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 (TNFα)
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 (Moriarity 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 (Moriarity 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

<table>
<thead>
<tr>
<th>Differences in Edge Weight</th>
<th>Elevated CRP</th>
<th>Non-elevated CRP</th>
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</thead>
<tbody>
<tr>
<td>Lack of Personal &amp; Social Interest—Social Anxiety</td>
<td>Somatic Depression—Harm Avoidance</td>
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<tr>
<td>Social Anxiety—Specific Phobia</td>
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<tr>
<td>Dysphoria—Specific Phobia</td>
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</tbody>
</table>
CENTRALITY - NODE STRENGTH

Elevated CRP

13 sig differences

Non-elevated CRP

11 sig differences
NETWORK COMPARISON TEST

**Graph 1:**
- Title: Maximum of difference
- Frequency distribution
- **p = 0.371**

**Graph 2:**
- Title: Difference in global strength
- Frequency distribution
- **p = 0.065**
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
ACKNOWLEDGEMENTS

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<table>
<thead>
<tr>
<th>Elevated CRP</th>
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