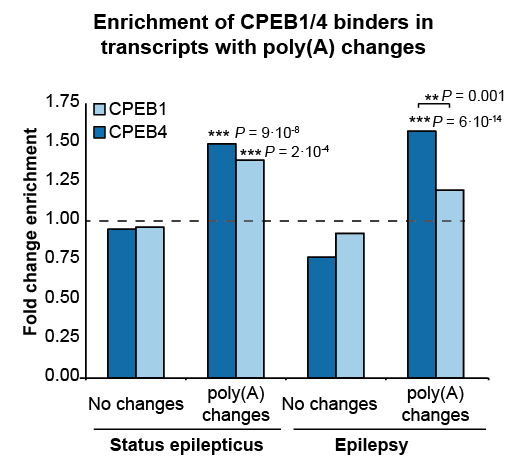
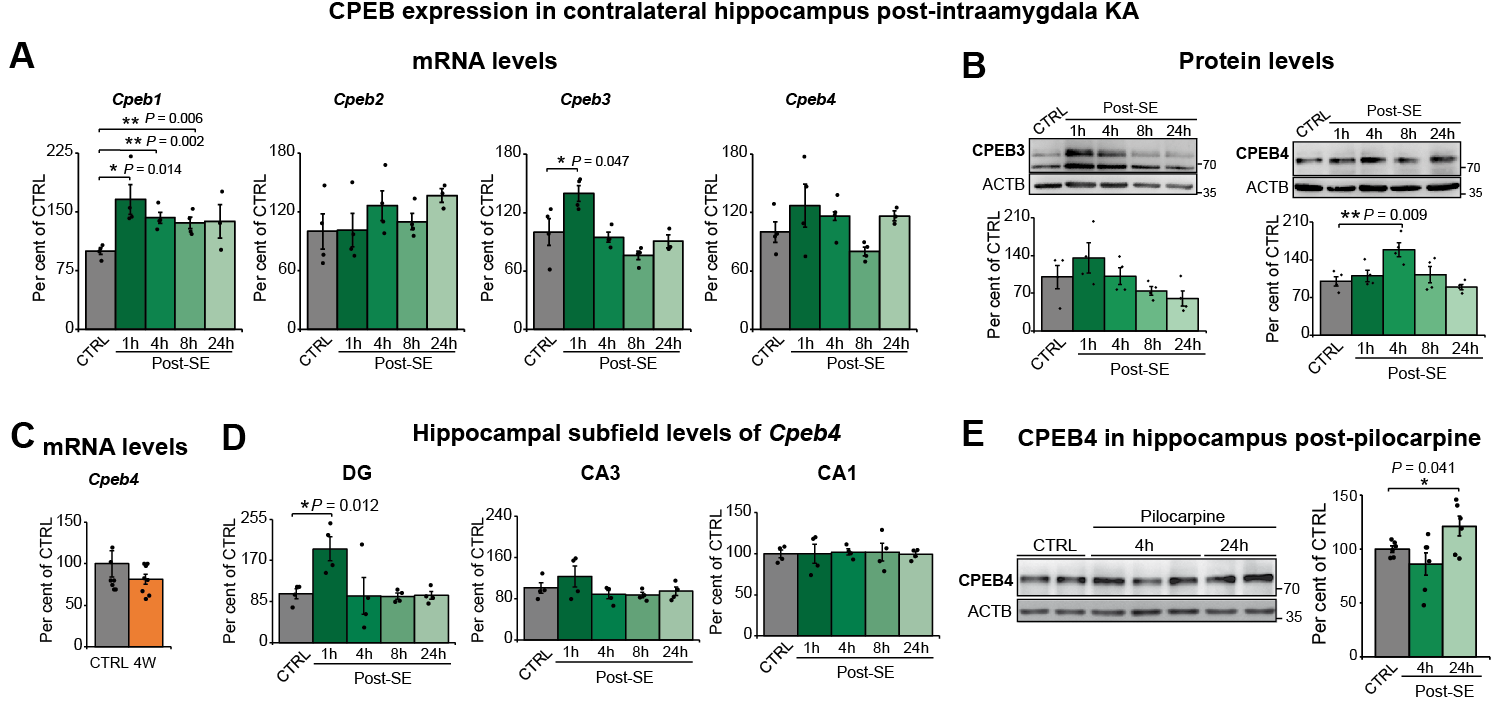
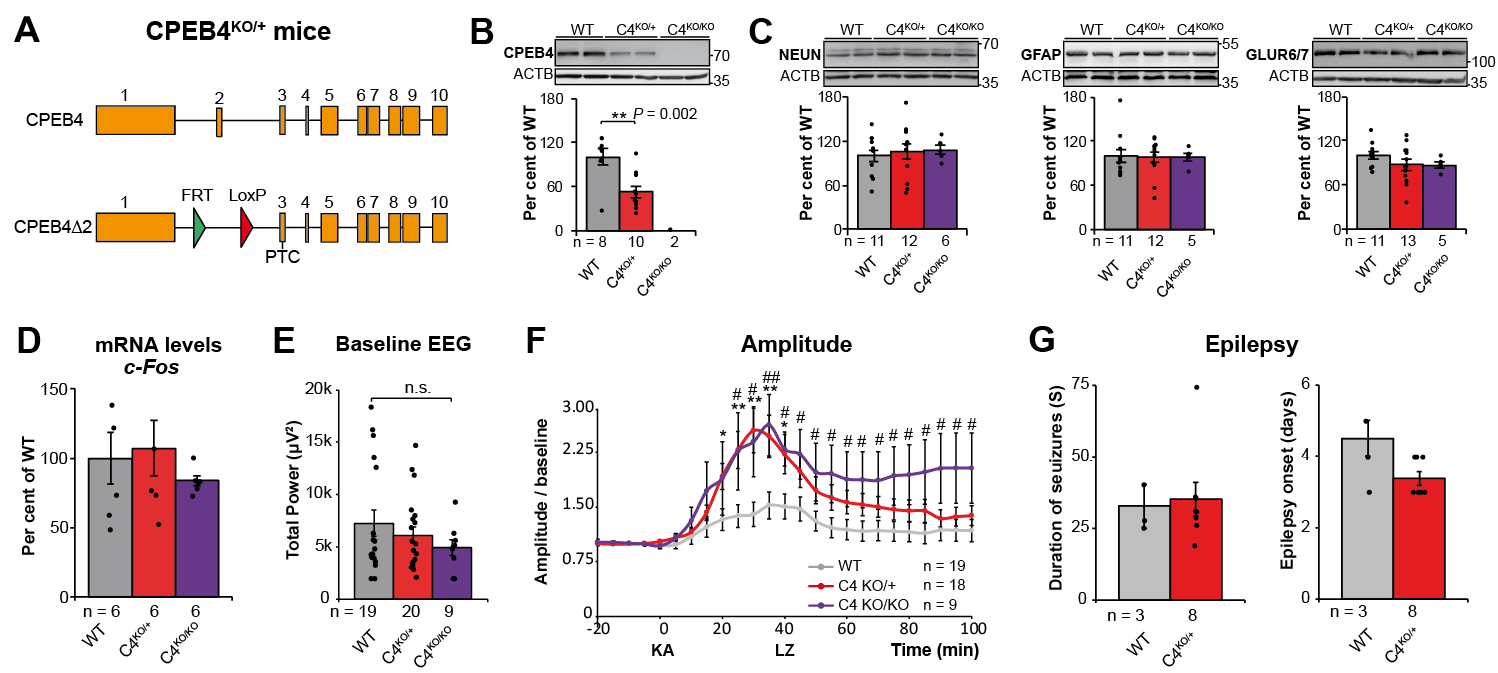


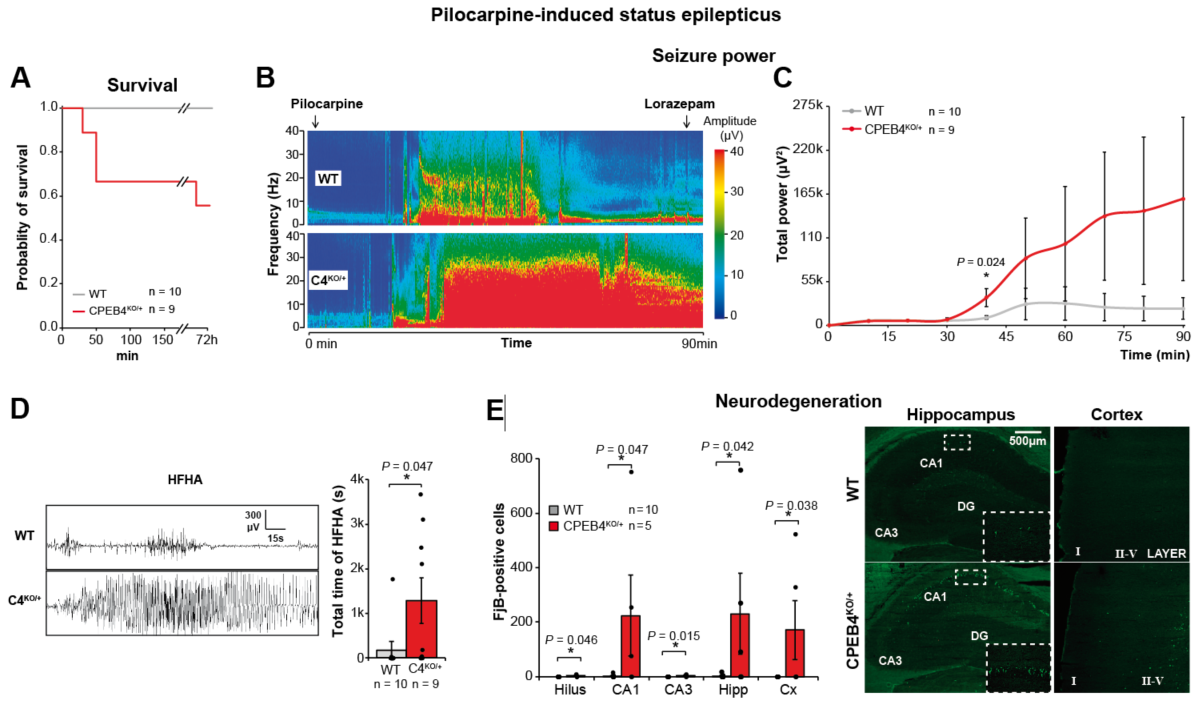
**Supplementary Fig.1 Pathway analysis and polyadenylation regulated genes.** (**A**) Top GO terms associated with biological process using DAVID resources of transcripts with poly(A) tail changes following status epilepticus and during epilepsy; the negative log10 of the *P* value is plotted on the X-axis. GO, Gene Ontology. (**B**) Percentage of transcriptswith poly(A) tail length changed and/or potential genes targeted by microRNA up- and down-regulated in the ipsilateral hippocampus 8 h post-intraamygdala KA-induced status epilepticus. RF, Representation Factor. (**C**) Percentage of transcripts with poly(A) tail length changes following intraamygdala KA-induced status epilepticus and during epilepsy in epilepsy-related genes compared vs. total number of transcripts and brain expressed genes. F.E., fold enrichment. (**D, F**) mRNA levels of *Stx6 and Mettl3* in the (**D**) ipsilateral (n = 4) and (**F**) contralateral (n = 4) hippocampus at 8 h post-status epilepticus, vehicle (control) vs. intraamygdala KA-treated (status epilepticus). Data were normalized to *Actb.* (**E, G**) Protein levels in the (**E**) ipsilateral hippocampus, METTL3 (n = 4) and STX6 (n = 8), and (**G**) contralateral hippocampus (n = 4) of mice injected with vehicle vs. KA at 8 h and 24 h post-status epilepticus. CTRL, control; SE, status epilepticus. Data were analyzed and normalized to the expression of ACTB. (**C**)One-sided Fisher’s exact test, *P* values of deadenylated epilepsy-related genes vs. total and brain transcriptome. (**B**) Hypergeometric test. (**D** - **G**) Two-sided unpaired t-test. Data are mean ± S.E.M. 95% CIs. \**P* < 0.05, \*\**P* < 0.01, \*\*\**P* < 0.001.

**Supplementary Fig.2 Poly(A) tail changes in CPEB1/4 binders.** Enrichment analysis of CPEB1- and CPEB4-only binders in transcripts with poly(A) changes post-status epilepticus and during epilepsy. One-sided Fisher’s exact test. \*\**P* < 0.01, \*\*\**P* < 0.001.

**Supplementary Fig.3 Additional data on CPEB expression post-status epilepticus and during epilepsy.** (**A**) mRNA levels of *Cpebs* in the contralateral hippocampus of WT mice injected with vehicle (CTRL) vs. intraamygdala KA at 1 h, 4 h, 8 h and 24 h post-status epilepticus (post-SE) (n = 4). (**B**) Protein levels of CPEB3 and CPEB4 in contralateral hippocampus of mice subjected to intraamygdala KA-induced status epilepticus at same time-points (n = 4). (**C**) mRNA levels of *Cpeb4* the ipsilateral hippocampusat 4 weeks after status epileptus (n = 8), and (**D**) in the hippocampal subfields CA1, CA3 and DG at different time points post-intraamygdala KA-induced status epilepticus (n = 4). DG, dentate gyrus. Data were analyzed and normalized to the expression of *Actb*. (**E**)CPEB4 protein levels in the hippocampus of WT mice 4 h and 24 h following intraperitoneal pilocarpine-induced status epilepticus (vehicle n = 9, pilocarpine n = 6). Protein quantity was normalized to the loading control (ACTB). (**A** - **E**) Two-sided unpaired t-test. Data are mean ± S.E.M. 95% CIs. \**P* < 0.05, \*\**P* < 0.01.



**Supplementary Fig.4 Additional information on CPEB4-deficient mice.** (**A**)Construct design. (**B**) CPEB4 protein levels in the hippocampus of CPEB4KO/+ and CPEB4KO/KO mice. (**C**)Western blot and corresponding graphs showing NEUN, GFAP and GLUR6/7-positive protein levels in the hippocampus of WT, CPEB4KO/+ and CPEB4KO/KO mice. Protein quantity was normalized to the loading control (ACTB). (**D**) *c-Fos* mRNA levels in the hippocampus of WT, CPEB4KO/+, CPEB4KO/KO mice. Data were analyzed and normalized to the expression of *Actb*. (**E**)Baseline EEG recordings of different genotypes. EEG, electroencephalogram. (**F)** Amplitude post-intraamygdala KA injection normalized to baseline. KA, kainic acid; LZ, lorazepam. (**G)** Duration and onset of spontaneous seizures in WT and CPEB4KO/+ mice during a 14 days after status epilepticus. Data are mean ± S.E.M. 95% CIs. WT vs CPEB4KO/+ \**P* < 0.05, \*\**P* < 0.01. WT vs CPEB4KO/KO #*P* < 0.05, ##*P* < 0.01.

**Supplementary Fig.5 CPEB4-deficiency aggravates intraperitoneal pilocarpine-induced seizures and neurodegeneration.** (**A**) Kaplan–Meier curve for cumulative survival. (**B**) Representative heatmaps showing increased total seizure power in CPEB4KO/+ during a 90 min recording period starting at intraperitoneal pilocarpine injection. (**C**) Total power measured in 10 min segments. (**D**) Total time of high-frequency high-amplitude (HFHA) polyspike discharges and representative EEG traces. (**E**) Quantitative analysis of FluoroJade-B (FjB)-positive cells and representative sections of neurodegeneration in hippocampus and cortex 72h post-intraperitoneal pilocarpine induced-status epilepticus. Data are mean ± S.E.M. 95% CIs. \**P* < 0.05.