

# 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:

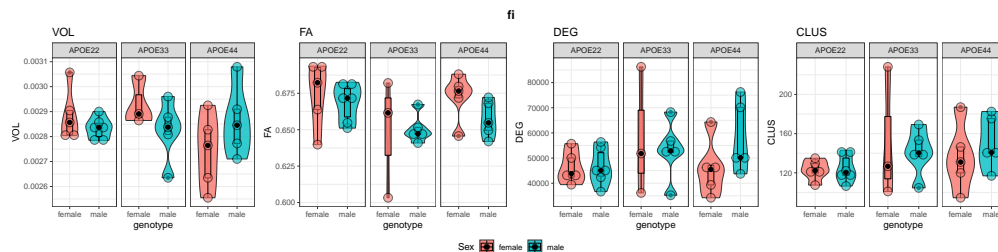
Morris Water Maze - testing spatial navigation memory Segmentation: regional volumes Microstructural properties: FA Tractography Based Connectivity: Degree, and Clustering Coefficient

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

## Plots for fi

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('fi')
```

```
## [1] "fi"
```

```
lm_fi_VOL <- lm(fi ~ Genotype*Sex, geno_combined_VOL)
summary(lm_fi_VOL)
```

```
##
## Call:
## lm(formula = fi ~ Genotype * Sex, data = geno_combined_VOL)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -1.889e-04 -6.864e-05  3.110e-07  5.381e-05  2.159e-04
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)      2.886e-03  5.090e-05  56.701  <2e-16 ***
## GenotypeAPOE33      4.727e-05  8.311e-05   0.569   0.5750
## GenotypeAPOE44     -1.444e-04  7.198e-05  -2.007   0.0567 .
## Sexmale           -5.189e-05  6.891e-05  -0.753   0.4591
## GenotypeAPOE33:Sexmale -5.738e-05  1.080e-04  -0.531   0.6002
## GenotypeAPOE44:Sexmale  1.740e-04  9.965e-05   1.746   0.0942 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.0001138 on 23 degrees of freedom
## Multiple R-squared:  0.2308, Adjusted R-squared:  0.06359
## F-statistic:  1.38 on 5 and 23 DF,  p-value: 0.2682

lm_fi_VOL_f <- lm(fi ~ Genotype, combo_f_FA)
#summary(lm_fi_VOL_f)
lm_fi_VOL_m <- lm(fi ~ Genotype, combo_m_FA)
#summary(lm_fi_VOL_f)

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

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

## [1] "omnibus testing"

joint_tests(ref_grid(lm_fi_VOL))

##   model term    df1 df2 F.ratio p.value
##   Genotype      2   23   1.117  0.3444
##   Sex           1   23   0.091  0.7660
##   Genotype:Sex   2   23   2.577  0.0978

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

## Sex = female:
##   model term df1 df2 F.ratio p.value
##   Genotype    2   23   3.285  0.0556
##
## Sex = male:
##   model term df1 df2 F.ratio p.value
##   Genotype    2   23   0.165  0.8486
```

```

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

## Genotype = APOE22:
## model term df1 df2 F.ratio p.value
## Sex          1  23   0.567  0.4591
##
## Genotype = APOE33:
## model term df1 df2 F.ratio p.value
## Sex          1  23   1.728  0.2016
##
## Genotype = APOE44:
## model term df1 df2 F.ratio p.value
## Sex          1  23   2.876  0.1034

'anova'

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

## Analysis of Variance Table
##
## Response: fi
##          Df      Sum Sq    Mean Sq F value    Pr(>F)
## Genotype    2 2.2405e-08  1.1202e-08   0.8649  0.43433
## Sex          1 2.3900e-10  2.3900e-10   0.0184  0.89315
## Genotype:Sex  2 6.6743e-08  3.3371e-08   2.5766  0.09779 .
## Residuals   23 2.9789e-07  1.2952e-08
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

#anova(lm_fi_VOL_f)
#anova(lm_fi_VOL_m)

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

## contrast          estimate      SE df t.ratio p.value
## APOE22 female effect  3.89e-05 4.68e-05 23   0.830  0.7688
## APOE33 female effect  8.62e-05 5.78e-05 23   1.490  0.4497
## APOE44 female effect -1.06e-04 4.68e-05 23  -2.253  0.2047
## APOE22 male effect   -1.30e-05 4.37e-05 23  -0.297  0.7688
## APOE33 male effect   -2.31e-05 4.68e-05 23  -0.493  0.7688
## APOE44 male effect    1.65e-05 4.68e-05 23   0.353  0.7688
##
## P value adjustment: fdr method for 6 tests
contrast(fi_VOL.emm, simple = list("Genotype", "Sex"))

## $`simple contrasts for Genotype`
## Sex = female:
## contrast          estimate      SE df t.ratio p.value
## APOE22 effect    3.24e-05 4.38e-05 23   0.739  0.4672
## APOE33 effect    7.97e-05 4.99e-05 23   1.595  0.1866
## APOE44 effect   -1.12e-04 4.38e-05 23  -2.558  0.0528
##

```

```
## Sex = male:
## contrast      estimate      SE df t.ratio p.value
## APOE22 effect -6.48e-06 3.92e-05 23 -0.165 0.8701
## APOE33 effect -1.66e-05 4.10e-05 23 -0.405 0.8701
## APOE44 effect  2.31e-05 4.10e-05 23  0.563 0.8701
##
## P value adjustment: fdr method for 3 tests
##
## `$simple contrasts for Sex`
## Genotype = APOE22:
## contrast      estimate      SE df t.ratio p.value
## female effect  2.59e-05 3.45e-05 23  0.753 0.4591
## male effect   -2.59e-05 3.45e-05 23 -0.753 0.4591
##
## Genotype = APOE33:
## contrast      estimate      SE df t.ratio p.value
## female effect  5.46e-05 4.16e-05 23  1.315 0.2016
## male effect   -5.46e-05 4.16e-05 23 -1.315 0.2016
##
## Genotype = APOE44:
## contrast      estimate      SE df t.ratio p.value
## female effect -6.10e-05 3.60e-05 23 -1.696 0.1034
## male effect    6.10e-05 3.60e-05 23  1.696 0.1034
##
## P value adjustment: fdr method for 2 tests
#post hoc tests
summary(glht(lm_fi_VOL, emm(pairwise ~ Genotype*Sex, contr="sidak"))) #consider save to file

##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_VOL)
##
## Linear Hypotheses:
##
##               Estimate Std. Error t value Pr(>|t|)
## APOE22 female - APOE33 female == 0 -4.727e-05 8.311e-05 -0.569 0.992
## APOE22 female - APOE44 female == 0  1.444e-04 7.198e-05  2.007 0.367
## APOE22 female - APOE22 male == 0   5.189e-05 6.891e-05  0.753 0.972
## APOE22 female - APOE33 male == 0   6.199e-05 7.198e-05  0.861 0.952
## APOE22 female - APOE44 male == 0   2.235e-05 7.198e-05  0.311 1.000
## APOE33 female - APOE44 female == 0  1.917e-04 8.311e-05  2.307 0.230
## APOE33 female - APOE22 male == 0   9.916e-05 8.047e-05  1.232 0.816
## APOE33 female - APOE33 male == 0   1.093e-04 8.311e-05  1.315 0.773
## APOE33 female - APOE44 male == 0   6.963e-05 8.311e-05  0.838 0.957
## APOE44 female - APOE22 male == 0  -9.254e-05 6.891e-05 -1.343 0.757
## APOE44 female - APOE33 male == 0  -8.244e-05 7.198e-05 -1.145 0.856
## APOE44 female - APOE44 male == 0  -1.221e-04 7.198e-05 -1.696 0.546
## APOE22 male - APOE33 male == 0     1.010e-05 6.891e-05  0.147 1.000
## APOE22 male - APOE44 male == 0    -2.953e-05 6.891e-05 -0.429 0.998
## APOE33 male - APOE44 male == 0    -3.964e-05 7.198e-05 -0.551 0.993
## (Adjusted p values reported -- single-step method)
res<-summary(glht(lm_fi_VOL, emm(pairwise ~ Genotype*Sex))) #consider save to file
#summary(as.glht(pairs(lm_fi_VOL.emm), by = NULL))
```

```
summary(glht(lm-fi_VOL, emm(pairwise ~ Genotype | Sex)))

## $`Sex = female`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_VOL)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## APOE22 - APOE33 == 0 -4.727e-05  8.311e-05 -0.569  0.8373
## APOE22 - APOE44 == 0  1.444e-04  7.198e-05  2.007  0.1326
## APOE33 - APOE44 == 0  1.917e-04  8.311e-05  2.307  0.0747 .
## ---
## 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 = fi ~ Genotype * Sex, data = geno_combined_VOL)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## APOE22 - APOE33 == 0  1.010e-05  6.891e-05  0.147  0.988
## APOE22 - APOE44 == 0 -2.953e-05  6.891e-05 -0.429  0.904
## APOE33 - APOE44 == 0 -3.964e-05  7.198e-05 -0.551  0.847
## (Adjusted p values reported -- single-step method)
summary(glht(lm-fi_VOL, emm(pairwise ~ Sex | Genotype)))

## $`Genotype = APOE22`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_VOL)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## female - male == 0 5.189e-05  6.891e-05  0.753  0.459
## (Adjusted p values reported -- single-step method)
##
##
## $`Genotype = APOE33`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_VOL)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## female - male == 0 1.093e-04  8.311e-05  1.315  0.202
```

```

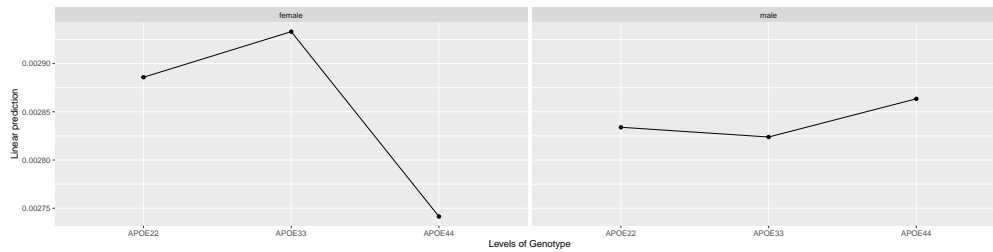
## (Adjusted p values reported -- single-step method)
##
##
## $`Genotype = APOE44`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_VOL)
##
## Linear Hypotheses:
##               Estimate Std. Error t value Pr(>|t|)
## female - male == 0 -1.221e-04  7.198e-05  -1.696    0.103
## (Adjusted p values reported -- single-step method)
mypairs<-pairs(fi_VOL.emm) #_consider save to file
pairs(fi_VOL.emm, by="Genotype")

## Genotype = APOE22:
## contrast      estimate      SE df t.ratio p.value
## female - male  5.19e-05 6.89e-05 23   0.753  0.4591
##
## Genotype = APOE33:
## contrast      estimate      SE df t.ratio p.value
## female - male  1.09e-04 8.31e-05 23   1.315  0.2016
##
## Genotype = APOE44:
## contrast      estimate      SE df t.ratio p.value
## female - male -1.22e-04 7.20e-05 23  -1.696  0.1034
pairs(fi_VOL.emm, by="Sex")

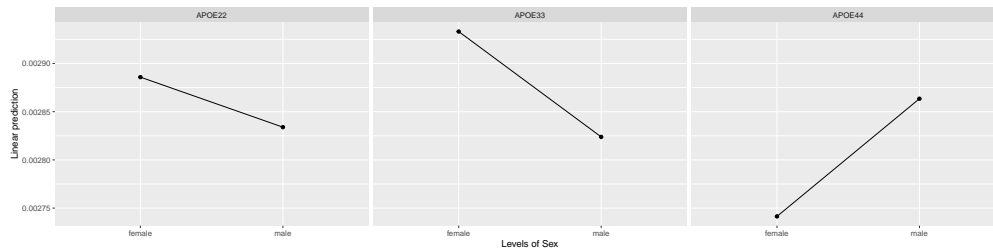
## Sex = female:
## contrast      estimate      SE df t.ratio p.value
## APOE22 - APOE33 -4.73e-05 8.31e-05 23  -0.569  0.8379
## APOE22 - APOE44  1.44e-04 7.20e-05 23   2.007  0.1332
## APOE33 - APOE44  1.92e-04 8.31e-05 23   2.307  0.0749
##
## Sex = male:
## contrast      estimate      SE df t.ratio p.value
## APOE22 - APOE33  1.01e-05 6.89e-05 23   0.147  0.9882
## APOE22 - APOE44 -2.95e-05 6.89e-05 23  -0.429  0.9041
## APOE33 - APOE44 -3.96e-05 7.20e-05 23  -0.551  0.8472
##
## P value adjustment: tukey method for comparing a family of 3 estimates
print('fi VOL')

## [1] "fi VOL"
emmip(lm-fi_VOL, ~ Genotype | Sex )

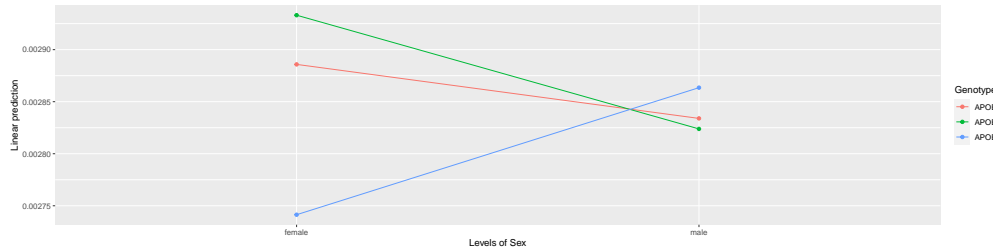
```



```
emmip(lm-fi_VOL, ~ Sex | Genotype )
```

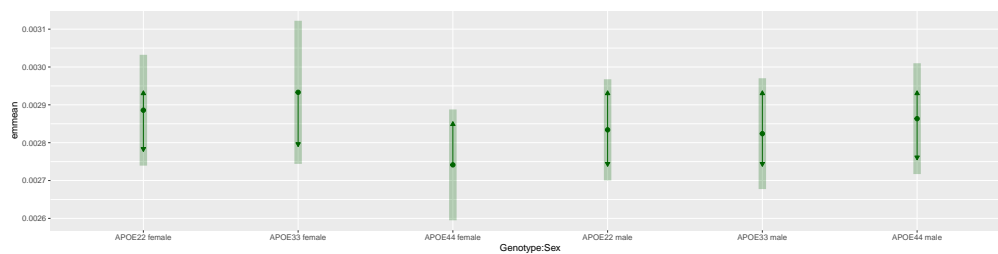


```
emmip(lm-fi_VOL, Genotype~ Sex )
```



```
sink()
```

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



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

```
'simple stats'
```

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

```
print('fi')
```

```
## [1] "fi"
```

```
lm-fi_FA <- lm(fi ~ Genotype*Sex, geno_combined_FA)
summary(lm-fi_FA)
```

```
##
## Call:
## lm(formula = fi ~ Genotype * Sex, data = geno_combined_FA)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.045696 -0.009889  0.002339  0.012594  0.033102
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)      0.674432   0.008517  79.184  <2e-16 ***
## GenotypeAPOE33    -0.025466   0.013909  -1.831   0.0801 .
## GenotypeAPOE44    -0.002072   0.012045  -0.172   0.8649
## Sexmale           -0.005803   0.011532  -0.503   0.6196
## GenotypeAPOE33:Sexmale  0.007586   0.018068   0.420   0.6785
## GenotypeAPOE44:Sexmale -0.009255   0.016676  -0.555   0.5843
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.01905 on 23 degrees of freedom
## Multiple R-squared:  0.2502, Adjusted R-squared:  0.08722
## F-statistic: 1.535 on 5 and 23 DF,  p-value: 0.2181
lm_fi_FA_f <- lm(fi ~ Genotype, combo_f_FA)
#summary(lm_fi_FA_f)
lm_fi_FA_m <- lm(fi ~ Genotype, combo_m_FA)
#summary(lm_fi_FA_f)

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

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

## [1] "omnibus testing"
joint_tests(ref_grid(lm_fi_FA))

##   model term    df1 df2 F.ratio p.value
##   Genotype      2   23   2.918  0.0742
##   Sex           1   23   0.772  0.3888
##   Genotype:Sex   2   23   0.428  0.6566
joint_tests(ref_grid(lm_fi_FA), by = "Sex", adjust = "sidak")

## Sex = female:
##   model term df1 df2 F.ratio p.value
##   Genotype   2   23   1.913  0.1703
##
## Sex = male:
##   model term df1 df2 F.ratio p.value
##   Genotype   2   23   1.250  0.3051
joint_tests(ref_grid(lm_fi_FA), by = "Genotype", adjust = "sidak" )

## Genotype = APOE22:
```



```
## model term df1 df2 F.ratio p.value
## Sex          1  23   0.253  0.6196
##
## Genotype = APOE33:
## model term df1 df2 F.ratio p.value
## Sex          1  23   0.016  0.8991
##
## Genotype = APOE44:
## model term df1 df2 F.ratio p.value
## Sex          1  23   1.563  0.2238

'anova'

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

## Analysis of Variance Table
##
## Response: fi
##           Df      Sum Sq    Mean Sq F value    Pr(>F)
## Genotype    2  0.0021195  0.00105977   2.9217  0.07402 .
## Sex          1  0.0003538  0.00035376   0.9753  0.33364
## Genotype:Sex  2  0.0003108  0.00015541   0.4285  0.65660
## Residuals   23  0.0083426  0.00036272
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

#anova(lm_fi_FA_f)
#anova(lm_fi_FA_m)

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

## contrast          estimate      SE df t.ratio p.value
## APOE22 female effect  0.01236 0.00784 23   1.576  0.3036
## APOE33 female effect -0.01311 0.00968 23  -1.354  0.3036
## APOE44 female effect  0.01029 0.00784 23   1.312  0.3036
## APOE22 male effect    0.00656 0.00731 23   0.897  0.4547
## APOE33 male effect   -0.01132 0.00784 23  -1.444  0.3036
## APOE44 male effect   -0.00477 0.00784 23  -0.608  0.5488
##
## P value adjustment: fdr method for 6 tests
contrast(fi_FA.emm, simple = list("Genotype", "Sex"))

## $`simple contrasts for Genotype`
## Sex = female:
## contrast          estimate      SE df t.ratio p.value
## APOE22 effect    0.00918 0.00733 23   1.252  0.3346
## APOE33 effect   -0.01629 0.00836 23  -1.949  0.1909
## APOE44 effect    0.00711 0.00733 23   0.970  0.3423
##
## Sex = male:
## contrast          estimate      SE df t.ratio p.value
## APOE22 effect    0.00974 0.00656 23   1.485  0.3705
```

```

## APOE33 effect -0.00814 0.00686 23 -1.188 0.3705
## APOE44 effect -0.00159 0.00686 23 -0.232 0.8186
##
## P value adjustment: fdr method for 3 tests
##
## $`simple contrasts for Sex`
## Genotype = APOE22:
## contrast estimate SE df t.ratio p.value
## female effect 0.002901 0.00577 23 0.503 0.6196
## male effect -0.002901 0.00577 23 -0.503 0.6196
##
## Genotype = APOE33:
## contrast estimate SE df t.ratio p.value
## female effect -0.000892 0.00695 23 -0.128 0.8991
## male effect 0.000892 0.00695 23 0.128 0.8991
##
## Genotype = APOE44:
## contrast estimate SE df t.ratio p.value
## female effect 0.007529 0.00602 23 1.250 0.2238
## male effect -0.007529 0.00602 23 -1.250 0.2238
##
## P value adjustment: fdr method for 2 tests
#post hoc tests
summary(glht(lm_fi_FA, emm(pairwise ~ Genotype*Sex, contr="sidak"))) #consider save to file

##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_FA)
##
## Linear Hypotheses:
##
## Estimate Std. Error t value Pr(>|t|)
## APOE22 female - APOE33 female == 0 0.025466 0.013909 1.831 0.465
## APOE22 female - APOE44 female == 0 0.002072 0.012045 0.172 1.000
## APOE22 female - APOE22 male == 0 0.005803 0.011532 0.503 0.996
## APOE22 female - APOE33 male == 0 0.023683 0.012045 1.966 0.389
## APOE22 female - APOE44 male == 0 0.017129 0.012045 1.422 0.712
## APOE33 female - APOE44 female == 0 -0.023394 0.013909 -1.682 0.554
## APOE33 female - APOE22 male == 0 -0.019664 0.013467 -1.460 0.690
## APOE33 female - APOE33 male == 0 -0.001783 0.013909 -0.128 1.000
## APOE33 female - APOE44 male == 0 -0.008337 0.013909 -0.599 0.990
## APOE44 female - APOE22 male == 0 0.003731 0.011532 0.323 0.999
## APOE44 female - APOE33 male == 0 0.021611 0.012045 1.794 0.487
## APOE44 female - APOE44 male == 0 0.015057 0.012045 1.250 0.807
## APOE22 male - APOE33 male == 0 0.017881 0.011532 1.550 0.635
## APOE22 male - APOE44 male == 0 0.011327 0.011532 0.982 0.918
## APOE33 male - APOE44 male == 0 -0.006554 0.012045 -0.544 0.994
## (Adjusted p values reported -- single-step method)
res<-summary(glht(lm_fi_FA, emm(pairwise ~ Genotype*Sex))) #consider save to file
#summary(as.glht(pairs(lm_fi_FA.emm), by = NULL))

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

```

```

## $`Sex = female`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_FA)
##
## Linear Hypotheses:
##           Estimate Std. Error t value Pr(>|t|)
## APOE22 - APOE33 == 0  0.025466   0.013909   1.831   0.181
## APOE22 - APOE44 == 0  0.002072   0.012045   0.172   0.984
## APOE33 - APOE44 == 0 -0.023394   0.013909  -1.682   0.232
## (Adjusted p values reported -- single-step method)
##
##
## $`Sex = male`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_FA)
##
## Linear Hypotheses:
##           Estimate Std. Error t value Pr(>|t|)
## APOE22 - APOE33 == 0  0.017881   0.011532   1.550   0.287
## APOE22 - APOE44 == 0  0.011327   0.011532   0.982   0.595
## APOE33 - APOE44 == 0 -0.006554   0.012045  -0.544   0.850
## (Adjusted p values reported -- single-step method)
summary(glht(lm-fi_FA, emm(pairwise ~ Sex | Genotype)))

## $`Genotype = APOE22`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_FA)
##
## Linear Hypotheses:
##           Estimate Std. Error t value Pr(>|t|)
## female - male == 0  0.005803   0.011532   0.503   0.62
## (Adjusted p values reported -- single-step method)
##
##
## $`Genotype = APOE33`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_FA)
##
## Linear Hypotheses:
##           Estimate Std. Error t value Pr(>|t|)
## female - male == 0 -0.001783   0.013909  -0.128   0.899
## (Adjusted p values reported -- single-step method)
##
##
## $`Genotype = APOE44`
##

```

```
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_FA)
##
## Linear Hypotheses:
##             Estimate Std. Error t value Pr(>|t|)
## female - male == 0  0.01506    0.01205   1.25  0.224
## (Adjusted p values reported -- single-step method)

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

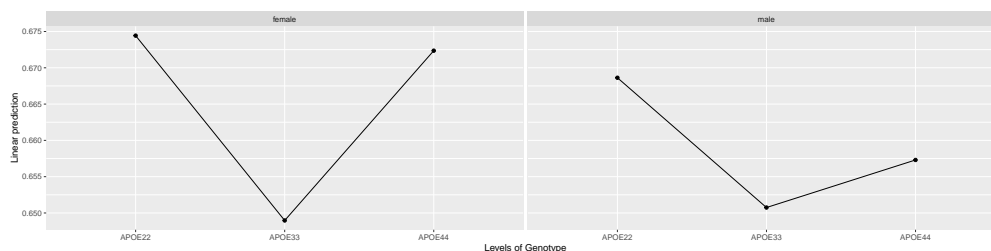
## Genotype = APOE22:
## contrast      estimate      SE df t.ratio p.value
## female - male  0.00580 0.0115 23   0.503  0.6196
##
## Genotype = APOE33:
## contrast      estimate      SE df t.ratio p.value
## female - male -0.00178 0.0139 23  -0.128  0.8991
##
## Genotype = APOE44:
## contrast      estimate      SE df t.ratio p.value
## female - male  0.01506 0.0120 23   1.250  0.2238

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

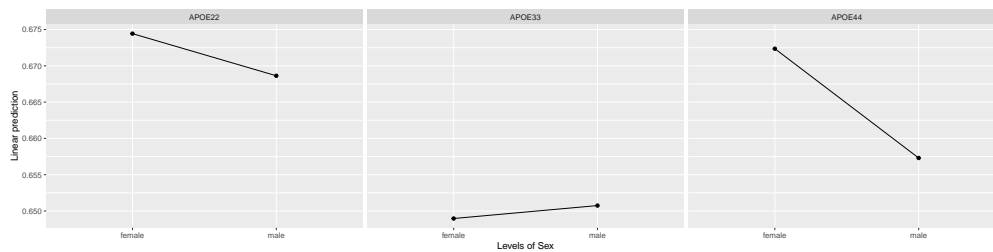
## Sex = female:
## contrast      estimate      SE df t.ratio p.value
## APOE22 - APOE33  0.02547 0.0139 23   1.831  0.1820
## APOE22 - APOE44  0.00207 0.0120 23   0.172  0.9838
## APOE33 - APOE44 -0.02339 0.0139 23  -1.682  0.2334
##
## Sex = male:
## contrast      estimate      SE df t.ratio p.value
## APOE22 - APOE33  0.01788 0.0115 23   1.550  0.2869
## APOE22 - APOE44  0.01133 0.0115 23   0.982  0.5952
## APOE33 - APOE44 -0.00655 0.0120 23  -0.544  0.8505
##
## P value adjustment: tukey method for comparing a family of 3 estimates
print('fi FA')

## [1] "fi FA"
```

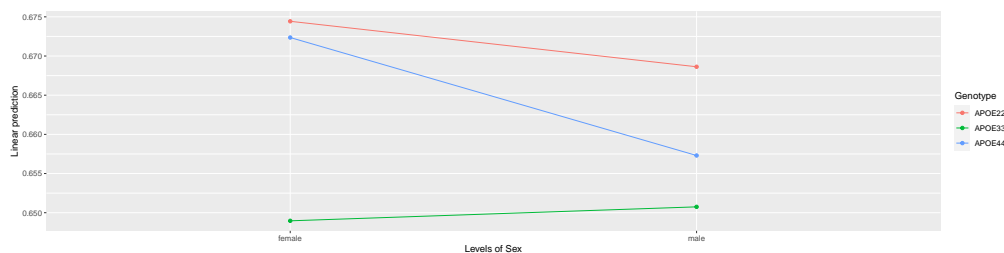
```
emmip(lm-fi_FA, ~ Genotype | Sex )
```



```
emmip(lm-fi_FA, ~ Sex | Genotype )
```

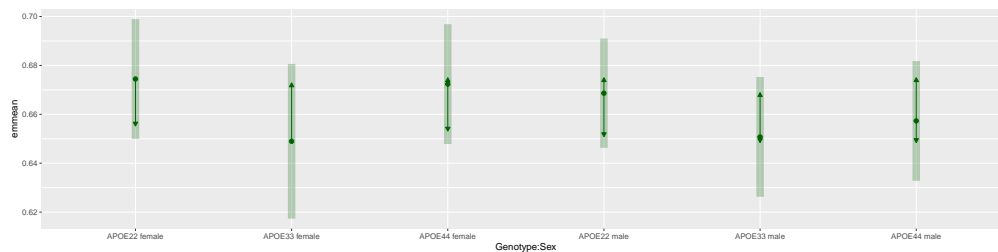


```
emmip(lm_fi_FA, Genotype~ Sex )
```



```
sink()
```

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



```
ggsave(paste(outpath, 'fi_FA_emmeans.pdf', sep=''), plot = last_plot(), device='pdf', scale=1, width=16, height=10)
```

```
'simple stats'
```

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

```
print('fi')
```

```
## [1] "fi"
```

```
lm_fi_DEG <- lm(fi ~ Genotype*Sex, geno_combined_DEG)
summary(lm_fi_DEG)
```

```
##
```

```
## Call:
```

```
## lm(formula = fi ~ Genotype * Sex, data = geno_combined_DEG)
```

```
##
```

```
## Residuals:
```

```
##      Min       1Q   Median       3Q      Max
## -21929.3  -6854.2   -855.8   7591.3  28195.7
```

```
##
```

```
## Coefficients:
```

```
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)    46291.2     5639.7   8.208 2.75e-08 ***
## GenotypeAPOE33  11781.1     9209.5   1.279   0.214
```

```

## GenotypeAPOE44          -198.8      7975.7 -0.025    0.980
## Sexmale                 340.5      7636.1  0.045    0.965
## GenotypeAPOE33:Sexmale -5351.0    11963.5 -0.447    0.659
## GenotypeAPOE44:Sexmale 11634.5    11041.8  1.054    0.303
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 12610 on 23 degrees of freedom
## Multiple R-squared:  0.173, Adjusted R-squared:  -0.006832
## F-statistic: 0.962 on 5 and 23 DF,  p-value: 0.4612

lm_fi_DEG_f <- lm(fi ~ Genotype, combo_f_FA)
#summary(lm_fi_DEG_f)
lm_fi_DEG_m <- lm(fi ~ Genotype, combo_m_FA)
#summary(lm_fi_DEG_f)

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

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

## [1] "omnibus testing"

joint_tests(ref_grid(lm_fi_DEG))

##   model term    df1 df2 F.ratio p.value
##   Genotype      2   23   1.233  0.3100
##   Sex           1   23   0.258  0.6163
##   Genotype:Sex   2   23   1.072  0.3588

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

## Sex = female:
##   model term df1 df2 F.ratio p.value
##   Genotype   2  23   1.024  0.3748
##
## Sex = male:
##   model term df1 df2 F.ratio p.value
##   Genotype   2  23   1.138  0.3379

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

## Genotype = APOE22:
##   model term df1 df2 F.ratio p.value
##   Sex        1  23   0.002  0.9648
##
## Genotype = APOE33:
##   model term df1 df2 F.ratio p.value
##   Sex        1  23   0.296  0.5916
##
## Genotype = APOE44:
##   model term df1 df2 F.ratio p.value
##   Sex        1  23   2.254  0.1468

```

```

'anova'

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

## Analysis of Variance Table
##
## Response: fi
##           Df      Sum Sq   Mean Sq F value Pr(>F)
## Genotype    2 359036685 179518342  1.1288 0.3407
## Sex          1  64911127  64911127  0.4082 0.5292
## Genotype:Sex  2 340979282 170489641  1.0721 0.3588
## Residuals   23 3657650816 159028296

#anova(lm_fi_DEG_f)
#anova(lm_fi_DEG_m)

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

## contrast           estimate    SE df t.ratio p.value
## APOE22 female effect   -5078 5191 23  -0.978  0.4057
## APOE33 female effect    6703 6410 23   1.046  0.4057
## APOE44 female effect   -5277 5191 23  -1.017  0.4057
## APOE22 male effect     -4738 4839 23  -0.979  0.4057
## APOE33 male effect      1692 5191 23   0.326  0.7474
## APOE44 male effect      6698 5191 23   1.290  0.4057
##
## P value adjustment: fdr method for 6 tests
contrast(fi_DEG.emm, simple = list("Genotype", "Sex"))

## $`simple contrasts for Genotype`
## Sex = female:
## contrast           estimate    SE df t.ratio p.value
## APOE22 effect     -3861 4854 23  -0.795  0.4345
## APOE33 effect      7920 5534 23   1.431  0.4345
## APOE44 effect     -4060 4854 23  -0.836  0.4345
##
## Sex = male:
## contrast           estimate    SE df t.ratio p.value
## APOE22 effect     -5955 4341 23  -1.372  0.3595
## APOE33 effect       475 4540 23   0.105  0.9176
## APOE44 effect      5480 4540 23   1.207  0.3595
##
## P value adjustment: fdr method for 3 tests
##
## $`simple contrasts for Sex`
## Genotype = APOE22:
## contrast           estimate    SE df t.ratio p.value
## female effect     -170 3818 23  -0.045  0.9648
## male effect        170 3818 23   0.045  0.9648
##
## Genotype = APOE33:

```

```

## contrast      estimate    SE df t.ratio p.value
## female effect    2505 4605 23   0.544  0.5916
## male effect     -2505 4605 23  -0.544  0.5916
##
## Genotype = APOE44:
## contrast      estimate    SE df t.ratio p.value
## female effect   -5988 3988 23  -1.501  0.1468
## male effect      5988 3988 23   1.501  0.1468
##
## P value adjustment: fdr method for 2 tests

#post hoc tests
summary(glht(lm_fi_DEG, emm(pairwise ~ Genotype*Sex, contr="sidak"))) #consider save to file

##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_DEG)
##
## Linear Hypotheses:
##
##               Estimate Std. Error t value Pr(>|t|)
## APOE22 female - APOE33 female == 0 -11781.133  9209.511  -1.279    0.792
## APOE22 female - APOE44 female == 0    198.800  7975.670   0.025    1.000
## APOE22 female - APOE22 male == 0    -340.467  7636.123  -0.045    1.000
## APOE22 female - APOE33 male == 0   -6770.600  7975.670  -0.849    0.954
## APOE22 female - APOE44 male == 0  -11776.200  7975.670  -1.477    0.680
## APOE33 female - APOE44 female == 0  11979.933  9209.511   1.301    0.780
## APOE33 female - APOE22 male == 0   11440.667  8917.071   1.283    0.790
## APOE33 female - APOE33 male == 0    5010.533  9209.511   0.544    0.994
## APOE33 female - APOE44 male == 0     4.933  9209.511   0.001    1.000
## APOE44 female - APOE22 male == 0   -539.267  7636.123  -0.071    1.000
## APOE44 female - APOE33 male == 0  -6969.400  7975.670  -0.874    0.949
## APOE44 female - APOE44 male == 0  -11975.000  7975.670  -1.501    0.665
## APOE22 male - APOE33 male == 0    -6430.133  7636.123  -0.842    0.956
## APOE22 male - APOE44 male == 0   -11435.733  7636.123  -1.498    0.667
## APOE33 male - APOE44 male == 0    -5005.600  7975.670  -0.628    0.988
## (Adjusted p values reported -- single-step method)

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

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

## $`Sex = female`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_DEG)
##
## Linear Hypotheses:
##
##               Estimate Std. Error t value Pr(>|t|)
## APOE22 - APOE33 == 0 -11781.1  9209.5  -1.279    0.420
## APOE22 - APOE44 == 0    198.8  7975.7   0.025    1.000
## APOE33 - APOE44 == 0  11979.9  9209.5   1.301    0.408
## (Adjusted p values reported -- single-step method)

```



```
##
##
## $`Sex = male`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_DEG)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## APOE22 - APOE33 == 0    -6430      7636  -0.842   0.681
## APOE22 - APOE44 == 0   -11436      7636  -1.498   0.310
## APOE33 - APOE44 == 0    -5006      7976  -0.628   0.806
## (Adjusted p values reported -- single-step method)
summary(glht(lm-fi_DEG, emm(pairwise ~ Sex | Genotype)))

## $`Genotype = APOE22`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_DEG)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## female - male == 0   -340.5      7636.1  -0.045   0.965
## (Adjusted p values reported -- single-step method)
##
##
## $`Genotype = APOE33`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_DEG)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## female - male == 0     5010      9210   0.544   0.592
## (Adjusted p values reported -- single-step method)
##
##
## $`Genotype = APOE44`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_DEG)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## female - male == 0   -11975      7976  -1.501   0.147
## (Adjusted p values reported -- single-step method)
mypairs<-pairs(fi_DEG.emm) #_consider save to file
pairs(fi_DEG.emm, by="Genotype")
```

```
## Genotype = APOE22:
## contrast      estimate    SE df t.ratio p.value
## female - male    -340 7636 23  -0.045  0.9648
##
## Genotype = APOE33:
## contrast      estimate    SE df t.ratio p.value
## female - male    5011 9210 23   0.544  0.5916
##
## Genotype = APOE44:
## contrast      estimate    SE df t.ratio p.value
## female - male   -11975 7976 23  -1.501  0.1468

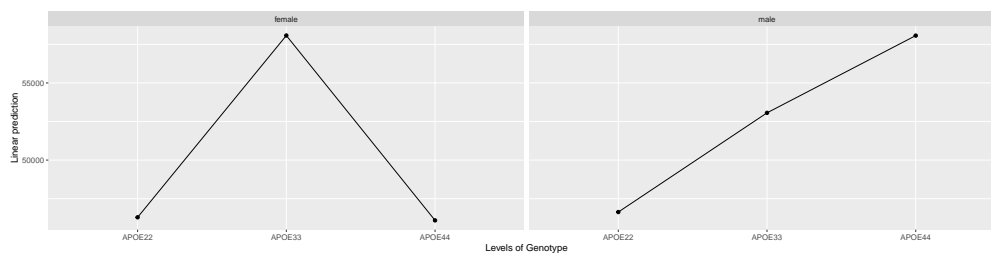
pairs(fi_DEG.emm, by="Sex")

## Sex = female:
## contrast      estimate    SE df t.ratio p.value
## APOE22 - APOE33  -11781 9210 23  -1.279  0.4207
## APOE22 - APOE44    199 7976 23   0.025  0.9997
## APOE33 - APOE44   11980 9210 23   1.301  0.4090
##
## Sex = male:
## contrast      estimate    SE df t.ratio p.value
## APOE22 - APOE33   -6430 7636 23  -0.842  0.6812
## APOE22 - APOE44  -11436 7636 23  -1.498  0.3106
## APOE33 - APOE44   -5006 7976 23  -0.628  0.8066
##
## P value adjustment: tukey method for comparing a family of 3 estimates

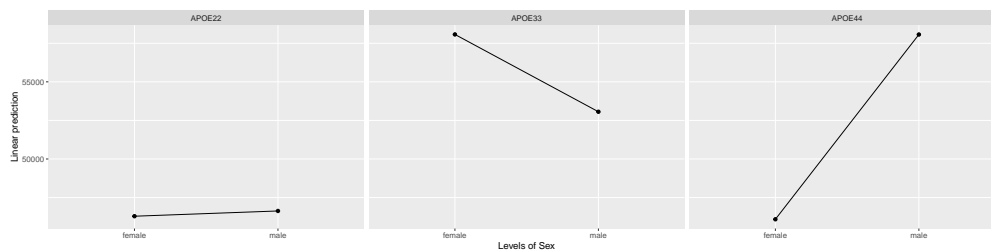
print('fi DEG')

## [1] "fi DEG"

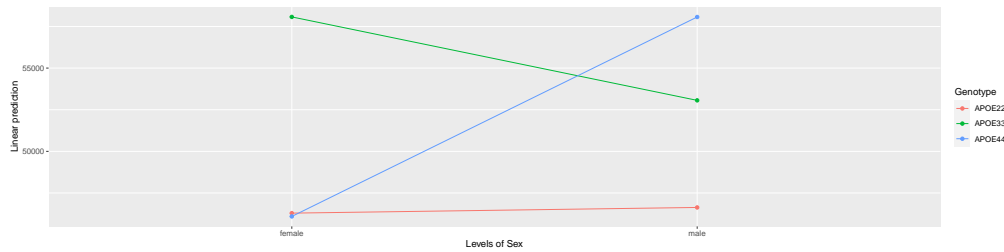
emmip(lm-fi_DEG, ~ Genotype | Sex )
```



```
emmip(lm-fi_DEG, ~ Sex | Genotype )
```

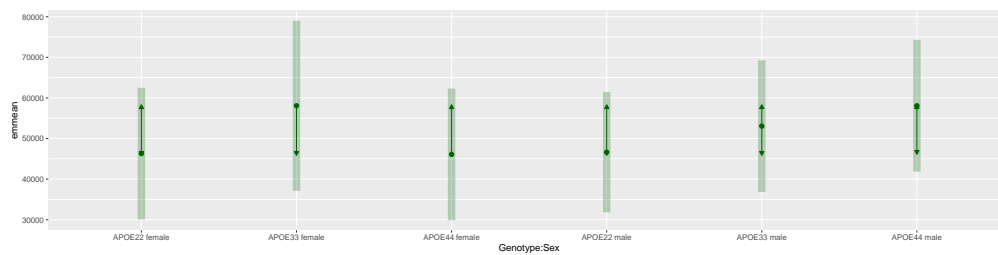


```
emmip(lm_fi_DEG, Genotype~ Sex )
```



```
sink()
```

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



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

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

```
print('fi')
```

```
## [1] "fi"
```

```
lm_fi_CLUS <- lm(fi ~ Genotype*Sex, geno_combined_CLUS)
summary(lm_fi_CLUS)
```

```
##
## Call:
## lm(formula = fi ~ Genotype * Sex, data = geno_combined_CLUS)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -50.937 -15.302  -3.082  12.532  76.223
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)    122.792     13.335   9.208 3.54e-09 ***
## GenotypeAPOE33     29.185     21.776   1.340  0.193
## GenotypeAPOE44     13.000     18.858   0.689  0.497
## Sexmale           1.635     18.055   0.091  0.929
## GenotypeAPOE33:Sexmale -12.713     28.287  -0.449  0.657
## GenotypeAPOE44:Sexmale  13.757     26.108   0.527  0.603
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
```

```

## Residual standard error: 29.82 on 23 degrees of freedom
## Multiple R-squared:  0.1536, Adjusted R-squared:  -0.03045
## F-statistic: 0.8345 on 5 and 23 DF,  p-value: 0.5387

lm_fi_CLUS_f <- lm(fi ~ Genotype, combo_f_FA)
#summary(lm_fi_CLUS_f)
lm_fi_CLUS_m <- lm(fi ~ Genotype, combo_m_FA)
#summary(lm_fi_CLUS_f)

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

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

## [1] "omnibus testing"

joint_tests(ref_grid(lm_fi_CLUS))

##   model term    df1 df2 F.ratio p.value
##   Genotype      2   23   1.710  0.2030
##   Sex            1   23   0.031  0.8627
##   Genotype:Sex    2   23   0.428  0.6571

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

## Sex = female:
##   model term df1 df2 F.ratio p.value
##   Genotype    2  23   0.905  0.4183
##
## Sex = male:
##   model term df1 df2 F.ratio p.value
##   Genotype    2  23   1.134  0.3391

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

## Genotype = APOE22:
##   model term df1 df2 F.ratio p.value
##   Sex          1  23   0.008  0.9286
##
## Genotype = APOE33:
##   model term df1 df2 F.ratio p.value
##   Sex          1  23   0.259  0.6158
##
## Genotype = APOE44:
##   model term df1 df2 F.ratio p.value
##   Sex          1  23   0.666  0.4228

'anova'

## [1] "anova"

anova(lm_fi_CLUS)

## Analysis of Variance Table
##
## Response: fi
##           Df Sum Sq Mean Sq F value Pr(>F)

```

```

## Genotype      2  2880.1 1440.06  1.6197 0.2197
## Sex           1    69.2   69.17  0.0778 0.7828
## Genotype:Sex  2   760.5  380.25  0.4277 0.6571
## Residuals    23 20448.9  889.08

#anova(lm_fi_CLUS_f)
#anova(lm_fi_CLUS_m)

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

## contrast            estimate    SE df t.ratio p.value
## APOE22 female effect  -15.05 12.3 23  -1.226  0.5412
## APOE33 female effect   14.13 15.2 23   0.932  0.5412
## APOE44 female effect   -2.05 12.3 23  -0.167  0.8687
## APOE22 male effect    -13.42 11.4 23  -1.173  0.5412
## APOE33 male effect      3.05 12.3 23   0.249  0.8687
## APOE44 male effect     13.34 12.3 23   1.087  0.5412
##
## P value adjustment: fdr method for 6 tests

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

## $`simple contrasts for Genotype`
## Sex = female:
## contrast      estimate    SE df t.ratio p.value
## APOE22 effect  -14.06 11.5 23  -1.225  0.3895
## APOE33 effect   15.12 13.1 23   1.156  0.3895
## APOE44 effect   -1.06 11.5 23  -0.092  0.9271
##
## Sex = male:
## contrast      estimate    SE df t.ratio p.value
## APOE22 effect  -14.41 10.3 23  -1.404  0.3928
## APOE33 effect    2.06 10.7 23   0.192  0.8494
## APOE44 effect   12.35 10.7 23   1.150  0.3928
##
## P value adjustment: fdr method for 3 tests
##
## $`simple contrasts for Sex`
## Genotype = APOE22:
## contrast      estimate    SE df t.ratio p.value
## female effect  -0.817  9.03 23  -0.091  0.9286
## male effect     0.817  9.03 23   0.091  0.9286
##
## Genotype = APOE33:
## contrast      estimate    SE df t.ratio p.value
## female effect   5.539 10.89 23   0.509  0.6158
## male effect    -5.539 10.89 23  -0.509  0.6158
##
## Genotype = APOE44:
## contrast      estimate    SE df t.ratio p.value
## female effect  -7.696  9.43 23  -0.816  0.4228
## male effect     7.696  9.43 23   0.816  0.4228
##

```

```
## P value adjustment: fdr method for 2 tests
#post hoc tests
summary(glht(lm_fi_CLUS, emm(pairwise ~ Genotype*Sex, contr="sidak"))) #consider save to file

##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_CLUS)
##
## Linear Hypotheses:
##
## Estimate Std. Error t value Pr(>|t|)
## APOE22 female - APOE33 female == 0 -29.1847 21.7756 -1.340 0.759
## APOE22 female - APOE44 female == 0 -13.0004 18.8582 -0.689 0.981
## APOE22 female - APOE22 male == 0 -1.6347 18.0554 -0.091 1.000
## APOE22 female - APOE33 male == 0 -18.1060 18.8582 -0.960 0.925
## APOE22 female - APOE44 male == 0 -28.3920 18.8582 -1.506 0.663
## APOE33 female - APOE44 female == 0 16.1843 21.7756 0.743 0.974
## APOE33 female - APOE22 male == 0 27.5500 21.0841 1.307 0.777
## APOE33 female - APOE33 male == 0 11.0787 21.7756 0.509 0.995
## APOE33 female - APOE44 male == 0 0.7927 21.7756 0.036 1.000
## APOE44 female - APOE22 male == 0 11.3657 18.0554 0.629 0.987
## APOE44 female - APOE33 male == 0 -5.1056 18.8582 -0.271 1.000
## APOE44 female - APOE44 male == 0 -15.3916 18.8582 -0.816 0.961
## APOE22 male - APOE33 male == 0 -16.4713 18.0554 -0.912 0.939
## APOE22 male - APOE44 male == 0 -26.7573 18.0554 -1.482 0.677
## APOE33 male - APOE44 male == 0 -10.2860 18.8582 -0.545 0.993
## (Adjusted p values reported -- single-step method)

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

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

## $`Sex = female`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_CLUS)
##
## Linear Hypotheses:
##
## Estimate Std. Error t value Pr(>|t|)
## APOE22 - APOE33 == 0 -29.18 21.78 -1.340 0.387
## APOE22 - APOE44 == 0 -13.00 18.86 -0.689 0.771
## APOE33 - APOE44 == 0 16.18 21.78 0.743 0.740
## (Adjusted p values reported -- single-step method)
##
##
## $`Sex = male`
##
## Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_CLUS)
##
## Linear Hypotheses:
```

```

##              Estimate Std. Error t value Pr(>|t|)
## APOE22 - APOE33 == 0   -16.47      18.06  -0.912   0.638
## APOE22 - APOE44 == 0   -26.76      18.06  -1.482   0.318
## APOE33 - APOE44 == 0   -10.29      18.86  -0.545   0.850
## (Adjusted p values reported -- single-step method)
summary(glht(lm_fi_CLUS, emm(pairwise ~ Sex | Genotype)))

## $`Genotype = APOE22`
##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_CLUS)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## female - male == 0   -1.635     18.055  -0.091   0.929
## (Adjusted p values reported -- single-step method)
##
## $`Genotype = APOE33`
##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_CLUS)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## female - male == 0    11.08      21.78   0.509   0.616
## (Adjusted p values reported -- single-step method)
##
## $`Genotype = APOE44`
##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = fi ~ Genotype * Sex, data = geno_combined_CLUS)
##
## Linear Hypotheses:
##              Estimate Std. Error t value Pr(>|t|)
## female - male == 0   -15.39      18.86  -0.816   0.423
## (Adjusted p values reported -- single-step method)
mypairs<-pairs(fi_CLUS.emm) #_consider save to file
pairs(fi_CLUS.emm, by="Genotype")

## Genotype = APOE22:
## contrast      estimate    SE df t.ratio p.value
## female - male   -1.63 18.1 23  -0.091  0.9286
##
## Genotype = APOE33:
## contrast      estimate    SE df t.ratio p.value
## female - male   11.08 21.8 23   0.509  0.6158
##
## Genotype = APOE44:

```

```
## contrast      estimate    SE df t.ratio p.value
## female - male   -15.39 18.9 23  -0.816  0.4228
```

```
pairs(fi_CLUS.emm, by="Sex")
```

```
## Sex = female:
## contrast      estimate    SE df t.ratio p.value
## APOE22 - APOE33   -29.2 21.8 23  -1.340  0.3881
## APOE22 - APOE44   -13.0 18.9 23  -0.689  0.7720
## APOE33 - APOE44    16.2 21.8 23   0.743  0.7407
##
```

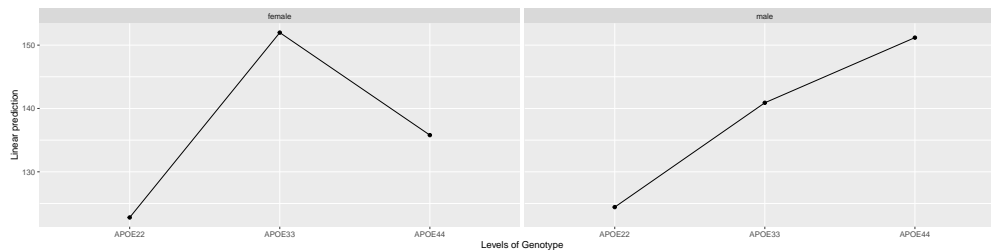
```
## Sex = male:
## contrast      estimate    SE df t.ratio p.value
## APOE22 - APOE33   -16.5 18.1 23  -0.912  0.6382
## APOE22 - APOE44   -26.8 18.1 23  -1.482  0.3178
## APOE33 - APOE44   -10.3 18.9 23  -0.545  0.8498
##
```

```
## P value adjustment: tukey method for comparing a family of 3 estimates
```

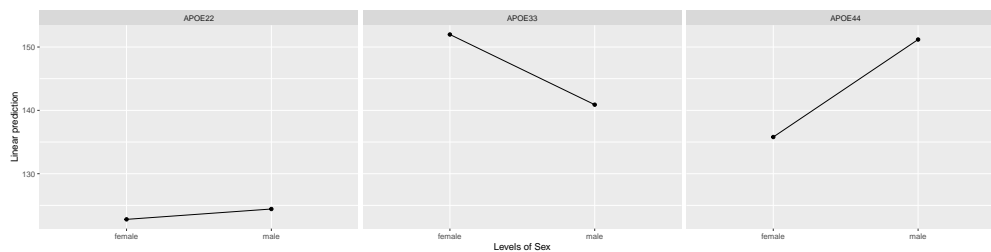
```
print('fi CLUS')
```

```
## [1] "fi CLUS"
```

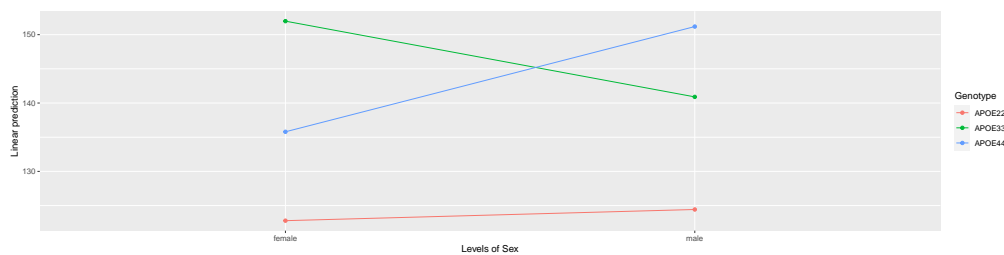
```
emmip(lm-fi_CLUS, ~ Genotype | Sex )
```



```
emmip(lm-fi_CLUS, ~ Sex | Genotype )
```



```
emmip(lm-fi_CLUS, Genotype~ Sex )
```

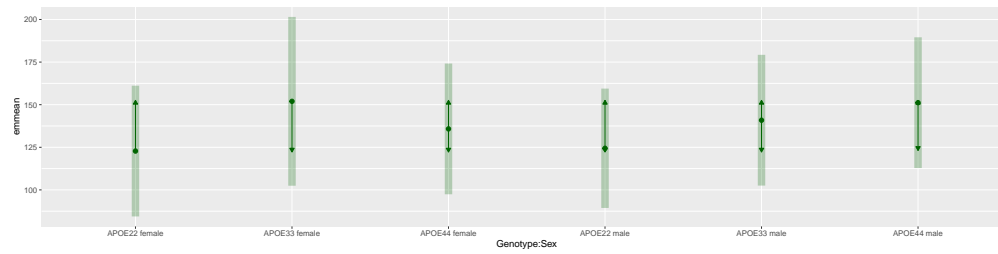


```
sink()
```

```
plot(fi_CLUS.emm, by = NULL, comparisons = TRUE, adjust = "mvt",
```



```
horizontal = FALSE, colors = "darkgreen", main = "fi CLUS")
```



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