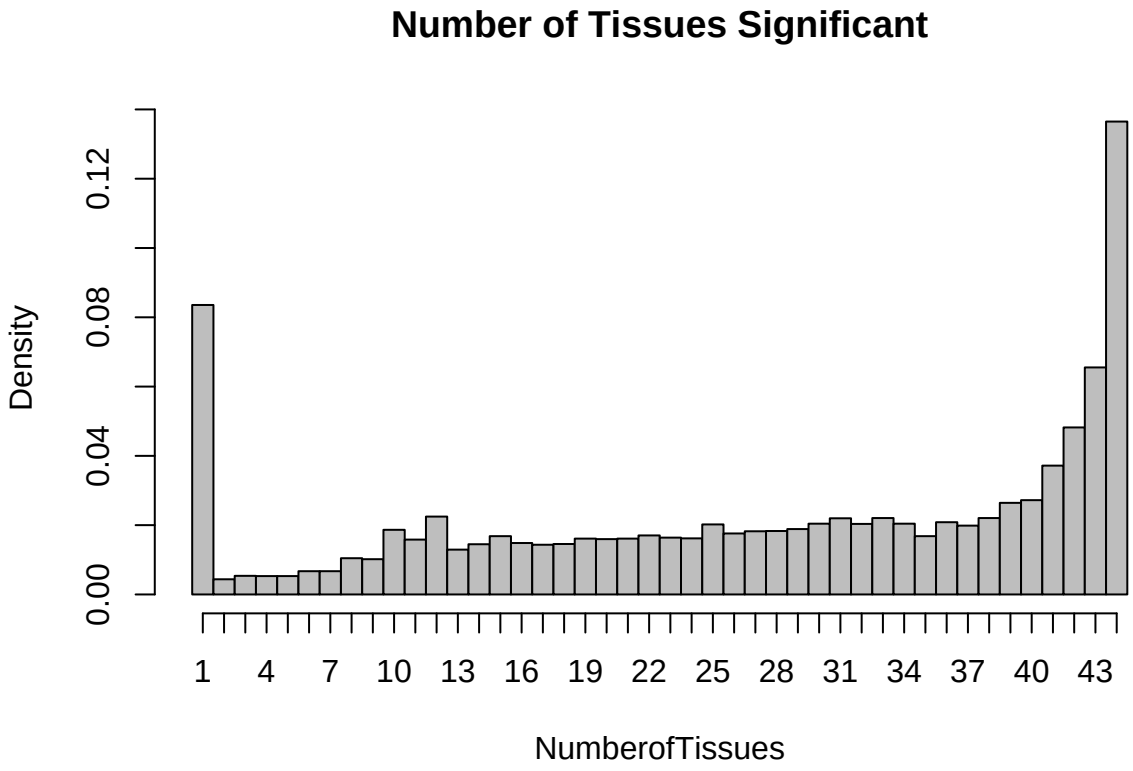
heterogeneitywithandwithoutbrainformatthew

Heterogeneity Analysis

First, we asked in how many tissues is a QTL signficiant.

```
##  [1] FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE
## [12] FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE
## [23] FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE
## [34] FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE
```



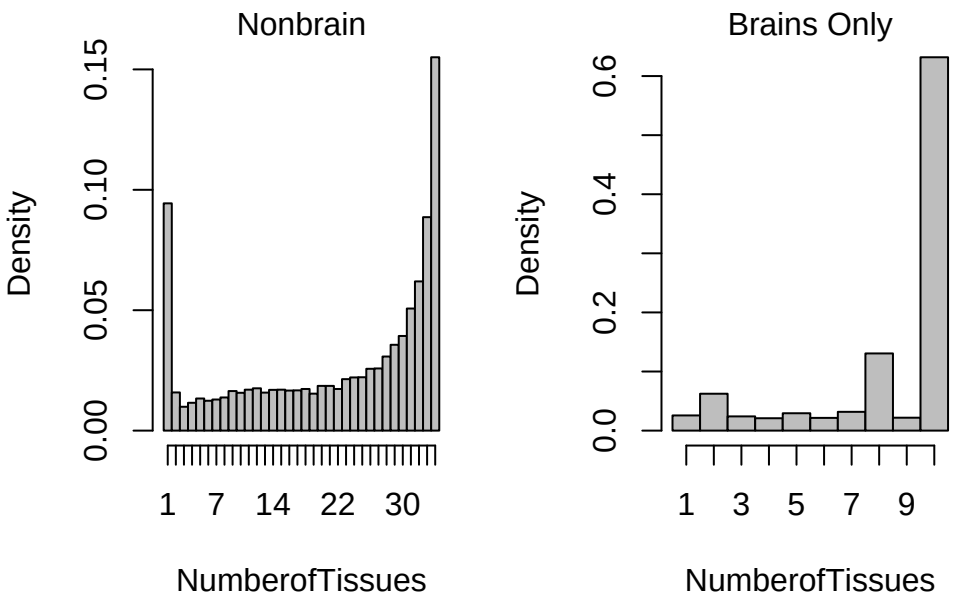

```
## [1] 0.6320675
```

Now make plot of lfsr for other groups of tissues and the comparison plot of Number of QTLs significant between Analysis subtype.

```
## [1] 0.6471221
```

```
## [1] 0.8364146
```

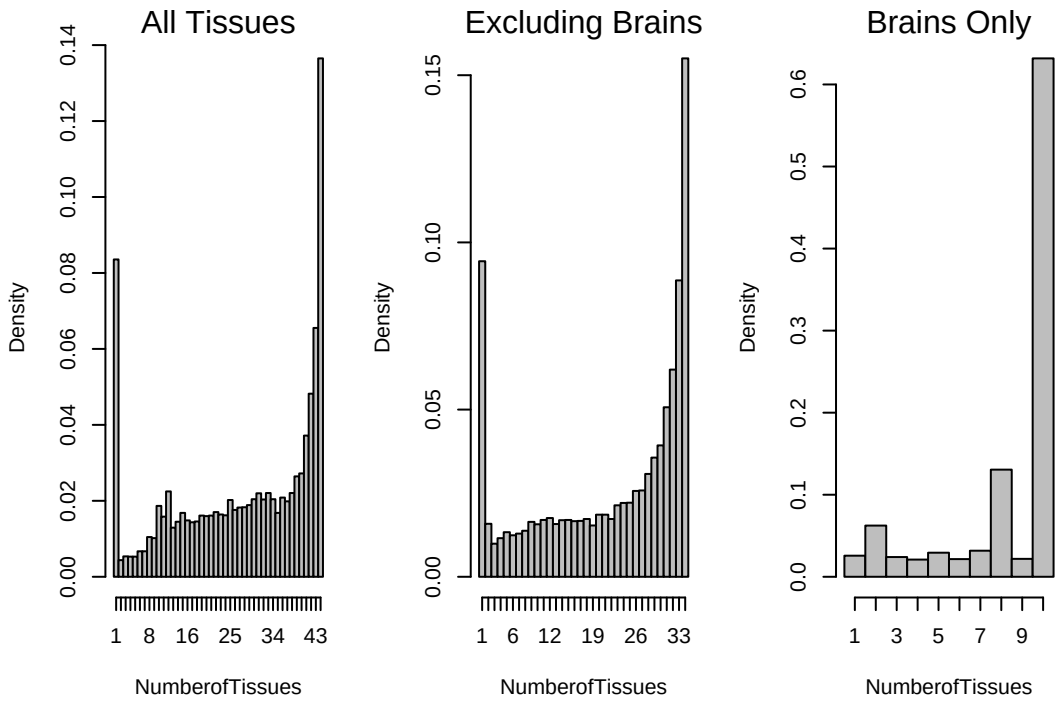
Number of Tissues Significant




```
## [1] 0.6471221
```

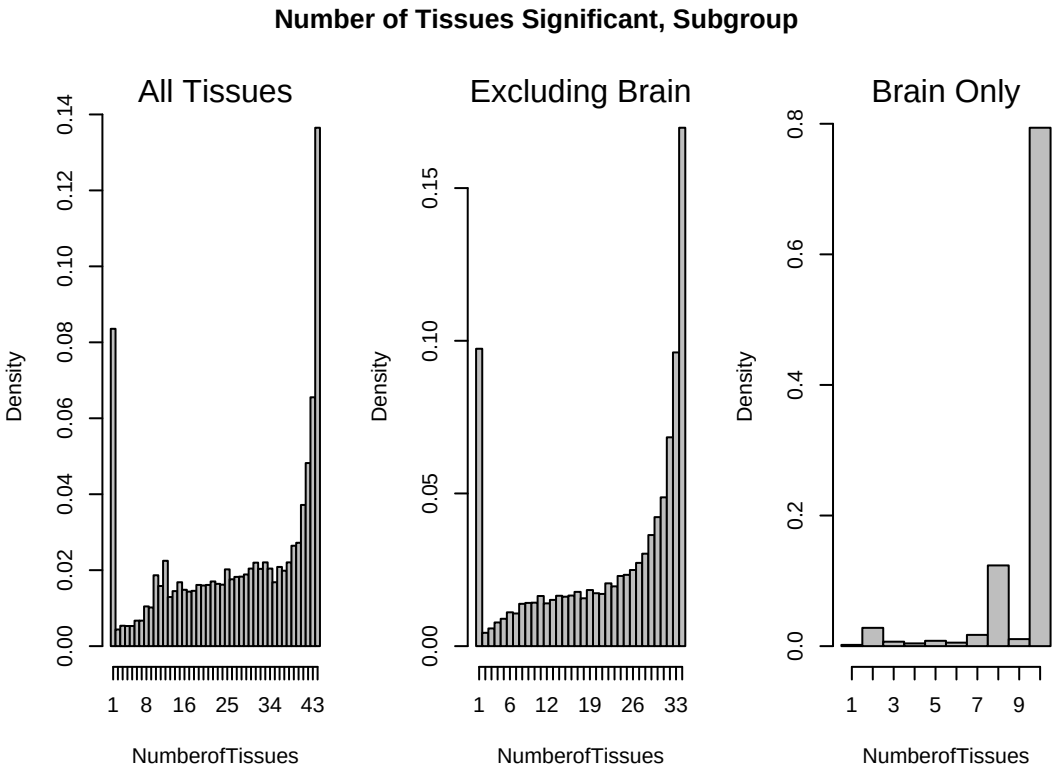
```
## [1] 0.8364146
```

Number of Tissues Significant, All Tissue




```
## [1] 0.6320675
```

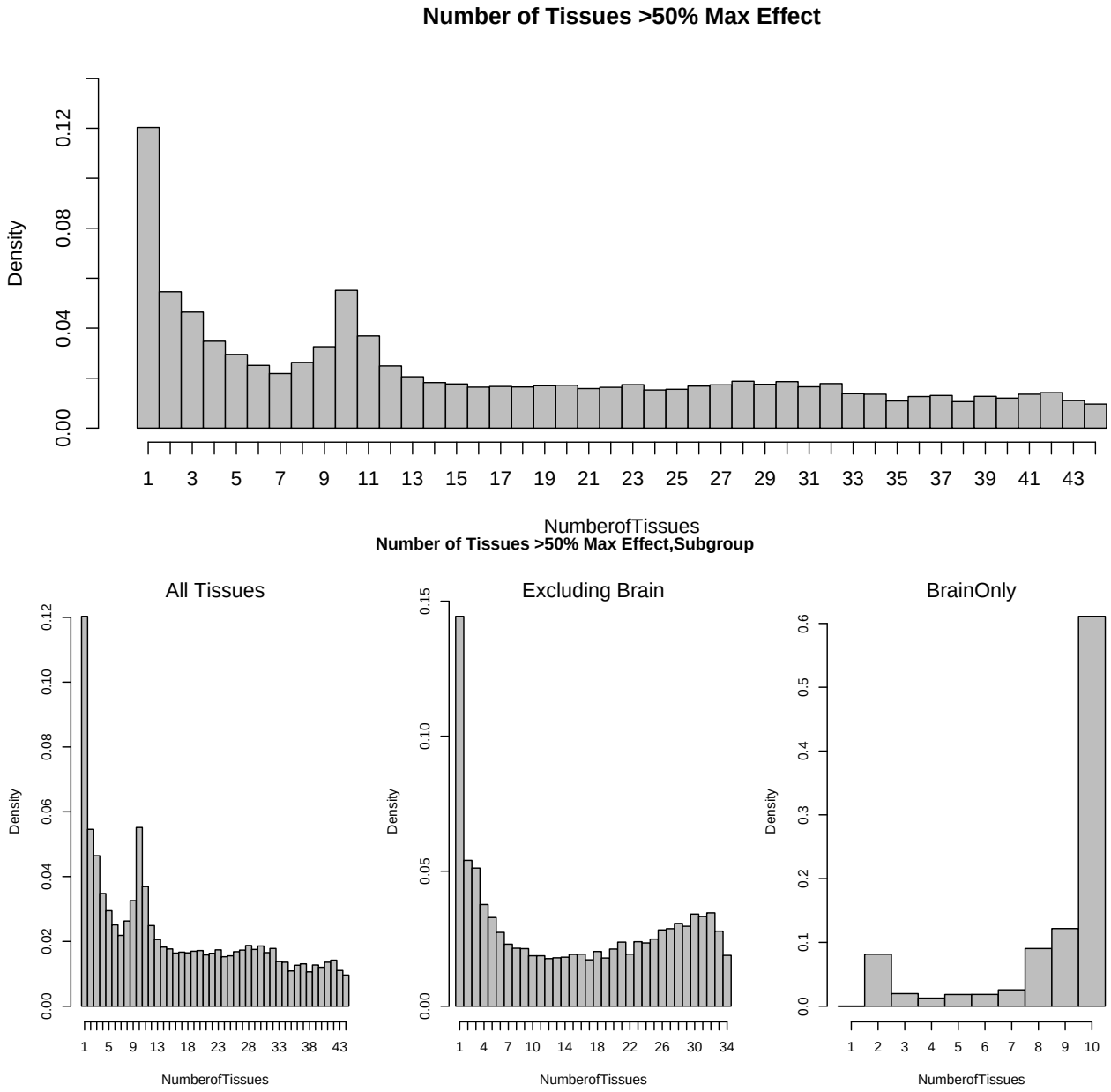
```
## [1] 0.6730104
```

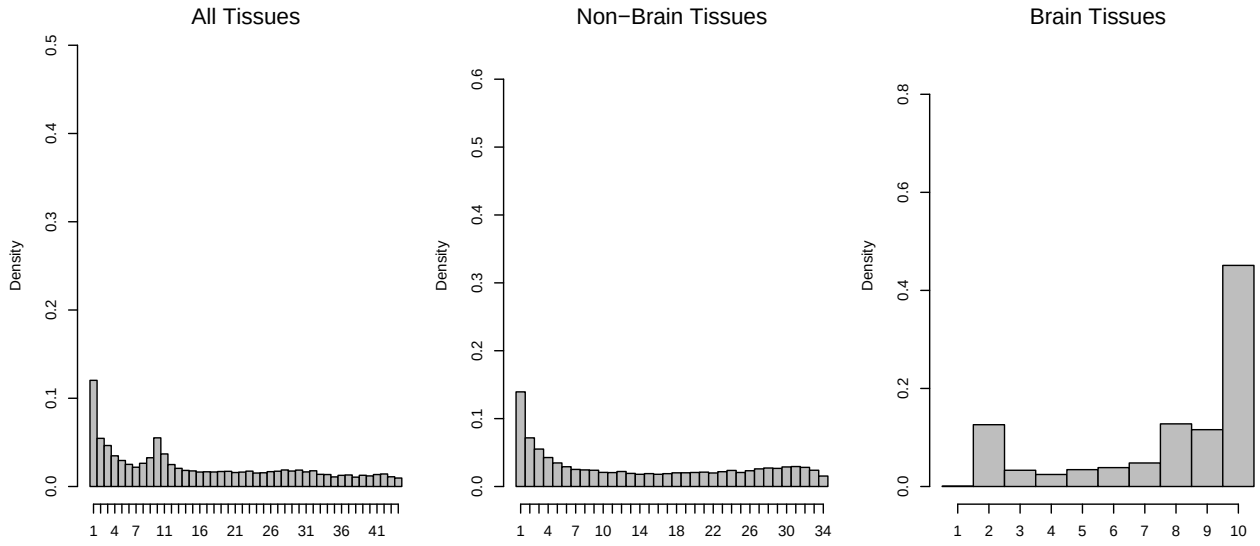



```
## [1] 0.9313826
```

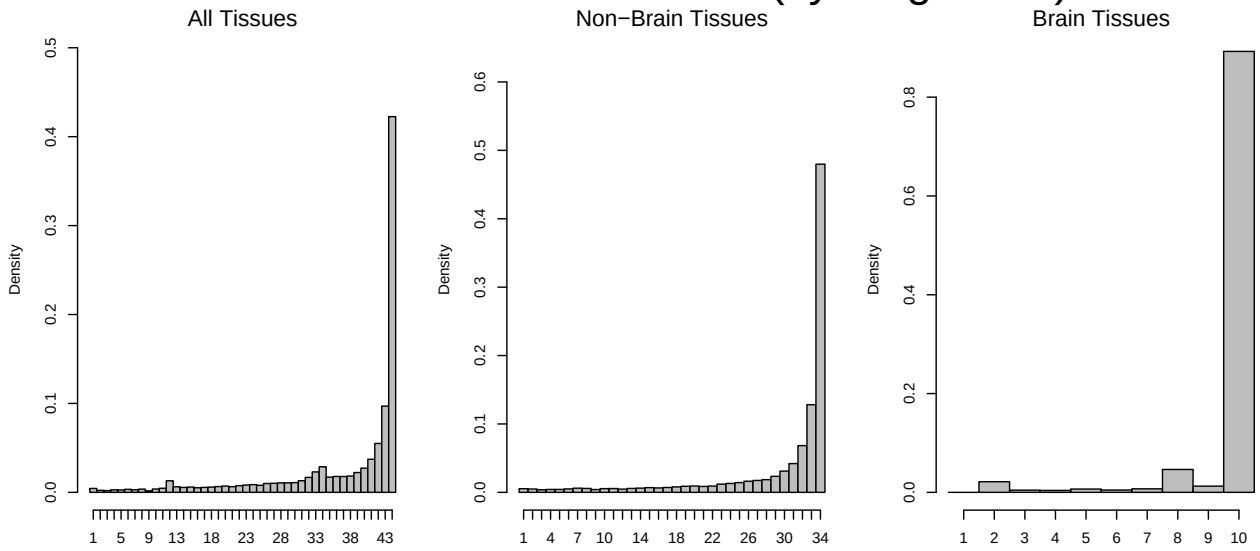
```
maxbeta=read.table("../Data/maxbetahats.txt")
maxz=read.table("../Data/maxz.txt")
#standard.error=maxbeta/maxz
standard.error=read.table("../Data/standard.error.txt")
pm.mash=as.matrix(read.table("../../Dropbox/Aug12/Aug13withEDposterior.means.txt")[,-1])

pm.mash.beta=pm.mash*standard.error

pm.mash.nobrain=as.matrix(read.table("../withoutbrain/nobrainposterior.means.txt")[,-1])*standard.error

pm.mash.brain.only=as.matrix(read.table("..//..//Dropbox/BrainOnly//brainonlyposterior.means.txt")[,-1])
```

But now, we can ask much more interesting questions.


Number of Tissues >50% Max Effect
Density
0.00
0.04
0.08
0.12
1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 33 35 37 39 41 43
NumberofTissues
Number of Tissues >50% Max Effect,Subgroup
All Tissues
Excluding Brain
BrainOnly
Density
NumberofTissues
1 5 9 13 18 23 28 33 38 43
1 4 7 10 14 18 22 26 30 34
1 2 3 4 5 6 7 8 9 10



Number of Tissues Shared (by magnitude)

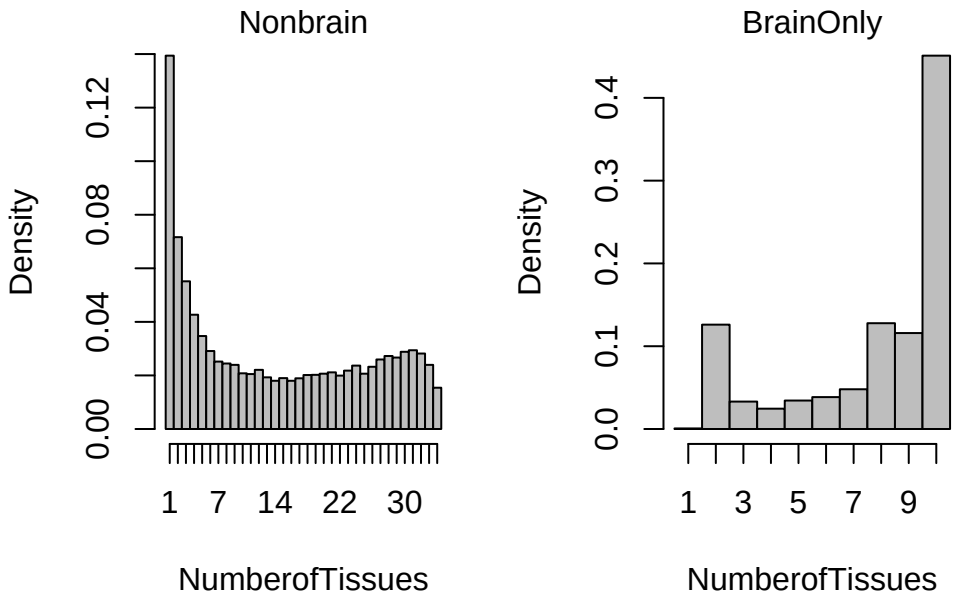


Number of Tissues Shared (by sign)

Generate the 2x1 plot for sharing of magnitudes for this subset:

```
par(mar=c(4,4.5,2,1))
par(oma=c(3,3,3,3) )
par(mfrow=c(1,2))
sigmat=(lfsr[,-c(7:16)]<=thresh)
nsig= rowSums(sigmat)

hist((het.func(het.norm(effectsize=pm.mash.beta[nsig>0,-c(7:16)]),threshold=0.5)),main="",xlab="Numbero
#,ylim=c(0,0.6))
mtext("Nonbrain")
axis(1, at=seq(1, 34, by=1), labels=c(1:34))
```

```
sigmat=(lfsr[,c(7:16)]<=thresh)
nsig= rowSums(sigmat)


brain.norm=het.norm(effectsize=pm.mash.beta[nsig>0,c(7:16)])
#hist(het.func(brain.norm,threshold=0.5),main="",xlab="NumberofTissues",nclass=12,col="grey",freq=FALSE
#hist(het.func(brain.norm,threshold=0.5),main="",xlab="NumberofTissues",breaks=seq(0,10,by=1),col="grey
hist(het.func(brain.norm,threshold=0.5),main="",xlab="NumberofTissues",breaks=0.5:10.5,col="grey",freq=
axis(1, at=seq(1, 10, by=1), labels=c(1:10))#,ylim=c(0,0.6))
#,ylim=c(0,0.6))
mtext("BrainOnly")

title(xlab="Number of Tissues >50% Max Effect, Global", outer=TRUE)
```




```
sigmat=(lfsr<=thresh)
nsig= rowSums(sigmat)
(signall=mean(het.norm(pm.mash.beta[nsig>0,])>0))
```

```
## [1] 0.8490723
```

```
sigmat=(lfsr.nobrain<=thresh)
nsig= rowSums(sigmat)
(signnobrain=mean(het.norm(pm.mash.nobrain[nsig>0,])>0))
```

```
## [1] 0.8823972
```

```
sigmat=(lfsr.brain.only<=thresh)
nsig= rowSums(sigmat)
(signbrainonly=mean(het.norm(pm.mash.brain.only[nsig>0,])>0))
```

```
## [1] 0.9840876
```

```
#

##show that results are robust###
sigmat=(lfsr[,-c(7:16)]<=thresh)
nsig= rowSums(sigmat)
(signall.nobrain=mean(het.norm(pm.mash.beta[,-c(7:16)])>0))
```

```
## [1] 0.8620526
```

```
sigmat=(lfsr[,c(7:16)]<=thresh)
nsig= rowSums(sigmat)
(signall.brainonly=mean(het.norm(pm.mash.beta[nsig>0,c(7:16)])>0))
```

```
## [1] 0.9593838
```

```
####
sigmat=(lfsr<=thresh)
nsig= rowSums(sigmat)
(magall=mean(het.norm(pm.mash.beta[nsig>0,])>0.5))
```

```
## [1] 0.3660784
```

```
(magall=mean(het.norm(pm.mash.beta[nsig>0,])>0.5&lfsr[nsig>0,]<0.05))
```

```
## [1] 0.3478738
```

```
sigmat=(lfsr.nobrain<=thresh)
nsig= rowSums(sigmat)
(magnobrain=mean(het.norm(pm.mash.nobrain[nsig>0,])>0.5))
```

```
## [1] 0.4445148
```

```
(magnobrain=mean(het.norm(pm.mash.nobrain[nsig>0,])>0.5&lfsr.nobrain[nsig>0,]<0.05))
```

```
## [1] 0.4209425
```

```
sigmat=(lfsr.brain.only<=thresh)
nsig= rowSums(sigmat)
(magbrain=mean(het.norm(pm.mash.brain.only[nsig>0,])>0.5))
```

```
## [1] 0.8586027
```

```
(magbrain=mean(het.norm(pm.mash.brain.only[nsig>0,])>0.5&lfsr.brain.only[nsig>0,]<0.05))
```

```
## [1] 0.8325508
```

```
##show that results are robust###
sigmat=(lfsr[,-c(7:16)]<=thresh)
nsig= rowSums(sigmat)
(magall.excludingbrain=mean(het.norm(pm.mash.beta[nsig>0,-c(7:16)])>0.5))
```

```
## [1] 0.4150992
```

```
(magall.excludingbrain=mean(het.norm(pm.mash.beta[nsig>0,-c(7:16)])>0.5&lfsr[nsig>0,-c(7:16)]<0.05))
```

```
## [1] 0.3924451
```

```
sigmat=(lfsr[,c(7:16)]<=thresh)
nsig= rowSums(sigmat)
(magall.brainonly=mean(het.norm(pm.mash.beta[nsig>0,c(7:16)])>0.5))
```

```
## [1] 0.7764802
```

```
(magall.brainonly=mean(het.norm(pm.mash.beta[nsig>0,c(7:16)])>0.5&lfsr[nsig>0,c(7:16)]<0.05))
```

```
## [1] 0.7259055
```

```
###let's also ask which significant associations are consistent in size
```

```
####
# (gene_cons_all=1-thresh_inconsistent(effect = pm.mash.beta,thresh=0.05,sigs =lfsr)/nrow(pm.mash.beta)
# (gene_cons_nobrain=1-thresh_inconsistent(effect=pm.mash.nobrain,thresh = 0.05,sigs = lfsr.nobrain)/nr
# (gene_cons_brainonly=1-thresh_inconsistent(effect=pm.mash.brain.only,thresh = 0.05,sigs = lfsr.brain.
#
#
# ##show that results are robust###
# (gene_cons_all.excludingbrain=1-thresh_inconsistent(effect = pm.mash.beta[,-c(7:16)],thresh=0.05,sigs
# (gene_cons_all.brainonly=1-thresh_inconsistent(effect = pm.mash.beta[,c(7:16)],thresh=0.05,sigs =lfsr
```

And plot the heatmaps of shared homogeneity:

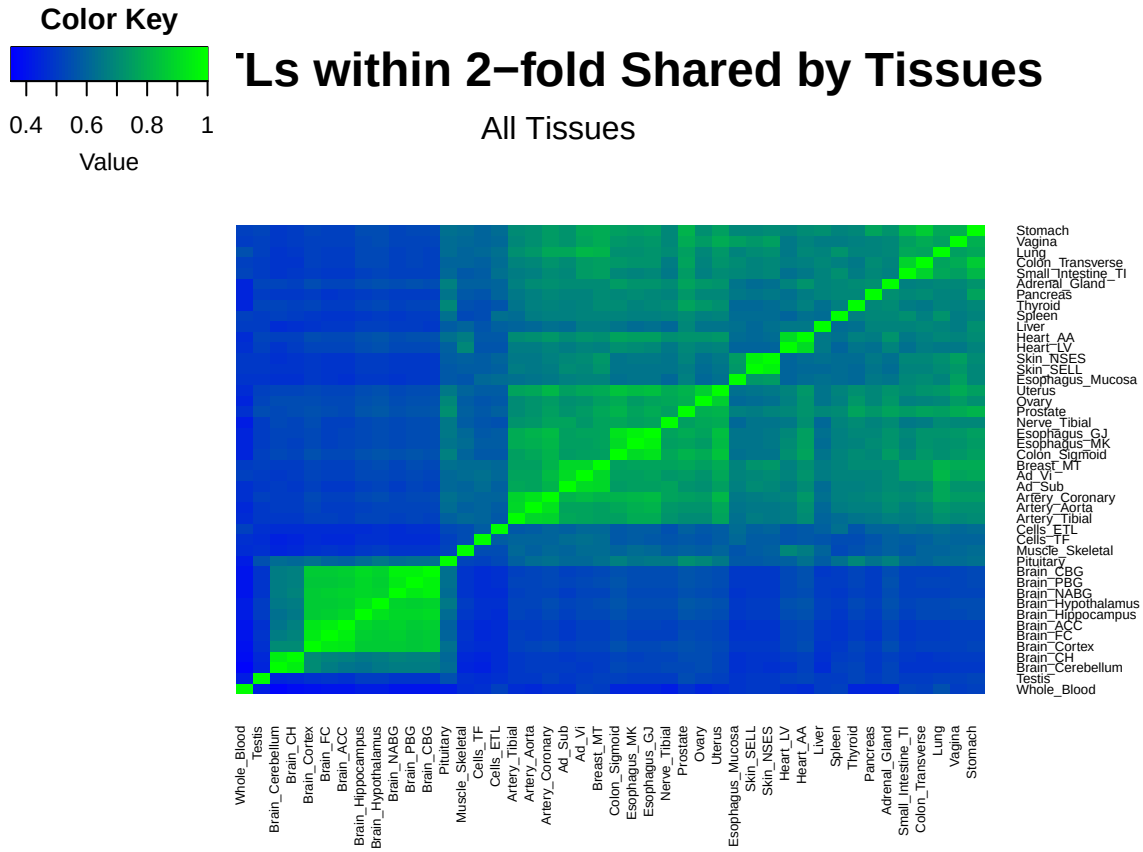
Now we can look at effect sizes which are within 2 fold of each other:

```
library(gplots)
```

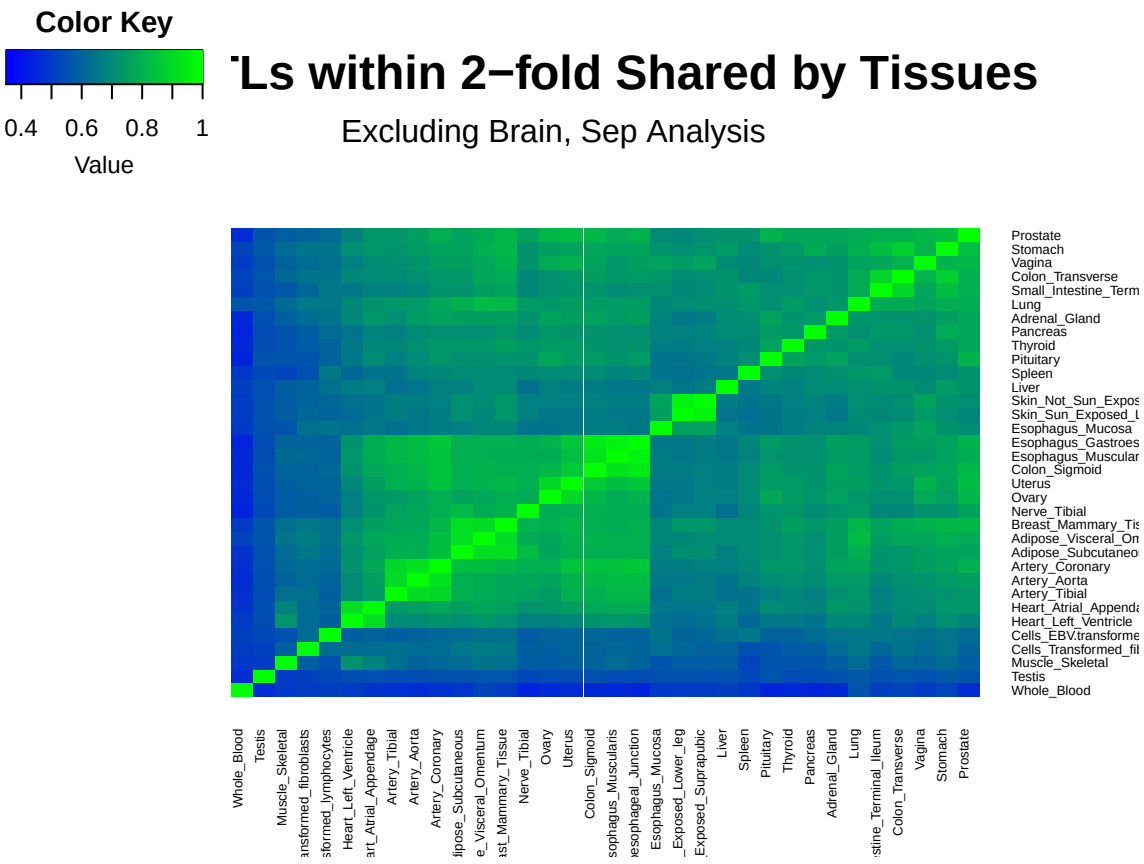
```
##
## Attaching package: 'gplots'
```

```
## The following object is masked from 'package:stats':
##
##     lowess
```

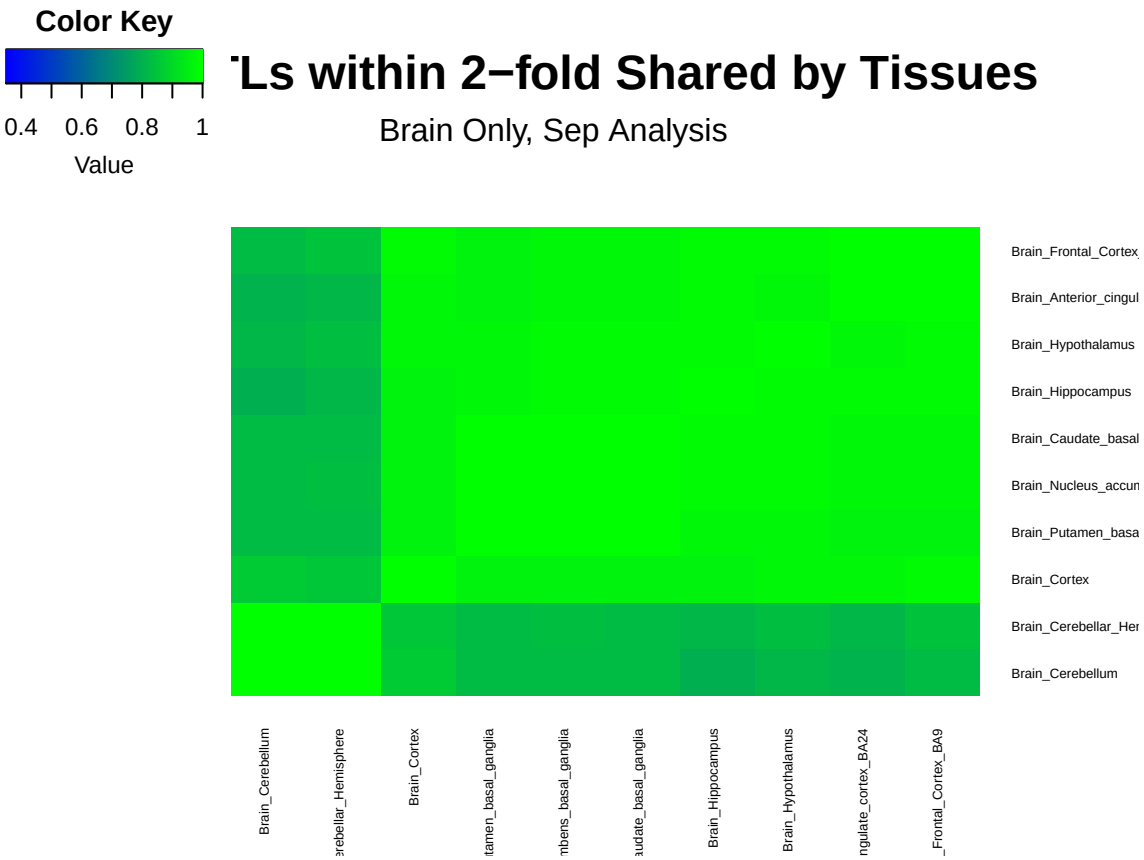
```
library(ggplot2)
library('colorRamps')
sigmat=lfsr<0.05
sigs=rowSums(sigmat)
a=pm.mash.beta[sigs>0,]##subset to ones that are significant in at least one tissue
thresh=0.05
R=ncol(a)
shared.het=matrix(NA,ncol=R,nrow=R)
colnames(shared.het)=rownames(shared.het)=tissue.names
for(i in 1:ncol(a)){
  for(j in 1:ncol(a)){
    quotient=abs(a[,i]/a[,j])##divide effect sizes


    shared.het[i,j]=mean(quotient>0.5&quotient<2)
 }

}

all.tissue.order=heatmap.2(shared.het,density="none",trace="none",dendrogram = "none",col=blue2green,ce

#write.table(all.tissue.order,"~/Dropbox/alltissueorder.txt",col.names = F,row.names = F)
mtext("All Tissues")
```



```
sigmat=lfsr.nobrain<0.05
sigs=rowSums(sigmat)
a=pm.mash.nobrain[sigs>0,]

a=pm.mash.nobrain
R=ncol(a)

thresh=0.05
shared.het=matrix(NA,ncol=R,nrow=R)
colnames(shared.het)=rownames(shared.het)=colnames(a)
for(i in 1:ncol(a)){
  for(j in 1:ncol(a)){
    quotient=abs(a[,i]/a[,j])##divide effect sizes


    shared.het[i,j]=mean(quotient>0.5&quotient<2)
 }

}



excludebrainorder=heatmap.2(shared.het,density="none",trace="none",dendrogram = "none",col=blue2green,c
mtext("Excluding Brain, Sep Analysis")
```



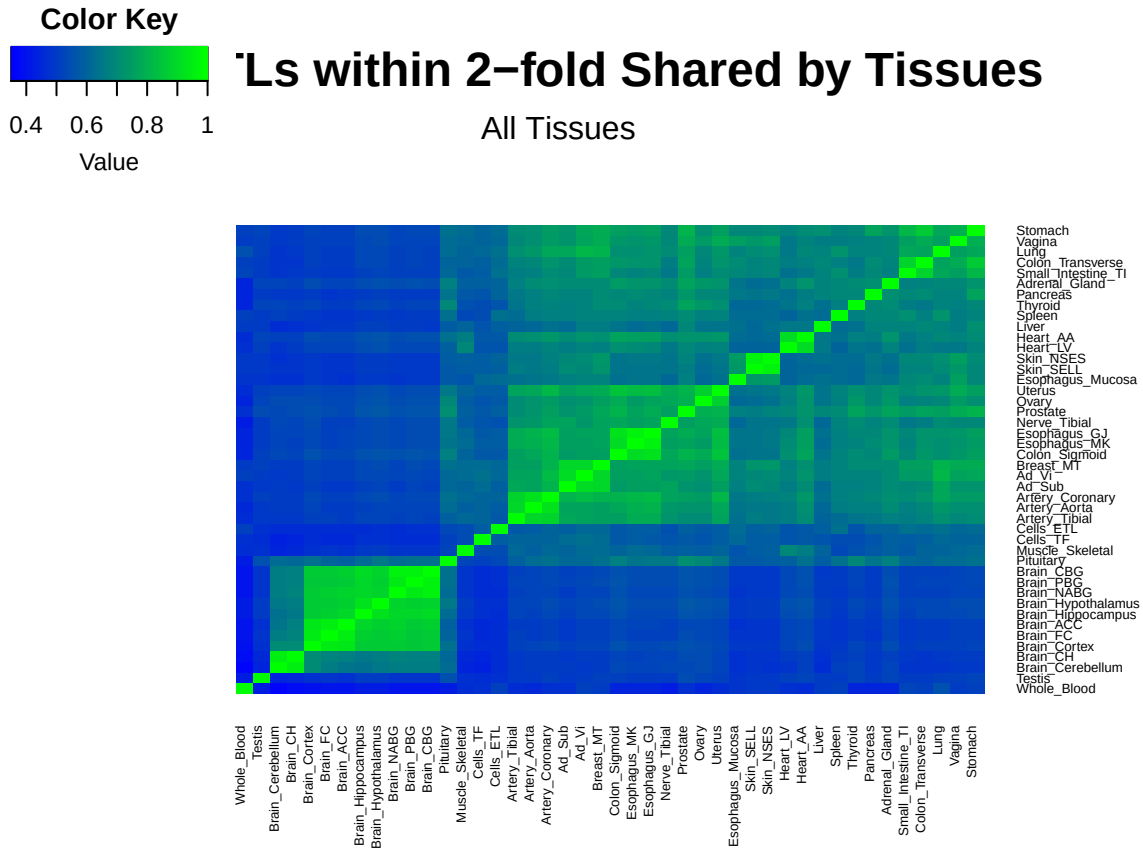
```
#write.table(excludebrainorder,"~/Dropbox/excludebrainorder.txt",col.names = F,row.names = F)

sigmat=lfsr.brain.only<0.05
sigs=rowSums(sigmat)
a=pm.mash.brain.only[sigs>0,]
R=ncol(a)

thresh=0.05
shared.het=matrix(NA,ncol=R,nrow=R)
colnames(shared.het)=rownames(shared.het)=colnames(a)
for(i in 1:ncol(a)){
  for(j in 1:ncol(a)){
    quotient=abs(a[,i]/a[,j])##divide effect sizes


    shared.het[i,j]=mean(quotient>0.5&quotient<2)
 }

}

brain.only.order=heatmap.2(shared.het,density="none",trace="none",dendrogram = "none",col=blue2green,ce
mtext("Brain Only, Sep Analysis")
```




```
#write.table(brain.only.order,"~/Dropbox/brain.only.order.txt",col.names = F,row.names = F)
```

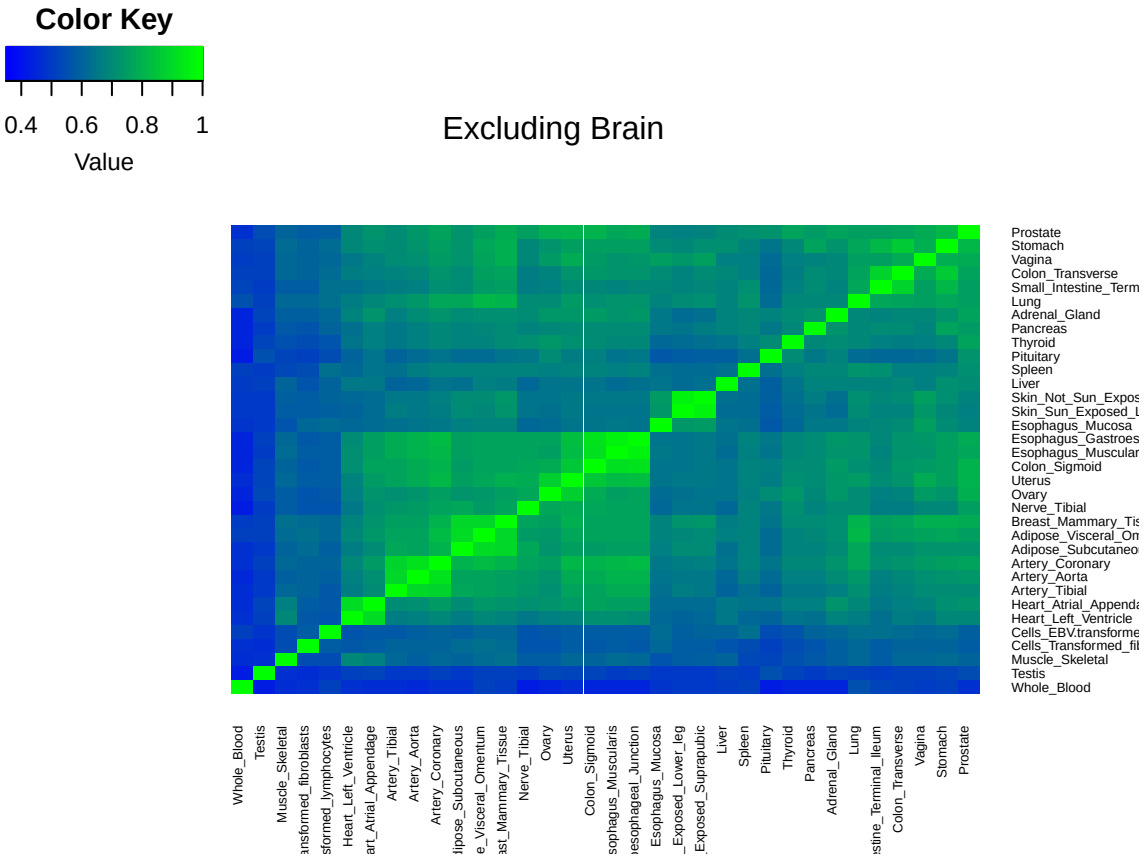
Now perform with subset of all tissue effects:

```
sigmat=lfsr<0.05
sigs=rowSums(sigmat)
a=pm.mash.beta[sigs>0,]

thresh=0.05
R=ncol(a)
shared.het=matrix(NA,ncol=R,nrow=R)
colnames(shared.het)=rownames(shared.het)=tissue.names
for(i in 1:ncol(a)){
  for(j in 1:ncol(a)){
    quotient=abs(a[,i]/a[,j])##divide effect sizes


    shared.het[i,j]=mean(quotient>0.5&quotient<2)
 }

}

heatmap.2(shared.het,density="none",trace="none",dendrogram = "none",col=blue2green,cexRow=0.5,cexCol=0
mtext("All Tissues")
```



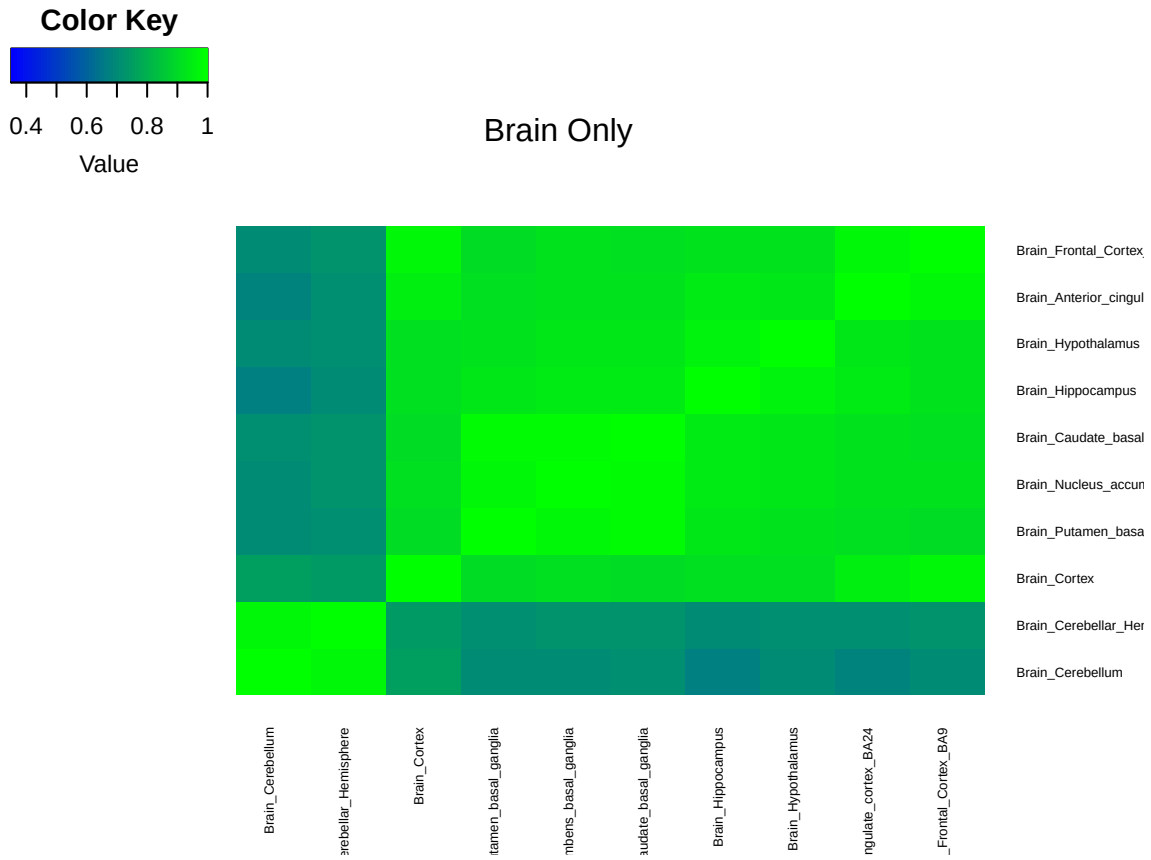

```
sigmat=lfsr[,-c(7:16)]<0.05
sigs=rowSums(sigmat)##subset significant
a=pm.mash.beta[sigs>0,-c(7:16)]

#a=pm.mash.beta[,-c(7:16)]
```

```
R=ncol(a)

thresh=0.05
shared.het=matrix(NA,ncol=R,nrow=R)
colnames(shared.het)=rownames(shared.het)=colnames(a)
for(i in 1:ncol(a)){
  for(j in 1:ncol(a)){
    quotient=abs(a[,i]/a[,j])##divide effect sizes


    shared.het[i,j]=mean(quotient>0.5&quotient<2)
 }

}

heatmap.2(shared.het[rev(excludebrainorder),(excludebrainorder)],density="none",trace="none",dendrogram
mtext("Excluding Brain")
```




```
sigmat=lfsr[,c(7:16)]<0.05
sigs=rowSums(sigmat)
a=pm.mash.beta[sigs>0,c(7:16)]
#a=pm.mash.beta[,c(7:16)]
R=ncol(a)

thresh=0.05
shared.het=matrix(NA,ncol=R,nrow=R)
```

```
colnames(shared.het)=rownames(shared.het)=colnames(a)
for(i in 1:ncol(a)){
  for(j in 1:ncol(a)){
    quotient=abs(a[,i]/a[,j])##divide effect sizes


    shared.het[i,j]=mean(quotient>0.5&quotient<2)
 }

}

heatmap.2(shared.het[rev(brain.only.order),brain.only.order],density="none",trace="none",dendrogram = "
          col=blue2green,main="",cexRow=0.5,cexCol=0.5,symm = T,Rowv = FALSE,Colv = FALSE,breaks=seq(0.3
mtext("Brain Only")
```



Let's also consider how our power changes when we perform the Subgroup analyses and when you do it on a per gene basis:

```
## [1] 82120
```

```
## [1] 86594
```

```
## [1] 303809
```

```
## [1] 306820
```

```
## [1] 8817

## [1] 10353

## [1] 13277

## [1] 13945
```