

# Do environmental interventions ameliorate gut dysbiosis in Huntington disease mice?

Data Analysis

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## Executive Summary

- The data were preprocessed to remove any samples with more than 80% missing data which resulted in removing four mice from the study.
- Except for the clinical variable clasping score, all other single time-point observations, such as Colon length, were modelled using Linear mixed models (LMMs). A LMM is an extension of a linear model to incorporate both fixed-effect terms and random effect terms. For repeated measures, time was added as covariate in the LMM. All two-way interactions between fixed effects were included in the LMM models.
- For the variable clasping score measured on an ordinal scale, we fitted a cumulative linear mixed model with Laplace approximation.
- For models with at least one significant effect, we performed a post-hoc contrast analysis on estimated marginal means to identify significant pairs using the emmeans R package (Lenth 2021). The emmeans method performs pairwise comparisons on the levels of significant main effects while controlling for other factors. For example, if genotype was significant in the LMM, a pairwise comparisons between two genotypes separately for each sex and housing type would be conducted. All the p-values from the pairwise comparisons were then adjusted for multiple comparisons using Tukey adjustment.

## 1 Data preprocessing (Removing insufficient samples)

Data from ‘210330\_Gubert\_EE-EX\_Data\_All.xlsx’ were analysed by combining the male and female details from ‘Female\_EEEX\_Data\_Final’ and ‘Male\_EEEX\_Data\_Final’.

First, the samples with more than 80% missing data were removed from the analysis (insufficient data). As a result, 4 mice were removed from the analysis. These four samples did not have any clinical information ( i.e. Colon Length, Gut Permeability, Fecal Water content at Week 12, Isobutyrate, 2-Methyl butyrate, Isovalerate). Those mice fell into the following combination of Sex, genotype and housing condition:

– Female/ HD/ EE      – Female/ HD/ EX      – Female/ WT/ SH      – Male/ HD/ EX

After the preprocessing, the composition of the samples are as follows:

##		Sex	Female	Male
##	Genotype Housing			
##	WT SH		12	12
##	EE		12	12
##	EX		12	11
##	HD SH		11	12
##	EE		11	12
##	EX		11	11

## 2 Effect of Housing, Genotype and Sex on Brain Weight

In this section, we use LMM to find the significant variables that are associated with the Brain weight of a mouse. LMM model considers both fixed and random effects. Fixed effects are variables that we expect

will have an impact on our response variable. For example, we expect Sex, genotype and housing would impact the brain weight of a mouse. Thus, those variables (i.e. Sex, genotype and housing) are considered fixed effects. Random effects are usually grouping factors that may have an impact on the response variable but we are not specifically interested in their impact. In this study, mice are housed within cages (random effect), while we are investigating the effect of sex (male, female); genotype (WT, HD) and housing (SH, EE, EX) (fixed effects).

```
##
## =====
##                               Dependent variable:
##                               -----
##                               Brain weight
##                               -----
## GenotypeHD                    -0.049**
##                               p = 0.002
##
## HousingEE                     0.019
##                               p = 0.205
##
## HousingEX                     0.021
##                               p = 0.155
##
## SexMale                      0.030*
##                               p = 0.039
##
## GenotypeHD:SexMale            0.018
##                               p = 0.211
##
## HousingEE:SexMale            -0.026
##                               p = 0.145
##
## HousingEX:SexMale            -0.010
##                               p = 0.553
##
## GenotypeHD:HousingEE         0.008
##                               p = 0.641
##
## GenotypeHD:HousingEX         0.013
##                               p = 0.458
##
## Constant                     0.435***
##                               p = 0.000
##
## -----
## Observations                  138
## Log Likelihood                250.526
## Akaike Inf. Crit.            -477.051
## Bayesian Inf. Crit.          -442.827
## =====
## Note:                        + p<0.1; * p<0.05; ** p<0.01; *** p<0.001
##                               Constants are significant (p<0.001)
```

- Based on the LMM, significant variables are:
  - Sex
  - Genotype

- A significant parameter with a positive value (i.e.  $> 0$ ) indicates a positive effect on the average brain weight. For example, the average brain weight is higher for male mice than female mice.

### 3 LMM for all interested variables

```
##
## =====
##                               Dependent variable:
##                               -----
##                               Gut permeability Gut transit time Colon length Caecum weight
##                               (1)           (2)           (3)           (4)
##                               -----
## GenotypeHD                    -0.059           -9.049           -0.642+           0.036
##                               p = 0.818           p = 0.658           p = 0.058           p = 0.232
##
## HousingEE                     -0.108           -33.768           -0.336           -0.014
##                               p = 0.692           p = 0.121           p = 0.329           p = 0.650
##
## HousingEX                     -0.350           -8.297           -0.329           0.036
##                               p = 0.273           p = 0.720           p = 0.339           p = 0.251
##
## SexMale                       -0.324           12.907           0.343           0.011
##                               p = 0.216           p = 0.553           p = 0.292           p = 0.715
##
## GenotypeHD:SexMale            0.341           -0.489           0.558+           -0.044
##                               p = 0.200           p = 0.983           p = 0.097           p = 0.144
##
## HousingEE:SexMale             0.098           7.170           -0.419           0.042
##                               p = 0.749           p = 0.786           p = 0.299           p = 0.249
##
## HousingEX:SexMale             0.096           -0.412           -0.288           0.045
##                               p = 0.767           p = 0.989           p = 0.473           p = 0.219
##
## GenotypeHD:HousingEE          0.097           42.821           0.504           -0.024
##                               p = 0.752           p = 0.111           p = 0.213           p = 0.509
##
## GenotypeHD:HousingEX          0.005           5.793           0.089           -0.036
##                               p = 0.988           p = 0.833           p = 0.825           p = 0.324
##
## Constant                      0.757***           141.487***           8.249***           0.300***
##                               p = 0.001           p = 0.000           p = 0.000           p = 0.000
##
## -----
## Observations                   89              110              134              138
## Log Likelihood                 -63.266           -527.645           -152.068           152.118
## Akaike Inf. Crit.             150.532           1079.290           328.136           -280.235
## Bayesian Inf. Crit.           178.965           1110.552           361.980           -246.011
## =====
## Note:                          + p<0.1; * p<0.05; ** p<0.01; *** p<0.001
##                               Constants are significant (p<0.001)
```

##	=====			
##	Dependent variable:			
##	-----			
##	Caecum length	Swing time forepaw	Swing time hind paw	Stride time forepaw
##	(1)	(2)	(3)	(4)
##	-----			
## GenotypeHD	0.219+	0.015*	0.011*	-0.017
##	p = 0.097	p = 0.042	p = 0.049	p = 0.637
##	-----			
## HousingEE	-0.199	0.001	0.004	0.024
##	p = 0.143	p = 0.930	p = 0.492	p = 0.526
##	-----			
## HousingEX	0.023	0.006	-0.003	-0.003
##	p = 0.861	p = 0.417	p = 0.623	p = 0.934
##	-----			
## SexMale	0.016	-0.002	-0.002	0.029
##	p = 0.900	p = 0.752	p = 0.739	p = 0.429
##	-----			
## GenotypeHD:SexMale	-0.218+	-0.006	0.001	-0.019
##	p = 0.098	p = 0.358	p = 0.862	p = 0.599
##	-----			
## HousingEE:SexMale	0.255	0.015+	0.005	-0.019
##	p = 0.113	p = 0.084	p = 0.400	p = 0.665
##	-----			
## HousingEX:SexMale	0.095	0.002	0.004	-0.014
##	p = 0.544	p = 0.786	p = 0.500	p = 0.761
##	-----			
## GenotypeHD:HousingEE	0.068	-0.004	-0.005	0.028
##	p = 0.665	p = 0.632	p = 0.426	p = 0.524
##	-----			
## GenotypeHD:HousingEX	-0.151	-0.002	-0.003	0.050
##	p = 0.338	p = 0.830	p = 0.686	p = 0.271
##	-----			
## Constant	2.542***	0.106***	0.093***	0.306***
##	p = 0.000	p = 0.000	p = 0.000	p = 0.000
##	-----			
## Observations	134	133	133	133
## Log Likelihood	-50.442	307.191	327.459	176.381
## Akaike Inf. Crit.	124.884	-590.382	-630.918	-328.762
## Bayesian Inf. Crit.	158.727	-556.636	-597.171	-295.016
##	=====			
## Note:	+ p<0.1; * p<0.05; ** p<0.01; *** p<0.001			
##	Constants are significant (p<0.001)			

##	=====		
##	Dependent variable:		
##	-----		
##	Stride time hind paw	Stride length forepaw	Stride length hindpaw
##	(1)	(2)	(3)
##	-----		
## GenotypeHD	-0.025	0.432*	0.357+
##	p = 0.508	p = 0.043	p = 0.071
##			
## HousingEE	0.024	0.039	0.042
##	p = 0.547	p = 0.856	p = 0.831
##			
## HousingEX	-0.006	0.420+	0.445*
##	p = 0.877	p = 0.063	p = 0.036
##			
## SexMale	0.029	-0.165	-0.161
##	p = 0.445	p = 0.417	p = 0.397
##			
## GenotypeHD:SexMale	-0.010	-0.368+	-0.236
##	p = 0.802	p = 0.086	p = 0.230
##			
## HousingEE:SexMale	-0.017	0.366	0.406+
##	p = 0.713	p = 0.153	p = 0.092
##			
## HousingEX:SexMale	-0.011	-0.067	-0.077
##	p = 0.809	p = 0.795	p = 0.748
##			
## GenotypeHD:HousingEE	0.035	-0.217	-0.171
##	p = 0.462	p = 0.390	p = 0.469
##			
## GenotypeHD:HousingEX	0.049	-0.436+	-0.538*
##	p = 0.298	p = 0.097	p = 0.031
##			
## Constant	0.311***	4.889***	4.956***
##	p = 0.000	p = 0.000	p = 0.000
##	-----		
## Observations	133	133	133
## Log Likelihood	178.083	-124.037	-115.346
## Akaike Inf. Crit.	-332.166	272.074	254.692
## Bayesian Inf. Crit.	-298.420	305.820	288.439
##	=====		
## Note:	+ p<0.1; * p<0.05; ** p<0.01; *** p<0.001		
##	Constants are significant (p<0.001)		

```
##
## =====
##                               Dependent variable:
##                               -----
##                               Absolute paw angle forepaw Absolute paw angle hindpaw
##                               (1)                               (2)
##                               -----
## GenotypeHD                -0.604                -0.352
##                               p = 0.747                p = 0.843
##
## HousingEE                  -0.491                -0.221
##                               p = 0.803                p = 0.905
##
## HousingEX                  -1.221                -2.144
##                               p = 0.541                p = 0.261
##
## SexMale                    -1.687                0.189
##                               p = 0.368                p = 0.914
##
## GenotypeHD:SexMale         2.140                -2.151
##                               p = 0.263                p = 0.237
##
## HousingEE:SexMale          -0.216                -1.872
##                               p = 0.925                p = 0.392
##
## HousingEX:SexMale          2.653                0.743
##                               p = 0.258                p = 0.737
##
## GenotypeHD:HousingEE       0.232                1.691
##                               p = 0.920                p = 0.439
##
## GenotypeHD:HousingEX       -0.826                0.387
##                               p = 0.722                p = 0.861
##
## Constant                   7.912***             13.897***
##                               p = 0.00000             p = 0.000
##
## -----
## Observations                133                133
## Log Likelihood              -370.485             -383.695
## Akaike Inf. Crit.           764.970             791.391
## Bayesian Inf. Crit.         798.716             825.137
## =====
## Note:                        + p<0.1; * p<0.05; ** p<0.01; *** p<0.001
##                               Constants are significant (p<0.001)
```

```
##
## =====
##                               Dependent variable:
##                               -----
##                               Stance width forepaw  Stance width hindpaw
##                               (1)                  (2)
##                               -----
## GenotypeHD                    -0.258**           -0.145
##                               p = 0.009           p = 0.305
##
## HousingEE                     -0.099            -0.240
##                               p = 0.305           p = 0.110
##
## HousingEX                     0.011             -0.043
##                               p = 0.914           p = 0.773
##
## SexMale                       0.219*            0.134
##                               p = 0.022           p = 0.336
##
## GenotypeHD:SexMale            -0.059            -0.161
##                               p = 0.528           p = 0.259
##
## HousingEE:SexMale             -0.225+           -0.021
##                               p = 0.054           p = 0.902
##
## HousingEX:SexMale             -0.196+           -0.130
##                               p = 0.095           p = 0.456
##
## GenotypeHD:HousingEE          0.189            0.082
##                               p = 0.102           p = 0.631
##
## GenotypeHD:HousingEX          0.098            0.069
##                               p = 0.398           p = 0.692
##
## Constant                      1.628***          2.558***
##                               p = 0.000           p = 0.000
##
## -----
## Observations                   133              133
## Log Likelihood                 -25.147           -58.494
## Akaike Inf. Crit.              74.295           140.989
## Bayesian Inf. Crit.            108.041          174.735
## =====
## Note:                          + p<0.1; * p<0.05; ** p<0.01; *** p<0.001
##                               Constants are significant (p<0.001)
```



```
##
## =====
##                               Dependent variable:
##                               -----
##                               propel:brake ratio forepaw propel:brake ratio hind paw
##                               (1)                               (2)
## -----
## GenotypeHD                0.895*                0.152
##                               p = 0.025                p = 0.830
##
## HousingEE                  0.738+                0.580
##                               p = 0.070                p = 0.434
##
## HousingEX                  0.044                -0.468
##                               p = 0.913                p = 0.535
##
## SexMale                    -0.493                -0.187
##                               p = 0.195                p = 0.790
##
## GenotypeHD:SexMale         0.088                1.183
##                               p = 0.820                p = 0.108
##
## HousingEE:SexMale          -0.355                -0.632
##                               p = 0.447                p = 0.468
##
## HousingEX:SexMale          0.153                0.005
##                               p = 0.745                p = 0.996
##
## GenotypeHD:HousingEE       0.057                0.002
##                               p = 0.902                p = 0.999
##
## GenotypeHD:HousingEX       -0.592                -0.495
##                               p = 0.216                p = 0.576
##
## Constant                   1.665***              4.222***
##                               p = 0.00000              p = 0.000
## -----
## Observations                133                133
## Log Likelihood              -194.767            -276.369
## Akaike Inf. Crit.           413.533            576.739
## Bayesian Inf. Crit.         447.279            610.485
## =====
## Note:                        + p<0.1; * p<0.05; ** p<0.01; *** p<0.001
##                               Constants are significant (p<0.001)
```

##	=====			
##	Dependent variable:			
##	-----			
##	Acetate	Propionate	Isobutyrate	Butyrate
##	(1)	(2)	(3)	(4)
##	-----			
## GenotypeHD	-8602.928	-25145.620	2277.939	6972.407
##	p = 0.822	p = 0.602	p = 0.237	p = 0.907
##				
## HousingEE	-1023.549	-6400.128	233.152	58994.610
##	p = 0.980	p = 0.899	p = 0.906	p = 0.352
##				
## HousingEX	4767.927	-10673.920	810.795	53362.420
##	p = 0.906	p = 0.833	p = 0.683	p = 0.401
##				
## SexMale	-21938.740	-23584.870	-130.173	67812.740
##	p = 0.566	p = 0.623	p = 0.945	p = 0.262
##				
## GenotypeHD:SexMale	23581.420	2152.242	-114.541	-44907.600
##	p = 0.539	p = 0.965	p = 0.952	p = 0.457
##				
## HousingEE:SexMale	-26735.560	-51662.690	-1119.766	-71501.210
##	p = 0.568	p = 0.384	p = 0.626	p = 0.332
##				
## HousingEX:SexMale	-32544.930	-49029.750	-2573.925	-161105.800*
##	p = 0.491	p = 0.413	p = 0.277	p = 0.043
##				
## GenotypeHD:HousingEE	14884.980	51773.530	-1296.484	-23170.360
##	p = 0.750	p = 0.383	p = 0.573	p = 0.750
##				
## GenotypeHD:HousingEX	8195.979	27804.550	-2257.265	83812.260
##	p = 0.861	p = 0.640	p = 0.338	p = 0.265
##				
## Constant	96084.230**	173487.900***	4510.105**	99543.590*
##	p = 0.002	p = 0.00002	p = 0.003	p = 0.033
##	-----			
## Observations	90	90	90	90
## Log Likelihood	-975.156	-1021.808	-764.875	-1046.152
## Akaike Inf. Crit.	1974.312	2067.616	1553.751	2116.303
## Bayesian Inf. Crit.	2002.896	2096.201	1582.335	2144.888
##	=====			
## Note:	+ p<0.1; * p<0.05; ** p<0.01; *** p<0.001			
##	Constants are significant (p<0.001)			

##	Dependent variable:			
##	Methylbutyrate2	Isovalerate	Valerate	Caproate
##	(1)	(2)	(3)	(4)
##	-----			
##	GenotypeHD	1548.701+	1747.519	5361.005
##		p = 0.070	p = 0.196	p = 0.193
##				p = 0.831
##	HousingEE	389.604	282.163	1263.034
##		p = 0.643	p = 0.838	p = 0.762
##				p = 0.734
##	HousingEX	891.358	480.120	6866.115
##		p = 0.300	p = 0.729	p = 0.117
##				p = 0.570
##	SexMale	276.116	-428.799	3540.237
##		p = 0.729	p = 0.742	p = 0.375
##				p = 0.667
##	GenotypeHD:SexMale	-65.593	75.254	-2968.780
##		p = 0.936	p = 0.955	p = 0.463
##				p = 0.568
##	HousingEE:SexMale	-592.407	-422.388	-21.168
##		p = 0.546	p = 0.792	p = 0.997
##				p = 0.880
##	HousingEX:SexMale	-1969.476+	-1446.633	-12036.940*
##		p = 0.064	p = 0.378	p = 0.027
##				p = 0.580
##	GenotypeHD:HousingEE	-1553.430	-1478.174	-5598.832
##		p = 0.127	p = 0.362	p = 0.258
##				p = 0.812
##	GenotypeHD:HousingEX	-1053.377	-1504.676	20.468
##		p = 0.300	p = 0.360	p = 0.997
##				p = 0.576
##	Constant	1924.892**	3195.218**	6791.438*
##		p = 0.003	p = 0.003	p = 0.029
##				p = 0.002
##	-----			
##	Observations	90	90	90
##	Log Likelihood	-716.723	-737.957	-845.783
##	Akaike Inf. Crit.	1457.446	1499.913	1715.565
##	Bayesian Inf. Crit.	1486.030	1528.497	1744.149
##	-----			
##	Note:	+ p<0.1; * p<0.05; ** p<0.01; *** p<0.001		
##		Constants are significant (p<0.001)		

## 4 LMM with Week as a covariate

##	=====					
##	Dependent variable:					
##	-----					
##	Food_Intake	Water_Intake	Weight	Rotarod	FH20	FOutput
##	(1)	(2)	(3)	(4)	(5)	(6)
##	-----					
## GenotypeHD	0.090	0.166	0.843	67.587*	4.573	4.530+
##	p = 0.578	p = 0.542	p = 0.437	p = 0.021	p = 0.470	p = 0.060
##						
## HousingEE	-0.031	-0.630+	0.989	78.859*	-8.670	-4.309
##	p = 0.872	p = 0.059	p = 0.407	p = 0.021	p = 0.235	p = 0.119
##						
## HousingEX	-0.037	-0.797*	2.709*	-20.350	10.050	-3.374
##	p = 0.848	p = 0.019	p = 0.030	p = 0.534	p = 0.173	p = 0.221
##						
## SexMale	-0.164	0.393	6.267***	8.769	10.498	2.498
##	p = 0.312	p = 0.156	p = 0.00001	p = 0.752	p = 0.105	p = 0.287
##						
## Week	-0.027	-0.031	0.820***	8.905***	0.777	0.457*
##	p = 0.141	p = 0.306	p = 0.000	p = 0.001	p = 0.130	p = 0.033
##						
## GenotypeHD:SexMale	-0.070	-0.313*	0.292	-9.084	-2.433	1.370
##	p = 0.405	p = 0.029	p = 0.758	p = 0.555	p = 0.586	p = 0.336
##						
## HousingEE:SexMale	0.061	0.297+	-1.293	36.296+	2.359	-1.076
##	p = 0.553	p = 0.084	p = 0.269	p = 0.062	p = 0.666	p = 0.534
##						
## HousingEX:SexMale	0.067	0.280	-1.824	16.699	-4.134	-1.066
##	p = 0.511	p = 0.102	p = 0.124	p = 0.378	p = 0.451	p = 0.539
##						
## GenotypeHD:Week	-0.007	0.066*	-0.218***	-14.385***	-0.490	-0.367+
##	p = 0.647	p = 0.017	p = 0.0002	p = 0.000	p = 0.295	p = 0.057
##						
## SexMale:Week	0.006	-0.084**	0.111+	-3.231	-0.732	-0.251
##	p = 0.687	p = 0.003	p = 0.053	p = 0.179	p = 0.118	p = 0.193
##						
## HousingEE:Week	0.005	0.074*	-0.256***	-4.354	0.758	0.217
##	p = 0.789	p = 0.029	p = 0.0003	p = 0.136	p = 0.183	p = 0.354
##						
## HousingEX:Week	0.034+	0.125***	-0.443***	-0.107	-0.683	0.114
##	p = 0.089	p = 0.0003	p = 0.000	p = 0.972	p = 0.232	p = 0.630
##						
## GenotypeHD:HousingEE	0.035	-0.100	1.290	-12.616	-0.715	-1.063
##	p = 0.735	p = 0.549	p = 0.270	p = 0.503	p = 0.896	p = 0.539
##						
## GenotypeHD:HousingEX	0.008	-0.186	1.154	25.184	-4.154	1.116
##	p = 0.939	p = 0.271	p = 0.323	p = 0.188	p = 0.448	p = 0.520
##						
## Constant	1.301***	1.685***	13.968***	119.417***	44.833***	7.738***
##	p = 0.000	p = 0.000	p = 0.000	p = 0.00003	p = 0.000	p = 0.001
##						

```
## -----
## Observations      215      216      973      834      803      834
## Log Likelihood    -3.316    -108.975  -1991.683  -4559.335  -3089.079  -2495.876
## Akaike Inf. Crit.  40.632    251.949   4017.366   9152.671   6212.158   5025.751
## Bayesian Inf. Crit. 96.704    308.105   4100.068   9232.708   6291.539   5105.789
## =====
## Note:                + p<0.1; * p<0.05; ** p<0.01; *** p<0.001
##                      Constants are significant (p<0.001)
```

## 5 Modelling the variable clasping

```
##           0  1  2  3  4
## Claspings_Week6 123  7  9  0  0
## Claspings_Week7 117 10 11  1  0
## Claspings_Week8 114 11 14  0  0
## Claspings_Week9  98 17 21  2  1
## Claspings_Week10 97 15 22  3  1
## Claspings_Week11 90 17 26  3  3
## Claspings_Week12 68  8 45  7 11
```

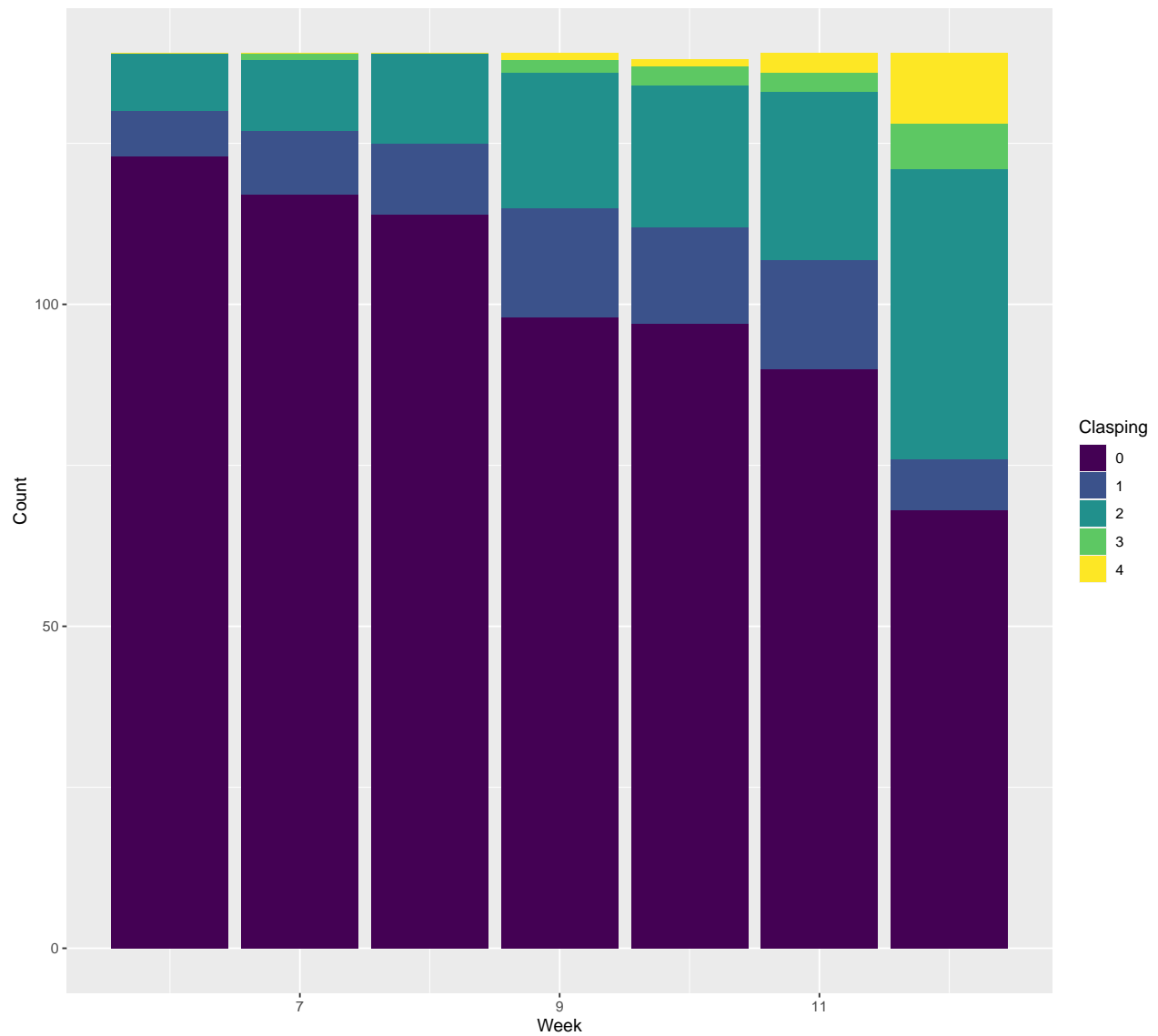


Figure 1: Bar plot for clasping over the 5 weeks

- Cumulative Link Mixed Models are used to model clasping variable

We will fit the following cumulative link mixed model to the Clasping variable( $Y_i$ ):

$\text{logit}(P(Y_i \leq j)) = \theta_j - \beta_1(\text{Genotype}_i) - \beta_2(\text{Housing}_i) - \beta_3(\text{Sex}_i) - \beta_4(\text{Week}_i) - u(\text{Box}_i)$  where  $i = 1, \dots, 973$  and  $j = 0, \dots, 4$ .

```
## Cumulative Link Mixed Model fitted with the Laplace approximation
##
## formula: Clasping ~ Genotype + Housing + Sex + Week + (1 | Box)
## data:    long_data_clasping_sorted
##
## link threshold nobs logLik AIC      niter      max.grad cond.H
## logit flexible  972  -752.18 1524.36 618(2477) 7.67e-05 6.4e+03
##
## Random effects:
## Groups Name      Variance Std.Dev.
## Box      (Intercept) 0.5998   0.7745
## Number of groups:  Box 36
##
## Coefficients:
##              Estimate Std. Error z value Pr(>|z|)
## GenotypeHD   0.804965   0.306927   2.623  0.00872 **
## HousingEE   -0.161811   0.375274  -0.431  0.66634
## HousingEX   -0.006249   0.372239  -0.017  0.98661
## SexMale      0.611638   0.306046   1.999  0.04566 *
## Week         0.413447   0.042902   9.637 < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Threshold coefficients:
##      Estimate Std. Error z value
## 0|1    5.6206    0.5535  10.15
## 1|2    6.2419    0.5617  11.11
## 2|3    8.4128    0.6054  13.90
## 3|4    9.1692    0.6350  14.44
## (1 observation deleted due to missingness)
```

The coefficients of Genotype HD, Male and Week are positive indicating that the clasping rate being higher is more likely for higher weeks, among males and for HD group. The odds ratio of clasping rate being in category  $j$  or above for male to female is 1.84.

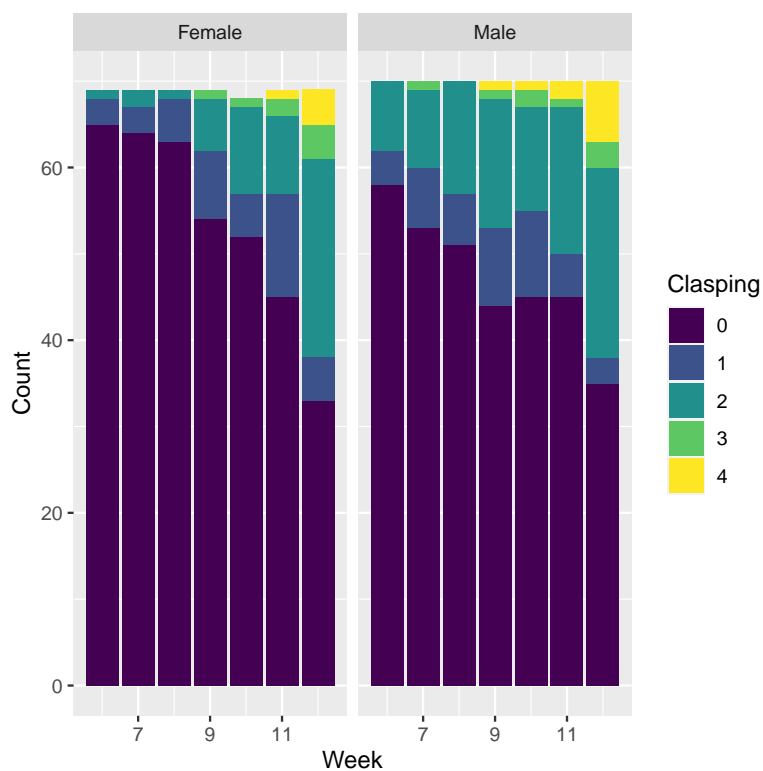


Figure 2: Bar plot for clasping over the 5 weeks between sex

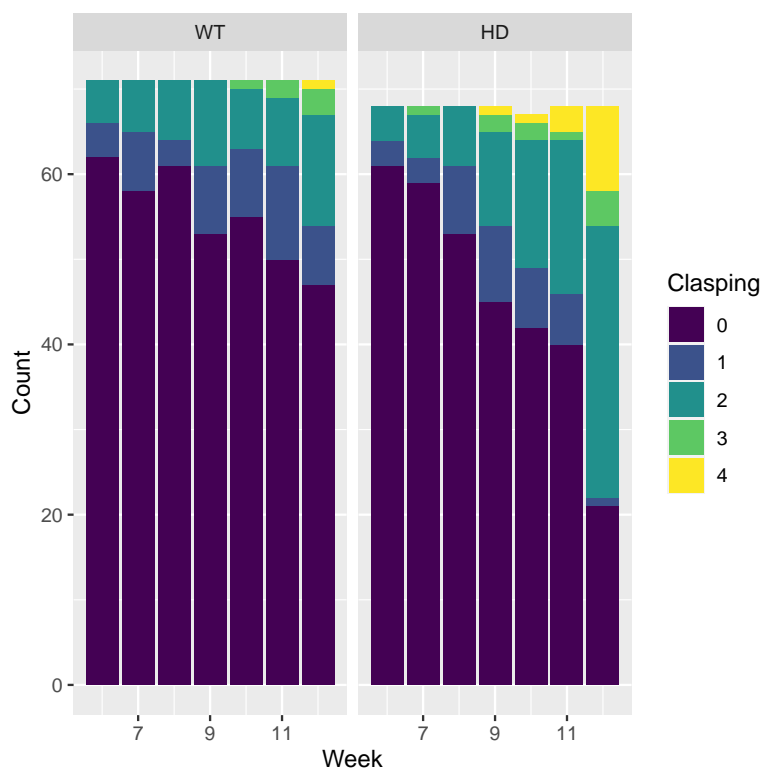


Figure 3: Bar plot for clasping over the 5 weeks between genotype



## 6 Post-Hoc test for Clinical variables

Except for the clasping score, we modelled all other clinical variables using Linear Mixed Models (LMMs). Since the clasping score was an ordinal response, a Cumulative Link Mixed Model was used instead of an LMM.

Example of interpretation for Table 1: Among different housing types, SH showed the highest number of significant pairwise differences in brain weight among different sex and genotype contrasts. With the exception of housing type EX, both the other housing types showed a significant increase in average brain weight in WT female mice compared to HD counterparts. In addition, HD male mice have greater brain weight than HD female mice on average in SH housing.

Figure 1 illustrates the pairwise comparisons. The blue bars are the confidence intervals for the estimated marginal means. However, pairwise comparisons are done using the red arrows, instead of using the confidence intervals directly. Pairwise comparison is considered to be significant if a red arrow from contrast does not overlap with another contrasts arrow. For instance in Figure 4, the two red arrows from WT male and HD female mice do not overlap in SH housing and are thus deemed significant.

### 6.1 Linear Mixed Model

#### 6.1.1 Brain weight

Table 1: Post-hoc results for genotype and sex given housing type in variable brain weight

contrast	Housing	estimate	SE	df	t.ratio	p.value
WT Female - HD Female	SH	0.0487	0.0139	26	3.5109	<b>0.0084</b>
WT Female - WT Male	SH	-0.0300	0.0138	26	-2.1780	0.1560
WT Female - HD Male	SH	0.0008	0.0168	26	0.0496	1.0000
HD Female - WT Male	SH	-0.0787	0.0170	26	-4.6282	<b>0.0005</b>
HD Female - HD Male	SH	-0.0479	0.0139	26	-3.4509	<b>0.0097</b>
WT Male - HD Male	SH	0.0309	0.0138	26	2.2384	0.1394
WT Female - HD Female	EE	0.0407	0.0140	26	2.9098	<b>0.0346</b>
WT Female - WT Male	EE	-0.0045	0.0138	26	-0.3266	0.9877
WT Female - HD Male	EE	0.0183	0.0168	26	1.0904	0.6984
HD Female - WT Male	EE	-0.0452	0.0172	26	-2.6237	0.0646
HD Female - HD Male	EE	-0.0223	0.0140	26	-1.5985	0.3969
WT Male - HD Male	EE	0.0228	0.0138	26	1.6541	0.3674
WT Female - HD Female	EX	0.0359	0.0139	26	2.5783	0.0710
WT Female - WT Male	EX	-0.0198	0.0139	26	-1.4236	0.4965
WT Female - HD Male	EX	-0.0018	0.0170	26	-0.1042	0.9996
HD Female - WT Male	EX	-0.0557	0.0172	26	-3.2347	<b>0.0164</b>
HD Female - HD Male	EX	-0.0376	0.0140	26	-2.6902	0.0561
WT Male - HD Male	EX	0.0180	0.0140	26	1.2887	0.5780

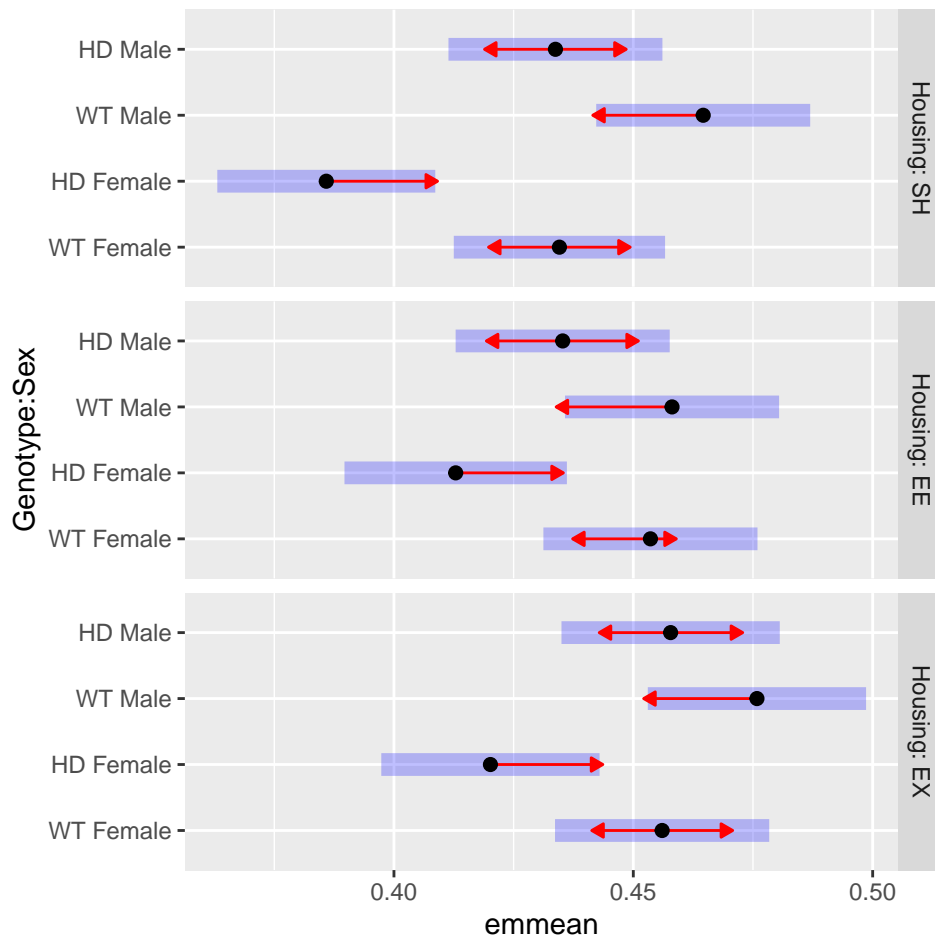


Figure 4: Graphical comparisons from emmeans method

### 6.1.2 Swing time forepaw

contrast	Housing	Sex	estimate	SE	df	t.ratio	p.value
WT - HD	SH	Female	-0.0146	0.0068	26	-2.1486	<b>0.0412</b>
WT - HD	EE	Female	-0.0106	0.0068	26	-1.5506	0.1331
WT - HD	EX	Female	-0.0128	0.0070	26	-1.8284	0.0790
WT - HD	SH	Male	-0.0082	0.0068	26	-1.2020	0.2402
WT - HD	EE	Male	-0.0041	0.0069	26	-0.6007	0.5532
WT - HD	EX	Male	-0.0063	0.0070	26	-0.9068	0.3728

### 6.1.3 Swing time hindpaw

contrast	Housing	Sex	estimate	SE	df	t.ratio	p.value
WT - HD	SH	Female	-0.0107	0.0052	26	-2.0699	<b>0.0485</b>
WT - HD	EE	Female	-0.0056	0.0052	26	-1.0745	0.2925
WT - HD	EX	Female	-0.0080	0.0053	26	-1.5060	0.1441
WT - HD	SH	Male	-0.0116	0.0052	26	-2.2483	<b>0.0333</b>
WT - HD	EE	Male	-0.0065	0.0052	26	-1.2391	0.2264

(continued)

contrast	Housing	Sex	estimate	SE	df	t.ratio	p.value
WT - HD	EX	Male	-0.0090	0.0053	26	-1.6785	0.1052

#### 6.1.4 Stride length forepaw

contrast	Housing	Sex	estimate	SE	df	t.ratio	p.value
WT - HD	SH	Female	-0.4323	0.2028	26	-2.1319	<b>0.0426</b>
WT - HD	EE	Female	-0.2148	0.2033	26	-1.0566	0.3004
WT - HD	EX	Female	0.0042	0.2099	26	0.0200	0.9842
WT - HD	SH	Male	-0.0643	0.2028	26	-0.3172	0.7536
WT - HD	EE	Male	0.1532	0.2055	26	0.7455	0.4627
WT - HD	EX	Male	0.3722	0.2099	26	1.7735	0.0879

#### 6.1.5 Stride length hindpaw

contrast	Genotype	Sex	estimate	SE	df	t.ratio	p.value
SH - EE	WT	Female	-0.0424	0.1968	26	-0.2156	0.9747
SH - EX	WT	Female	-0.4451	0.2010	26	-2.2147	0.0874
EE - EX	WT	Female	-0.4027	0.2013	26	-2.0004	0.1322
SH - EE	HD	Female	0.1281	0.2027	26	0.6322	0.8039
SH - EX	HD	Female	0.0928	0.2072	26	0.4481	0.8957
EE - EX	HD	Female	-0.0353	0.2076	26	-0.1699	0.9842
SH - EE	WT	Male	-0.4487	0.1998	26	-2.2454	0.0822
SH - EX	WT	Male	-0.3685	0.2010	26	-1.8337	0.1786
EE - EX	WT	Male	0.0801	0.2042	26	0.3923	0.9189
SH - EE	HD	Male	-0.2781	0.2027	26	-1.3723	0.3696
SH - EX	HD	Male	0.1694	0.2072	26	0.8177	0.6956
EE - EX	HD	Male	0.4475	0.2076	26	2.1561	0.0981

contrast	Genotype	estimate	SE	df	t.ratio	p.value
SH - EE	WT	-0.2455	0.1611	26	-1.5246	0.2962
SH - EX	WT	-0.4068	0.1629	26	-2.4979	<b>0.0486</b>
EE - EX	WT	-0.1613	0.1646	26	-0.9798	0.5959
SH - EE	HD	-0.0750	0.1664	26	-0.4508	0.8945
SH - EX	HD	0.1311	0.1705	26	0.7692	0.7248
EE - EX	HD	0.2061	0.1705	26	1.2092	0.4585

#### 6.1.6 Stance width forepaw

contrast	Housing	Sex	estimate	SE	df	t.ratio	p.value
WT - HD	SH	Female	0.1446	0.1380	26	1.0480	0.3043
WT - HD	EE	Female	0.0624	0.1382	26	0.4515	0.6554
WT - HD	EX	Female	0.0758	0.1414	26	0.5360	0.5965
WT - HD	SH	Male	0.3054	0.1380	26	2.2140	<b>0.0358</b>

(continued)

contrast	Housing	Sex	estimate	SE	df	t.ratio	p.value
WT - HD	EE	Male	0.2233	0.1393	26	1.6027	0.1211
WT - HD	EX	Male	0.2366	0.1414	26	1.6736	0.1062

### 6.1.7 Propel:brake ratio forepaw

contrast	Housing	Sex	estimate	SE	df	t.ratio	p.value
WT - HD	SH	Female	-0.8954	0.3743	26	-2.3923	<b>0.0243</b>
WT - HD	EE	Female	-0.9525	0.3751	26	-2.5391	<b>0.0174</b>
WT - HD	EX	Female	-0.3031	0.3863	26	-0.7847	0.4397
WT - HD	SH	Male	-0.9829	0.3743	26	-2.6261	<b>0.0143</b>
WT - HD	EE	Male	-1.0401	0.3789	26	-2.7449	<b>0.0108</b>
WT - HD	EX	Male	-0.3906	0.3863	26	-1.0112	0.3212

### 6.1.8 Butyrate

contrast	Housing	estimate	SE	df	t.ratio	p.value
Female - Male	SH	-45358.94	50238.70	14	-0.9029	0.3819
Female - Male	EE	26142.26	50238.70	14	0.5204	0.6109
Female - Male	EX	115746.88	51709.47	14	2.2384	<b>0.0420</b>

### 6.1.9 Valerate

contrast	Housing	estimate	SE	df	t.ratio	p.value
Female - Male	SH	-2055.847	3354.713	14	-0.6128	0.5498
Female - Male	EE	-2034.679	3354.713	14	-0.6065	0.5539
Female - Male	EX	9981.096	3498.810	14	2.8527	<b>0.0128</b>

### 6.1.10 Water Intake

contrast	estimate	SE	df	t.ratio	p.value
WT SH Female - HD SH Female	-0.7278	0.1348	26	-5.3993	<b>0.0006</b>
WT SH Female - WT EE Female	0.0042	0.1430	26	0.0292	1.0000
WT SH Female - HD EE Female	-0.6233	0.1581	26	-3.9432	<b>0.0218</b>
WT SH Female - WT EX Female	-0.2646	0.1430	26	-1.8510	0.7767
WT SH Female - HD EX Female	-0.8068	0.1581	26	-5.1040	<b>0.0013</b>
WT SH Female - WT SH Male	0.3183	0.1348	26	2.3615	0.4627
WT SH Female - HD SH Male	-0.0968	0.1651	26	-0.5866	1.0000
WT SH Female - WT EE Male	0.0254	0.1581	26	0.1605	1.0000
WT SH Female - HD EE Male	-0.2894	0.1430	26	-2.0245	0.6745
WT SH Female - WT EX Male	-0.2262	0.1581	26	-1.4310	0.9461
WT SH Female - HD EX Male	-0.4557	0.1430	26	-3.1871	0.1145
HD SH Female - WT EE Female	0.7320	0.1581	26	4.6309	<b>0.0041</b>
HD SH Female - HD EE Female	0.1045	0.1430	26	0.7311	0.9998

(continued)

contrast	estimate	SE	df	t.ratio	p.value
HD SH Female - WT EX Female	0.4632	0.1581	26	2.9302	0.1876
HD SH Female - HD EX Female	-0.0790	0.1430	26	-0.5522	1.0000
HD SH Female - WT SH Male	1.0461	0.1651	26	6.3366	<b>0.0001</b>
HD SH Female - HD SH Male	0.6310	0.1348	26	4.6808	<b>0.0036</b>
HD SH Female - WT EE Male	0.7532	0.1430	26	5.2679	<b>0.0008</b>
HD SH Female - HD EE Male	0.4384	0.1581	26	2.7733	0.2477
HD SH Female - WT EX Male	0.5016	0.1430	26	3.5084	0.0583
HD SH Female - HD EX Male	0.2721	0.1581	26	1.7217	0.8427
WT EE Female - HD EE Female	-0.6274	0.1348	26	-4.6548	<b>0.0039</b>
WT EE Female - WT EX Female	-0.2688	0.1430	26	-1.8802	0.7604
WT EE Female - HD EX Female	-0.8109	0.1581	26	-5.1304	<b>0.0012</b>
WT EE Female - WT SH Male	0.3141	0.1581	26	1.9875	0.6972
WT EE Female - HD SH Male	-0.1010	0.1430	26	-0.7065	0.9998
WT EE Female - WT EE Male	0.0212	0.1348	26	0.1572	1.0000
WT EE Female - HD EE Male	-0.2936	0.1651	26	-1.7785	0.8150
WT EE Female - WT EX Male	-0.2304	0.1581	26	-1.4574	0.9394
WT EE Female - HD EX Male	-0.4598	0.1430	26	-3.2163	0.1079
HD EE Female - WT EX Female	0.3586	0.1581	26	2.2690	0.5199
HD EE Female - HD EX Female	-0.1835	0.1430	26	-1.2833	0.9742
HD EE Female - WT SH Male	0.9416	0.1430	26	6.5858	<b>0.0000</b>
HD EE Female - HD SH Male	0.5264	0.1581	26	3.3305	0.0853
HD EE Female - WT EE Male	0.6486	0.1651	26	3.9290	<b>0.0225</b>
HD EE Female - HD EE Male	0.3338	0.1348	26	2.4766	0.3952
HD EE Female - WT EX Male	0.3971	0.1430	26	2.7773	0.2460
HD EE Female - HD EX Male	0.1676	0.1581	26	1.0604	0.9940
WT EX Female - HD EX Female	-0.5421	0.1348	26	-4.0217	<b>0.0181</b>
WT EX Female - WT SH Male	0.5830	0.1581	26	3.6881	<b>0.0392</b>
WT EX Female - HD SH Male	0.1678	0.1430	26	1.1736	0.9867
WT EX Female - WT EE Male	0.2900	0.1581	26	1.8347	0.7855
WT EX Female - HD EE Male	-0.0248	0.1430	26	-0.1735	1.0000
WT EX Female - WT EX Male	0.0384	0.1348	26	0.2852	1.0000
WT EX Female - HD EX Male	-0.1910	0.1651	26	-1.1571	0.9881
HD EX Female - WT SH Male	1.1251	0.1430	26	7.8691	<b>0.0000</b>
HD EX Female - HD SH Male	0.7099	0.1581	26	4.4913	<b>0.0058</b>
HD EX Female - WT EE Male	0.8321	0.1430	26	5.8201	<b>0.0002</b>
HD EX Female - HD EE Male	0.5173	0.1581	26	3.2728	0.0962
HD EX Female - WT EX Male	0.5806	0.1651	26	3.5166	0.0573
HD EX Female - HD EX Male	0.3511	0.1348	26	2.6046	0.3263
WT SH Male - HD SH Male	-0.4152	0.1348	26	-3.0799	0.1414
WT SH Male - WT EE Male	-0.2930	0.1430	26	-2.0490	0.6592
WT SH Male - HD EE Male	-0.6078	0.1581	26	-3.8451	<b>0.0274</b>
WT SH Male - WT EX Male	-0.5445	0.1430	26	-3.8085	<b>0.0298</b>
WT SH Male - HD EX Male	-0.7740	0.1581	26	-4.8967	<b>0.0021</b>
HD SH Male - WT EE Male	0.1222	0.1581	26	0.7732	0.9996
HD SH Male - HD EE Male	-0.1926	0.1430	26	-1.3471	0.9639
HD SH Male - WT EX Male	-0.1293	0.1581	26	-0.8183	0.9994
HD SH Male - HD EX Male	-0.3588	0.1430	26	-2.5097	0.3766
WT EE Male - HD EE Male	-0.3148	0.1348	26	-2.3354	0.4786
WT EE Male - WT EX Male	-0.2516	0.1430	26	-1.7595	0.8245
WT EE Male - HD EX Male	-0.4810	0.1581	26	-3.0433	0.1518
HD EE Male - WT EX Male	0.0633	0.1581	26	0.4002	1.0000

(continued)

contrast	estimate	SE	df	t.ratio	p.value
HD EE Male - HD EX Male	-0.1662	0.1430	26	-1.1626	0.9876
WT EX Male - HD EX Male	-0.2295	0.1348	26	-1.7024	0.8515

### 6.1.11 Weight

contrast	estimate	SE	df	t.ratio	p.value
WT SH Female - HD SH Female	1.1150	0.9349	26	1.1927	0.9849
WT SH Female - WT EE Female	1.3180	0.9905	26	1.3306	0.9668
WT SH Female - HD EE Female	1.1430	1.0966	26	1.0423	0.9948
WT SH Female - WT EX Female	1.2805	0.9908	26	1.2923	0.9729
WT SH Female - HD EX Female	1.2416	1.0965	26	1.1324	0.9899
WT SH Female - WT SH Male	-7.2667	0.9341	26	-7.7790	<b>0.0000</b>
WT SH Female - HD SH Male	-6.4438	1.1435	26	-5.6353	<b>0.0003</b>
WT SH Female - WT EE Male	-4.6556	1.0950	26	-4.2517	<b>0.0104</b>
WT SH Female - HD EE Male	-5.1228	0.9905	26	-5.1717	<b>0.0011</b>
WT SH Female - WT EX Male	-4.1622	1.0965	26	-3.7960	<b>0.0306</b>
WT SH Female - HD EX Male	-4.4932	0.9919	26	-4.5301	<b>0.0053</b>
HD SH Female - WT EE Female	0.2030	1.0966	26	0.1851	1.0000
HD SH Female - HD EE Female	0.0279	0.9926	26	0.0281	1.0000
HD SH Female - WT EX Female	0.1654	1.0965	26	0.1509	1.0000
HD SH Female - HD EX Female	0.1266	0.9929	26	0.1275	1.0000
HD SH Female - WT SH Male	-8.3817	1.1453	26	-7.3184	<b>0.0000</b>
HD SH Female - HD SH Male	-7.5588	0.9349	26	-8.0854	<b>0.0000</b>
HD SH Female - WT EE Male	-5.7706	0.9916	26	-5.8195	<b>0.0002</b>
HD SH Female - HD EE Male	-6.2378	1.0966	26	-5.6886	<b>0.0003</b>
HD SH Female - WT EX Male	-5.2772	0.9929	26	-5.3150	<b>0.0007</b>
HD SH Female - HD EX Male	-5.6082	1.0981	26	-5.1074	<b>0.0012</b>
WT EE Female - HD EE Female	-0.1751	0.9349	26	-0.1873	1.0000
WT EE Female - WT EX Female	-0.0376	0.9908	26	-0.0379	1.0000
WT EE Female - HD EX Female	-0.0764	1.0965	26	-0.0697	1.0000
WT EE Female - WT SH Male	-8.5847	1.0950	26	-7.8401	<b>0.0000</b>
WT EE Female - HD SH Male	-7.7618	0.9905	26	-7.8360	<b>0.0000</b>
WT EE Female - WT EE Male	-5.9736	0.9341	26	-6.3948	<b>0.0000</b>
WT EE Female - HD EE Male	-6.4408	1.1435	26	-5.6327	<b>0.0003</b>
WT EE Female - WT EX Male	-5.4802	1.0965	26	-4.9980	<b>0.0016</b>
WT EE Female - HD EX Male	-5.8112	0.9919	26	-5.8590	<b>0.0002</b>
HD EE Female - WT EX Female	0.1375	1.0965	26	0.1254	1.0000
HD EE Female - HD EX Female	0.0987	0.9929	26	0.0994	1.0000
HD EE Female - WT SH Male	-8.4096	0.9916	26	-8.4810	<b>0.0000</b>
HD EE Female - HD SH Male	-7.5868	1.0966	26	-6.9187	<b>0.0000</b>
HD EE Female - WT EE Male	-5.7985	1.1453	26	-5.0629	<b>0.0014</b>
HD EE Female - HD EE Male	-6.2657	0.9349	26	-6.7022	<b>0.0000</b>
HD EE Female - WT EX Male	-5.3051	0.9929	26	-5.3431	<b>0.0007</b>
HD EE Female - HD EX Male	-5.6361	1.0981	26	-5.1328	<b>0.0012</b>
WT EX Female - HD EX Female	-0.0388	0.9352	26	-0.0415	1.0000
WT EX Female - WT SH Male	-8.5471	1.0949	26	-7.8063	<b>0.0000</b>
WT EX Female - HD SH Male	-7.7243	0.9908	26	-7.7960	<b>0.0000</b>
WT EX Female - WT EE Male	-5.9360	1.0949	26	-5.4215	<b>0.0006</b>
WT EX Female - HD EE Male	-6.4032	0.9908	26	-6.4627	<b>0.0000</b>

(continued)

contrast	estimate	SE	df	t.ratio	p.value
WT EX Female - WT EX Male	-5.4426	0.9352	26	-5.8195	<b>0.0002</b>
WT EX Female - HD EX Male	-5.7736	1.1453	26	-5.0412	<b>0.0015</b>
HD EX Female - WT SH Male	-8.5083	0.9919	26	-8.5782	<b>0.0000</b>
HD EX Female - HD SH Male	-7.6854	1.0965	26	-7.0092	<b>0.0000</b>
HD EX Female - WT EE Male	-5.8972	0.9919	26	-5.9456	<b>0.0002</b>
HD EX Female - HD EE Male	-6.3644	1.0965	26	-5.8044	<b>0.0002</b>
HD EX Female - WT EX Male	-5.4038	1.1471	26	-4.7108	<b>0.0034</b>
HD EX Female - HD EX Male	-5.7348	0.9360	26	-6.1270	<b>0.0001</b>
WT SH Male - HD SH Male	0.8229	0.9341	26	0.8809	0.9988
WT SH Male - WT EE Male	2.6111	0.9905	26	2.6361	0.3106
WT SH Male - HD EE Male	2.1439	1.0950	26	1.9579	0.7151
WT SH Male - WT EX Male	3.1045	0.9919	26	3.1300	0.1282
WT SH Male - HD EX Male	2.7735	1.0965	26	2.5295	0.3658
HD SH Male - WT EE Male	1.7883	1.0950	26	1.6331	0.8811
HD SH Male - HD EE Male	1.3210	0.9905	26	1.3336	0.9663
HD SH Male - WT EX Male	2.2816	1.0965	26	2.0809	0.6392
HD SH Male - HD EX Male	1.9506	0.9919	26	1.9667	0.7098
WT EE Male - HD EE Male	-0.4672	0.9341	26	-0.5002	1.0000
WT EE Male - WT EX Male	0.4934	0.9919	26	0.4974	1.0000
WT EE Male - HD EX Male	0.1624	1.0965	26	0.1481	1.0000
HD EE Male - WT EX Male	0.9606	1.0965	26	0.8761	0.9988
HD EE Male - HD EX Male	0.6296	0.9919	26	0.6348	0.9999
WT EX Male - HD EX Male	-0.3310	0.9360	26	-0.3536	1.0000

### 6.1.12 Rotarod

contrast	Sex	estimate	SE	df	t.ratio	p.value
WT SH - HD SH	Female	69.0738	15.1751	26	4.5518	<b>0.0014</b>
WT SH - WT EE	Female	-37.4977	16.0165	26	-2.3412	0.2141
WT SH - HD EE	Female	44.1919	17.8178	26	2.4802	0.1668
WT SH - WT EX	Female	21.3658	16.0359	26	1.3324	0.7648
WT SH - HD EX	Female	65.2560	17.8120	26	3.6636	<b>0.0127</b>
HD SH - WT EE	Female	-106.5715	17.8178	26	-5.9812	<b>0.0000</b>
HD SH - HD EE	Female	-24.8819	16.1731	26	-1.5385	0.6438
HD SH - WT EX	Female	-47.7080	17.8116	26	-2.6785	0.1141
HD SH - HD EX	Female	-3.8178	16.1934	26	-0.2358	0.9999
WT EE - HD EE	Female	81.6896	15.1751	26	5.3831	<b>0.0002</b>
WT EE - WT EX	Female	58.8635	16.0359	26	3.6707	<b>0.0125</b>
WT EE - HD EX	Female	102.7537	17.8120	26	5.7688	<b>0.0001</b>
HD EE - WT EX	Female	-22.8261	17.8116	26	-1.2815	0.7921
HD EE - HD EX	Female	21.0641	16.1934	26	1.3008	0.7819
WT EX - HD EX	Female	43.8902	15.2031	26	2.8869	0.0745
WT SH - HD SH	Male	78.1574	15.1189	26	5.1695	<b>0.0003</b>
WT SH - WT EE	Male	-73.7940	16.0165	26	-4.6074	<b>0.0012</b>
WT SH - HD EE	Male	16.9791	17.6989	26	0.9593	0.9266
WT SH - WT EX	Male	4.6670	16.1154	26	0.2896	0.9997
WT SH - HD EX	Male	57.6408	17.8120	26	3.2361	<b>0.0347</b>
HD SH - WT EE	Male	-151.9514	17.6989	26	-8.5854	<b>0.0000</b>
HD SH - HD EE	Male	-61.1782	16.0165	26	-3.8197	<b>0.0087</b>



(continued)

contrast	Sex	estimate	SE	df	t.ratio	p.value
HD SH - WT EX	Male	-73.4904	17.8120	26	-4.1259	<b>0.0041</b>
HD SH - HD EX	Male	-20.5166	16.1154	26	-1.2731	0.7965
WT EE - HD EE	Male	90.7731	15.1189	26	6.0039	<b>0.0000</b>
WT EE - WT EX	Male	78.4610	16.1154	26	4.8687	<b>0.0006</b>
WT EE - HD EX	Male	131.4347	17.8120	26	7.3790	<b>0.0000</b>
HD EE - WT EX	Male	-12.3121	17.8120	26	-0.6912	0.9814
HD EE - HD EX	Male	40.6616	16.1154	26	2.5231	0.1540
WT EX - HD EX	Male	52.9738	15.2581	26	3.4718	<b>0.0201</b>

## 6.2 Cumulative Link Mixed Model

### 6.2.1 Clasping Score

contrast	Housing	estimate	SE	df	z.ratio	p.value
WT Female - HD Female	SH	-0.8050	0.3069	Inf	-2.6227	<b>0.0433</b>
WT Female - WT Male	SH	-0.6116	0.3060	Inf	-1.9985	0.1885
WT Female - HD Male	SH	-1.4166	0.4382	Inf	-3.2325	<b>0.0067</b>
HD Female - WT Male	SH	0.1933	0.4286	Inf	0.4511	0.9694
HD Female - HD Male	SH	-0.6116	0.3060	Inf	-1.9985	0.1885
WT Male - HD Male	SH	-0.8050	0.3069	Inf	-2.6227	<b>0.0433</b>
WT Female - HD Female	EE	-0.8050	0.3069	Inf	-2.6227	<b>0.0433</b>
WT Female - WT Male	EE	-0.6116	0.3060	Inf	-1.9985	0.1885
WT Female - HD Male	EE	-1.4166	0.4382	Inf	-3.2325	<b>0.0067</b>
HD Female - WT Male	EE	0.1933	0.4286	Inf	0.4511	0.9694
HD Female - HD Male	EE	-0.6116	0.3060	Inf	-1.9985	0.1885
WT Male - HD Male	EE	-0.8050	0.3069	Inf	-2.6227	<b>0.0433</b>
WT Female - HD Female	EX	-0.8050	0.3069	Inf	-2.6227	<b>0.0433</b>
WT Female - WT Male	EX	-0.6116	0.3060	Inf	-1.9985	0.1885
WT Female - HD Male	EX	-1.4166	0.4382	Inf	-3.2325	<b>0.0067</b>
HD Female - WT Male	EX	0.1933	0.4286	Inf	0.4511	0.9694
HD Female - HD Male	EX	-0.6116	0.3060	Inf	-1.9985	0.1885
WT Male - HD Male	EX	-0.8050	0.3069	Inf	-2.6227	<b>0.0433</b>

## References

Lenth, Russell V. 2021. *Emmeans: Estimated Marginal Means, Aka Least-Squares Means*. <https://CRAN.R-project.org/package=emmeans>.

## R session information

```
sessionInfo()
```

```
## R version 4.1.0 (2021-05-18)
## Platform: x86_64-apple-darwin17.0 (64-bit)
## Running under: macOS Big Sur 10.16
```



```
##
## Matrix products: default
## BLAS: /Library/Frameworks/R.framework/Versions/4.1/Resources/lib/libRblas.dylib
## LAPACK: /Library/Frameworks/R.framework/Versions/4.1/Resources/lib/libRlapack.dylib
##
## locale:
## [1] en_AU.UTF-8/en_AU.UTF-8/en_AU.UTF-8/C/en_AU.UTF-8/en_AU.UTF-8
##
## attached base packages:
## [1] stats      graphics  grDevices  utils      datasets  methods    base
##
## other attached packages:
## [1] kableExtra_1.3.4 patchwork_1.1.1 rstatix_0.7.0 lmerTest_3.1-3
## [5] lme4_1.1-27.1 Matrix_1.3-4 viridis_0.6.1 viridisLite_0.4.0
## [9] ordinal_2019.12-10 tidyr_1.1.4 emmeans_1.7.0 jtools_2.1.4
## [13] TSA_1.3 xtable_1.8-4 sjPlot_2.8.9 dotwhisker_0.7.4
## [17] stargazer_5.2.2 nlme_3.1-153 car_3.0-11 carData_3.0-4
## [21] ggpubr_0.4.0 ggplot2_3.3.5 magrittr_2.0.1 readxl_1.3.1
## [25] dplyr_1.0.7 knitr_1.36
##
## loaded via a namespace (and not attached):
## [1] TH.data_1.1-0 minqa_1.2.4 colorspace_2.0-2
## [4] ggsignif_0.6.3 ellipsis_0.3.2 rio_0.5.27
## [7] sjlabelled_1.1.8 estimability_1.3 ggstance_0.3.5
## [10] parameters_0.14.0 rstudioapi_0.13 farver_2.1.0
## [13] fansi_0.5.0 mvtnorm_1.1-2 xml2_1.3.2
## [16] codetools_0.2-18 splines_4.1.0 leaps_3.1
## [19] sjmisc_2.8.7 nloptr_1.2.2.2 ggeffects_1.1.1
## [22] broom_0.7.9 effectsize_0.5 compiler_4.1.0
## [25] httr_1.4.2 sjstats_0.18.1 backports_1.2.1
## [28] assertthat_0.2.1 fastmap_1.1.0 htmltools_0.5.2
## [31] tools_4.1.0 coda_0.19-4 gtable_0.3.0
## [34] glue_1.4.2 Rcpp_1.0.7 cellranger_1.1.0
## [37] vctr_0.3.8 svglite_2.0.0 insight_0.14.4
## [40] xfun_0.26 stringr_1.4.0 openxlsx_4.2.4
## [43] rvest_1.0.1 lifecycle_1.0.1 MASS_7.3-54
## [46] zoo_1.8-9 scales_1.1.1 hms_1.1.1
## [49] sandwich_3.0-1 yaml_2.2.1 curl_4.3.2
## [52] gridExtra_2.3 pander_0.6.4 stringi_1.7.5
## [55] ucminf_1.1-4 bayestestR_0.11.0 boot_1.3-28
## [58] zip_2.2.0 rlang_0.4.11 pkgconfig_2.0.3
## [61] systemfonts_1.0.2 evaluate_0.14 lattice_0.20-45
## [64] purrr_0.3.4 labeling_0.4.2 tidyselect_1.1.1
## [67] R6_2.5.1 generics_0.1.0 multcomp_1.4-17
## [70] DBI_1.1.1 pillar_1.6.3 haven_2.4.3
## [73] foreign_0.8-81 withr_2.4.2 mgcv_1.8-37
## [76] survival_3.2-13 datawizard_0.2.1 abind_1.4-5
## [79] tibble_3.1.5 performance_0.8.0 modelr_0.1.8
## [82] crayon_1.4.1 utf8_1.2.2 rmarkdown_2.11
## [85] locfit_1.5-9.4 grid_4.1.0 data.table_1.14.2
## [88] forcats_0.5.1 digest_0.6.28 webshot_0.5.2
## [91] numDeriv_2016.8-1.1 munsell_0.5.0
```