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Supplementary Figures

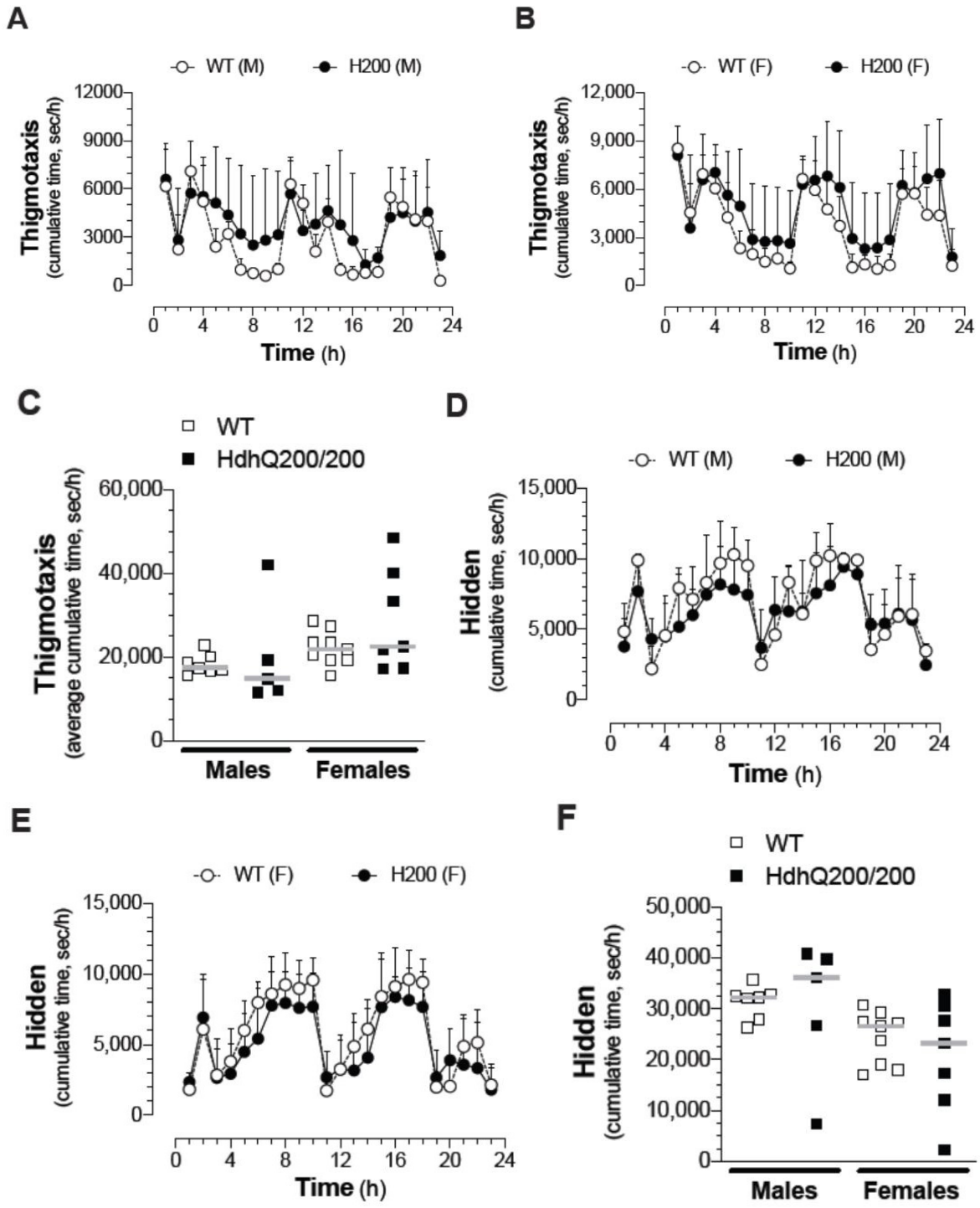

Figure 1: Comparable time spent in the thigmotaxis and hidden zones in male and female HdhQ200/200 mice at 8 months of age.

Mice were housed in PhenoTyper home-cages for 72 hours and the cumulative time spent in the thigmotaxis and hidden zones were measured during dark phase. At 8 months of age, both female and male HdhQ200/200 mice spent similar amounts of time (i.e. total seconds in zone/h) in the **(A and B)** Thigmotaxis zone and **(D and E)** hidden zone when compared to respective wild-type littermates Statisticalanalysis: One-way ANOVA analysis (multiple comparison using Tukey) of the cumulative time spent in the **(C)** thigmotaxis zone and **(F)** hidden zone resulted in no difference. N = 5-9 mice per condition and error bars represent S.E.M.

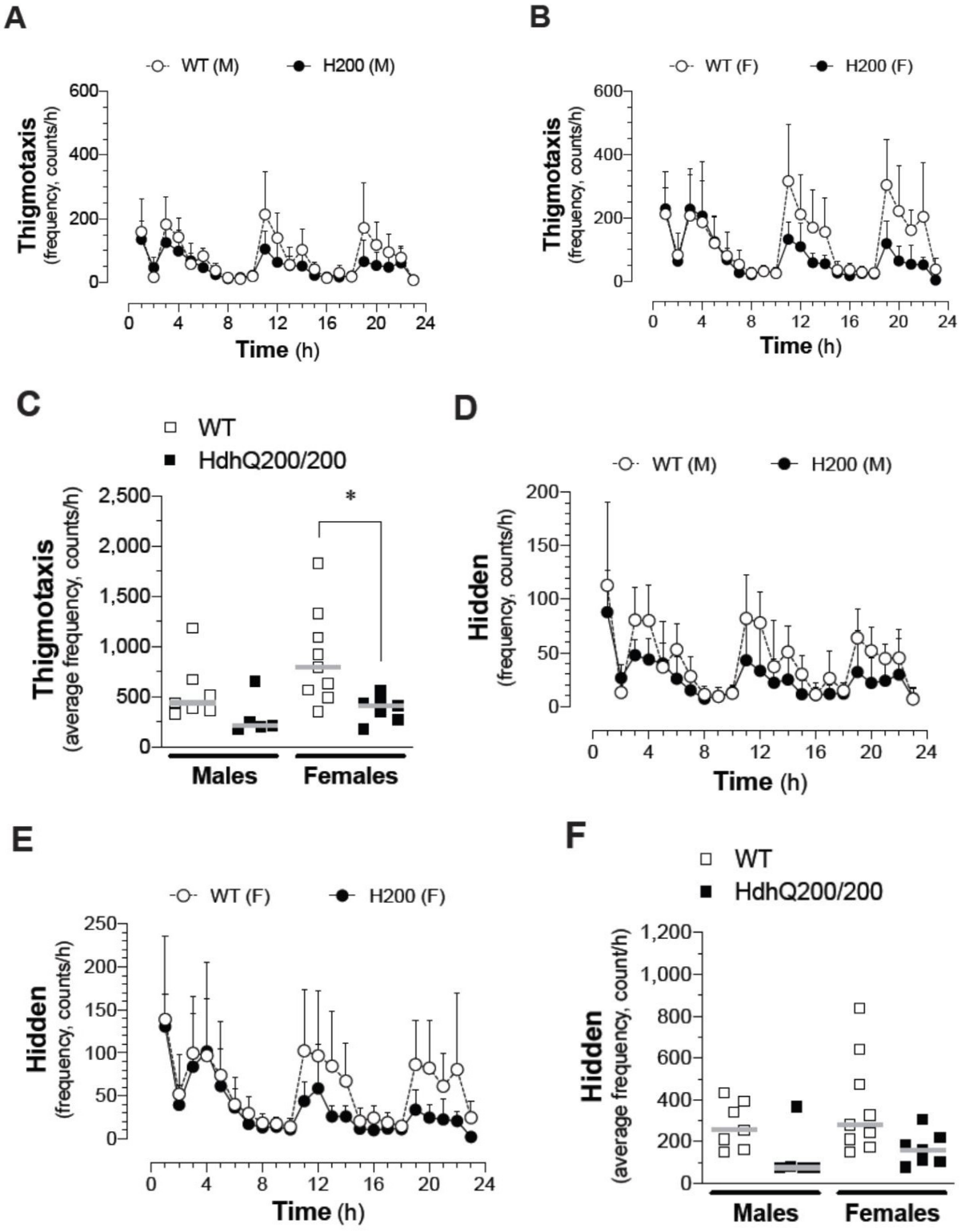

Figure 2: Reduced frequency to enter the thigmotaxis and hidden zones in female HdhQ200/200 mice at 8 months of age.

PhenoTyper analysis for the frequency to enter the thigmotaxis and hidden zones indicated that female, but not male, HdhQ200/200 mice less frequently entered (i.e. number of entry/h) the **(A and B)** thigmotaxis zone and **(D and E)** hidden zone when compared to respective wild-type littermates. Statistical analysis: One-way ANOVA analysis (multiple comparison using Tukey) of the frequency to enter the **(C)** thigmotaxis zone but not **(F)** hidden zone resulted in significant differences compared to wild-type female littermates. N = 5-9 mice per condition, error bars represent S.E.M. and *$p < 0.05$.

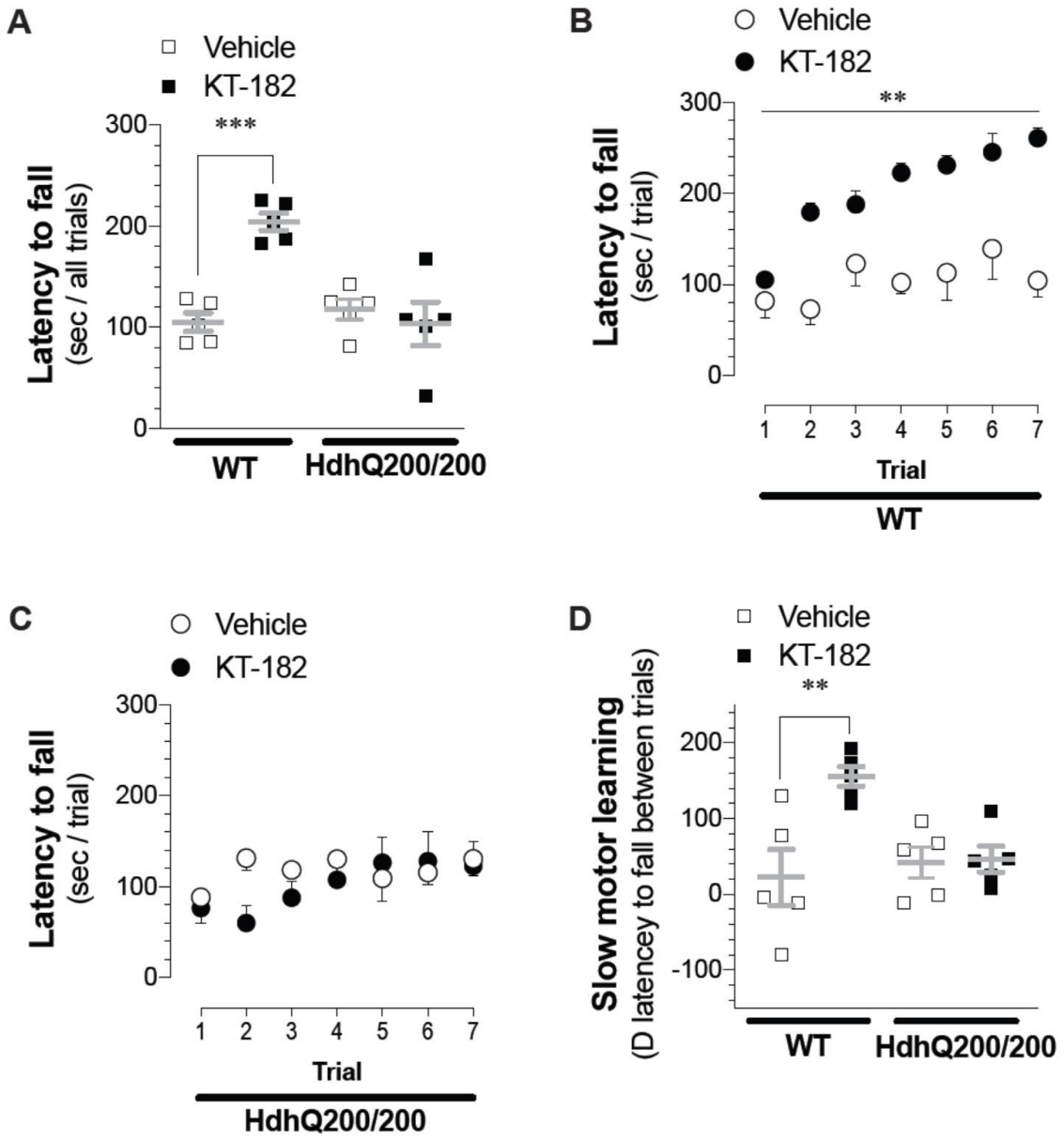

Figure 3: Improved motor coordination in wild-type male mice after acute KT-182 treatment.

(A) KT-182 increased motor coordination in male wild-type (WT) mice but not male HdhQ200/200 mice. Statistical analysis: One-way ANOVA analysis (multiple comparison using Tukey) indicated 2- fold improvement in latency to fall in male WT mice triggered by KT-182 but no difference between treatments in male HdhQ200/200 mice. **(B and C)** KT-182 improved latency to fall in male (B) WT mice but did not affect the latency to fall in (C) HdhQ200/200 mice. Statistical analysis: Two-way ANOVA with a Bonferroni post-hoc analysis indicated significant improvement of motor coordination in male WT mice treated with KT-182 compared to vehicle-treated male WT mice; **(D)** Slow motor learning was significantly enhanced in male WT mice by KT-182 but unaffected in HdhQ200/200 mice. Statistical analysis: One-way ANOVA analysis (multiple comparison using Tukey) indicated an 8-fold improvement. N = 5 mice per condition, error bars represent S.E.M. and **p<0.01, ***p<0.001.