Absolute Winding Number Differentiates Spatial Navigation Strategies with Genetic Risk for Alzheimer's disease

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Contents

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

##Setup

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

Plots for Winding Number

We embed plots for day 5 and day 8 probe trials:

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

Winding Number Probe Day 5

Winding Number Probe Day 8
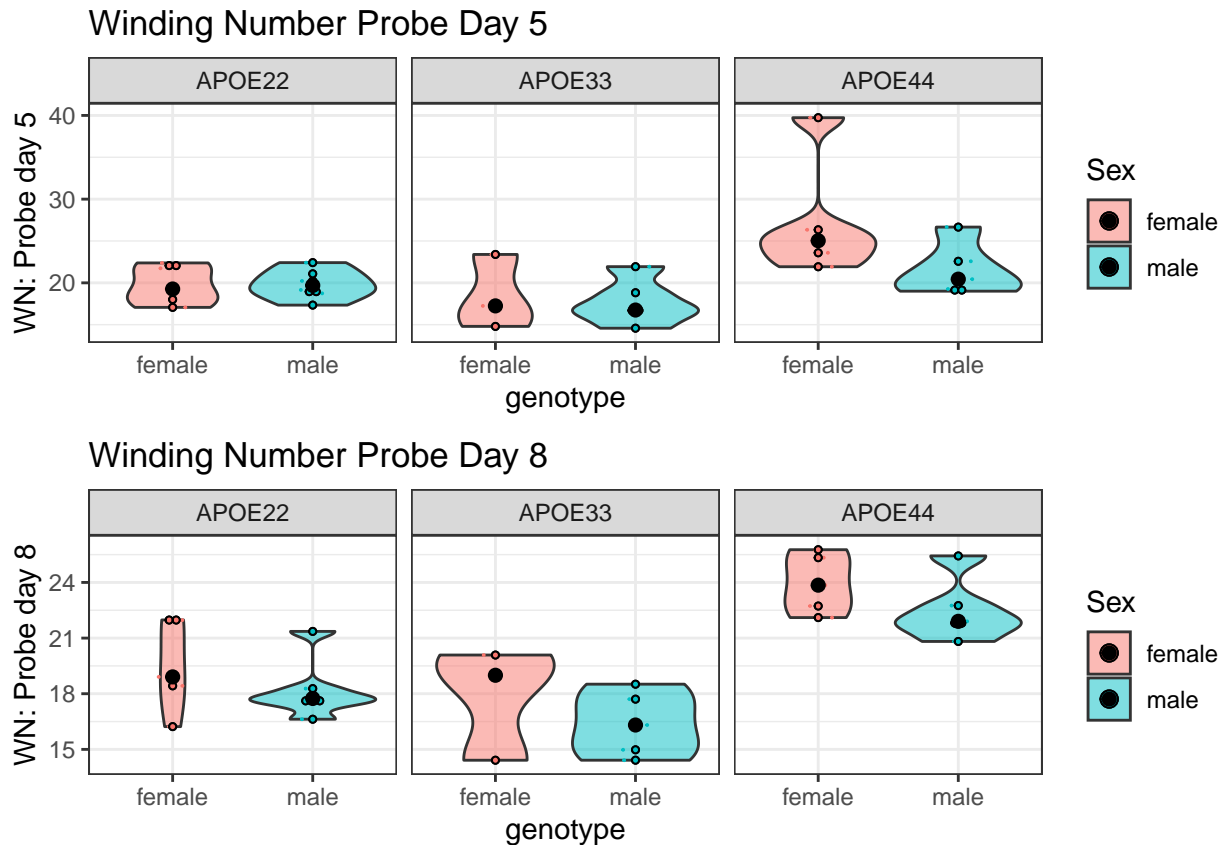

```
## [1] "Probe day 5"

##
## Call:
## lm(formula = Probe_d5 ~ Genotype * Sex, data = geno_combined_FA)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -5.4015 -2.3246 -0.9962  1.2548 12.4058
##
## Coefficients:
##                      Estimate Std. Error t value Pr(>|t|)
## (Intercept)           19.6924     1.7469  11.273 7.62e-11 ***
## GenotypeAPOE33        -1.2129     2.8527  -0.425  0.67466
## GenotypeAPOE44         7.6319     2.4705   3.089  0.00518 **
## Sexmale                0.1352     2.3654   0.057  0.95493
## GenotypeAPOE33:Sexmale -0.8661    3.7058  -0.234  0.81728
## GenotypeAPOE44:Sexmale -5.8705    3.4203  -1.716  0.09953 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 3.906 on 23 degrees of freedom
## Multiple R-squared:  0.4526, Adjusted R-squared:  0.3336
## F-statistic: 3.803 on 5 and 23 DF,  p-value: 0.01174

##
## Call:
## lm(formula = Probe_d5 ~ Genotype, data = combo_f_FA)
```

```
## 
## Residuals:
##    Min     1Q Median     3Q    Max
## -5.402 -2.623 -1.232  2.046 12.406
## 
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept)     19.692      2.297   8.574 6.38e-06 ***
## GenotypeAPOE33   -1.213      3.750  -0.323   0.7531
## GenotypeAPOE44    7.632      3.248   2.350   0.0407 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## 
## Residual standard error: 5.136 on 10 degrees of freedom
## Multiple R-squared:  0.4361, Adjusted R-squared:  0.3233
## F-statistic: 3.867 on 2 and 10 DF,  p-value: 0.05701

## 
## Call:
## lm(formula = Probe_d5 ~ Genotype, data = combo_m_FA)
## 
## Residuals:
##     Min      1Q  Median      3Q     Max
## -3.1660 -1.4438 -0.8342  1.1177  5.0717
## 
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept)     19.828      1.057  18.751 8.55e-11 ***
## GenotypeAPOE33   -2.079      1.568  -1.326    0.208
## GenotypeAPOE44    1.761      1.568   1.123    0.282
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## 
## Residual standard error: 2.59 on 13 degrees of freedom
## Multiple R-squared:  0.2977, Adjusted R-squared:  0.1896
## F-statistic: 2.755 on 2 and 13 DF,  p-value: 0.1006

## Analysis of Variance Table
## 
## Response: Probe_d5
##              Df Sum Sq Mean Sq F value   Pr(>F)
## Genotype      2 206.87 103.434  6.7786 0.004849 **
## Sex           1  33.13  33.134  2.1715 0.154148
## Genotype:Sex  2  50.15  25.077  1.6434 0.215215
## Residuals    23 350.95  15.259
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

## Analysis of Variance Table
## 
## Response: Probe_d5
##           Df Sum Sq Mean Sq F value  Pr(>F)
## Genotype   2 203.97 101.987  3.8669 0.05701 .
## Residuals 10 263.74  26.374
## ---
```

```
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## Analysis of Variance Table
##
## Response: Probe_d5
##           Df Sum Sq Mean Sq F value Pr(>F)
## Genotype   2 36.965 18.4826  2.7551 0.1006
## Residuals 13 87.212  6.7086

##  contrast             estimate   SE df t.ratio p.value
##  APOE22 female effect   -1.084 1.61 23  -0.674  0.6184
##  APOE33 female effect   -2.297 1.99 23  -1.157  0.5182
##  APOE44 female effect    6.547 1.61 23   4.072  0.0028
##  APOE22 male effect     -0.949 1.50 23  -0.633  0.6184
##  APOE33 male effect     -3.028 1.61 23  -1.883  0.2171
##  APOE44 male effect      0.812 1.61 23   0.505  0.6184
##
## P value adjustment: fdr method for 6 tests

## $`simple contrasts for Genotype`
## Sex = female:
##  contrast       estimate   SE df t.ratio p.value
##  APOE22 effect    -2.140 1.50 23  -1.423  0.1681
##  APOE33 effect    -3.353 1.71 23  -1.956  0.0941
##  APOE44 effect     5.492 1.50 23   3.653  0.0040
##
## Sex = male:
##  contrast       estimate   SE df t.ratio p.value
##  APOE22 effect     0.106 1.34 23   0.079  0.9379
##  APOE33 effect    -1.973 1.41 23  -1.403  0.2960
##  APOE44 effect     1.867 1.41 23   1.328  0.2960
##
## P value adjustment: fdr method for 3 tests
##
## $`simple contrasts for Sex`
## Genotype = APOE22:
##  contrast       estimate   SE df t.ratio p.value
##  female effect  -0.0676 1.18 23  -0.057  0.9549
##  male effect     0.0676 1.18 23   0.057  0.9549
##
## Genotype = APOE33:
##  contrast       estimate   SE df t.ratio p.value
##  female effect   0.3655 1.43 23   0.256  0.8001
##  male effect    -0.3655 1.43 23  -0.256  0.8001
##
## Genotype = APOE44:
##  contrast       estimate   SE df t.ratio p.value
##  female effect   2.8677 1.24 23   2.322  0.0295
##  male effect    -2.8677 1.24 23  -2.322  0.0295
##
## P value adjustment: fdr method for 2 tests
```
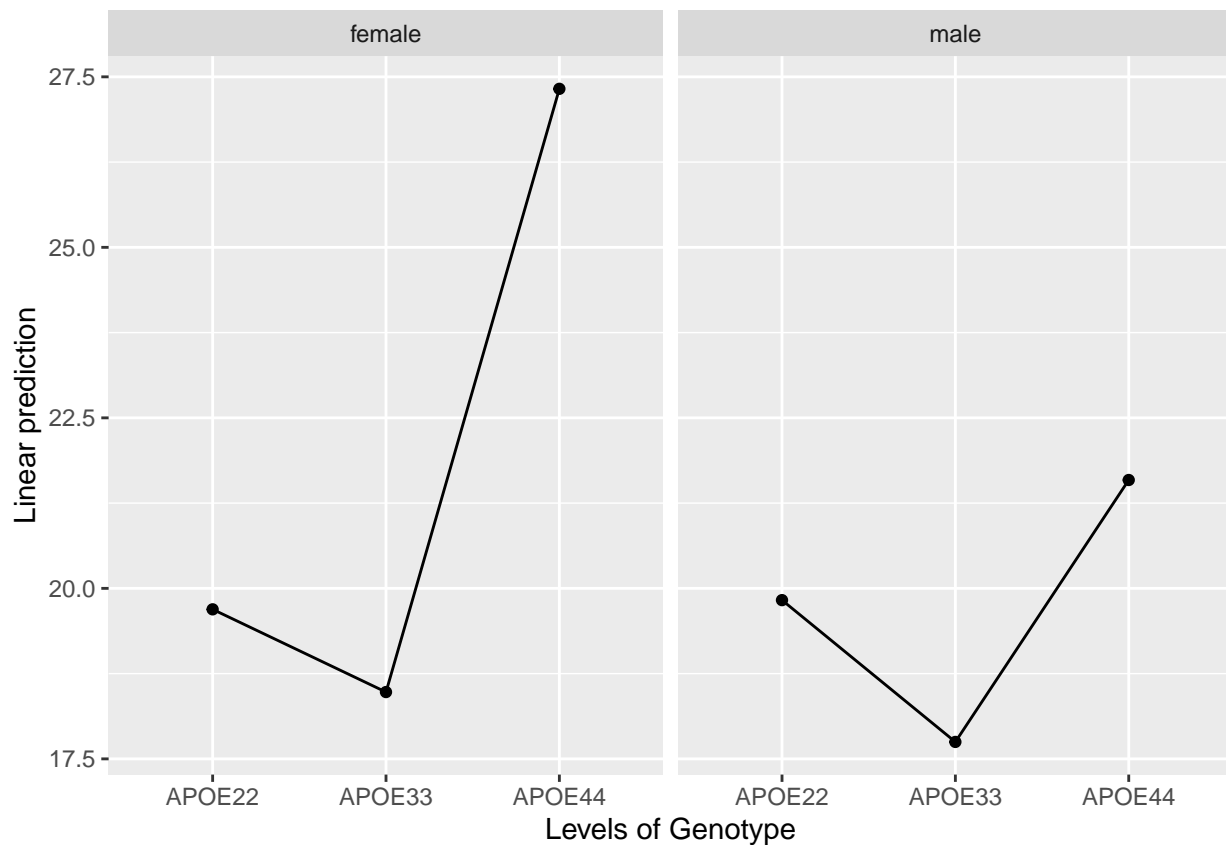
```
## Genotype_poly Sex_consec  estimate   SE df t.ratio p.value
## linear         male - female    -5.87 3.42 23  -1.716  0.0995
## quadratic      male - female    -4.14 6.65 23  -0.622  0.5400

##   Genotype    Sex c.1 c.2
## 1   APOE22 female   1  -1
## 2   APOE33 female   0   2
## 3   APOE44 female  -1  -1
## 4   APOE22   male  -1   1
## 5   APOE33   male   0  -2
## 6   APOE44   male   1   1

## $emmeans
##  Genotype Sex     emmean   SE df lower.CL upper.CL
##  APOE22   female   19.7 1.75 23     16.1     23.3
##  APOE33   female   18.5 2.26 23     13.8     23.1
##  APOE44   female   27.3 1.75 23     23.7     30.9
##  APOE22   male     19.8 1.59 23     16.5     23.1
##  APOE33   male     17.7 1.75 23     14.1     21.4
##  APOE44   male     21.6 1.75 23     18.0     25.2
##
## Confidence level used: 0.95
##
## $contrasts
##  contrast                      estimate   SE df t.ratio p.value
##  APOE22 female - APOE33 female    1.213 2.85 23   0.425  0.9980
##  APOE22 female - APOE44 female   -7.632 2.47 23  -3.089  0.0515
##  APOE22 female - APOE22 male     -0.135 2.37 23  -0.057  1.0000
```

```
##  APOE22 female - APOE33 male       1.944 2.47 23   0.787  0.9670
##  APOE22 female - APOE44 male      -1.896 2.47 23  -0.768  0.9703
##  APOE33 female - APOE44 female    -8.845 2.85 23  -3.100  0.0503
##  APOE33 female - APOE22 male      -1.348 2.76 23  -0.488  0.9961
##  APOE33 female - APOE33 male       0.731 2.85 23   0.256  0.9998
##  APOE33 female - APOE44 male      -3.109 2.85 23  -1.090  0.8804
##  APOE44 female - APOE22 male       7.497 2.37 23   3.169  0.0434
##  APOE44 female - APOE33 male       9.576 2.47 23   3.876  0.0088
##  APOE44 female - APOE44 male       5.735 2.47 23   2.322  0.2259
##  APOE22 male - APOE33 male         2.079 2.37 23   0.879  0.9478
##  APOE22 male - APOE44 male        -1.761 2.37 23  -0.745  0.9739
##  APOE33 male - APOE44 male        -3.840 2.47 23  -1.554  0.6346
##
## P value adjustment: tukey method for comparing a family of 6 estimates

## Sex = female:
##  contrast         estimate   SE df t.ratio p.value
##  APOE22 - APOE33      1.21 2.85 23   0.425  0.9056
##  APOE22 - APOE44     -7.63 2.47 23  -3.089  0.0138
##  APOE33 - APOE44     -8.84 2.85 23  -3.100  0.0134
##
## Sex = male:
##  contrast         estimate   SE df t.ratio p.value
##  APOE22 - APOE33      2.08 2.37 23   0.879  0.6587
##  APOE22 - APOE44     -1.76 2.37 23  -0.745  0.7398
##  APOE33 - APOE44     -3.84 2.47 23  -1.554  0.2851
##
## P value adjustment: tukey method for comparing a family of 3 estimates

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Linear Hypotheses:
##                              Estimate Std. Error t value Pr(>|t|)
## APOE22 - APOE33, female == 0    1.213      2.853   0.425   0.9904
## APOE22 - APOE44, female == 0   -7.632      2.471  -3.089   0.0269 *
## APOE33 - APOE44, female == 0   -8.845      2.853  -3.100   0.0263 *
## APOE22 - APOE33, male == 0      2.079      2.365   0.879   0.8767
## APOE22 - APOE44, male == 0     -1.761      2.365  -0.745   0.9279
## APOE33 - APOE44, male == 0     -3.840      2.471  -1.554   0.4776
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Adjusted p values reported -- single-step method)

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Probe_d5 ~ Genotype * Sex, data = geno_combined_FA)
##
## Linear Hypotheses:
##                                 Estimate Std. Error t value Pr(>|t|)
## APOE22 female - APOE33 female == 0  1.2129     2.8527   0.425  0.99797
## APOE22 female - APOE44 female == 0 -7.6319     2.4705  -3.089  0.05111 .
## APOE22 female - APOE22 male == 0   -0.1352     2.3654  -0.057  1.00000
## APOE22 female - APOE33 male == 0    1.9439     2.4705   0.787  0.96673
```

```
## APOE22 female - APOE44 male == 0      -1.8965      2.4705   -0.768   0.97004
## APOE33 female - APOE44 female == 0   -8.8448      2.8527   -3.100   0.04994 *
## APOE33 female - APOE22 male == 0      -1.3481      2.7621   -0.488   0.99610
## APOE33 female - APOE33 male == 0       0.7309      2.8527    0.256   0.99983
## APOE33 female - APOE44 male == 0      -3.1094      2.8527   -1.090   0.87950
## APOE44 female - APOE22 male == 0       7.4967      2.3654    3.169   0.04301 *
## APOE44 female - APOE33 male == 0       9.5757      2.4705    3.876   0.00866 **
## APOE44 female - APOE44 male == 0       5.7354      2.4705    2.322   0.22472
## APOE22 male - APOE33 male == 0         2.0790      2.3654    0.879   0.94739
## APOE22 male - APOE44 male == 0        -1.7613      2.3654   -0.745   0.97370
## APOE33 male - APOE44 male == 0        -3.8403      2.4705   -1.554   0.63275
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Adjusted p values reported -- single-step method)

## $`Sex = female`
##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = Probe_d5 ~ Genotype * Sex, data = geno_combined_FA)
##
## Linear Hypotheses:
##                    Estimate Std. Error t value Pr(>|t|)
## APOE22 - APOE33 == 0    1.213      2.853    0.425    0.9052
## APOE22 - APOE44 == 0   -7.632      2.471   -3.089    0.0138 *
## APOE33 - APOE44 == 0   -8.845      2.853   -3.100    0.0134 *
## ---
## 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 = Probe_d5 ~ Genotype * Sex, data = geno_combined_FA)
##
## Linear Hypotheses:
##                    Estimate Std. Error t value Pr(>|t|)
## APOE22 - APOE33 == 0    2.079      2.365    0.879    0.659
## APOE22 - APOE44 == 0   -1.761      2.365   -0.745    0.740
## APOE33 - APOE44 == 0   -3.840      2.471   -1.554    0.285
## (Adjusted p values reported -- single-step method)
```
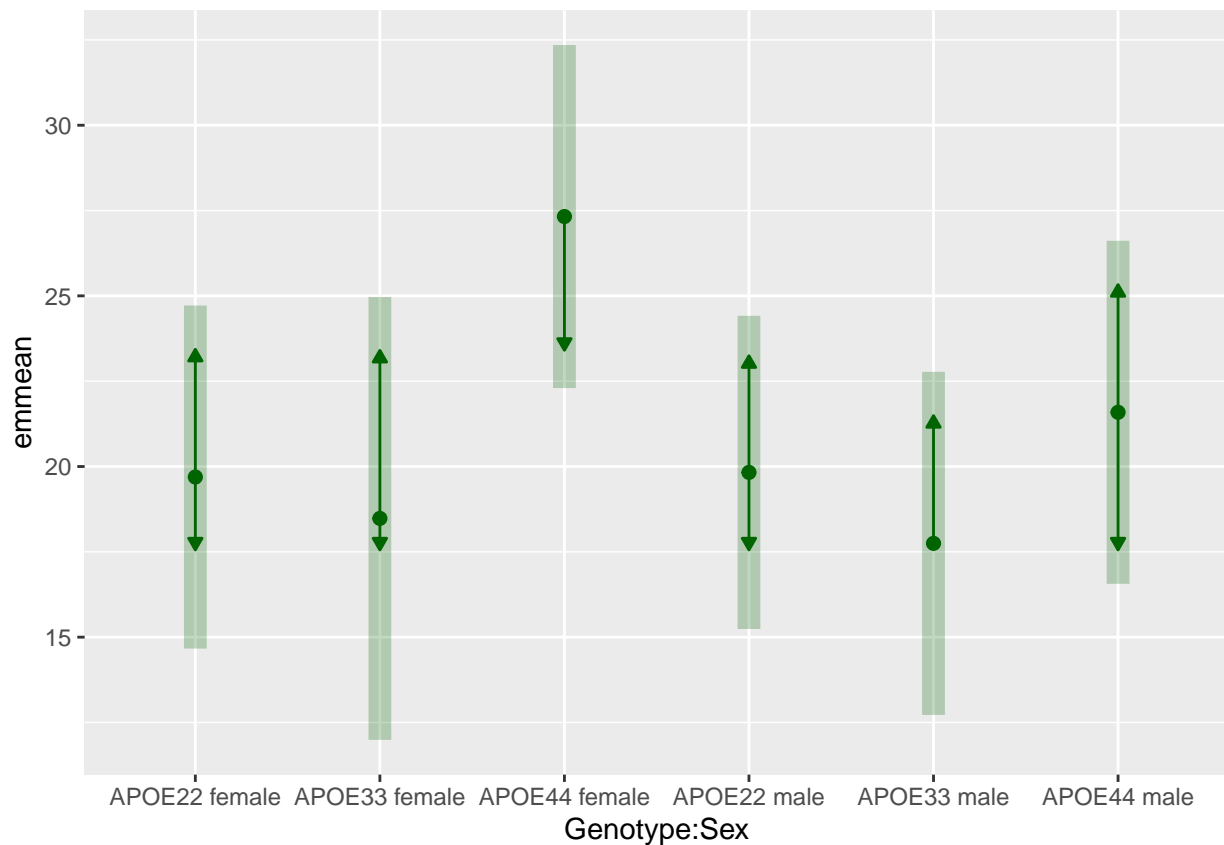
```
##   Sex     Genotype contrast          estimate   SE df t.ratio p.value
##   female  .        APOE22 - APOE33       1.213 2.85 23   0.425  0.9968
##   female  .        APOE22 - APOE44      -7.632 2.47 23  -3.089  0.0368
##   female  .        APOE33 - APOE44      -8.845 2.85 23  -3.100  0.0355
##   male    .        APOE22 - APOE33       2.079 2.37 23   0.879  0.9256
##   male    .        APOE22 - APOE44      -1.761 2.37 23  -0.745  0.9615
##   male    .        APOE33 - APOE44      -3.840 2.47 23  -1.554  0.5598
##   .       APOE22   female - male        -0.135 2.37 23  -0.057  1.0000
##   .       APOE33   female - male         0.731 2.85 23   0.256  0.9997
##   .       APOE44   female - male         5.735 2.47 23   2.322  0.1752
##
## P value adjustment: mvt method for 9 tests

##   Sex     contrast        estimate   SE df t.ratio p.value
##   female  APOE22 - APOE33     1.21 2.85 23   0.425  0.6747
##   female  APOE22 - APOE44    -7.63 2.47 23  -3.089  0.0155
##   female  APOE33 - APOE44    -8.84 2.85 23  -3.100  0.0155
##   male    APOE22 - APOE33     2.08 2.37 23   0.879  0.5568
##   male    APOE22 - APOE44    -1.76 2.37 23  -0.745  0.5568
##   male    APOE33 - APOE44    -3.84 2.47 23  -1.554  0.2675
##   female  APOE22 - APOE33     1.21 2.85 23   0.425  0.6747
##   female  APOE22 - APOE44    -7.63 2.47 23  -3.089  0.0155
##   female  APOE33 - APOE44    -8.84 2.85 23  -3.100  0.0155
##   male    APOE22 - APOE33     2.08 2.37 23   0.879  0.5568
##   male    APOE22 - APOE44    -1.76 2.37 23  -0.745  0.5568
##   male    APOE33 - APOE44    -3.84 2.47 23  -1.554  0.2675
##
```

```
## P value adjustment: fdr method for 12 tests

## [1] "Probe day 8"

##
## Call:
## lm(formula = Probe_d8 ~ Genotype * Sex, data = geno_combined_FA)
##
## Residuals:
##     Min     1Q  Median     3Q     Max
## -3.4167 -1.2288 -0.4318  1.3781  3.1566
##
## Coefficients:
##                         Estimate Std. Error t value Pr(>|t|)
## (Intercept)             19.5012     0.8881  21.959  < 2e-16 ***
## GenotypeAPOE33          -1.6686     1.4502  -1.151  0.26171
## GenotypeAPOE44           4.4562     1.2559   3.548  0.00171 **
## Sexmale                 -1.2979     1.2024  -1.079  0.29161
## GenotypeAPOE33:Sexmale  -0.1483     1.8839  -0.079  0.93796
## GenotypeAPOE44:Sexmale  -0.1366     1.7387  -0.079  0.93808
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 1.986 on 23 degrees of freedom
## Multiple R-squared:  0.6975, Adjusted R-squared:  0.6317
## F-statistic: 10.61 on 5 and 23 DF,  p-value: 2.242e-05

##
## Call:
## lm(formula = Probe_d8 ~ Genotype, data = combo_f_FA)
##
## Residuals:
##     Min     1Q  Median     3Q     Max
## -3.4167 -1.2288 -0.1041  1.8071  2.4777
##
## Coefficients:
##                Estimate Std. Error t value Pr(>|t|)
## (Intercept)      19.501      1.026  19.000 3.54e-09 ***
## GenotypeAPOE33   -1.669      1.676  -0.996   0.3429
## GenotypeAPOE44    4.456      1.452   3.070   0.0118 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 2.295 on 10 degrees of freedom
## Multiple R-squared:  0.6165, Adjusted R-squared:  0.5398
## F-statistic: 8.039 on 2 and 10 DF,  p-value: 0.008292

##
## Call:
## lm(formula = Probe_d8 ~ Genotype, data = combo_m_FA)
##
## Residuals:
##     Min     1Q  Median     3Q     Max
## -1.9692 -0.9598 -0.4575  0.5022  3.1566
##
## Coefficients:
```

```
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept)    18.2034     0.6982  26.072 1.31e-12 ***
## GenotypeAPOE33 -1.8169     1.0356  -1.754   0.1029
## GenotypeAPOE44  4.3196     1.0356   4.171   0.0011 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 1.71 on 13 degrees of freedom
## Multiple R-squared:  0.7246, Adjusted R-squared:  0.6822
## F-statistic:  17.1 on 2 and 13 DF,  p-value: 0.0002292

## Analysis of Variance Table
##
## Response: Probe_d8
##              Df  Sum Sq Mean Sq F value     Pr(>F)
## Genotype      2 195.444  97.722 24.7824 1.826e-06 ***
## Sex           1  13.625  13.625  3.4554   0.07589 .
## Genotype:Sex  2   0.034   0.017  0.0043   0.99572
## Residuals    23  90.694   3.943
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

## Analysis of Variance Table
##
## Response: Probe_d8
##           Df Sum Sq Mean Sq F value   Pr(>F)
## Genotype   2 84.685  42.342  8.0389 0.008292 **
## Residuals 10 52.672   5.267
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

## Analysis of Variance Table
##
## Response: Probe_d8
##           Df  Sum Sq Mean Sq F value    Pr(>F)
## Genotype   2 100.014  50.007  17.098 0.0002292 ***
## Residuals 13  38.022   2.925
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```
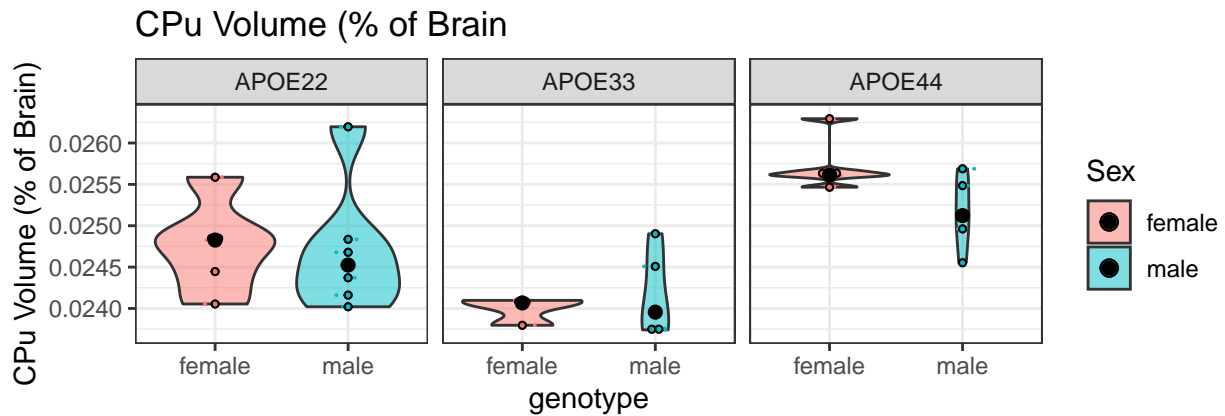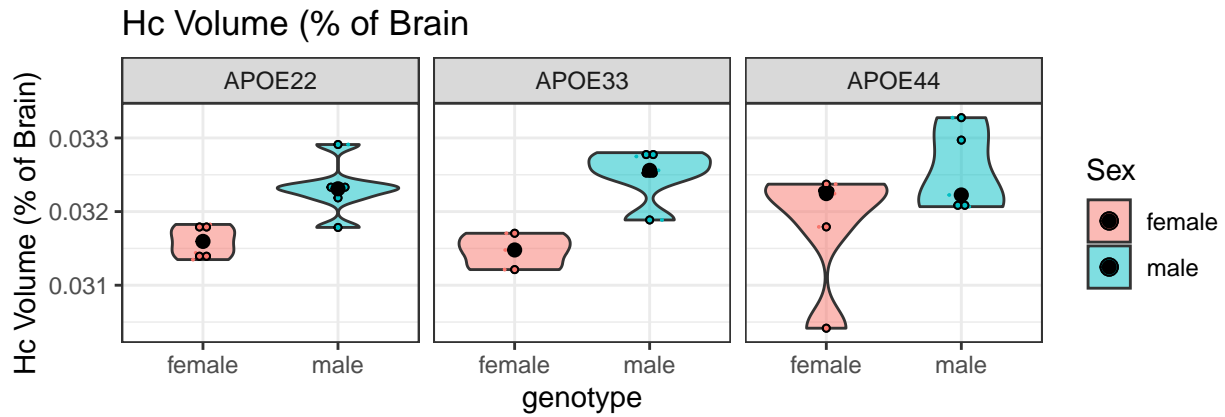
Plots for Volume

Hippocampus, Caudate Putamen, Brain

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

Hc Volume (% of Brain

CPu Volume (% of Brain


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

Brain Volume (mm3
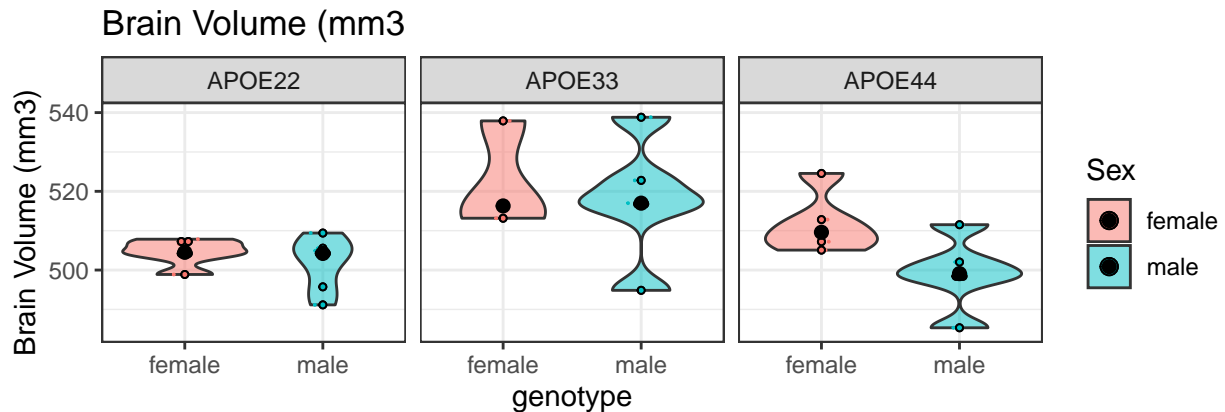

```
## [1] "Hc Volume"

##
## 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

##
## Call:
## lm(formula = Hc ~ Genotype, data = combo_f_VOL)
##
## Residuals:
##        Min         1Q     Median         3Q        Max
## -1.413e-03 -1.529e-04  1.321e-05  2.401e-04  5.422e-04
##
## Coefficients:
##                Estimate Std. Error t value Pr(>|t|)
## (Intercept)     0.0315929  0.0002448 129.072   <2e-16 ***
## GenotypeAPOE33 -0.0001273  0.0003997  -0.319    0.757
## GenotypeAPOE44  0.0002371  0.0003462   0.685    0.509
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.0005473 on 10 degrees of freedom
## Multiple R-squared:  0.08551,    Adjusted R-squared:  -0.09739
## F-statistic: 0.4675 on 2 and 10 DF,  p-value: 0.6396

##
## Call:
## lm(formula = Hc ~ Genotype, data = combo_m_VOL)
##
## Residuals:
##        Min         1Q     Median         3Q        Max
## -0.0006101 -0.0003333  0.0000013  0.0002651  0.0007467
##
## Coefficients:
##                Estimate Std. Error t value Pr(>|t|)
## (Intercept)     0.0323112  0.0001764 183.195   <2e-16 ***
## GenotypeAPOE33  0.0001852  0.0002616   0.708    0.492
## GenotypeAPOE44  0.0002172  0.0002616   0.830    0.421
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.000432 on 13 degrees of freedom
## Multiple R-squared:  0.0598, Adjusted R-squared:  -0.08484
## F-statistic: 0.4134 on 2 and 13 DF,  p-value: 0.6698

## 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

## Analysis of Variance Table
## 
## Response: Hc
##           Df    Sum Sq    Mean Sq F value Pr(>F)
## Genotype   2 2.8010e-07 1.4005e-07  0.4675 0.6396
## Residuals 10 2.9956e-06 2.9956e-07

## Analysis of Variance Table
## 
## Response: Hc
##           Df    Sum Sq    Mean Sq F value Pr(>F)
## Genotype   2 1.5434e-07 7.7170e-08  0.4134 0.6698
## Residuals 13 2.4265e-06 1.8665e-07

## [1] "CPu Volume"

## 
## Call:
## lm(formula = CPu ~ Genotype * Sex, data = geno_combined_VOL)
## 
## Residuals:
##        Min         1Q     Median         3Q        Max
## -7.026e-04 -3.106e-04 -6.856e-05  1.250e-04  1.486e-03
## 
## Coefficients:
##                          Estimate Std. Error t value Pr(>|t|)
## (Intercept)             2.476e-02  2.420e-04 102.283  < 2e-16 ***
## GenotypeAPOE33         -7.692e-04  3.952e-04  -1.946  0.06395 .
## GenotypeAPOE44          9.720e-04  3.423e-04   2.840  0.00928 **
## Sexmale                -4.568e-05  3.277e-04  -0.139  0.89036
## GenotypeAPOE33:Sexmale  2.317e-04  5.134e-04   0.451  0.65601
## GenotypeAPOE44:Sexmale -5.205e-04  4.739e-04  -1.098  0.28336
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## 
## Residual standard error: 0.0005412 on 23 degrees of freedom
## Multiple R-squared:  0.5711, Adjusted R-squared:  0.4778
## F-statistic: 6.124 on 5 and 23 DF,  p-value: 0.0009559

## 
## Call:
## lm(formula = CPu ~ Genotype, data = combo_f_VOL)
## 
## Residuals:
##        Min         1Q     Median         3Q        Max
## -7.026e-04 -1.906e-04 -6.856e-05  1.107e-04  8.300e-04
```

```
##
## Coefficients:
##                 Estimate Std. Error t value Pr(>|t|)
## (Intercept)     0.0247562  0.0001883 131.487  < 2e-16 ***
## GenotypeAPOE33 -0.0007692  0.0003075  -2.502  0.03135 *
## GenotypeAPOE44  0.0009720  0.0002663   3.651  0.00446 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.000421 on 10 degrees of freedom
## Multiple R-squared:  0.7719, Adjusted R-squared:  0.7263
## F-statistic: 16.92 on 2 and 10 DF,  p-value: 0.0006174

##
## Call:
## lm(formula = CPu ~ Genotype, data = combo_m_VOL)
##
## Residuals:
##        Min         1Q     Median         3Q        Max
## -0.0006900 -0.0004200 -0.0001197  0.0003258  0.0014856
##
## Coefficients:
##                 Estimate Std. Error t value Pr(>|t|)
## (Intercept)     0.0247106  0.0002523  97.948   <2e-16 ***
## GenotypeAPOE33 -0.0005375  0.0003742  -1.436    0.175
## GenotypeAPOE44  0.0004515  0.0003742   1.207    0.249
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.000618 on 13 degrees of freedom
## Multiple R-squared:  0.3306, Adjusted R-squared:  0.2277
## F-statistic: 3.211 on 2 and 13 DF,  p-value: 0.07358
## Analysis of Variance Table
##
## Response: CPu
##               Df    Sum Sq   Mean Sq F value    Pr(>F)
## Genotype       2 8.0970e-06 4.0485e-06 13.8218 0.0001142 ***
## Sex            1 1.9980e-07 1.9980e-07  0.6822 0.4173028
## Genotype:Sex   2 6.7230e-07 3.3610e-07  1.1476 0.3349205
## Residuals     23 6.7368e-06 2.9290e-07
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## Analysis of Variance Table
##
## Response: CPu
##            Df    Sum Sq   Mean Sq F value    Pr(>F)
## Genotype    2 5.9982e-06 2.9991e-06  16.921 0.0006174 ***
## Residuals  10 1.7724e-06 1.7724e-07
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## Analysis of Variance Table
##
## Response: CPu
```

```
##            Df      Sum Sq    Mean Sq F value  Pr(>F)
## Genotype    2 2.4523e-06 1.2261e-06  3.2108 0.07358 .
## Residuals  13 4.9644e-06 3.8188e-07
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

## [1] "Brain Volume"

##
## Call:
## lm(formula = Brain ~ Genotype * Sex, data = geno_combined_VOL)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -23.1520  -5.4838  -0.0532   3.4798  20.8142
##
## Coefficients:
##                       Estimate Std. Error t value Pr(>|t|)
## (Intercept)            504.359      4.403 114.561   <2e-16 ***
## GenotypeAPOE33          18.090      7.189   2.516   0.0193 *
## GenotypeAPOE44           7.488      6.226   1.203   0.2413
## Sexmale                 -2.641      5.961  -0.443   0.6619
## GenotypeAPOE33:Sexmale  -1.806      9.339  -0.193   0.8483
## GenotypeAPOE44:Sexmale -10.056      8.620  -1.167   0.2553
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 9.844 on 23 degrees of freedom
## Multiple R-squared:  0.4588, Adjusted R-squared:  0.3412
## F-statistic:   3.9 on 5 and 23 DF,  p-value: 0.01047

##
## Call:
## lm(formula = Brain ~ Genotype, data = combo_f_VOL)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -9.2858 -5.4838 -0.4342  2.2928 15.4434
##
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept)    504.359      3.592 140.421   <2e-16 ***
## GenotypeAPOE33  18.090      5.865   3.084   0.0116 *
## GenotypeAPOE44   7.488      5.080   1.474   0.1712
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 8.031 on 10 degrees of freedom
## Multiple R-squared:  0.4881, Adjusted R-squared:  0.3858
## F-statistic: 4.768 on 2 and 10 DF,  p-value: 0.03514

##
## Call:
## lm(formula = Brain ~ Genotype, data = combo_m_VOL)
##
## Residuals:
```

```
##        Min       1Q    Median       3Q       Max
## -23.1520  -2.5670    0.8804    4.0770   20.8142
##
## Coefficients:
##                 Estimate Std. Error t value Pr(>|t|)
## (Intercept)      501.718      4.506 111.337   <2e-16 ***
## GenotypeAPOE33    16.284      6.684   2.436    0.030 *
## GenotypeAPOE44    -2.568      6.684  -0.384    0.707
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 11.04 on 13 degrees of freedom
## Multiple R-squared:  0.402,  Adjusted R-squared:   0.31
## F-statistic:  4.37 on 2 and 13 DF,  p-value: 0.03535

## Analysis of Variance Table
##
## Response: Brain
##               Df  Sum Sq Mean Sq F value   Pr(>F)
## Genotype       2 1430.77  715.38  7.3818 0.003338 **
## Sex            1  314.81  314.81  3.2485 0.084612 .
## Genotype:Sex   2  144.35   72.18  0.7448 0.485956
## Residuals     23 2228.96   96.91
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

## Analysis of Variance Table
##
## Response: Brain
##           Df Sum Sq Mean Sq F value  Pr(>F)
## Genotype   2 615.15 307.574  4.7683 0.03514 *
## Residuals 10 645.04  64.504
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

## Analysis of Variance Table
##
## Response: Brain
##           Df Sum Sq Mean Sq F value  Pr(>F)
## Genotype   2 1064.9  532.45    4.37 0.03535 *
## Residuals 13 1583.9  121.84
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```
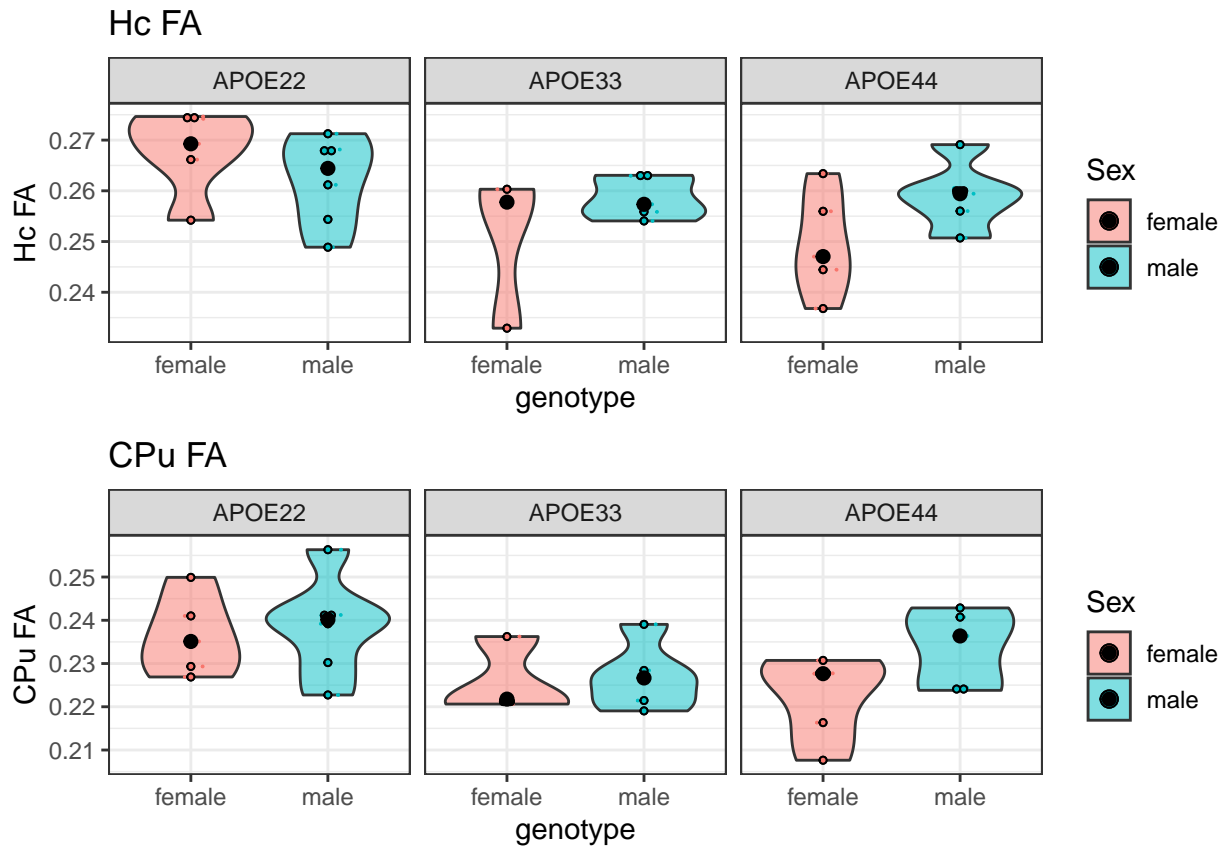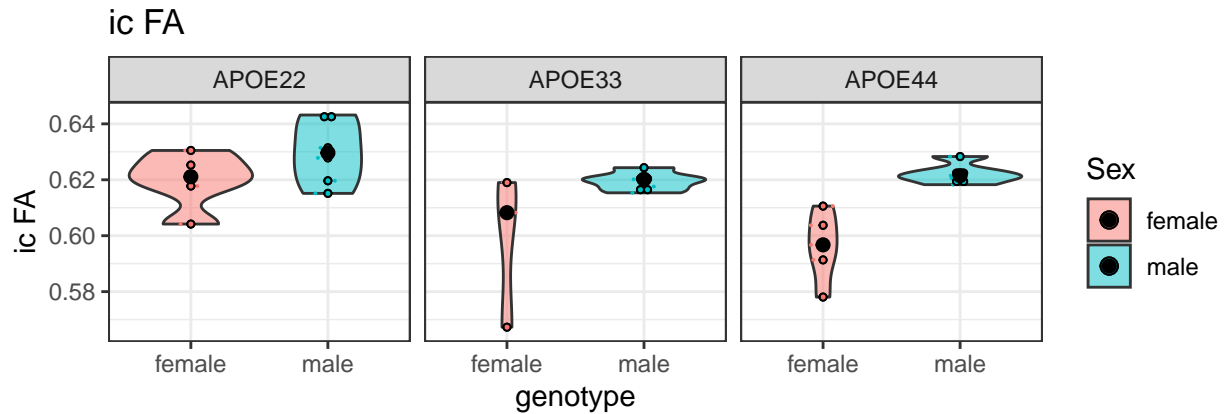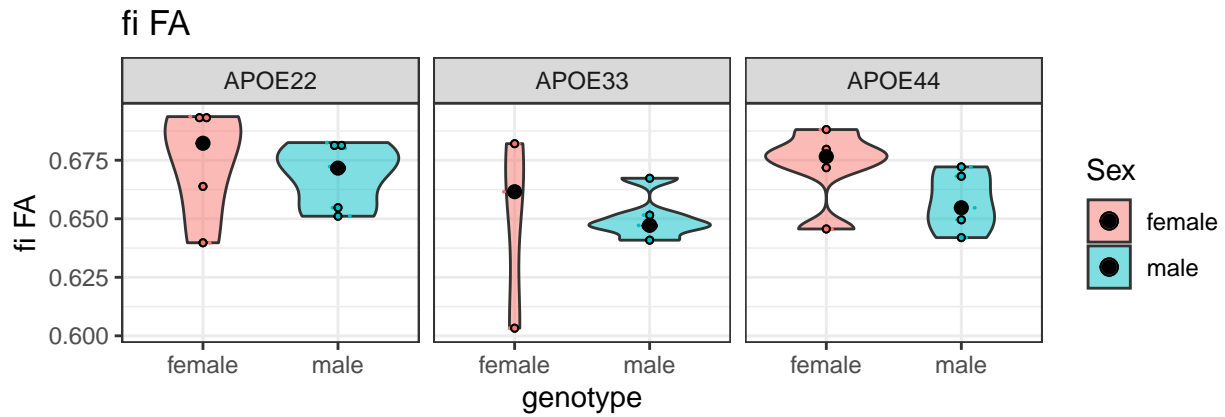
Plots for FA

Gray Matter of hippocampus and caudate putamen (Hc and CPu) ; white matter of fimbria (fi), fornix (fx) and internal capsule (ic)

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

Hc FA

CPu FA


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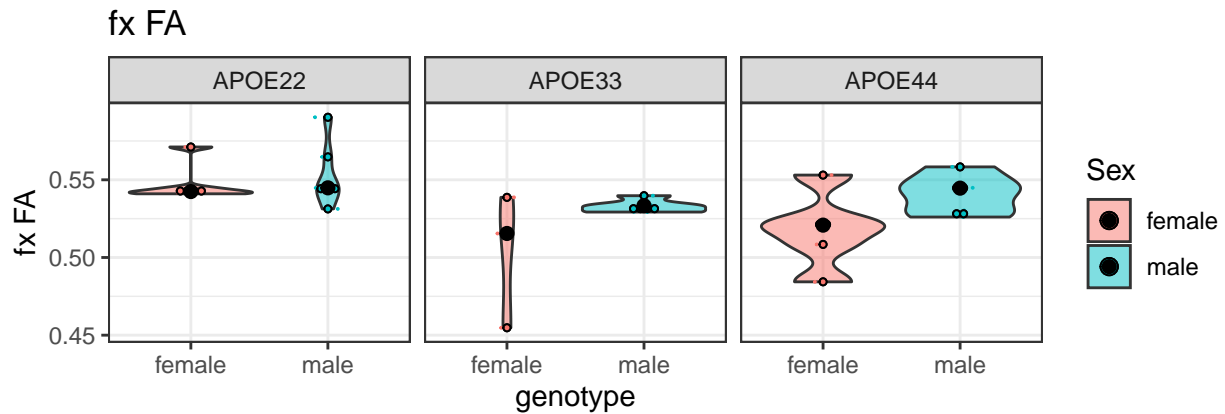
fi FA

ic FA


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

fx FA


```
## [1] "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

##
## Call:
## lm(formula = Hc ~ Genotype, data = combo_f_FA)
##
## Residuals:
##       Min        1Q    Median        3Q       Max
## -0.017413 -0.005077  0.001575  0.006957  0.013862
##
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept)    0.267691   0.004822  55.509 8.73e-14 ***
## GenotypeAPOE33 -0.017357   0.007875  -2.204   0.0521 .
## GenotypeAPOE44 -0.018166   0.006820  -2.664   0.0237 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.01078 on 10 degrees of freedom
## Multiple R-squared:  0.4581, Adjusted R-squared:  0.3497
## F-statistic: 4.227 on 2 and 10 DF,  p-value: 0.04673

##
## Call:
## lm(formula = Hc ~ Genotype, data = combo_m_FA)
##
## Residuals:
##        Min         1Q     Median         3Q        Max
## -0.0130315 -0.0035130 -0.0002347  0.0047378  0.0099443
##
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept)    0.261915   0.002858   91.64   <2e-16 ***
## GenotypeAPOE33 -0.003263   0.004239   -0.77    0.455
## GenotypeAPOE44 -0.002755   0.004239   -0.65    0.527
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.007001 on 13 degrees of freedom
## Multiple R-squared:  0.0515, Adjusted R-squared:  -0.09442
## F-statistic: 0.3529 on 2 and 13 DF,  p-value: 0.7091

## 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

## Analysis of Variance Table
## 
## Response: Hc
##           Df     Sum Sq    Mean Sq F value  Pr(>F)
## Genotype   2 0.00098301 0.00049151  4.2269 0.04673 *
## Residuals 10 0.00116280 0.00011628
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

## Analysis of Variance Table
## 
## Response: Hc
##           Df     Sum Sq    Mean Sq F value Pr(>F)
## Genotype   2 0.00003460 1.7298e-05  0.3529 0.7091
## Residuals 13 0.00063715 4.9012e-05

## [1] "CPu FA"

## 
## Call:
## lm(formula = CPu ~ Genotype * Sex, data = geno_combined_FA)
## 
## Residuals:
##        Min         1Q     Median         3Q        Max
## -0.0157390 -0.0071250  0.0007236  0.0057157  0.0178542
## 
## Coefficients:
##                        Estimate Std. Error t value Pr(>|t|)
## (Intercept)            0.236449   0.004266  55.423   <2e-16 ***
## GenotypeAPOE33        -0.010244   0.006967  -1.470   0.1550
## GenotypeAPOE44        -0.014434   0.006033  -2.392   0.0253 *
## Sexmale                0.002017   0.005777   0.349   0.7302
## GenotypeAPOE33:Sexmale -0.001301   0.009050  -0.144   0.8869
## GenotypeAPOE44:Sexmale  0.009600   0.008353   1.149   0.2623
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## 
## Residual standard error: 0.00954 on 23 degrees of freedom
## Multiple R-squared:  0.3388, Adjusted R-squared:  0.195
## F-statistic: 2.357 on 5 and 23 DF,  p-value: 0.07251

## 
## Call:
## lm(formula = CPu ~ Genotype, data = combo_f_FA)
## 
## Residuals:
```

```
##        Min        1Q     Median        3Q       Max
## -0.014377 -0.005680 -0.001346  0.005716  0.013471
##
## Coefficients:
##                Estimate Std. Error t value Pr(>|t|)
## (Intercept)     0.236449   0.004188  56.462 7.37e-14 ***
## GenotypeAPOE33 -0.010244   0.006839  -1.498    0.165
## GenotypeAPOE44 -0.014434   0.005922  -2.437    0.035 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.009364 on 10 degrees of freedom
## Multiple R-squared:  0.382,  Adjusted R-squared:  0.2584
## F-statistic: 3.091 on 2 and 10 DF,  p-value: 0.09015

##
## Call:
## lm(formula = CPu ~ Genotype, data = combo_m_FA)
##
## Residuals:
##        Min        1Q     Median        3Q       Max
## -0.015739 -0.007968  0.001099  0.003847  0.017854
##
## Coefficients:
##                Estimate Std. Error t value Pr(>|t|)
## (Intercept)     0.238466   0.003949  60.389   <2e-16 ***
## GenotypeAPOE33 -0.011545   0.005857  -1.971   0.0704 .
## GenotypeAPOE44 -0.004835   0.005857  -0.825   0.4240
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.009673 on 13 degrees of freedom
## Multiple R-squared:  0.2304, Adjusted R-squared:  0.112
## F-statistic: 1.946 on 2 and 13 DF,  p-value: 0.1823

## Analysis of Variance Table
##
## Response: CPu
##              Df     Sum Sq    Mean Sq F value  Pr(>F)
## Genotype      2 0.00072293 0.00036146  3.9719 0.03298 *
## Sex           1 0.00018127 0.00018127  1.9919 0.17153
## Genotype:Sex  2 0.00016811 0.00008405  0.9236 0.41131
## Residuals    23 0.00209312 0.00009101
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

## Analysis of Variance Table
##
## Response: CPu
##           Df     Sum Sq    Mean Sq F value  Pr(>F)
## Genotype   2 0.00054200 2.7100e-04  3.0906 0.09015 .
## Residuals 10 0.00087686 8.7686e-05
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

## Analysis of Variance Table
```

```
##
## Response: CPu
##            Df     Sum Sq    Mean Sq F value Pr(>F)
## Genotype    2 0.00036413 1.8206e-04   1.946 0.1823
## Residuals  13 0.00121626 9.3559e-05

## [1] "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

##
## Call:
## lm(formula = fi ~ Genotype, data = combo_f_FA)
##
## Residuals:
##       Min        1Q    Median        3Q       Max
## -0.045696 -0.010606  0.007315  0.015746  0.033102
##
## Coefficients:
##                Estimate Std. Error t value Pr(>|t|)
## (Intercept)    0.674432   0.011362  59.357 4.47e-14 ***
## GenotypeAPOE33 -0.025466   0.018555  -1.373      0.2
## GenotypeAPOE44 -0.002072   0.016069  -0.129      0.9
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.02541 on 10 degrees of freedom
## Multiple R-squared:  0.177,  Adjusted R-squared:  0.01237
## F-statistic: 1.075 on 2 and 10 DF,  p-value: 0.3776

##
## Call:
## lm(formula = fi ~ Genotype, data = combo_m_FA)
##
## Residuals:
```

```
##         Min         1Q      Median          3Q         Max
## -0.0175431 -0.0082795 -0.0008975  0.0110151  0.0165586
##
## Coefficients:
##                Estimate Std. Error t value Pr(>|t|)
## (Intercept)     0.668630   0.004919 135.923   <2e-16 ***
## GenotypeAPOE33 -0.017881   0.007296  -2.451   0.0292 *
## GenotypeAPOE44 -0.011327   0.007296  -1.552   0.1446
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.01205 on 13 degrees of freedom
## Multiple R-squared:  0.3246, Adjusted R-squared:  0.2207
## F-statistic: 3.124 on 2 and 13 DF,  p-value: 0.078

## 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

## Analysis of Variance Table
##
## Response: fi
##          Df    Sum Sq    Mean Sq F value Pr(>F)
## Genotype  2 0.0013881 0.00069404  1.0752 0.3776
## Residuals 10 0.0064552 0.00064552

## Analysis of Variance Table
##
## Response: fi
##          Df     Sum Sq    Mean Sq F value Pr(>F)
## Genotype  2 0.00090716 0.00045358   3.124  0.078 .
## Residuals 13 0.00188746 0.00014519
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

## [1] "ic FA"

##
## Call:
## lm(formula = ic ~ Genotype * Sex, data = geno_combined_FA)
##
## Residuals:
##         Min         1Q      Median          3Q         Max
## -0.0308930 -0.0041263  0.0006374  0.0059384  0.0208270
##
## Coefficients:
##                       Estimate Std. Error t value Pr(>|t|)
## (Intercept)           0.619760   0.005320 116.495  < 2e-16 ***
## GenotypeAPOE33       -0.021588   0.008688  -2.485  0.02067 *
```

23

```
## GenotypeAPOE44          -0.023672   0.007524  -3.146  0.00452 **
## Sexmale                  0.010103   0.007203   1.403  0.17412
## GenotypeAPOE33:Sexmale  0.011325   0.011286   1.004  0.32604
## GenotypeAPOE44:Sexmale  0.016188   0.010416   1.554  0.13380
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.0119 on 23 degrees of freedom
## Multiple R-squared:  0.5763, Adjusted R-squared:  0.4842
## F-statistic: 6.258 on 5 and 23 DF,  p-value: 0.000839

##
## Call:
## lm(formula = ic ~ Genotype, data = combo_f_FA)
##
## Residuals:
##      Min        1Q    Median        3Q       Max
## -0.030893 -0.004746  0.001343  0.010066  0.020827
##
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept)    0.619760   0.007072  87.633 9.16e-16 ***
## GenotypeAPOE33 -0.021588   0.011549  -1.869   0.0911 .
## GenotypeAPOE44 -0.023672   0.010002  -2.367   0.0395 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.01581 on 10 degrees of freedom
## Multiple R-squared:  0.3932, Adjusted R-squared:  0.2718
## F-statistic:  3.24 on 2 and 10 DF,  p-value: 0.08228

##
## Call:
## lm(formula = ic ~ Genotype, data = combo_m_FA)
##
## Residuals:
##       Min        1Q    Median        3Q       Max
## -0.014724 -0.002558 -0.000158  0.002379  0.013310
##
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept)    0.629862   0.003109 202.585   <2e-16 ***
## GenotypeAPOE33 -0.010262   0.004612  -2.225   0.0444 *
## GenotypeAPOE44 -0.007484   0.004612  -1.623   0.1286
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.007616 on 13 degrees of freedom
## Multiple R-squared:  0.2944, Adjusted R-squared:  0.1858
## F-statistic: 2.712 on 2 and 13 DF,  p-value: 0.1037
## Analysis of Variance Table
##
## Response: ic
##               Df    Sum Sq   Mean Sq F value    Pr(>F)
```

```
## Genotype      2 0.0015605 0.00078027   5.5137 0.0110621 *
## Sex            1 0.0025078 0.00250781  17.7213 0.0003339 ***
## Genotype:Sex   2 0.0003595 0.00017977   1.2703 0.2997152
## Residuals     23 0.0032548 0.00014151
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

## Analysis of Variance Table
##
## Response: ic
##           Df    Sum Sq    Mean Sq F value  Pr(>F)
## Genotype   2 0.0016204 0.00081017   3.2396 0.08228 .
## Residuals 10 0.0025008 0.00025008
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

## Analysis of Variance Table
##
## Response: ic
##           Df     Sum Sq    Mean Sq F value Pr(>F)
## Genotype   2 0.00031453 0.00015727   2.7115 0.1037
## Residuals 13 0.00075400 0.00005800

## [1] "fx FA"

##
## Call:
## lm(formula = fx ~ Genotype * Sex, data = geno_combined_FA)
##
## Residuals:
##       Min        1Q    Median        3Q       Max
## -0.048213 -0.008483 -0.003539  0.006695  0.036991
##
## Coefficients:
##                        Estimate Std. Error t value Pr(>|t|)
## (Intercept)            0.548151   0.009258  59.211  < 2e-16 ***
## GenotypeAPOE33        -0.045172   0.015118  -2.988  0.00657 **
## GenotypeAPOE44        -0.030483   0.013092  -2.328  0.02905 *
## Sexmale                0.005117   0.012535   0.408  0.68688
## GenotypeAPOE33:Sexmale 0.024983   0.019638   1.272  0.21602
## GenotypeAPOE44:Sexmale 0.018041   0.018125   0.995  0.32993
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.0207 on 23 degrees of freedom
## Multiple R-squared:  0.4363, Adjusted R-squared:  0.3138
## F-statistic: 3.56 on 5 and 23 DF,  p-value: 0.01572

##
## Call:
## lm(formula = fx ~ Genotype, data = combo_f_FA)
##
## Residuals:
##       Min        1Q    Median        3Q       Max
## -0.048213 -0.007154 -0.003539  0.012483  0.035729
##
```

```
## Coefficients:
##                Estimate Std. Error t value Pr(>|t|)
## (Intercept)     0.54815    0.01175  46.668 4.92e-13 ***
## GenotypeAPOE33 -0.04517    0.01918  -2.355   0.0403 *
## GenotypeAPOE44 -0.03048    0.01661  -1.835   0.0964 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.02626 on 10 degrees of freedom
## Multiple R-squared:  0.3889, Adjusted R-squared:  0.2667
## F-statistic: 3.182 on 2 and 10 DF,  p-value: 0.08521

##
## Call:
## lm(formula = fx ~ Genotype, data = combo_m_FA)
##
## Residuals:
##       Min        1Q    Median        3Q       Max
## -0.021995 -0.008767 -0.001684  0.004700  0.036991
##
## Coefficients:
##                 Estimate Std. Error t value Pr(>|t|)
## (Intercept)     0.553269   0.006158  89.851   <2e-16 ***
## GenotypeAPOE33 -0.020189   0.009133  -2.210   0.0456 *
## GenotypeAPOE44 -0.012442   0.009133  -1.362   0.1962
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.01508 on 13 degrees of freedom
## Multiple R-squared:  0.2797, Adjusted R-squared:  0.1689
## F-statistic: 2.524 on 2 and 13 DF,  p-value: 0.1186
## Analysis of Variance Table
##
## Response: fx
##              Df    Sum Sq    Mean Sq F value  Pr(>F)
## Genotype      2 0.0045172 0.00225862  5.2709 0.01305 *
## Sex           1 0.0023173 0.00231728  5.4078 0.02923 *
## Genotype:Sex  2 0.0007937 0.00039683  0.9261 0.41038
## Residuals    23 0.0098557 0.00042851
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## Analysis of Variance Table
##
## Response: fx
##           Df    Sum Sq    Mean Sq F value  Pr(>F)
## Genotype   2 0.0043904 0.00219518  3.1822 0.08521 .
## Residuals 10 0.0068983 0.00068983
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## Analysis of Variance Table
##
## Response: fx
##           Df    Sum Sq    Mean Sq F value Pr(>F)
```
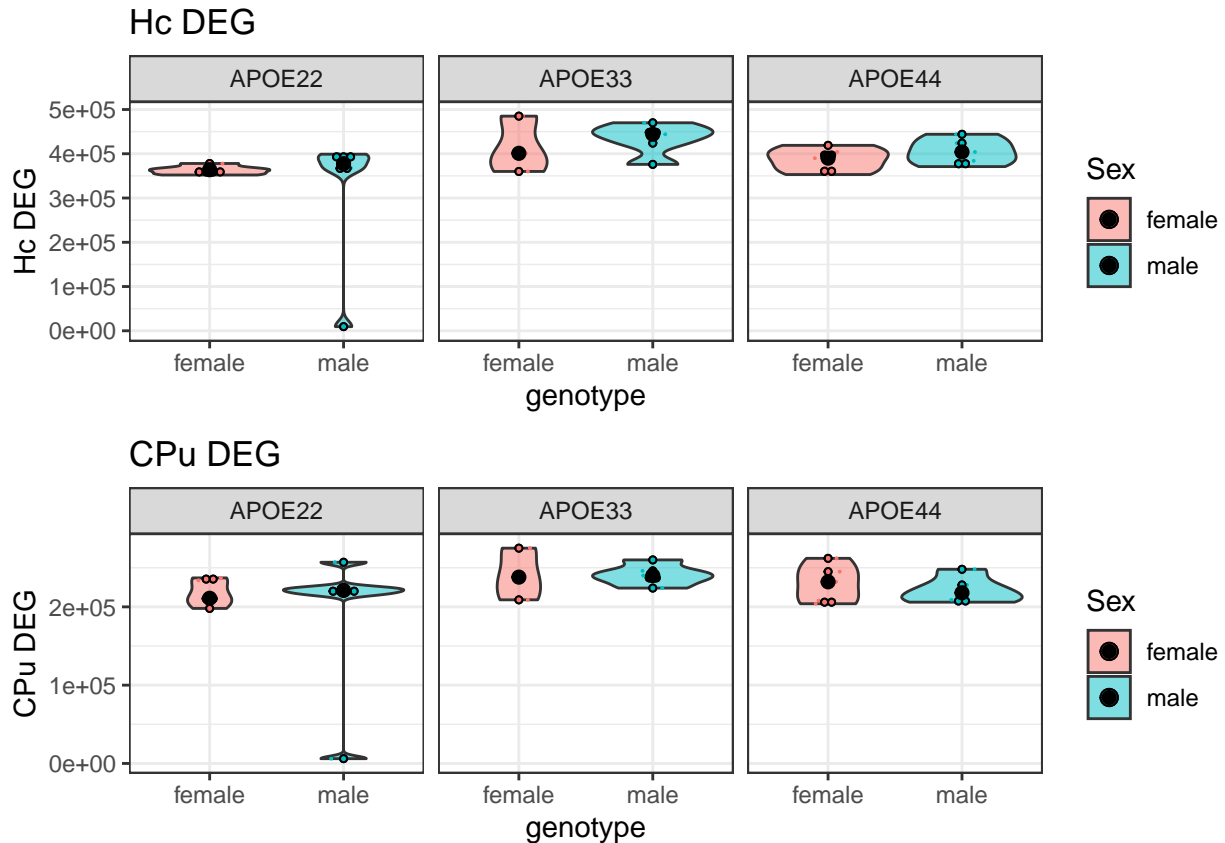
```
## Genotype    2 0.0011483 0.00057414  2.5237 0.1186
## Residuals 13 0.0029575 0.00022750
```
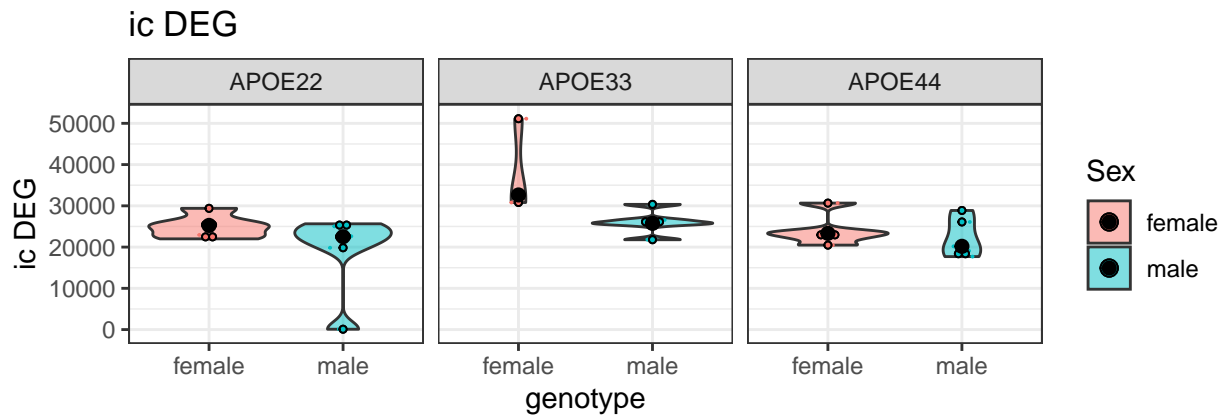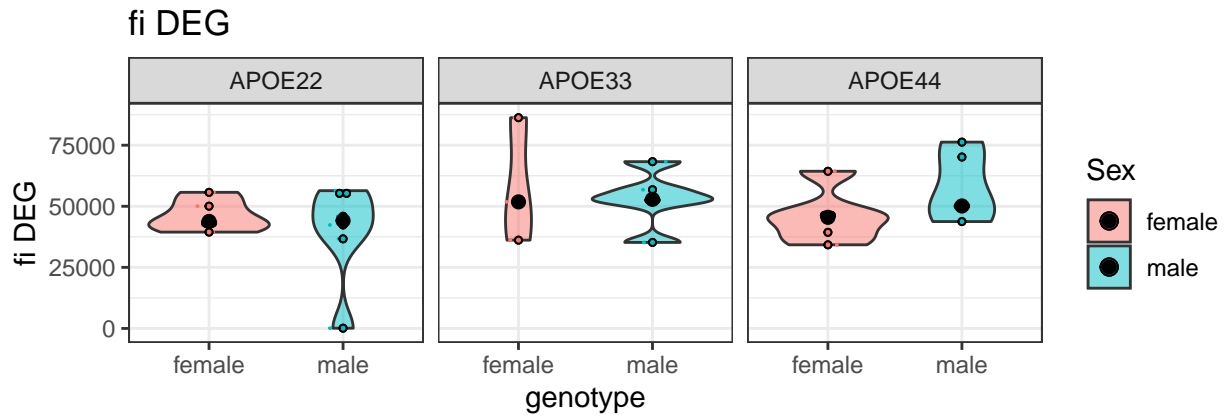
Plots for Connectivity Degree

Hc and CPu

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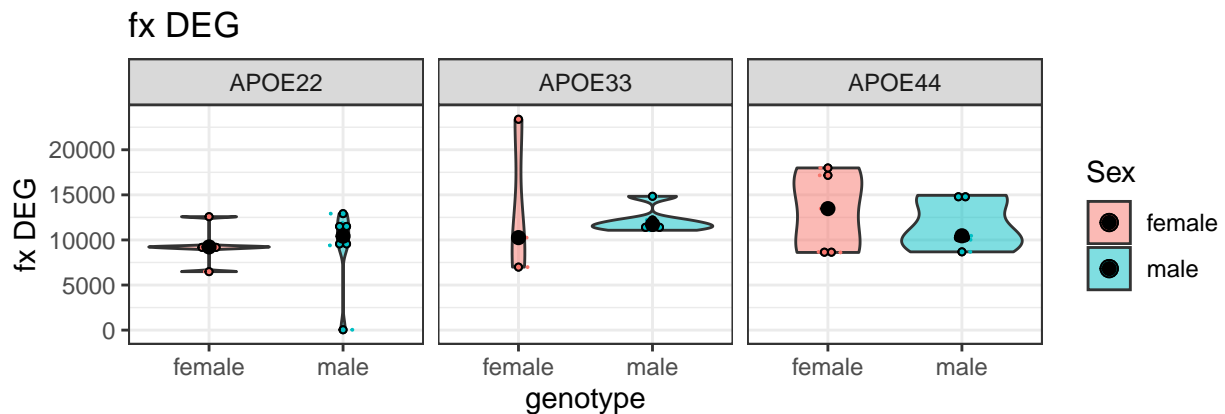


```
## Bin width defaults to 1/30 of the range of the data. Pick better value with `binwidth`.
## Bin width defaults to 1/30 of the range of the data. Pick better value with `binwidth`.
## Bin width defaults to 1/30 of the range of the data. Pick better value with `binwidth`.
## Bin width defaults to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

fi DEG

ic DEG


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

fx DEG


```
## [1] "Hc DEG"
##
## Call:
## lm(formula = Hc ~ Genotype * Sex, data = geno_combined_DEG)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -311690  -14333    3200   36800   77938
##
## Coefficients:
```

```
##                      Estimate Std. Error t value Pr(>|t|)
## (Intercept)             363200      34589  10.500 3.02e-10 ***
## GenotypeAPOE33           52133      56484   0.923    0.366
## GenotypeAPOE44           23600      48916   0.482    0.634
## Sexmale                 -42138      46834  -0.900    0.378
## GenotypeAPOE33:Sexmale   60005      73374   0.818    0.422
## GenotypeAPOE44:Sexmale   60738      67722   0.897    0.379
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 77340 on 23 degrees of freedom
## Multiple R-squared:  0.2393, Adjusted R-squared:  0.07399
## F-statistic: 1.447 on 5 and 23 DF,  p-value: 0.2453

##
## Call:
## lm(formula = Hc ~ Genotype, data = combo_f_DEG)
##
## Residuals:
##    Min     1Q Median     3Q    Max
## -55333 -14333    800  14800  69667
##
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept)     363200      15076  24.091 3.46e-10 ***
## GenotypeAPOE33   52133      24619   2.118   0.0603 .
## GenotypeAPOE44   23600      21321   1.107   0.2942
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 33710 on 10 degrees of freedom
## Multiple R-squared:  0.3117, Adjusted R-squared:  0.174
## F-statistic: 2.264 on 2 and 10 DF,  p-value: 0.1545

##
## Call:
## lm(formula = Hc ~ Genotype, data = combo_m_DEG)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -311690  -12250   18700   45438   77938
##
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept)     321062      40227   7.981 2.29e-06 ***
## GenotypeAPOE33  112138      59667   1.879   0.0828 .
## GenotypeAPOE44   84338      59667   1.413   0.1810
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 98540 on 13 degrees of freedom
## Multiple R-squared: 0.232,  Adjusted R-squared:  0.1138
## F-statistic: 1.963 on 2 and 13 DF,  p-value: 0.1799

## Analysis of Variance Table
```

```
## 
## Response: Hc
##               Df      Sum Sq    Mean Sq F value  Pr(>F)
## Genotype       2 3.6987e+10 1.8494e+10  3.0915 0.06469 .
## Sex            1 1.7171e+08 1.7171e+08  0.0287 0.86694
## Genotype:Sex   2 6.1343e+09 3.0671e+09  0.5127 0.60554
## Residuals     23 1.3759e+11 5.9820e+09
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

## Analysis of Variance Table
## 
## Response: Hc
##           Df     Sum Sq    Mean Sq F value Pr(>F)
## Genotype   2 5.1465e+09 2573251282  2.2643 0.1545
## Residuals 10 1.1364e+10 1136426667

## Analysis of Variance Table
## 
## Response: Hc
##           Df     Sum Sq    Mean Sq F value Pr(>F)
## Genotype   2 3.8122e+10 1.9061e+10  1.9632 0.1799
## Residuals 13 1.2622e+11 9.7094e+09

## [1] "CPu DEG"

## 
## Call:
## lm(formula = CPu ~ Genotype * Sex, data = geno_combined_DEG)
## 
## Residuals:
##     Min      1Q  Median      3Q     Max
## -184742  -12800    1800   25148   66149
## 
## Coefficients:
##                      Estimate Std. Error t value Pr(>|t|)
## (Intercept)            218000      20783  10.489 3.08e-10 ***
## GenotypeAPOE33          22667      33938   0.668    0.511
## GenotypeAPOE44          12200      29391   0.415    0.682
## Sexmale                -27148      28140  -0.965    0.345
## GenotypeAPOE33:Sexmale  27282      44087   0.619    0.542
## GenotypeAPOE44:Sexmale  18748      40690   0.461    0.649
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## 
## Residual standard error: 46470 on 23 degrees of freedom
## Multiple R-squared:  0.154,  Adjusted R-squared:  -0.02994
## F-statistic: 0.8372 on 5 and 23 DF,  p-value: 0.5369

## 
## Call:
## lm(formula = CPu ~ Genotype, data = combo_f_DEG)
## 
## Residuals:
##    Min     1Q Median     3Q    Max
## -31667 -20000  -2667  16000  34333
```

```
##
## Coefficients:
##                 Estimate Std. Error t value Pr(>|t|)
## (Intercept)       218000      10706  20.361  1.8e-09 ***
## GenotypeAPOE33     22667      17484   1.296    0.224
## GenotypeAPOE44     12200      15141   0.806    0.439
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 23940 on 10 degrees of freedom
## Multiple R-squared:  0.1492, Adjusted R-squared:  -0.02091
## F-statistic: 0.8771 on 2 and 10 DF,  p-value: 0.4457

##
## Call:
## lm(formula = CPu ~ Genotype, data = combo_m_DEG)
##
## Residuals:
##      Min      1Q  Median      3Q     Max
## -184742   -8300    5700   26687   66149
##
## Coefficients:
##                 Estimate Std. Error t value Pr(>|t|)
## (Intercept)       190852      23735   8.041 2.11e-06 ***
## GenotypeAPOE33     49948      35204   1.419    0.179
## GenotypeAPOE44     30948      35204   0.879    0.395
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 58140 on 13 degrees of freedom
## Multiple R-squared:  0.1381, Adjusted R-squared:  0.005449
## F-statistic: 1.041 on 2 and 13 DF,  p-value: 0.3807

## Analysis of Variance Table
##
## Response: CPu
##              Df      Sum Sq      Mean Sq F value Pr(>F)
## Genotype      2 6.8539e+09   3426962109  1.5868 0.2262
## Sex           1 1.2651e+09   1265144689  0.5858 0.4518
## Genotype:Sex  2 9.2140e+08    460700303  0.2133 0.8095
## Residuals    23 4.9672e+10   2159635488

## Analysis of Variance Table
##
## Response: CPu
##          Df     Sum Sq   Mean Sq F value Pr(>F)
## Genotype  2 1005456410 502728205  0.8771 0.4457
## Residuals 10 5731466667 573146667

## Analysis of Variance Table
##
## Response: CPu
##          Df     Sum Sq    Mean Sq F value Pr(>F)
## Genotype  2 7.0378e+09 3518902160  1.0411 0.3807
## Residuals 13 4.3940e+10 3380011505
```

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

##
## Call:
## lm(formula = fi ~ Genotype * Sex, data = geno_combined_DEG)
##
## Residuals:
##    Min    1Q Median    3Q    Max
## -39176  -6854   -608   9418  28196
##
## Coefficients:
##                        Estimate Std. Error t value Pr(>|t|)
## (Intercept)            46291.2     6910.9   6.698 7.83e-07 ***
## GenotypeAPOE33         11781.1    11285.5   1.044    0.307
## GenotypeAPOE44          -198.8     9773.5  -0.020    0.984
## Sexmale                -7016.4     9357.4  -0.750    0.461
## GenotypeAPOE33:Sexmale  2005.8    14660.3   0.137    0.892
## GenotypeAPOE44:Sexmale 18991.4    13530.8   1.404    0.174
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 15450 on 23 degrees of freedom
## Multiple R-squared:  0.2014, Adjusted R-squared:  0.02784
## F-statistic:  1.16 on 5 and 23 DF,  p-value: 0.3583

##
## Call:
## lm(formula = fi ~ Genotype, data = combo_f_DEG)
##
## Residuals:
##    Min    1Q Median    3Q    Max
## -21929  -6759  -2484   3752  28196
##
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept)    46291.2     6334.6   7.308 2.58e-05 ***
## GenotypeAPOE33 11781.1    10344.3   1.139    0.281
## GenotypeAPOE44  -198.8     8958.4  -0.022    0.983
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 14160 on 10 degrees of freedom
## Multiple R-squared:  0.1397, Adjusted R-squared:  -0.03235
## F-statistic: 0.812 on 2 and 10 DF,  p-value: 0.4712

##
## Call:
## lm(formula = fi ~ Genotype, data = combo_m_DEG)
##
## Residuals:
##    Min    1Q Median    3Q    Max
## -39176  -7967   1428  12813  18196
##
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
```

```
## (Intercept)        39275        6685    5.875 5.46e-05 ***
## GenotypeAPOE33      13787        9916    1.390   0.1878
## GenotypeAPOE44      18793        9916    1.895   0.0805 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 16380 on 13 degrees of freedom
## Multiple R-squared:  0.2328, Adjusted R-squared:  0.1147
## F-statistic: 1.972 on 2 and 13 DF,  p-value: 0.1786

## Analysis of Variance Table
##
## Response: fi
##               Df      Sum Sq     Mean Sq F value Pr(>F)
## Genotype       2  845671422   422835711   1.7706 0.1926
## Sex            1      278816      278816   0.0012 0.9730
## Genotype:Sex   2  539557458   269778729   1.1297 0.3404
## Residuals     23 5492481834   238803558

## Analysis of Variance Table
##
## Response: fi
##           Df      Sum Sq    Mean Sq F value Pr(>F)
## Genotype   2  325822817  162911408   0.812 0.4712
## Residuals 10 2006327623  200632762

## Analysis of Variance Table
##
## Response: fi
##           Df      Sum Sq    Mean Sq F value Pr(>F)
## Genotype   2 1057726946  528863473   1.9722 0.1786
## Residuals 13 3486154211  268165709

## [1] "ic DEG"

##
## Call:
## lm(formula = ic ~ Genotype * Sex, data = geno_combined_DEG)
##
## Residuals:
##      Min        1Q    Median        3Q       Max
## -19180.5  -3038.0   -276.2    3704.0   12936.3
##
## Coefficients:
##                       Estimate Std. Error t value Pr(>|t|)
## (Intercept)            25034.0     2858.8   8.757 8.79e-09 ***
## GenotypeAPOE33         13151.7     4668.4   2.817  0.00978 **
## GenotypeAPOE44          -952.8     4043.0  -0.236  0.81578
## Sexmale                -5765.5     3870.8  -1.489  0.14995
## GenotypeAPOE33:Sexmale -6393.0     6064.4  -1.054  0.30275
## GenotypeAPOE44:Sexmale  4071.3     5597.2   0.727  0.47433
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 6392 on 23 degrees of freedom
## Multiple R-squared:  0.4473, Adjusted R-squared:  0.3271
```

```
## F-statistic: 3.722 on 5 and 23 DF,  p-value: 0.01293

##
## Call:
## lm(formula = ic ~ Genotype, data = combo_f_DEG)
##
## Residuals:
##     Min     1Q  Median     3Q     Max
## -7382.7 -3038.0  -749.2   545.0 12936.3
##
## Coefficients:
##                Estimate Std. Error t value Pr(>|t|)
## (Intercept)     25034.0     2630.8   9.516  2.5e-06 ***
## GenotypeAPOE33  13151.7     4296.1   3.061    0.012 *
## GenotypeAPOE44   -952.8     3720.5  -0.256    0.803
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 5883 on 10 degrees of freedom
## Multiple R-squared:  0.5546, Adjusted R-squared:  0.4655
## F-statistic: 6.225 on 2 and 10 DF,  p-value: 0.01753

##
## Call:
## lm(formula = ic ~ Genotype, data = combo_m_DEG)
##
## Residuals:
##      Min      1Q   Median      3Q      Max
## -19180.5  -2475.2    558.1   3860.4   6488.0
##
## Coefficients:
##                Estimate Std. Error t value Pr(>|t|)
## (Intercept)       19268       2759   6.983 9.57e-06 ***
## GenotypeAPOE33     6759       4092   1.651    0.123
## GenotypeAPOE44     3118       4092   0.762    0.460
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 6759 on 13 degrees of freedom
## Multiple R-squared:  0.1734, Adjusted R-squared:  0.04626
## F-statistic: 1.364 on 2 and 13 DF,  p-value: 0.29

## Analysis of Variance Table
##
## Response: ic
##               Df     Sum Sq    Mean Sq F value  Pr(>F)
## Genotype       2  385536001  192768000  4.7173 0.01920 *
## Sex            1  257401655  257401655  6.2990 0.01957 *
## Genotype:Sex   2  117609459   58804730  1.4390 0.25772
## Residuals     23  939863844   40863645
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

## Analysis of Variance Table
##
## Response: ic
```

```
##            Df    Sum Sq   Mean Sq F value  Pr(>F)
## Genotype   2 430863880 215431940  6.2253 0.01753 *
## Residuals 10 346057481  34605748
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

## Analysis of Variance Table
##
## Response: ic
##            Df    Sum Sq  Mean Sq F value Pr(>F)
## Genotype   2 124589277 62294639  1.3638   0.29
## Residuals 13 593806362 45677412

## [1] "fx DEG"

##
## Call:
## lm(formula = fx ~ Genotype * Sex, data = geno_combined_DEG)
##
## Residuals:
##     Min     1Q  Median      3Q     Max
## -9142.5 -1727.0   -52.8  2705.5  9842.7
##
## Coefficients:
##                      Estimate Std. Error t value Pr(>|t|)
## (Intercept)            9329.8     1865.6   5.001 4.65e-05 ***
## GenotypeAPOE33         4213.5     3046.6   1.383    0.180
## GenotypeAPOE44         3852.4     2638.4   1.460    0.158
## Sexmale                -150.3     2526.1  -0.059    0.953
## GenotypeAPOE33:Sexmale -1131.2     3957.6  -0.286    0.778
## GenotypeAPOE44:Sexmale -1283.9     3652.7  -0.351    0.728
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 4172 on 23 degrees of freedom
## Multiple R-squared:  0.1748, Adjusted R-squared:  -0.004537
## F-statistic: 0.9747 on 5 and 23 DF,  p-value: 0.454

##
## Call:
## lm(formula = fx ~ Genotype, data = combo_f_DEG)
##
## Residuals:
##     Min     1Q  Median      3Q     Max
## -6556.3 -3286.3  -103.8  3252.2  9842.7
##
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept)       9330       2235   4.175   0.0019 **
## GenotypeAPOE33    4214       3649   1.155   0.2751
## GenotypeAPOE44    3852       3160   1.219   0.2508
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 4997 on 10 degrees of freedom
## Multiple R-squared:  0.1646, Adjusted R-squared:  -0.002534
```
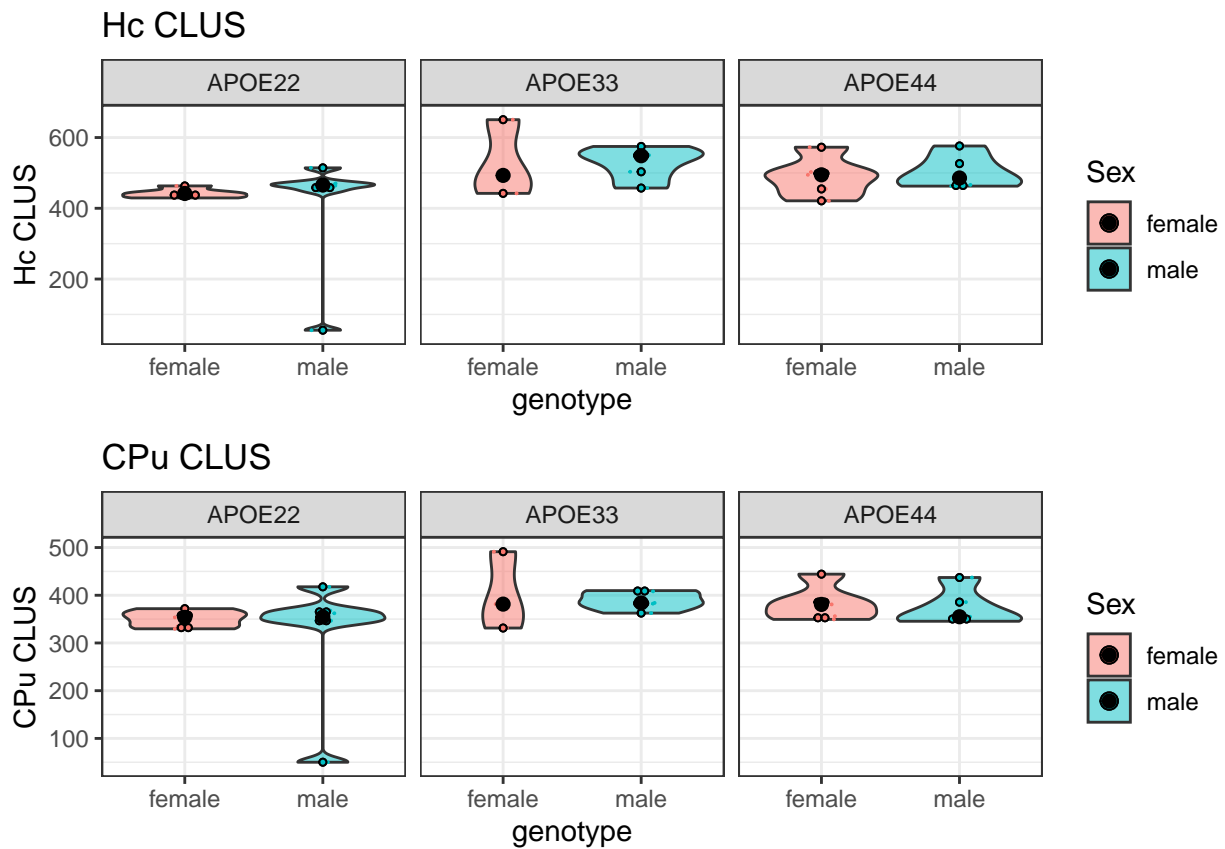
```
## F-statistic: 0.9848 on 2 and 10 DF,  p-value: 0.407

##
## Call:
## lm(formula = fx ~ Genotype, data = combo_m_DEG)
##
## Residuals:
##     Min     1Q  Median      3Q     Max
## -9142.5 -1212.6    86.3  2610.0  3739.5
##
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept)       9180       1390   6.606  1.7e-05 ***
## GenotypeAPOE33    3082       2061   1.496    0.159
## GenotypeAPOE44    2568       2061   1.246    0.235
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 3404 on 13 degrees of freedom
## Multiple R-squared:  0.1689, Adjusted R-squared:  0.04098
## F-statistic: 1.321 on 2 and 13 DF,  p-value: 0.3005

## Analysis of Variance Table
##
## Response: fx
##               Df     Sum Sq   Mean Sq F value Pr(>F)
## Genotype       2   76531013  38265506  2.1988 0.1337
## Sex            1    5764076   5764076  0.3312 0.5705
## Genotype:Sex   2    2519222   1259611  0.0724 0.9304
## Residuals     23  400268775  17402990

## Analysis of Variance Table
##
## Response: fx
##           Df     Sum Sq   Mean Sq F value Pr(>F)
## Genotype   2   49176065  24588033  0.9848  0.407
## Residuals 10  249666606  24966661

## Analysis of Variance Table
##
## Response: fx
##           Df     Sum Sq   Mean Sq F value Pr(>F)
## Genotype   2   30595795  15297898  1.3205 0.3005
## Residuals 13  150602168  11584782
```
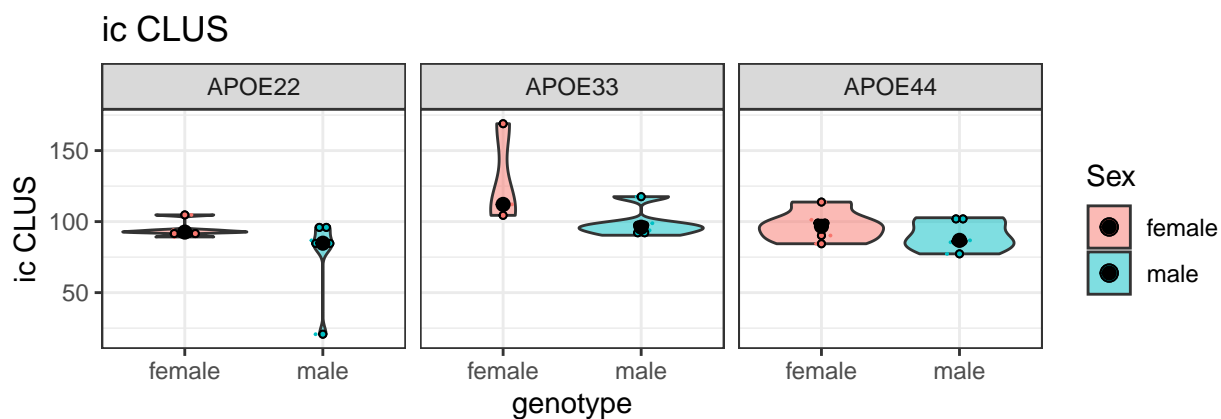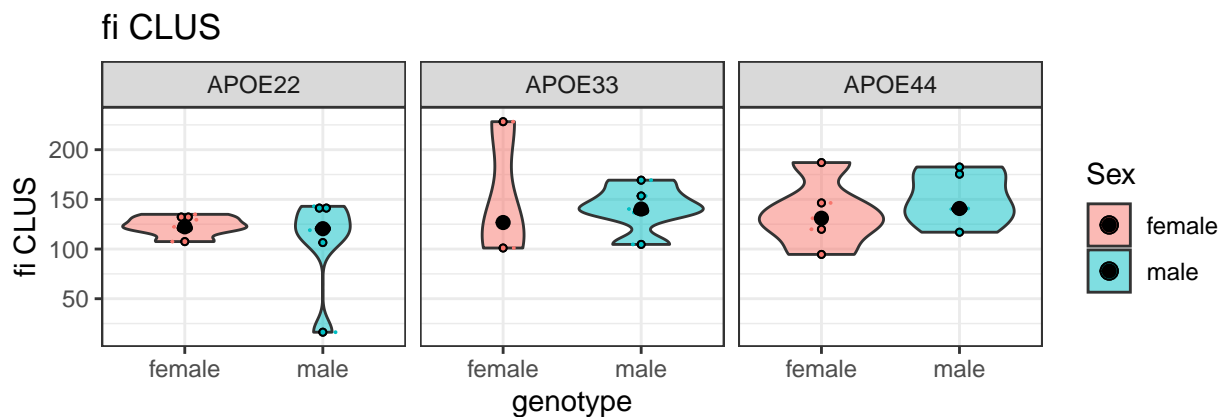
Plots for Clustering Coefficient

Hc and CPu, fi, fx, ic

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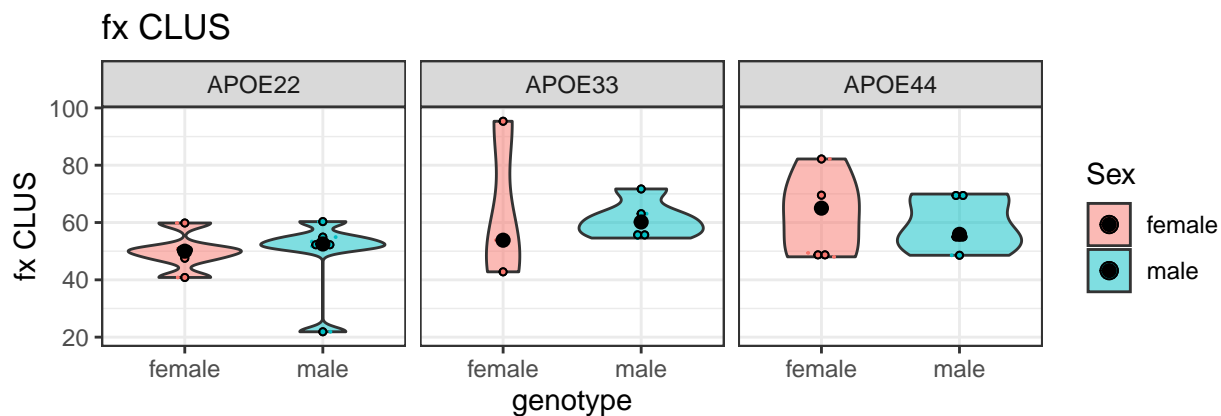
Hc CLUS

CPu CLUS


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

fi CLUS

ic CLUS


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

fx CLUS


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

##
## Call:
## lm(formula = Hc ~ Genotype * Sex, data = geno_combined_CLUS)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -348.08  -34.42    5.53   47.99  121.92
##
## Coefficients:
```

```
##                          Estimate Std. Error t value Pr(>|t|)
## (Intercept)                442.45       42.01  10.532 2.85e-10 ***
## GenotypeAPOE33              86.11        68.61   1.255    0.222
## GenotypeAPOE44              46.66        59.41   0.785    0.440
## Sexmale                    -39.00        56.88  -0.686    0.500
## GenotypeAPOE33:Sexmale      37.22        89.12   0.418    0.680
## GenotypeAPOE44:Sexmale      53.28        82.25   0.648    0.524
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 93.94 on 23 degrees of freedom
## Multiple R-squared:  0.2369, Adjusted R-squared:  0.07095
## F-statistic: 1.428 on 5 and 23 DF,  p-value: 0.2518

##
## Call:
## lm(formula = Hc ~ Genotype, data = combo_f_CLUS)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -86.377 -34.420  -0.572  13.380 121.923
##
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept)     442.45      27.31  16.199 1.67e-08 ***
## GenotypeAPOE33   86.11      44.60   1.931   0.0823 .
## GenotypeAPOE44   46.66      38.63   1.208   0.2549
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 61.08 on 10 degrees of freedom
## Multiple R-squared:  0.2805, Adjusted R-squared:  0.1365
## F-statistic: 1.949 on 2 and 10 DF,  p-value: 0.1929

##
## Call:
## lm(formula = Hc ~ Genotype, data = combo_m_CLUS)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -348.08  -26.94   23.16   61.39  110.88
##
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept)     403.45      46.09   8.754 8.23e-07 ***
## GenotypeAPOE33  123.33      68.36   1.804   0.0944 .
## GenotypeAPOE44   99.93      68.36   1.462   0.1675
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 112.9 on 13 degrees of freedom
## Multiple R-squared: 0.225,  Adjusted R-squared:  0.1058
## F-statistic: 1.887 on 2 and 13 DF,  p-value: 0.1907

## Analysis of Variance Table
```

```
##
## Response: Hc
##               Df Sum Sq Mean Sq F value  Pr(>F)
## Genotype      2  58333 29166.7  3.3050 0.05474 .
## Sex           1    771   771.1  0.0874 0.77019
## Genotype:Sex  2   3892  1946.2  0.2205 0.80377
## Residuals    23 202975  8825.0
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

## Analysis of Variance Table
##
## Response: Hc
##           Df Sum Sq Mean Sq F value Pr(>F)
## Genotype   2  14539  7269.7  1.9488 0.1929
## Residuals 10  37303  3730.3

## Analysis of Variance Table
##
## Response: Hc
##           Df Sum Sq Mean Sq F value Pr(>F)
## Genotype   2  48101   24051  1.8872 0.1907
## Residuals 13 165672   12744

## [1] "CPu CLUS"

##
## Call:
## lm(formula = CPu ~ Genotype * Sex, data = geno_combined_CLUS)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -265.086  -20.644    3.266   31.367  102.497
##
## Coefficients:
##                        Estimate Std. Error t value Pr(>|t|)
## (Intercept)              350.33      31.71  11.048 1.13e-10 ***
## GenotypeAPOE33            50.99      51.78   0.985    0.335
## GenotypeAPOE44            33.83      44.84   0.754    0.458
## Sexmale                  -35.15      42.93  -0.819    0.421
## GenotypeAPOE33:Sexmale    23.17      67.26   0.344    0.734
## GenotypeAPOE44:Sexmale    25.12      62.08   0.405    0.689
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 70.9 on 23 degrees of freedom
## Multiple R-squared:  0.1786, Adjusted R-squared:  2.57e-05
## F-statistic:     1 on 5 and 23 DF,  p-value: 0.4397

##
## Call:
## lm(formula = CPu ~ Genotype, data = combo_f_CLUS)
##
## Residuals:
##    Min     1Q Median     3Q    Max
## -70.02 -20.64  -3.34  11.70  89.93
```

```
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)    350.33      20.16  17.377 8.44e-09 ***
## GenotypeAPOE33  50.99      32.92   1.549    0.152
## GenotypeAPOE44  33.83      28.51   1.186    0.263
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 45.08 on 10 degrees of freedom
## Multiple R-squared:  0.2142, Adjusted R-squared:  0.05707
## F-statistic: 1.363 on 2 and 10 DF,  p-value: 0.2996

##
## Call:
## lm(formula = CPu ~ Genotype, data = combo_m_CLUS)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -265.09  -21.05   15.09   35.36  102.50
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)    315.18      34.95   9.017  5.9e-07 ***
## GenotypeAPOE33  74.16      51.85   1.430    0.176
## GenotypeAPOE44  58.95      51.85   1.137    0.276
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 85.62 on 13 degrees of freedom
## Multiple R-squared:  0.1528, Adjusted R-squared:  0.02246
## F-statistic: 1.172 on 2 and 13 DF,  p-value: 0.3403
## Analysis of Variance Table
##
## Response: CPu
##              Df Sum Sq Mean Sq F value Pr(>F)
## Genotype      2  21249 10624.7  2.1134 0.1437
## Sex           1   2896  2895.7  0.5760 0.4556
## Genotype:Sex  2    995   497.4  0.0989 0.9062
## Residuals    23 115627  5027.3

## Analysis of Variance Table
##
## Response: CPu
##           Df  Sum Sq Mean Sq F value Pr(>F)
## Genotype   2  5540.7  2770.3  1.3631 0.2996
## Residuals 10 20323.4  2032.3

## Analysis of Variance Table
##
## Response: CPu
##           Df Sum Sq Mean Sq F value Pr(>F)
## Genotype   2  17189  8594.4  1.1723 0.3403
## Residuals 13  95304  7331.1
```

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

##
## Call:
## lm(formula = fi ~ Genotype * Sex, data = geno_combined_CLUS)
##
## Residuals:
##     Min     1Q Median     3Q    Max
## -91.418 -15.302  -0.618  14.281  76.223
##
## Coefficients:
##                        Estimate Std. Error t value Pr(>|t|)
## (Intercept)             122.792     16.260   7.552 1.14e-07 ***
## GenotypeAPOE33           29.185     26.552   1.099    0.283
## GenotypeAPOE44           13.000     22.995   0.565    0.577
## Sexmale                 -15.083     22.016  -0.685    0.500
## GenotypeAPOE33:Sexmale    4.005     34.492   0.116    0.909
## GenotypeAPOE44:Sexmale   30.475     31.835   0.957    0.348
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 36.36 on 23 degrees of freedom
## Multiple R-squared:  0.1967, Adjusted R-squared:  0.02203
## F-statistic: 1.126 on 5 and 23 DF,  p-value: 0.3745

##
## Call:
## lm(formula = fi ~ Genotype, data = combo_f_CLUS)
##
## Residuals:
##     Min     1Q Median     3Q    Max
## -50.937 -15.872  -3.082  10.638  76.223
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)    122.79      16.85   7.288 2.64e-05 ***
## GenotypeAPOE33  29.18      27.51   1.061    0.314
## GenotypeAPOE44  13.00      23.83   0.546    0.597
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 37.67 on 10 degrees of freedom
## Multiple R-squared:  0.1019, Adjusted R-squared:  -0.07773
## F-statistic: 0.5672 on 2 and 10 DF,  p-value: 0.5843

##
## Call:
## lm(formula = fi ~ Genotype, data = combo_m_CLUS)
##
## Residuals:
##     Min     1Q Median     3Q    Max
## -91.418 -10.512   5.327  25.267  35.282
##
## Coefficients:
##                 Estimate Std. Error t value Pr(>|t|)
```

```
## (Intercept)      107.71     14.42   7.471 4.69e-06 ***
## GenotypeAPOE33    33.19      21.38   1.552    0.145
## GenotypeAPOE44    43.48      21.38   2.033    0.063 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 35.31 on 13 degrees of freedom
## Multiple R-squared:  0.2626, Adjusted R-squared:  0.1492
## F-statistic: 2.315 on 2 and 13 DF,  p-value: 0.138

## Analysis of Variance Table
##
## Response: fi
##               Df  Sum Sq Mean Sq F value Pr(>F)
## Genotype       2  6000.5 3000.27  2.2696 0.1260
## Sex            1    77.3   77.30  0.0585 0.8111
## Genotype:Sex   2  1365.6  682.79  0.5165 0.6034
## Residuals     23 30404.0 1321.91

## Analysis of Variance Table
##
## Response: fi
##           Df Sum Sq Mean Sq F value Pr(>F)
## Genotype   2   1610  805.01  0.5672 0.5843
## Residuals 10  14192 1419.18

## Analysis of Variance Table
##
## Response: fi
##           Df  Sum Sq Mean Sq F value Pr(>F)
## Genotype   2  5774.7  2887.3  2.3153  0.138
## Residuals 13 16212.1  1247.1

## [1] "ic CLUS"

##
## Call:
## lm(formula = ic ~ Genotype * Sex, data = geno_combined_CLUS)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -56.732  -5.469  -0.669  10.092  40.447
##
## Coefficients:
##                       Estimate Std. Error t value Pr(>|t|)
## (Intercept)             94.638      8.392  11.277 7.56e-11 ***
## GenotypeAPOE33          33.855     13.704   2.470   0.0213 *
## GenotypeAPOE44           2.640     11.868   0.222   0.8259
## Sexmale                -17.184     11.363  -1.512   0.1441
## GenotypeAPOE33:Sexmale -11.950     17.802  -0.671   0.5087
## GenotypeAPOE44:Sexmale  10.595     16.431   0.645   0.5254
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 18.77 on 23 degrees of freedom
## Multiple R-squared:  0.4012, Adjusted R-squared:  0.271
```

```
## F-statistic: 3.082 on 5 and 23 DF,  p-value: 0.0284

##
## Call:
## lm(formula = ic ~ Genotype, data = combo_f_CLUS)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -24.073  -7.060  -1.994   3.992  40.447
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)    94.638      7.908  11.968    3e-07 ***
## GenotypeAPOE33 33.855     12.913   2.622   0.0255 *
## GenotypeAPOE44  2.640     11.183   0.236   0.8181
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 17.68 on 10 degrees of freedom
## Multiple R-squared:  0.4404, Adjusted R-squared:  0.3284
## F-statistic: 3.934 on 2 and 10 DF,  p-value: 0.0549

##
## Call:
## lm(formula = ic ~ Genotype, data = combo_m_CLUS)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -56.732  -5.268   2.275  10.825  19.429
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)    77.455      7.984   9.701 2.56e-07 ***
## GenotypeAPOE33 21.905     11.843   1.850   0.0872 .
## GenotypeAPOE44 13.235     11.843   1.118   0.2840
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 19.56 on 13 degrees of freedom
## Multiple R-squared:  0.213,  Adjusted R-squared:  0.09188
## F-statistic: 1.759 on 2 and 13 DF,  p-value: 0.2108

## Analysis of Variance Table
##
## Response: ic
##             Df Sum Sq Mean Sq F value  Pr(>F)
## Genotype     2 2920.8 1460.42  4.1472 0.02897 *
## Sex          1 1959.2 1959.22  5.5637 0.02721 *
## Genotype:Sex 2  546.1  273.03  0.7753 0.47222
## Residuals   23 8099.3  352.14
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

## Analysis of Variance Table
##
## Response: ic
```

```
##           Df Sum Sq Mean Sq F value Pr(>F)
## Genotype   2 2460.2 1230.10  3.9342 0.0549 .
## Residuals 10 3126.7  312.67
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

## Analysis of Variance Table
##
## Response: ic
##           Df Sum Sq Mean Sq F value Pr(>F)
## Genotype   2 1345.6  672.78  1.7589 0.2108
## Residuals 13 4972.6  382.51

## [1] "fx CLUS"

##
## Call:
## lm(formula = fx ~ Genotype * Sex, data = geno_combined_CLUS)
##
## Residuals:
##     Min     1Q  Median     3Q     Max
## -27.008  -6.689   1.052   6.705  31.356
##
## Coefficients:
##                      Estimate Std. Error t value Pr(>|t|)
## (Intercept)           49.8136     5.9088   8.430 1.73e-08 ***
## GenotypeAPOE33        14.1734     9.6490   1.469    0.155
## GenotypeAPOE44        13.0186     8.3563   1.558    0.133
## Sexmale               -0.9349     8.0005  -0.117    0.908
## GenotypeAPOE33:Sexmale -1.7829   12.5344  -0.142    0.888
## GenotypeAPOE44:Sexmale -2.4195   11.5687  -0.209    0.836
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 13.21 on 23 degrees of freedom
## Multiple R-squared:  0.2139, Adjusted R-squared:  0.04297
## F-statistic: 1.251 on 5 and 23 DF,  p-value: 0.3181

##
## Call:
## lm(formula = fx ~ Genotype, data = combo_f_CLUS)
##
## Residuals:
##      Min      1Q  Median      3Q      Max
## -21.2000 -10.1560  0.1914   6.7048  31.3560
##
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept)     49.814      7.137   6.980 3.81e-05 ***
## GenotypeAPOE33  14.173     11.655   1.216    0.252
## GenotypeAPOE44  13.019     10.093   1.290    0.226
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 15.96 on 10 degrees of freedom
## Multiple R-squared:  0.1801, Adjusted R-squared:  0.01606
```

```
## F-statistic: 1.098 on 2 and 10 DF,  p-value: 0.3706

##
## Call:
## lm(formula = fx ~ Genotype, data = combo_m_CLUS)
##
## Residuals:
##     Min     1Q  Median     3Q    Max
## -27.008  -4.717   2.044   6.893  11.441
##
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept)     48.879      4.339  11.266 4.44e-08 ***
## GenotypeAPOE33  12.391      6.435   1.925   0.0763 .
## GenotypeAPOE44  10.599      6.435   1.647   0.1235
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 10.63 on 13 degrees of freedom
## Multiple R-squared:  0.2554, Adjusted R-squared:  0.1408
## F-statistic: 2.229 on 2 and 13 DF,  p-value: 0.1471

## Analysis of Variance Table
##
## Response: fx
##              Df Sum Sq Mean Sq F value  Pr(>F)
## Genotype      2 1047.9  523.96  3.0015 0.06947 .
## Sex           1   36.2   36.19  0.2073 0.65316
## Genotype:Sex  2    8.2    4.09  0.0234 0.97688
## Residuals    23 4015.1  174.57
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

## Analysis of Variance Table
##
## Response: fx
##           Df  Sum Sq Mean Sq F value Pr(>F)
## Genotype   2  559.26  279.63  1.0979 0.3706
## Residuals 10 2546.85  254.69

## Analysis of Variance Table
##
## Response: fx
##           Df  Sum Sq Mean Sq F value Pr(>F)
## Genotype   2  503.51  251.76  2.2291 0.1471
## Residuals 13 1468.21  112.94
```

Note that the `echo = FALSE` parameter was added to the code chunk to prevent printing of the R code that generated the plot.