Supplemental information

Reduced inhibition in depression impairs stimulus

processing in human cortical microcircuits

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Supplemental Materials

Data type	Animal Source
Neuron electrophysiological features	Human
Neuron morphologies	Human
Pyr-Pyr, SST-Pyr, Pyr-SST, PV-Pyr, Pyr-PV synaptic connections	Human
Other synaptic connections	Rodent
Pyr-Pyr connection probability	Human
Other connection probabilities	Rodent
SST gene expression in health and depression	Human
In-vivo Pyr baseline firing rate	Human
In-vivo SST, PV, VIP interneuron baseline firing rates	Rodent
In-vivo response firing rates across neuron types	Rodent

Table S1. Animal sources of data constraints for the models. Related "Human L2/3 Microcircuit Models" of STAR methods.

	Current Step (pA)	Experimental	Best Fit
Passive Features			
Voltage base (mV)	-100	-74.97	-74.21
Sag amplitude (mV)	-100	0.98	0.7
	-200	1.54	1.78
	-300	2.12	3.2
Voltage deflection (mV)	-100	-10.02	-6.7
	-200	-17.81	-12.25
	-300	-24.23	-17.16
Decay time constant after the stimulus (ms)	-100	11.38	11.56
Firing Features			
Firing rate (Hz)	100	12.32	11.88
	200	18.06	17.6
	300	22.56	22.22
Absolute AHP depth (mV)	100	-53.17	-71.97
	200	-49.54	-71.5
	300	-46.53	-69.82
AP half-width (ms)	100	3.18	1.02
AP peak voltage (mV)	100	21.90	31.55
ISI CV	100	0.47	0.1
	200	0.34	0.15
	300	0.32	0.16
First ISI (ms)	100	67.22	49.7
	200	24.13	22.3
	300	16.06	14.5
Second ISI (ms)	100	126.29	75.2
	200	47.69	36.0
	300	27.4	26.4
Third ISI (ms)	100	130.62	97.0
	200	59.72	52.7
	300	49.39	36.4
Adaptation index	100	0.065	0.03
	200	0.08	0.03
	300	0.11	0.02
Time to first spike (ms)	100	110.02	25.0
	200	44.20	10.2

		300	25.75	6.4

Table S2. Electrophysiology features used in the optimization of the Pyr neuron model. AP – action potential, AHP – after-hyperpolarization, ISI – inter-spike interval, CV – coefficient of variation. Related to Figure 1 and "Neuron Models" and "Experimental Models and Subject Details" of the STAR methods.

	Current Step (pA)	Experimental	Best Fit
Passive Features			
Voltage base (mV)	-10	-77.6	-77.8
Sag amplitude (mV)	-10	0.37	0.24
	-30	1.06	1.04
	-90	4.13	5.14
Voltage deflection (mV)	-10	-1.99	-2.11
	-30	-5.74	-6.03
	-90	-15.37	-14.74
Firing Features			
Firing rate (Hz)	70	9	12.29
	100	13	17.94
	190	46	45.7
Absolute AHP depth (mV)	70	-73.5	-75.2
	100	-73.2	-74.81
	190	-71	-74.03
AP half-width (ms)	70	0.42	0.56
AP peak voltage (mV)	70	16.3	13.5
ISI CV	70	0.22	0.23
	100	0.23	0.23
	190	0.11	0.07
First ISI (ms)	70	62.5	50.1
	100	38.35	26.9
	190	12.1	13.6
Second ISI (ms)	70	77.9	58.0
	100	48.58	32.7
	190	14.4	16.0
Last ISI (ms)	70	130.4	110.3
	100	99.68	71.8
	190	24.9	23.0
Adaptation index	70	0.043	0.05
	100	0.035	0.04
	190	0.006	0.01

Table S3. Electrophysiology features used in the optimization of the SST interneuron model. Related to Figure 1 and "Neuron Models" and "Experimental Models and Subject Details" of the STAR methods.

	Current Step (pA)	Experimental	Best Fit
Passive Features			
R_{in} (MΩ)	-110	90.64	98.09
	-50	96.84	98.91
Voltage base (mV)	-110	-83.41	-83.40
Sag amplitude (mV)	-110	0.50	0.39
	-50	0.38	0.11
Voltage decay time constant (ms)	-50	12.28	12.25
Firing Features			
Firing rate (Hz)	170	11	12

	210	39	39
	250	60	59
	250 (axon)	N/A	59
AHP depth (mV)	170	-80.52	-79.41
	210	-81.11	-79.13
	250	-81.71	-78.93
	250 (axon)	N/A	-82.96
AP half-width (ms)	170	0.24	0.46
	210	0.24	0.46
	250	0.23	0.47
AP peak voltage (mV)	170	7.76	19.35
	210	10.05	20.05
	250	10.40	20.47
	250 (axon)	N/A	2.80
ISI CV	210	0.115	0.069
	250	0.120	0.058

Table S4. Electrophysiology features used in the optimization of the PV interneuron model. Related to Figure 1 and "Neuron Models" and "Experimental Models and Subject Details" of the STAR methods.

	Current Step (pA)	Experimental	Best Fit
Passive Features			
R_{in} (MΩ)	-110	164.62	175.10
	-30	241.09	203.23
Voltage base (mV)	-110	-81.28	-81.30
Sag amplitude (mV)	-110	2.48	2.53
	-30	1.16	0.26
Voltage decay time constant (ms)	-30	23.83	23.92
Firing Features			
Firing rate (Hz)	90	8	5
	150	22	21
	210	32	33
	210 (axon)	N/A	33
AHP depth (mV)	90	-72.46	-70.46
	150	-71.10	-69.17
	210	-69.28	-67.10
	210 (axon)	N/A	-69.01
AP half-width (ms)	90	0.39	0.64
	150	0.39	0.66
	210	0.39	0.66
AP peak voltage (mV)	90	18.24	19.06
	150	15.68	18.26
	210	12.98	15.38
	210 (axon)	N/A	13.93
ISI CV	150	0.240	0.034
	210	0.240	0.064
Inverse first ISI (Hz)	150	11.92	15.04
	210	17.79	19.57
AHP time (ms)	150	0.91	2.14
	210	0.93	2.12
AHP depth, slow (mV)	150	-65.82	-66.87
	210	-62.94	-64.39

Table S5. Electrophysiology features used in the optimization of the VIP interneuron model. Related to Figure 1 and "Neuron Models" and "Experimental Models and Subject Details" of the STAR methods.

Parameter	Pyr	SST	PV	VIP
$c_{m,soma}$	1	1	2	2
$c_{m,dend}$	2	1	2	2
$c_{m,apic}$	2			
$c_{m,axon}$	1	1	2	2
$c_{m,myelin}$	0.02	0.02		
E_{pas}	-80	-81.5	-83.93	-79.74
G_{pas}	9.54e-5	2.32e-5	1.18e-4	2.58e-5
$G_{H,soma}$	1.48e-4	4.31e-5	2.77e-5	4.27e-5
$G_{H,apic}$	(see methods)			
$G_{H,dend}$	7.09e-7	9.49e-5	2.77e-5	4.27e-5
$G_{H,axon}$			2.77e-5	4.27e-5
$G_{NaT,soma}$	0.272	0.127	0.500	0.115
$G_{NaT,axon}$	1.38	0.343	0.109	0.201
$G_{Nap,soma}$			8.79e-3	1.89e-4
$G_{Nap,axon}$	8.42e-3	4.44e-4	1.20e-3	6.25e-4
$G_{KP,soma}$	2.08e-4	1.11e-2	9.61e-6	9.92e-4
$G_{KP,axon}$	0.338	2.95e-2	0.685	0.264
$G_{KT,soma}$	6.05e-2		1.17e-3	9.05e-3
$G_{KT,axon}$	4.24e-2	2.23e-2	7.60e-2	1.44e-2
$G_{Kv3.1,soma}$	4.24e-2	0.871	2.99	0.312
$G_{Kv3.1,axon}$	0.941	0.984	2.99	1.12e-3
$G_{M,soma}$	3.06e-4	1.58e-4	4.21e-2	3.68e-4
$G_{M,axon}$		3.17e-4	2.96e-2	1.39e-4
$G_{SK,soma}$	8.53e-4		3.73e-6	0.165
$G_{SK,axon}$	1.45e-2	1.13e-3	0.512	0.703
$G_{Ca\_HVA,soma}$	1.55e-3	3.55e-3	1.79e-4	4.38e-5
$G_{Ca,HVA,axon}$	3.06e-4	1.45e-3	2.96e-3	2.82e-5
$G_{Ca\_LVA,soma}$	2.96e-3	3.14e-3	9.25e-2	3.45e-3
$G_{Ca,LVA,axon}$	4.39e-2	6.27e-3	5.95e-5	1.03e-2
$CaDynamics_{decay,soma}$	20	465	531	25.16
$CaDynamics_{decay,axon}$	226	469	163	75.79

Table S6. Neuron model parameter values. Maximal conductance (G) values are in S/cm^2. Related to Figure 1 and "Neuron Models" of the STAR methods.

Connection Type	p_{con}	G_{syn} (nS)	Contacts Per Connection	Facilitation	Depression	Use
Pyr to Pyr	0.15	0.2482	3	17	670	0.46
Pyr to SST	0.19	0.38	8	670	140	0.09
Pyr to PV	0.09	0.337	8	180	510	0.88
Pyr to VIP	0.09	0.31	4	17	670	0.5
SST to Pyr	0.19	1.24	12	2	1300	0.3
SST to SST	0.04	0.34	12	21	720	0.25
SST to PV	0.20	0.33	13	21	710	0.25
SST to VIP	0.06	0.46	5	25	890	0.31
PV to Pyr	0.094	2.91	17	23	710	0.08
PV to SST	0.05	0.33	16	21	700	0.25
PV to PV	0.37	0.33	15	21	710	0.25

PV to VIP	0.03	0.34	7	21	720	0.26
VIP to Pyr	0	0	0	160	300	0.23
VIP to SST	0.35	0.36	9	22	760	0.27
VIP to PV	0.10	0.34	11	21	720	0.25
VIP to VIP	0.05	0.34	7	21	720	0.26

Table S7. Microcircuit model synaptic and connectivity parameter values. Related to Figure 1 and "Synaptic Connectivity Models" of the STAR methods.