

Robust symptom networks in recurrent major depression across different levels of genetic and environmental risk

HM van Loo, CD van Borkulo, RE Peterson, EI Fried, SH Aggen, D Borsboom, KS Kendler

J Aff Disorders, 2017

Set up: load libraries and data

```
# Load libraries
library(IsingFit); library(qgraph); library(NetworkComparisonTest); library(knitr)

# Load data
load('CONVERGE.networks.Rdata')
nrow(data) # 5784

# Column names of symptoms
all.sx <- c("DSM_A3a", "DSM_A3b", "DSM_A3c", "DSM_A3d", "DSM_A4a", "DSM_A4b",
           "DSM_A5a", "DSM_A5b", "fDSM_A6", "fDSM_A7", "fDSM_A8", "fDSM_A9",
           "nDSM_10", "nDSM_12", "nDSM_13", "nDSM_14", "nDSM_15", "nDSM_16",
           "nDSM_17", "nDSM_18", "nDSM_19", "nDSM_20", "nDSM_21", "nDSM_22")

# Abbreviations of symptoms
varnames_4 <- c("appl", "wgtl", "appg", "wgtg", "inso", "hyso", "reta",
               "agit", "fati", "guil", "conc", "suic",
               "intl", "self", "conf", "qual", "diur", "libi",
               "reac", "irri", "hope", "cryi", "help", "nerv")
```

Network for total sample (n=5784) of all 24 symptoms

```
# Network including all 24 symptoms
nw0 <- IsingFit(na.omit(data[, all.sx]), plot = F, progressBar = F) #
nrow(na.omit(data[, all.sx])) # 5784

# Edge weights (lasso penalized ORs)
ORs <- exp(nw0$weiadj)

# Thresholds
Thresholds <- exp(nw0$thresholds)

# Node strength
node.strength0 <- centrality(nw0$weiadj)$InDegree
node.betweenness0 <- centrality(nw0$weiadj)$Betweenness
node.closeness0 <- centrality(nw0$weiadj)$Closeness
```

Subset data for network comparisons tests

```
# Family history (FH)
data1 <- subset(na.omit(data[, c(all.sx, "fh.pos.strict")]), fh.pos.strict == 0) # n=3907
data2 <- subset(na.omit(data[, c(all.sx, "fh.pos.strict")]), fh.pos.strict == 1) # n=1494
```

```

# Stress
data3 <- subset(na.omit(data[, c(all.sx, "adversity_all")] ), adversity_all == 0) # n=3511
data4 <- subset(na.omit(data[, c(all.sx, "adversity_all")] ), adversity_all == 1) # n=1812

# High polygenic risk score (PRS)
data5 <- subset(na.omit(data[, c(all.sx, "highPRS.blup")] ), highPRS.blup == 0) # n=3909
data6 <- subset(na.omit(data[, c(all.sx, "highPRS.blup")] ), highPRS.blup == 1) # n=1301

# Early age at onset (AAO)
data7 <- subset(na.omit(data[, c(all.sx, "aao_early")] ), aao_early == 0) # n=4149
data8 <- subset(na.omit(data[, c(all.sx, "aao_early")] ), aao_early == 1) # n=1477

```

Network comparison tests (NCT)

```

# FH
nct1 <- NCT(data1[, -25], data2[, -25], gamma = 0.25, it = 1000, binary.data = T,
  test.edges = T, edges = "all")
# Stress
nct2 <- NCT(data3[, -25], data4[, -25], gamma = 0.25, it = 1000, binary.data = T,
  test.edges = T, edges = "all")
# PRS BLUP
nct3 <- NCT(data5[, -25], data6[, -25], gamma = 0.25, it = 1000, binary.data = T,
  test.edges = T, edges = "all")
# Early AAO (AAO <28 y)
nct4 <- NCT(data7[, -25], data8[, -25], gamma = 0.25, it = 1000, binary.data = T,
  test.edges = T, edges = "all")

# Assess NCT results
nct1$glstrinv.pval # p-value global strength
nct1$nwinv.pval # p-value maximum difference in edge weights
nct1$einv.pvals[nct1$einv.pvals[, 3] < 0.05, ] # p-values < 0.05 for individual edges

plot(nct1, what = "network") # maximum difference in edge weights
plot(nct1, what = "strength") # global strength

# nct2, nct3, nct4 have been analyzed in a similar way

```

Compare networks for subsamples

```

# Family history networks
res1 <- IsingFit(data1[, !colnames(data1) %in% "fh.pos.strict"]) # Fam Hist = 0
res2 <- IsingFit(data2[, !colnames(data2) %in% "fh.pos.strict"]) # Fam Hist = 1

# Test for similarity in networks by comparing weighted adjacency matrix
plot(res1$weiadj[lower.tri(res1$weiadj)], res2$weiadj[lower.tri(res2$weiadj)])
cor(res1$weiadj[lower.tri(res1$weiadj)], res2$weiadj[lower.tri(res2$weiadj)], method = "spearman")
cor(res1$weiadj[lower.tri(res1$weiadj)], res2$weiadj[lower.tri(res2$weiadj)], method = "pearson")

```

```

# Network plots
q1 <- qgraph(res1$weiadj, layout = "spring", title = paste("no fam.history, n =",
  3907), labels = varnames_4)
q2 <- qgraph(res2$weiadj, layout = q1$layout, title = paste("fam. history, n =",
  1494), labels = varnames_4)

# Networks for subsamples with higher vs lower polygenic risk score (PRS), age
# at onset (AAO) or adversity have been tested similarly

## R version 3.4.0 (2017-04-21)
## Platform: x86_64-apple-darwin15.6.0 (64-bit)
## Running under: macOS Sierra 10.12.6
##
## Matrix products: default
## BLAS: /Library/Frameworks/R.framework/Versions/3.4/Resources/lib/libRblas.0.dylib
## LAPACK: /Library/Frameworks/R.framework/Versions/3.4/Resources/lib/libRlapack.dylib
##
## locale:
## [1] en_US.UTF-8/en_US.UTF-8/en_US.UTF-8/C/en_US.UTF-8/en_US.UTF-8
##
## attached base packages:
## [1] stats      graphics  grDevices  utils      datasets  methods   base
##
## other attached packages:
## [1] knitr_1.15.1      NetworkComparisonTest_2.0.1
## [3] qgraph_1.4.3     IsingFit_0.3.1
##
## loaded via a namespace (and not attached):
## [1] foreach_1.4.3      splines_3.4.0      ellipse_0.3-8
## [4] gtools_3.5.0       network_1.13.0     Formula_1.2-1
## [7] stats4_3.4.0       latticeExtra_0.6-28 yaml_2.1.14
## [10] d3Network_0.5.2.1 pbivnorm_0.6.0     backports_1.0.5
## [13] lattice_0.20-35    quadprog_1.5-5     digest_0.6.12
## [16] RColorBrewer_1.1-2 checkmate_1.8.2     ggml_2.3
## [19] minqa_1.2.4        colorspace_1.3-2   htmltools_0.3.5
## [22] Matrix_1.2-9       plyr_1.8.4         psych_1.7.3.21
## [25] corpcor_1.6.9      scales_0.4.1       glasso_1.8
## [28] sna_2.4            whisker_0.3-2      jpeg_0.1-8
## [31] fdrtool_1.2.15     lme4_1.1-13        huge_1.2.7
## [34] arm_1.9-3          htmlTable_1.9      tibble_1.3.0
## [37] ggplot2_2.2.1      nnet_7.3-12        lazyeval_0.2.0
## [40] mnormt_1.5-5       survival_2.41-3     magrittr_1.5
## [43] statnet.common_3.3.0 evaluate_0.10       nlme_3.1-131
## [46] MASS_7.3-47        foreign_0.8-67     tools_3.4.0
## [49] data.table_1.10.4  formatR_1.5        stringr_1.2.0
## [52] glmnet_2.0-5       munsell_0.4.3      cluster_2.0.6
## [55] IsingSampler_0.2   compiler_3.4.0     sem_3.1-8
## [58] grid_3.4.0         nloptr_1.0.4       iterators_1.0.8
## [61] rjson_0.2.15       htmlwidgets_0.8    igraph_1.0.1
## [64] lavaan_0.5-23.1097 base64enc_0.1-3     rmarkdown_1.4
## [67] boot_1.3-19        mi_1.0             codetools_0.2-15
## [70] gtable_0.2.0       abind_1.4-5        reshape2_1.4.2
## [73] gridExtra_2.2.1    Hmisc_4.0-2        rprojroot_1.2
## [76] stringi_1.1.5      matrixcalc_1.0-3   parallel_3.4.0

```

```
## [79] Rcpp_0.12.10      rpart_4.1-11      acepack_1.4.1
## [82] png_0.1-7            coda_0.19-1
```