Gastrointestinal Symptoms in 2- to 5-Year-Old Children

Interagency Autism Coordinating Committee
Full Committee Meeting

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Gastrointestinal Symptoms (GIS) in ASD

Questions
- Prevalence ranges from 9-70%
- Etiology
- Phenotypic subtype

Needs
- Diverse, non-clinic based sample
- Large sample with comparison groups
- Well characterized sample
Methods

Sample
- ASD (n=672), DD (n=938), POP (n=851)
- Stool diary: ASD (n=423), DD (n=551), and POP (n=597)

GI symptoms
- Parent Completed Gastrointestinal Questionnaire (yes/no)
- Stool Diary using Bristol Stool Scale (7 point Likert Scale)
- GI Medications used in previous month

Associations with GIS
- ADOS Calibrated Severity Scale - \textbf{ASD only}
- ADI-R Regression Questions - \textbf{ASD only}
- Child Behavior Checklist (CBCL)
- Children’s Sleep Habits Questionnaire (CSHQ)
GI Symptoms Methods

Parent Report
- Any GIS
- Diarrhea
- Loose Stools
- Constipation
- Loose Stool alternating w/constipation
- Vomiting
- Abdominal pain
- Gas

Parent Report Plus Stool Diary
- Stool Consistency
- Stool Frequency
- Laxative or Stool Softener use
- Vomiting
- Abdominal Pain
- Gas

GIS Diagnosis (+/-)
Analysis

- Multivariable logistic regression
- Generalized estimating equation (GEE) models
- All models adjusted for
  - Maternal race/ethnicity, education level, and age at child's birth
  - Child sex and cognitive skills
  - Site
GIS Prevalence in SEED

<table>
<thead>
<tr>
<th></th>
<th>ASD</th>
<th>DD</th>
<th>POP</th>
<th>ASD vs DD</th>
<th>ASD vs POP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ASD</td>
<td></td>
<td></td>
<td>Adjusted OR</td>
<td>Adjusted OR</td>
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<tr>
<td></td>
<td>(95% CI)</td>
<td>(95% CI)</td>
<td></td>
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<tr>
<td>Parent Report Only</td>
<td></td>
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</tr>
<tr>
<td>GIS</td>
<td>34.6%</td>
<td>22.1%</td>
<td>12.0%</td>
<td>1.85 (1.54-2.22)*</td>
<td>3.42 (2.11-5.54)*</td>
</tr>
<tr>
<td>Parent Report with Stool Diary</td>
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<tr>
<td>GIS</td>
<td>50.4%</td>
<td>42.6%</td>
<td>30.6%</td>
<td>1.29 (1.07-1.56)**</td>
<td>2.22 (1.56-3.14)*</td>
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</table>

* p-value < 0.001, ** p-value < 0.05
Association between GIS and regression and autism severity in Children with ASD

- Children with ASD and Regression are 1.5 times more likely to have GIS
  - Adjusted Odds Ratio = 1.53 (95% CI, 1.33-1.77), p<0.05

- No Difference in Autism Severity Score in Children with ASD with and without GIS
## Association between GIS and behavior

<table>
<thead>
<tr>
<th></th>
<th>Mean Difference (95% CI)</th>
<th>p-value</th>
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<tbody>
<tr>
<td><strong>CBCL - Anxious Depressed Subscale</strong></td>
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<tr>
<td>ASD</td>
<td>0.74(0.22-1.27)</td>
<td>0.0056</td>
</tr>
<tr>
<td>DD</td>
<td>0.66(0.31-1)</td>
<td>0.0002</td>
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<tr>
<td>POP</td>
<td>0.73(0.27-1.18)</td>
<td>0.0017</td>
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<tr>
<td><strong>CBCL - Aggressive Behavior Subscale</strong></td>
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<tr>
<td>ASD</td>
<td>2.35(1.58-3.12)</td>
<td>&lt;.0001</td>
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<tr>
<td>DD</td>
<td>2.87(1.82-3.91)</td>
<td>&lt;.0001</td>
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<tr>
<td>POP</td>
<td>2.13(1.32-2.94)</td>
<td>&lt;.0001</td>
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<tr>
<td></td>
<td>CSHQ Score &gt; 48</td>
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<tr>
<td><strong>OR (95% CI)</strong></td>
<td><strong>p-value</strong></td>
<td></td>
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<tr>
<td><strong>Case</strong></td>
<td>2.07(1.57-2.71)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>DD</strong></td>
<td>1.67(1.18-2.36)</td>
<td>0.004</td>
</tr>
<tr>
<td><strong>POP</strong></td>
<td>2.08(1.36-3.18)</td>
<td>0.0007</td>
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Limitations

- No clinical diagnosis of GIS
- Questionnaire has not been validated

Stool Diary
- Differences in demographic variables
- 51% completed SD during a typical week
- Children with ASD using treatment for constipation were less likely to have a SD
- Children with ASD were more likely to use a treatment for constipation other than a laxative or stool softener
Implications / Future Directions

Gastrointestinal Symptoms
ASD>DD>POP

Motility
- Anxiety
  - Arousal
  - Autonomic
  - Hypotonia

Limited Diet

Cognitive Behavioral

Immune
- Food Allergy
  - Eosinophilic Esophagitis

Microbiome
- Perinatal Risk Factors

Genetic
- GWAS
- GxE

Dysregulation

Anxiety

Dysfunction

Hypotonia
Thank You

Children and Their Families
SEED Study Staff
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