Supplementary Figure 1

SI Figure 1. Influence of chronic unpredictable stress (CUS) on the expression of synapse related genes. Expression of the mRNA of the five dysregulated genes that were previously confirmed by PCR analysis were analyzed with a $^{35}$S-labeled antisense riboprobe, including (a) calmodulin II (Calm 2), (b) synapsin I (Syn1), (c) Rab3A (Rab3a), (d) Rab4B (Rab4b), and (e) tubulin 4 (Tubb4). Representative images of the control (top) and CUS (bottom) autoradiographs are shown, and quantitative analysis (bar graphs) are shown. Results represent the means ± S.E.M. ($n = 5$). *$P < 0.05$ compared to control (unpaired t-test). (Scale bar, 1 mm)
**Supplementary Figure 2**

(a) Expression of GATA1 was analyzed by qRT-PCR. Results represent the mean fold change relative to matched controls ± S.E.M (n = 9 for Control and All MDD, n = 4 for unmedicated patients, or MDD/no meds), P = 0.0001 (One-way ANOVA). (b) Spine synapses were quantified in layer II/III of dlPFC, and the results represent the mean ± S.E.M (n = 5 for Control and All MDD, n = 2 for MDD/no meds); P = 0.0001 (One-way ANOVA). *P < 0.05 compared to control (tukey’s posthoc analysis).

**Supplementary Figure 3**

(a) Expression of GATA1 was analyzed by qRT-PCR. Results represent the mean fold change relative to matched controls ± S.E.M (n = 9 for Control and All MDD, n = 3 for age of onset <40yr, and n = 6 for age of onset ≥40yr), P = 0.001 (One-way ANOVA). (b) Spine synapses were quantified in layer II/III of dlPFC, and the results represent the mean ± S.E.M (n = 5 for Control and All MDD, n = 3 for age of onset <40yr, and n = 2 for age of onset ≥40yr); P = 5.18E-05 (One-way ANOVA). *P < 0.05 compared to control (tukey’s posthoc analysis).
Supplementary Figure 4

(a) Expression of GATA1 was analyzed by qRT-PCR. Results represent the mean fold change relative to matched controls ± S.E.M (n = 9 for Control and All MDD, n = 6 for non-suicide MDD patients), P = 0.002 (One-way ANOVA). (b) Spine synapses were quantified in layer II/III of dIPFC, and the results represent the mean ± S.E.M (n = 5 for Control and All MDD, n = 2 for non-suicide MDD patients); P = 0.0001 (One-way ANOVA). *P <0.05 compared to control (Tukey’s posthoc analysis).

Supplementary Figure 5

Expression of GATA1 was analyzed by qRT-PCR. Results represent the mean fold change relative to matched controls ± S.E.M (n = 9 for Control and All MDD, n = 2 for single episode, and n = 7 for multiple episodes), P = 0.001 (One-way ANOVA). *P <0.05 compared to control (Tukey’s posthoc analysis).
Supplementary Figure 6

SI Figure 6. Antidepressant treatment does not reverse the behavioral effects of viral GATA1 expression.

rAAV-control or rAAV-GATA1 were infused into the medial PFC, and then rats were administered vehicle or antidepressant, and behavior in the forced swim test was determined. Anti-depressant treatments included fluoxetine (15 mg kg$^{-1}$, i.p., 28 d), washout for 7 d, and then imipramine (15 mg kg$^{-1}$, i.p., 4 d). Rats expressing Gata1 did not respond to either fluoxetine (not shown) or imipramine treatment. Results represent the mean immobility time (during the 5–10 min swim test) ± S.E.M. ($n = 4–8$ per group). (One-way ANOVA). *$P < 0.05$, #$P = 0.056$ compared to rAAV-control saline (Fisher's posthoc analysis).
SI Figure 7. Efficiency of shRNA knockdown on the expression of Gata1 mRNA in HEK cells and rat PFC.

(a) Different amounts of GATA1shRNA plasmid were transfected into HEK cells to determine the efficiency of knockdown of Gata1 mRNA expression, analyzed by qRT-PCR. Results represent the mean ± S.E.M. (n = 2 per group); *P < 0.05, Students t-test. (b) Infusion of rAAV-GATA1shRNA into rat PFC resulted in knockdown of Gata1 mRNA in the microdissected regions of medial PFC. rAAV-GATA1shRNA or rAAV-Scr were infused into PFC and rats were exposed to CUS or remained in the home cage (Control). Results represent the mean ± S.E.M. (n = 4–5 per group). Two-way ANOVA demonstrates that there was an overall main effect of rAAV-GATA1shRNA compared to rAAV-Scr (P < 0.05). There was also significant difference between animals receiving rAAV-GATA1shRNA vs. rAAV-Scr in the CUS groups (*P < 0.05, Fisher's posthoc analysis). There was no significant effect of CUS compared to control, possibly due to the behavioral testing, which could explain the variability.