

STOPPD cortical thickness analysis (left hemisphere only)

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This script analyses cortical thickness in the left hemisphere.

```
#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("O", "P"),
                      labels = c("Olanzapine", "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)
```

Exclusions from this analysis and reasons

subject 210030 (MAS): serious outlier.. it appears that this participants baseline is acutally a mislabeled repeat of the subject 210022's baseline data. Calculating the difference in cortical thinkness between two different people was a relatively large value..

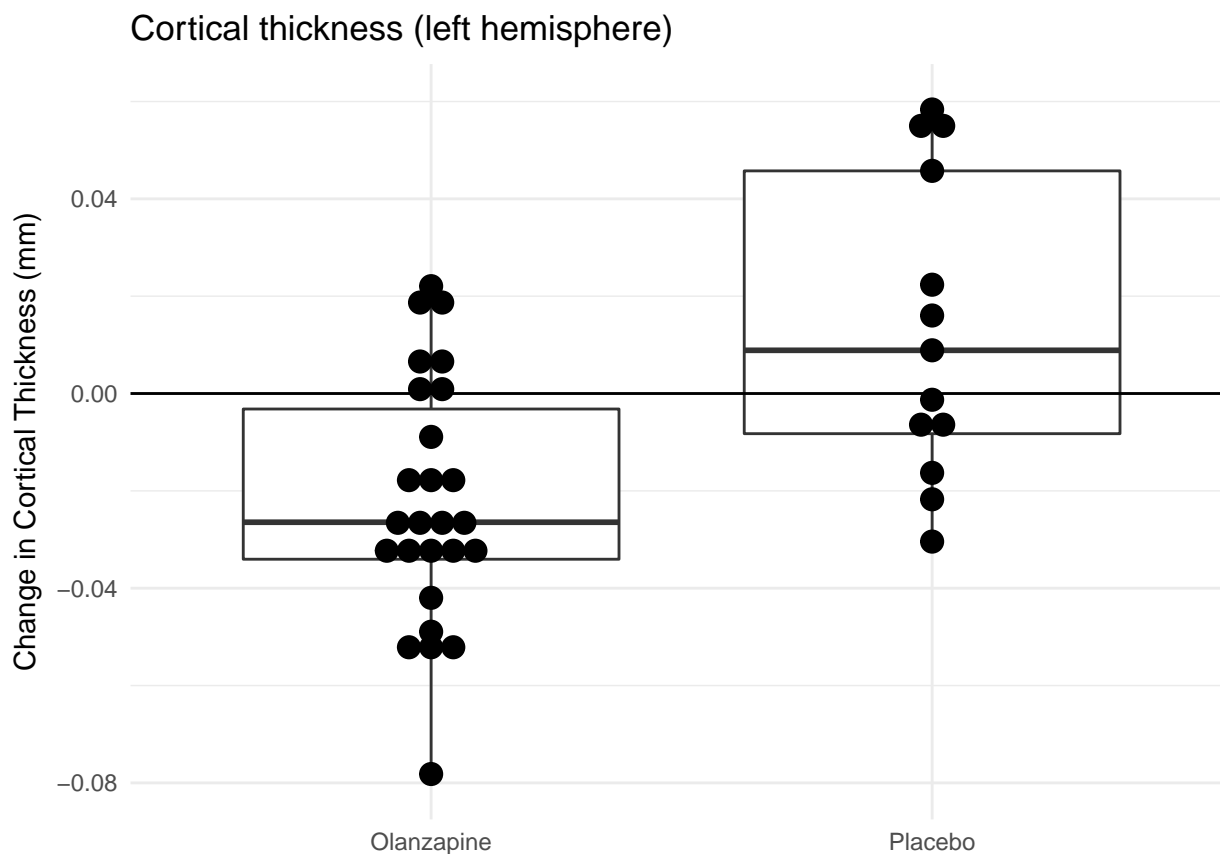
subject 320032 (PMC): incidental findings more atrophy, should excluded

```
RCT_CT <- filter(RCT_CT, !(STUDYID %in% c("210030", "320032")))
RCTRelapse_CT <- filter(RCTRelapse_CT, !(STUDYID %in% c("210030", "320032")))
```

RCT only

```
#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      0.03629
summary(fit_rct)
```

```
##
## Call:
## lm(formula = LDifference ~ RandomArm, data = RCT_CT)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.055651 -0.018879 -0.004877  0.023429  0.044603
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)   -0.022529   0.005364  -4.200 0.000161 ***
## RandomArmPlacebo  0.036286   0.009291   3.906 0.000384 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.02735 on 37 degrees of freedom
## Multiple R-squared:  0.2919, Adjusted R-squared:  0.2728
## F-statistic: 15.25 on 1 and 37 DF,  p-value: 0.0003845
#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
##      -0.0049692      0.0394312      0.0091736     -0.0004173
summary(fit_rct)

##
## Call:
## lm(formula = LDifference ~ RandomArm + sex + age, data = RCT_CT)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.054434 -0.020198 -0.000047  0.020688  0.050722
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)   -0.0049692   0.0172200  -0.289 0.774614
## RandomArmPlacebo  0.0394312   0.0095104   4.146 0.000204 ***
## sexM           0.0091736   0.0090735   1.011 0.318938
## age          -0.0004173   0.0003220  -1.296 0.203458
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.02727 on 35 degrees of freedom
## Multiple R-squared:  0.3341, Adjusted R-squared:  0.277
## F-statistic: 5.853 on 3 and 35 DF,  p-value: 0.00238
#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
##      0.0004801      0.0406154      0.0128779      -0.0003194
##      siteMAS      siteNKI      sitePMC
##      -0.0191304      -0.0212857      -0.0287078

summary(fit_rct)

##
## Call:
## lm(formula = LDifference ~ RandomArm + sex + age + site, data = RCT_CT)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.045158 -0.014002 -0.001631  0.017064  0.052044
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)    0.0004801   0.0180872    0.027   0.9790
## RandomArmPlacebo 0.0406154   0.0090358    4.495 8.57e-05 ***
## sexM            0.0128779   0.0086482    1.489   0.1463
## age            -0.0003194   0.0003328   -0.960   0.3444
## siteMAS        -0.0191304   0.0116128   -1.647   0.1093
## siteNKI        -0.0212857   0.0107606   -1.978   0.0566 .
## sitePMC        -0.0287078   0.0132075   -2.174   0.0372 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.02566 on 32 degrees of freedom
## Multiple R-squared:  0.4611, Adjusted R-squared:  0.3601
## F-statistic: 4.564 on 6 and 32 DF,  p-value: 0.001887

```

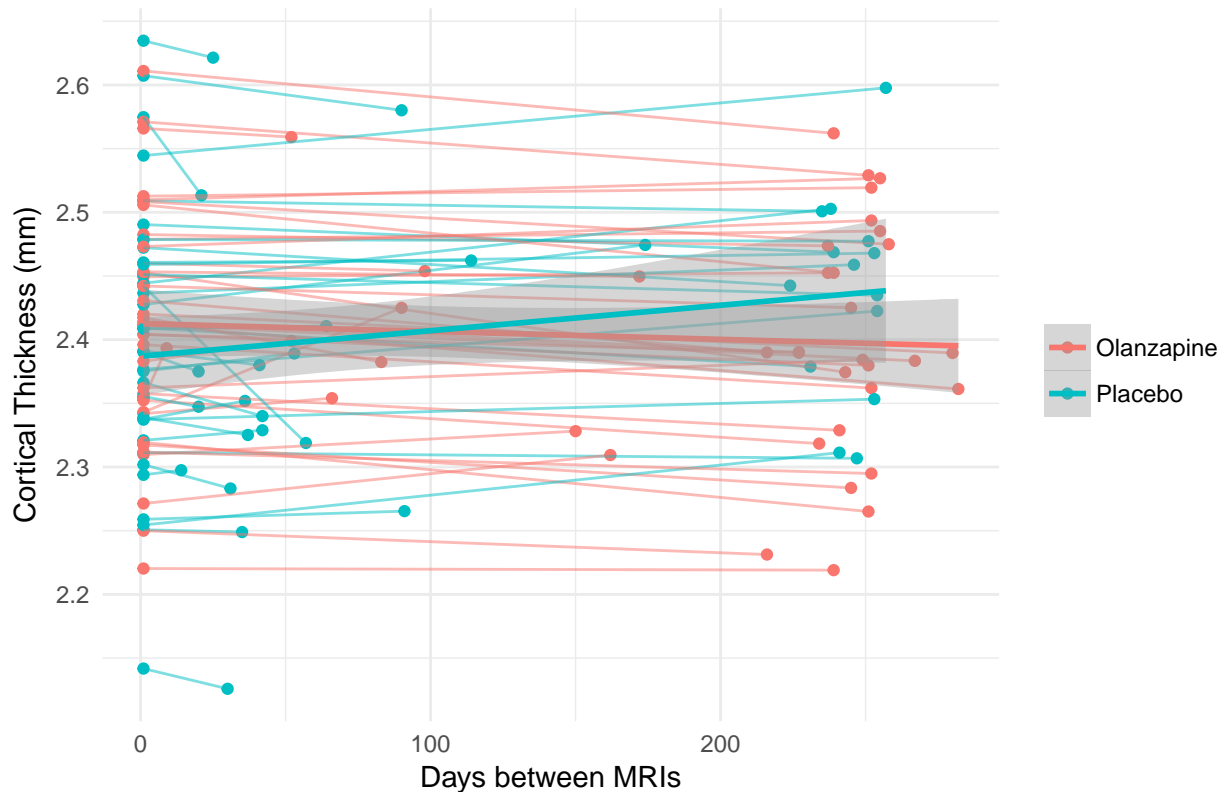
RCT & Relapse (with time as factor)

```

#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()

```

Cortical thickness in left hemisphere over time



```
#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: -395.9
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.86368 -0.40010 -0.02013  0.40442  2.77636
##
## Random effects:
## Groups Name Variance Std.Dev.
## STUDYID (Intercept) 0.0054333 0.07371
## Residual 0.0004976 0.02231
## Number of obs: 144, groups: STUDYID, 72
##
## Fixed effects:
##              Estimate Std. Error    df t value
## (Intercept)  2.627e+00  3.458e-02 6.865e+01  75.967
## RandomArmPlacebo -1.243e-02  1.815e-02 7.226e+01  -0.685
## model_days -8.005e-05  2.346e-05 7.056e+01  -3.413
## sexM -8.324e-03  1.800e-02 6.784e+01  -0.462
```

```

## age -3.807e-03 5.834e-04 6.784e+01 -6.525
## RandomArmPlacebo:model_days 1.274e-04 4.030e-05 7.159e+01 3.161
## Pr(>|t|)
## (Intercept) < 2e-16 ***
## RandomArmPlacebo 0.49553
## model_days 0.00107 **
## sexM 0.64530
## age 1.01e-08 ***
## RandomArmPlacebo:model_days 0.00231 **
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
## (Intr) RndmAP mdl_dy sexM age
## RndmArmPlcb -0.216
## model_days -0.078 0.133
## sexM -0.155 0.065 0.001
## age -0.900 -0.051 0.008 -0.100
## RndmArmPl:_ 0.045 -0.174 -0.582 0.005 -0.006

#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: -381.2
##
## Scaled residuals:
## Min 1Q Median 3Q Max
## -2.91914 -0.37912 -0.00243 0.41014 2.72028
##
## Random effects:
## Groups Name Variance Std.Dev.
## STUDYID (Intercept) 0.0054994 0.07416
## Residual 0.0004975 0.02231
## Number of obs: 144, groups: STUDYID, 72
##
## Fixed effects:
## Estimate Std. Error df t value
## (Intercept) 2.627e+00 3.628e-02 6.558e+01 72.427
## RandomArmPlacebo -1.310e-02 1.841e-02 6.898e+01 -0.712
## model_days -8.028e-05 2.346e-05 7.052e+01 -3.422
## sexM -1.206e-02 1.840e-02 6.485e+01 -0.655
## age -3.867e-03 5.896e-04 6.485e+01 -6.559
## siteMAS -8.584e-03 2.324e-02 6.485e+01 -0.369
## siteNKI 8.004e-03 2.552e-02 6.485e+01 0.314
## sitePMC 3.256e-02 2.629e-02 6.484e+01 1.239
## RandomArmPlacebo:model_days 1.273e-04 4.030e-05 7.157e+01 3.158
## Pr(>|t|)
## (Intercept) < 2e-16 ***

```

```

## RandomArmPlacebo          0.47915
## model_days                0.00104 **
## sexM                      0.51453
## age                       1.05e-08 ***
## siteMAS                   0.71304
## siteNKI                   0.75481
## sitePMC                   0.21994
## RandomArmPlacebo:model_days 0.00232 **
## ---
## 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 -0.170
## model_days  -0.075  0.132
## sexM         -0.119  0.082  0.002
## age          -0.877 -0.056  0.009 -0.093
## siteMAS      -0.272 -0.106  0.009 -0.051  0.083
## siteNKI      -0.161 -0.107 -0.010 -0.131  0.000  0.339
## sitePMC      -0.140 -0.078  0.000 -0.154 -0.018  0.326  0.313
## RndmArmPl:_  0.043 -0.172 -0.582  0.005 -0.006  0.000  0.006  0.000

```