Advantage of two scans in small populations demonstrated with a transgender dataset.

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Introduction

We have a dataset where FreeSurfer was used to determine cortical and subcortical brain anatomy in cis- and transgender population. For every participant two scans were administered (T1 and T2) and an average of both scans was computed. In this report we analyze the data from one scan and the average of both scans. Later on we show the advantage and increase in power obtained by administering 2 scans.

One participant (P22) was removed from the analysis because no anatomical data was available for this participant.

Startup

We first read in the data. In data. all available measurements are stored (descriptive and anatomical) while in data.hyp the anatomical results for every region of interest stored. Both files contain data of T1, T2 and the average.

```
# Libraries
library(knitr)

# Read in data
data.all <- read.csv("../1.Data/Behzad_all.csv", sep=";", dec=",")
data.hyp <- read.csv("../1.Data/Behzad_hyp.csv", sep=";", dec=",")

# Check data
dim(data.hyp)

## [1] 140 68
dim(data.all)

## [1] 140 820</pre>
```

The regions we are interested in are the cerebellum, caudate, putamen, nucleus accumenbens, thalamus, fusiform, pre-central gyrus, post-central gyrus, frontal poles and inferior parietal gyrus. Here we list the variables we selected from FreeSurfer that comply with these regions.

```
# Regions of interest
names(data.hyp[,47:68])
```

```
[1] "Tavg_L_fusiform_volume"
                                           "Tavg_L_inferiorparietal_volume"
##
   [3] "Tavg_L_postcentral_volume"
                                           "Tavg_L_precentral_volume"
   [5] "Tavg_L_frontalpole_volume"
                                           "Tavg_R_fusiform_volume"
   [7] "Tavg_R_inferiorparietal_volume"
##
                                           "Tavg_R_postcentral_volume"
##
   [9] "Tavg_R_precentral_volume"
                                           "Tavg_R_frontalpole_volume"
  [11] "Tavg_LeftCerebellumWhiteMatter"
                                           "Tavg_LeftCerebellumCortex"
##
  [13] "Tavg_RightCerebellumWhiteMatter"
                                           "Tavg_RightCerebellumCortex"
## [15] "Tavg LeftThalamusProper"
                                           "Tavg LeftCaudate"
## [17] "Tavg_LeftPutamen"
                                           "Tavg LeftAccumbensarea"
## [19] "Tavg_RightThalamusProper"
                                           "Tavg_RightCaudate"
## [21] "Tavg_RightPutamen"
                                           "Tavg_RightAccumbensarea"
```

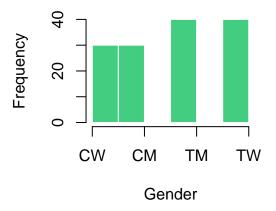
Descriptives

In this section population parameters are presented.

Gender

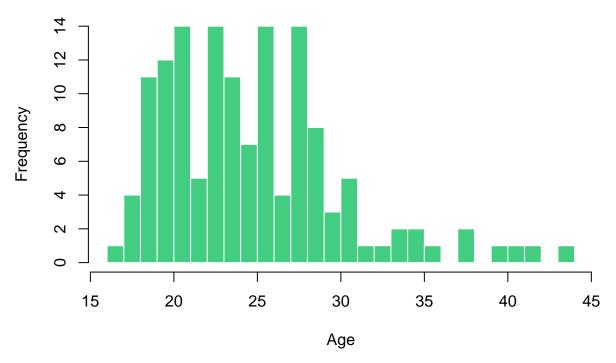
There were 60 cisgender and 80 transgender participants. One participant (P22) was removed from the analysis because no anatomical data was available for this participant.

Frequency of gender



Age

Histogram of age distribution



Age of the participants ranged from 16 to 44. If we look at the distribution of age in the cis- and transgender group we see that the range is similar in both groups.

```
# Cisqender group
summary(data.all[data.all[,2]<3,4])</pre>
      Min. 1st Qu.
                                Mean 3rd Qu.
##
                     Median
                                                 Max.
##
     19.00
             23.00
                      25.00
                               25.92
                                       29.00
                                                41.00
# Transgender group
summary(data.all[data.all[,2]>2,4])
##
      Min. 1st Qu.
                     Median
                                Mean 3rd Qu.
                                                 Max.
     16.00
             20.75
                      24.00
                                       26.25
##
                               24.62
                                                44.00
```

Social-Economic Status

I don't know the interpretation of the numbers below (e.g. to which SES which number refers), I just added the frequency tables.

```
table(data.all[,5])
##
## 1 2 3
## 19 87 34
```

Level of education

```
table(data.all[,6])
```

```
##
## 2 3 4 5
## 22 76 28 14
Handedness
table(data.all[,7])
##
##
        2
   1
## 129 11
Gender identity
summary(data.all[,8])
##
     Min. 1st Qu. Median
                             Mean 3rd Qu.
                                             Max.
           0.000
                    5.000
                            5.036 10.000 10.000
table(data.all[,8])
##
## 0 1 2 3 7 8 9 10
## 49 4 13 4 1 9 16 44
# Cisqender women
summary(data.all[data.all[,2]==1,8])
     Min. 1st Qu. Median
                             Mean 3rd Qu.
                                             Max.
    7.000
           9.000
                    9.500
                            9.267 10.000 10.000
##
# Cisqender men
summary(data.all[data.all[,2]==2,8])
     Min. 1st Qu. Median
                             Mean 3rd Qu.
                                             Max.
      0.0
              0.0
                      0.0
                              0.9
                                      2.0
                                              3.0
##
# Transgender men
summary(data.all[data.all[,2]==3,8])
     Min. 1st Qu. Median
##
                             Mean 3rd Qu.
                                             Max.
##
     0.000
           0.000
                    0.000
                            0.375
                                    0.000
                                            3.000
# Transgender women
summary(data.all[data.all[,2]==4,8])
     Min. 1st Qu. Median
                             Mean 3rd Qu.
           9.000 10.000 9.625 10.000 10.000
##
     8.000
Sexual orientation
summary(data.all[,9])
```

Max.

Mean 3rd Qu.

4.957 10.000 10.000

##

##

Min. 1st Qu. Median

0.000 0.000 5.000

```
table(data.all[,9])
##
##
   0 1 2 3 7
                   8 9 10
## 50 12 7 1 1
                   9 14 46
# Cisgender women
summary(data.all[data.all[,2]==1,9])
##
      Min. 1st Qu. Median
                               Mean 3rd Qu.
                                                Max.
##
    0.0000 \quad 0.0000 \quad 0.0000 \quad 0.5333 \quad 1.0000 \quad 2.0000
# Cisqender men
summary(data.all[data.all[,2]==2,9])
##
      Min. 1st Qu. Median
                               Mean 3rd Qu.
                                                Max.
     7.000
             9.250 10.000
                              9.533 10.000
                                              10.000
##
# Transgender women
summary(data.all[data.all[,2]==3,9])
##
      Min. 1st Qu. Median
                               Mean 3rd Qu.
                                                Max.
                              9.475 10.000
##
     8.000
             9.000 10.000
                                              10.000
# Transgender men
summary(data.all[data.all[,2]==4,9])
##
                    Median
                               Mean 3rd Qu.
      Min. 1st Qu.
                                                Max.
     0.000
            0.000
                      0.000
                                       0.000
##
                              0.325
                                               3.000
Mental illnesses
There are no available measures for the cisgender group. ####Somatization
table(data.all[,22])
##
## #NULL!
               0
                       1
##
       60
              67
                      13
Obsessive-compulsive disorder
table(data.all[,23])
##
## #NULL!
               0
                       1
               58
Among the cisgender participants 1 had a history of obsession.
Interpersonal sensitivity
```

```
## #NULL! 0 1
## 60 57 23
```

Depression

```
table(data.all[,25])
```

```
## #NULL! 0 1 2
## 60 42 37 1
```

Among the cisgender participants 3 had a history of depression.

Anxiety

```
table(data.all[,26])
```

```
## ## #NULL! 0 1 2
## 60 54 25 1
```

Among the cisgender participants 1 had a history of a general anxiety disorder.

Hostility

```
table(data.all[,27])
```

```
## ## #NULL! 0 1 2
## 60 64 15 1
```

Phobic anxiety

```
table(data.all[,28])
```

```
## #NULL! 0 1
## 60 67 13
```

Paranoia

```
table(data.all[,29])
```

```
## #NULL! 0 1
## 60 46 34
```

Psychotism

```
table(data.all[,30])
```

```
## #NULL! 0 1
## 60 67 13
```

Global severity

```
table(data.all[,31])
```

```
## #NULL! 0 1
## 60 59 21
```

Cisgender group

Past psychiatric condition Out of 60 cisgender participants 3 had a history of depression, 1 reported a general anxiety disorder and 1 had a history of obsession.

Past medical condition Out of 60 cisgender participants 3 reported migraine, 1 reported left ear surgery, 1 participant had suffered from heart palpitations, 1 participants reported a history of meningitis, 1 participant reported they had asthma as a child and 1 participants reported favism.

Analysis of the data

Analysis of one measurement

We compute an ANOVA on all hypothesis regions with the data from T1.

```
bg.one <- 3
nd.one <- 24
ln <- nd.one-bg.one
fac <- c(rep("CW",30), rep("CM",30), rep("TM",40), rep("TW",40))  # factor for participant group
# Object to save p-values of ANOVA
pan.one <- array(data=NA, dim = ln)
# Compute ANOVA for every predictor and save p-value
for(i in bg.one:nd.one){
   tempan <- aov(data.hyp[,i] ~ as.factor(data.hyp[,2]))
   pan.one[i-bg.one+1] <- unlist(summary(tempan))[9]
}
# FDR correction on p-values to correct for multiple testing
pancorr.one <- p.adjust(pan.one, method = "fdr")
sum(pancorr.one < 0.05)
## [1] 20</pre>
```

kable(cbind(names(data.hyp[,bg.one:nd.one]), round(pancorr.one, 3)))

T1_L_fusiform_volume	0
T1_L_inferiorparietal_volume	0.001
T1_L_postcentral_volume	0.002
T1_L_precentral_volume	0.032
T1_L_frontalpole_volume	0.006
T1_R_fusiform_volume	0
T1_R_inferiorparietal_volume	0.001
T1_R_postcentral_volume	0.014
T1_R_precentral_volume	0.002
T1_R_frontalpole_volume	0.001
${\bf T1_LeftCerebellumWhiteMatter}$	0.001
T1_LeftCerebellumCortex	0
T1_RightCerebellumWhiteMatter	0.001
T1_RightCerebellumCortex	0
T1_LeftThalamusProper	0
T1_LeftCaudate	0.002
T1_LeftPutamen	0.006
T1_LeftAccumbensarea	0.453
T1_RightThalamusProper	0
T1_RightCaudate	0.002
T1_RightPutamen	0
T1_RightAccumbensarea	0.119

Analysis of the average

We computed the same ANOVA on the average.

```
bg.avg <- 47
nd.avg <- 68
ln <- nd.avg-bg.avg+1
fac <- c(rep("CW",30), rep("CM",30), rep("TM",40), rep("TW",40)) # factor for participant group

# Object to save p-values of ANOVA
pan.avg <- array(data=NA, dim = ln)

# Compute ANOVA for every predictor and save p-value
for(i in bg.avg:nd.avg){
   tempan <- aov(data.hyp[,i] ~ as.factor(data.hyp[,2]))
   pan.avg[i-bg.avg+1] <- unlist(summary(tempan))[9]
}

# FDR correction on p-values to correct for multiple testing
pancorr.avg <- p.adjust(pan.avg, method = "fdr")
sum(pancorr.avg < 0.05)</pre>
## [1] 19
```

kable(cbind(names(data.hyp[,bg.avg:nd.avg]), round(pancorr.avg, 3)))

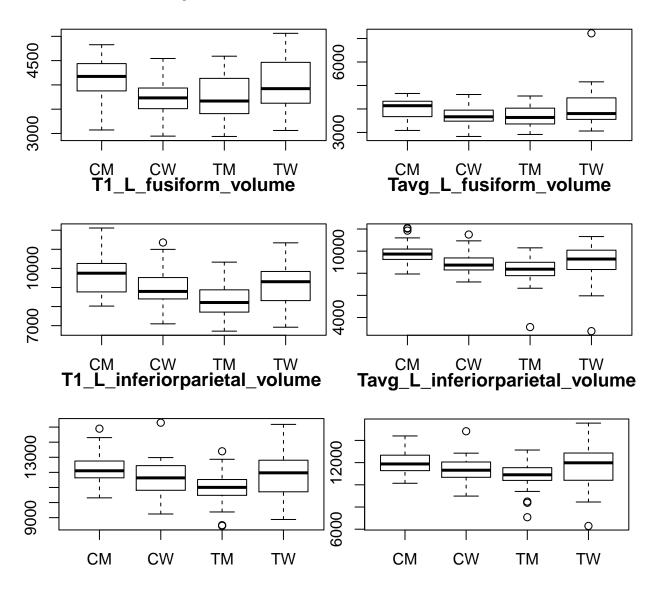
Tavg_L_fusiform_volume	0			
$Tavg_L_inferior parietal_volume$	0.005			
$Tavg_L_postcentral_volume$	0.005			
$Tavg_L_precentral_volume$	0.128			
$Tavg_L_frontalpole_volume$	0.101			
Tavg_R_fusiform_volume	0.001			
$Tavg_R_inferior parietal_volume$	0.004			
$Tavg_R_postcentral_volume$	0.049			
$Tavg_R_precentral_volume$	0.01			
$Tavg_R_frontalpole_volume$	0.003			
$Tavg_LeftCerebellumWhiteMatter$	0.004			
$Tavg_LeftCerebellumCortex$	0			
$Tavg_RightCerebellumWhiteMatter$	0.003			
$Tavg_RightCerebellumCortex$	0			
Tavg_LeftThalamusProper	0			
Tavg_LeftCaudate	0.005			
Tavg_LeftPutamen				
Tavg_LeftAccumbensarea	0.387			
Tavg_RightThalamusProper				
Tavg_RightCaudate				
Tavg_RightPutamen	0.002			
Tavg_RightAccumbensarea	0.014			

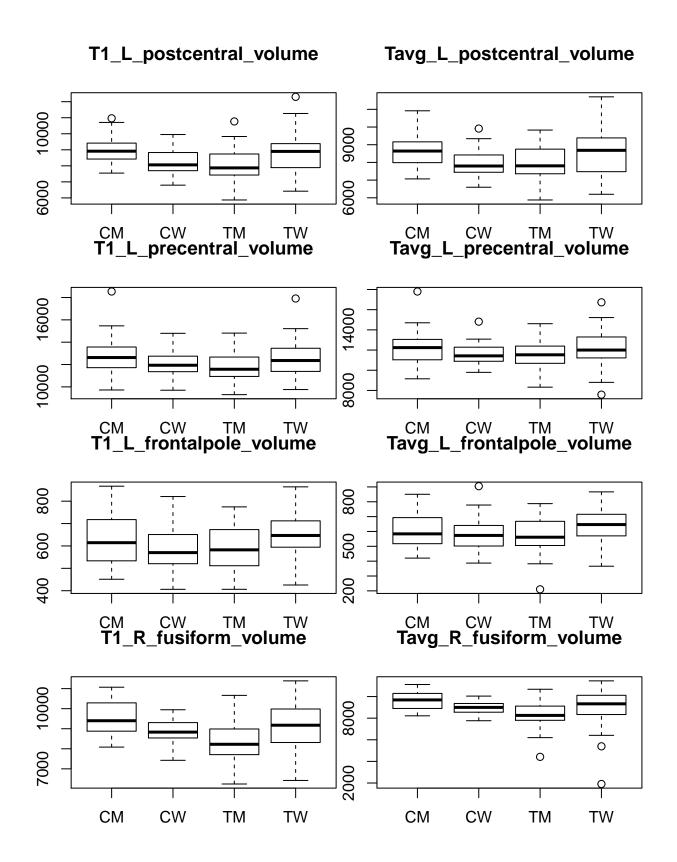
Why are there less regions for which the difference is statistically significant when the average is used compared to when one measure is used? To investigate this we look at the difference between the boxplots for one statistically significant region.

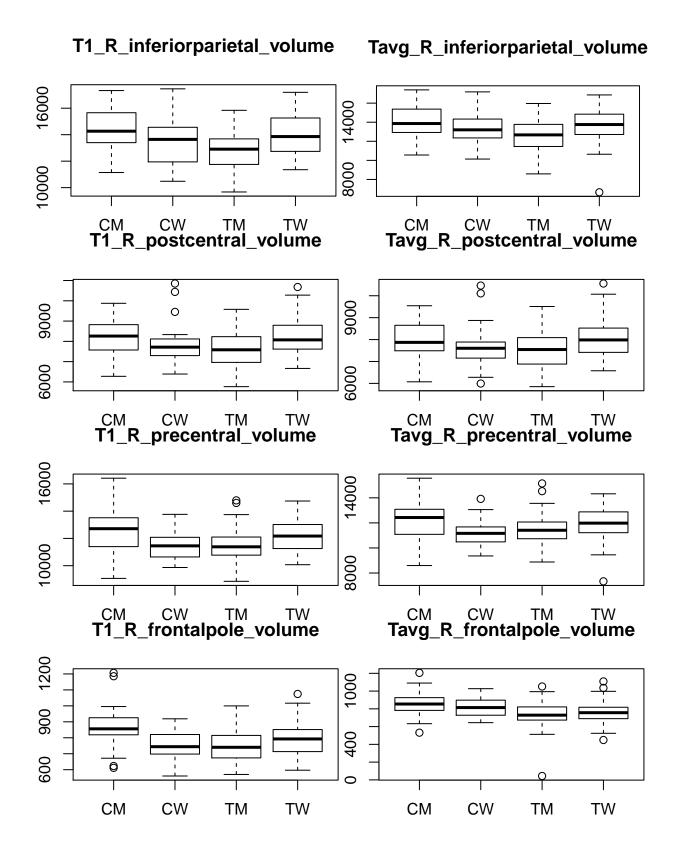
```
boxplot(data.hyp[,22] ~ fac, main = names(data.hyp)[26])
boxplot(data.hyp[,66] ~ fac, main = names(data.hyp)[78])

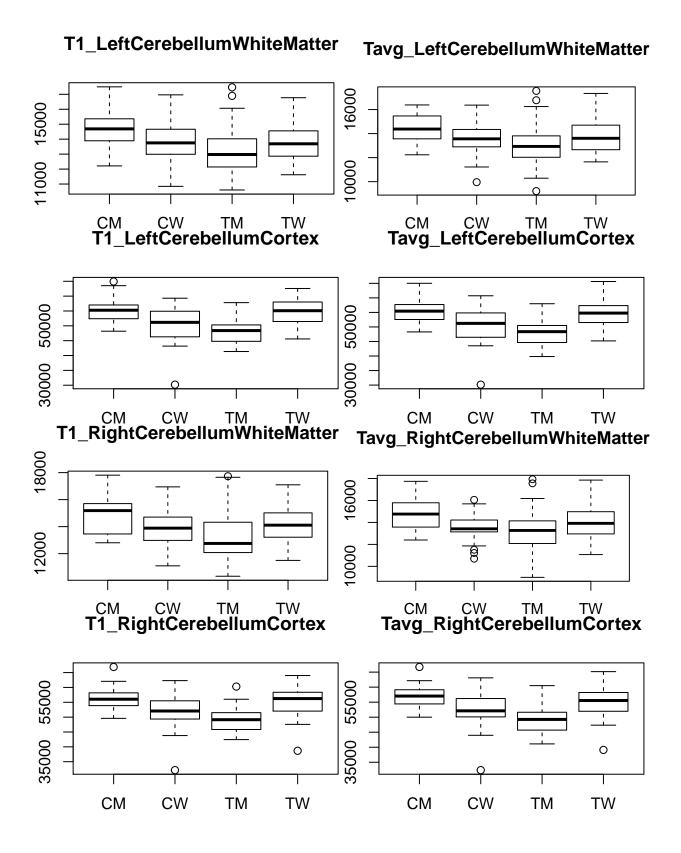
for(i in bg.one:nd.one){
    # construct boxplot for every region
    boxplot(data.hyp[,i] ~ fac, main = names(data.hyp)[i])
    boxplot(data.hyp[,i + 44] ~ fac, main = names(data.hyp)[i + 44])
}
```

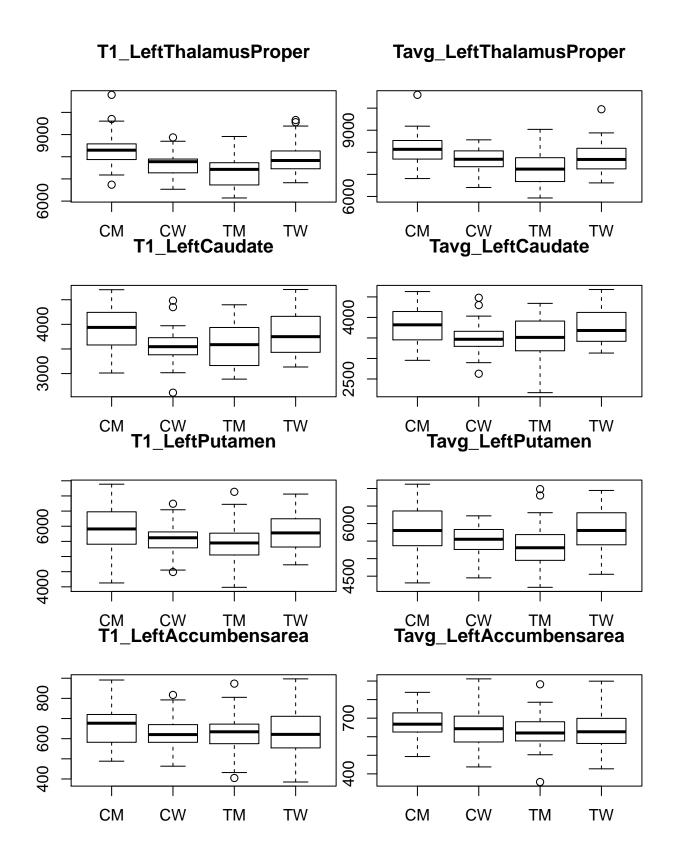
T2_L_inferiorparietal_volume

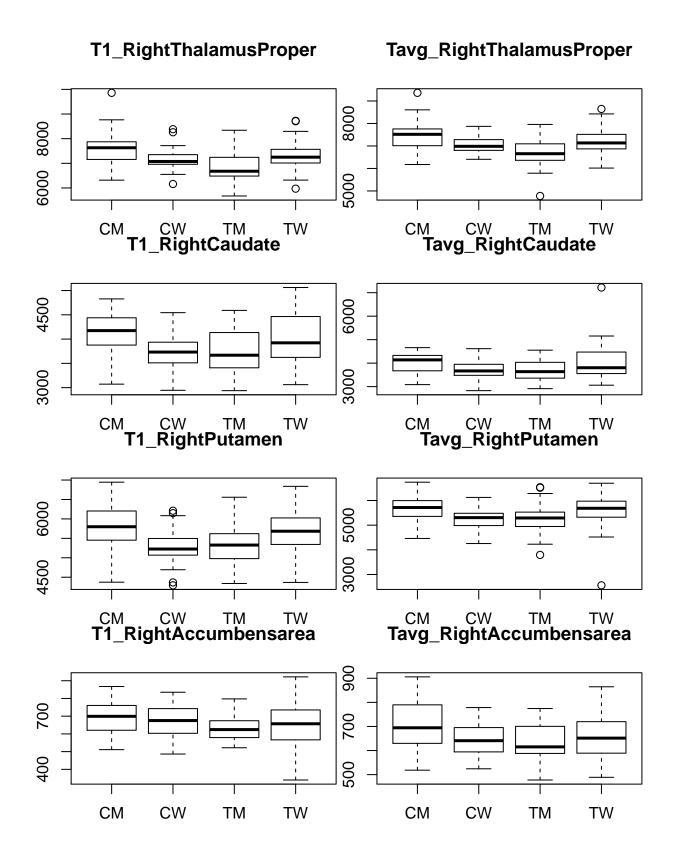












Post-hoc tests

We conduct post-hoc t-tests on the statistically significant regions to determine which group differences cause the effect. The p-values are uncorrected at this point and I computed them for every region.

```
# create an object with all possible combinations
  allcomb \leftarrow combn(c(1:4),2)
  allcomb.txt <- array(data=NA, dim = dim(allcomb)[2])
  labels.g <- c("CW", "CM", "TM", "TW")
  for(i in 1:dim(allcomb)[2]){
    allcomb.txt[i] \gets paste(labels.g[allcomb[1,i]], "vs", labels.g[allcomb[2,i]], sep="")
  }
# create object to save results
 pt.one <- array(data = NA, dim = c(length(pan.one),dim(allcomb)[2]))</pre>
 pt.avg <- array(data = NA, dim = c(length(pan.avg),dim(allcomb)[2]))</pre>
# Left Cerebellum White Matter
  # 1 measure
  bg.one \leftarrow 3
 nd.one \leftarrow 24
 pt.corr.one <- array(data=NA, dim=dim(pt.one))</pre>
  for(r in bg.one:nd.one){
    if (pan.one[r-bg.one+1] > 0.05) {
        pt.one[r-bg.one+1,] <- rep(NA,dim(allcomb)[2])
    }else{
      for(i in 1:dim(allcomb)[2]){
        pt.one[r-bg.one+1,i] <- unlist(t.test(data.hyp[data.hyp[,2]==allcomb[1,i],r], data.hyp[data.hyp
        pt.corr.one[r - bg.one + 1,] <- p.adjust(pt.one[r - bg.one + 1,], method = "bonferroni")</pre>
    }
  }
  kable(cbind(c(" ",names(data.hyp[,bg.one:nd.one])),rbind(c("CW vs CM","CW vs TM","CW vs TW","CM vs TM
```

	CW vs CM	CW vs TM	CW vs TW	CM vs TM	CM vs TW	TM vs TW
T1_L_fusiform_volume	0.014	0.047	1	0	0.202	0.001
T1_L_inferiorparietal_volume	0.137	0.158	1	0	0.949	0.025
$T1_L_postcentral_volume$	0.01	1	0.233	0.002	1	0.06
$T1_L_precentral_volume$	0.284	1	0.807	0.087	1	0.243
$T1_L_frontalpole_volume$	0.929	1	0.015	0.998	1	0.009
$T1_R_{instructure}$ fusiform_volume	0.013	0.02	1	0	0.78	0.006
T1_R_inferiorparietal_volume	0.162	0.568	1	0.001	1	0.006
T1_R_postcentral_volume	0.87	1	0.534	0.067	1	0.018
T1_R_precentral_volume	0.014	1	0.026	0.034	1	0.087
T1_R_frontalpole_volume	0.004	1	0.624	0.005	0.177	0.724
${\bf T1_LeftCerebellumWhiteMatter}$	0.036	0.775	1	0	0.01	0.677
$T1_LeftCerebellumCortex$	0.005	0.587	0.009	0	1	0
${\bf T1_RightCerebellumWhiteMatter}$	0.04	1	1	0.001	0.133	0.221
T1_RightCerebellumCortex	0.003	0.227	0.058	0	1	0
T1_LeftThalamusProper	0.004	0.196	0.61	0	0.174	0.002
T1_LeftCaudate	0.021	1	0.072	0.02	1	0.066
T1_LeftPutamen	0.14	1	0.417	0.032	1	0.069

T1_LeftAccumbensarea	NA	NA	NA	NA	NA	NA
$T1$ _RightThalamusProper	0.127	0.047	1	0	0.775	0.004
T1_RightCaudate	0.003	1	0.124	0.007	1	0.203
T1_RightPutamen	0	1	0.002	0.001	1	0.03
$T1$ _RightAccumbensarea	NA	NA	NA	NA	NA	NA

```
# Average
bg.avg <- 47
nd.avg <- 68
pt.corr.avg <- array(data=NA, dim=dim(pt.avg))
for(r in bg.avg:nd.avg){
    if (pan.avg[r-bg.avg+1] > 0.05) {
        pt.avg[r-bg.avg+1,] <- rep(NA,dim(allcomb)[2])
}else{
        for(i in 1:dim(allcomb)[2]){
            pt.avg[r-bg.avg+1,i] <- unlist(t.test(data.hyp[data.hyp[,2]==allcomb[1,i],r], data.hyp[data.hyp
            pt.corr.avg[r - bg.avg + 1,] <- p.adjust(pt.avg[r - bg.avg + 1,], method = "bonferroni")
        }
    }
}
kable(cbind(c(" ",names(data.hyp[,bg.avg:nd.avg])),rbind(c("CW vs CM","CW vs TM","CW vs TW","CM vs TM</pre>
```

	CW vs CM	CW vs TM	CW vs TW	CM vs TM	CM vs TW	TM vs TW
$Tavg_L_fusiform_volume$	0.015	0.137	1	0	0.15	0.102
$Tavg_L_inferior parietal_volume$	0.147	0.39	1	0	1	0.074
$Tavg_L_postcentral_volume$	0.008	1	0.146	0.011	1	0.187
$Tavg_L_precentral_volume$	NA	NA	NA	NA	NA	NA
$Tavg_L_frontalpole_volume$	NA	NA	NA	NA	NA	NA
Tavg_R_fusiform_volume	0.005	0.022	1	0	0.389	0.225
Tavg_R_inferiorparietal_volume	0.353	0.597	1	0.004	1	0.02
$Tavg_R_postcentral_volume$	1	1	0.213	0.729	1	0.071
$Tavg_R_precentral_volume$	0.023	1	0.012	0.411	1	0.452
$Tavg_R_frontalpole_volume$	1	0.062	0.236	0.008	0.028	1
$Tavg_LeftCerebellumWhiteMatter$	0.088	0.916	1	0.001	0.35	0.176
${\bf Tavg_LeftCerebellumCortex}$	0.004	0.282	0.03	0	1	0
$Tavg_RightCerebellumWhiteMatter$	0.009	1	1	0.002	0.332	0.283
$Tavg_RightCerebellumCortex$	0.002	0.134	0.098	0	0.97	0
$Tavg_LeftThalamusProper$	0.037	0.091	1	0	0.144	0.024
Tavg_LeftCaudate	0.048	1	0.021	0.103	1	0.052
Tavg_LeftPutamen	0.043	1	0.045	0.009	1	0.007
Tavg_LeftAccumbensarea	NA	NA	NA	NA	NA	NA
$Tavg_RightThalamusProper$	0.024	0.073	0.494	0	0.909	0.003
Tavg_RightCaudate	0.009	1	0.087	0.024	1	0.168
Tavg_RightPutamen	0.004	1	0.027	0.015	1	0.081
$Tavg_RightAccumbens are a$	0.18	1	1	0.02	0.395	1

Correlations

```
between T1 and T2
bg <- 36
nd <- 108
ln <- nd-bg+1</pre>
# Object to save correlations
corrall <- array(data=NA, dim = ln)</pre>
# Compute ANOVA for every predictor and save p-value
for(i in bg:nd){
  corrall[i-bg+1] \leftarrow cor(x = data.all[,i], y = data.all[,i + ln + 1])
summary(corrall)
      Min. 1st Qu. Median Mean 3rd Qu.
## 0.6334 0.7950 0.8243 0.8216 0.8466 0.9985
bg.one <- 3
nd.one <- 24
ln <- nd.one-bg.one+1</pre>
# Object to save correlations
corrhyp <- array(data=NA, dim = ln)</pre>
# Compute ANOVA for every predictor and save p-value
for(i in bg.one:nd.one){
  corrhyp[i-bg.one+1] \leftarrow cor(x = data.hyp[,i], y = data.hyp[,i + ln])
summary(corrhyp)
      Min. 1st Qu. Median
                              Mean 3rd Qu.
## 0.7046 0.8897 0.9313 0.8990 0.9492 0.9963
# plot with correlations? Which region lies where?
```

Simulations

Intro

Code

First we need to define the parameters of our simulations.

```
# variance/sd epsilon
seps <- 1

# Number of simulations
asim <- 5000

# Effect size
delta <- 0.8

# Number of participants
n <- 30
n.1 <- n/2  # in the first group
n.2 <- n/2  # in the second group

# Level of statistical significance
alpha <- 0.05

# Correlation between first and second measurement
rho <- seq(0.01,0.99,0.01)</pre>
```

Then we prepare objects to store our results

```
# Number of simulations
pow.mean1<-vector("numeric",length(rho))</pre>
pow.mean2<-vector("numeric",length(rho))</pre>
pow.mean3<-vector("numeric",length(rho))</pre>
pow.mean4<-vector("numeric",length(rho))</pre>
# Loop over preset correlations between measure 1 and measure 2
for(i in 1:length(rho)){
  # Create objects to store power in for every simulations
  pow.1<-vector("numeric",asim)</pre>
  pow.2<-vector("numeric",asim)</pre>
  pow.3<-vector("numeric",asim)</pre>
  pow.4<-vector("numeric",asim)</pre>
  for(k in 1:asim){
    # Scenario 1: lower bound of power curve
    # two groups with equal amount of subjects, groups differ with an effect size delta
    # Construct a vector that determines in which group each subject falls
    x < -c(rep(1,n.1), rep(0,n.2))
    # Vector with observations in the set of participants
    y < -rnorm(n, 0, seps)
    # Add an effect size to the first group
    y[1:n.1] < -y[1:n.1] + delta
```

```
# Boolean of whether an effect is detected, this is later used to compute the power
 pow.1[k] < -summary(lm(y~x))$coef[2,4] <alpha
  # Scenario 2: upper bound of power curve
  # two groups with equal amount of subjects, twice as many as scenario 1, groups differ with an effe
  # Construct a vector that determines in which group each subject falls
 x2 < -c(rep(1,(n.1*2)),rep(0,(n.2*2)))
  # Vector with observations in the set of participants
 y2 < -rnorm(n*2, 0, seps)
  # Add an effect size to the first group
 y2[1:(n.1*2)]<-y2[1:(n.1*2)]+delta
  # Boolean of whether an effect is detected, this is later used to compute the power
 pow.2[k] < -summary(lm(y2~x2))$coef[2,4] <alpha
  # Scenario 3: two measurements for every subject, same amount of subjects as in scenario 1
  # two groups with equal amount of subjects, correlation between measurements, groups differ with an
  # Construct a vector that determines in which group each subject falls
 x3<-c(rep(1,n.1),rep(0,n.2),rep(1,n.1),rep(0,n.2))
  # Vector with first observation of every participant
 y3 < -rnorm(n, 0, seps)
  # Factor to multiply second set of observations with to obtain results in line with predefined corr
 alpac<-sqrt(rho[i]^2/(1-rho[i]^2)*seps)</pre>
  # Construct second set of observations that are correlated with first set (y3)
 y3.2u<-alpac*y3+rnorm(n)
 y3.2 < -y3.2u/sqrt(var(y3.2u))
  # Add effect size to the first group of participants
 y3[1:n.1] < -y3[1:n.1] + delta
 y3.2[1:n.1]<-y3.2[1:n.1]+delta
  \# Combine both observations in 1 vector
 y3o < -c(y3, y3.2)
  # Define subject numbers
 subject<-rep(1:n,2)</pre>
  # Construct mixed model
 mm < -lmer(y3o \sim x3 + (1 \mid subject))
  # Boolean of whether an effect is detected, this is later used to compute the power
 pow.3[k] <-summary (mm) $coef [2,5] <alpha
  # Scenario 4: What if we work with the average?
 y3m < -(y3+y3.2)/2
  # Boolean of whether an effect is detected, this is later used to compute the power
 pow.4[k] < -summary(lm(y3m-x))$coef[2,4] <alpha
pow.mean1[i] <-mean(pow.1)</pre>
pow.mean2[i] <-mean(pow.2)</pre>
pow.mean3[i] <-mean(pow.3)</pre>
pow.mean4[i]<-mean(pow.4)
```

Warning in optwrap(optimizer, devfun, getStart(start, rho\$lower, rho\$pp), :
convergence code 3 from bobyqa: bobyqa -- a trust region step failed to

```
## reduce q

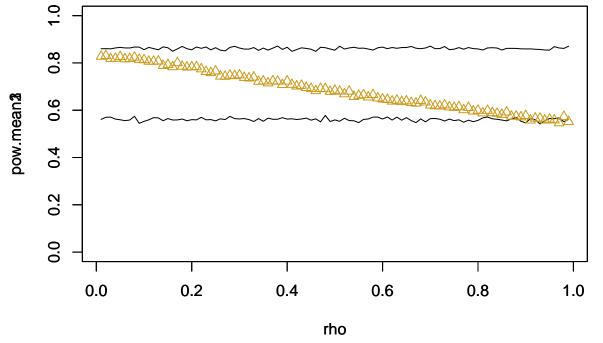
## Warning in optwrap(optimizer, devfun, getStart(start, rho$lower, rho$pp), :
## convergence code 3 from bobyqa: bobyqa -- a trust region step failed to
## reduce q

## Warning in optwrap(optimizer, devfun, getStart(start, rho$lower, rho$pp), :
## convergence code 3 from bobyqa: bobyqa -- a trust region step failed to
## warning in optwrap(optimizer, devfun, getStart(start, rho$lower, rho$pp), :
## convergence code 3 from bobyqa: bobyqa -- a trust region step failed to
## reduce q

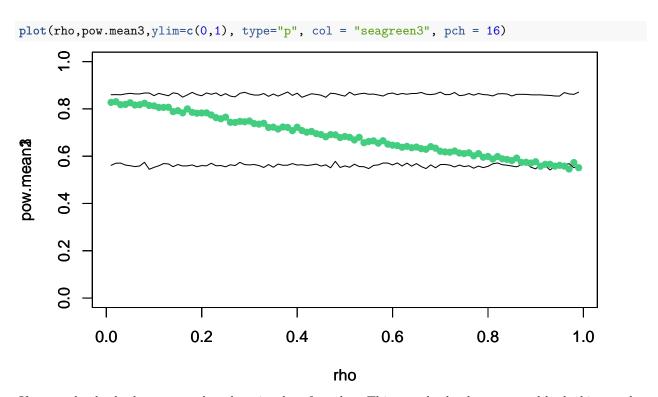
## Warning in optwrap(optimizer, devfun, getStart(start, rho$lower, rho$pp), :
## convergence code 3 from bobyqa: bobyqa -- a trust region step failed to
## reduce q
```

Results

```
# power of taking both measures into account
plot(rho,pow.mean1,ylim=c(0,1), type="l")
par(new = TRUE)
plot(rho,pow.mean2,ylim=c(0,1), type="l")
par(new = TRUE)
plot(rho,pow.mean3,ylim=c(0,1), type="p", col = "goldenrod3", pch = 2)
```



```
# power of using the average
plot(rho,pow.mean1,ylim=c(0,1), type="l")
par(new = TRUE)
plot(rho,pow.mean2,ylim=c(0,1), type="l")
par(new = TRUE)
```

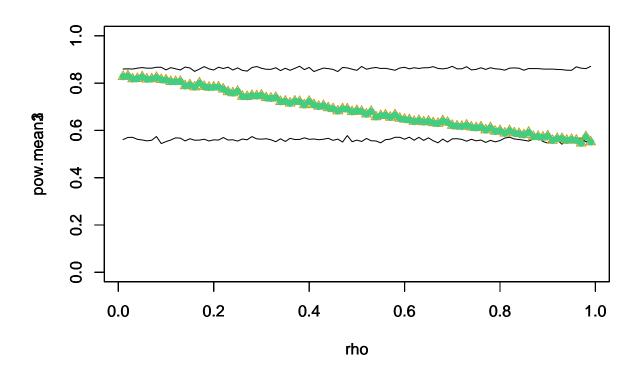


If we overlay both plots we see that there is a lot of overlap. This can also be demonstrated by looking at the results that are exactly the same.

```
table(pow.mean3==pow.mean4)

##
## FALSE TRUE
## 36 63

# Overlap of both plots
plot(rho,pow.mean1,ylim=c(0,1), type="l")
par(new = TRUE)
plot(rho,pow.mean2,ylim=c(0,1), type="l")
par(new = TRUE)
plot(rho,pow.mean3,ylim=c(0,1), type="p", col = "goldenrod3", pch = 2)
par(new = TRUE)
plot(rho,pow.mean3,ylim=c(0,1), type="p", col = "seagreen3", pch = 16)
```



Discussion