

SimpleViolins

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Data sources

We evaluate genotype and sex differences in mouse models of Alzheimer's disease risk, based on APOE alleles: APOE2 is protective, APOE3 is control, and APOE4 represents genetic risk for AD. One allele increases risk by 3 times, and two APOE4 alleles increase risk by 10 times (ref) in relation to APOE3 . We use multiple data sources:

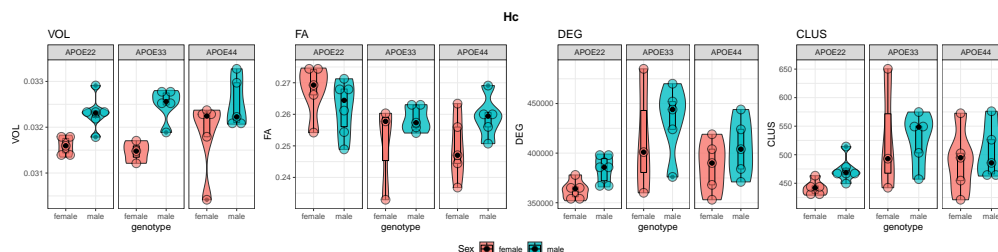
Morris Water Maze - testing spatial navigation memory Segmentation: regional volumes Microstructural properties: FA Tractography Based Connectivity: Degree, and Clustering Coefficient

We read the data and normalize volumes to the whole brain.

Plots for Hc

We embed plots for day d8 probe trials:

```
## Bin width defaults to 1/30 of the range of the data. Pick better value with `binwidth`.
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## Bin width defaults to 1/30 of the range of the data. Pick better value with `binwidth`.
```



```
print('Hc')
```

```
## [1] "Hc"
```

```
lm_Hc_VOL <- lm(Hc ~ Genotype*Sex, geno_combined_VOL)
summary(lm_Hc_VOL)
```

```
##
## Call:
## lm(formula = Hc ~ Genotype * Sex, data = geno_combined_VOL)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -1.413e-03 -2.449e-04  1.222e-05  2.522e-04  7.467e-04
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)      3.159e-02  2.171e-04 145.497  <2e-16 ***
## GenotypeAPOE33    -1.273e-04  3.546e-04  -0.359   0.7228
## GenotypeAPOE44     2.371e-04  3.071e-04   0.772   0.4478
## Sexmale           7.183e-04  2.940e-04   2.443   0.0227 *
## GenotypeAPOE33:Sexmale  3.125e-04  4.606e-04   0.678   0.5043
## GenotypeAPOE44:Sexmale -1.995e-05  4.251e-04  -0.047   0.9630
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.0004855 on 23 degrees of freedom
## Multiple R-squared:  0.4708, Adjusted R-squared:  0.3557
## F-statistic: 4.092 on 5 and 23 DF,  p-value: 0.00837

lm_Hc_VOL_f <- lm(Hc ~ Genotype, combo_f_FA)
#summary(lm_Hc_VOL_f)
lm_Hc_VOL_m <- lm(Hc ~ Genotype, combo_m_FA)
#summary(lm_Hc_VOL_f)

#omnibus testing
#https://cran.r-project.org/web/packages/emmeans/vignettes/confidence-intervals.html#adjust

sink(paste(outpath, "Hc_VOL_SimpleStats.txt", sep=''))
'omnibus testing'

## [1] "omnibus testing"

joint_tests(ref_grid(lm_Hc_VOL))

##   model term    df1 df2 F.ratio p.value
##   Genotype      2   23   0.645  0.5337
##   Sex           1   23  19.545  0.0002
##   Genotype:Sex   2   23   0.305  0.7403

joint_tests(ref_grid(lm_Hc_VOL), by = "Sex", adjust = "sidak")

## Sex = female:
##   model term df1 df2 F.ratio p.value
##   Genotype    2  23   0.594  0.5603
##
## Sex = male:
##   model term df1 df2 F.ratio p.value
##   Genotype    2  23   0.327  0.7241
```

```

joint_tests(ref_grid(lm_Hc_VOL), by = "Genotype", adjust = "sidak" )

## Genotype = APOE22:
## model term df1 df2 F.ratio p.value
## Sex          1  23   5.969  0.0227
##
## Genotype = APOE33:
## model term df1 df2 F.ratio p.value
## Sex          1  23   8.451  0.0079
##
## Genotype = APOE44:
## model term df1 df2 F.ratio p.value
## Sex          1  23   5.172  0.0326

'anova'

## [1] "anova"
anova(lm_Hc_VOL)

## Analysis of Variance Table
##
## Response: Hc
##          Df      Sum Sq    Mean Sq F value    Pr(>F)
## Genotype    2 2.0430e-07 1.0210e-07   0.4333 0.6535491
## Sex          1 4.4749e-06 4.4749e-06  18.9821 0.0002313 ***
## Genotype:Sex  2 1.4360e-07 7.1800e-08   0.3047 0.7402957
## Residuals   23 5.4221e-06 2.3570e-07
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

#anova(lm_Hc_VOL_f)
#anova(lm_Hc_VOL_m)

#post hoc comparison
Hc_VOL.emm <- emmeans(lm_Hc_VOL , ~ Genotype | Sex, adjust = "sidak")
contrast(Hc_VOL.emm, simple = c("Genotype", "Sex")) #FDR

## contrast          estimate      SE df t.ratio p.value
## APOE22 female effect -0.000445 0.000200 23  -2.224  0.0544
## APOE33 female effect -0.000572 0.000247 23  -2.317  0.0544
## APOE44 female effect -0.000207 0.000200 23  -1.038  0.3103
## APOE22 male effect    0.000274 0.000186 23   1.470  0.1863
## APOE33 male effect    0.000459 0.000200 23   2.296  0.0544
## APOE44 male effect    0.000491 0.000200 23   2.456  0.0544
##
## P value adjustment: fdr method for 6 tests
contrast(Hc_VOL.emm, simple = list("Genotype", "Sex"))

## $`simple contrasts for Genotype`
## Sex = female:
## contrast          estimate      SE df t.ratio p.value
## APOE22 effect -3.66e-05 0.000187 23  -0.196  0.8464
## APOE33 effect -1.64e-04 0.000213 23  -0.769  0.6743
## APOE44 effect  2.01e-04 0.000187 23   1.073  0.6743
##

```

```

## Sex = male:
## contrast      estimate      SE df t.ratio p.value
## APOE22 effect -1.34e-04 0.000167 23 -0.802 0.7728
## APOE33 effect  5.11e-05 0.000175 23  0.292 0.7728
## APOE44 effect  8.31e-05 0.000175 23  0.475 0.7728
##
## P value adjustment: fdr method for 3 tests
##
## $`simple contrasts for Sex`
## Genotype = APOE22:
## contrast      estimate      SE df t.ratio p.value
## female effect -0.000359 0.000147 23 -2.443 0.0227
## male effect    0.000359 0.000147 23  2.443 0.0227
##
## Genotype = APOE33:
## contrast      estimate      SE df t.ratio p.value
## female effect -0.000515 0.000177 23 -2.907 0.0079
## male effect    0.000515 0.000177 23  2.907 0.0079
##
## Genotype = APOE44:
## contrast      estimate      SE df t.ratio p.value
## female effect -0.000349 0.000154 23 -2.274 0.0326
## male effect    0.000349 0.000154 23  2.274 0.0326
##
## P value adjustment: fdr method for 2 tests
#post hoc tests
summary(glht(lm_Hc_VOL, emm(pairwise ~ Genotype*Sex, contr="sidak"))) #consider save to file

##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_VOL)
##
## Linear Hypotheses:
##
## Estimate Std. Error t value Pr(>|t|)
## APOE22 female - APOE33 female == 0 1.273e-04 3.546e-04 0.359 0.9991
## APOE22 female - APOE44 female == 0 -2.371e-04 3.071e-04 -0.772 0.9693
## APOE22 female - APOE22 male == 0 -7.183e-04 2.940e-04 -2.443 0.1820
## APOE22 female - APOE33 male == 0 -9.035e-04 3.071e-04 -2.942 0.0695 .
## APOE22 female - APOE44 male == 0 -9.355e-04 3.071e-04 -3.046 0.0557 .
## APOE33 female - APOE44 female == 0 -3.644e-04 3.546e-04 -1.028 0.9030
## APOE33 female - APOE22 male == 0 -8.456e-04 3.433e-04 -2.463 0.1755
## APOE33 female - APOE33 male == 0 -1.031e-03 3.546e-04 -2.907 0.0745 .
## APOE33 female - APOE44 male == 0 -1.063e-03 3.546e-04 -2.997 0.0620 .
## APOE44 female - APOE22 male == 0 -4.812e-04 2.940e-04 -1.637 0.5824
## APOE44 female - APOE33 male == 0 -6.663e-04 3.071e-04 -2.170 0.2874
## APOE44 female - APOE44 male == 0 -6.983e-04 3.071e-04 -2.274 0.2430
## APOE22 male - APOE33 male == 0 -1.852e-04 2.940e-04 -0.630 0.9874
## APOE22 male - APOE44 male == 0 -2.172e-04 2.940e-04 -0.739 0.9746
## APOE33 male - APOE44 male == 0 -3.199e-05 3.071e-04 -0.104 1.0000
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Adjusted p values reported -- single-step method)

```

```
res<-summary(glht(lm_Hc_VOL, emm(pairwise ~ Genotype*Sex))) #consider save to file
#summary(as.glht(pairs(lm_Hc_VOL.emm), by = NULL))
```

```
summary(glht(lm_Hc_VOL, emm(pairwise ~ Genotype | Sex)))
```

```
## $`Sex = female`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_VOL)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## APOE22 - APOE33 == 0  0.0001273  0.0003546   0.359   0.931
## APOE22 - APOE44 == 0 -0.0002371  0.0003071  -0.772   0.723
## APOE33 - APOE44 == 0 -0.0003645  0.0003546  -1.028   0.566
## (Adjusted p values reported -- single-step method)
```

```
##
## $`Sex = male`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_VOL)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## APOE22 - APOE33 == 0 -1.852e-04  2.940e-04  -0.630   0.805
## APOE22 - APOE44 == 0 -2.172e-04  2.940e-04  -0.739   0.743
## APOE33 - APOE44 == 0 -3.199e-05  3.071e-04  -0.104   0.994
## (Adjusted p values reported -- single-step method)
```

```
summary(glht(lm_Hc_VOL, emm(pairwise ~ Sex | Genotype)))
```

```
## $`Genotype = APOE22`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_VOL)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## female - male == 0 -0.0007183  0.0002940  -2.443   0.0227 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Adjusted p values reported -- single-step method)
```

```
##
## $`Genotype = APOE33`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_VOL)
##
```

```

## Linear Hypotheses:
##               Estimate Std. Error t value Pr(>|t|)
## female - male == 0 -0.0010308  0.0003546  -2.907  0.00794 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Adjusted p values reported -- single-step method)
##
##
## $`Genotype = APOE44`
##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_VOL)
##
## Linear Hypotheses:
##               Estimate Std. Error t value Pr(>|t|)
## female - male == 0 -0.0006983  0.0003071  -2.274  0.0326 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Adjusted p values reported -- single-step method)
mypairs<-pairs(Hc_VOL.emm) #_consider save to file
pairs(Hc_VOL.emm, by="Genotype")

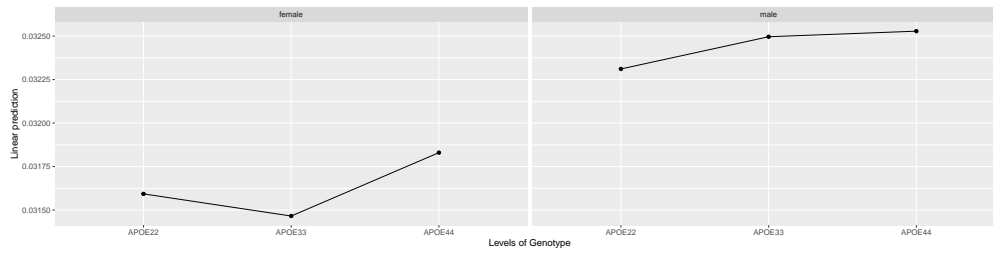
## Genotype = APOE22:
## contrast      estimate      SE df t.ratio p.value
## female - male -0.000718 0.000294 23  -2.443  0.0227
##
## Genotype = APOE33:
## contrast      estimate      SE df t.ratio p.value
## female - male -0.001031 0.000355 23  -2.907  0.0079
##
## Genotype = APOE44:
## contrast      estimate      SE df t.ratio p.value
## female - male -0.000698 0.000307 23  -2.274  0.0326
pairs(Hc_VOL.emm, by="Sex")

## Sex = female:
## contrast      estimate      SE df t.ratio p.value
## APOE22 - APOE33  0.000127 0.000355 23   0.359  0.9316
## APOE22 - APOE44 -0.000237 0.000307 23  -0.772  0.7234
## APOE33 - APOE44 -0.000364 0.000355 23  -1.028  0.5673
##
## Sex = male:
## contrast      estimate      SE df t.ratio p.value
## APOE22 - APOE33 -0.000185 0.000294 23  -0.630  0.8053
## APOE22 - APOE44 -0.000217 0.000294 23  -0.739  0.7433
## APOE33 - APOE44 -0.000032 0.000307 23  -0.104  0.9940
##
## P value adjustment: tukey method for comparing a family of 3 estimates
print('Hc VOL')

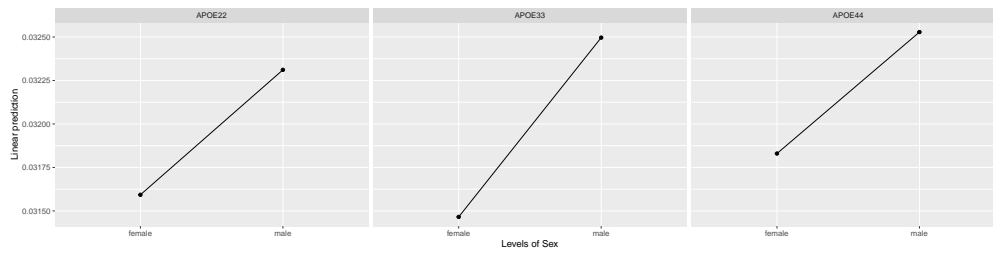
## [1] "Hc VOL"

```

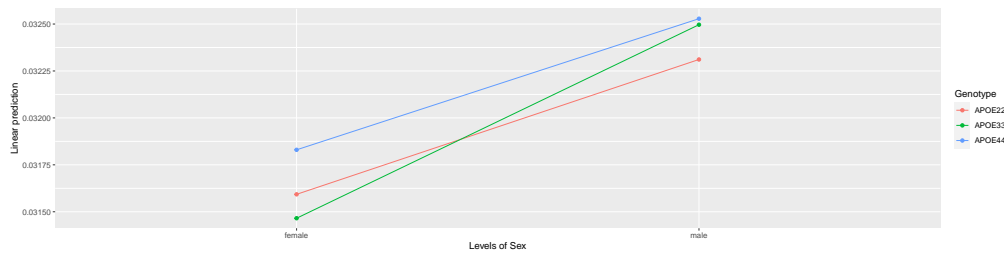
```
emmip(lm_Hc_VOL, ~ Genotype | Sex )
```



```
emmip(lm_Hc_VOL, ~ Sex | Genotype )
```

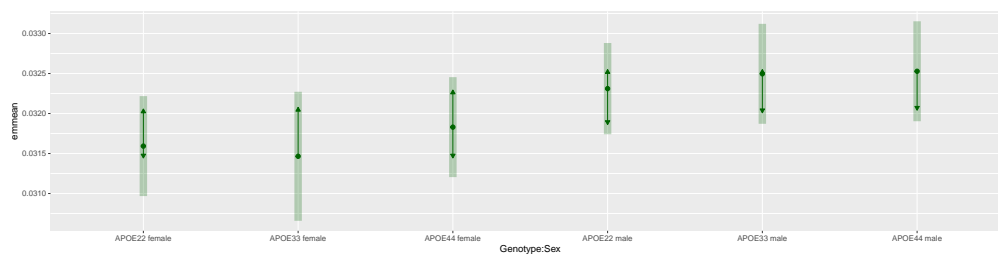


```
emmip(lm_Hc_VOL, Genotype~ Sex )
```



```
sink()
```

```
plot(Hc_VOL.emm, by = NULL, comparisons = TRUE, adjust = "mvt",  
horizontal = FALSE, colors = "darkgreen", main = "Hc VOL")
```



```
ggsave(paste(outpath, 'Hc_VOL_emmeans.pdf', sep = ''), plot = last_plot(), device = 'pdf', scale = 1, width = 16,  
'simple stats')
```

```
## [1] "simple stats"
```

```
print('Hc')
```

```
## [1] "Hc"
```

```

lm_Hc_FA <- lm(Hc ~ Genotype*Sex, geno_combined_FA)
summary(lm_Hc_FA)

##
## Call:
## lm(formula = Hc ~ Genotype * Sex, data = geno_combined_FA)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.0174129 -0.0045908  0.0002655  0.0064382  0.0138615
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)      0.267691   0.003956  67.663 < 2e-16 ***
## GenotypeAPOE33    -0.017357   0.006460  -2.687  0.01317 *
## GenotypeAPOE44    -0.018166   0.005595  -3.247  0.00356 **
## Sexmale           -0.005776   0.005357  -1.078  0.29211
## GenotypeAPOE33:Sexmale  0.014094   0.008392   1.679  0.10661
## GenotypeAPOE44:Sexmale  0.015411   0.007746   1.990  0.05866 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.008846 on 23 degrees of freedom
## Multiple R-squared:  0.3788, Adjusted R-squared:  0.2437
## F-statistic: 2.805 on 5 and 23 DF,  p-value: 0.04041

lm_Hc_FA_f <- lm(Hc ~ Genotype, combo_f_FA)
#summary(lm_Hc_FA_f)
lm_Hc_FA_m <- lm(Hc ~ Genotype, combo_m_FA)
#summary(lm_Hc_FA_f)

#omnibus testing
#https://cran.r-project.org/web/packages/emmeans/vignettes/confidence-intervals.html#adjust

sink(paste(outpath, "Hc_FA_SimpleStats.txt", sep=''))
'omnibus testing'

## [1] "omnibus testing"

joint_tests(ref_grid(lm_Hc_FA))

##   model term    df1 df2 F.ratio p.value
##   Genotype      2   23   4.641  0.0203
##   Sex           1   23   1.458  0.2396
##   Genotype:Sex   2   23   2.378  0.1152

joint_tests(ref_grid(lm_Hc_FA), by = "Sex", adjust = "sidak")

## Sex = female:
##   model term df1 df2 F.ratio p.value
##   Genotype   2   23   6.281  0.0067
##
## Sex = male:
##   model term df1 df2 F.ratio p.value
##   Genotype   2   23   0.221  0.8034

```



```
joint_tests(ref_grid(lm_Hc_FA), by = "Genotype", adjust = "sidak" )
```

```
## Genotype = APOE22:
## model term df1 df2 F.ratio p.value
## Sex          1  23   1.163  0.2921
##
## Genotype = APOE33:
## model term df1 df2 F.ratio p.value
## Sex          1  23   1.658  0.2107
##
## Genotype = APOE44:
## model term df1 df2 F.ratio p.value
## Sex          1  23   2.966  0.0985
```

```
'anova'
```

```
## [1] "anova"
```

```
anova(lm_Hc_FA)
```

```
## Analysis of Variance Table
##
## Response: Hc
##          Df      Sum Sq    Mean Sq F value    Pr(>F)
## Genotype    2 0.00064461  0.00032230   4.1185 0.02959 *
## Sex          1 0.00008065  0.00008065   1.0306 0.32059
## Genotype:Sex  2 0.00037217  0.00018609   2.3778 0.11517
## Residuals   23 0.00179995  0.00007826
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
#anova(lm_Hc_FA_f)
```

```
#anova(lm_Hc_FA_m)
```

```
#post hoc comparison
```

```
Hc_FA.emm <- emmeans(lm_Hc_FA , ~ Genotype | Sex, adjust = "sidak")
contrast(Hc_FA.emm, simple = c("Genotype", "Sex")) #FDR
```

```
## contrast          estimate      SE df t.ratio p.value
## APOE22 female effect  0.009811 0.00364 23   2.694  0.0777
## APOE33 female effect -0.007546 0.00450 23  -1.678  0.2137
## APOE44 female effect -0.008355 0.00364 23  -2.294  0.0937
## APOE22 male effect    0.004036 0.00339 23   1.189  0.3699
## APOE33 male effect    0.000773 0.00364 23   0.212  0.8338
## APOE44 male effect    0.001281 0.00364 23   0.352  0.8338
##
```

```
## P value adjustment: fdr method for 6 tests
```

```
contrast(Hc_FA.emm, simple = list("Genotype", "Sex"))
```

```
## $`simple contrasts for Genotype`
```

```
## Sex = female:
```

```
## contrast          estimate      SE df t.ratio p.value
## APOE22 effect  0.011841 0.00340 23   3.478  0.0061
## APOE33 effect -0.005516 0.00388 23  -1.421  0.1688
## APOE44 effect -0.006325 0.00340 23  -1.858  0.1141
##
```

```

## Sex = male:
## contrast      estimate      SE df t.ratio p.value
## APOE22 effect  0.002006 0.00305 23   0.659  0.8161
## APOE33 effect -0.001257 0.00319 23  -0.395  0.8161
## APOE44 effect -0.000749 0.00319 23  -0.235  0.8161
##
## P value adjustment: fdr method for 3 tests
##
## `$simple contrasts for Sex`
## Genotype = APOE22:
## contrast      estimate      SE df t.ratio p.value
## female effect  0.00289 0.00268 23   1.078  0.2921
## male effect   -0.00289 0.00268 23  -1.078  0.2921
##
## Genotype = APOE33:
## contrast      estimate      SE df t.ratio p.value
## female effect -0.00416 0.00323 23  -1.288  0.2107
## male effect    0.00416 0.00323 23   1.288  0.2107
##
## Genotype = APOE44:
## contrast      estimate      SE df t.ratio p.value
## female effect -0.00482 0.00280 23  -1.722  0.0985
## male effect    0.00482 0.00280 23   1.722  0.0985
##
## P value adjustment: fdr method for 2 tests
#post hoc tests
summary(glht(lm_Hc_FA, emm(pairwise ~ Genotype*Sex, contr="sidak"))) #consider save to file

##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_FA)
##
## Linear Hypotheses:
##
##               Estimate Std. Error t value Pr(>|t|)
## APOE22 female - APOE33 female == 0  0.0173571  0.0064605   2.687  0.1158
## APOE22 female - APOE44 female == 0  0.0181662  0.0055949   3.247  0.0364 *
## APOE22 female - APOE22 male == 0    0.0057758  0.0053568   1.078  0.8842
## APOE22 female - APOE33 male == 0    0.0090386  0.0055949   1.615  0.5954
## APOE22 female - APOE44 male == 0    0.0085309  0.0055949   1.525  0.6509
## APOE33 female - APOE44 female == 0  0.0008091  0.0064605   0.125  1.0000
## APOE33 female - APOE22 male == 0   -0.0115814  0.0062553  -1.851  0.4530
## APOE33 female - APOE33 male == 0   -0.0083185  0.0064605  -1.288  0.7872
## APOE33 female - APOE44 male == 0   -0.0088262  0.0064605  -1.366  0.7444
## APOE44 female - APOE22 male == 0   -0.0123904  0.0053568  -2.313  0.2279
## APOE44 female - APOE33 male == 0   -0.0091276  0.0055949  -1.631  0.5856
## APOE44 female - APOE44 male == 0   -0.0096353  0.0055949  -1.722  0.5299
## APOE22 male - APOE33 male == 0      0.0032628  0.0053568   0.609  0.9892
## APOE22 male - APOE44 male == 0      0.0027551  0.0053568   0.514  0.9950
## APOE33 male - APOE44 male == 0     -0.0005077  0.0055949  -0.091  1.0000
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Adjusted p values reported -- single-step method)

```

```
res<-summary(glht(lm_Hc_FA, emm(pairwise ~ Genotype*Sex))) #consider save to file
#summary(as.glht(pairs(lm_Hc_FA.emm), by = NULL))
```

```
summary(glht(lm_Hc_FA, emm(pairwise ~ Genotype | Sex)))
```

```
## $`Sex = female`
##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_FA)
##
## Linear Hypotheses:
##               Estimate Std. Error t value Pr(>|t|)
## APOE22 - APOE33 == 0  0.0173571  0.0064605   2.687  0.03357 *
## APOE22 - APOE44 == 0  0.0181662  0.0055949   3.247  0.00947 **
## APOE33 - APOE44 == 0  0.0008091  0.0064605   0.125  0.99137
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Adjusted p values reported -- single-step method)
##
```

```
## $`Sex = male`
##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_FA)
##
## Linear Hypotheses:
##               Estimate Std. Error t value Pr(>|t|)
## APOE22 - APOE33 == 0  0.0032628  0.0053568   0.609   0.817
## APOE22 - APOE44 == 0  0.0027551  0.0053568   0.514   0.865
## APOE33 - APOE44 == 0 -0.0005077  0.0055949  -0.091   0.995
## (Adjusted p values reported -- single-step method)
```

```
summary(glht(lm_Hc_FA, emm(pairwise ~ Sex | Genotype)))
```

```
## $`Genotype = APOE22`
##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_FA)
##
## Linear Hypotheses:
##               Estimate Std. Error t value Pr(>|t|)
## female - male == 0  0.005776   0.005357   1.078   0.292
## (Adjusted p values reported -- single-step method)
##
```

```
## $`Genotype = APOE33`
##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_FA)
##
```

```

## Linear Hypotheses:
##               Estimate Std. Error t value Pr(>|t|)
## female - male == 0 -0.008319  0.006460 -1.288  0.211
## (Adjusted p values reported -- single-step method)
##
##
## $`Genotype = APOE44`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_FA)
##
## Linear Hypotheses:
##               Estimate Std. Error t value Pr(>|t|)
## female - male == 0 -0.009635  0.005595 -1.722  0.0985 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Adjusted p values reported -- single-step method)
mypairs<-pairs(Hc_FA.emm) #_consider save to file
pairs(Hc_FA.emm, by="Genotype")

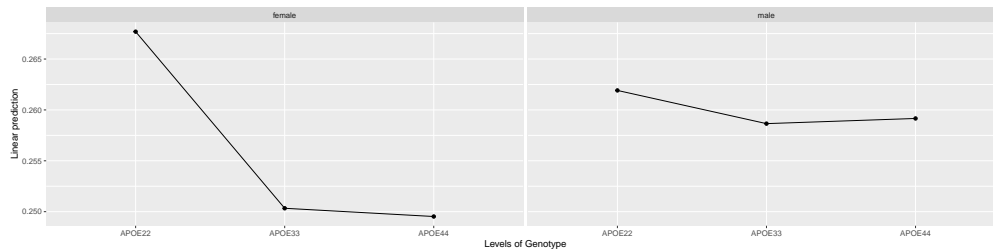
## Genotype = APOE22:
## contrast      estimate      SE df t.ratio p.value
## female - male  0.00578 0.00536 23  1.078  0.2921
##
## Genotype = APOE33:
## contrast      estimate      SE df t.ratio p.value
## female - male -0.00832 0.00646 23 -1.288  0.2107
##
## Genotype = APOE44:
## contrast      estimate      SE df t.ratio p.value
## female - male -0.00964 0.00559 23 -1.722  0.0985

pairs(Hc_FA.emm, by="Sex")

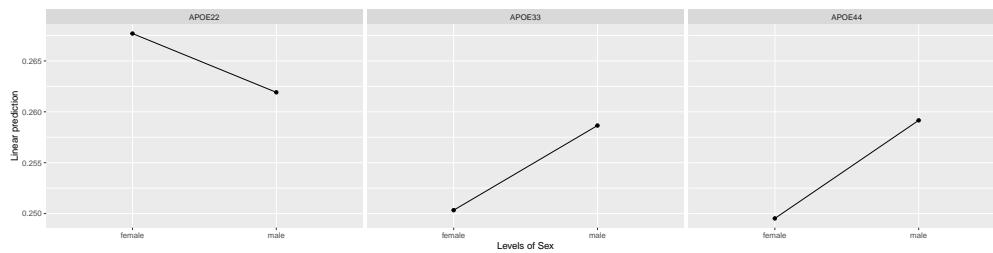
## Sex = female:
## contrast      estimate      SE df t.ratio p.value
## APOE22 - APOE33  0.017357 0.00646 23  2.687  0.0339
## APOE22 - APOE44  0.018166 0.00559 23  3.247  0.0096
## APOE33 - APOE44  0.000809 0.00646 23  0.125  0.9914
##
## Sex = male:
## contrast      estimate      SE df t.ratio p.value
## APOE22 - APOE33  0.003263 0.00536 23  0.609  0.8166
## APOE22 - APOE44  0.002755 0.00536 23  0.514  0.8652
## APOE33 - APOE44 -0.000508 0.00559 23 -0.091  0.9955
##
## P value adjustment: tukey method for comparing a family of 3 estimates
print('Hc FA')

## [1] "Hc FA"
emmip(lm_Hc_FA, ~ Genotype | Sex )

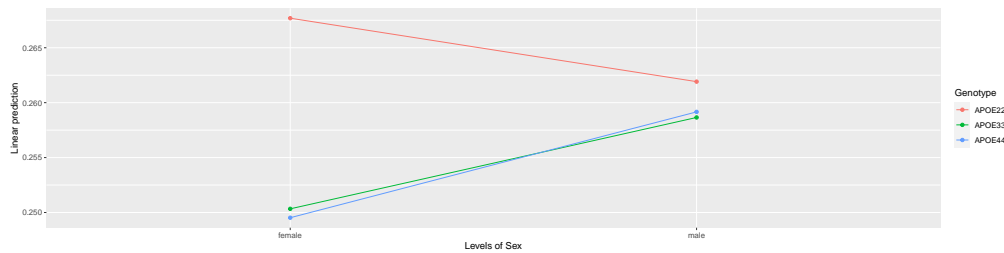
```



```
emmip(lm_Hc_FA, ~ Sex | Genotype )
```

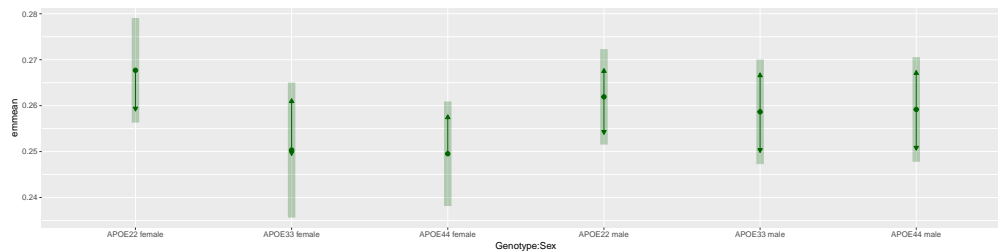


```
emmip(lm_Hc_FA, Genotype~ Sex )
```



```
sink()
```

```
plot(Hc_FA.emm, by = NULL, comparisons = TRUE, adjust = "mvt",
horizontal = FALSE, colors = "darkgreen", main = "Hc FA")
```



```
ggsave(paste(outpath, 'Hc_FA_emmeans.pdf', sep=''), plot = last_plot(), device='pdf', scale=1, width=16, height=16)
```

```
'simple stats'
```

```
## [1] "simple stats"
```

```
print('Hc')
```

```
## [1] "Hc"
```

```
lm_Hc_DEG <- lm(Hc ~ Genotype*Sex, geno_combined_DEG)
summary(lm_Hc_DEG)
```

```
##
```

```
## Call:
```

```

## lm(formula = Hc ~ Genotype * Sex, data = geno_combined_DEG)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -57200 -15583    917  15417  69667
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)      363200      13515  26.873  <2e-16 ***
## GenotypeAPOE33       52133       22070   2.362   0.027 *
## GenotypeAPOE44       23600       19114   1.235   0.229
## Sexmale             20383       18300   1.114   0.277
## GenotypeAPOE33:Sexmale -2517       28670  -0.088   0.931
## GenotypeAPOE44:Sexmale -1783       26462  -0.067   0.947
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 30220 on 23 degrees of freedom
## Multiple R-squared:  0.4199, Adjusted R-squared:  0.2938
## F-statistic:  3.33 on 5 and 23 DF,  p-value: 0.02083

lm_Hc_DEG_f <- lm(Hc ~ Genotype, combo_f_FA)
#summary(lm_Hc_DEG_f)
lm_Hc_DEG_m <- lm(Hc ~ Genotype, combo_m_FA)
#summary(lm_Hc_DEG_f)

#omnibus testing
#https://cran.r-project.org/web/packages/emmeans/vignettes/confidence-intervals.html#adjust

sink(paste(outpath, "Hc_DEG_SimpleStats.txt", sep=''))
'omnibus testing'

## [1] "omnibus testing"

joint_tests(ref_grid(lm_Hc_DEG))

##   model term    df1 df2 F.ratio p.value
##   Genotype      2   23   6.311  0.0065
##   Sex           1   23   2.722  0.1126
##   Genotype:Sex   2   23   0.004  0.9956

joint_tests(ref_grid(lm_Hc_DEG), by = "Sex", adjust = "sidak")

## Sex = female:
##   model term df1 df2 F.ratio p.value
##   Genotype    2  23   2.817  0.0805
##
## Sex = male:
##   model term df1 df2 F.ratio p.value
##   Genotype    2  23   3.677  0.0412

joint_tests(ref_grid(lm_Hc_DEG), by = "Genotype", adjust = "sidak" )

## Genotype = APOE22:
##   model term df1 df2 F.ratio p.value
##   Sex        1  23   1.241  0.2768

```

```
##
## Genotype = APOE33:
## model term df1 df2 F.ratio p.value
## Sex          1  23   0.655  0.4265
##
## Genotype = APOE44:
## model term df1 df2 F.ratio p.value
## Sex          1  23   0.947  0.3406
'anova'

## [1] "anova"
anova(lm_Hc_DEG)

## Analysis of Variance Table
##
## Response: Hc
##           Df      Sum Sq    Mean Sq F value    Pr(>F)
## Genotype    2 1.2612e+10 6305878370   6.9043 0.004482 **
## Sex          1 2.5886e+09 2588593164   2.8343 0.105800
## Genotype:Sex  2 7.9682e+06   3984100   0.0044 0.995648
## Residuals   23 2.1006e+10 913325000
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

#anova(lm_Hc_DEG_f)
#anova(lm_Hc_DEG_m)

#post hoc comparison
Hc_DEG.emm <- emmeans(lm_Hc_DEG , ~ Genotype | Sex, adjust = "sidak")
contrast(Hc_DEG.emm, simple = c("Genotype", "Sex")) #FDR

## contrast            estimate      SE df t.ratio p.value
## APOE22 female effect  -34719 12440 23  -2.791  0.0312
## APOE33 female effect   17414 15360 23   1.134  0.4029
## APOE44 female effect  -11119 12440 23  -0.894  0.4568
## APOE22 male effect    -14336 11596 23  -1.236  0.4029
## APOE33 male effect     35281 12440 23   2.836  0.0312
## APOE44 male effect      7481 12440 23   0.601  0.5535
##
## P value adjustment: fdr method for 6 tests
contrast(Hc_DEG.emm, simple = list("Genotype", "Sex"))

## `$`simple contrasts for Genotype`
## Sex = female:
## contrast            estimate      SE df t.ratio p.value
## APOE22 effect      -25244 11632 23  -2.170  0.0815
## APOE33 effect       26889 13263 23   2.027  0.0815
## APOE44 effect      -1644 11632 23  -0.141  0.8888
##
## Sex = male:
## contrast            estimate      SE df t.ratio p.value
## APOE22 effect      -23811 10404 23  -2.289  0.0474
## APOE33 effect       25806 10881 23   2.372  0.0474
## APOE44 effect      -1994 10881 23  -0.183  0.8562
```

```
##
## P value adjustment: fdr method for 3 tests
##
## `$simple contrasts for Sex`
## Genotype = APOE22:
## contrast      estimate      SE df t.ratio p.value
## female effect  -10192  9150 23  -1.114  0.2768
## male effect    10192  9150 23   1.114  0.2768
##
## Genotype = APOE33:
## contrast      estimate      SE df t.ratio p.value
## female effect  -8933 11035 23  -0.810  0.4265
## male effect    8933 11035 23   0.810  0.4265
##
## Genotype = APOE44:
## contrast      estimate      SE df t.ratio p.value
## female effect  -9300  9557 23  -0.973  0.3406
## male effect    9300  9557 23   0.973  0.3406
##
## P value adjustment: fdr method for 2 tests
#post hoc tests
summary(glht(lm_Hc_DEG, emm(pairwise ~ Genotype*Sex, contr="sidak"))) #consider save to file

##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_DEG)
##
## Linear Hypotheses:
##
##               Estimate Std. Error t value Pr(>|t|)
## APOE22 female - APOE33 female == 0  -52133      22070  -2.362  0.2095
## APOE22 female - APOE44 female == 0  -23600      19114  -1.235  0.8143
## APOE22 female - APOE22 male == 0    -20383      18300  -1.114  0.8697
## APOE22 female - APOE33 male == 0   -70000      19114  -3.662  0.0144 *
## APOE22 female - APOE44 male == 0   -42200      19114  -2.208  0.2705
## APOE33 female - APOE44 female == 0    28533      22070   1.293  0.7845
## APOE33 female - APOE22 male == 0     31750      21370   1.486  0.6745
## APOE33 female - APOE33 male == 0   -17867      22070  -0.810  0.9625
## APOE33 female - APOE44 male == 0     9933      22070   0.450  0.9973
## APOE44 female - APOE22 male == 0     3217      18300   0.176  1.0000
## APOE44 female - APOE33 male == 0   -46400      19114  -2.428  0.1870
## APOE44 female - APOE44 male == 0   -18600      19114  -0.973  0.9212
## APOE22 male - APOE33 male == 0    -49617      18300  -2.711  0.1104
## APOE22 male - APOE44 male == 0    -21817      18300  -1.192  0.8349
## APOE33 male - APOE44 male == 0     27800      19114   1.454  0.6933
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Adjusted p values reported -- single-step method)
res<-summary(glht(lm_Hc_DEG, emm(pairwise ~ Genotype*Sex))) #consider save to file
#summary(as.glht(pairs(lm_Hc_DEG.emm), by = NULL))

summary(glht(lm_Hc_DEG, emm(pairwise ~ Genotype | Sex)))
```



```

## $`Sex = female`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_DEG)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## APOE22 - APOE33 == 0   -52133      22070  -2.362   0.0666 .
## APOE22 - APOE44 == 0   -23600      19114  -1.235   0.4444
## APOE33 - APOE44 == 0    28533      22070   1.293   0.4122
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Adjusted p values reported -- single-step method)
##
##
## $`Sex = male`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_DEG)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## APOE22 - APOE33 == 0   -49617      18300  -2.711   0.032 *
## APOE22 - APOE44 == 0   -21817      18300  -1.192   0.469
## APOE33 - APOE44 == 0    27800      19114   1.454   0.331
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Adjusted p values reported -- single-step method)
summary(glht(lm_Hc_DEG, emm(pairwise ~ Sex | Genotype)))

## $`Genotype = APOE22`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_DEG)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## female - male == 0   -20383      18300  -1.114   0.277
## (Adjusted p values reported -- single-step method)
##
##
## $`Genotype = APOE33`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_DEG)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## female - male == 0   -17867      22070  -0.81    0.427
## (Adjusted p values reported -- single-step method)

```

```
##
##
## $`Genotype = APOE44`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_DEG)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## female - male == 0   -18600      19114  -0.973   0.341
## (Adjusted p values reported -- single-step method)

mypairs<-pairs(Hc_DEG.emm) #_consider save to file
pairs(Hc_DEG.emm, by="Genotype")

## Genotype = APOE22:
## contrast      estimate      SE df t.ratio p.value
## female - male  -20383 18300 23  -1.114  0.2768
##
## Genotype = APOE33:
## contrast      estimate      SE df t.ratio p.value
## female - male  -17867 22070 23  -0.810  0.4265
##
## Genotype = APOE44:
## contrast      estimate      SE df t.ratio p.value
## female - male  -18600 19114 23  -0.973  0.3406

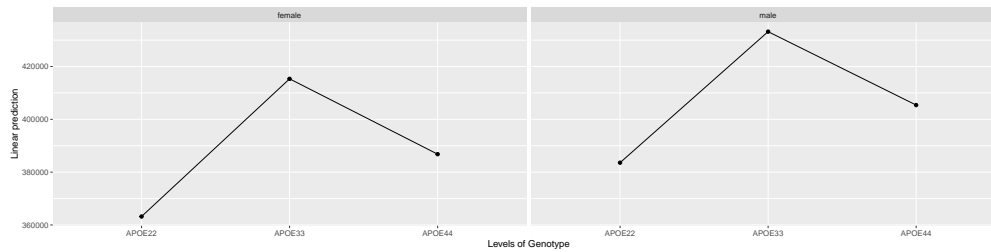
pairs(Hc_DEG.emm, by="Sex")

## Sex = female:
## contrast      estimate      SE df t.ratio p.value
## APOE22 - APOE33  -52133 22070 23  -2.362  0.0670
## APOE22 - APOE44  -23600 19114 23  -1.235  0.4454
## APOE33 - APOE44   28533 22070 23   1.293  0.4133
##
## Sex = male:
## contrast      estimate      SE df t.ratio p.value
## APOE22 - APOE33  -49617 18300 23  -2.711  0.0322
## APOE22 - APOE44  -21817 18300 23  -1.192  0.4696
## APOE33 - APOE44   27800 19114 23   1.454  0.3308
##
## P value adjustment: tukey method for comparing a family of 3 estimates

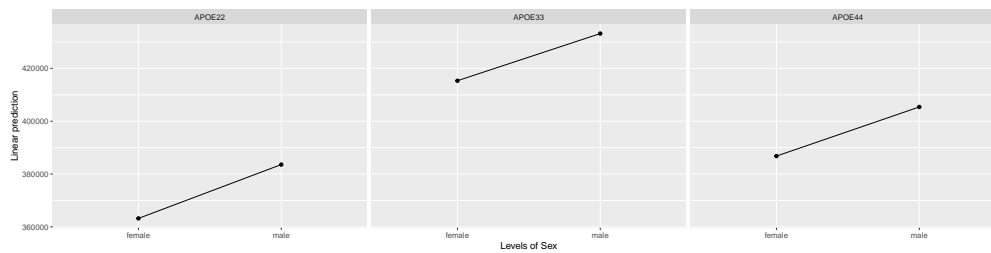
print('Hc DEG')

## [1] "Hc DEG"

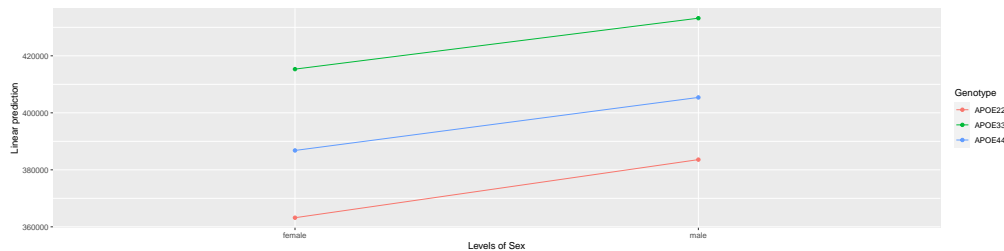
emmip(lm_Hc_DEG, ~ Genotype | Sex )
```



```
emmip(lm_Hc_DEG, ~ Sex | Genotype )
```

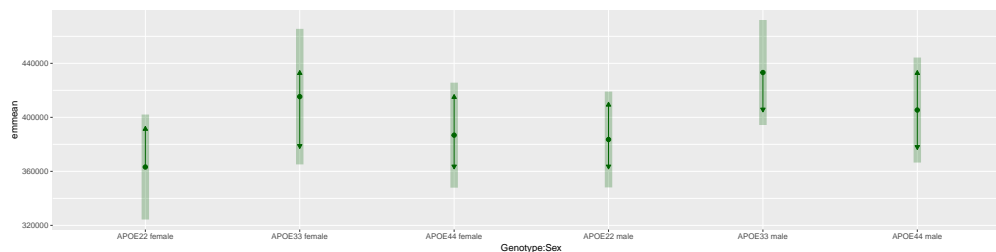


```
emmip(lm_Hc_DEG, Genotype~ Sex )
```



```
sink()
```

```
plot(Hc_DEG.emm, by = NULL, comparisons = TRUE, adjust = "mvt",
horizontal = FALSE, colors = "darkgreen", main = "Hc DEG")
```



```
ggsave(paste(outpath, 'Hc_DEG_emmeans.pdf', sep = ''), plot = last_plot(), device = 'pdf', scale = 1, width = 16,
```

```
'simple stats')
```

```
## [1] "simple stats"
```

```
print('Hc')
```

```
## [1] "Hc"
```

```
lm_Hc_CLUS <- lm(Hc ~ Genotype*Sex, geno_combined_CLUS)
summary(lm_Hc_CLUS)
```

```
##
```

```
## Call:
```

```

## lm(formula = Hc ~ Genotype * Sex, data = geno_combined_CLUS)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -86.377 -24.544  -3.834  21.724 121.923
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)      442.45      22.38  19.769 6.23e-16 ***
## GenotypeAPOE33       86.11      36.55   2.356  0.0274 *
## GenotypeAPOE44       46.66      31.65   1.474  0.1540
## Sexmale             31.52      30.30   1.040  0.3091
## GenotypeAPOE33:Sexmale -33.30      47.48  -0.701  0.4901
## GenotypeAPOE44:Sexmale -17.24      43.82  -0.394  0.6976
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 50.05 on 23 degrees of freedom
## Multiple R-squared:  0.3022, Adjusted R-squared:  0.1505
## F-statistic: 1.992 on 5 and 23 DF,  p-value: 0.1179

lm_Hc_CLUS_f <- lm(Hc ~ Genotype, combo_f_FA)
#summary(lm_Hc_CLUS_f)
lm_Hc_CLUS_m <- lm(Hc ~ Genotype, combo_m_FA)
#summary(lm_Hc_CLUS_f)

#omnibus testing
#https://cran.r-project.org/web/packages/emmeans/vignettes/confidence-intervals.html#adjust

sink(paste(outpath, "Hc_CLUS_SimpleStats.txt", sep=''))
'omnibus testing'

## [1] "omnibus testing"

joint_tests(ref_grid(lm_Hc_CLUS))

##   model term    df1 df2 F.ratio p.value
##   Genotype      2   23   4.404  0.0240
##   Sex           1   23   0.595  0.4483
##   Genotype:Sex   2   23   0.250  0.7806

joint_tests(ref_grid(lm_Hc_CLUS), by = "Sex", adjust = "sidak")

## Sex = female:
##   model term df1 df2 F.ratio p.value
##   Genotype    2  23   2.903  0.0752
##
## Sex = male:
##   model term df1 df2 F.ratio p.value
##   Genotype    2  23   1.539  0.2360

joint_tests(ref_grid(lm_Hc_CLUS), by = "Genotype", adjust = "sidak" )

## Genotype = APOE22:
##   model term df1 df2 F.ratio p.value
##   Sex        1  23   1.082  0.3091

```

```
##
## Genotype = APOE33:
## model term df1 df2 F.ratio p.value
## Sex          1  23   0.002  0.9616
##
## Genotype = APOE44:
## model term df1 df2 F.ratio p.value
## Sex          1  23   0.203  0.6561
'anova'

## [1] "anova"
anova(lm_Hc_CLUS)

## Analysis of Variance Table
##
## Response: Hc
##           Df Sum Sq Mean Sq F value  Pr(>F)
## Genotype    2  21720  10860.2   4.3361 0.02524 *
## Sex          1   1971   1971.3   0.7871 0.38416
## Genotype:Sex  2   1254    627.1   0.2504 0.78060
## Residuals   23  57605   2504.6
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

#anova(lm_Hc_CLUS_f)
#anova(lm_Hc_CLUS_m)

#post hoc comparison
Hc_CLUS.emm <- emmeans(lm_Hc_CLUS , ~ Genotype | Sex, adjust = "sidak")
contrast(Hc_CLUS.emm, simple = c("Genotype", "Sex")) #FDR

## contrast            estimate    SE df t.ratio p.value
## APOE22 female effect  -51.59 20.6 23  -2.504  0.1188
## APOE33 female effect   34.52 25.4 23   1.357  0.3758
## APOE44 female effect   -4.94 20.6 23  -0.240  0.8128
## APOE22 male effect    -20.07 19.2 23  -1.045  0.4601
## APOE33 male effect     32.74 20.6 23   1.589  0.3758
## APOE44 male effect      9.34 20.6 23   0.453  0.7853
##
## P value adjustment: fdr method for 6 tests
contrast(Hc_CLUS.emm, simple = list("Genotype", "Sex"))

## `$`simple contrasts for Genotype`
## Sex = female:
## contrast            estimate    SE df t.ratio p.value
## APOE22 effect      -44.26 19.3 23  -2.298  0.0931
## APOE33 effect       41.86 22.0 23   1.906  0.1039
## APOE44 effect        2.40 19.3 23   0.125  0.9019
##
## Sex = male:
## contrast            estimate    SE df t.ratio p.value
## APOE22 effect      -27.41 17.2 23  -1.591  0.2579
## APOE33 effect       25.40 18.0 23   1.410  0.2579
## APOE44 effect        2.01 18.0 23   0.111  0.9124
```

```
##
## P value adjustment: fdr method for 3 tests
##
## `$simple contrasts for Sex`
## Genotype = APOE22:
## contrast      estimate    SE df t.ratio p.value
## female effect  -15.76 15.2 23  -1.040  0.3091
## male effect    15.76 15.2 23   1.040  0.3091
##
## Genotype = APOE33:
## contrast      estimate    SE df t.ratio p.value
## female effect   0.89 18.3 23   0.049  0.9616
## male effect    -0.89 18.3 23  -0.049  0.9616
##
## Genotype = APOE44:
## contrast      estimate    SE df t.ratio p.value
## female effect  -7.14 15.8 23  -0.451  0.6561
## male effect    7.14 15.8 23   0.451  0.6561
##
## P value adjustment: fdr method for 2 tests
#post hoc tests
summary(glht(lm_Hc_CLUS, emm(pairwise ~ Genotype*Sex, contr="sidak"))) #consider save to file

##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_CLUS)
##
## Linear Hypotheses:
##
##               Estimate Std. Error t value Pr(>|t|)
## APOE22 female - APOE33 female == 0 -86.115    36.548  -2.356    0.212
## APOE22 female - APOE44 female == 0 -46.658    31.652  -1.474    0.681
## APOE22 female - APOE22 male == 0  -31.522    30.304  -1.040    0.899
## APOE22 female - APOE33 male == 0  -84.334    31.652  -2.664    0.121
## APOE22 female - APOE44 male == 0  -60.936    31.652  -1.925    0.411
## APOE33 female - APOE44 female == 0  39.457    36.548   1.080    0.884
## APOE33 female - APOE22 male == 0   54.593    35.388   1.543    0.640
## APOE33 female - APOE33 male == 0    1.781    36.548   0.049    1.000
## APOE33 female - APOE44 male == 0   25.179    36.548   0.689    0.981
## APOE44 female - APOE22 male == 0   15.136    30.304   0.499    0.996
## APOE44 female - APOE33 male == 0  -37.676    31.652  -1.190    0.836
## APOE44 female - APOE44 male == 0  -14.278    31.652  -0.451    0.997
## APOE22 male - APOE33 male == 0   -52.812    30.304  -1.743    0.517
## APOE22 male - APOE44 male == 0   -29.414    30.304  -0.971    0.922
## APOE33 male - APOE44 male == 0    23.398    31.652   0.739    0.975
## (Adjusted p values reported -- single-step method)
res<-summary(glht(lm_Hc_CLUS, emm(pairwise ~ Genotype*Sex))) #consider save to file
#summary(as.glht(pairs(lm_Hc_CLUS.emm), by = NULL))

summary(glht(lm_Hc_CLUS, emm(pairwise ~ Genotype | Sex)))

## `$Sex = female`
##
```

```

## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_CLUS)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## APOE22 - APOE33 == 0   -86.11      36.55  -2.356  0.0674 .
## APOE22 - APOE44 == 0   -46.66      31.65  -1.474  0.3205
## APOE33 - APOE44 == 0    39.46      36.55   1.080  0.5349
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Adjusted p values reported -- single-step method)
##
##
## $`Sex = male`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_CLUS)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## APOE22 - APOE33 == 0   -52.81      30.30  -1.743  0.211
## APOE22 - APOE44 == 0   -29.41      30.30  -0.971  0.602
## APOE33 - APOE44 == 0    23.40      31.65   0.739  0.743
## (Adjusted p values reported -- single-step method)
summary(glht(lm_Hc_CLUS, emm(pairwise ~ Sex | Genotype)))

## $`Genotype = APOE22`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_CLUS)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## female - male == 0   -31.52      30.30  -1.04   0.309
## (Adjusted p values reported -- single-step method)
##
##
## $`Genotype = APOE33`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_CLUS)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## female - male == 0    1.781      36.548  0.049  0.962
## (Adjusted p values reported -- single-step method)
##
##
## $`Genotype = APOE44`
##

```

```
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Hc ~ Genotype * Sex, data = geno_combined_CLUS)
##
## Linear Hypotheses:
##           Estimate Std. Error t value Pr(>|t|)
## female - male == 0   -14.28    31.65  -0.451   0.656
## (Adjusted p values reported -- single-step method)

mypairs<-pairs(Hc_CLUS.emm) #_consider save to file
pairs(Hc_CLUS.emm, by="Genotype")

## Genotype = APOE22:
## contrast      estimate    SE df t.ratio p.value
## female - male  -31.52 30.3 23  -1.040  0.3091
##
## Genotype = APOE33:
## contrast      estimate    SE df t.ratio p.value
## female - male    1.78 36.5 23   0.049  0.9616
##
## Genotype = APOE44:
## contrast      estimate    SE df t.ratio p.value
## female - male  -14.28 31.7 23  -0.451  0.6561

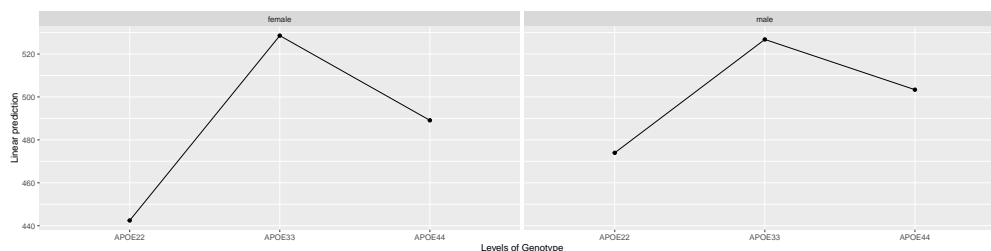
pairs(Hc_CLUS.emm, by="Sex")

## Sex = female:
## contrast      estimate    SE df t.ratio p.value
## APOE22 - APOE33  -86.1 36.5 23  -2.356  0.0678
## APOE22 - APOE44  -46.7 31.7 23  -1.474  0.3215
## APOE33 - APOE44   39.5 36.5 23   1.080  0.5359
##
## Sex = male:
## contrast      estimate    SE df t.ratio p.value
## APOE22 - APOE33  -52.8 30.3 23  -1.743  0.2113
## APOE22 - APOE44  -29.4 30.3 23  -0.971  0.6023
## APOE33 - APOE44   23.4 31.7 23   0.739  0.7430
##
## P value adjustment: tukey method for comparing a family of 3 estimates

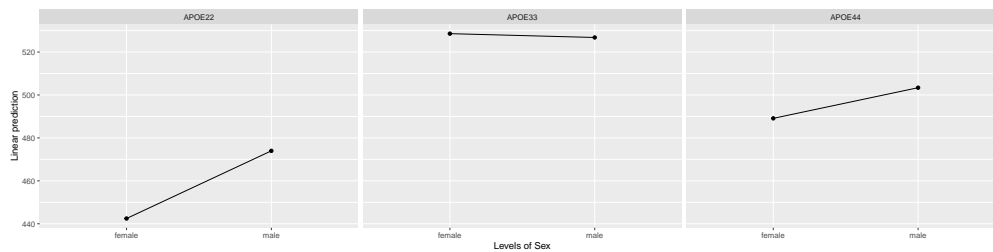
print('Hc CLUS')

## [1] "Hc CLUS"

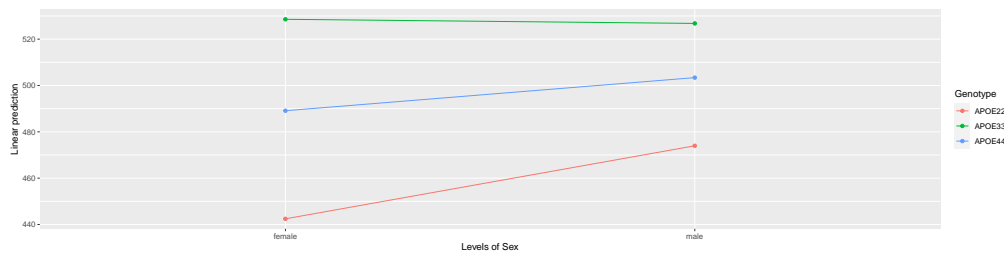
emmip(lm_Hc_CLUS, ~ Genotype | Sex )
```



```
emmip(lm_Hc_CLUS, ~ Sex | Genotype )
```

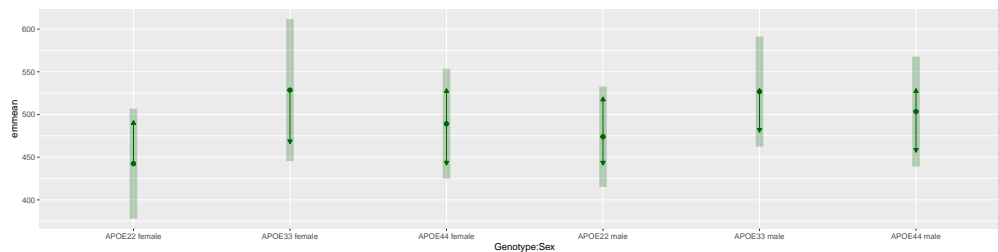



```
emmip(lm_Hc_CLUS, Genotype~ Sex )
```



```
sink()
```

```
plot(Hc_CLUS.emm, by = NULL, comparisons = TRUE, adjust = "mvt",
horizontal = FALSE, colors = "darkgreen", main = "Hc CLUS")
```



```
ggsave(paste(outpath, 'Hc_CLUS_emmeans.pdf', sep=''), plot = last_plot(), device='pdf', scale=1, width=16
```