# Supplementary figures

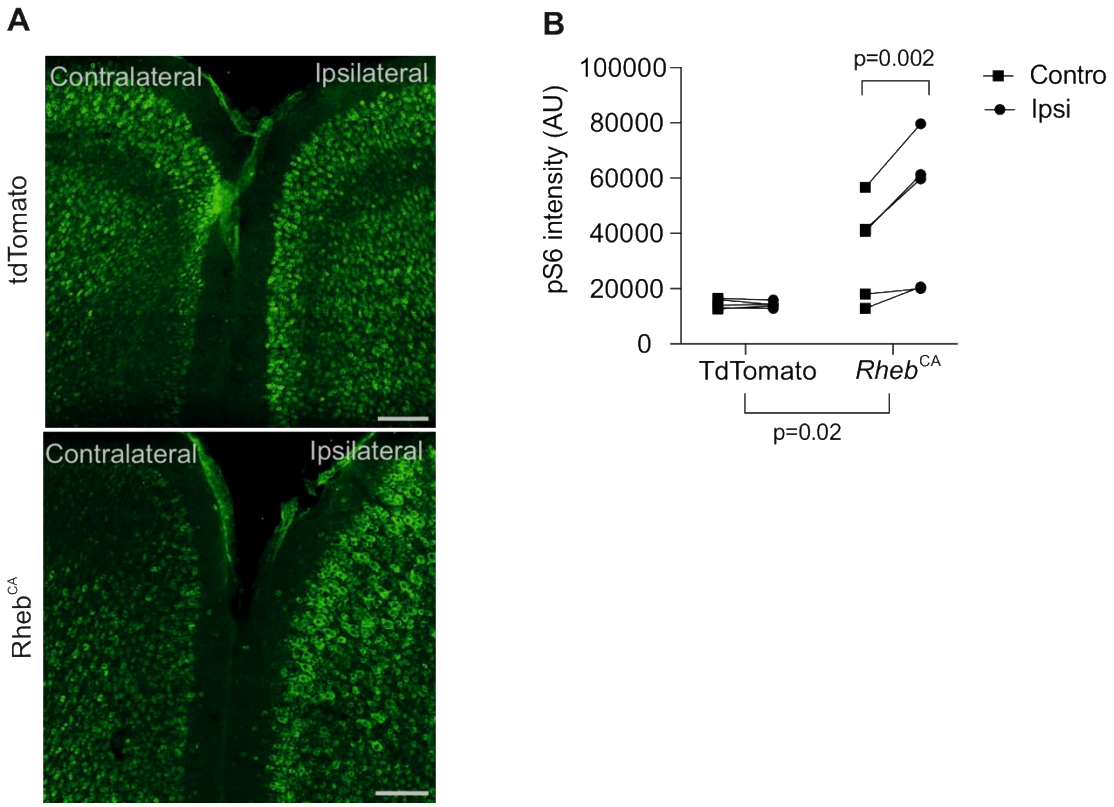


**Fig.S1. *Rheb*$^{CA}$ mice shows higher pS6 fluorescence intensity in the electroporated (ipsilateral) hemisphere compared to tdTomato (control). A.** Representative images of pS6 fluorescence in tdTomato or tdTomato-*RHEB*$^{CA}$ mice. **B.** Slope graph of pS6 intensity for tdTomato or tdTomato-*RHEB*$^{CA}$ mice (n=5 mice, 2-4 slices per mouse, 2-way ANOVA followed by Bonferroni multiple comparison test).

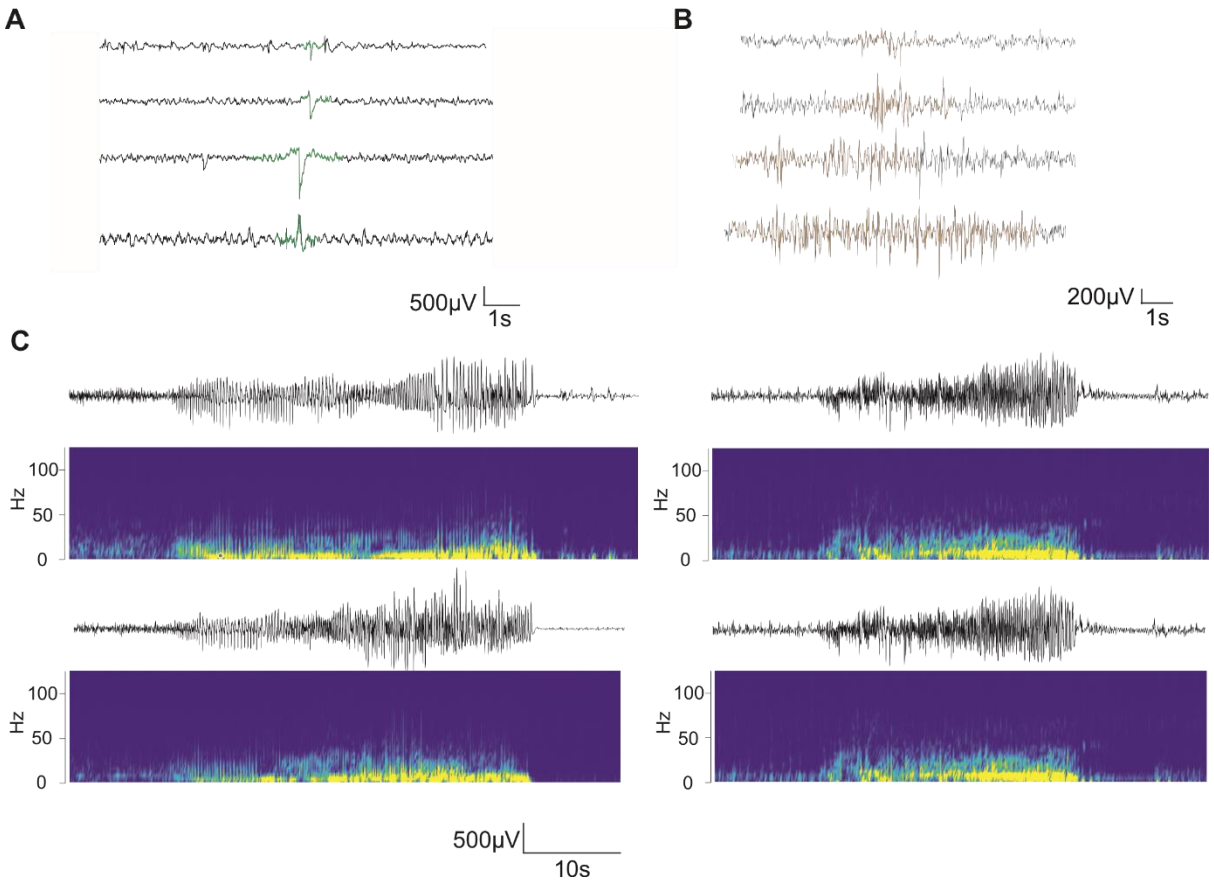


**Fig.S2. Representative epileptiform activity in mice electroporated with *RHEB*$^{CA}$ . A.** Interictal spikes not present in mice electroporated with control tdTomato. **B.** Examples of polyspikes. **C.** Examples of generalised seizures with spectrograms, associated with tonic-clonic convulsions.

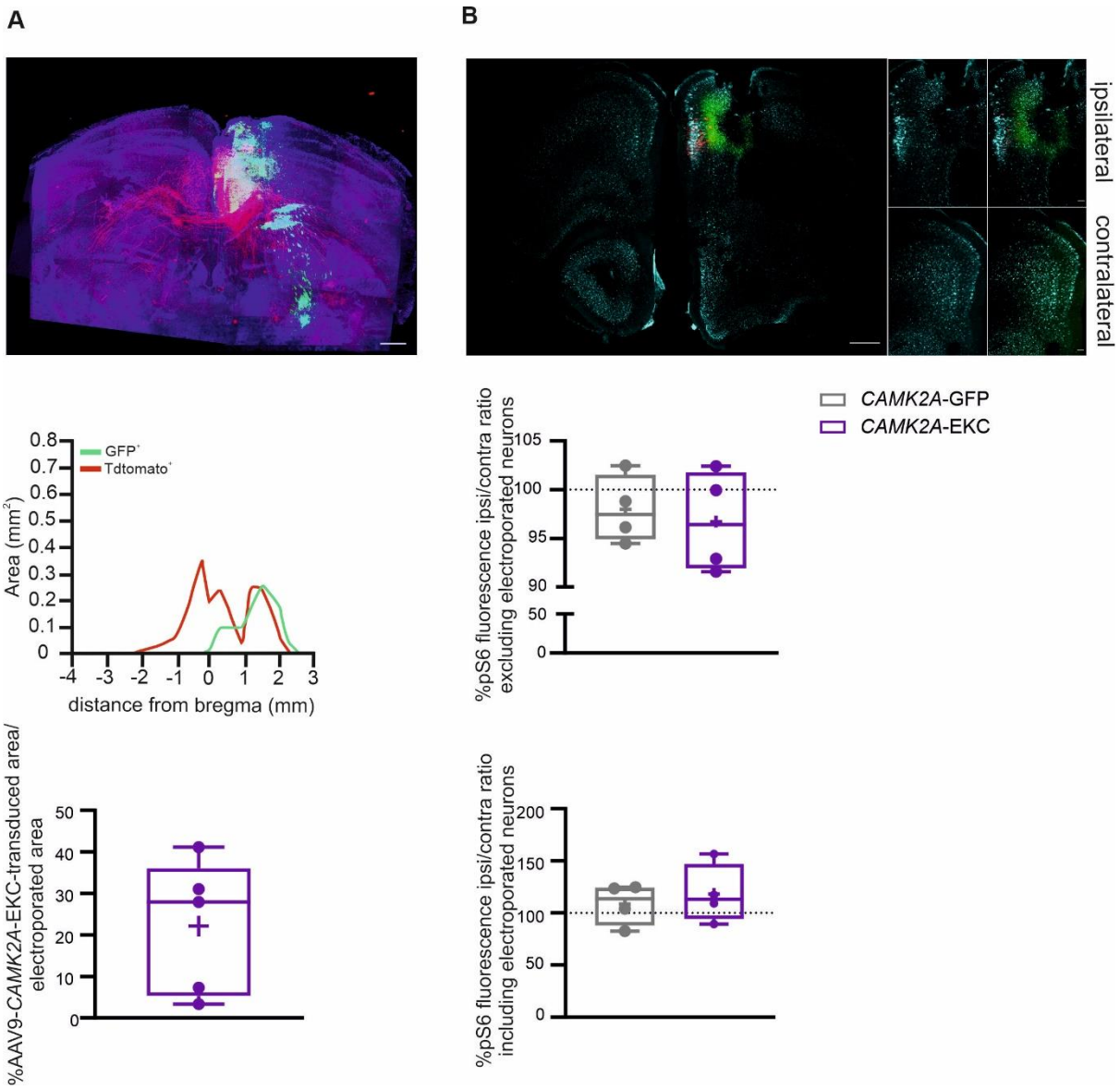


**Fig. S3. *CAMK2A*-EKC therapy spreads in the dysplastic region and does not reduce mTORC1 activity A.** 3D reconstruction of the spread of the dysplastic area (tdTomato, red fluorescence) and its overlap with expression of the GFP reporter included in the *CAMK2A*-EKC therapy, scale bar=500µm. (*middle*) Line graph displaying the anatomical overlap of the transduced ($GFP^+$) and electroporated ($tdTomato^+$) areas. (*bottom*) Box plot showing the percentage of electroporated area (tdTomato) overlapping with *CAMK2A*-EKC transduced area (GFP+) (n=5 *CAMK2A*-EKC-GFP mice). **B.** Immunofluorescence pictures of prefrontal cortical slice presenting a cortical dysplastic area (left panel: Two frontal hemispheres labelled with GFP (EKC) and pS6 antibody (cyan), scale bar=500µm; middle panels: Zoom in the ipsilateral hemisphere (top) and contralateral hemisphere (bottom) showing the pS6 expression (cyan); right panels: ipsilateral hemisphere (top) and contralateral hemisphere (bottom), scale bar=100µm . (*right*) Box plots displaying the % of pS6 fluorescence between the two hemispheres (ipsi = electroporated hemisphere) in animals from both groups (grey = *CAMK2A*-GFP, purple = *CAMK2A*-EKC, n=4 mice per group). Data are plotted as box and whiskers, representing interquartile range (box), median (horizontal line), mean (+ symbol) and maximum and minimum (whiskers), together with all the points.

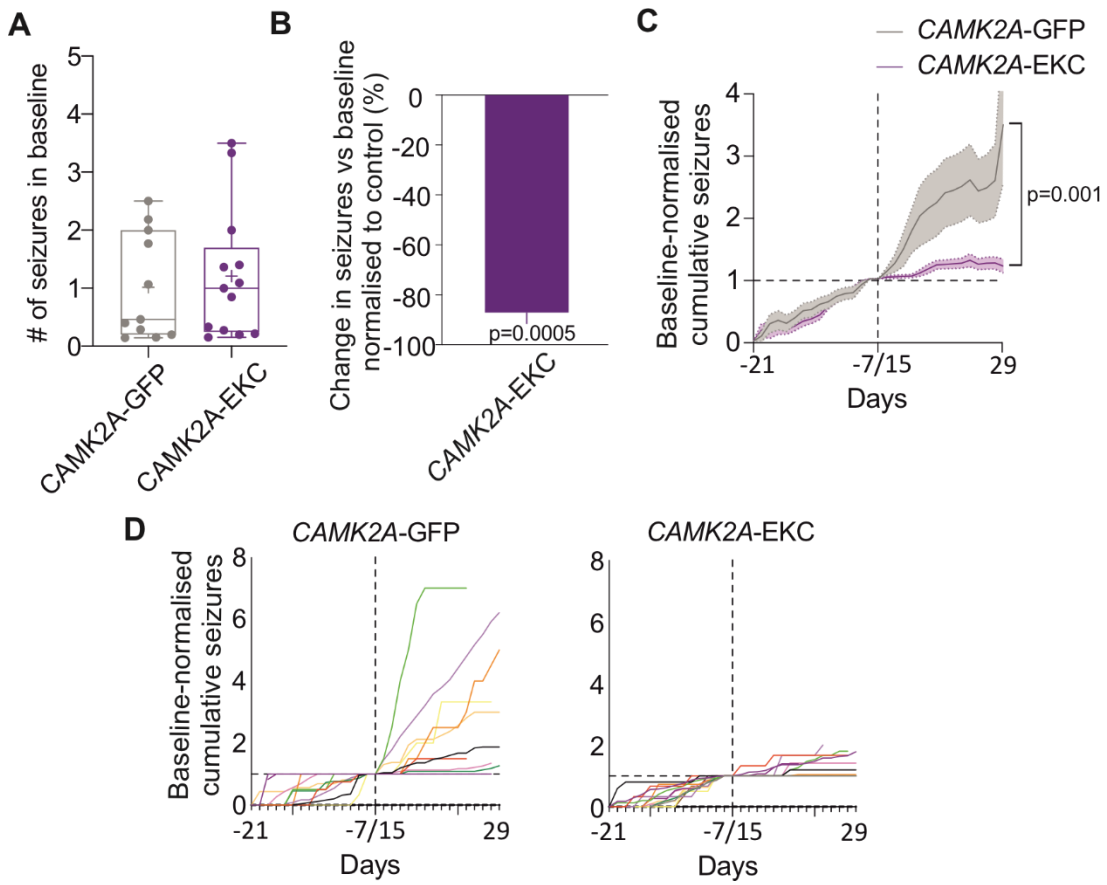


**Fig.S4. *CAMK2A*-EKC and *CAMK2A*-GFP treated animals had similar baseline seizure frequencies. A.** Box plot displaying the average seizure frequency recorded prior to AAV injection with either *CAMK2A*-EKC (n=13 mice) or *CAMK2A*-GFP (n=11 mice) (p=0.65, unpaired t-test). Data are plotted as box and whiskers, representing interquartile range (box), median (horizontal line), mean (+ symbol) and maximum and minimum (whiskers), together with all the points.
**B.** Graph displaying the change in number of seizures in animals treated with *CAMK2A*-EKC normalised to the average change in *CAMK2A*-GFP treated animals. **C.** Cumulative seizures normalised to baseline (*CAMK2A*-GFP n=11 mice, *CAMK2A*-EKC n=13 mice, Mixed effects analysis followed by Sidak's multiple comparison test). **D.** Cumulative seizures normalised to baseline for each animal; *left*: *CAMK2A*-GFP, *right*: *CAMK2A*-EKC

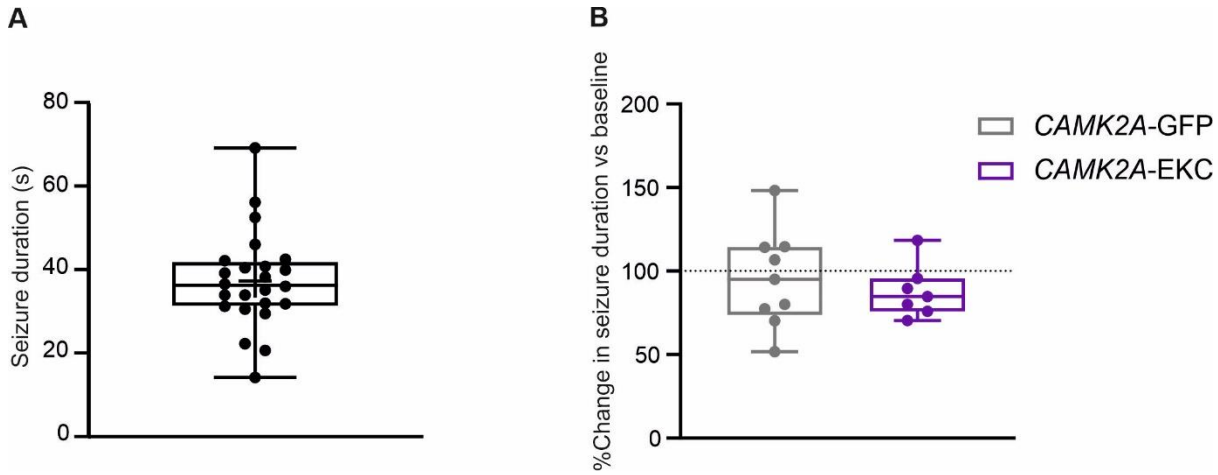


**Fig. S5. *CAMK2A*-EKC therapy does not change seizure duration A.** Box plot displaying the average durations of seizures recorded prior to AAV injection (n=24 mice). **B.** Box plot displaying the change in seizure duration normalised to baseline for *CAMK2A*-EKC (n=7 mice) and *CAMK2A*-GFP (n=9 mice) groups (p=0.5455, unpaired t-test). Data are plotted as box and whiskers, representing interquartile range (box), median (horizontal line), mean (+ symbol) and maximum and minimum (whiskers), together with all the points.

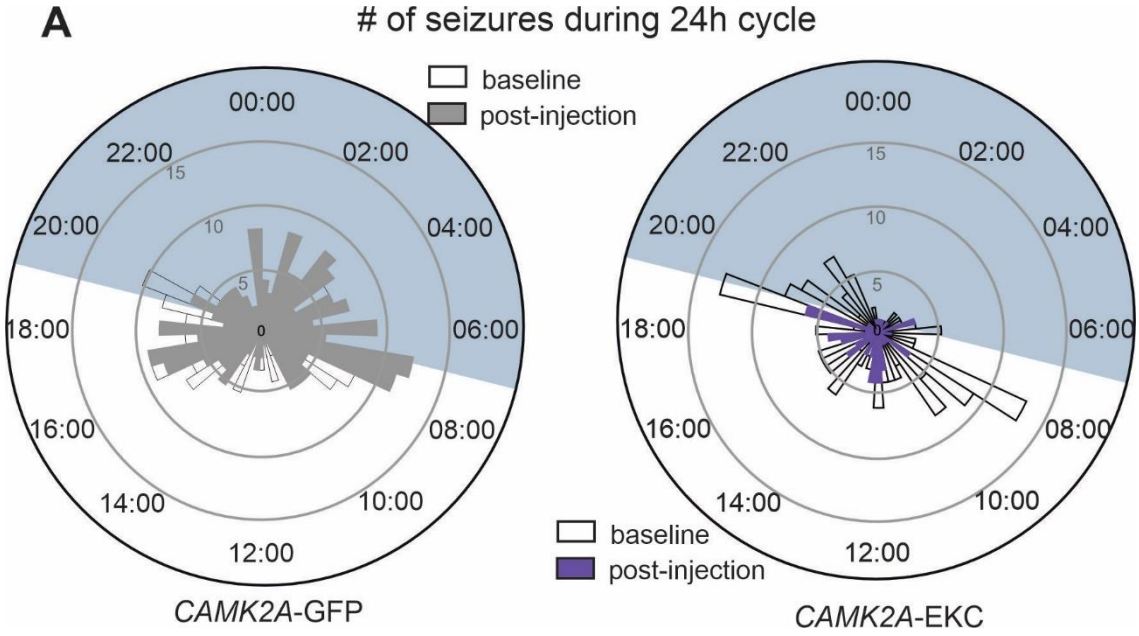


**Fig. S6. *CAMK2A*-EKC therapy does not change the light-dark cycle pattern of seizure occurrence.** Circular graph displaying the number of seizures before (empty rectangles) and after the therapy (filled rectangles) over 24h cycles for animals injected with either *CAMK2A*-GFP (n=11 mice) or *CAMK2A*-EKC (n=13 mice).

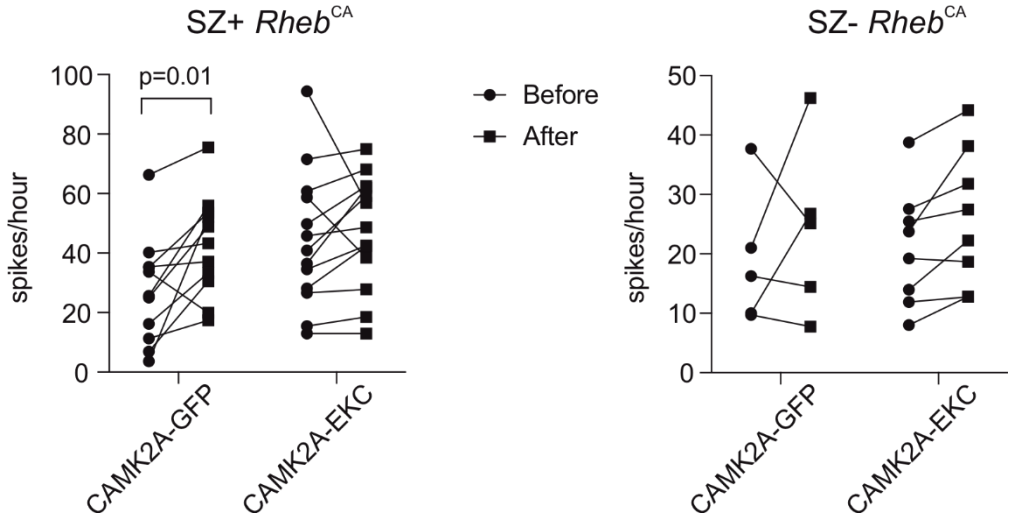


**Fig.S7. *CAMK2A*-EKC therapy prevented an increase in interictal spike frequency in *RHEB*$^{CA}$ animals with seizures.** Slope graphs displaying spikes per hour in SZ+ *RHEB*$^{CA}$ animals before and after treatment (*CAMK2A*-GFP n =11 mice, *CAMK2A*-EKC n =13 mice, 2-way ANOVA followed by Bonferroni multiple comparison test) and in SZ- *RHEB*$^{CA}$ animals (*CAMK2A*-GFP n =5 mice, *CAMK2A*-EKC, n =8 mice).