Supplemental figures

SI Figure 1. LD screening of an inbred population of genetically similar mice allows identification of at-risk mice with an inherent susceptibility. At-risk individuals are characterized by behavioral and molecular signatures of susceptibility, such as light avoidance, high hippocampal levels of mineralocorticoid receptor MR and reduced ability to cope with stress due to an over activation of the glutamate system in hippocampus[1].
(a) Time spent in the light chamber of a light dark box distinguish at-risk mice with an anxiety prone phenotype and low susceptible mice, which spent a significantly higher time in the light. Panel B is adapted from previous reports[2]. Bars represent mean+s.e.m., *indicate significant comparisons, ***P<0.001.

SI Figure 2. Prolonged 21day CRS results in a significant increase in adrenal to body weight ratio compared with non-stressed Ctrl mice, indicating the validity of the chronic stress paradigm. Bars represent mean+s.e.m., *indicate significant comparisons, **P<0.01.

SI Figure 3. Pairwise 2-way analyses for comparisons of all conditions (+/- stress, +/- LAC treatment) for Sholl analyses of MeA dendritic length and number of intersections in incremental steps of 15μm from the soma show that MeA stellate neurons underwent the most pronounced decrease in length (a) and number of intersections (e) in CRS mice starting from a distance of 105μm from the soma. 3 days of LAC oral treatment promotes dendritic plasticity of MeA stellate neurons at the closer distance of 75μm from the soma (c,g), suggesting that LAC prophylactic treatment induced growth of novel primary and secondary dendrites rather than reversing a pathological phenotype by elongation of CRS-shrink dendrites. In agreement with previous findings, pairwise 2-way ANOVA for Sholl analyses also shows that LAC has no effects effect in naïve mice (b,d,f and h). (a: $F_{22,345}$=61.3, p<0.0001 (distance); $F_{1,345}$=51.1, p<0.0001 (stress); b: $F_{22,207}$=36.8, p<0.0001 (distance); $F_{1,207}$=1.1, p=0.28 (treatment); c: $F_{22,345}$=78, p<0.0001 (distance); $F_{1,345}$=87.4, p<0.0001 (treatment); d: $F_{22,207}$=52.3, p<0.0001 (distance); $F_{1,207}$=0.22, p=0.64 (stress); e: $F_{22,345}$=53, p<0.0001 (distance); $F_{1,345}$=44.2, p<0.0001 (stress); f: $F_{20,189}$=29, p<0.0001 (distance); $F_{1,189}$=0.002, p=0.96 (treatment); g: $F_{22,345}$=67.7, p<0.0001 (distance); $F_{1,345}$=73.6, p<0.0001 (treatment); h: $F_{20,189}$=41.2, p<0.0001 (distance); $F_{1,189}$=0.45, p=0.50 (stress)).

Supplemental References

1. Nasca, C., Bigio, B., Zelli, D., Nicoletti, F. & McEwen, B.S. Mind the gap: glucocorticoids modulate hippocampal glutamate tone underlying individual differences in stress susceptibility. *Molecular psychiatry* **20**, 755-763 (2015).
2. McEwen, B.S., Nasca, C. & Gray, J.D. Stress Effects on Neuronal Structure: Hippocampus, Amygdala, and Prefrontal Cortex. *Neuropsychopharmacology* (2015).