,city}}$	–	0.467	0.612	–	–
$P_{\text{phase,village}}$	–	0.195	0.415	–	–
RR ≈ 1.33					

g = 0.22 corresponds to the full transfer of the mean peak narrowing (11 % ΔFWHM) into the phase domain.

Supplementary Table S46. Epidemiological studies and the β coefficient

#	Author (year)	Population	Endpoint	RR	95 % CI	log RR	SE² (log RR)	β = (RR−1)/0.28
1	(Nishimura et al. 2020)	Taiwan	Suicide attempts	1.15	1.05-1.25	0.140	0.00197	0.54
2	(Kay 1994)	Scotland	Depression (hospital)	1.36	1.12-1.66	0.308	0.00996	1.29
3	(Raps et al. 1992)	Israel	Psychiatric admissions	1.15	n/a	0.140	n/a	0.54
4	(Tada et al. 2014)	Japan	Suicides	1.18	1.05-1.32	0.165	0.00341	0.64
5	(Partonen et al. 2004)	Finland	Suicides	1.22	1.10-1.35	0.199	0.00265	0.79
6	(Feigin et al. 2014)	6 countries	First stroke	1.19	1.04-1.36	0.174	0.00468	0.68
7	(Shaposhnikov et al. 2014)	Moscow	Stroke hospitalisations	1.25	1.10-1.42	0.223	0.00424	0.89
8	(Villoresi et al. 1998)	Italy	Myocardial infarction	1.11	1.06-1.38	0.104	0.00453	0.39
Pooled (DL)	–	–	–	1.19	1.14-1.25	0.176	0.00052	0.69
Heterogeneity	–	–	–	Q = 4.25 (df = 6; p = 0.64)	–	–	–	I^2 = 0 %
Leave-one-out	–	–	–	pooled β range:	–	–	–	–

				0.62 – 0.70				

$$\log RR = \ln(RR)\,;\ \mathrm{Var} = SE^2,\ \text{where } SE = \frac{\ln(\mathrm{CI_{upper}}) - \ln(\mathrm{CI_{lower}})}{(2 \times 1.96)}$$

CI: 0.48 – 0.85

(Raps et al. 1992) does not report a 95 % confidence interval; the study was assigned a weight of 0 in the random-effects model.

Removing (Nishimura et al. 2020) raises β_{pooled} to 0.70, whereas removing (Kay 1994) lowers it to 0.62.

The β column has been recalculated using Δ = 0.28 as the denominator.
The updated values are: 0.54 · 1.29 · 0.54 · 0.64 · 0.79 · 0.68 · 0.89 · 0.39.
The exact median is 0.66.

For consistency across the manuscript we retain β = 0.67 (rounded to two decimal places); the 0.01 difference is < 2 % in relative terms and has no material impact on β_{pooled} (0.69 vs 0.67) or on the final RR_{hosp} estimate (1.192 vs 1.188).

Supplementary Table S47. Sensitivity analysis – impact of uncertainty in Δ and β on RR_{hosp}

ΔN_{hit} / N_{hit}	β	$RR_{hosp} = 1 + \beta \cdot \Delta$
0.25	0.60	1.15
0.25	0.67	1.17
0.25	0.85	1.21
0.29	0.60	1.17
0.29	0.67	1.19
0.29	0.85	1.25
0.33	0.60	1.20
0.33	0.67	1.22
0.33	0.85	1.28

Legend: Δ – relative increase in N_{hit} (0.25 – 0.33, ± 15 %);

The span β = 0.60 – 0.85 covers the leave-one-out interval (0.62 – 0.70) and the upper section of the 95 % CI.
The lower 95 % bound (β = 0.48) would give RR ≈ 1.14 for Δ = 0.28 and can be obtained by linear interpolation.

Supplementary Table S48. Margins at V_{margin} = 5.7 mV (± 10 %)

Parameter	Nominal value	± 10 % range
V_{margin}	5.7 mV	5.13 – 6.27 mV
Margin after – 55 %	2.57 mV	2.31 – 2.82 mV
Caffeine (1 mV)	1.57 mV	1.40 – 1.74 mV

Supplementary Table S49. Matrix of parameter transfer – fear loop (schizophrenia)

#	Parameter / effect	Original region & species	Source (year)	Value in source	Rule	k	Model use	Evidence	Timescale
1	DA ↑ (fear reminder) †	mPFC, rat	(Yoshioka et al. 1996)	Significant DA increase (microdialysis)	R4	1.0	Neuromodulatory gain	Qnt	minutes
2	Cortisol ↑ (acute stress) †	Saliva, human	(Schwabe and Wolf 2012)	Robust AUC elevation	R4	1.0	Global hormonal drive	Qnt	minutes –hours

				with stressors					
3	4 Hz mPFC–VTA coupling; θ-locking to HPC †	mPFC–VTA–HPC, rat	(Fujisawa and Buzsáki 2011)	4 Hz mPFC–VTA rhythm (δ/θ border), θ-locked to HPC	R2	1.0	Tempo-phase coordination	Qnt	seconds
4	Glutamatergic metabolite ↓	mPFC, human	(Rowland et al. 2016)	Glx lower by ~0.6 IU vs controls	R1	1.0	E/I shift (glutamatergic tone)	Qnt	chronic
5	GABA ↓ (older SZ)	mPFC, human	(Rowland et al. 2016)	Lower GABA in older cohort	R1	1.0	E/I shift (inhibitory tone)	Qnt	chronic
6	Redox dysregulation (GSH↓) → PV vulnerability †	PFC/HPC, rodent & human	(Cabungcal et al. 2013; Steullet et al. 2017; Perkins et al. 2020)	PV-IN sensitive to GSH deficit	R1	1.0	Redox → PV/PNN axis	Ql/Qnt	chronic
7	PNN density ↓	DLPFC, human	(Mauney et al. 2013)	~70–76% reduction (layers III/V)	R1	1.0	PV network destabilisation	Qnt	chronic
8	PV-IR neurons ↓ (stress) †	Hippocampus, tree shrew	(Czeh et al. 2005)	−28% to −33%	R1	1.0	PV loss proxy	Qnt	weeks
9	θ–γ PAC ↑ during AVH †	Left frontotemporal, human	(Koutsoukos et al. 2013)	Increased θ–γ coupling (AVH)	R2	1.0	State marker	Qnt	state-dependent
10	β/γ synchrony deficits	Cortex, human	(Uhlhaas and Singer 2010)	Reduced γ/β power & synchrony	R1/R2	1.0	Network signature	Ql/Qnt	chronic
11	Apical dendrites −20% †	mPFC (II/III), rat	(Radley et al. 2004)	~20% shortening (chronic stress)	R1	1.0	Validation anchor (top-down)	Qnt	weeks
12	BDNF H3/H4 acetylation ↑ (fear) †	Hippocampus, mouse	(Lubin et al. 2008)	Increased promoter acetylation	R1	1.0	Plasticity stabilisation	Qnt	hours–days
13	AMPAR synaptic incorporation ↑ †	Lateral amygdala, rodent	(Rumpel et al. 2005)	AMPAR insertion after fear	R1	1.0	Limbic potentiation	Qnt	hours–days

Legend: † measured outside vCA1; transferred per R-rules; k = 1.0 unless stated. Evidence: Qnt quantitative; Ql qualitative. Timescale refers to the source paradigm.

Supplementary Table S50 — Matrix of parameter transfer: sadness loop (MDD)

#	Parameter / effect	Original region & species	Source (year)	Value in source	Rule†	k	Model use	Timescale

1	HVA ↓; 5-HIAA n.s. (dopamine proxy)	CSF, human	(Ogawa et al. 2018)	HVA g≈−0.30; 5-HIAA n.s.	R4	1.0	Global monoaminergic set-point	cross-sectional meta
2	CSF CRF ↑	CSF, human	(Nemeroff et al. 1984)	Elevated vs controls (RIAs)	R4	1.0	HPA/CRF disinhibition	minutes–hours
3	GABA ↓; Glx trend ↓ (E/I tilt)	sgACC/ACC, human (MRS; meta-analiza)	(Godfrey et al. 2018)	GABA reduction; Glx ↓ trend	R1	1.0	Local E/I shift	chronic
4	Redox dysregulation → PV vulnerability	PFC/HPC, rodent & human transl.	(Cabungcal et al. 2013; Steullet et al. 2017)	PNNs protect PV; redox load injures PV	R1	1.0	Redox→PNN/PV axis	weeks–chronic
5	PNN density ↓ (depression-like)	PrL mPFC, rat	(Yu et al. 2020)	Decreased PNNs under CUMS	R1	1.0	PV network destabilisation	weeks
6	Altered α/β power (rumination-linked	Scalp EEG, human	(Forner-Phillips et al. 2020)	Altered α/β dynamics with rumination (direction context-dependent)	R2/R4	—	Network signature	task-state
7	PCC↔sgPFC connectivity ↑ (rumination)	EEG connectivity, human	(Benschop et al. 2021)	Elevated functional connectivity vs controls; correlates with rumination	R2	—	DMN coupling marker	resting-state
8	Synapse/spine reduction in dlPFC	dlPFC, human post-mortem	(Kang et al. 2012)	↓ synapse-related genes; ↓ synapses	R1	1.0	Morphology anchor	chronic
9	ACC GM loss explained by spine/dendrite loss	ACC/HPC, mouse	(Kassem et al. 2013)	ACC GM −10%; spine loss up to ~60%; dendritic length −40%	R1	1.0	Morphology anchor	weeks
10	Stress → dendritic/spine loss in PFC (review)	PFC, rodent/human	(Qiao et al. 2016)	Robust dendritic atrophy/spine loss	descriptive	—	Convergent evidence	review

† Variables measured outside vCA1; transferred according to Supplementary Methods S2.18.1 with k = 1.0. Values are differences vs control where reported; otherwise qualitative.

Supplementary Table S51 — Matrix of parameter transfer: trauma loop (PTSD)

#	Parameter / effect	Original region & species	Source (year)	Value in source	Rule†	k	Model use	Timescale
1	NE release with LC→BLA activation †	BLA, mouse	(McCall et al. 2017)	Robust NE release (FSCV); β-AR-dependent anxiety	R4	1.0	Neuromodulatory gain	seconds–minutes
2	DA modulation of BLA excitability †	BLA, rat	(Rosenkranz and Grace 2002)	DA increases principal-cell excitability	R4	1.0	Limbic salience bias	minutes–hours
3	CSF CRF ↑ in PTSD †	CSF, human	(Bremner et al. 1997)	Higher CRF vs controls	R4	1.0	Global HPA/CRF drive	minutes–hours
4a	Hippocampal Glu ↑ (7 T) †	R hippocampus, human	(Rosso et al. 2017)	Glu higher in PTSD	R1	1.0	Local E/I tilt	chronic
4b	Insular GABA ↓ (7 T) †	Ant. insula, human	(Rosso et al. 2014)	~30% lower GABA/Cr	R2 (δ/θ coupling)	1.0	Local E/I tilt	chronic
5	CA1 E_GABA depolarizing shift †	dCA1, rodent	(PVN: Inoue et al. 2013; dCA1: MacKenzie and Maguire 2015)	Depolarizing shift after stress	R2	—	Inhibitory weakening	days–weeks
6	PV/PNN vulnerability	PFC/HPC/limbic	(Cabungcal et al. 2013; Perlman et al. 2021)	PV sensitive to redox; PNN involvement	R1	1.0	γ-network fragility	weeks–chronic
7	PNN alterations with stress	Limbic cortex	(Murthy et al. 2019; Fawcett et al. 2022)	Stress/ELS alter PNNs & ECM	R1	1.0	Consolidation substrate	weeks–chronic
8	vmPFC hypoactivity during recall †	vmPFC, human	(Shin and Liberzon 2010)	Hypoactivity in PTSD recall	R4	1.0	Executive control ↓	state-dependent
9	α suppression / fast-band abnormalities †	MEG/EEG, human	(Dunkley et al. 2015; Shaw et al. 2023)	Altered α power and frequency-specific fast-band changes during trauma-related processing	R4	—	Oscillatory signature	state-dependent
10	BDNF promoter methylation ↑ †	mPFC, rodent	(Roth et al. 2009)	↑ methylation with stress	R1	—	Plasticity lock-in	days–weeks

1 1	vCA1↔BA plasticity facilit.	BA↔vCA1, rodent	(Kim and Cho 2020; Sun et al. 2020)	Fear learning enables synaptic LTP	R1	—	Engram susceptibility	hours–days

† Variables measured outside vCA1; transferred per Supplementary Methods S2.18.1 (R-rules) with k = 1.0. Values are differences vs. control where reported; otherwise directional.

Supplementary Table S52. Rescue E⁺ protocol (precision window)

Phase	Activated axes	Mechanistic class (examples only)	Intended biophysical / network effect	Decision gate & outcomes
Preparation	–	Safety screen (ECG/SpO_2/electrolytes per SOP)	Eligibility for session	Proceed vs reschedule
Reconsolidation window	C (+D)	Plasticity window opener (class level; parameters locked in SAP)	Transient ↑ plasticity / BDNF window enabling targeted engram modification	Window achieved (Y/N)
Entrainment overlay	D (phenotype-specific band)	Oscillatory entrainment in target band (class-level; parameters locked)	Narrower γ/θ window; ↑ PV "brake"	PAC width ↓ vs baseline
Low-ELF context	F (optional if relevant per pre-specified criteria)	ELF-attenuated environment (quality index Q_{ELF} pre-specified)	Reduce phase-locked reactivation	Q_{ELF} achieved (Y/N)
Engram rewrite	E	CBT-p / EMDR / recall+β-blockade (class-level only)	Damp hot spot reactivation	EMA intrusions ↓ (expl.)
Assessment	–	PET-KCC2 (if available), MEG γ-burst, 5-min HRV	Map to ΔV_{margin} per Supplementary Discussion SD8	Session success per E⁺ criteria (see Supplementary Discussion SD9.4)

The table lists mechanistic classes, decision gates and outcome rules only; operational parameters (timings, doses, device settings) will be specified in the SAP at trial registration.

Supplementary Table S53. β-loop (ELF → clinic): three-stage causal test before activating axis F

Stage	Research question	Data / analysis	Success criterion
0 — Geomagnetic storms (retrospective 5–10 yr)	Does $K_p \geq 6$ (± 48 h) or ΔFWHM 7.83 Hz ≥ 13 % increase daily ICD-10 F + I admissions?	ΔFWHM from global SRN stations (35°–65° N/S); admissions from WHO / Eurostat / HCUP; quasi-Poisson GAM (nspline DOY + DOW + T_{max} + RH).	95 % CI of β_{macro} excludes 0
1 — Daily noise (prospective 12 mo)	Do day-to-day fluctuations of the 7.83 Hz peak (ΔFWHM, Hz; amplitude, Arms in pT; lags 0–7 d) predict admissions?	1–300 Hz magnetometer (≤ 1 pT RMS); 1-h FFT windows; DLNM.	β_{micro} ($p < 0.05$) with the same sign as β_{macro}

2 — Bayesian hierarchy (after 24 mo)	Does $\beta_{pooled} \neq 0$ after adjusting for season / weather / smog?	Hierarchical model (countries / cities); prior N(0, 1); $\hat{R} < 1.1$.	95 % CrI of β_{pooled} excludes 0

FWHM is reported in Hz (peak width), amplitude as A_{rms} in pT; both are extracted from 1-h FFT windows. The primary β_{macro} endpoint uses ΔFWHM; amplitude is a pre-specified sensitivity analysis.

Assumptions & quality control

- ELF data: SRN stations within ± 10° geomagnetic latitude; urban magnetometer calibrated in a μ-metal chamber.
- Hospital admissions: ICD-10 F00–F99 + I00–I99, UTC day 00–24 h.
- Control variables: DOY, DOW, T_{max}, RH; sensitivity analyses include $PM_{2.5}$ (CAMS EU) and a "COVID dummy."
- Statistical power (α = 0.05): stage 0 > 0.99; stage 1 ≈ 0.85 (β ≈ 0.04, N = 365).

Supplementary Table S54. PET KCC2 → ΔE_{GABA} → ΔV_{margin} (ROI vCA1; SUVR normalised to cerebellum)

Step	Equation / Assumption	Input data	Result (+15 % SUVR)	Sources
1	$\Delta[Cl^-]_i$ (%) ≈ –0.90 × ΔSUVR (%)	+15 % SUVR	–13.5 %	(Keramidis et al. 2023)
2	ΔE_{GABA} (mV) ≈ 0.267 mV × $\Delta[Cl^-]_i$ (%) (37 °C; first-order Nernst linearisation around baseline $[Cl^-]_i$) *Full (non-linear) form at 37 °C: ΔE_{GABA} = 26.7 mV × ln(1 + $\Delta[Cl^-]_{i,frac}$), where $\Delta[Cl^-]_{i,frac}$ = $\Delta[Cl^-]_i$(%) / 100.	–13.5 %	–3.60 mV	Nernst equation @ 37 °C
3	ΔV_{margin} (mV) ≈ −0.60 × ΔE_{GABA}	–3.60 mV	+2.16 mV	Table SD8

The factor 0.60 accounts for partial contribution of E_{GABA} to the total excitability margin within the PET-defined vCA1 ROI, based on simulations with g_{Cl} = 0.15 and the relative weighting of somatic versus dendritic compartments. Without this correction the relationship would be 1:1, as in Supplementary Methods 2.10.3.

Coefficient –0.90 was chosen as a conservative scaling factor informed by the effect sizes for KCC2 restoration and chloride homeostasis in (Keramidis et al. 2023); see Supplementary Methods 2.10.3.

Supplementary Table S55. MEG γ burst → $\Delta gain_{dend}$ → ΔV_{margin}

Step	Equation / assumption	Input data	Result (–35 % γ burst)	Source / note
1	$\Delta gain_{dend}$ (%) ≈ 0.90 × Δburst (%)	–35 %	–31.5 %	NEURON simulation (*gamma_gain.hoc*)
2	$\Delta V_{effEPSP}$ (mV) ≈ 0.032 mV × $\Delta gain_{dend}$ (%)	–31.5 %	–1.0 mV	(Kim and Johnston 2015; Malik and Johnston 2017)
3	ΔV_{margin} (mV) ≈ − $\Delta V_{effEPSP}$	–1.0 mV	+1.0 mV	Multicompartment model

95 % confidence interval for the coefficient 0.032 mV %⁻¹: 0.028 – 0.036 mV %⁻¹ (patch-clamp, n = 48).

Supplementary Table S56. HRV (rMSSD) → ΔV_{rest} → ΔV_{margin}

Step	Equation / assumption	Input data	Result (+5 ms rMSSD)	Source / note
1	ΔV_{rest} (mV) ≈ – 0.08 mV·ms⁻¹ × ΔrMSSD	+5 ms	–0.40 mV	(Rowland et al. 2016; Keerthy et al. 2021)
2	$\Delta V_{margin} \approx -\Delta V_{rest}$	–0.40 mV	+0.40 mV	Margin definition

The −0.08 mV·ms⁻¹ coefficient was estimated from a meta-regression of HRV versus excitability (patch-clamp n = 54 plus TMS-MEP/MRS studies) and will be re-validated empirically in the pilot phase.

Interpretative conversion to ΔV_{margin}; gating of the pilot relies on MEG primary per Supplementary Discussion SD9.4; HRV is supportive/auxiliary.

Supplementary Table S57. Projected sensitivity of HRV (rMSSD) and its contribution to ΔV_{margin} in the pilot study

Sub-cohort*	N (planned)	rMSSD baseline (mean ± SD, ms)	Δ rMSSD at $T_{4\ weeks}$ ± SE (ms)‡	p (paired t)	Estimated contribution ΔV_{margin} (mV)§
A – "low stim" (caffeine < 200 mg day⁻¹ & nicotine < 5 cig day⁻¹)	17	27.8 ± 7.1	+5.6 ± 1.2	0.001	+0.45
B – "high stim" (caffeine ≥ 200 mg day⁻¹ or nicotine ≥ 5 cig day⁻¹)	13	24.2 ± 8.4	+2.1 ± 1.5	0.09	+0.17
Combined (A + B)	30	26.2 ± 7.8	+4.1 ± 1.0	0.002	+0.33

* Split by daily caffeine and nicotine intake; cohort B has lower planned power (~0.56 for an expected +5 ms effect; see †) and is considered exploratory.

† Power calculation for α = 0.05, expected effect +5 ms, SD = 5 ms: power ≈ 0.82 (package *pwr* v1.3, R 4.4).

‡SE = SD / √N; $SD_{\text{low stim}}$ = 5 ms, $SD_{\text{high stim}}$ = 7 ms (Shaffer and Ginsberg 2017). § Conversion uses a conservative composite coefficient of 0.08 mV·ms^{-1}.

This estimate is anchored in patch-clamp CA1 data showing mV-scale changes in excitability per ΔE_{GABA} shift (Rowland et al. 2016), and scaled using published autonomic–excitability coupling slopes relating rMSSD to cortical excitability (MEP amplitude and intracortical inhibition) (Keerthy et al. 2021).

The coefficient is intentionally conservative and used only for order-of-magnitude estimation.

Supplementary Table S58. Rescue F (ELF screen)

Block	Exposure mode	Environment spec (public)	Parallel A–D / E procedures	Mandatory assessments	Exit criterion
F-Block A	Continuous ELF attenuation (duty-cycle target pre-specified)	Meets Q_{ELF} index (unitless quality score defined in SAP)	Standard A–D cycle; 1 session of E inside environment (timing pre-specified)	MEG γ-burst; ΔV_{margin} composite	Meet ≥ 1: γ-burst ↓ ≥ 35 % or PET KCC2 ↑ ≥ 15 % (exploratory, if available) or $\Delta V_{margin} \geq +3$ mV.
F-Block B (optional)	Extended attenuation (same duty-cycle)	Q_{ELF} maintained	Continue A–D; optional neuromodulatory adjuncts (class-level only)	Repeat measures	Same as above

Inclusion for Rescue F (public): $\Delta V_{margin} < 3$ mV despite ≥ 1 E^{+}; β-loop stages 0–2 positive; consent to continuous attenuation.

PET KCC2 is an exploratory biomarker; tracers are under development and may not be available at study initiation.

The table lists exposure modes, quality criteria (Q_{ELF}) and decision rules only; operational specifications will be pre-specified in the SAP at trial registration.

Q_{ELF} is a unitless pass/fail quality index derived from blinded device logs against pre-specified attenuation/stability bands; numeric thresholds are defined in the SAP.

Supplementary Table S59. Secondary or domain-specific limitations

Area / module	Technical or secondary limitation
Valence cascades	The valence-tuned neuromodulatory cascades (fear, sadness, trauma) are reconstructed via reverse-engineering from convergent but separate literatures rather than demonstrated as a single, continuous causal chain within one model system. The proposed sequences (e.g., fear-biased replay → DA/CRF surges → oxidative load → PNN/PV erosion → γ desynchronisation) integrate results from patch-clamp, behavioural, imaging and molecular studies performed in different species, paradigms and timescales. No in-vivo experiment has yet combined a low-ΔV_{margin} state with repeated engram-specific reactivation over days–weeks to observe the full cascade in one preparation. These pathways should therefore be

	interpreted as mechanistically coherent hypotheses generated from convergent evidence, not as experimentally verified end-to-end trajectories.
Biomarker coverage	Current biomarkers capture only a fraction of the putative 7–9 mV range: MEG γ-burst and HRV rMSSD likely constrain ~20–25% of ΔV_{margin}, with PET-KCC2 raising coverage toward ~70–80%. Near-complete mapping will require next-generation ligands, particularly PET Kir4.1 and PET PV, which are not yet available. Nevertheless, the present biomarker panel is sufficient for falsifying the central ΔV_{margin} predictions at the population level, while full mV-level coverage would mainly enable precise remission forecasting and individualised threshold estimation.
Replay load	Replay load (N_{hit}) is treated as a static driver of short-term risk. It remains unknown whether chronic high replay in stress-sensitised circuits leads to homeostatic recovery or to progressive structural vulnerability (e.g., dendritic spine loss, interneuron stress or persistent ΔV_{margin} lowering). Our use of N_{hit} is therefore conservative and does not address long-term circuit evolution. These uncertainties motivate, rather than undermine, the proposed future experiments.
Axis F – urban ELF fields and Schumann-resonance sub-branch	For urban rail-power exposure around 16.7 Hz at $B_{rms} \approx 0.15$ μT, the magnetite-chain model yields $\Delta V_{soma} \approx 0.06$ mV, corresponding to roughly 1% of the residual excitability margin in our CRS → hot-spot → allele scenarios. In principle, such a subthreshold bias could contribute a small phase modulation of θ/ripple timing in chronically stress-primed, low-ΔV_{margin} networks with weakened PV/γ control, although this remains untested. By contrast, even under the upper-bound parameterisation, the 7.83 Hz Schumann mode at ≈ 1 pT produces ΔV_{soma} values that remain ~10^5–10^6-fold below the phase-locking criterion, even for pathologically reduced ΔV_{margin} (see Supplementary Methods S2.11). Any effect of the fundamental Schumann mode would therefore require critically narrowed excitability margins, summation over very large ensembles and many repeated cycles, and favourable coherence of both the field and the theta generator. These conditions have not yet been tested in chronically stressed human vCA1. Existing EEG–Schumann studies have so far focused on healthy participants and macroscopic spectral correlations; some report partial α/θ–Schumann convergence, others do not, and overall the evidence is inconsistent and non-specific. They therefore neither confirm nor refute the conditional, low-ΔV_{margin}, ensemble-based phase-bias mechanism considered here. In the present EMM, the Schumann sub-branch is treated only as a boundary-case phase perturbation, not as a robust driver of replay or symptoms.

Supplementary Table S60. Detailed research directions and proposed methods

Research goal / knowledge gap	Key methods
Micro-to-meso calibration of ΔV_{margin} in ventral CA1.	Stress-sensitised rodent models with CRS ± risk-allele knock-in; laminar vCA1 LFP and unit recordings during θ/SWR; perforated-patch measurements of V_{rest}, V_{thr} and E_{GABA} in identified pyramidal cells; dynamic-clamp to impose "CRS → hot-spot → allele" stacks; parallel source-resolved MEG in patients to derive meso-scale gain curves that can be linked back to cellular ΔV_{margin}.
Long-term impact of elevated replay load (N_{hit}) on circuit integrity.	Longitudinal in-vivo calcium imaging or multi-unit recordings in vCA1–BLA–mPFC during repeated emotional-memory reactivation in stress-sensitised animals; chronic manipulation of replay rate (e.g. optogenetic cueing) to generate low- vs high-N_{hit} trajectories; post-hoc morphometry (pyramidal dendrites, PV/PNN integrity, KCC2/NKA expression). Computational models incorporating slow structural plasticity (activity-dependent spine loss, inhibitory rebalancing) to test whether very high N_{hit} leads to a stable attractor or progressive failure of ΔV_{margin}.
Positive engrams and "protective replay" trajectories.	Future work could test whether sustained activation of positively valenced engrams has long-term effects on excitability margins that differ from those seen with negatively valenced content. In stress-sensitised animals, activity-dependent tagging and reactivation of positively valenced vCA1–BLA–mPFC engrams (e.g. via opto/chemogenetics) could be combined with measurements of ΔV_{margin}-linked variables (V_{rest}, V_{thr}, R_{in}, E_{GABA}, γ/θ coupling) and autonomic output (HRV), together with morphometric readouts of PV/PNN integrity and dendritic structure. In humans, neurofeedback or imaging paradigms that up-regulate positive affect while tracking vCA1–amygdala connectivity and MEG γ-burst metrics could probe whether positive-valence replay is associated with stabilisation or widening of ΔV_{margin}, or whether it remains neutral. These studies would explore whether the valence of replayed content

	systematically biases the long-term stability of ΔV_{margin}, without implying any specific clinical intervention.
Second-generation "mV-meter": closer to full ΔV_{margin} coverage.	Development and validation of PET ligands for Kir4.1 and PV, combined with existing PET-KCC2 to expand coverage of the excitability margin. Joint modelling of MEG γ-burst, HRV rMSSD and PET signals across symptom states would yield multi-modal estimates of ΔV_{margin}, calibrated against invasive measurements in animal models to define remission-grade thresholds.
Identification of an ELF biosensor (conditional on positive β-loop).	In-vitro screens of candidate field-sensitive structures (magnetite assemblies, cryptochromes, TRP channels, disordered protein aggregates) in low-ΔV_{margin} networks; application of weak 7–30 Hz magnetic fields at environmentally relevant amplitudes; readouts: changes in membrane potential, spike timing, θ/γ phase relationships and phase-locking statistics. Use of pharmacological / genetic perturbations to test necessity of specific biosensors for any observed phase bias.
Phenotype extrapolation: narrow-margin disorders beyond SZ, MDD and PTSD.	Systematic estimation of region-specific ΔV_{margin} in candidate ignition sites across disorders (GAD, ChAD/BD, ADHD, OCD, high-functioning autism/Asperger, Rett, Fragile X, TLE, Dravet, SCN8A EIEE, KCNQ2 EE, Alzheimer's/MCI, Parkinson's cognitive subtype, MS + epilepsy, chronic migraine, addictions). Approaches: laminar LFP/MEG and oscillatory fingerprints in patients; matched animal models with patch-clamp measurements; mapping of chronic triggers (IL-6/TNFα, DA surges, Aβ/ROS, channelopathies) onto ΔV_{margin} changes. Test whether each phenotype corresponds to collapse of the same ΔV_{margin} threshold in distinct network loci (PFC–LC, CA3/dCA1, CSTC, entorhinal–dorsal hippocampus, etc.).
End-to-end validation of valence-tuned neuromodulatory cascades under low-ΔV_{margin} conditions	A feasible, hypothesis-driven multi-stage research programme could combine complementary approaches to explore whether, under experimentally narrowed ΔV_{margin}, chronically elevated replay load from engrams of defined valence drives distinct neuromodulatory trajectories. In stress-sensitised mice (CRS/CUS), activity-dependent tagging of vCA1→BLA engrams of different valences (fear, anhedonia-like, trauma-intensity) could be performed in separate cohorts. Low-ΔV_{margin} states could be induced using established manipulations (e.g., mild vCA1 KCC2 reduction, IL-6 mimetics, or combined stress plus a single genetic susceptibility factor), after which each valence-tagged engram would be repeatedly reactivated over days to weeks—using natural cues or opto/chemogenetic recall—to approximate a high replay-load regime (order-of-magnitude ≈10^3–10^4 unintended activations per day, as suggested by the model). Early-phase readouts (days to ~3 weeks) could include neuromodulatory signatures (DA/NA/CRF and corticosterone proxies), local E/I indicators (Glx/GABA ratios, E_{GABA} shifts, R_{in}), and circuit-level dynamics (θ/γ coupling and replay rate across vCA1↔BLA↔mPFC), alongside behavioural outputs (psychosis-like, anhedonic and avoidance phenotypes). Late-phase readouts (≥3–6 weeks) could examine redox/GSH status, microglial engagement, PV/PNN integrity and dendritic morphology in mPFC and amygdala. In humans, the potential daily replay-hit window can only be coarsely approximated using EEG/MEG markers — including hippocampal ripple proxies, burstiness, micro-events and phase-slip dynamics — which, under high rumination, intrusive thought, auditory verbal hallucination or OCD-like perseveration, may reach the 10^3–10^4 range per day. These estimates refer to replay-permissive burst opportunities rather than conscious thought episodes and are intended as model-informed order-of-magnitude bounds rather than direct measurements. Across this programme, the central hypothesis test would be whether, under broadly matched low-ΔV_{margin} conditions and chronically high replay load, engrams of different valence tend to bias distinct neuromodulatory and oscillatory cascades in a reproducible way, yielding SZ-like, MDD-like or PTSD-like signatures at the level of circuit dynamics and behaviour, as predicted by the EMM. Any such programme would be technically demanding and long-term, but it provides a conceptually direct route to end-to-end validation (or falsification) of the valence-tuned cascade component of the model.

Supplementary Table S61. Hypothetical triggers that may launch the ΔV_{margin} narrowing cascade in clinical phenotypes other than SZ, MDD, and PTSD

Phenotype	Chronic trigger	Dominant neuromod./cytokine axis	Expected network motif	Documentation of four markers*

GAD	"Worry loop" without extinction phase	CRF ↑ + tonic LC-NE	θ with β (15–25 Hz)	✓ τ_{EPSP}, PV, R_{in} ✗ V_{thr}
ChAD / BD	Repeated DA surges in mania	DA ↑ + cortical Glu→vHPC	γ 35–50 Hz ↔ θ	✓ τ_{EPSP}, PV ~ R_{in} ✗ V_{thr}
ASD (FMR1, MECP2)	Early sensory-social overload	5-HT / OXT ↓, mGluR5 ↑	δ–θ dominant, γ deficit	✓ τ_{EPSP}, PV, R_{in} ✗ V_{thr}
TLE	Partial seizures – Glu/K^+ re-entry	ACh & NE bursts	δ–θ interictal, high γ ictal	✓ (full)
Addictions	Cue-induced craving (NAc↔vCA1)	DA ↑ + Glu potentiation	β–γ "salience burst"	✓ τ_{EPSP}, PV ~ R_{in}, V_{thr}
AD / MCI	Aβ-driven "memory wandering"	Aβ → ROS → IL-1β	θ–β dominant, γ deficit	✓ (full)
MS + epilepsy	Chronic IL-6 / TNFα	NKCC1 ↑, Kir ↓	δ–θ + epileptiform γ	✓ τ_{EPSP}, PV, R_{in} ~ V_{thr}
Dravet (SCN1A LoF)	Febrile seizures, Nav1.1 PV ↓	Homeostatic NE / ACh	high γ / fast ripples	✓ (full)
SCN8A EIEE	SCN8A GoF, Nav1.6 hyper	Nav-driven intrinsic burst	very high γ / FR	✓ τ_{EPSP}, PV, R_{in}, V_{thr}
KCNQ2 EE	KCNQ2 LoF (M-current ↓)	Intrinsic excitability ↑	broad γ shift	✓ τ_{EPSP}, PV ✗ R_{in}, V_{thr}
OCD	"Error loop" cortico-striatal	DA ↑ + 5-HT ↓	high β-γ in CSTC	~ τ_{EPSP}, PV; others weak
ADHD	Early stress / sleep loss / high-sugar diet	LC-NE & DA hypofunction (PFC)	↑θ/β ratio, γ deficit (fronto-hippocampal)	~ τEPSP, PV; ✗ Rin, Vthr
High-functioning autism / Asperger	Sustained sensory overload	5-HT/OXT ↓, E/I shift	δ–θ ↑, γ coherence ↓	~ τEPSP, PV; ✗ Rin, Vthr
Chronic migraine	Recurrent cortical spreading depolarisation	Glu ↑, CGRP ↑, TRP ↑	α suppression, paroxysmal γ	~ τEPSP; ✗ PV, Rin, Vthr
Parkinson's (cognitive)	DA depletion + cholinergic dysregul.	DA ↓, ACh ↑, NE ↓	θ–β ↑, hippocampal γ coupling ↓	~ τEPSP; ✗ PV, Rin, Vthr
Tourette/OCD spectrum	Habit loop overtraining	DA ↑ in CSTC	β–γ bursts (CSTC)	~ (network); ✗ cellular

* ✓ = ≥ 1 patch-clamp or in vivo study; ~ = partial data; ✗ = gap highlighted in the text.

Supplementary Table S62. List of Abbreviations

Abbreviation	Full term / definition
1H-MRS	Proton magnetic resonance spectroscopy
23Na-MRI	Sodium-23 magnetic resonance imaging
5-HIAA	5-Hydroxyindoleacetic acid
5-HT	5-Hydroxytryptamine (serotonin)
5-HT1A	5-HT1A receptor
A1	Adenosine A1 receptor
ACC	Anterior cingulate cortex
ACh	Acetylcholine
ACS	Acute coronary syndrome
ACSF	Artificial cerebrospinal fluid
AD	Alzheimer's disease
AD/MCI	Alzheimer's disease / mild cognitive impairment
ADHD	Attention-deficit/hyperactivity disorder
ADP	Adenosine diphosphate

AE	Adverse event
AGE	Advanced glycation endproduct
AGEs	Advanced glycation endproducts
AHP	Afterhyperpolarisation
AIS	Axon initial segment
AMPA	α-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
AMPAR	AMPA receptor
AMPH	Amphetamine
Ams	Root mean square magnetic field amplitude
ASD	Autism spectrum disorder
ATP	Adenosine triphosphate
Att	Electrotonic attenuation factor
AUC	Area under the curve
AVH	Auditory verbal hallucinations
Axis A	Axis A of FAR (ionic buffer / astroglial support axis)
Axis B	Axis B of FAR (chloride reset / KCC2–NKCC1 axis)
Axis C	Axis C of FAR (plasticity window / neuromodulatory gating)
Axis D	Axis D of FAR (oscillatory entrainment axis)
Axis E	Axis E of FAR (engram rewrite / CBT-EMDR axis)
Axis F	Axis F of FAR (ELF attenuation / screen axis)
Aβ	Amyloid-β peptide
BA25	Brodmann area 25 (subgenual cingulate)
BA32/24	Brodmann areas 32/24 (medial prefrontal / cingulate)
BA9	Brodmann area 9 (dorsolateral prefrontal cortex)
BD	Bipolar disorder
BDNF	Brain-derived neurotrophic factor
BfS	Bundesamt für Strahlenschutz (German radiation protection office)
BLA	Basolateral amygdala
BOLD	Blood-oxygen-level-dependent signal
BPRS	Brief Psychiatric Rating Scale
Brms	Root mean square magnetic flux density
C4A	Complement component 4A
CA1	Cornu ammonis 1 (hippocampal subfield)
CA2	Cornu ammonis 2 (hippocampal subfield)
CA3	Cornu ammonis 3 (hippocampal subfield)
CACNA1C	Calcium voltage-gated channel subunit alpha1 C
CaMKII	Calcium/calmodulin-dependent protein kinase II
CAMS	Copernicus Atmosphere Monitoring Service
CAPEX	Capital expenditure
CAPS-5	Clinician-Administered PTSD Scale for DSM-5
CaV1.2	L-type voltage-gated calcium channel Cav1.2
Ca^{2+}	Calcium ion
CBT	Cognitive behavioural therapy
CBT p	Cognitive behavioural therapy for psychosis
CC BY 4.0	Creative Commons Attribution 4.0 International licence
CEST	Chemical exchange saturation transfer (MRI)
CGRP	Calcitonin gene-related peptide
ChAD/BD	Recurrent depressive disorder / bipolar disorder
CI	Confidence interval
CIE	Chronic intermittent ethanol
ClinicalTrials.gov	ClinicalTrials.gov trial registry
ClopHensorN	Genetically encoded chloride/pH sensor ClopHensorN
CLP 257	Experimental KCC2 positive allosteric modulator CLP-257
COMT	Catechol-O-methyltransferase
COVID	Coronavirus disease 2019
CP-AMPAR	Ca^{2+}-permeable AMPA receptor
CRF	Corticotropin-releasing factor

CrI	Bayesian credible interval
CRS	Chronic restraint stress
CSF	Cerebrospinal fluid
CSTC	Cortico–striato–thalamo–cortical circuit
CUMS	Chronic unpredictable mild stress
DA	Dopamine
dCA1	Dorsal CA1
deep TMS	Deep transcranial magnetic stimulation
DG	Dentate gyrus
dHPC	Dorsal hippocampus
DLNM	Distributed lag non-linear model
DLPFC	Dorsolateral prefrontal cortex
DMN	Default mode network
dmPFC	Dorsomedial prefrontal cortex
DOI	Digital object identifier
DOW	Day of week
DOY	Day of year
DSMB	Data and Safety Monitoring Board
dTMS	Deep transcranial magnetic stimulation
E/I	Excitation/inhibition balance
EC	Entorhinal cortex
ECG	Electrocardiogram
ECS	Extracellular space
EE	Epileptic encephalopathy
EEG	Electroencephalogram
EFSA	European Food Safety Authority
E_{GABA}	GABAA reversal potential
EIEE	Early infantile epileptic encephalopathy
ELF	Extremely low-frequency electromagnetic field
EMA	Ecological momentary assessment
EMDR	Eye movement desensitisation and reprocessing
EMM	Excitability-Margin Model
EPA	Eicosapentaenoic acid
EPSC	Excitatory postsynaptic current
EPSP	Excitatory postsynaptic potential
EPSPs	Excitatory postsynaptic potentials
FAR	Four-Axis Reset
FDR	False discovery rate
FEP	First-episode psychosis
FMR1	Fragile X mental retardation 1 gene
FS	Fast-spiking (interneuron)
FWHM	Full width at half maximum
GABA	Gamma-aminobutyric acid
GABAA	GABAA receptor
GABRA1	GABAA receptor α1 subunit
GAD	Generalised anxiety disorder
GAM	Generalised additive model
GBD	Global Burden of Disease study
GBM	Gradient boosting machine
GENUS	Gamma Entrainment Using Sensory stimuli
GHO	WHO Global Health Observatory
GI	Glycaemic index
ginh	Inhibitory synaptic conductance
GIRK	G protein-activated inward-rectifying K^+ channel
GL	Glycaemic load
GLT-1	Glutamate transporter GLT-1 (EAAT2)
Glu	Glutamate
GluN	NMDA receptor GluN subunit family

Glx	Glutamate + glutamine (MRS peak)
GM	Grey matter
GoF	Gain-of-function (mutation)
GSH	Glutathione
HAM A	Hamilton Anxiety Rating Scale
HapICE	Neuregulin-1 (NRG1) schizophrenia-risk haplotype (Icelandic)
HCN	Hyperpolarisation-activated cyclic nucleotide-gated channel
HCUP	Healthcare Cost and Utilization Project
HDRS	Hamilton Depression Rating Scale
HPA	Hypothalamic–pituitary–adrenal axis
HPC	Hippocampus
HRV	Heart rate variability
HVA	Homovanillic acid
i.v.	Intravenous
ICD-10	International Classification of Diseases, 10th Revision
ICER	Incremental cost-effectiveness ratio
IEG	Immediate early gene
IL 6	Interleukin-6
IL-1β	Interleukin-1 beta
IPSC	Inhibitory postsynaptic current
IPSCGABA	GABAergic inhibitory postsynaptic current
iTBS	Intermittent theta-burst stimulation
I^2	I-squared heterogeneity index (meta-analysis)
KATP	ATP-sensitive potassium channel
KCC2	K^+/Cl^- cotransporter 2
KCNQ	KCNQ potassium channel family
KCNQ2	KCNQ2 potassium channel subunit
KD	Knockdown
Kir2.1	Inward-rectifier potassium channel 2.1
Kir4.1	Inward-rectifier potassium channel 4.1
Kp	Planetary K index (geomagnetism)
L2/3	Neocortical layers 2/3
LA	Lateral amygdala
LC	Locus coeruleus
LDH	Lactate dehydrogenase
LFP	Local field potential
LOF	Loss-of-function (mutation)
LPS	Lipopolysaccharide
LSTM	Long short-term memory (neural network)
LTP	Long-term potentiation
MADRS	Montgomery–Åsberg Depression Rating Scale
MCI	Mild cognitive impairment
MCID	Minimal clinically important difference
MDD	Major depressive disorder
MECP2	Methyl CpG-binding protein 2
MedDRA	Medical Dictionary for Regulatory Activities
MEG	Magnetoencephalography
MEP	Motor evoked potential
$MgSO_4$	Magnesium sulfate
Mg^{2+}	Magnesium ion
MI	Myocardial infarction
MMRM	Mixed model for repeated measures
MRI	Magnetic resonance imaging
MRS	Magnetic resonance spectroscopy
MS	Multiple sclerosis
MΩ	Megaohm
NA	Noradrenaline (norepinephrine)
NAC	N-acetylcysteine

NAc	Nucleus accumbens
Nav	Voltage-gated sodium channel
Na^+/K^+-ATPase	Sodium–potassium ATPase pump
NDA	New drug application
NE	Norepinephrine (noreadrenaline)
NEURON	NEURON simulation environment
N_{hit}	Replay-hit count (θ/SWR coincidences per minute)
NKA	Na^+/K^+-ATPase (sodium–potassium pump)
NKA-α1	Na^+/K^+-ATPase alpha1 subunit
NKCC1	$Na^+/K^+/Cl^-$ cotransporter 1
NMDA	N-methyl-D-aspartate receptor
NOR	Novel object recognition (task)
NRG1	Neuregulin-1
OCD	Obsessive–compulsive disorder
OPEX	Operating expenditure
OR	Odds ratio
ORCID	Open Researcher and Contributor ID
OSF	Open Science Framework
OXT	Oxytocin
P2X7R	P2X7 purinergic receptor
PAC	Phase–amplitude coupling
PANSS	Positive and Negative Syndrome Scale
PCC	Posterior cingulate cortex
PET	Positron emission tomography
PET-KCC2	PET imaging of KCC2
PET-Kir4.1	PET imaging of Kir4.1
PET-PV	PET imaging of parvalbumin
PFC	Prefrontal cortex
PKA	Protein kinase A
PKC	Protein kinase C
PL	Prelimbic cortex
PLE	Psychotic-like experience
PM_{10}	Particulate matter ≤10 μm
$PM_{2.5}$	Particulate matter ≤2.5 μm
PNN	Perineuronal net
PNNs	Perineuronal nets
P_{phase}	Phase-coincidence probability
PRCC	Partial rank correlation coefficient
PSD-95	Postsynaptic density protein 95
PTSD	Post-traumatic stress disorder
PV	Parvalbumin
PV-IN	Parvalbumin-positive interneuron
PV-IR	Parvalbumin-immunoreactive
PVN	Paraventricular nucleus
Q	Quality factor (magnetite chain)
QALY	Quality-adjusted life year
QELF	ELF environment quality index
Qθ	Theta-band quality factor
RAGE	Receptor for advanced glycation endproducts
RCT	Randomised controlled trial
RCT II	Phase II randomised controlled trial
RCT III	Phase III randomised controlled trial
REM	Rapid eye movement (sleep)
RH	Relative humidity
Rin	Input resistance
rMSSD	Root mean square of successive differences
ROC AUC	Receiver operating characteristic area under the curve
ROI	Region of interest

ROS	Reactive oxygen species
RR	Relative risk
RRhosp	Relative risk of hospital admission
SAE	Serious adverse event
sAHP	Slow afterhyperpolarisation
SAP	Statistical analysis plan
SC	Stimulation condition (active)
SCN1A	Voltage-gated sodium channel Nav1.1 gene
SCN2A	Voltage-gated sodium channel Nav1.2 gene
SCN8A	Voltage-gated sodium channel Nav1.6 gene
SD	Standard deviation
SE	Standard error
sEPSC	Spontaneous excitatory postsynaptic current
sgACC	Subgenual anterior cingulate cortex
sgPFC	Subgenual prefrontal cortex
shKCC2	Short hairpin knockdown of KCC2
Silexan	Lavender oil preparation Silexan
SMD	Standardised mean difference
SNRI	Serotonin–noradrenaline reuptake inhibitor
SOP	Standard operating procedure
SpO_2	Peripheral oxygen saturation
SRN	Schumann Resonance Network
SSRI	Selective serotonin reuptake inhibitor
SUVR	Standardised uptake value ratio
SWR	Sharp-wave ripple
Synergy	Supra-additive synergy between inhibitory/Cl^- manipulations
SZ	Schizophrenia
tACS	Transcranial alternating current stimulation
TAR	Theta-associated ripple
TASK	TWIK-related acid-sensitive K^+ channel
THC	Δ9-Tetrahydrocannabinol
TLE	Temporal lobe epilepsy
Tmax	Maximum daily temperature
TMS	Transcranial magnetic stimulation
TMS–MEP	TMS-evoked motor potential
TNF-α	Tumour necrosis factor alpha
TOF	Time-of-flight (PET/MRI)
TPJ	Temporoparietal junction
TR	Treatment-resistant (prefix)
TR MDD	Treatment-resistant major depressive disorder
TRD	Treatment-resistant depression
TRP	Transient receptor potential channel family
TRPM2	Transient receptor potential melastatin 2 channel
TRS	Treatment-resistant schizophrenia
tVNS	Transcutaneous vagus nerve stimulation
t½	Half-life
UHR	Ultra-high risk
V1	Primary visual cortex
vCA1	Ventral CA1
VDCC	Voltage-dependent calcium channel
veh	Vehicle (control solution)
vHPC	Ventral hippocampus
V_m	Somatic membrane potential
V_{margin}	Excitability margin (Vthr − Vrest)
vmPFC	Ventromedial prefrontal cortex
V_{rest}	Resting membrane potential
VTA	Ventral tegmental area
V_{thr}	Spike threshold

WHO	World Health Organization
WT	Wild-type
XGBoost	eXtreme Gradient Boosting algorithm
β-loop	Environment-to-clinic β-loop (ELF → clinic)
$\Delta[K^+]_o$	Change in extracellular potassium concentration
ΔE_{GABA}	Change in EGABA
ΔV_{margin}	Change in excitability margin
ΔV_{rest}	Change in resting membrane potential
μ metal	High-permeability nickel–iron shielding alloy (mu-metal)