

STOPPD cortical thickness analysis (left hemisphere only)

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This script analyses cortical thickness in the left hemisphere.

```
#load libraries
library(tidyverse)
library(lme4)
library(lmerTest)
library(growthmodels)

#bring in data
df <- read_csv('../generated_csvs/STOPPD_participantsCT_20181105.csv') #generated by 05_STOPPD_error in

#make sure that STUDYID is an interger not a number
df$STUDYID <- as.character(df$STUDYID)

#make sure that dateDiff is a number, not an interger
df$dateDiff <- as.numeric(df$dateDiff)

#make a difference score
df$LDifference <- df$LThickness_02 - df$LThickness_01 #we're only concerned with left thickness (as p

df$RandomArm <- factor(df$randomization,
                      levels = c("0", "P"),
                      labels = c("0lanzapine", "Placebo"))

#restructure data for RCT completers' only (N=41)
RCT_CT <- df[(df$category == "RCT"),]

#restructure data for RCT & Relapse participants (N=74)
RCTRelapse_CT <- df %>%
  gather(thick_oldcolname, thickness, LThickness_01, LThickness_02) %>%
  mutate(model_days = if_else(thick_oldcolname == "LThickness_01", 1, dateDiff))

#write out clean dataframe
# write.csv(RCT_CT, '../generated_data/df_leftCT.csv', row.names=FALSE)
```

Print the N's

RCT only

```
RCT_CT %>% count(randomization) %>% knitr::kable()
```

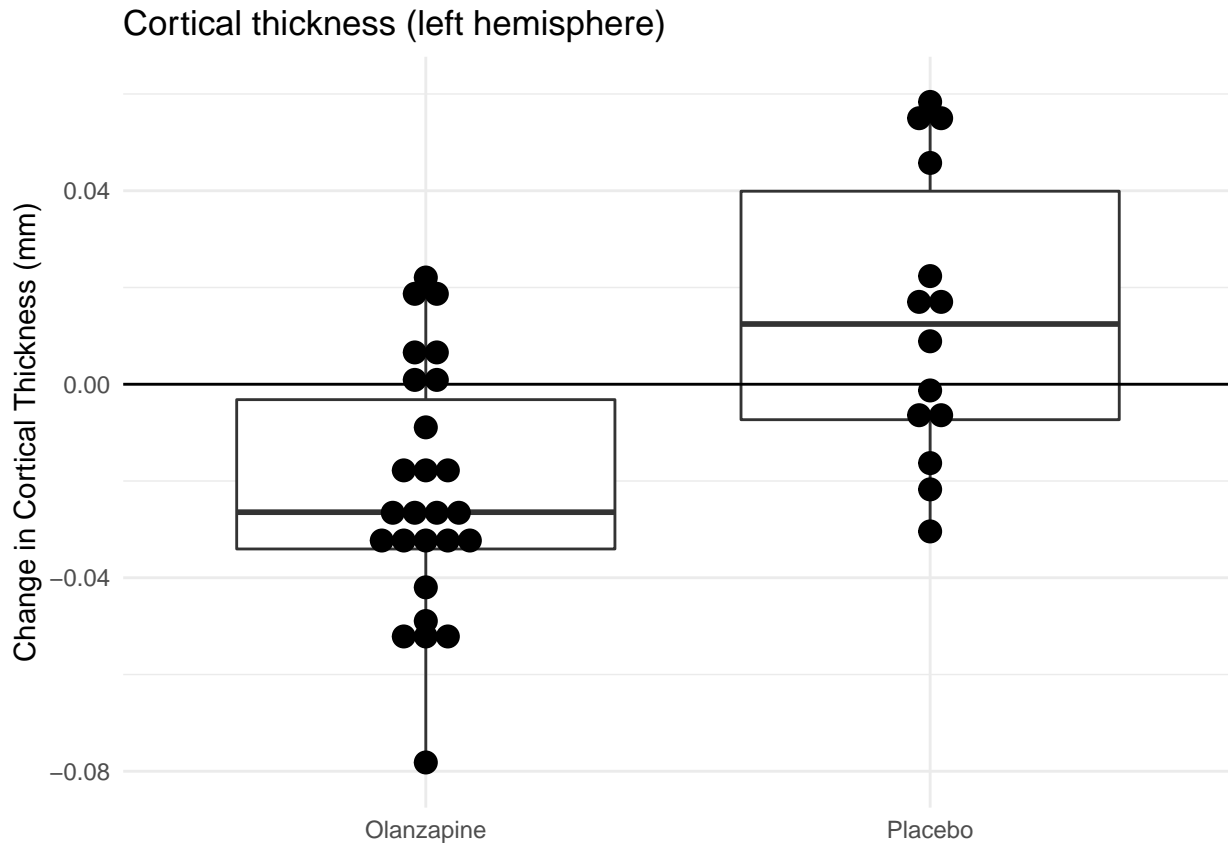
randomization	n
O	26
P	14

```
RCT_CT %>% count(randomization) %>% knitr::kable()
```

randomization	n
O	26
P	14

```
#boxplot of difference in thickness (y axis) by randomization group (x axis)
(plot <- ggplot(RCT_CT, aes(x= RandomArm, y = LDifference)) +
  geom_boxplot(outlier.shape = NA) +
  geom_dotplot(binaxis = 'y', stackdir = 'center') +
  geom_hline(yintercept = 0) +
  ggtitle("Cortical thickness (left hemisphere)") +
  xlab(NULL) +
  ylab("Change in Cortical Thickness (mm)")) +
  theme_minimal()
```

```
## `stat_bindot()` using `bins = 30`. Pick better value with `binwidth`.
```



```
#run linear model without covariates
fit_rct <- lm(LDifference ~ RandomArm, data= RCT_CT)
print(fit_rct)
```

```
##
## Call:
## lm(formula = LDifference ~ RandomArm, data = RCT_CT)
##
## Coefficients:
##      (Intercept)  RandomArmPlacebo
##          -0.02253           0.03659
```

```
summary(fit_rct)
```

```
##
## Call:
## lm(formula = LDifference ~ RandomArm, data = RCT_CT)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.055651 -0.018822 -0.003541  0.022344  0.044589
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)   -0.022529   0.005294  -4.255 0.000131 ***
## RandomArmPlacebo  0.036591   0.008949   4.089 0.000217 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
##
## Residual standard error: 0.027 on 38 degrees of freedom
## Multiple R-squared:  0.3055, Adjusted R-squared:  0.2873
## F-statistic: 16.72 on 1 and 38 DF,  p-value: 0.0002168

#run linear model with covariates of sex and age
fit_rct <- lm(LDifference ~ RandomArm + sex + age, data= RCT_CT)
print(fit_rct)

##
## Call:
## lm(formula = LDifference ~ RandomArm + sex + age, data = RCT_CT)
##
## Coefficients:
##      (Intercept)  RandomArmPlacebo          sexM          age
##      -0.0053535       0.0389342       0.0087658      -0.0004063

summary(fit_rct)

##
## Call:
## lm(formula = LDifference ~ RandomArm + sex + age, data = RCT_CT)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.054543 -0.019130 -0.001897  0.019599  0.050858
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)   -0.0053535   0.0168885   -0.317  0.753081
## RandomArmPlacebo  0.0389342   0.0090734    4.291  0.000128 ***
## sexM           0.0087658   0.0087344    1.004  0.322272
## age          -0.0004063   0.0003132   -1.297  0.202857
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.02691 on 36 degrees of freedom
## Multiple R-squared:  0.3465, Adjusted R-squared:  0.292
## F-statistic: 6.363 on 3 and 36 DF,  p-value: 0.001424

#run linear model with covariates of sex and age
fit_rct <- lm(LDifference ~ RandomArm + sex + age + site, data= RCT_CT)
print(fit_rct)

##
## Call:
## lm(formula = LDifference ~ RandomArm + sex + age + site, data = RCT_CT)
##
## Coefficients:
##      (Intercept)  RandomArmPlacebo          sexM          age
##      0.0003982       0.0404923       0.0127657      -0.0003164
##      siteMAS       siteNKI          sitePMC
##      -0.0193116      -0.0212567      -0.0287115

summary(fit_rct)

##
```

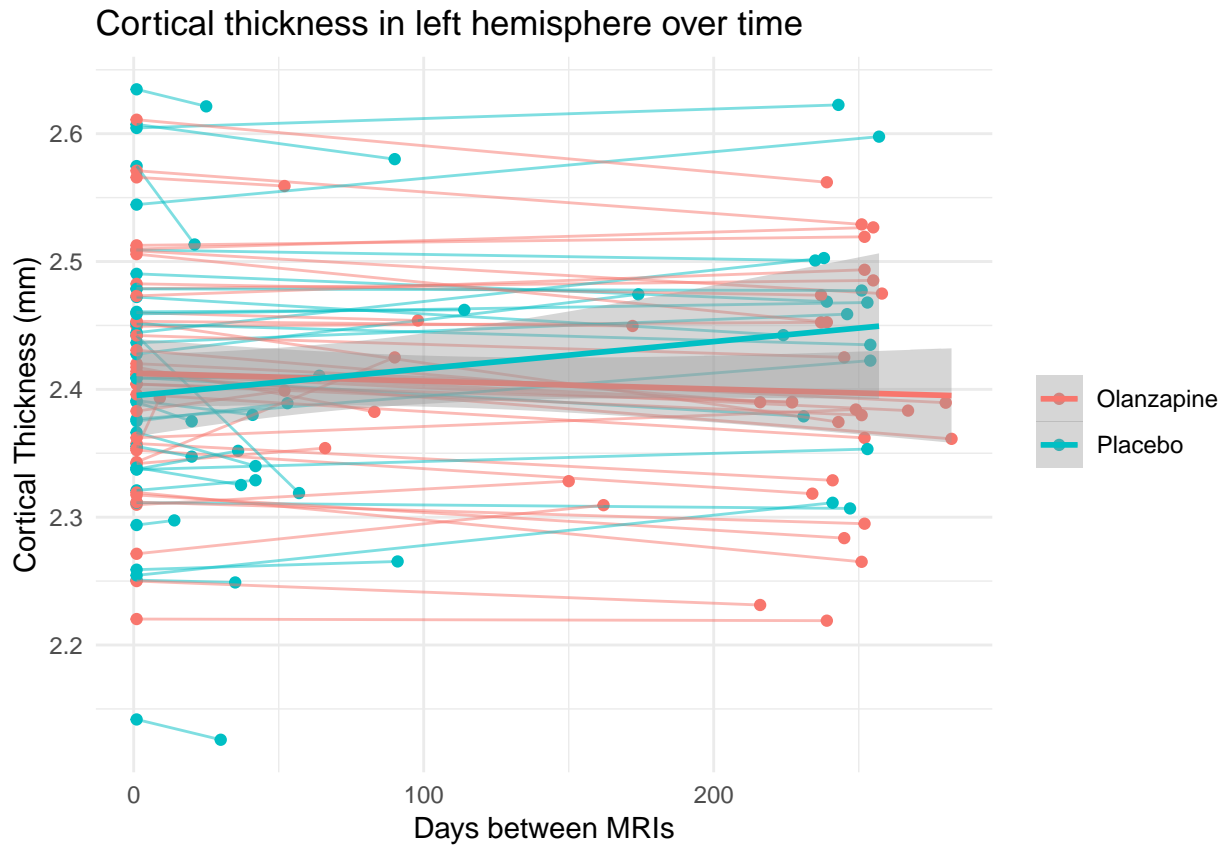
```
## Call:
## lm(formula = LDifference ~ RandomArm + sex + age + site, data = RCT_CT)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.045029 -0.013484 -0.001428  0.017054  0.052285
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)    0.0003982   0.0177658    0.022   0.9823
## RandomArmPlacebo  0.0404923   0.0086868    4.661 4.99e-05 ***
## sexM            0.0127657   0.0083335    1.532   0.1351
## age            -0.0003164   0.0003244   -0.975   0.3365
## siteMAS        -0.0193116   0.0110783   -1.743   0.0906 .
## siteNKI        -0.0212567   0.0105872   -2.008   0.0529 .
## sitePMC        -0.0287115   0.0130066   -2.207   0.0343 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.02527 on 33 degrees of freedom
## Multiple R-squared:  0.4717, Adjusted R-squared:  0.3757
## F-statistic: 4.911 on 6 and 33 DF,  p-value: 0.001094
```

RCT & Relapse (with time as factor)

```
RCTRelapse_CT %>% filter(model_days == 1) %>% count(randomization) %>% knitr::kable()
```

randomization	n
O	38
P	34

```
#plot all data, including outlier (participant 210030)
RCTRelapse_CT %>%
  ggplot(aes(x=model_days, y=thickness, colour=RandomArm)) +
  geom_point() +
  geom_line(aes(group=STUDYID), alpha = 0.5) +
  geom_smooth(method="lm", formula=y~poly(x,1)) +
  ggtitle("Cortical thickness in left hemisphere over time") +
  labs(x = "Days between MRIs", y = "Cortical Thickness (mm)", colour = NULL) +
  theme_minimal()
```



```
#run mixed linear model, with covariates
fit_all <- lmer(thickness ~ RandomArm*model_days + sex + age + (1|STUDYID), data= RCTRelapse_CT)
summary(fit_all)
```

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: thickness ~ RandomArm * model_days + sex + age + (1 | STUDYID)
## Data: RCTRelapse_CT
##
## REML criterion at convergence: -396
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.89073 -0.39603 -0.02082  0.40944  2.76834
##
## Random effects:
## Groups Name Variance Std.Dev.
## STUDYID (Intercept) 0.0054535 0.07385
## Residual 0.0004953 0.02225
## Number of obs: 144, groups: STUDYID, 72
##
## Fixed effects:
##              Estimate Std. Error    df t value
## (Intercept)  2.639e+00  3.484e-02 6.864e+01  75.756
## RandomArmPlacebo -2.035e-03  1.816e-02 7.233e+01  -0.112
## model_days -8.012e-05  2.340e-05 7.056e+01  -3.424
## sexM -6.099e-03  1.792e-02 6.784e+01  -0.340
```

```
## age -4.053e-03 5.853e-04 6.785e+01 -6.924
## RandomArmPlacebo:model_days 1.297e-04 3.942e-05 7.148e+01 3.291
## Pr(>|t|)
## (Intercept) < 2e-16 ***
## RandomArmPlacebo 0.91106
## model_days 0.00103 **
## sexM 0.73470
## age 1.96e-09 ***
## RandomArmPlacebo:model_days 0.00155 **
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
## (Intr) RndmAP mdl_dy sexM age
## RndmArmPlcb -0.206
## model_days -0.077 0.133
## sexM -0.171 0.036 0.001
## age -0.901 -0.053 0.008 -0.079
## RndmArmPl:_ 0.043 -0.176 -0.594 0.004 -0.003
```

#run mixed linear model, with covariates

```
fit_all <- lmer(thickness ~ RandomArm*model_days + sex + age + site + (1|STUDYID), data= RCTRelapse_CT
summary(fit_all)
```

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: thickness ~ RandomArm * model_days + sex + age + site + (1 |
## STUDYID)
## Data: RCTRelapse_CT
##
## REML criterion at convergence: -380.4
##
## Scaled residuals:
## Min 1Q Median 3Q Max
## -2.93368 -0.37860 -0.00129 0.40530 2.72488
##
## Random effects:
## Groups Name Variance Std.Dev.
## STUDYID (Intercept) 0.0055987 0.07482
## Residual 0.0004952 0.02225
## Number of obs: 144, groups: STUDYID, 72
##
## Fixed effects:
## Estimate Std. Error df t value
## (Intercept) 2.640e+00 3.703e-02 6.556e+01 71.309
## RandomArmPlacebo -1.963e-03 1.863e-02 6.894e+01 -0.105
## model_days -8.021e-05 2.341e-05 7.051e+01 -3.427
## sexM -8.192e-03 1.840e-02 6.485e+01 -0.445
## age -4.101e-03 5.970e-04 6.486e+01 -6.869
## siteMAS -6.325e-03 2.335e-02 6.486e+01 -0.271
## siteNKI 1.359e-04 2.587e-02 6.486e+01 0.005
## sitePMC 2.516e-02 2.662e-02 6.485e+01 0.945
## RandomArmPlacebo:model_days 1.296e-04 3.942e-05 7.143e+01 3.286
## Pr(>|t|)
## (Intercept) < 2e-16 ***
```

```

## RandomArmPlacebo          0.91640
## model_days                0.00102 **
## sexM                      0.65759
## age                      2.98e-09 ***
## siteMAS                   0.78731
## siteNKI                   0.99582
## sitePMC                   0.34814
## RandomArmPlacebo:model_days 0.00158 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##      (Intr) RndmAP mdl_dy sexM   age    sitMAS sitNKI sitPMC
## RndmArmPlcb -0.145
## model_days  -0.074  0.129
## sexM         -0.130  0.054  0.002
## age          -0.880 -0.064  0.009 -0.076
## siteMAS      -0.291 -0.145  0.009 -0.066  0.108
## siteNKI      -0.174 -0.119 -0.010 -0.119  0.010  0.357
## sitePMC      -0.153 -0.088  0.000 -0.144 -0.009  0.343  0.319
## RndmArmPl:_  0.040 -0.172 -0.594  0.003 -0.003  0.000  0.009  0.002

```