

Expanded View Figures

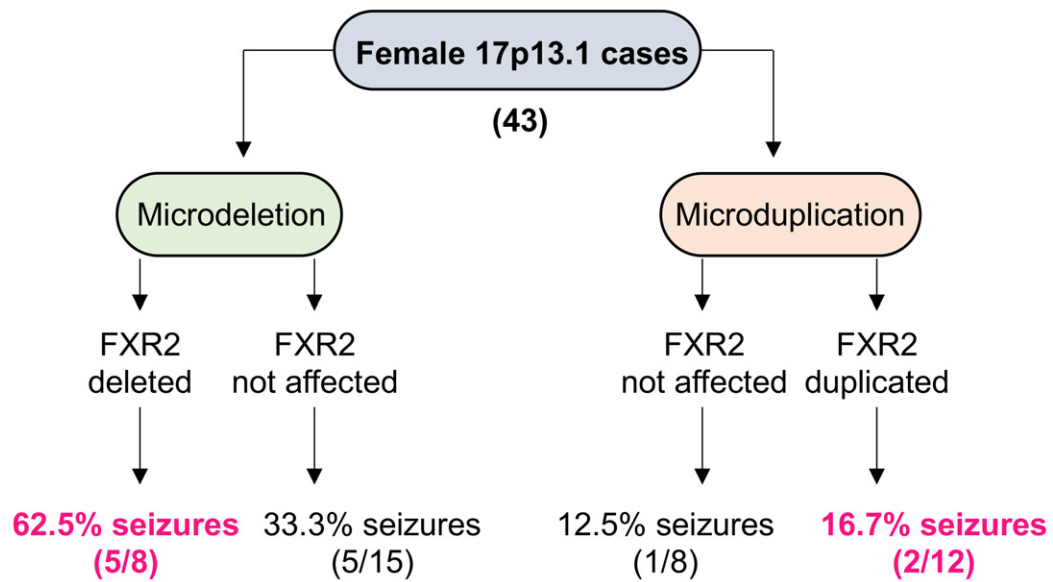


Figure EV1. Frequency of seizures in females with 17p13.1 deletion/duplication.

The analysis consists of 43 females described in the DECIPHER database and the CNV database from center of Medical Genetics in Antwerp (Belgium). 23 Patients carried a microdeletion of the 17p13.1 locus whereas 20 patients carried a microduplication.

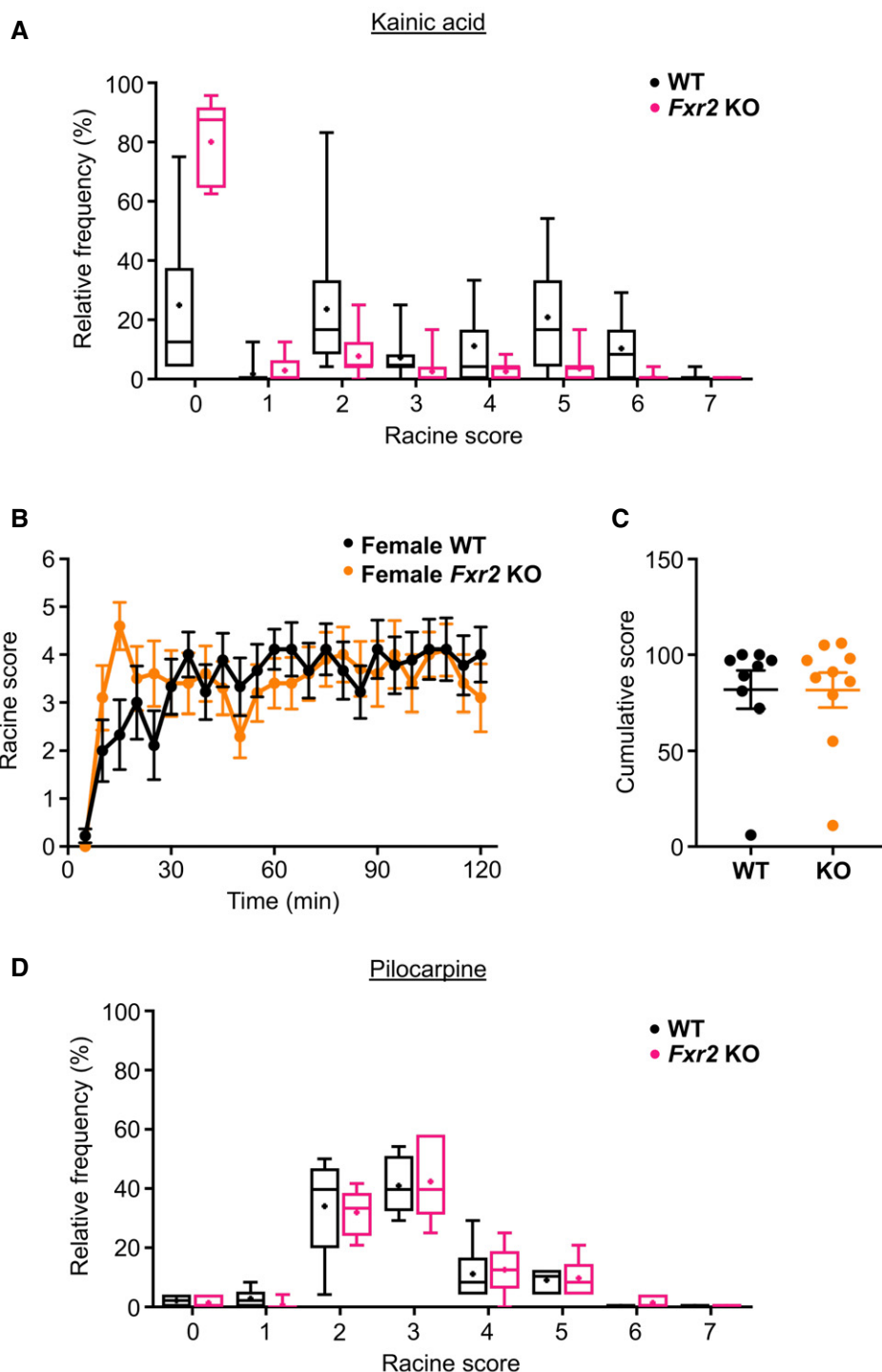


Figure EV2. Seizure distribution based on convulsant and gender.

- A Relative frequency of the different Racine scores in WT (black, $n = 16$) and *Fxr2* KO (magenta, $n = 12$) upon KA administration (Chi-square test; $\chi^2_7 = 175.67$, $P < 0.001$). Data are presented boxplots defined by median, quantiles 0.25 and 0.75. The length of the whiskers indicates 1.5 times the interquartile range (IQR).
- B Average seizure score of female KA-treated WT ($n = 9$) and *Fxr2* KO mice ($n = 10$) over time from $t = 0$ (injection time) to 2 h. No genotype-dependent differences observed (two-way repeated measures ANOVA). Data are presented as mean \pm SEM.
- C Responsiveness to KA of female WT (black, $n = 9$) and female *Fxr2* KO mice (orange, $n = 10$). KA-treated WT mice ($n = 9$), KA-treated *Fxr2* KO mice ($n = 10$; two-tailed Student's t -test). Data are presented as mean \pm SEM.
- D Relative frequency of the different Racine scores in WT ($n = 6$) and *Fxr2* KO mice ($n = 6$) upon pilocarpine administration (Chi-square test). Data are presented boxplots defined by median, quantiles 0.25 and 0.75. The length of the whiskers indicates 1.5 times the interquartile range (IQR).

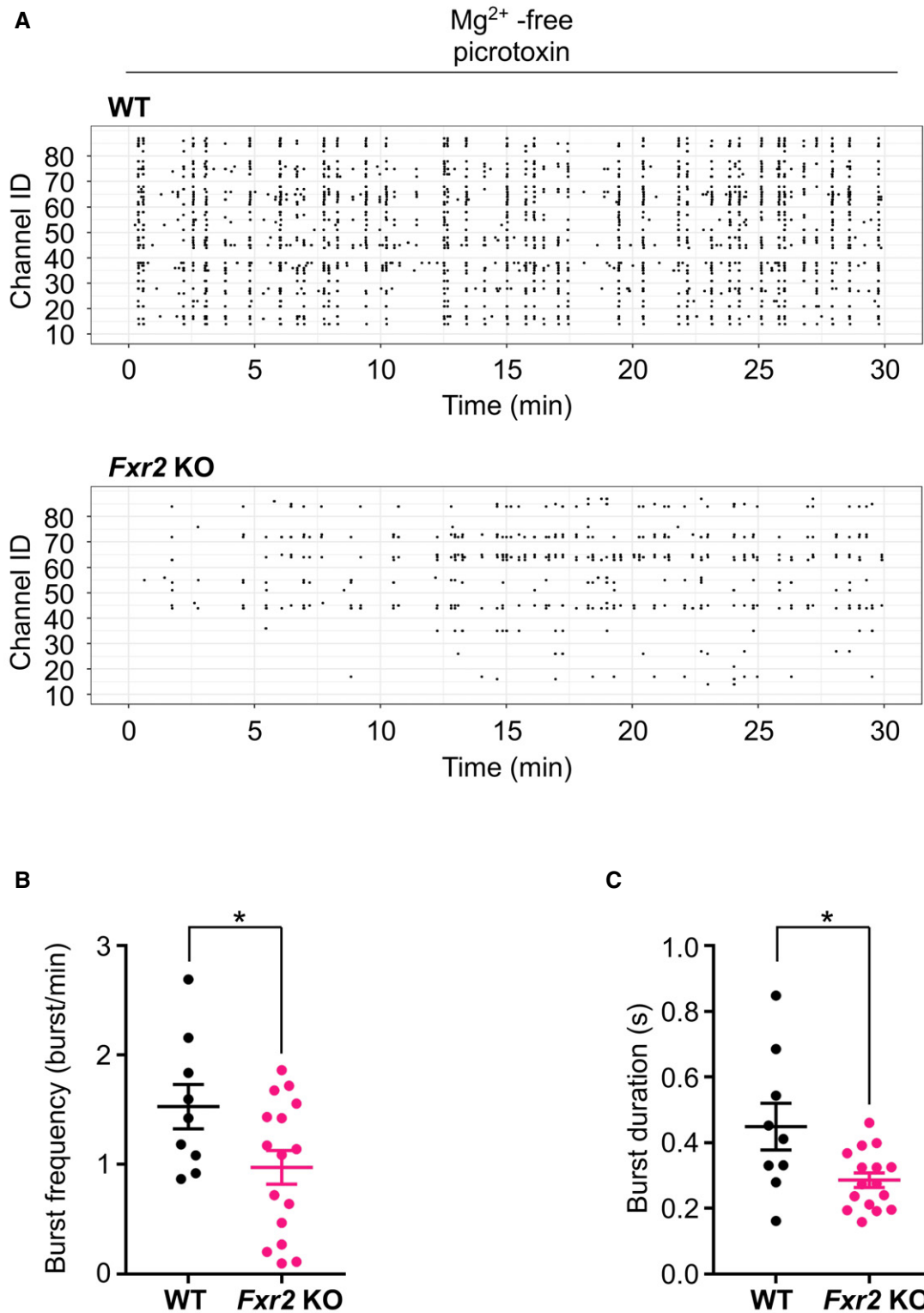


Figure EV3. Multi-electrode array recording in WT and *Fxr2* KO hippocampi.

A Representative rasterplot showing burst activity from a WT (top) and *Fxr2* KO (bottom) hippocampal slice recorded in a multi-electrode array (MEA) preparation.
 B, C Burst frequency and burst duration. * $P < 0.05$, significant difference compared with WT slices. ($n = 9$ slices taken from 6 WT mice, 16 slices taken from 8 *Fxr2* KO mice; two-tailed Student's t -test: burst frequency: $t_{23} = 2.17$, $P < 0.05$; burst duration: $t_{23} = 2.71$, $P < 0.05$). Data are presented as mean \pm SEM.

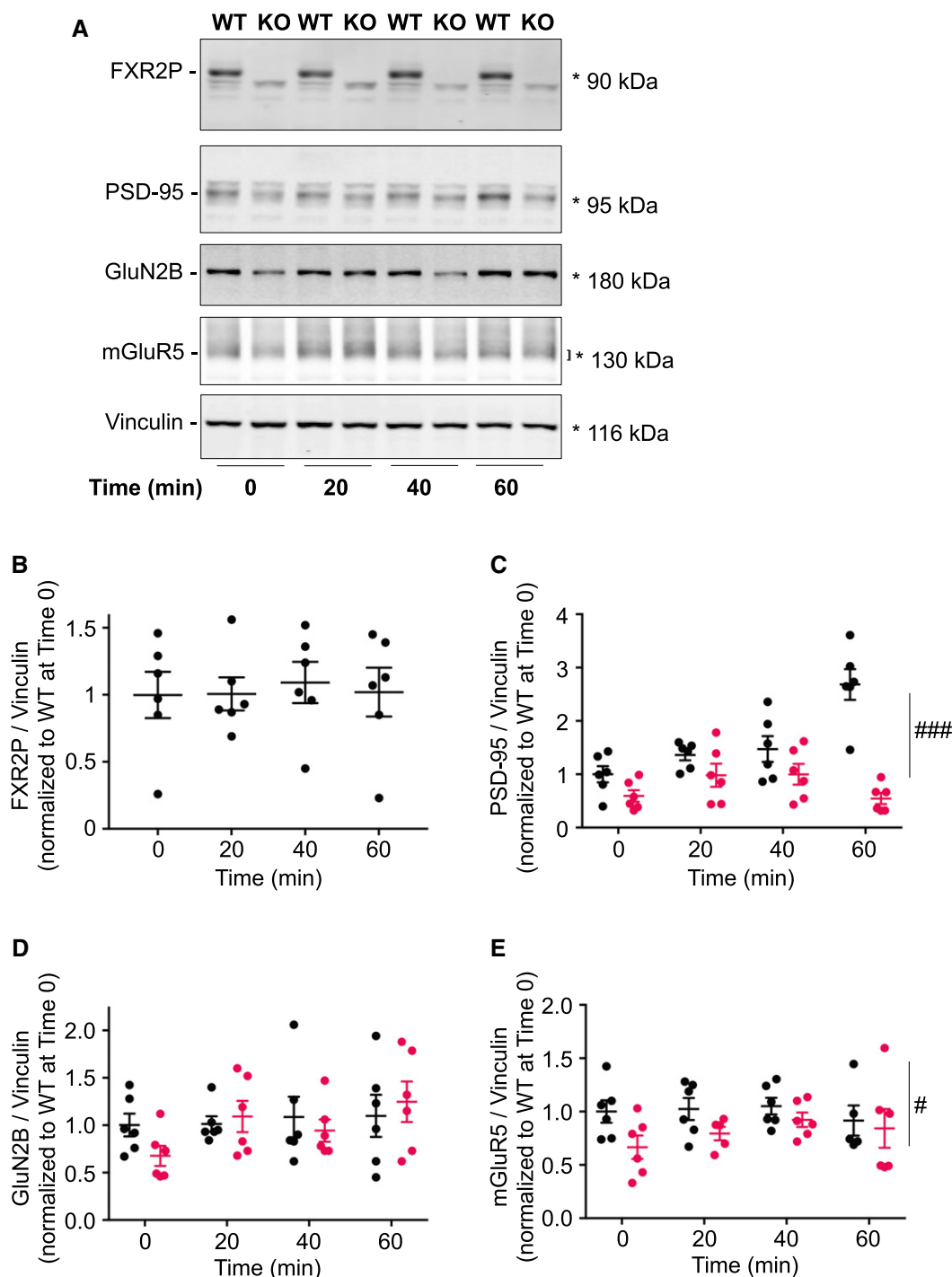


Figure EV4. FXR2P and glutamatergic protein expression in KA-treated WT and *Fxr2* KO mice at different time intervals.

A Representative Western blot to detect the expression of FXR2P, PSD-95, GluN2B, and mGluR5 proteins over different time intervals (0, 20, 40, and 60 min) in WT and *Fxr2* KO hippocampi. Quantified bands are highlighted with an asterisk or squared bracket.

B Bar plot showing FXR2P expression over Vinculin in KA-treated WT sacrificed at different time intervals (one-way ANOVA). Data are presented as mean \pm SEM.

C Bar plot showing PSD-95 expression in control and KA-treated WT and *Fxr2* KO mice. ### $P < 0.001$, overall significant difference between WT and *Fxr2* KO samples (two-way ANOVA: Genotype effect, $F_{1,40} = 40.90$, $P < 0.001$; Interaction of genotype and time, $F_{3,40} = 10.49$, $P < 0.001$). Data are presented as mean \pm SEM.

D Barplot showing GluN2B expression in control and KA-treated WT and *Fxr2* KO mice (two-way ANOVA). Data are presented as mean \pm SEM.

E Barplot showing mGluR5 expression in control and KA-treated WT and *Fxr2* KO mice. # $P < 0.05$, overall significant difference between WT and *Fxr2* KO samples (two-way ANOVA: Genotype effect, $F_{1,38} = 5.90$, $P = 0.02$). Data are presented as mean \pm SEM. Group sizes were $n = 6$ for each genotype and interval throughout the figure.