

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

Melissa Mulraney

27th July 2019



Melbourne Children's
A world leader in child and adolescent health



The Royal Children's Hospital Melbourne



murdoch children's research institute



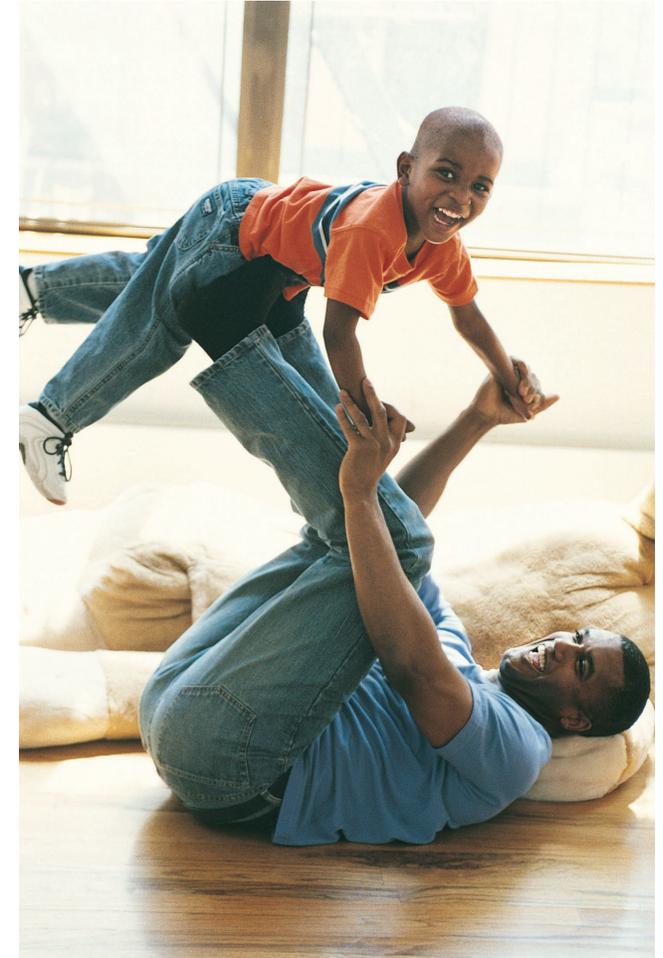
THE UNIVERSITY OF MELBOURNE

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
- Multi-informant: child, parent, teacher, direct assessment.
- 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.

Sciberras et al. *BMC Psychiatry* 2013, 13:18
<http://www.biomedcentral.com/1471-244X/13/18>



STUDY PROTOCOL

Open Access

The Children's Attention Project: a community-based longitudinal study of children with ADHD and non-ADHD controls

Emma Sciberras^{1,2,11*}, Daryl Efron^{1,2,10}, Elizabeth J Schilpzand¹, Vicki Anderson^{1,4,5,10}, Brad Jongeling^{6,7}, Philip Hazell⁸, Obioha C Ukoumunne⁹ and Jan M Nicholson^{1,3}

Silk et al. *BMC Psychiatry* (2016) 16:59
DOI 10.1186/s12888-016-0770-4

BMC Psychiatry

STUDY PROTOCOL

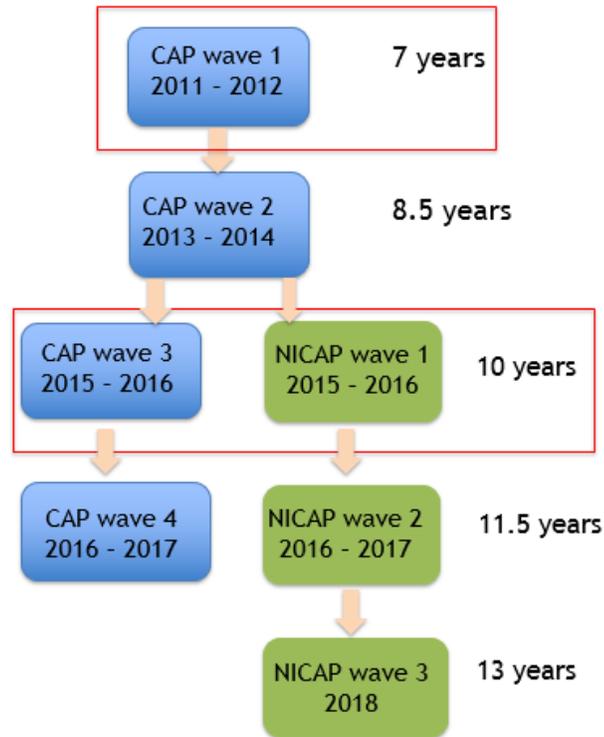
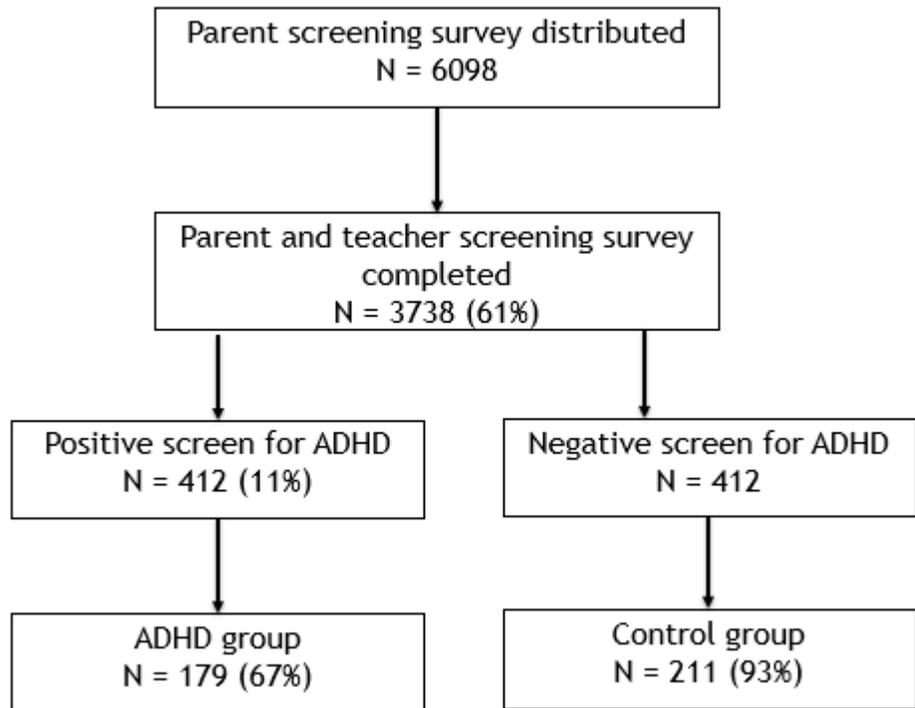
Open Access

Developmental brain trajectories in children with ADHD and controls: a longitudinal neuroimaging study

Timothy J. Silk^{1,3*}, Sila Genc¹, Vicki Anderson^{1,2}, Daryl Efron^{1,2,3}, Philip Hazell⁴, Jan M. Nicholson^{1,5}, Michael Kean^{1,2}, Charles B. Malpas¹ and Emma Sciberras^{1,2,3,6}



Participants



AIM 1

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

AIM 2

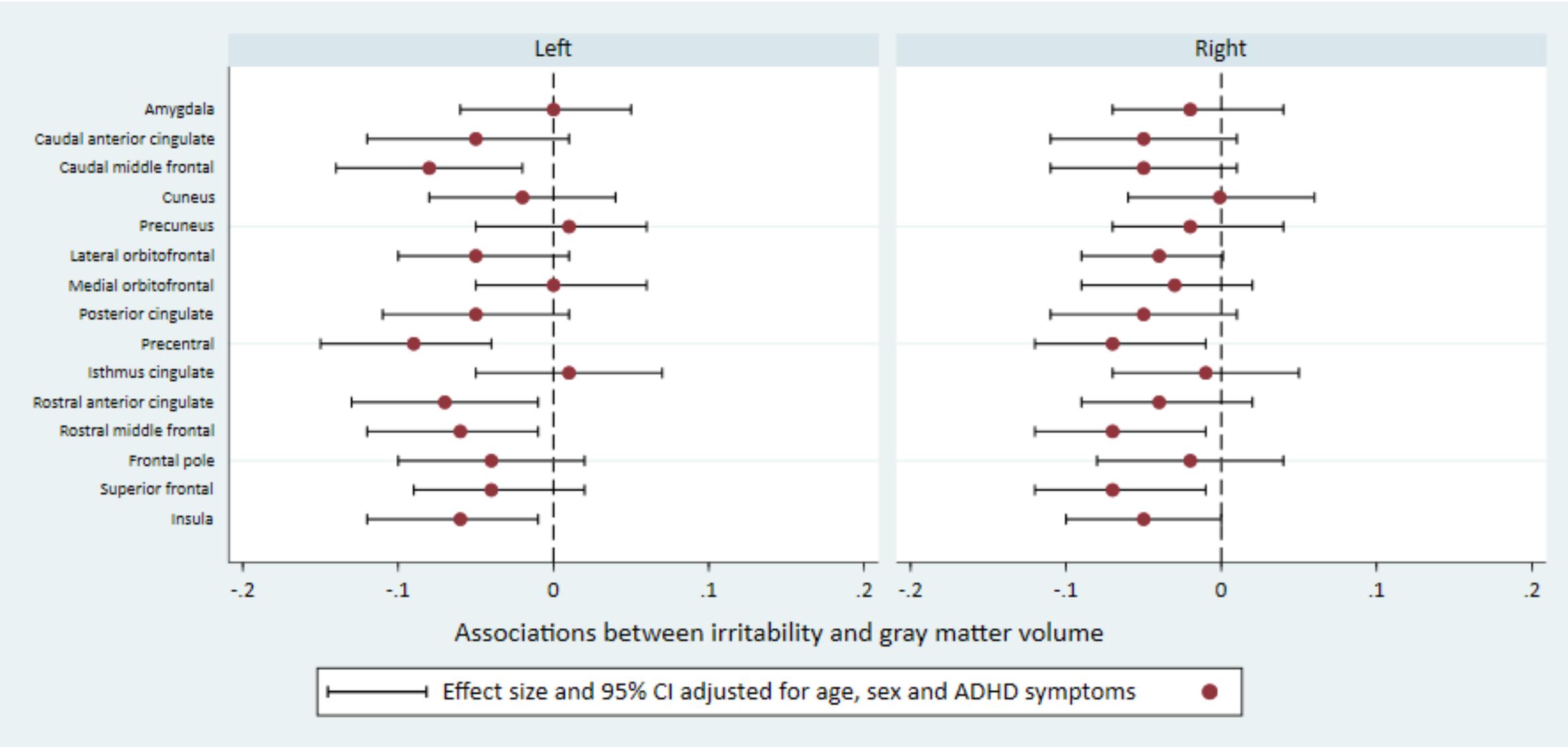
- Children from NICAP with DISC-IV at age 7 and 10 and had imaging data (n=162)
 - 19 ADHD+DMDD
 - 58 ADHD-DMDD
 - 85 controls

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



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?

JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY
Volume 26, Number 1, 2016
© Mary Ann Liebert, Inc.
Pp. 49–57
DOI: 10.1089/cap.2015.0100

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,^{2,5,6}
Daniel S. Pine, MD,⁷ and Ellen Leibenluft, MD¹



Thank you

Co-investigators:

A/Prof Tim Silk

A/Prof Daryl Efron

Prof Philip Hazell

Ms Alisha Gulenc

A/Prof Emma Sciberras

Funding:

Australian National Health
& Medical Research Council

Contact:

melissa.mulraney@mcri.edu.au



Melbourne
Children's

A world leader
in child and
adolescent
health



The Royal
Children's
Hospital
Melbourne



murdoch
children's
research
institute



THE UNIVERSITY OF
MELBOURNE

Sample characteristics at age 10

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

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

