

Multiple Testing

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Preparation

Load the GEO GSE1572 Brain Aging study - transcriptional profiling of the human frontal cortex from individuals ranging from 26 to 106 years of age

<https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE1572>

Dataset - Transcript (RNA) abundance in aging human brain tissue samples

Load also the annotation file for this dataframe

```
dat <- read.table('./agingStudy11FCortexAffy.txt', header=T, row.names=1)
dim(dat)
```

```
## [1] 12625    30
```

```
#dat
dat[1:5,]
```

```
##          GSM27015.26.M GSM27016.26.M GSM27018.29.M GSM27021.37.M
## 31307_at      179.8630      106.4950      265.5860      301.2430
## 31308_at      559.0780      411.4830      481.1760      570.7330
## 31309_r_at     20.7697       30.6415       50.2153       42.6892
## 31310_at     154.1910     224.4460     188.8230     177.8630
## 31311_at     956.7970     648.3100     933.6560    1016.4100
##          GSM27023.40.M GSM27024.42.M GSM27025.45.M GSM27027.52.M
## 31307_at     218.5090     224.6100     256.0590     137.9230
## 31308_at     333.5390     370.0790     558.0270     310.9570
## 31309_r_at     27.1059      21.5762      10.6286      47.6724
## 31310_at     233.4630     120.9080     217.8070      66.0645
## 31311_at     762.0130    1040.2900    1058.2000     695.9470
##          GSM27028.53.M GSM27031.66.M GSM27032.70.M GSM27034.73.M
## 31307_at     139.180       50.7749      260.5160      226.349
## 31308_at     404.723      426.2720     478.3090     447.678
## 31309_r_at     11.073       39.8862       15.7331       47.437
## 31310_at     205.010      126.1900     196.9490     157.376
## 31311_at     1185.670     658.6110     881.6030     658.250
##          GSM27035.77.M GSM27036.80.M GSM27038.85.M GSM27040.90.M
## 31307_at     173.98100     192.7170     141.1460     229.2120
## 31308_at     479.22900     445.5770     505.1160     379.0360
## 31309_r_at      7.34582      42.8014      26.7969      24.2459
## 31310_at     195.44200     339.7540     161.6910     157.2240
## 31311_at     870.22500     812.7340     849.2230     922.9160
##          GSM27042.91.M GSM27043.95.M GSM27017.27.F GSM27019.30.F
```

```
## 31307_at      251.251      378.7240      323.9430      193.1300
## 31308_at      437.748      339.7580      295.5310      457.5170
## 31309_r_at     48.923       53.0538      42.7983      33.8314
## 31310_at      273.100      345.5750      167.6910      223.6410
## 31311_at      767.145      516.2440      643.6290      821.7430
##      GSM27020.36.F GSM27022.38.F GSM27026.48.F GSM27029.56.F
## 31307_at      196.1630      183.3520      127.5160      154.1870
## 31308_at      446.2050      391.7210      238.4240      511.7930
## 31309_r_at     33.8327      32.3855      23.8202      18.0976
## 31310_at      164.8950      152.4320      183.8300      233.1270
## 31311_at      789.4560      831.7770      1703.3100      859.2930
##      GSM27030.61.F GSM27033.71.F GSM27037.81.F GSM27039.87.F
## 31307_at      188.3010      152.1210      139.1030      199.679
## 31308_at      300.5500      468.0530      463.4340      525.637
## 31309_r_at     27.0145      13.8967      14.9957      19.525
## 31310_at      98.7380      230.4060      68.8964      245.693
## 31311_at      820.1260      1128.4400      854.6600      755.398
##      GSM27041.90.F GSM27044.106.F
## 31307_at      114.8440      217.9670
## 31308_at      373.7830      385.1110
## 31309_r_at     43.4167      55.4229
## 31310_at      447.8360      246.6050
## 31311_at      899.7910      790.3100
```

```
ann <- read.table('./agingStudy1FCortexAffyAnn.txt', header=T, row.names=1)
dim(ann)
```

```
## [1] 30 2
```

```
ann
```

```
##      Gender Age
## GSM27015      M 26
## GSM27016      M 26
## GSM27018      M 29
## GSM27021      M 37
## GSM27023      M 40
## GSM27024      M 42
## GSM27025      M 45
## GSM27027      M 52
## GSM27028      M 53
## GSM27031      M 66
## GSM27032      M 70
## GSM27034      M 73
## GSM27035      M 77
## GSM27036      M 80
## GSM27038      M 85
## GSM27040      M 90
## GSM27042      M 91
## GSM27043      M 95
## GSM27017      F 27
## GSM27019      F 30
## GSM27020      F 36
```

```
## GSM27022      F  38
## GSM27026      F  48
## GSM27029      F  56
## GSM27030      F  61
## GSM27033      F  71
## GSM27037      F  81
## GSM27039      F  87
## GSM27041      F  90
## GSM27044      F 106
```

Create 2 vectors for sample (group) comparison:

1. between male and female patients
2. between patients ≥ 50 years of age and those < 50 years of age.

```
M <- row.names(ann[ann$Gender == "M",]); F <- row.names(ann[ann$Gender == "F",])
M; F
```

```
## [1] "GSM27015" "GSM27016" "GSM27018" "GSM27021" "GSM27023" "GSM27024"
## [7] "GSM27025" "GSM27027" "GSM27028" "GSM27031" "GSM27032" "GSM27034"
## [13] "GSM27035" "GSM27036" "GSM27038" "GSM27040" "GSM27042" "GSM27043"

## [1] "GSM27017" "GSM27019" "GSM27020" "GSM27022" "GSM27026" "GSM27029"
## [7] "GSM27030" "GSM27033" "GSM27037" "GSM27039" "GSM27041" "GSM27044"
```

```
length(M); length(F)
```

```
## [1] 18
```

```
## [1] 12
```

```
O <- row.names(ann[ann$Age >=50,]); Y <- row.names(ann[ann$Age < 50,])
O; Y
```

```
## [1] "GSM27027" "GSM27028" "GSM27031" "GSM27032" "GSM27034" "GSM27035"
## [7] "GSM27036" "GSM27038" "GSM27040" "GSM27042" "GSM27043" "GSM27029"
## [13] "GSM27030" "GSM27033" "GSM27037" "GSM27039" "GSM27041" "GSM27044"

## [1] "GSM27015" "GSM27016" "GSM27018" "GSM27021" "GSM27023" "GSM27024"
## [7] "GSM27025" "GSM27017" "GSM27019" "GSM27020" "GSM27022" "GSM27026"
```

```
length(O); length(Y)
```

```
## [1] 18
```

```
## [1] 12
```

Gene vectors (indices of specific genes/rows) for gender and age comparisons:

```
g.g <- c(1394, 1474, 1917, 2099, 2367, 2428, 2625, 3168, 3181, 3641, 3832, 4526,
        4731, 4863, 6062, 6356, 6684, 6787, 6900, 7223, 7244, 7299, 8086, 8652,
        8959, 9073, 9145, 9389, 10219, 11238, 11669, 11674, 11793)

g.a <- c(25, 302, 1847, 2324, 246, 2757, 3222, 3675, 4429, 4430, 4912, 5640, 5835,
        5856, 6803, 7229, 7833, 8133, 8579, 8822, 8994, 10101, 11433, 12039, 12353,
        12404, 12442, 67, 88, 100)
```

Statistical hypothesis testing

Are there significant differences between the groups?

Calculate Student's two-sample t-test on all genes at once

```
# s1 and s2 are dimensions of the two samples/groups
# returns the p-value for the t-test
# p-value is a measure of the probability that an observed difference could have occurred
# just by random chance.
# The lower the p-value, the greater the statistical significance of the observed difference

t.test.all.genes <- function(x, s1, s2) {
  x1 <- x[s1]
  x2 <- x[s2]
  x1 <- as.numeric(x1)
  x2 <- as.numeric(x2)
  t.out <- t.test(x1, x2, alternative='two.sided', var.equal = TRUE)
  out <- as.numeric(t.out$p.value)
  return(out)
}
```

Gender comparison

```
dat2 <- dat[g.g,]
dim(dat2)
```

```
## [1] 33 30
```

```
names(dat2) <- substr(names(dat2),1,8)

# apply(X, MARGIN, FUN) MARGIN=1 on rows, =2 on columns
rawp.gender <- apply(dat2,1,t.test.all.genes,s1=M,s2=F)
length(rawp.gender)
```

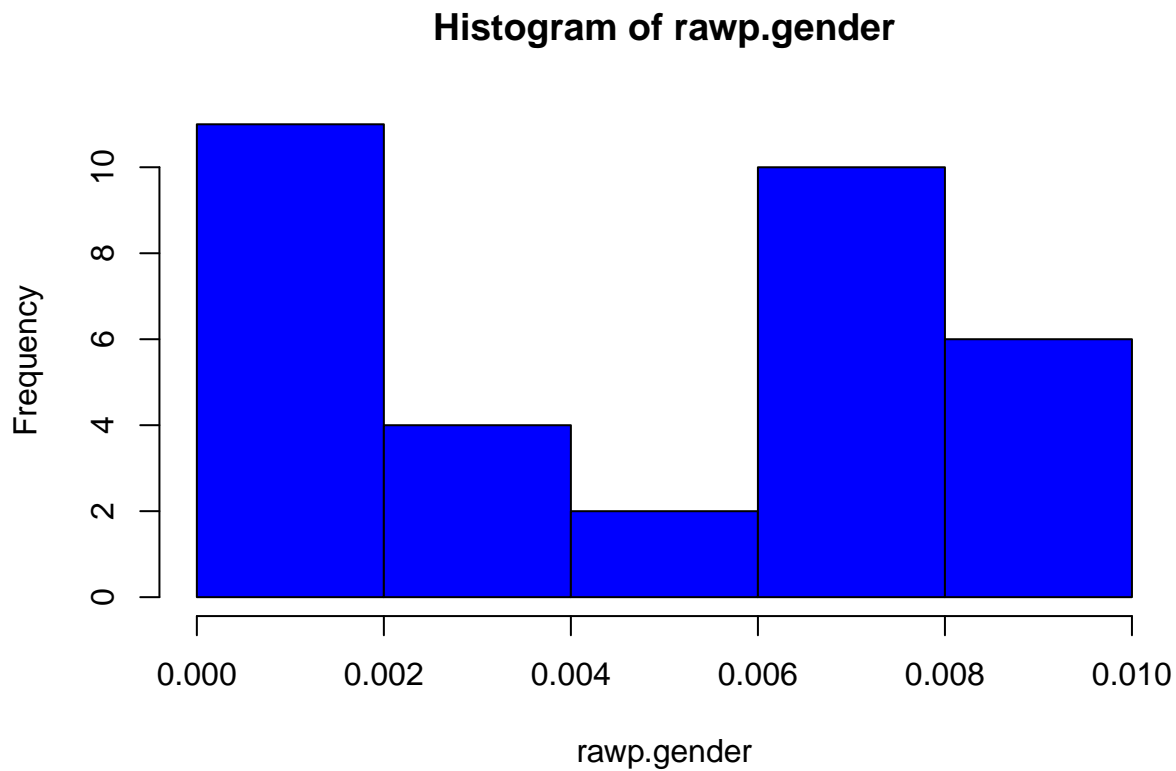
```
## [1] 33
```

```
rawp.gender
```

```
##      35570_at      36367_at      33937_at      34477_at      35465_at      35885_at
## 9.133044e-03 7.329210e-05 7.742819e-03 1.172742e-10 1.429817e-03 4.842837e-09
##      36321_at      38182_at      38195_at      39613_at      40044_at      31859_at
## 6.369457e-07 4.202946e-03 9.128972e-03 3.275208e-03 7.113820e-03 3.666085e-03
```

```
##      32660_at      33269_at      37583_at      38355_at      39402_at      39744_at
## 4.344341e-03 7.388762e-03 1.092557e-08 8.557945e-09 6.718808e-03 6.297030e-03
##      40097_at      41138_at      41159_at      41214_at      34870_at      36995_at
## 4.060825e-08 1.174762e-03 3.830846e-03 3.497619e-17 8.625123e-03 9.904404e-03
##      38020_at      38374_at      38446_at      39168_at      41556_s_at      1425_at
## 7.358727e-03 6.730852e-03 1.466001e-09 6.008340e-03 6.262977e-03 6.120252e-03
##      963_at      968_i_at      865_at
## 9.965919e-03 3.281164e-03 9.986787e-03
```

```
# look at distribution of p-values
hist(rawp.gender, col="blue")
```



Age comparison

```
dat3 <- dat[g.a,]
dim(dat3)
```

```
## [1] 30 30
```

```
names(dat3) <- substr(names(dat3),1,8)
```

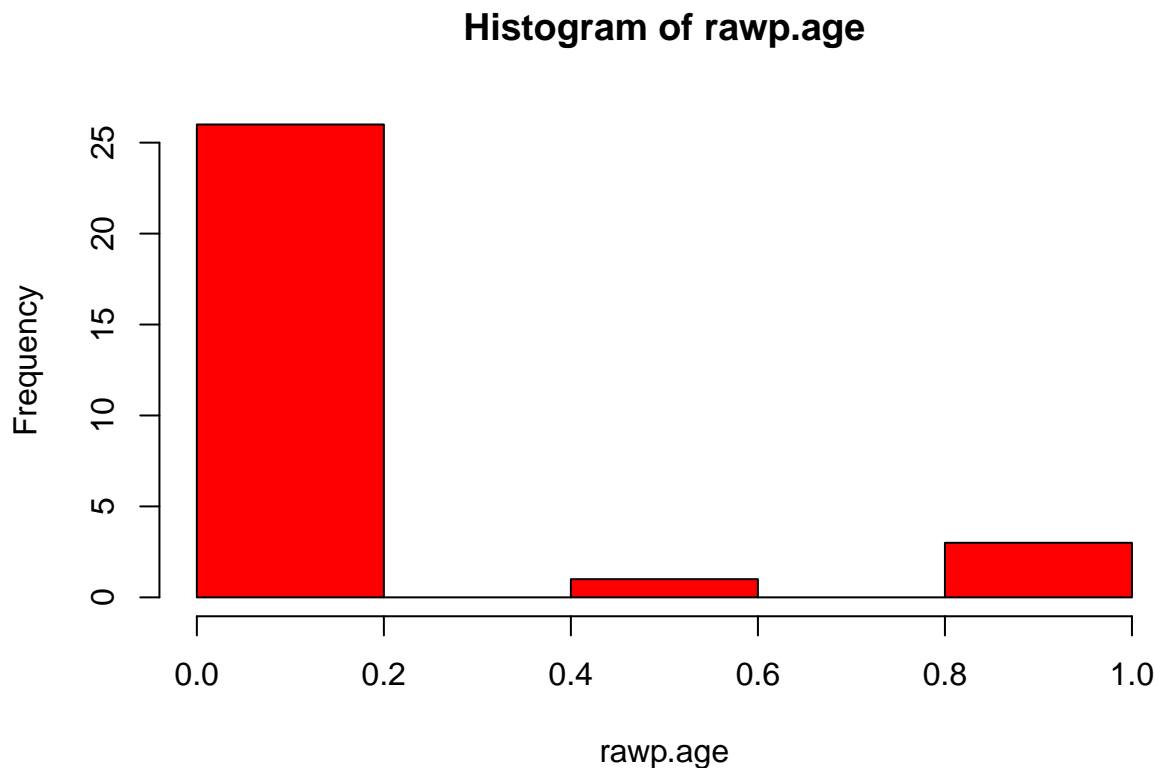
```
rawp.age <- apply(dat3,1,t.test.all.genes,s1=0,s2=Y)
length(rawp.age)
```

```
## [1] 30
```

```
rawp.age
```

```
##      31331_at      31608_g_at      33508_at      35422_at      31552_at      37053_at
## 1.888846e-01 2.324440e-05 2.009749e-05 6.328615e-05 8.325103e-01 2.362355e-05
##      38236_at      39647_s_at      41719_i_at      41720_r_at      33318_at      36083_at
## 1.120295e-05 4.043077e-05 3.956832e-05 1.194430e-05 2.992936e-05 3.313534e-05
##      36876_at      36897_at      39760_at      41144_g_at      33899_at      35277_at
## 8.613102e-05 2.402103e-05 9.338328e-05 7.430589e-05 5.165266e-05 1.446101e-05
##      36681_at      37405_at      38055_at      41318_g_at      1217_g_at      622_at
## 8.052295e-06 5.475056e-05 4.247644e-05 7.339560e-05 1.575925e-05 3.638745e-05
##       275_at       235_at       183_at      31373_at      31394_at      31406_at
## 1.543055e-05 3.100816e-05 6.585517e-05 8.316885e-01 9.162546e-01 5.754686e-01
```

```
# look at distribution of p-values
hist(rawp.age, col="red")
```



Multiple testing

When conducting a statistical test, under the null hypothesis (samples' means are equal), the p-value (observed significance) is the chance of getting a test statistic more extreme than the observed test statistic

When conducting a single statistical test, this probability is a good estimate

When conducting multiple statistical tests, the likelihood of getting a significant p-value increases due to the sheer number of independent tests: - Effect of testing too many genes can result in high false positive

rate - For 100 t-tests, the number of significant results occurring by chance at $\alpha=0.05$ is 5 - Alpha level (α) represents the probability of making a Type I error and is the p-value below which the null hypothesis that there is no difference between means is rejected. A p-value of 0.05 indicates accepting a 5% chance of being wrong when rejecting the null hypothesis. A p-value < 0.05 indicates rejection of the null hypothesis and existence of a significant difference.

There is a need to adjust the raw p-values (or criteria) to compensate for multiple tests (genes)

Adjust the raw p-values for multiple testing corrections with the Holm's step-down procedure for strong control of the family-wise Type I error rate (FWER)

FWER - the probability of at least one type I error (false positive) Type I error - incorrect rejection of a true null hypothesis

```
if (!requireNamespace("BiocManager", quietly = TRUE))
  install.packages("BiocManager")

BiocManager::install("multtest")
```

```
library(multtest)

procs <- c("Holm")
p.gender.mt.cor.h <- mt.rawp2adjp(rawp.gender,procs)
p.age.mt.cor.h <- mt.rawp2adjp(rawp.age,procs)
p.gender.mt.cor.h;p.age.mt.cor.h
```

```
## $adjp
##           rawp           Holm
## [1,] 3.497619e-17 1.154214e-15
## [2,] 1.172742e-10 3.752775e-09
## [3,] 1.466001e-09 4.544603e-08
## [4,] 4.842837e-09 1.452851e-07
## [5,] 8.557945e-09 2.481804e-07
## [6,] 1.092557e-08 3.059159e-07
## [7,] 4.060825e-08 1.096423e-06
## [8,] 6.369457e-07 1.656059e-05
## [9,] 7.329210e-05 1.832303e-03
## [10,] 1.174762e-03 2.819430e-02
## [11,] 1.429817e-03 3.288579e-02
## [12,] 3.275208e-03 7.205458e-02
## [13,] 3.281164e-03 7.205458e-02
## [14,] 3.666085e-03 7.332169e-02
## [15,] 3.830846e-03 7.332169e-02
## [16,] 4.202946e-03 7.565303e-02
## [17,] 4.344341e-03 7.565303e-02
## [18,] 6.008340e-03 9.613344e-02
## [19,] 6.120252e-03 9.613344e-02
## [20,] 6.262977e-03 9.613344e-02
## [21,] 6.297030e-03 9.613344e-02
## [22,] 6.718808e-03 9.613344e-02
## [23,] 6.730852e-03 9.613344e-02
## [24,] 7.113820e-03 9.613344e-02
## [25,] 7.358727e-03 9.613344e-02
## [26,] 7.388762e-03 9.613344e-02
## [27,] 7.742819e-03 9.613344e-02
```

```

## [28,] 8.625123e-03 9.613344e-02
## [29,] 9.128972e-03 9.613344e-02
## [30,] 9.133044e-03 9.613344e-02
## [31,] 9.904404e-03 9.613344e-02
## [32,] 9.965919e-03 9.613344e-02
## [33,] 9.986787e-03 9.613344e-02
##
## $index
## [1] 22 4 27 6 16 15 19 7 2 20 5 10 32 12 21 8 13 28 30 29 18 17 26 11 25
## [26] 14 3 23 9 1 24 31 33
##
## $h0.ABH
## NULL
##
## $h0.TSBH
## NULL

## $adjp
##          rawp          Holm
## [1,] 8.052295e-06 0.0002415688
## [2,] 1.120295e-05 0.0003248855
## [3,] 1.194430e-05 0.0003344405
## [4,] 1.446101e-05 0.0003904471
## [5,] 1.543055e-05 0.0004011944
## [6,] 1.575925e-05 0.0004011944
## [7,] 2.009749e-05 0.0004823398
## [8,] 2.324440e-05 0.0005346211
## [9,] 2.362355e-05 0.0005346211
## [10,] 2.402103e-05 0.0005346211
## [11,] 2.992936e-05 0.0005985871
## [12,] 3.100816e-05 0.0005985871
## [13,] 3.313534e-05 0.0005985871
## [14,] 3.638745e-05 0.0006185867
## [15,] 3.956832e-05 0.0006330930
## [16,] 4.043077e-05 0.0006330930
## [17,] 4.247644e-05 0.0006330930
## [18,] 5.165266e-05 0.0006714846
## [19,] 5.475056e-05 0.0006714846
## [20,] 6.328615e-05 0.0006961476
## [21,] 6.585517e-05 0.0006961476
## [22,] 7.339560e-05 0.0006961476
## [23,] 7.430589e-05 0.0006961476
## [24,] 8.613102e-05 0.0006961476
## [25,] 9.338328e-05 0.0006961476
## [26,] 1.888846e-01 0.9444230890
## [27,] 5.754686e-01 1.0000000000
## [28,] 8.316885e-01 1.0000000000
## [29,] 8.325103e-01 1.0000000000
## [30,] 9.162546e-01 1.0000000000
##
## $index
## [1] 19 7 10 18 25 23 3 2 6 14 11 26 12 24 9 8 21 17 20 4 27 22 16 13 15
## [26] 1 30 28 5 29
##

```



```
## $h0.ABH
## NULL
##
## $h0.TSBH
## NULL
```

The `mt.rawp2adjp` function sorts the raw and adjusted p-values and returns a list with components:

`adjp` A matrix of adjusted p-values, with rows corresponding to hypotheses (genes) and columns to multiple testing procedures. Hypotheses are sorted in increasing order of their raw (unadjusted) p-values.

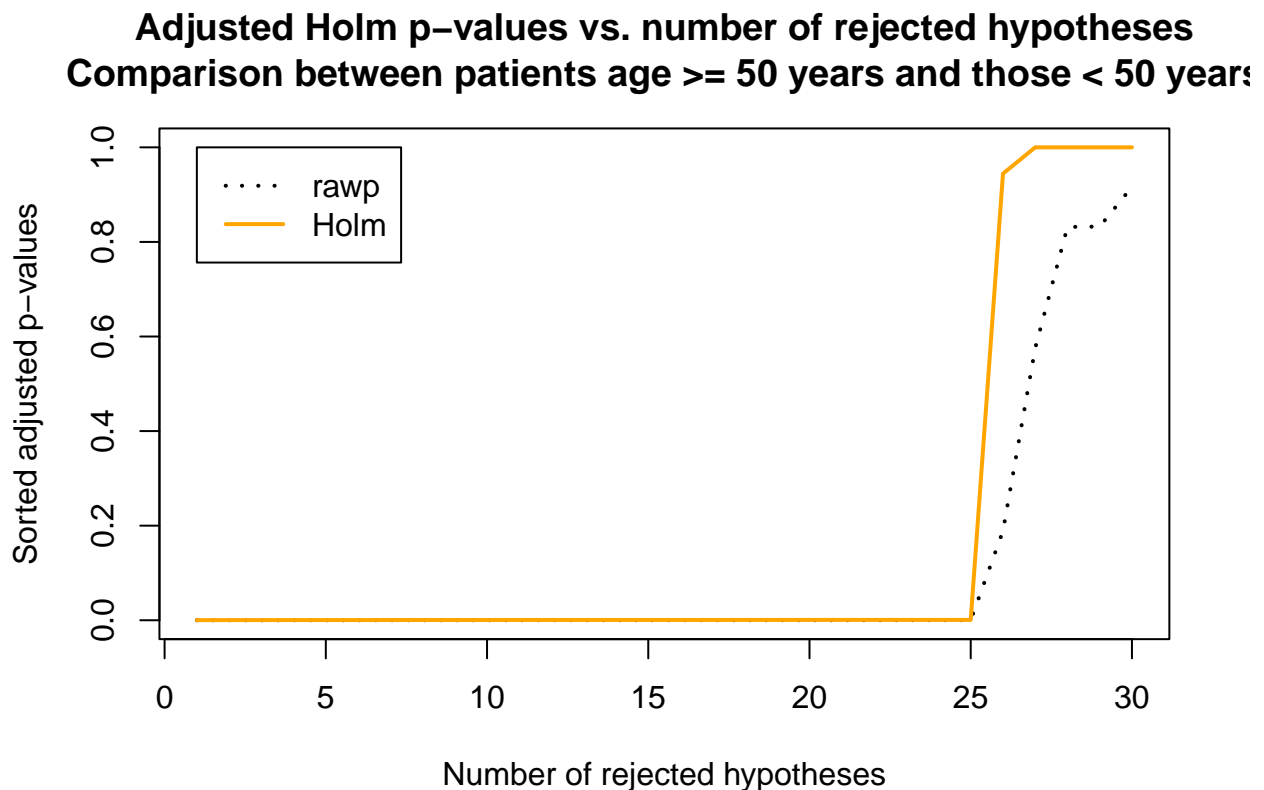
`index` A vector of row indices, between 1 and `length(rawp)`, where rows are sorted according to their raw (unadjusted) p-values. To obtain the adjusted p-values in the original data order, use `adjp[order(index),]`.

`as.data.frame(p.gender.mt.cor.h$adjp)$Holm` – gives the sorted adjusted p-values

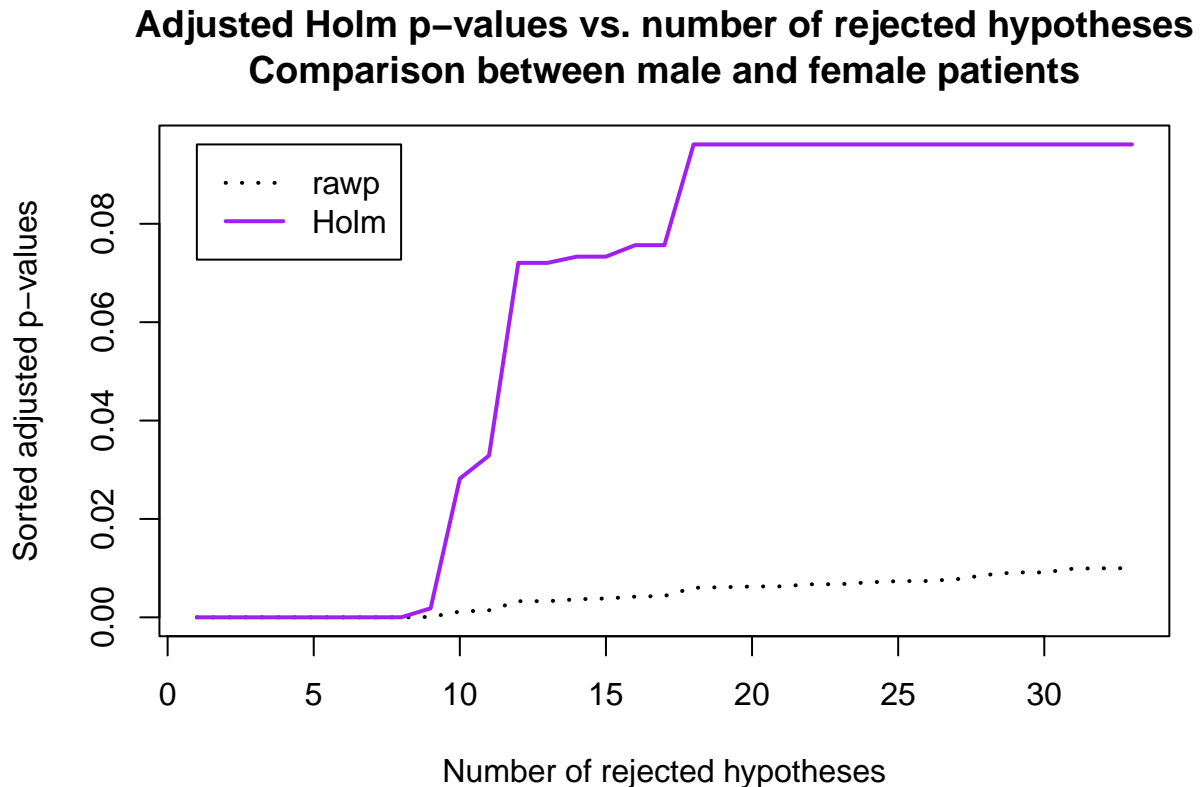
`as.data.frame(p.gender.mt.cor.h$adjp)$rawp` – gives the sorted non-adjusted p-values

Plotting results from multiple testing procedures

```
procs <- c("rawp","Holm")
cols <- c("black","orange")
ltypes <- c(3,1)
mt.plot(p.age.mt.cor.h$adjp, plottype='pvsr',proc=procs,
        leg=c(1, max(as.data.frame(p.age.mt.cor.h$adjp)$Holm)), lty=ltypes,col=cols,lwd=2,
        main="Adjusted Holm p-values vs. number of rejected hypotheses\nComparison between patients age
```



```
procs <- c("rawp","Holm")
cols <- c("black","purple")
ltyes <- c(3,1)
mt.plot(p.gender.mt.cor.h$adjp, plottype='pvsr',proc=procs,
        leg=c(1, max(as.data.frame(p.gender.mt.cor.h$adjp)$Holm)), lty=ltyes,col=cols,lwd=2,
        main="Adjusted Holm p-values vs. number of rejected hypotheses\nComparison between male and female patients")
```



Adjust the raw p-values for multiple testing corrections with the Bonferroni's single step procedure for strong control of the family-wise Type I error rate (FWER)

Only dependent on the number of tests (genes)

More conservative method compared to Holm's: - p-values larger reducing the possibility of getting a statistically significant result - appropriate when a single false positive would be a problem - useful for small number of multiple comparisons and looking for one or two that might be significant

```
#library(multtest)

procs <- c("Bonferroni")
p.gender.mt.cor.b <- mt.rawp2adjp(rawp.gender,procs)
p.age.mt.cor.b <- mt.rawp2adjp(rawp.age,procs)
p.gender.mt.cor.b;p.age.mt.cor.b
```

```
## $adjp
##          rawp  Bonferroni
## [1,] 3.497619e-17 1.154214e-15
```

```

## [2,] 1.172742e-10 3.870049e-09
## [3,] 1.466001e-09 4.837803e-08
## [4,] 4.842837e-09 1.598136e-07
## [5,] 8.557945e-09 2.824122e-07
## [6,] 1.092557e-08 3.605438e-07
## [7,] 4.060825e-08 1.340072e-06
## [8,] 6.369457e-07 2.101921e-05
## [9,] 7.329210e-05 2.418639e-03
## [10,] 1.174762e-03 3.876716e-02
## [11,] 1.429817e-03 4.718396e-02
## [12,] 3.275208e-03 1.080819e-01
## [13,] 3.281164e-03 1.082784e-01
## [14,] 3.666085e-03 1.209808e-01
## [15,] 3.830846e-03 1.264179e-01
## [16,] 4.202946e-03 1.386972e-01
## [17,] 4.344341e-03 1.433633e-01
## [18,] 6.008340e-03 1.982752e-01
## [19,] 6.120252e-03 2.019683e-01
## [20,] 6.262977e-03 2.066782e-01
## [21,] 6.297030e-03 2.078020e-01
## [22,] 6.718808e-03 2.217207e-01
## [23,] 6.730852e-03 2.221181e-01
## [24,] 7.113820e-03 2.347561e-01
## [25,] 7.358727e-03 2.428380e-01
## [26,] 7.388762e-03 2.438291e-01
## [27,] 7.742819e-03 2.555130e-01
## [28,] 8.625123e-03 2.846291e-01
## [29,] 9.128972e-03 3.012561e-01
## [30,] 9.133044e-03 3.013905e-01
## [31,] 9.904404e-03 3.268453e-01
## [32,] 9.965919e-03 3.288753e-01
## [33,] 9.986787e-03 3.295640e-01
##
## $index
## [1] 22 4 27 6 16 15 19 7 2 20 5 10 32 12 21 8 13 28 30 29 18 17 26 11 25
## [26] 14 3 23 9 1 24 31 33
##
## $h0.ABH
## NULL
##
## $h0.TSBH
## NULL

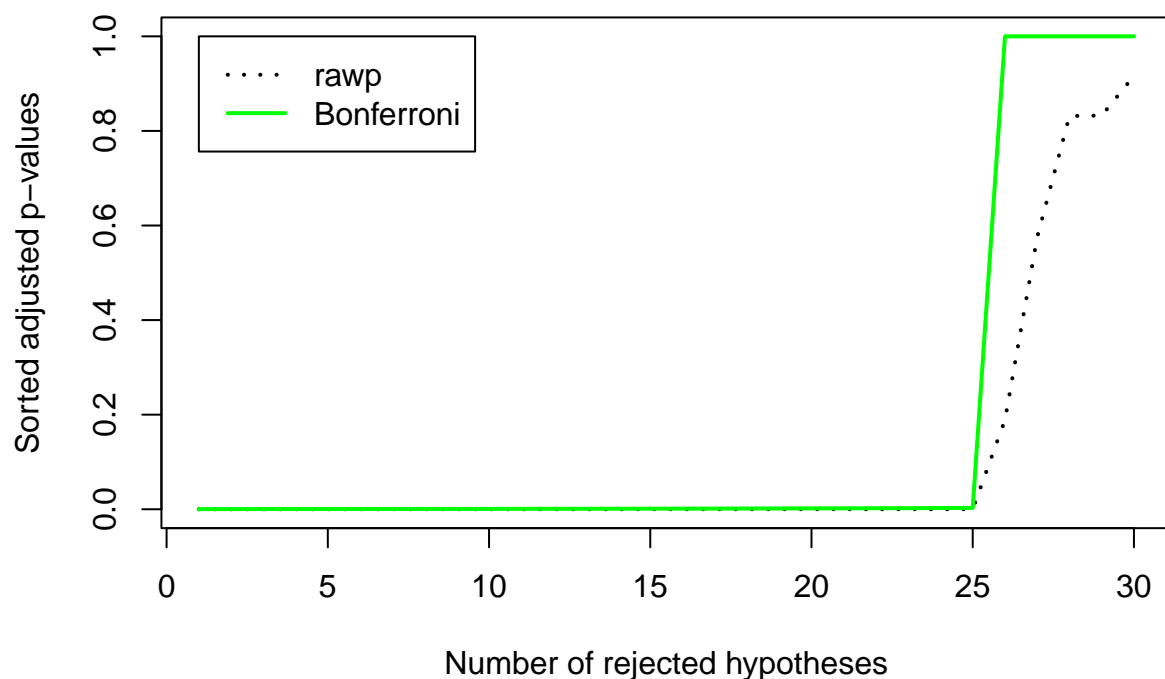
## $adjp
##          rawp      Bonferroni
## [1,] 8.052295e-06 0.0002415688
## [2,] 1.120295e-05 0.0003360885
## [3,] 1.194430e-05 0.0003583291
## [4,] 1.446101e-05 0.0004338302
## [5,] 1.543055e-05 0.0004629166
## [6,] 1.575925e-05 0.0004727775
## [7,] 2.009749e-05 0.0006029247
## [8,] 2.324440e-05 0.0006973319
## [9,] 2.362355e-05 0.0007087064

```

```
## [10,] 2.402103e-05 0.0007206309
## [11,] 2.992936e-05 0.0008978807
## [12,] 3.100816e-05 0.0009302448
## [13,] 3.313534e-05 0.0009940601
## [14,] 3.638745e-05 0.0010916235
## [15,] 3.956832e-05 0.0011870495
## [16,] 4.043077e-05 0.0012129230
## [17,] 4.247644e-05 0.0012742931
## [18,] 5.165266e-05 0.0015495799
## [19,] 5.475056e-05 0.0016425168
## [20,] 6.328615e-05 0.0018985845
## [21,] 6.585517e-05 0.0019756550
## [22,] 7.339560e-05 0.0022018679
## [23,] 7.430589e-05 0.0022291766
## [24,] 8.613102e-05 0.0025839305
## [25,] 9.338328e-05 0.0028014985
## [26,] 1.888846e-01 1.0000000000
## [27,] 5.754686e-01 1.0000000000
## [28,] 8.316885e-01 1.0000000000
## [29,] 8.325103e-01 1.0000000000
## [30,] 9.162546e-01 1.0000000000
##
## $index
## [1] 19 7 10 18 25 23 3 2 6 14 11 26 12 24 9 8 21 17 20 4 27 22 16 13 15
## [26] 1 30 28 5 29
##
## $h0.ABH
## NULL
##
## $h0.TSBH
## NULL
```

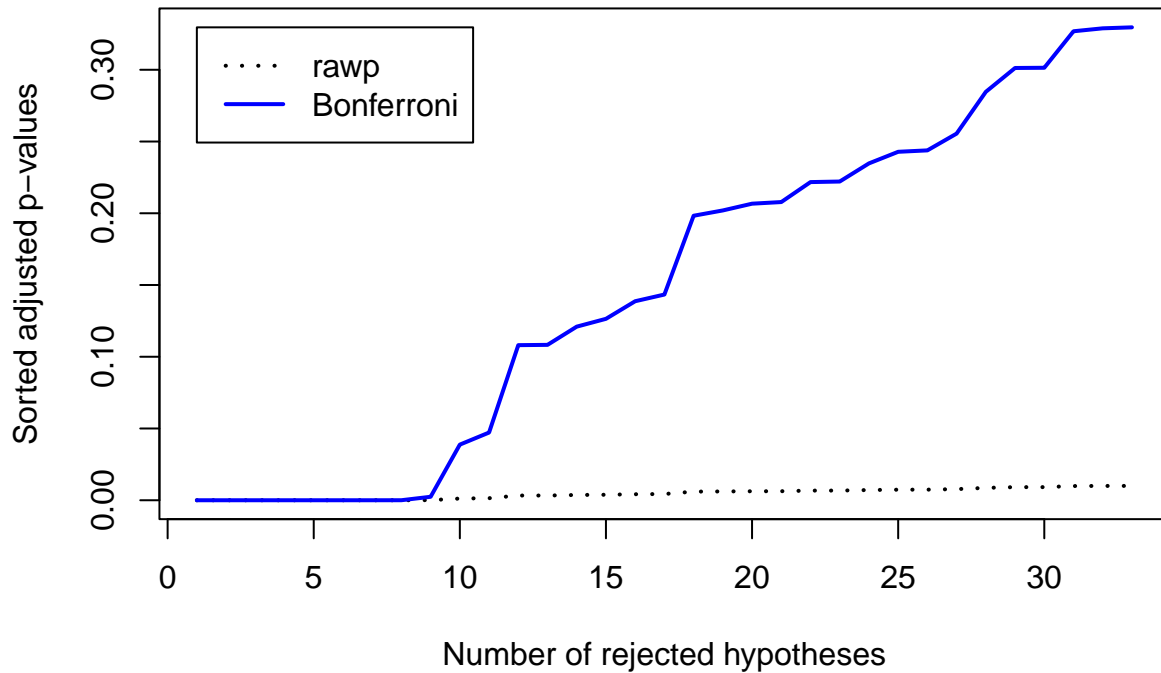
```
procs <- c("rawp","Bonferroni")
cols <- c("black","green")
ltypes <- c(3,1)
mt.plot(p.age.mt.cor.b$adjp, plottype='pvsr',proc=procs,
        leg=c(1, max(as.data.frame(p.age.mt.cor.b$adjp)$Bonferroni)), lty=ltypes,col=cols,lwd=2,
        main="Adjusted Bonferroni p-values vs. number of rejected hypotheses\nComparison between patient
```

Adjusted Bonferroni p-values vs. number of rejected hypotheses Comparison between patients age ≥ 50 years and those < 50 years



```
procs <- c("rawp","Bonferroni")
cols <- c("black","blue")
ltyes <- c(3,1)
mt.plot(p.gender.mt.cor.b$adjp, plottype='pvsr',proc=procs,
       leg=c(1, max(as.data.frame(p.gender.mt.cor.b$adjp)$Bonferroni)),
       lty=ltyes,col=cols,lwd=2, main="Adjusted Bonferroni p-values vs. number of rejected hypotheses")
```

Adjusted Bonferroni p-values vs. number of rejected hypotheses Comparison between male and female patients



```
#library(multtest)
```

```
procs <- c("Bonferroni", "Holm")
p.gender.mt.cor.bh <- mt.rawp2adjp(rawp.gender,procs)
p.age.mt.cor.bh <- mt.rawp2adjp(rawp.age,procs)
p.gender.mt.cor.bh;p.age.mt.cor.bh
```

```
## $adjp
##          rawp    Bonferroni      Holm
## [1,] 3.497619e-17 1.154214e-15 1.154214e-15
## [2,] 1.172742e-10 3.870049e-09 3.752775e-09
## [3,] 1.466001e-09 4.837803e-08 4.544603e-08
## [4,] 4.842837e-09 1.598136e-07 1.452851e-07
## [5,] 8.557945e-09 2.824122e-07 2.481804e-07
## [6,] 1.092557e-08 3.605438e-07 3.059159e-07
## [7,] 4.060825e-08 1.340072e-06 1.096423e-06
## [8,] 6.369457e-07 2.101921e-05 1.656059e-05
## [9,] 7.329210e-05 2.418639e-03 1.832303e-03
## [10,] 1.174762e-03 3.876716e-02 2.819430e-02
## [11,] 1.429817e-03 4.718396e-02 3.288579e-02
## [12,] 3.275208e-03 1.080819e-01 7.205458e-02
## [13,] 3.281164e-03 1.082784e-01 7.205458e-02
## [14,] 3.666085e-03 1.209808e-01 7.332169e-02
## [15,] 3.830846e-03 1.264179e-01 7.332169e-02
## [16,] 4.202946e-03 1.386972e-01 7.565303e-02
```

```

## [17,] 4.344341e-03 1.433633e-01 7.565303e-02
## [18,] 6.008340e-03 1.982752e-01 9.613344e-02
## [19,] 6.120252e-03 2.019683e-01 9.613344e-02
## [20,] 6.262977e-03 2.066782e-01 9.613344e-02
## [21,] 6.297030e-03 2.078020e-01 9.613344e-02
## [22,] 6.718808e-03 2.217207e-01 9.613344e-02
## [23,] 6.730852e-03 2.221181e-01 9.613344e-02
## [24,] 7.113820e-03 2.347561e-01 9.613344e-02
## [25,] 7.358727e-03 2.428380e-01 9.613344e-02
## [26,] 7.388762e-03 2.438291e-01 9.613344e-02
## [27,] 7.742819e-03 2.555130e-01 9.613344e-02
## [28,] 8.625123e-03 2.846291e-01 9.613344e-02
## [29,] 9.128972e-03 3.012561e-01 9.613344e-02
## [30,] 9.133044e-03 3.013905e-01 9.613344e-02
## [31,] 9.904404e-03 3.268453e-01 9.613344e-02
## [32,] 9.965919e-03 3.288753e-01 9.613344e-02
## [33,] 9.986787e-03 3.295640e-01 9.613344e-02
##
## $index
## [1] 22 4 27 6 16 15 19 7 2 20 5 10 32 12 21 8 13 28 30 29 18 17 26 11 25
## [26] 14 3 23 9 1 24 31 33
##
## $h0.ABH
## NULL
##
## $h0.TSBH
## NULL

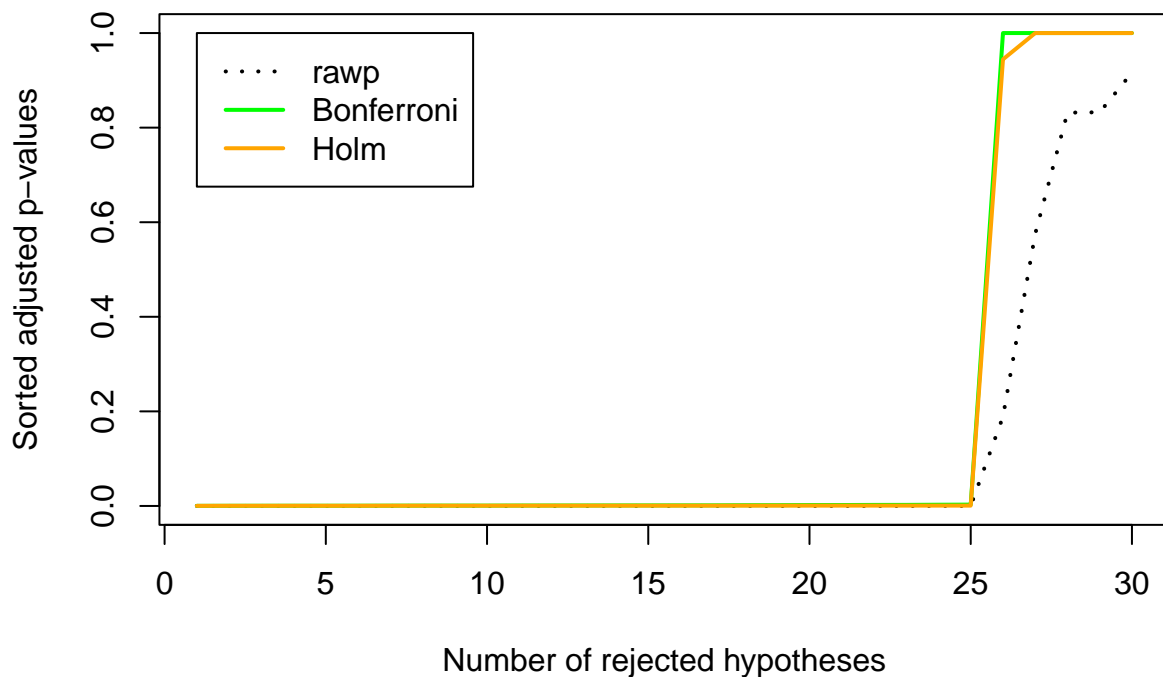
## $adjp
##          rawp      Bonferroni      Holm
## [1,] 8.052295e-06 0.0002415688 0.0002415688
## [2,] 1.120295e-05 0.0003360885 0.0003248855
## [3,] 1.194430e-05 0.0003583291 0.0003344405
## [4,] 1.446101e-05 0.0004338302 0.0003904471
## [5,] 1.543055e-05 0.0004629166 0.0004011944
## [6,] 1.575925e-05 0.0004727775 0.0004011944
## [7,] 2.009749e-05 0.0006029247 0.0004823398
## [8,] 2.324440e-05 0.0006973319 0.0005346211
## [9,] 2.362355e-05 0.0007087064 0.0005346211
## [10,] 2.402103e-05 0.0007206309 0.0005346211
## [11,] 2.992936e-05 0.0008978807 0.0005985871
## [12,] 3.100816e-05 0.0009302448 0.0005985871
## [13,] 3.313534e-05 0.0009940601 0.0005985871
## [14,] 3.638745e-05 0.0010916235 0.0006185867
## [15,] 3.956832e-05 0.0011870495 0.0006330930
## [16,] 4.043077e-05 0.0012129230 0.0006330930
## [17,] 4.247644e-05 0.0012742931 0.0006330930
## [18,] 5.165266e-05 0.0015495799 0.0006714846
## [19,] 5.475056e-05 0.0016425168 0.0006714846
## [20,] 6.328615e-05 0.0018985845 0.0006961476
## [21,] 6.585517e-05 0.0019756550 0.0006961476
## [22,] 7.339560e-05 0.0022018679 0.0006961476
## [23,] 7.430589e-05 0.0022291766 0.0006961476
## [24,] 8.613102e-05 0.0025839305 0.0006961476

```

```
## [25,] 9.338328e-05 0.0028014985 0.0006961476
## [26,] 1.888846e-01 1.0000000000 0.9444230890
## [27,] 5.754686e-01 1.0000000000 1.0000000000
## [28,] 8.316885e-01 1.0000000000 1.0000000000
## [29,] 8.325103e-01 1.0000000000 1.0000000000
## [30,] 9.162546e-01 1.0000000000 1.0000000000
##
## $index
## [1] 19 7 10 18 25 23 3 2 6 14 11 26 12 24 9 8 21 17 20 4 27 22 16 13 15
## [26] 1 30 28 5 29
##
## $h0.ABH
## NULL
##
## $h0.TSBH
## NULL
```

```
procs <- c("rawp", "Bonferroni", "Holm")
cols <- c("black", "green", "orange")
ltypes <- c(3, rep(1, 2))
mt.plot(p.age.mt.cor.bh$adjp, plottype='pvsr', proc=procs,
        leg=c(1, max(max(as.data.frame(p.age.mt.cor.bh$adjp)$Bonferroni),
                        max(as.data.frame(p.age.mt.cor.bh$adjp)$Holm))), lty=ltypes, col=cols, lwd=2,
        main="Adjusted p-values (Type I Error Rate) vs. number of rejected hypotheses\nComparison between
```

Adjusted p-values (Type I Error Rate) vs. number of rejected hypotheses Comparison between patients age ≥ 50 years and those < 50 years




```

procs<-c("rawp","Bonferroni", "Holm")
cols<-c("black","blue", "purple")
ltypes<-c(3,rep(1,2))
mt.plot(p.gender.mt.cor.bh$adjp, plottype='pvsr',proc=procs,
        leg=c(1, max(max(as.data.frame(p.gender.mt.cor.bh$adjp)$Bonferroni),
                        max(as.data.frame(p.gender.mt.cor.bh$adjp)$Holm))), lty=ltypes,col=cols,lwd=2,
        main="Adjusted p-values (Type I Error Rate) vs. number of rejected hypotheses\nComparison between

```

Adjusted p-values (Type I Error Rate) vs. number of rejected hypotheses Comparison between male and female patients

