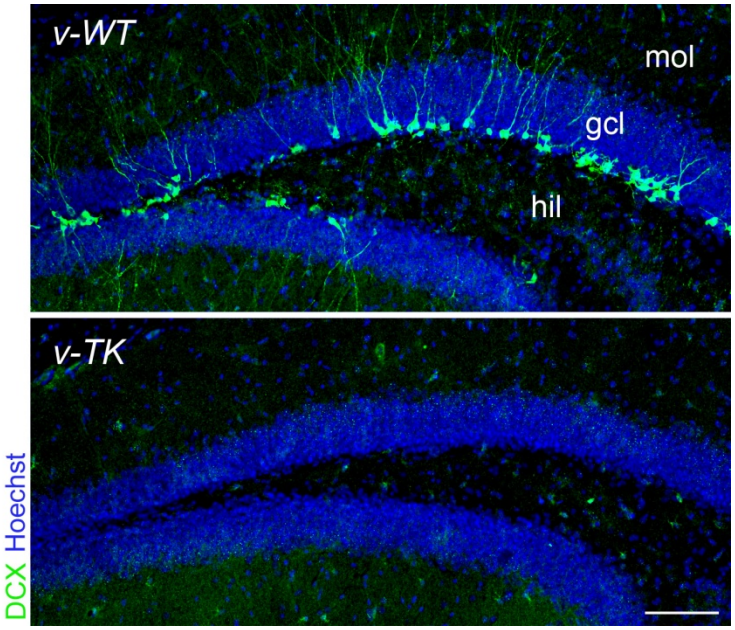
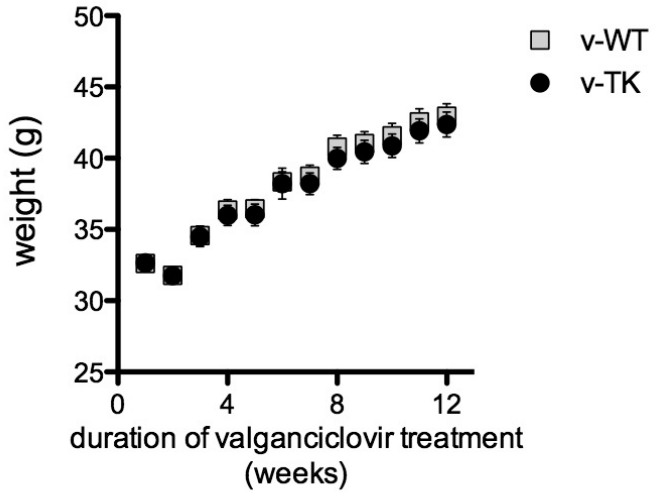
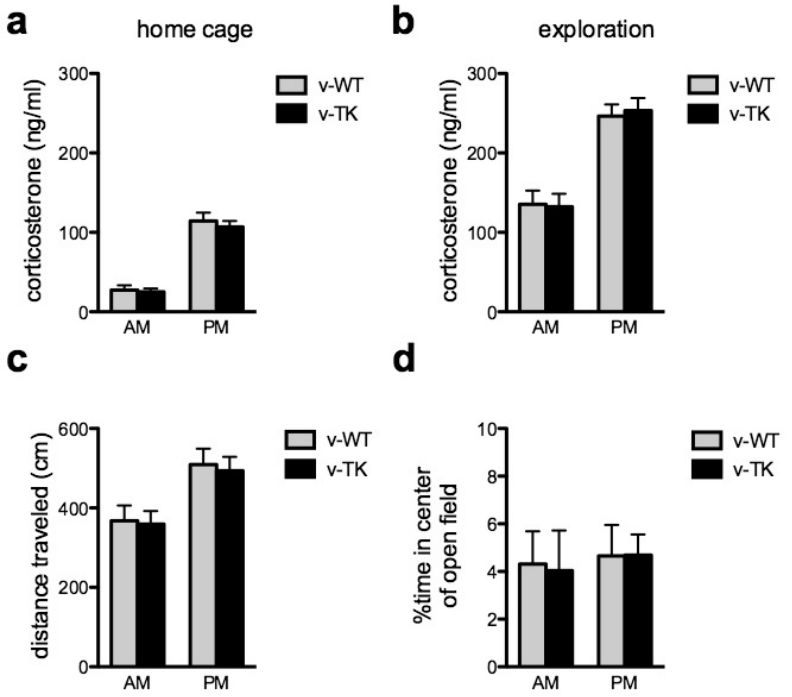
doi:10.1038/nature10287



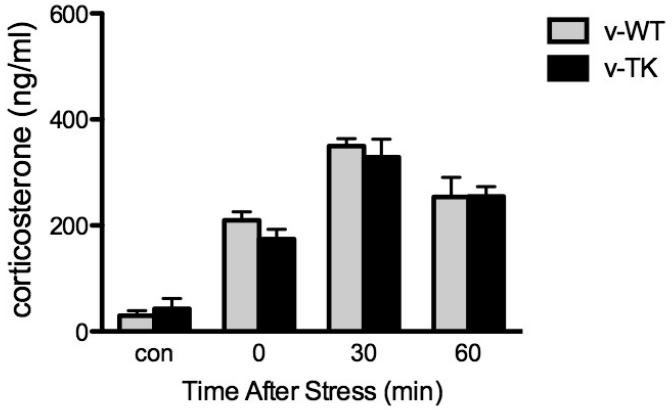
Supplementary Figure 1: Confocal photograph of doublecortin immunostaining following 12 weeks of valganciclovir treatment. Extending the 4 week treatment results in Fig. 1, neurogenesis remained suppressed in v-TK mice after longer valganciclovir treatments, as employed in the endocrine and behavior experiments. Scale bar 100 μm. Mol, molecular layer; gcl, granule cell layer; hil, hilus.



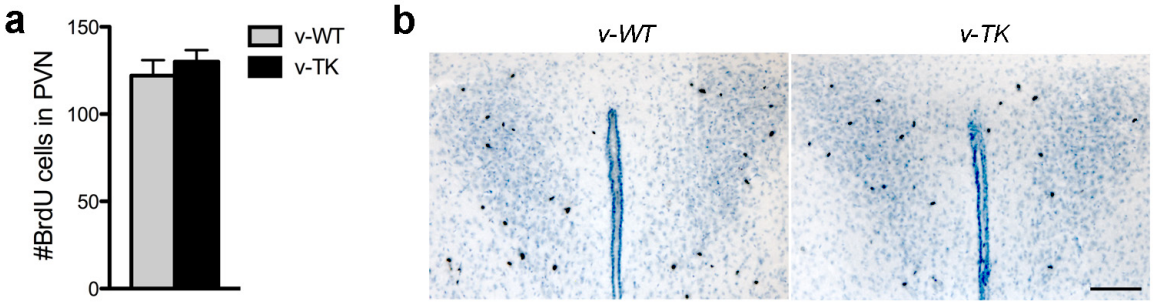
Supplementary Figure 2: Body weights were not significantly different in v-WT and v-TK mice (2-way repeated measures ANOVA, genotype effect $F_{1,759}$=0.2, P=0.69, duration effect $F_{11,759}$= 239, P<0.0001, genotype x duration interaction $F_{11,759}$=0.4, P=0.97).



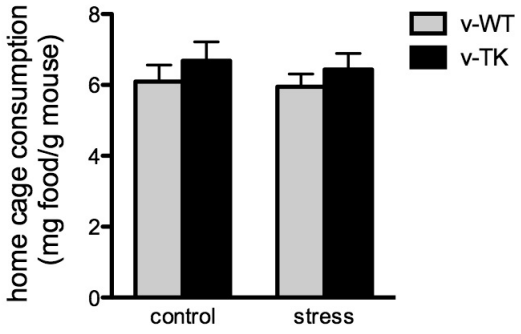
Supplementary Figure 3: Circadian fluctuations in corticosterone and baseline exploratory behavior. a) Circadian fluctuation in serum corticosterone in the home cage condition is normal in treated v-TK mice (genotype effect $F_{1,64}$=0.4, P=0.52; time of day effect $F_{1,64}$=123, P<0.001). b) Corticosterone levels did not differ between v-WT and v-TK mice following exposure to a novel open field, a mild stressor (genotype effect $F_{1,66}$=0.02, P=0.90; time of day effect $F_{1,66}$=53, P<0.001). c) Total locomotor distance did not differ between v-WT and v-TK mice during exploration of the novel environment (genotype and interaction effects $F_{1,66}$<1, P>0.7, time of day effect $F_{1,66}$=14, P<0.001). d) Time spent in the center of the open field (10 cm x 10 cm) did not differ between v-WT and v-TK mice (genotype and interaction effects both $F_{1,66}$<1, P>0.7; time of day effect $F_{1,66}$=4, P<0.001).



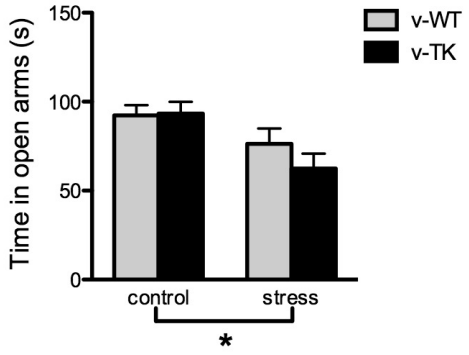
Supplementary Figure 4: Corticosterone response to isoflurane anesthesia, a moderate physical stressor, was unchanged in v-TK mice (genotype effect $F_{1,31}$=0.4, P=0.55; time effect $F_{3,31}$=49, P<0.001; interaction $F_{3,31}$=0.3, P=0.8).



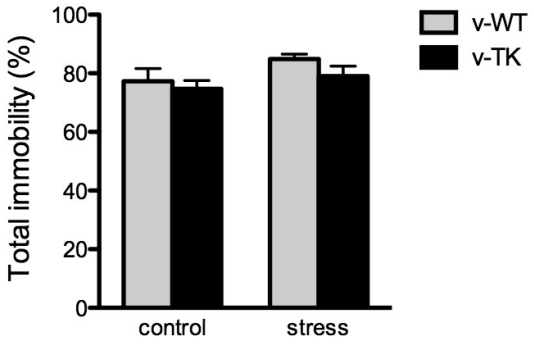
Supplementary Figure 5: Cell addition in the hypothalamic paraventricular nucleus (PVN), which drives the HPA response to stress, is not reduced in v-TK mice (T_{11} = 0.7, P=0.5), suggesting that any neurogenesis that might occur in the adult PVN is not altered in our transgenic model. b) BrdU immunostaining (black) in the PVN, as seen with Nissl counterstain (blue). Scale bar 100 μm.



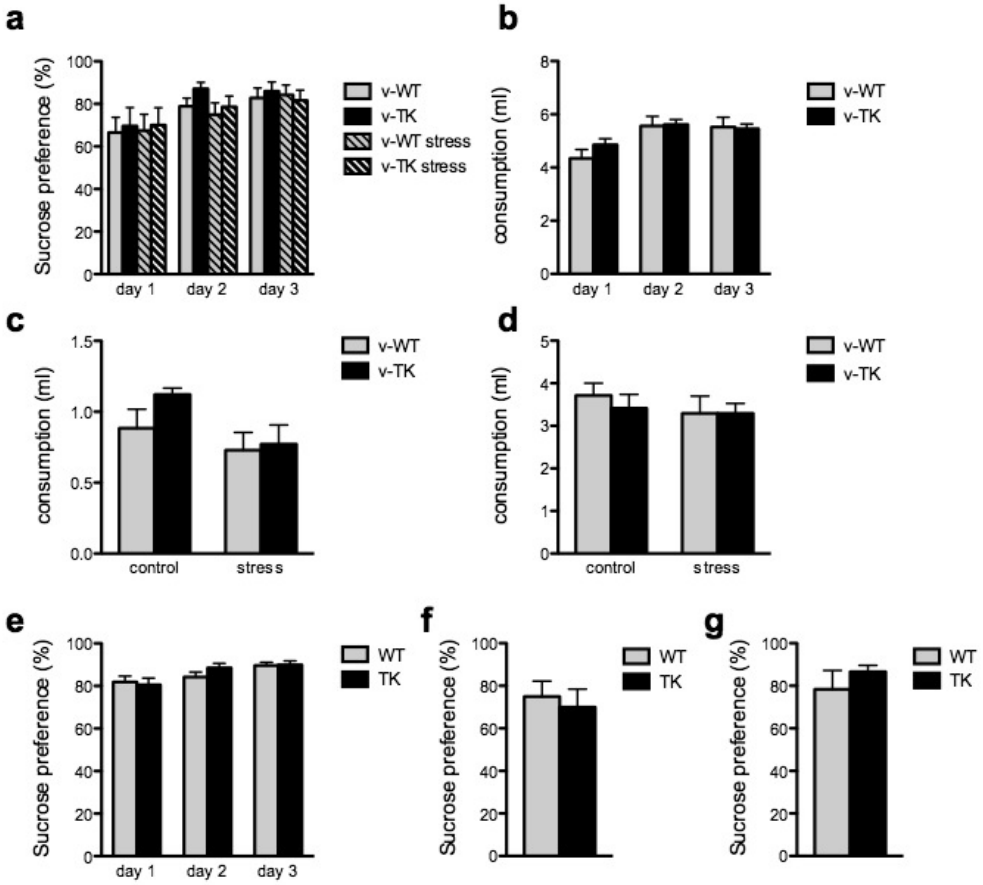
Supplementary Figure 6: Home cage food consumption following the NSF test. v-WT and v-TK mice did not consume different amounts of food upon returning to their home cage (genotype effect $F_{1,82}$=1.3, P=0.2; stress effect $F_{1,82}$=0.2, P=0.7; interaction $F_{1,82}$=0.01, P=0.9).



Supplementary Figure 7: Anxiety-related behavior in the elevated plus maze. Stress signficantly reduced time spent in the open arms of the maze in both genotypes. Stressed v-TK mice spent 18% less time in the open arms than stressed v-WT mice, which was not significantly different (genotype effect $F_{1,46}$=0.7, P=0.4; stress effect $F_{1,46}$=9, P<0.01; interaction $F_{1,46}$=0.9, P=0.3).



Supplementary Figure 8: v-WT and v-TK mice did not show differences in total immobility during minutes 2-6 of forced swim testing (genotype effect $F_{1,88}$=1.9, P=0.2; stress effect $F_{1,88}$=3.9, P=0.05; genotype x stress interaction $F_{1,88}$=0.3, P=0.6).



Supplementary Figure 9: Sucrose preference habituation and consumption (a-d) and sucrose preference in mice not treated with valganciclovir (e-g). a) Pre-test habituation. Sucrose preference during habituation was not different between v-WT and v-TK mice; both groups showed increased sucrose preference across days of habituation (2 way repeated measures ANOVA, control and to-be-stressed mice pooled; genotype effect $F_{1,42}$<0.1, P=0.9; day effect $F_{2,42}$=12, P<0.0001; interaction $F_{2,42}$=0.4, P=0.7; day 3 vs. day 1 post hoc P<0.05 for both v-WT and v-TK). b) Total consumption (sucrose + water) was not different in v-WT and v-TK mice (2 way repeated measures ANOVA, control and to-be-stressed mice pooled; genotype effect $F_{1,42}$=0.2, P=0.6; day effect $F_{2,42}$=16, P<0.0001; interaction $F_{2,42}$=1.2, P=0.3). c)

Total consumption during the 10 min test was not signficantly different between groups but there was a trend for stress to reduce overall consumption (genotype effect $F_{1,20}$=1.1, P=0.3; stress effect $F_{1,20}$=3.5, P=0.08; interaction $F_{1,20}$=0.5, P=0.5). d) There were no neurogenesis- or stress-related differences in total consumption on the night following the 10 min test (genotype effect $F_{1,20}$=0.2, P=0.7; stress effect $F_{1,20}$=0.6, P=0.4; interaction $F_{1,20}$=0.2, P=0.7). e) Pre-test habituation in WT and TK mice (not treated with valganciclovir) revealed no genotype differences in sucrose preference (genotype effect $F_{1,20}$=0.2, P=0.3; effect of day $F_{2,20}$=11.5, P=0.0005; interaction $F_{2,20}$=1.3, P=0.3). f) There was no difference in sucrose preference in untreated WT and TK mice during the 10 min test (T_{10}=0.4, P=0.7). g) There was no overnight difference in sucrose preference in untreated WT and TK mice during the dark cycle immediately following 10 min test (T_{10}=0.9, P=0.4).