Shank3 Modulates Sleep and Expression of Circadian Transcription Factors differential expression

october 25, 2018

Contents

Analysis for activity

```
wt <- read_xlsx("Activity_analysis_4_R.xlsx", sheet = 1)
mut <- read_xlsx("Activity_analysis_4_R.xlsx", sheet = 2)

wt <- wt %>%
  bind_cols(WT.M=rep("WT", nrow(wt)), time = decimal_date(ymd(wt$`Total_revolutions/day`)), .) %>%
  gather(mice, activity, -c(1:5))  %>%
  mutate(time = time-min(time)) %>%
  select(-`Total_revolutions/day`)

mut <- mut %>%
  bind_cols(WT.M=rep("M", nrow(mut)), time = decimal_date(ymd(mut$`Total_revolutions/day`)), .) %>%
  gather(mice, activity, -c(1:5))  %>%
  mutate(time = time-min(time)) %>%
  select(-`Total_revolutions/day`)

data <- wt %>% bind_rows(mut)

data <- data %>% filter(week>=3)

data$mice <- factor(data$mice, levels= unique(data$mice))
data$time_scaled <- scale(data$time, scale=FALSE)
data$period <- factor(data$period, levels= unique(data$period))
data$WT.M <-factor(data$WT.M, levels=c("WT", "M"))

mod <- lme(activity ~ time_scaled * WT.M, random=~1|mice, data = data)

cat("Estimates, errors and the significance")
```

```
## Estimates, errors and the significance
```

```
summary(mod)
```

```
## Linear mixed-effects model fit by REML
##  Data: data
##        AIC      BIC   logLik
```

```
##   8681.339 8705.303 -4334.67
##
## Random effects:
##  Formula: ~1 | mice
##         (Intercept) Residual
## StdDev:    14936.81 11161.46
##
## Fixed effects: activity ~ time_scaled * WT.M
##                         Value Std.Error  DF   t-value p-value
## (Intercept)          38778.45   5335.29 388  7.268296  0.0000
## time_scaled         -20486.52  35588.68 388 -0.575647  0.5652
## WT.MM               -20324.26   7810.06  13 -2.602317  0.0219
## time_scaled:WT.MM -289880.69  52096.49 388 -5.564304  0.0000
##  Correlation:
##                     (Intr) tm_scl WT.MM
## time_scaled          0.000
## WT.MM               -0.683  0.000
## time_scaled:WT.MM    0.000 -0.683  0.000
##
## Standardized Within-Group Residuals:
##         Min          Q1         Med          Q3         Max
## -2.69133816 -0.63470177  0.03277689  0.63109234  3.19701990
##
## Number of Observations: 405
## Number of Groups: 15
```

```
cat("Bootstrap confidence intervals for the estimates")
```

```
## Bootstrap confidence intervals for the estimates
```

```
mod_lmer <- lmer(activity ~ time_scaled * WT.M + (1|mice), data = data)
confint.merMod(mod_lmer, method = "boot", nsim = 999)
```

```
## Computing bootstrap confidence intervals ...
```

```
##                           2.5 %      97.5 %
## .sig01                 9168.051   20867.781
## .sigma                10340.936   11949.842
## (Intercept)           28714.922   49160.714
## time_scaled          -97516.675   47096.142
## WT.MM                -36220.231   -5146.717
## time_scaled:WT.MM -391310.705 -192338.249
```

```
cat("ANOVA table")
```

```
## ANOVA table
```

```
anova.lme(mod, type = "marginal", adjustSigma = F)
```

```
##                   numDF denDF  F-value p-value
## (Intercept)           1   388 52.82812  <.0001
## time_scaled           1   388  0.33137  0.5652
## WT.M                  1    13  6.77206  0.0219
## time_scaled:WT.M      1   388 30.96148  <.0001
```

Analysis for alpha

```
wt <- read_xlsx("Alpha_Activity_analysis_4_R.xlsx", sheet = 1, na = "NA")
mut <- read_xlsx("Alpha_Activity_analysis_4_R.xlsx", sheet = 2, na = "NA")

wt <- wt %>%
  bind_cols(WT.M = rep("WT", nrow(wt)), time = decimal_date(ymd(wt$`Total_revolutions/day`)), .)%>%
  gather(mice, alpha, -c(1:5))  %>%
  mutate(time = time-min(time)) %>%
  select(-`Total_revolutions/day`)

mut <- mut %>%
  bind_cols(WT.M=rep("M", nrow(mut)), time = decimal_date(ymd(mut$`Total_revolutions/day`)), .)%>%
  gather(mice, alpha, -c(1:5))  %>%
  mutate(time = time-min(time)) %>%
  select(-`Total_revolutions/day`)

alpha_data <- wt %>% bind_rows(mut)

alpha_data <- alpha_data %>% filter(week>=3)
alpha_data<- na.omit(alpha_data)

alpha_data$mice <- factor(alpha_data$mice, levels= unique(alpha_data$mice))
alpha_data$time_scaled <- scale(alpha_data$time, scale=FALSE)
alpha_data$period <- factor(alpha_data$period, levels= unique(alpha_data$period))
alpha_data$WT.M <- factor(alpha_data$WT.M, levels=c("WT", "M"))
alpha_data$alpha <-  as.numeric(alpha_data$alpha)

mod1 <- lme(alpha ~ time_scaled * WT.M, random=~1|mice, data = alpha_data, na.action = na.omit)

cat("Estimates, errors and the significance")
```

```
## Estimates, errors and the significance
```

```
summary(mod1)
```

```
## Linear mixed-effects model fit by REML
##  Data: alpha_data
##        AIC      BIC    logLik
##   2068.243 2091.978 -1028.121
##
## Random effects:
##  Formula: ~1 | mice
##         (Intercept) Residual
## StdDev:   0.6720236 3.405597
##
## Fixed effects: alpha ~ time_scaled * WT.M
##                         Value Std.Error  DF   t-value p-value
## (Intercept)        10.101010  0.334981 373 30.154013  0.0000
## time_scaled       -16.267322 11.031558 373 -1.474617  0.1412
## WT.MM              -0.714526  0.490361  13 -1.457142  0.1688
## time_scaled:WT.MM   2.360361 16.148547 373  0.146166  0.8839
##  Correlation:
##                   (Intr) tm_scl WT.MM
```

```
## time_scaled        0.000
## WT.MM             -0.683  0.000
## time_scaled:WT.MM  0.000 -0.683  0.000
##
## Standardized Within-Group Residuals:
##         Min          Q1         Med          Q3         Max
## -2.73631345 -0.48276146  0.06646042  0.49709145  3.94949030
##
## Number of Observations: 390
## Number of Groups: 15
```

```
cat("Bootstrap confidence intervals for the estimates")
```

```
## Bootstrap confidence intervals for the estimates
```

```
mod1_lmer <- lmer(alpha ~ time_scaled * WT.M + (1|mice), data = alpha_data)
confint.merMod(mod1_lmer, method = "boot", nsim = 999)
```

```
## Computing bootstrap confidence intervals ...
```

```
##                            2.5 %     97.5 %
## .sig01              3.696040e-09  1.1421226
## .sigma              3.155698e+00  3.6478932
## (Intercept)         9.441383e+00 10.7525585
## time_scaled        -3.651272e+01  5.2414428
## WT.MM              -1.704223e+00  0.2816872
## time_scaled:WT.MM -3.097407e+01 32.6586697
```

```
cat("ANOVA table")
```

```
## ANOVA table
```

```
anova.lme(mod1, type = "marginal", adjustSigma = F)
```

```
##                   numDF denDF  F-value p-value
## (Intercept)           1   373 909.2645  <.0001
## time_scaled           1   373   2.1745  0.1412
## WT.M                  1    13   2.1233  0.1688
## time_scaled:WT.M      1   373   0.0214  0.8839
```

Analysis for period

```
wt <- read_xlsx("Period_analysis_4_R.xlsx", sheet = 1)  %>% gather(mice, value, -1)
wt <- data.frame(WT.M=rep("WT", nrow(wt))) %>% bind_cols(wt)
mut <- read_xlsx("Period_analysis_4_R.xlsx", sheet = 2)  %>% gather(mice, value, -1)
mut <- data.frame(WT.M=rep("M", nrow(mut))) %>% bind_cols(mut)

period_data <- wt %>% bind_rows(mut)
period_data$value <- as.numeric(period_data$value)

mod2 <- lme(value~ week * WT.M, random = ~1|mice, data = period_data)

cat("Estimates, errors and the significance")
```

```
## Estimates, errors and the significance
```

```r
summary(mod2)
```

```
## Linear mixed-effects model fit by REML
##  Data: period_data
##        AIC   BIC    logLik
##   309.1875 328.7 -144.5938
##
## Random effects:
##  Formula: ~1 | mice
##         (Intercept) Residual
## StdDev:   0.7251103 3.268825
##
## Fixed effects: value ~ week * WT.M
##                            Value Std.Error DF   t-value p-value
## (Intercept)           23.721429  1.265532 39 18.744234  0.0000
## weekDD_Week_2         -3.381429  1.747260 39 -1.935275  0.0602
## weekDD_Week_3          2.055714  1.747260 39  1.176536  0.2465
## weekLD_Week_3          0.208571  1.747260 39  0.119371  0.9056
## WT.MWT                 0.137321  1.732901 13  0.079244  0.9380
## weekDD_Week_2:WT.MWT   3.251429  2.392535 39  1.358989  0.1820
## weekDD_Week_3:WT.MWT -2.426964  2.392535 39 -1.014390  0.3166
## weekLD_Week_3:WT.MWT -0.063571  2.392535 39 -0.026571  0.9789
##  Correlation:
##                       (Intr) wkDD_W_2 wkDD_W_3 wkLD_W_3 WT.MWT wDD_W_2:
## weekDD_Week_2         -0.690
## weekDD_Week_3         -0.690  0.500
## weekLD_Week_3         -0.690  0.500    0.500
## WT.MWT                -0.730  0.504    0.504    0.504
## weekDD_Week_2:WT.MWT   0.504 -0.730   -0.365   -0.365   -0.690
## weekDD_Week_3:WT.MWT   0.504 -0.365   -0.730   -0.365   -0.690  0.500
## weekLD_Week_3:WT.MWT   0.504 -0.365   -0.365   -0.730   -0.690  0.500
##                       wDD_W_3:
## weekDD_Week_2
## weekDD_Week_3
## weekLD_Week_3
## WT.MWT
## weekDD_Week_2:WT.MWT
## weekDD_Week_3:WT.MWT
## weekLD_Week_3:WT.MWT   0.500
##
## Standardized Within-Group Residuals:
##          Min           Q1          Med           Q3          Max
## -5.938352181 -0.067963537 -0.001414478  0.093674882  1.778532447
##
## Number of Observations: 60
## Number of Groups: 15
```

```r
cat("Bootstrap confidence intervals for the estimates")
```

```
## Bootstrap confidence intervals for the estimates
```

```r
mod2_lmer <- lmer(value ~ week * WT.M + (1|mice), data = period_data)
confint.merMod(mod2_lmer, method = "boot", nsim = 999)
```

```
## Computing bootstrap confidence intervals ...
```

```
##                            2.5 %      97.5 %
## .sig01                  0.000000  2.04676228
## .sigma                  2.446744  3.89218064
## (Intercept)            21.341927 26.39535290
## weekDD_Week_2          -6.882343  0.09411144
## weekDD_Week_3          -1.445615  5.57006947
## weekLD_Week_3          -3.244210  3.70052742
## WT.MWT                 -3.064934  3.50727475
## weekDD_Week_2:WT.MWT   -1.460366  8.01695360
## weekDD_Week_3:WT.MWT   -6.998269  2.29216137
## weekLD_Week_3:WT.MWT   -5.115730  4.66459328
```

```
cat("ANOVA table")
```

```
## ANOVA table
```

```
anova.lme(mod2, type = "marginal", adjustSigma = F)
```

```
##              numDF denDF  F-value p-value
## (Intercept)      1    39 351.3463  <.0001
## week             3    39   3.3611  0.0282
## WT.M             1    13   0.0063  0.9380
## week:WT.M        3    39   1.9008  0.1454
```