

Supplemental information

**Mineralocorticoid receptors dampen
glucocorticoid receptor sensitivity
to stress via regulation of FKBP5**

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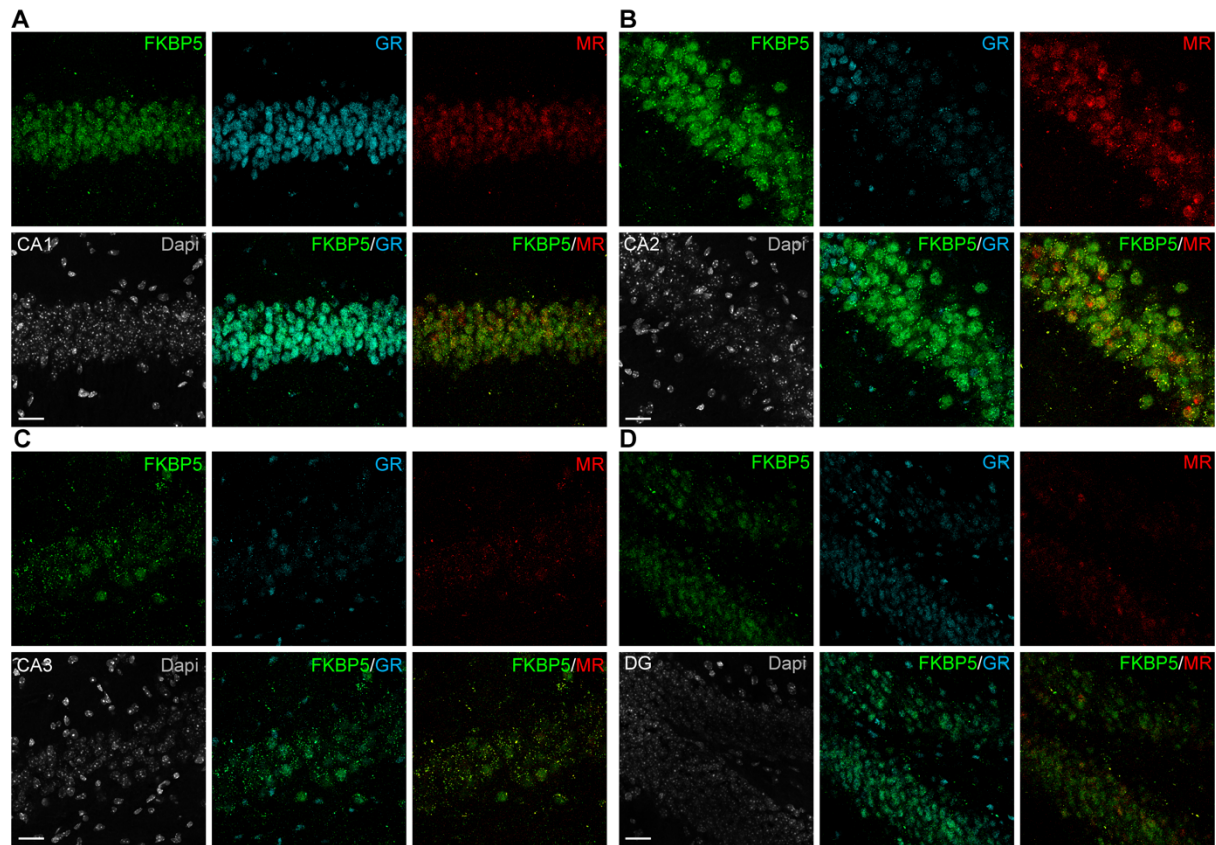


Figure S1. FKBP5, GR and MR protein expression patterns in the mouse hippocampus, related to Figure 2. (A) CA1, (B) CA2, (C) CA3 and (D) dentate gyrus (DG). Coronal sections of C57BL/6J mice ($n = 5$ mice) were stained for FKBP5, GR and MR protein as well as DAPI (4,6-diamidino-2-phenylindole). FKBP5 and MR exhibit similar expression patterns in the hippocampus, which is distinct from that of the GR. FKBP5 and MR expression is most prominent in hippocampal subregion CA2, whereas GR expression is strongly expressed in the CA1. Scale bar, 25 μm .

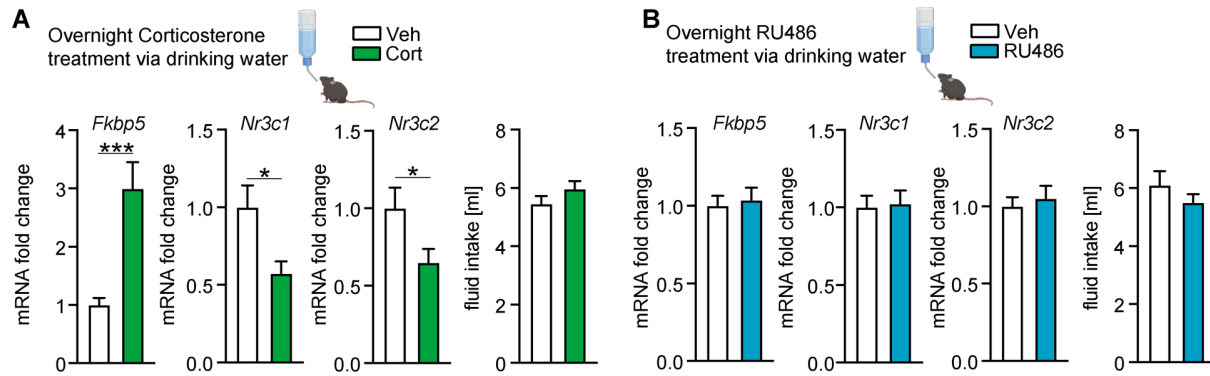


Figure S2. *Fkbp5*, *Nr3c1* and *Nr3c2* mRNA expression in the hippocampus of C57BL/6J mice following overnight corticosterone or RU486 treatment via drinking water, related to Figure 5A-C. **(A)** *Fkbp5* mRNA expression is increased in the hippocampus of C57BL/6J mice following overnight treatment with corticosterone (*Fkbp5*, $t_{17} = 4.039$, $p < 0.001$), while *Nr3c1* and *Nr3c2* mRNA levels are decreased (*Nr3c1*, $t_{18} = 2.650$, $p < 0.05$; *Nr3c2*, $t_{18} = 2.213$, $p < 0.05$). Overnight fluid intake did not differ between vehicle and corticosterone treated mice. **(B)** Overnight treatment with the GR antagonist RU486 did not alter the expression of *Fkbp5*, *Nr3c1* and *Nr3c2* mRNA. Overnight fluid intake did not differ between vehicle and RU486 treated mice. Unpaired, two-tailed Student's t-test; * = $p < 0.05$; *** = $p < 0.001$. Data are presented as mean + SEM. $n = 9-10$ mice per group.

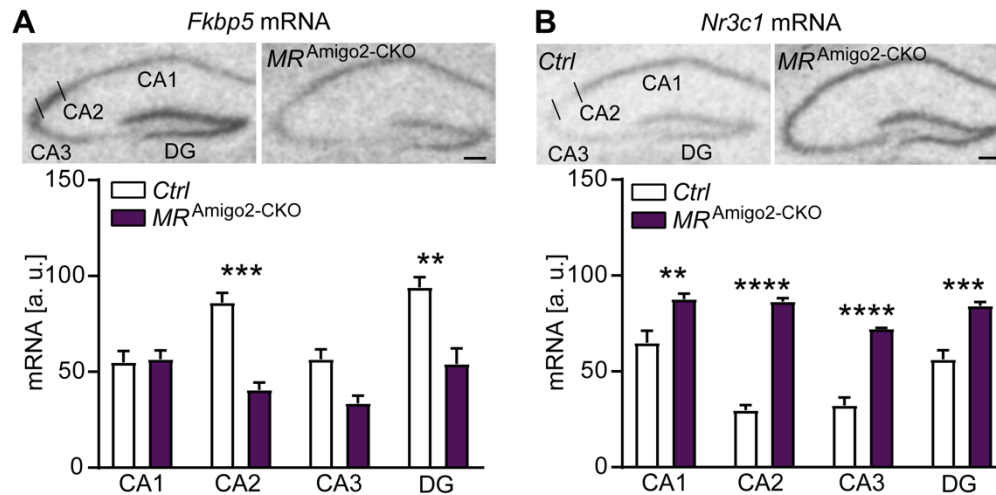


Figure S3. *Fkbp5* and *Nr3c1* mRNA expression in the hippocampus of MR^{Amigo2}-CKO mice, related to Figure 5D and E. (A) MR^{Amigo2}-CKO mice show lower *Fkbp5* mRNA levels (genotype x hippocampal sub-region interaction $F_{3,16} = 7.66$, $p < 0.01$), while *Nr3c1* mRNA expression **(B)** is increased in the hippocampus determined by ISH (genotype x sub-region interaction $F_{3,16} = 8.76$, $p < 0.001$). Top panels - representative autoradiographs of hippocampal *Fkbp5* or *Nr3c1* mRNA expression. Lower panel - quantified expression of *Fkbp5* or *Nr3c1* mRNA. Two-way ANOVA + Bonferroni post hoc test; ** = $p < 0.01$; *** = $p < 0.001$; **** = $p < 0.0001$. Data are presented as mean + SEM. $n = 3$ mice per group. Scale bar, 250 μm .

Table S1. Key information about each donor, related to Figure 1D-E and STAR Methods.

Donor	Sex	Age (y)	Race/Ethnicity	Postmortem Interval (h)
H0351.1009	Male	57	Caucasian	25.5
H0351.1012	Male	31	Caucasian	17.5
H0351.1015	Female	49	Hispanic	30
H0351.1016	Male	55	Caucasian	18
H0351.2001	Male	24	African American	23
H0351.2002	Male	39	African American	10