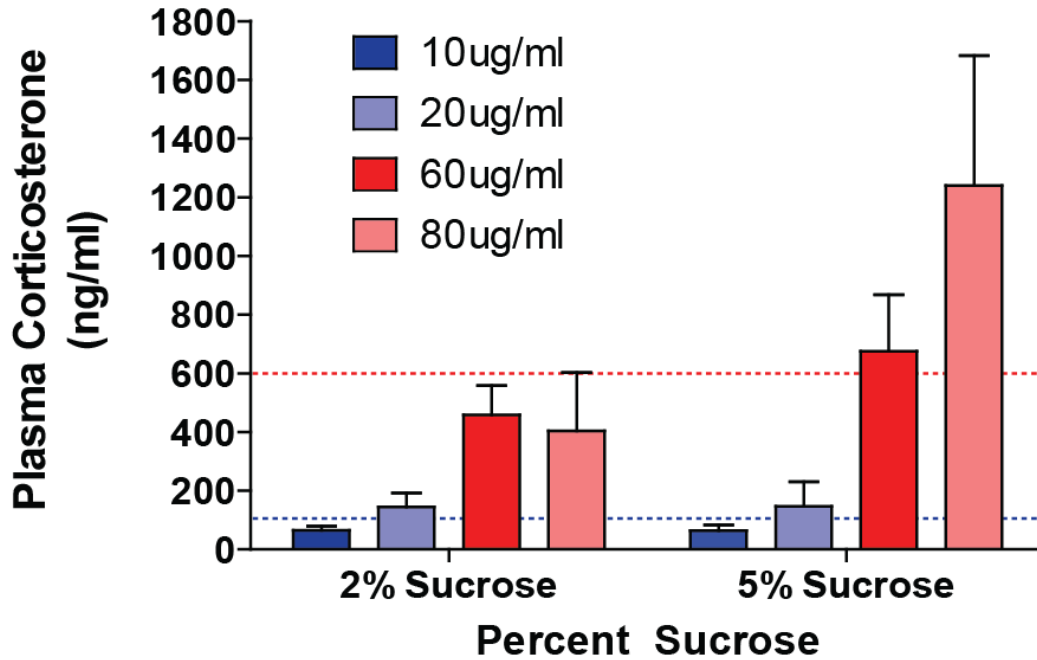
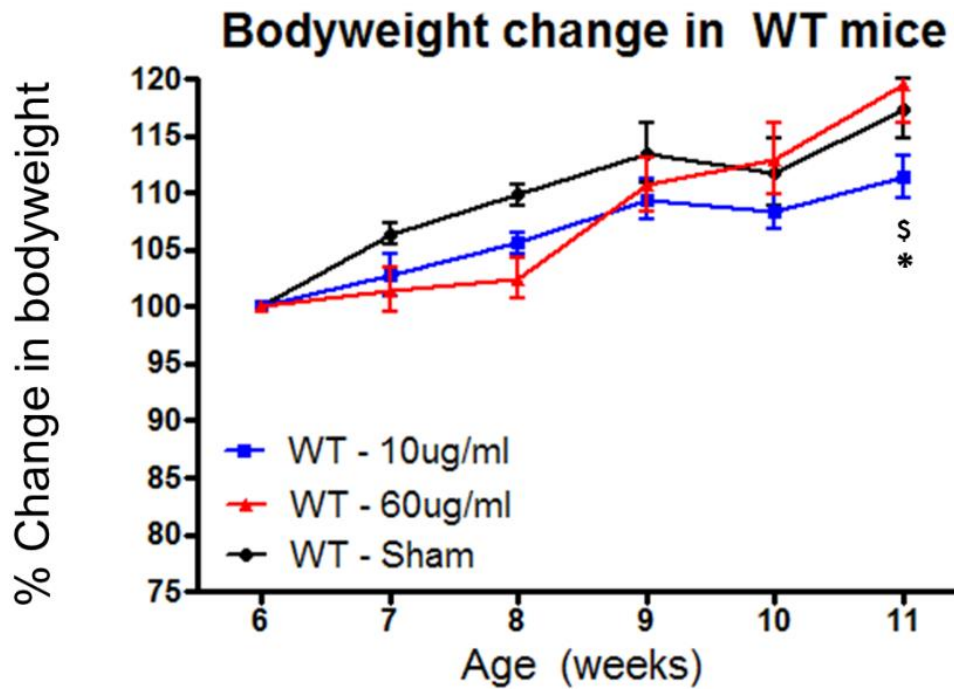


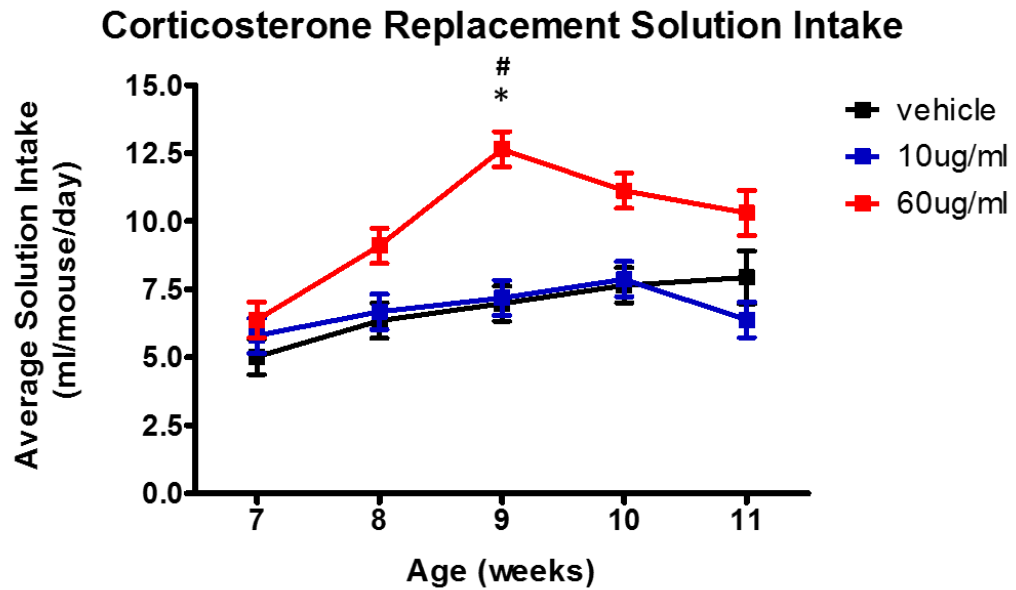
## Dose Response Pilot



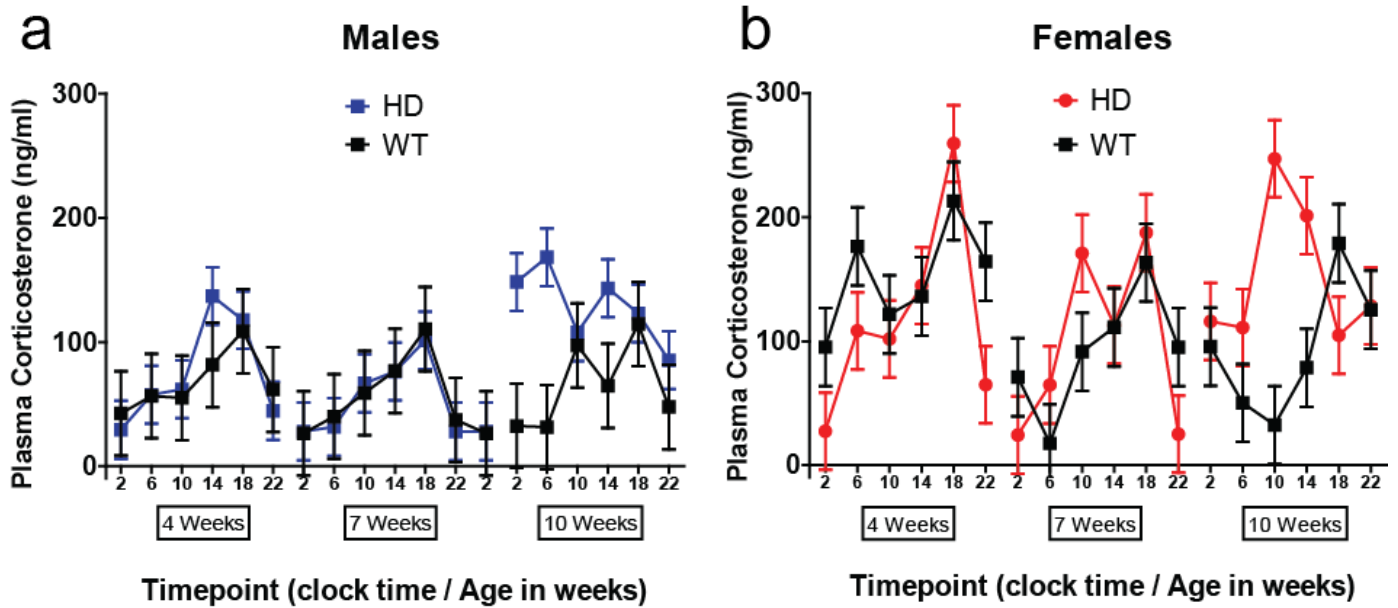
**Supplemental Figure 1. Dose Response Pilot.** Mice were adrenalectomized and given one of 4 levels of CORT replacement (10ug/ml, 20ug/ml, 60ug/ml, and 80ug/ml). The goal of this study was to identify the CORT replacement doses that would reach the target plasma CORT levels – 100ng/ml for WT-levels (dotted blue line) and 600ng/ml for HD-levels (dotted red line). Replacement solutions were either supplemented with 2% or 5% sucrose, to increase palatability and thus increase solution intake and plasma CORT level. Replacement solution also contained 0.9% saline. Target WT-levels were achieved with 10 $\mu$ g/ml and HD-levels with 60 $\mu$ g/ml (both with 2% sucrose supplementation, which were the doses chosen for the larger adrenalectomy and CORT replacement study).



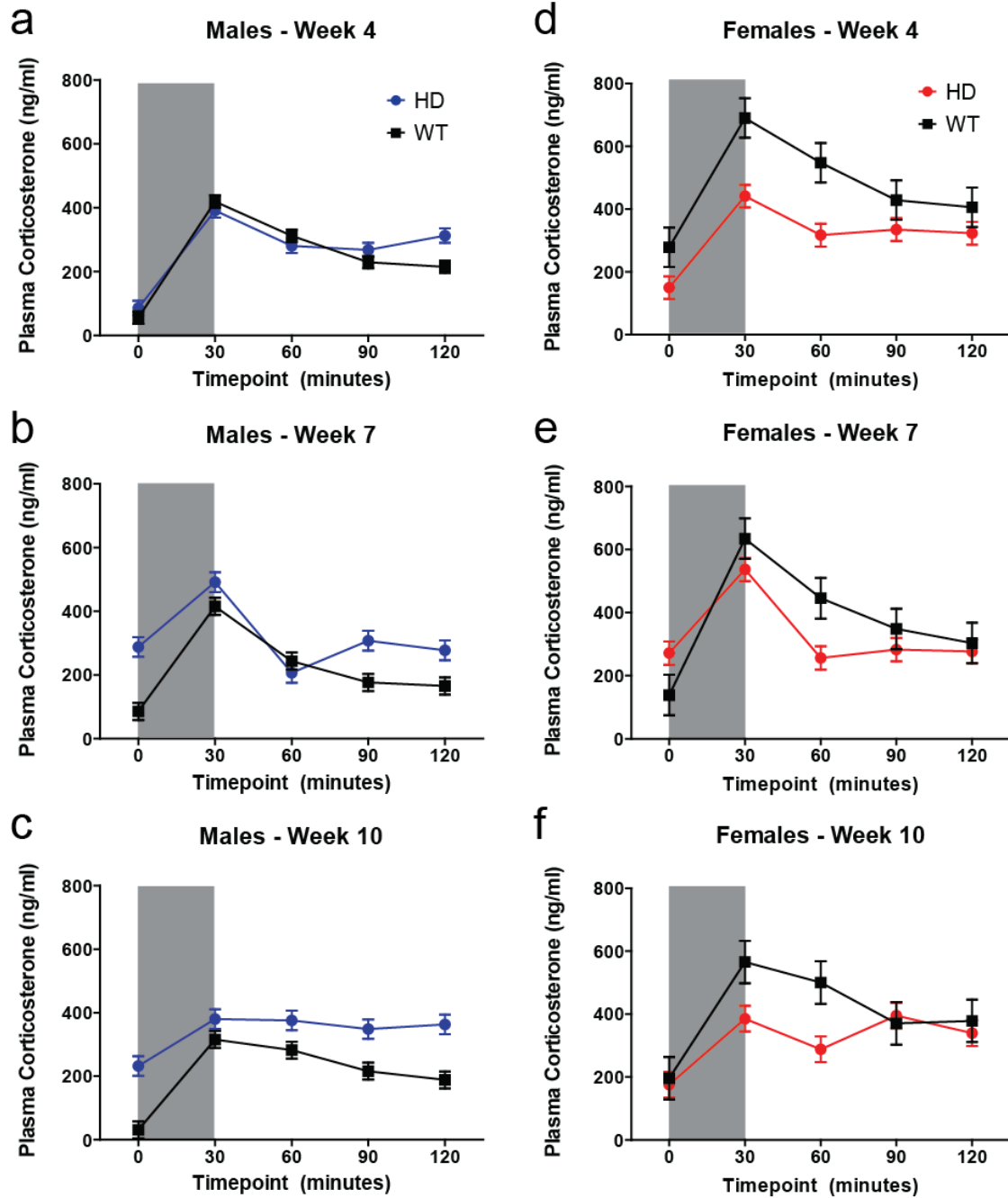
**Supplemental Figure 2 – Body weight in wild-type mice.** WT mice showed a consistent but small increase in bodyweight throughout the study, regardless of treatment. At the 11 week timepoint, mice on low-dose CORT showed a small but significant decrease in the amount of weight-gain relative to both the high dose CORT (\* Tukey's post-hoc  $p < .05$ ) and sham treated groups (\$ Tukey's post-hoc  $p < .05$ ).



**Supplemental Figure 3 – Corticosterone solution intake.** Cage scores were taken daily for consumption of corticosterone solution, and averaged across the number of mice per cage. Weekly averages are presented here. There is a significant elevation of intake in the high dose (60ug/ml) group at 9 weeks of age, relative to the low dose (\* Tukey's  $p < .05$ ) for both and vehicle control groups (#Tukey's  $p < .05$ ).



**Supplemental Figure 4. Circadian CORT release in males and females.** Since there wasn't a statistically significant effect of sex (or its interactions) on plasma CORT levels in the circadian study, data was collapsed across sex for Fig 2. For qualitative purposes, circadian CORT profiles of (a) male and (b) female mice are presented here, separately.



**Supplemental Figure 5. Stress induced CORT release at 4, 7, and 10 weeks of age.** Since there wasn't a statistically significant effect of age (nor age\*genotype) on stress induced CORT release in this study, data was collapsed across age for Fig 3. However, stress-induced CORT release profiles for male and female mice at 4, 7, and 10 weeks of age are also included here for qualitative purposes.