Gene	log$_2$FC	StdErr	*p*- adj	Direction	Biological function
Activity-dependent signaling					
Egr1	0.554	0.093	9.69×10^{-6}	↑	Immediate early gene, LTP and memory consolidation
Egr2	1.352	0.279	1.75×10^{-3}	↑	Immediate early gene, hindbrain segmentation and development
Nr4a1	0.666	0.104	1.30×10^{-6}	↑	Immediate early gene, synaptic plasticity, dendritic spine regulation
Nr4a3	0.284	0.071	4.46×10^{-2}	↑	Immediate early gene, memory formation
Bdnf	0.27	0.065	2.80×10^{-2}	↑	Neurotrophic factor, synaptic maturation and plasticity
Synaptic modulation					
Chrm3	0.304	0.073	2.80×10^{-2}	↑	Muscarinic M3 receptor, hippocampal GABAergic modulation
Sparc	−0.341	0.072	3.15×10^{-3}	↓	ECM glycoprotein, negative regulator of synaptogenesis
Structural					
Emp2	−0.533	0.117	6.36×10^{-3}	↓	Membrane protein, cell surface protein trafficking
Sclt1	−0.799	0.131	5.70×10^{-6}	↓	Ciliogenesis and cellular structure
Vascular, metabolic and stress					
Agt	−0.581	0.142	3.38×10^{-2}	↓	Vascular regulation
Nos3	−0.502	0.12	2.59×10^{-2}	↓	Endothelial nitric oxide synthase (eNOS), vascular tone regulation
Tlcd3b	−0.195	0.049	4.19×10^{-2}	↓	Membrane lipid metabolism
Immune response					
Gbp2b	−5.153	1.016	7.37×10^{-4}	↓	Interferon-induced GTPase, innate immune response
Clec16a	0.418	0.07	9.69×10^{-6}	↑	Autophagy and mitophagy regulation
Transcriptional regulation					
Cbfa2t3	−0.347	0.065	2.58×10^{-4}	↓	Transcriptional corepressor, cell differentiation
Zfp366	−0.710	0.168	2.26×10^{-2}	↓	Transcriptional repression activity
Tiparp	0.467	0.09	5.06×10^{-4}	↑	Mono-ADP-ribosyltransferase, transcriptional regulation
Id4	0.26	0.064	3.43×10^{-2}	↑	Transcriptional regulator, neural progenitor proliferation and differentiation
Epilepsy / neurodevelopment					
Cdkl5	0.674	0.083	1.48×10^{-11}	↑	CDD causal gene
Other / limited annotation					
Ermardl2	0.619	0.088	2.73×10^{-8}	↑	Poorly characterized
Ermardl1	4.554	0.928	1.40×10^{-3}	↑	Poorly characterized
Ddx4	1.021	0.228	8.08×10^{-3}	↑	RNA helicase; germline expression
Gm5148	−1.466	0.257	3.50×10^{-5}	↓	Predicted gene, unknown function
Gm26881	−2.447	0.546	8.00×10^{-3}	↓	Predicted gene, unknown function
Gm3764	−0.282	0.07	3.61×10^{-2}	↓	Predicted gene, unknown function
Gm12532	−4.139	1.021	3.61×10^{-2}	↓	Predicted gene, unknown function
Gm36823	−6.116	1.209	7.37×10^{-4}	↓	Predicted gene, unknown function
Armh4	0.238	0.056	1.98×10^{-2}	↑	Partially characterized; transcriptional context
Nr1d1	−0.458	0.097	2.84×10^{-3}	↓	Circadian clock gene

Per1	0.288	0.073	4.63×10^{-2}	↑	Circadian activity-dependent gene
Rnf38	−0.324	0.072	7.12×10^{-3}	↓	E3 ubiquitin ligase
2210418O10Rik	−1.299	0.321	3.61×10^{-2}	↓	Uncharacterized gene
E230020A03Rik	−1.255	0.248	7.37×10^{-4}	↓	Uncharacterized gene
F730043M19Rik	−0.476	0.084	3.50×10^{-5}	↓	Uncharacterized gene
Gm43488	0.869	0.219	4.64×10^{-2}	↑	Predicted gene, unknown function
Junb	0.502	0.116	1.58×10^{-2}	↑	AP-1 transcription factor
Pisd-ps1	−1.329	0.267	1.05×10^{-3}	↓	Poorly characterized

Table S4. Functional classification of genes differentially expressed in the hippocampus of heterozygous *Cdkl5* +/– female mice at 12 months. Genes were identified through RNA sequencing of hippocampal tissue from wild-type and *Cdkl5* +/– female mice at 12 months of age, followed by differential expression analysis using DESeq2. Log$_2$ fold change (log$_2$FC) values and their standard error (StdErr) represent differential expression between genotypes at 12 months. Direction indicates upregulation (↑) or downregulation (↓) in heterozygous mice relative to wild-type controls. Genes are grouped by biological function. All genes with an adjusted *p* -value (*p* -adj) < 0.05 are shown. This classification highlights the convergence of increased activity-dependent signaling with reduced structural and homeostatic support pathways.