

# **COMPARISON OF THE NETWORKS OF DEPRESSION AND ANXIETY SYMPTOMS IN ADOLESCENTS AS A FUNCTION OF INFLAMMATION**

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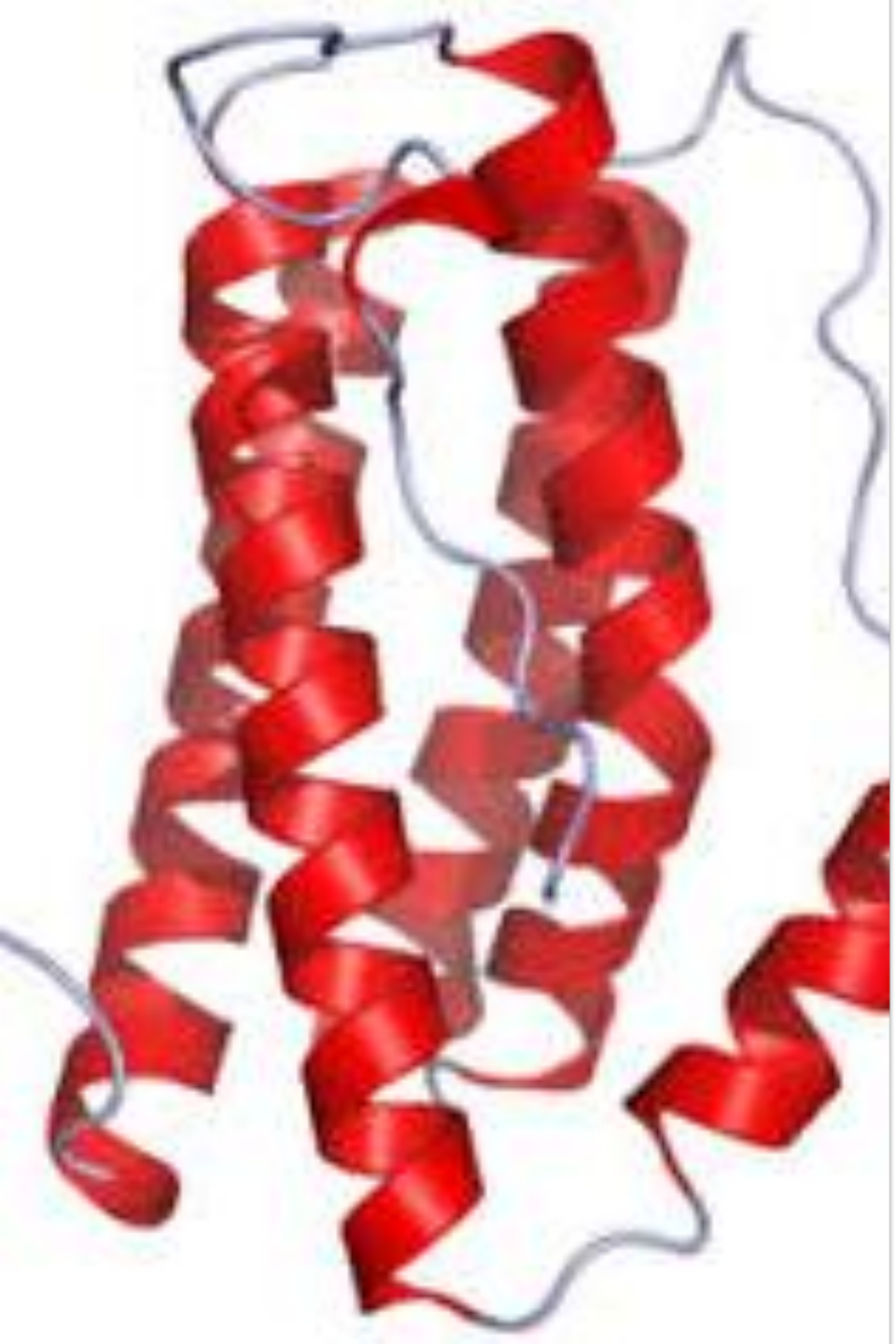
# MAJOR DEPRESSION + ANXIETY COMORBIDITY

- In a sample of almost 500 psychiatric outpatients with major depressive disorder (Zimmerman, Chelminski, & McDermut, 2002)
  - 64.1% had a comorbid psychiatric disorder
  - 36.7% had at least 2 comorbid psychiatric disorders
  - Anxiety disorders accounted for 56.8% of psychiatric comorbidities



# COMORBIDITY- WHY?

- Construct overlap
- Anxiety as a risk factor for depression (Starr et al., 2016) and vice-versa (Hamilton et al., 2016)
- Both caused by similar underlying processes



# INFLAMMATION

- Inflammation is one of the body's first lines of defense for physical injury and infection (Dantzer, 2001)
- E.g. C-reactive Protein (CRP), interleukin (IL)-6, and tumor necrosis factor alpha (TNF $\alpha$ )



# INFLAMMATION AS A SHARED BIOLOGICAL CORRELATE

- Elevated levels of proinflammatory biomarkers are seen in depressed participants vs. controls (Dhabhar et al., 2009; Dowlati et al., 2010; Howren, Lamkin, & Suls, 2009).
- More mixed evidence for anxiety disorders (see Michopoulos et al., 2016 for a review)
  - More consistent positive associations between inflammation and phobic disorders than GAD or PTSD
- IL-6 has been found to mediate the relationship between symptoms of anxiety and depression (Moriarty et al., 2018).

# INFLAMMATORY PHENOTYPE

- Inflammatory states associated with “sickness behaviors” that map onto depressive symptoms (Dantzer & Kelley, 2007)
  - Elevated inflammation is only seen in a subset of depressed individuals
- More consistent positive associations between inflammation and phobic disorders than GAD or PTSD (see Michopoulos et al., 2016 for a review)
- Differential associations between discrete inflammatory biomarkers and subtypes of depressive symptoms (Moriarty et al., 2019; Capuron et al., 2004)



# INFLAMMATORY PHENOTYPE

- Most work has adapted a latent factor model of psychopathology
- Network analysis can be a powerful tool for expanding how we think about phenotypes.
  - Not just presence/intensity of symptoms
  - Relationships among symptoms and patterns of symptom activation and maintenance

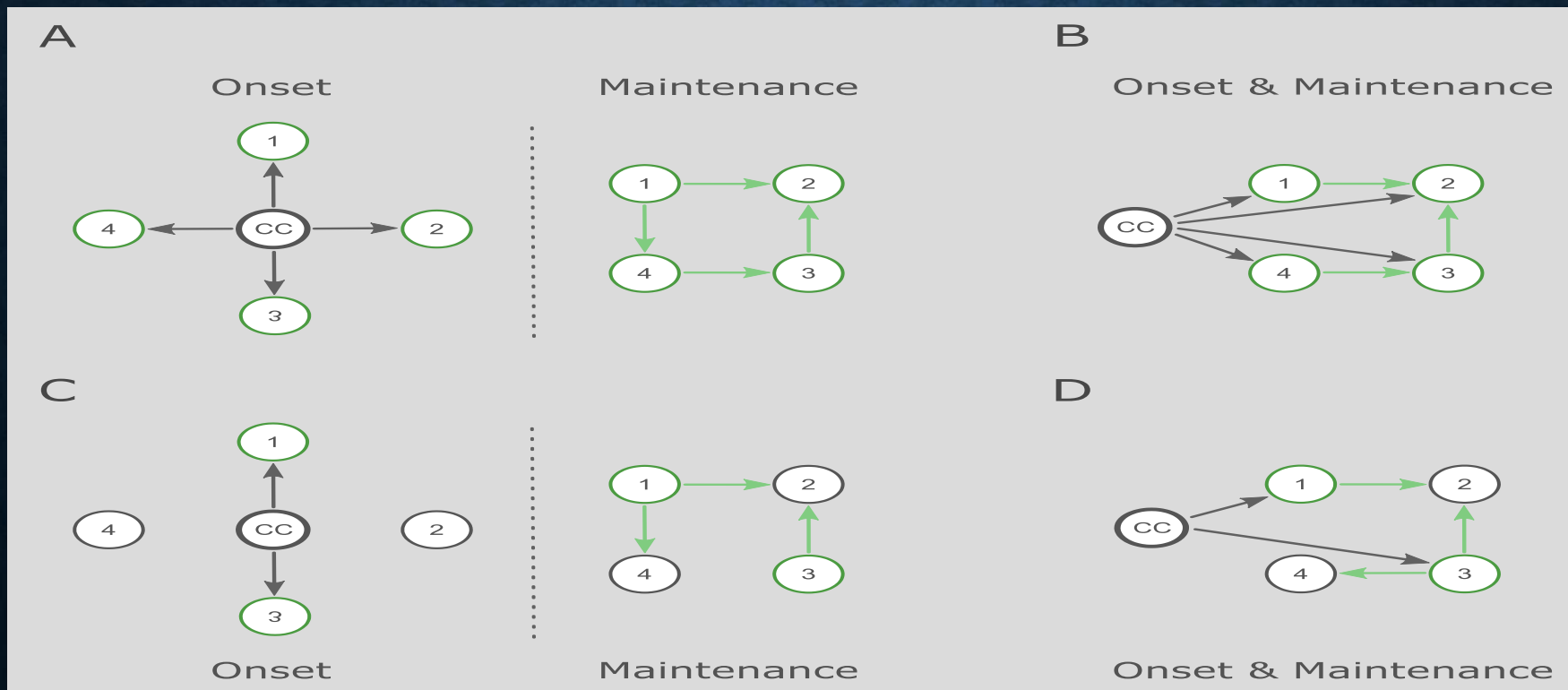
# LATENT FACTOR VS. NETWORK ANALYSIS

- Not mutually exclusive



# HYBRID LATENT/NETWORK MODEL

- Common causes for some sets of symptoms?
  - Trauma → PTSD symptoms



# **THE CURRENT STUDY**



# PARTICIPANTS

- Participants were drawn from the Adolescent Cognition and Emotion (ACE) Project at Temple University, a longitudinal study of adolescent depression
  - 307 adolescents (mean age =17) who completed a blood draw
  - 40% were Caucasian, 54% were African American, and 6% were biracial
  - 52% female
- 2 groups
  - Elevated Inflammation (CRP > 2.0 mg/L [n=150])
  - Non-elevated inflammation (CRP < 2.0 mg/L [n=150])

# HYPOTHESES

- More/greater differences in node strength centrality in an elevated CRP group vs. non-elevated group
- More significantly stronger edges in elevated CRP group vs. non-elevated group
- Explore differences in structure and global strength using NetworkComparisonTest

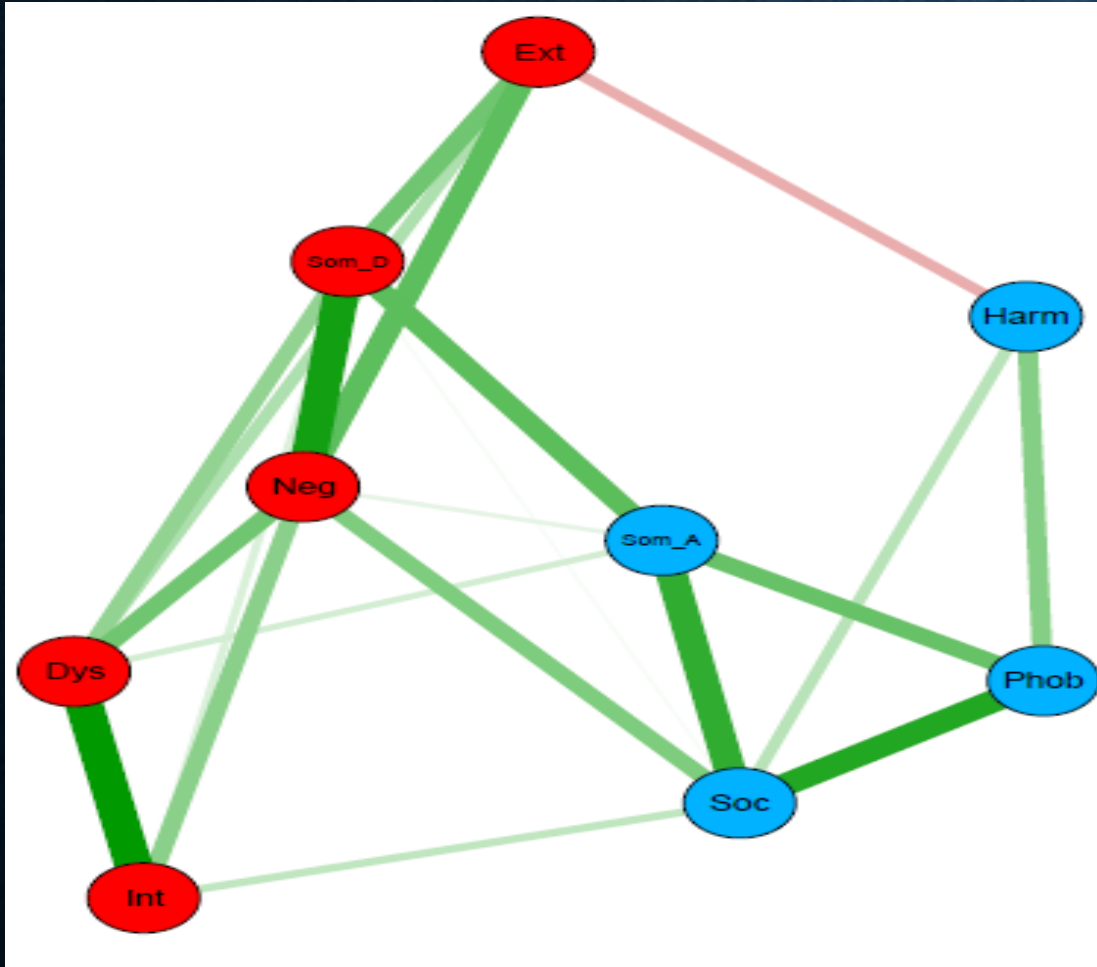


# MEASURES

- Depressive Symptoms
  - Children's Depression Inventory (CDI; Kovacs, 1985)
    - Somatic Concerns, Externalizing, Negative Self-Concept, Lack of Personal and Social Interest, Dysphoric Mood
- Anxiety Symptoms
  - Multidimensional Anxiety Scale for Children (MASC; March, Parker, Sullivan, Stallings, & Conners, 1997)
    - Social Anxiety, Separation Anxiety, Specific Phobia, Harm Avoidance
- Inflammation
  - High-sensitivity C-reactive protein (CRP) was determined in singleplex assay, using an electrochemiluminescence platform and a QuickPlex SQ 120 imager for analyte detection (Meso Scale Discovery, Gaithersburg, MD).

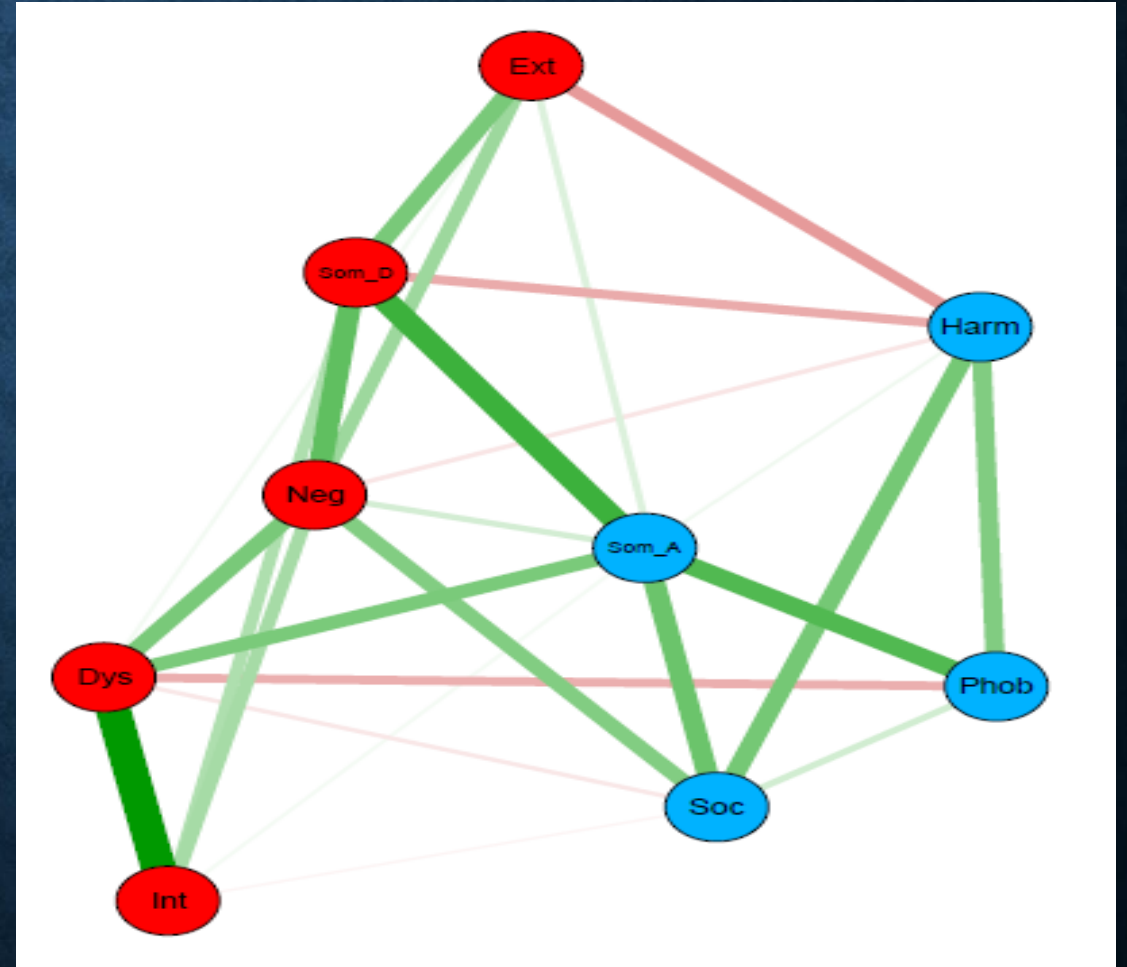
# GLASSO NETWORKS

Elevated CRP



21 surviving edges

Non-elevated CRP



26 surviving edges

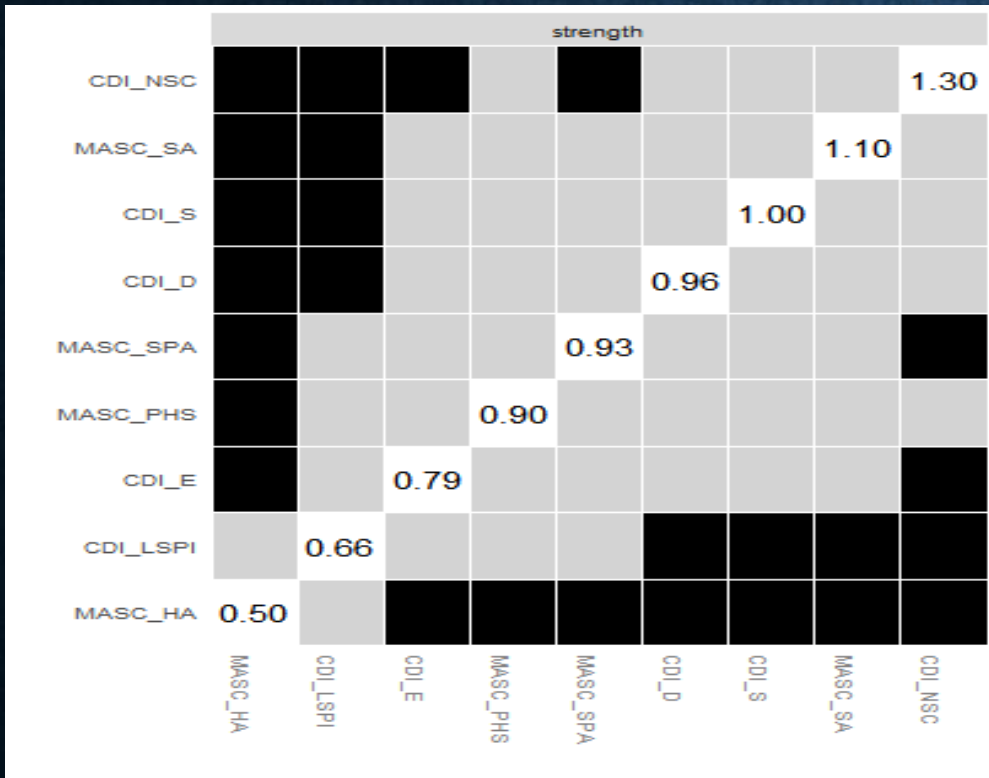


# NETWORK COMPARISON TEST

Differences in Edge Weight	
Elevated CRP	Non-elevated CRP
Lack of Personal & Social Interest—Social Anxiety	Somatic Depression—Harm Avoidance
Social Anxiety—Specific Phobia	
Dysphoria—Specific Phobia	

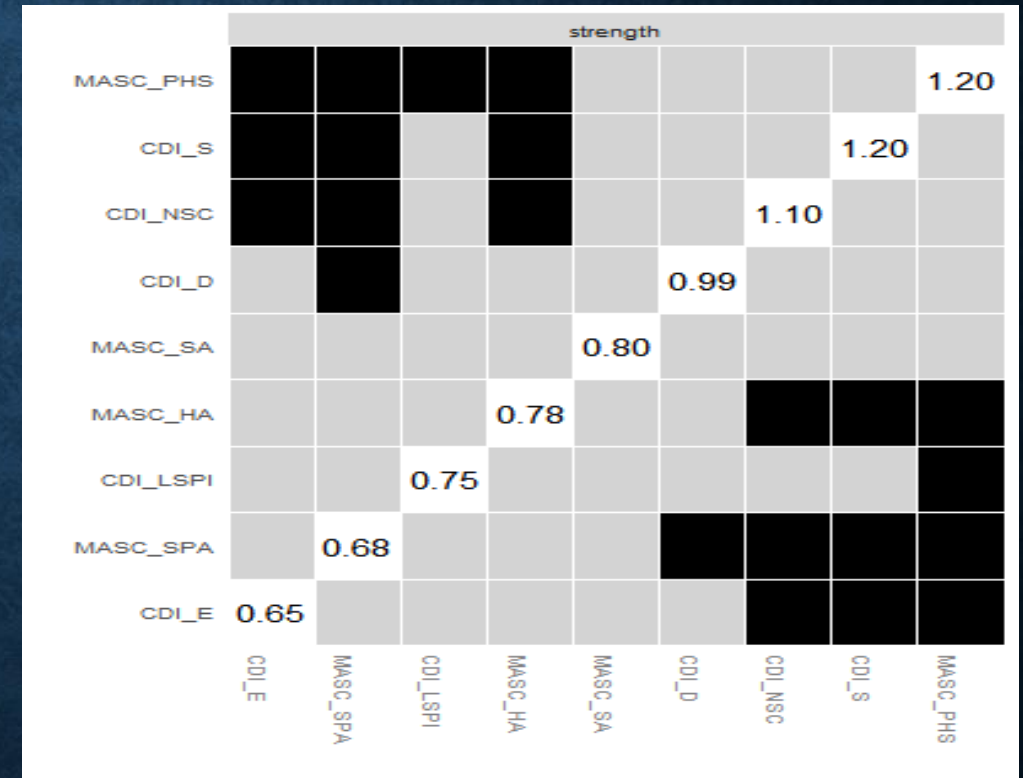
# CENTRALITY- NODE STRENGTH

Elevated CRP



13 sig differences

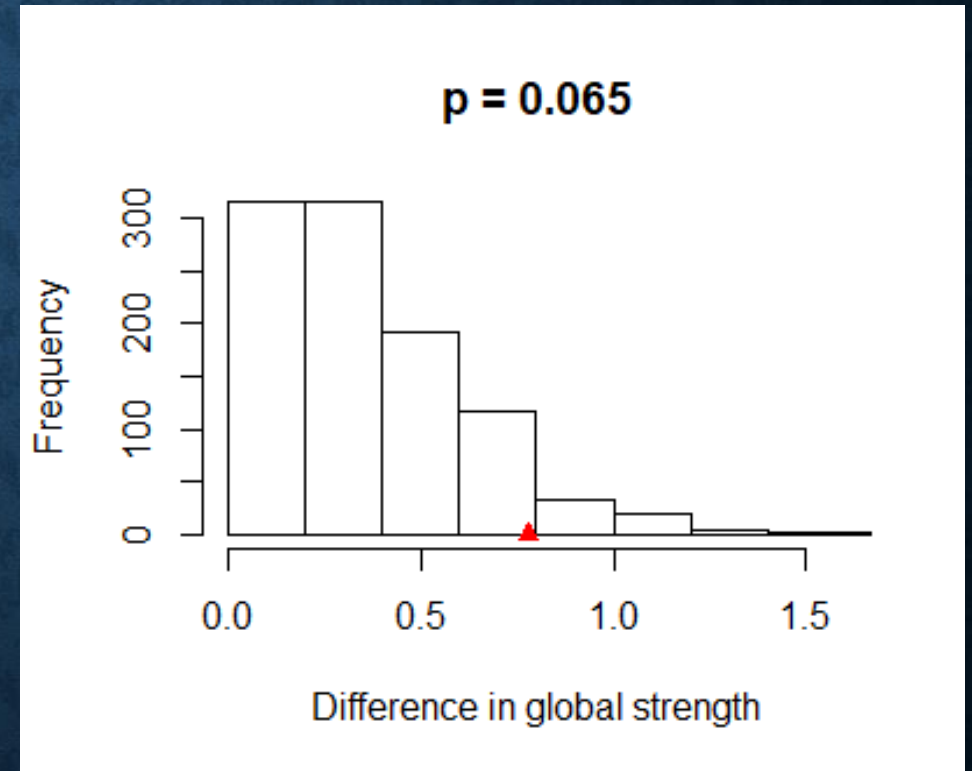
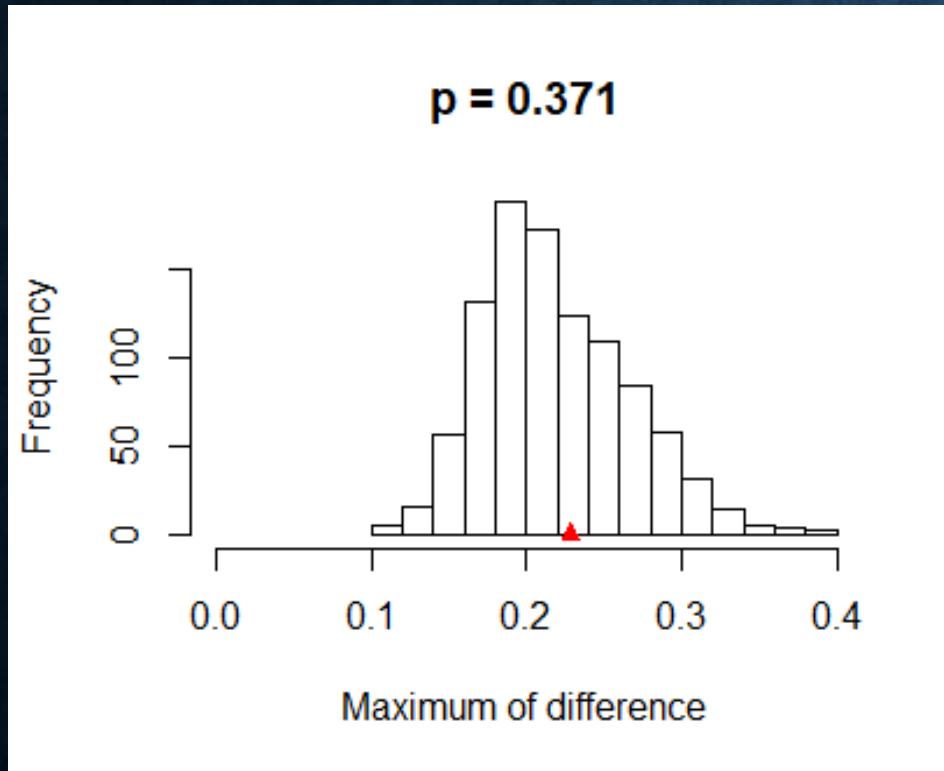
Non-elevated CRP



11 sig differences



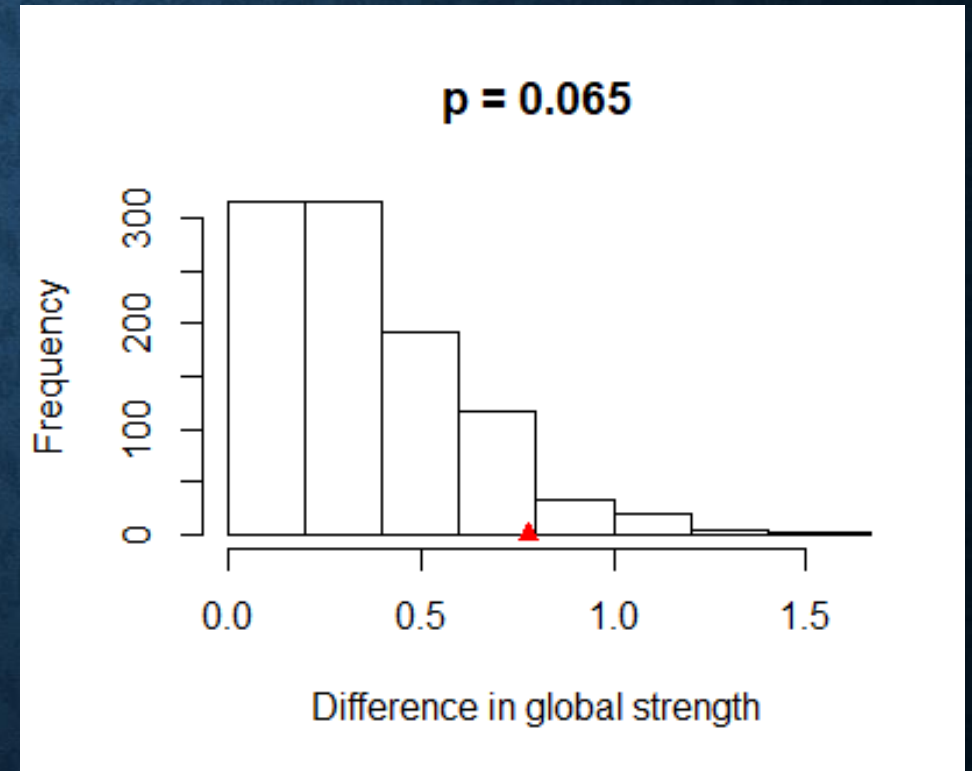
# NETWORK COMPARISON TEST



# NETWORK COMPARISON TEST

Elevated CRP: Global strength = 3.60

Non-elevated CRP: Global strength = 4.38





# LIMITATIONS

- While boot-strapped CIs were stable, relatively small N
- Cross-sectional
- No inclusion of third variable confounds (e.g. exercise)
- Participants were at the upper end of the age range the self-report measures were validated on

# IMPLICATIONS/FUTURE DIRECTIONS

- Evidence for an inflammatory phenotype of depression/anxiety symptoms
- NetworkComparisonTest or Model-based Recursive Partitioning of Network Models (R package: networktree)
- Future directions:
  - Replication
  - How do these networks change with anti-inflammatory treatment? Do the central symptoms disappear first?
  - Different biomarkers



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Elevated CRP	Non-elevated CRP
CDI_LSPI-CDI_D=.36	CDI_LSPI-CDI_D=.45
CDI_S-CDI_NSC=.33	CDI_S-MASC_PHS=.35
MASC_SA-MASC_SPA=.31	MASC_PHS-MASC_SPA=.31
MASC_PHS-MASC_SA=.29	CDI_S-CDI_NSC=.28
CDI_S-MASC_PHS=.23	MASC_PHS-MASC_SA=.265
CDI_E-CDI_NSC=.23	CDI_S-CDI_E=.24
MASC_PHS-MASC_SPA=.21	CDI_NSC-CDI_D=.24
CDI_NSC-CDI_D=.20	MASC_HA-MASC_SA=.24
CDI_S-CDI_E=.20	CDI_D-MASC_PHS=.23
CDI_NSC-MASC_SA=.18	MASC_HA-MASC_SPA=.22
MASC_HA-MASC_SPA=.17	CDI_NSC-MASC_SA=.22
CDI_NSC-CDI_LSPI=.16	CDI_E-CDI_NSC=.17
CDI_S-CDI_D=.15	CDI_NSC-CDI_LSPI=.16
CDI_E-CDI_D=.11	CDI_S-CDI_LSPI=.14
MASC_HA-MASC_SA=.10	MASC_SA-MASC_SPA=.08
CDI_LSPI-MASC_SA=.09	CDI_E-MASC_SA=.08
CDI_D-MASC_PHS=.06	CDI_NSC-MASC_PHS=.08
CDI_S-CDI_LSPI=.05	MASC_PHS-MASC_HA=.03
CDI_NSC-MASC_PHS=.04	CDI_LSPI-MASC_PHS=.02
CDI_E-MASC_HA= -.12	CDI_E-CDI_D=.02
	CDI_LSPI-MASC_SA=-.02
	CDI_D-MASC_SA=-.04
	CDI_NSC-MASC_HA=-.05
	CDI_D-MASC_SPA=-.14
	CDI_S-MASC_HA=-.15
	CDI_E-MASC_HA=-.18