

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_20181111.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)

# label the randomization variable
df$RandomArm <- factor(df$randomization,
                      levels = c("O", "P"),
                      labels = c("Olanzapine", "Placebo"))

#restructure data for RCT completers' only (N=40)
RCT_CT <- df %>%
  filter(category == "RCT")

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

RCT only

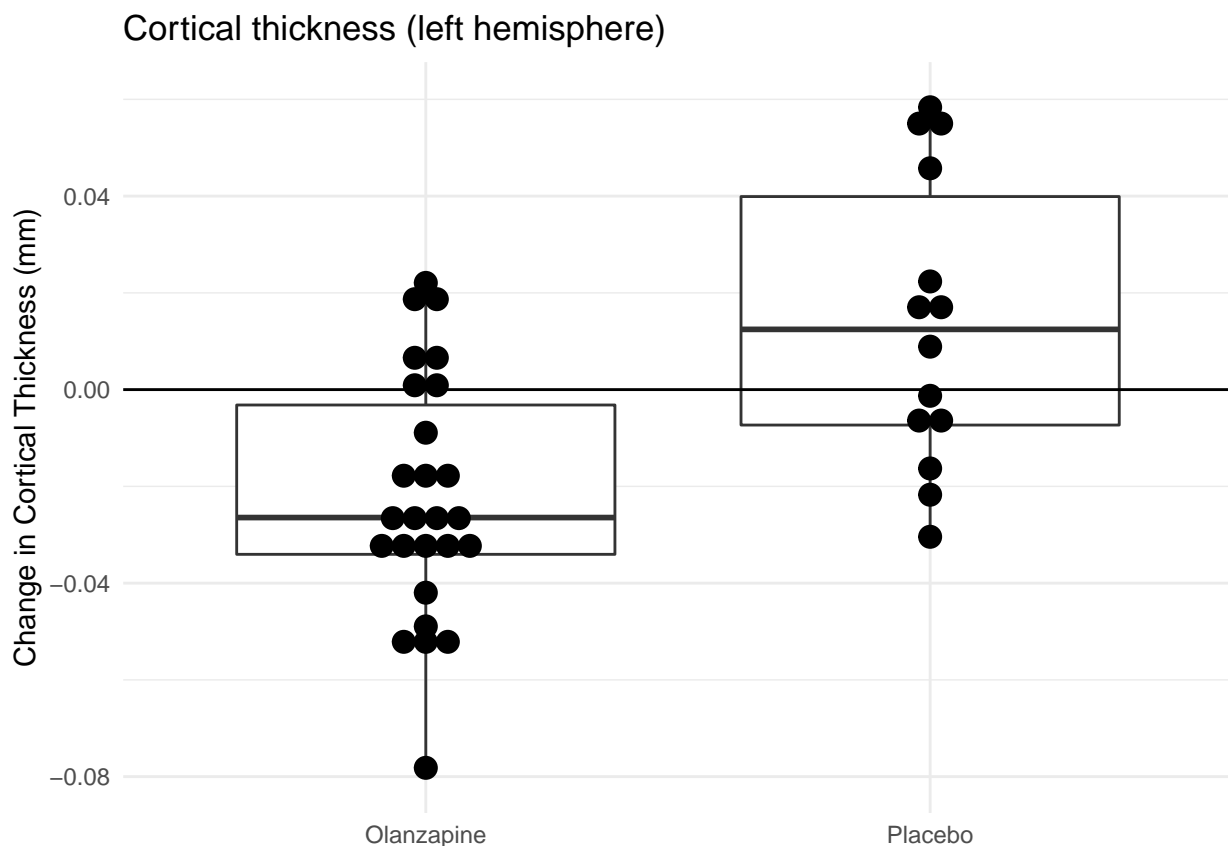
```
RCT_CT %>% count(randomization) %>% knitr::kable()
```

randomization	n
O	26

randomization	n
P	14

```
#boxplot of difference in thickness (y axis) by randomization group (x axis)
ggplot(RCT_CT, aes(x= RandomArm, y = LThickness_change)) +
  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(LThickness_change ~ RandomArm, data= RCT_CT)
print(fit_rct)
```

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

```
summary(fit_rct)
```

```
##
## Call:
## lm(formula = LThickness_change ~ 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(LThickness_change ~ RandomArm + sex + age, data= RCT_CT)
print(fit_rct)
```

```
##
## Call:
## lm(formula = LThickness_change ~ 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 = LThickness_change ~ 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(LThickness_change ~ RandomArm + sex + age + site, data= RCT_CT)
print(fit_rct)
```

```
##
## Call:
## lm(formula = LThickness_change ~ 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
```

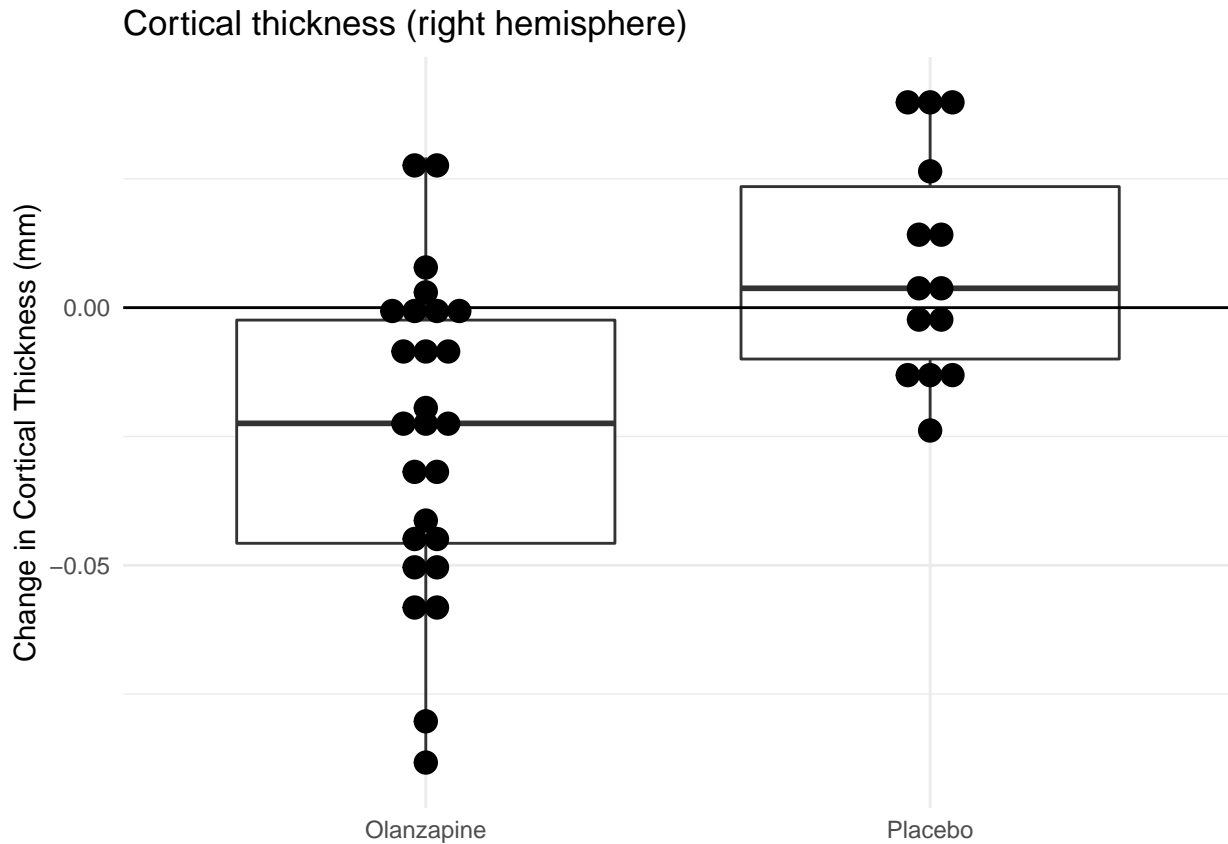
```
summary(fit_rct)
```

```
##
## Call:
## lm(formula = LThickness_change ~ 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
```

looking at the same thing for Right CT

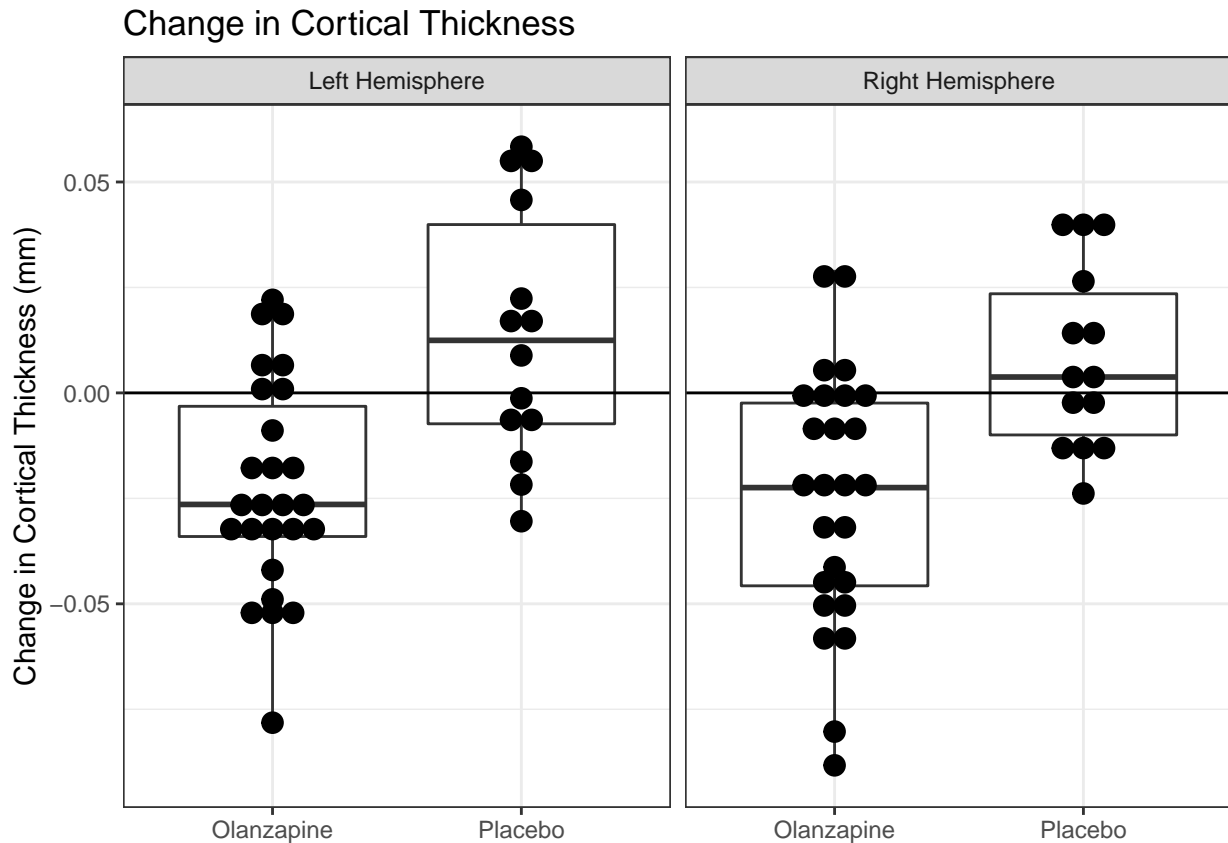
```
#boxplot of difference in thickness (y axis) by randomization group (x axis)
ggplot(RCT_CT, aes(x= RandomArm, y = RThickness_change)) +
  geom_boxplot(outlier.shape = NA) +
  geom_dotplot(binaxis = 'y', stackdir = 'center') +
  geom_hline(yintercept = 0) +
  ggtitle("Cortical thickness (right hemisphere)")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

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



```
#boxplot of difference in thickness (y axis) by randomization group (x axis)
RCT_CT %>%
  gather(TCT, mm, LThickness_change, RThickness_change) %>%
  mutate(ThickChange = factor(TCT, levels = c("LThickness_change", "RThickness_change"),
                                labels = c("Left Hemisphere", "Right Hemisphere"))) %>%
  ggplot(aes(x= RandomArm, y = mm)) +
    geom_boxplot(outlier.shape = NA) +
    geom_dotplot(binaxis = 'y', stackdir = 'center') +
    geom_hline(yintercept = 0) +
    labs(title = "Change in Cortical Thickness", x = NULL, y = "Change in Cortical Thickness (mm)") +
    facet_wrap(~ ThickChange) +
    theme_bw()
```

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



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

##
## Call:
## lm(formula = RThickness_change ~ RandomArm, data = RCT_CT)
##
## Coefficients:
##      (Intercept)  RandomArmPlacebo
##          -0.02434           0.03260

summary(fit_rct)

##
## Call:
## lm(formula = RThickness_change ~ RandomArm, data = RCT_CT)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.06395 -0.02029  0.00013  0.02178  0.05351
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)  -0.024340   0.005360  -4.542  5.5e-05 ***
## RandomArmPlacebo  0.032596   0.009059   3.598 0.000912 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
##
## Residual standard error: 0.02733 on 38 degrees of freedom
## Multiple R-squared:  0.2541, Adjusted R-squared:  0.2345
## F-statistic: 12.95 on 1 and 38 DF,  p-value: 0.0009116

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

##
## Call:
## lm(formula = RThickness_change ~ RandomArm + sex + age, data = RCT_CT)
##
## Coefficients:
##      (Intercept) RandomArmPlacebo          sexM          age
##      -0.0097657      0.0336641      -0.0044117      -0.0002401

summary(fit_rct)

##
## Call:
## lm(formula = RThickness_change ~ RandomArm + sex + age, data = RCT_CT)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.06700 -0.01799 -0.00128  0.01847  0.04950
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)  -0.0097657  0.0173882  -0.562 0.577851
## RandomArmPlacebo  0.0336641  0.0093419   3.604 0.000941 ***
## sexM          -0.0044117  0.0089928  -0.491 0.626698
## age          -0.0002401  0.0003225  -0.744 0.461500
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.0277 on 36 degrees of freedom
## Multiple R-squared:  0.2739, Adjusted R-squared:  0.2134
## F-statistic: 4.527 on 3 and 36 DF,  p-value: 0.008575

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

##
## Call:
## lm(formula = RThickness_change ~ RandomArm + sex + age + site,
##     data = RCT_CT)
##
## Coefficients:
##      (Intercept) RandomArmPlacebo          sexM          age
##      -1.111e-02      3.389e-02      -1.632e-03      -9.043e-05
##      siteMAS      siteNKI          sitePMC
##      -1.010e-02      -1.044e-02      -2.463e-02

summary(fit_rct)
```

```
##
## Call:
## lm(formula = RThickness_change ~ RandomArm + sex + age + site,
##     data = RCT_CT)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.072836 -0.015554  0.000948  0.019346  0.044262
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)   -1.111e-02  1.939e-02  -0.573  0.57042
## RandomArmPlacebo  3.389e-02  9.480e-03   3.575  0.00111 **
## sexM          -1.632e-03  9.095e-03  -0.179  0.85869
## age           -9.043e-05  3.540e-04  -0.255  0.79998
## siteMAS       -1.010e-02  1.209e-02  -0.835  0.40968
## siteNKI       -1.044e-02  1.155e-02  -0.903  0.37287
## sitePMC       -2.463e-02  1.419e-02  -1.735  0.09208 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.02758 on 33 degrees of freedom
## Multiple R-squared:  0.3405, Adjusted R-squared:  0.2206
## F-statistic:  2.84 on 6 and 33 DF,  p-value: 0.02429
```

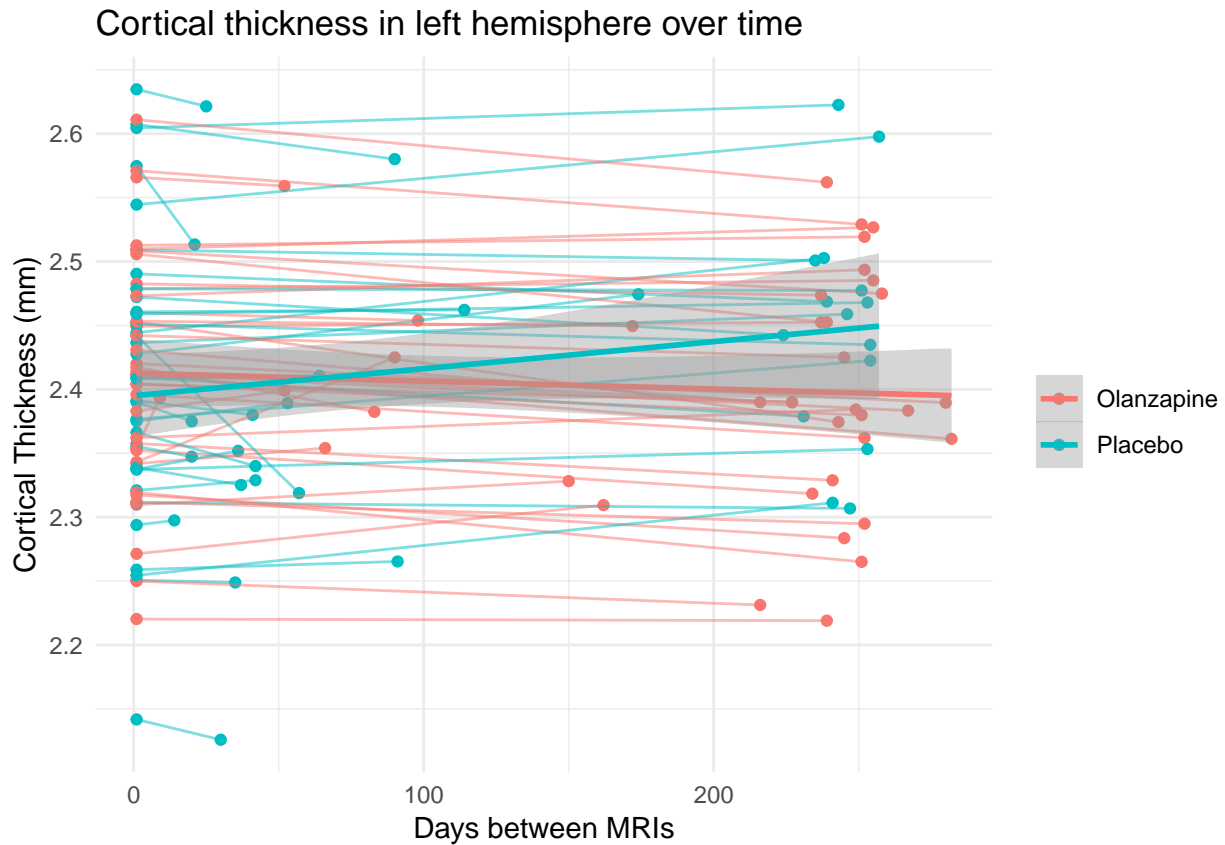
RCT & Relapse (with time as factor)

```
#restructure data for RCT & Relapse participants (N=72)
RCTRelapse_LCT <- df %>%
  gather(thick_oldcolname, thickness, LThickness_01, LThickness_02) %>%
  mutate(model_days = if_else(thick_oldcolname == "LThickness_01", 1, dateDiff))

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

randomization	n
O	38
P	34

```
#plot all data, including outlier (participant 210030)
RCTRelapse_LCT %>%
  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_LCT)
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_LCT
##
## 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_LCT)
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_LCT
##
## 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

```

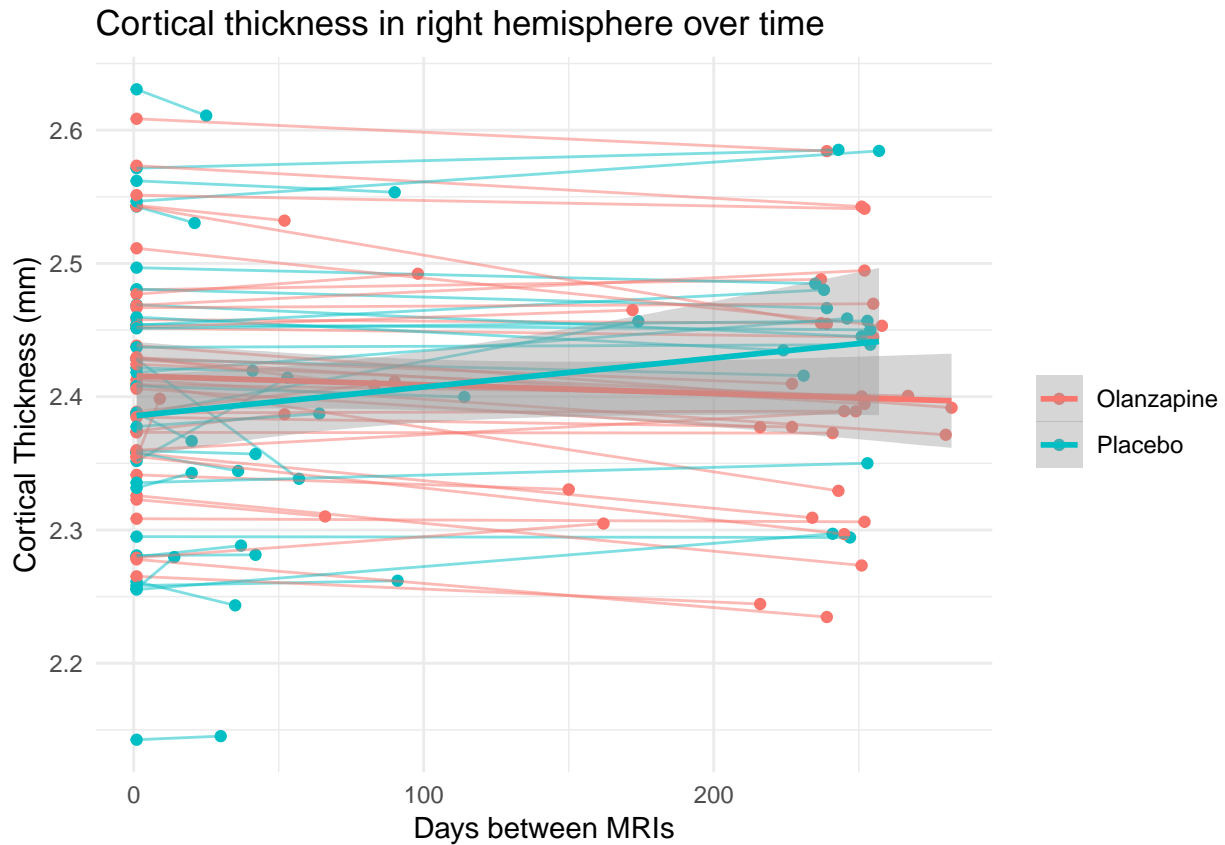
Running the right hemisphere RCTRelapse

```

#restructure data for RCT & Relapse participants (N=72)
RCTRelapse_RCT <- df %>%
  gather(thick_oldcolname, thickness, RThickness_01, RThickness_02) %>%
  mutate(model_days = if_else(thick_oldcolname == "RThickness_01", 1, dateDiff))

#plot all data, including outlier (participant 210030)
RCTRelapse_RCT %>%
  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 right 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_RCT)
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_RCT
##
## REML criterion at convergence: -409
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.34720 -0.42608 -0.01215  0.43733  2.27881
##
## Random effects:
## Groups Name Variance Std.Dev.
## STUDYID (Intercept) 0.0057442 0.07579
## Residual 0.0003947 0.01987
## Number of obs: 144, groups: STUDYID, 72
##
## Fixed effects:
##              Estimate Std. Error    df t value
## (Intercept)  2.618e+00  3.554e-02 6.847e+01  73.658
## RandomArmPlacebo -1.455e-02  1.847e-02 7.131e+01  -0.788
## model_days -8.813e-05  2.090e-05 7.041e+01  -4.216
## sexM -7.789e-03  1.830e-02 6.786e+01  -0.426
```

```

## age -3.588e-03 5.975e-04 6.786e+01 -6.004
## RandomArmPlacebo:model_days 1.281e-04 3.524e-05 7.112e+01 3.635
## Pr(>|t|)
## (Intercept) < 2e-16 ***
## RandomArmPlacebo 0.433361
## model_days 7.28e-05 ***
## sexM 0.671706
## age 8.40e-08 ***
## RandomArmPlacebo:model_days 0.000522 ***
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
## (Intr) RndmAP mdl_dy sexM age
## RndmArmPlcb -0.205
## model_days -0.067 0.117
## sexM -0.172 0.036 0.001
## age -0.902 -0.053 0.007 -0.079
## RndmArmPl:_ 0.037 -0.155 -0.593 0.003 -0.002

#run mixed linear model, with covariates
fit_all <- lmer(thickness ~ RandomArm*model_days + sex + age + site + (1|STUDYID), data= RCTRelapse_R
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_RCT
##
## REML criterion at convergence: -393.2
##
## Scaled residuals:
## Min 1Q Median 3Q Max
## -2.37660 -0.44552 -0.00537 0.43115 2.24882
##
## Random effects:
## Groups Name Variance Std.Dev.
## STUDYID (Intercept) 0.0059298 0.07701
## Residual 0.0003947 0.01987
## Number of obs: 144, groups: STUDYID, 72
##
## Fixed effects:
## Estimate Std. Error df t value
## (Intercept) 2.619e+00 3.788e-02 6.541e+01 69.150
## RandomArmPlacebo -1.446e-02 1.900e-02 6.800e+01 -0.761
## model_days -8.825e-05 2.091e-05 7.037e+01 -4.221
## sexM -9.731e-03 1.883e-02 6.487e+01 -0.517
## age -3.638e-03 6.112e-04 6.487e+01 -5.952
## siteMAS -7.805e-03 2.390e-02 6.488e+01 -0.327
## siteNKI 4.352e-03 2.649e-02 6.488e+01 0.164
## sitePMC 2.024e-02 2.725e-02 6.487e+01 0.743
## RandomArmPlacebo:model_days 1.280e-04 3.524e-05 7.108e+01 3.631
## Pr(>|t|)
## (Intercept) < 2e-16 ***

```

```

## RandomArmPlacebo          0.449288
## model_days                7.14e-05 ***
## sexM                      0.607158
## age                      1.18e-07 ***
## siteMAS                   0.745036
## siteNKI                   0.870002
## sitePMC                   0.460300
## RandomArmPlacebo:model_days 0.000529 ***
## ---
## 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 -0.144
## model_days -0.064  0.113
## sexM       -0.130  0.055  0.002
## age        -0.881 -0.065  0.008 -0.076
## siteMAS    -0.291 -0.146  0.007 -0.066  0.108
## siteNKI    -0.175 -0.119 -0.008 -0.119  0.010  0.357
## sitePMC    -0.153 -0.089  0.000 -0.144 -0.009  0.343  0.319
## RndmArmPl:_ 0.035 -0.151 -0.593  0.003 -0.003  0.000  0.008  0.002

```