Persistence and neural correlates of Disruptive Mood Dysregulation Disorder in 10-year-old children with ADHD

Melissa Mulraney

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Background

• Approximately 40% of children with ADHD frequently experience irritable moods and temper outbursts (Mayes et al. 2015; Stringaris et al. 2009) and 22% of children with ADHD meet diagnostic criteria for Disruptive Mood Dysregulation Disorder (Mulraney et al. 2016).

• Irritability and DMDD in ADHD is associated with:
  • Increased rates of comorbidities
  • More severe ADHD symptoms
  • Poor social functioning

• 40% of children aged 6-12 years with DMDD still meet criteria 2 years later (Axelson et al., 2012) & 29% 8 years later (Mayes et al., 2015) but to date no longitudinal studies have examined DMDD in children with ADHD.

• There is some evidence that irritability is associated with reduced gray matter volume in frontal and cingulate regions (Ball et al. 2019) and greater gray matter volume in the insula (Adleman et al. 2012).
Aims

1) To determine the proportion of children with ADHD who have persistent DMDD from 7 to 10 years of age, and the proportion with new-onset DMDD at age 10; and

2) To explore whether irritability, measured dimensionally, is associated with gray matter volume.
Children’s Attention Project (CAP) & Neuroimaging of CAP (NICAP)

**CAP**
- Longitudinal, community-based cohort study
- Population screening approach; 43 Melbourne primary schools
- Identify risk & protective factors associated with poor versus better outcomes

**NICAP**
- Collect longitudinal, multi-modal MRI data in a community cohort (n=180)
  - 3 timepoints at 18-month intervals from ages 9-12 years
  - 3.5hr assessment including cognitive assessment, a self-report survey, parent and teacher questionnaires, training mock scan and an MRI scan.
Participants

AIM 1
- Children from CAP whose parents completed the DISC-IV when their child was 7 and 10 (n=280).

AIM 2
- Children from NICAP with DISC-IV at age 7 and 10 and had imaging data (n=162)
  - 19 ADHD+DMDD
  - 58 ADHD-DMDD
  - 85 controls
Aim 1 – persistent and new onset DMDD

• 38 children (27.9%) met criteria for DMDD at either age 7 or 10:
  • 8 (21.1%) had persistent DMDD
  • 21 (57.9%) remitted
  • 8 (21.1%) had new onset DMDD at age 10

• 6 control children met criteria for DMDD at either age 7 or 10:
  • 3 (50%) remitted
  • 3 (50%) new onset at age 10
Aim 2 - irritability and gray matter volume

Associations between irritability and gray matter volume

Effect size and 95% CI adjusted for age, sex and ADHD symptoms
Summary & Future directions

- One in five children with ADHD had persistent comorbid DMDD from age 7 to 10.
- Irritability was associated with reduced GMV across multiple frontal regions, cingulate, and insula. Consistent with findings that irritability is associated with poor emotion regulation, abnormal reward processing, and poor executive functioning.

- Is irritability associated with a different trajectory of GMV development?
- Do interventions targeting executive functioning, emotion and reward processing result in reduced irritability?
- Are such changes associated with neurological changes?

An Open Pilot Study of Training Hostile Interpretation Bias to Treat Disruptive Mood Dysregulation Disorder

Joel Stoddard, MD,1 Banafsheh Sharif-Askary, BS,1 Elizabeth A. Harkins, BA,1 Heather R. Frank, BA,1 Melissa A. Brotman, PhD,1 Ian S. Penton-Voak, PhD,2 Keren Maoz, MA,3 Yair Bar-Haim, PhD,3,4 Marcus Munafò, PhD,5,6 Daniel S. Pine, MD,7 and Ellen Leibenluft, MD1
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Co-investigators:
A/Prof Tim Silk
A/Prof Daryl Efron
Prof Philip Hazell
Ms Alisha Gulenc
A/Prof Emma Sciberras

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Contact:
melissa.mulraney@mcri.edu.au
### Sample characteristics at age 10

<table>
<thead>
<tr>
<th></th>
<th>ADHD+DMDD (n=38)</th>
<th>ADHD-DMDD (n=98)</th>
<th>Controls (n=144)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child age, M (SD), y</td>
<td>10.5 (0.6)</td>
<td>10.5 (0.5)</td>
<td>10.5 (0.5)</td>
</tr>
<tr>
<td>Male, N (%)</td>
<td>28 (73.7)</td>
<td>68 (69.4)</td>
<td>88 (61.1)</td>
</tr>
<tr>
<td>ADHD medication use, N</td>
<td>15 (39.5)</td>
<td>22 (22.4)</td>
<td>-</td>
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<tr>
<td>ADHD subtype, N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combined</td>
<td>20 (52.6)</td>
<td>16 (16.3)</td>
<td>-</td>
</tr>
<tr>
<td>Inattentive</td>
<td>9 (23.7)</td>
<td>42 (42.9)</td>
<td>-</td>
</tr>
<tr>
<td>Hyperactive/impulsive</td>
<td>1 (2.6)</td>
<td>7 (7.1)</td>
<td>-</td>
</tr>
<tr>
<td>Comorbidities, N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Internalising</td>
<td>13 (35.1)</td>
<td>21 (22.8)</td>
<td>10 (7.0)</td>
</tr>
<tr>
<td>Externalising</td>
<td>29 (78.4)</td>
<td>37 (40.2)</td>
<td>13 (9.2)</td>
</tr>
<tr>
<td>ASD</td>
<td>10 (27.8)</td>
<td>28 (30.8)</td>
<td>3 (2.3)</td>
</tr>
<tr>
<td>SEIFA, M (SD)</td>
<td>1004.7 (39.0)</td>
<td>1020.9 (45.1)</td>
<td>1017.3 (48.0)</td>
</tr>
<tr>
<td>ARI total score, M (SD)</td>
<td>7.0 (3.5)</td>
<td>4.5 (3.1)</td>
<td>1.7 (2.4)</td>
</tr>
</tbody>
</table>
MRI

- Acquired on a 3T Siemens Tim Trio MRI scanner
- Multi-echo MPRAGE T1-weighted structural images (voxel size = 0.9mm$^3$)
- In-scanner motion correction (MoCo)
- To derive our cortical ROIs, parcellation was conducted in Freesurfer (v5.3.0) using Desikan-Killiany parcellation atlas