Neurocognitive profile of youth with conduct disorder: A focus on callous-unemotional traits and sex

Stephane De Brito, PhD
Centre for Human Brain Health
School of Psychology
University of Birmingham
Acknowledgments

- SCAN lab at UoB:
Acknowledgments (con’t)

● FemNAT-CD consortium ([www.femnat-cd.eu](http://www.femnat-cd.eu)):

● Funding: 

---

FemNAT-CD is funded by the European Commission within the 7th Framework Programme
Preamble

Getting the phenotypes right: an essential ingredient for understanding aetiological mechanisms underlying persistent violence and developing effective treatments

Sheilagh Hodgins¹ *, Stephane de Brito¹², Emily Simonoff³, Timo Vloet⁴ and Essi Viding²

“If neuroscience is to shed light on psychopathology, it is imperative that we improve our phenotyping instruments. As neuroscientists have known for many years, the success in elucidating the neural underpinning of a given behaviour depends to a great degree on how carefully and specifically the behaviour is described.” (Nelson and Jeste, 2008, p. 157)
Most violent crimes are committed by a small group of men who show an early onset and life-long pattern of antisocial behaviour

(Farrington & West, 1993; Kratzer & Hodgins, 1999; Moffitt, 1993; Wolfgang, 1972)
Antisocial Personality Disorder vs Psychopathy

Hare, *Psychopathy Checklist-Revised*, 2003

Male prisoners

- 15 – 20% Psychopathy
- 50-80% of prisoners
- Community: ~3% ASPD
- Community: 1% psychopathy
- Psychopathy
- CD/ASPD

FemNAT-CD is funded by the European Commission within the 7th Framework Programme
Psychopathy

- Greater numbers of crimes
- More violent crimes
- More likely to recidivate
- **Key characteristics:** lack empathy and remorse; manipulative; start offending at young age; premeditated violence; persistent and versatile offenders

**Affective-interpersonal domain**
- Glibness/superficial charm
- Grandiose sense of self-worth
- Pathological lying
- Conning/manipulative
- Lack of remorse or guilt
- Shallow affect
- Callous/lack of empathy
- Failure to accept responsibility for own actions

**Antisocial impulsive domain**
- Need for stimulation/proneness to boredom
- Parasitic lifestyle
- Poor behavioural control
- Early behavioural problems
- Lack of realistic, long term goals
- Impulsivity
- Irresponsibility
- Juvenile delinquency
- Revocation of conditional release

Psychopathy Checklist Revised, Hare 2001; Porter and Woodworth, 2007
It has been suggested that antisocial personality disorder and psychopathy are neurodevelopmental disorders.

The neurobiology of psychopathy: A neurodevelopmental perspective

Yu Gao¹, Andrea L. Glenn¹, Robert A. Schug², Yaling Yang³, Adrian Raine⁴

(see also Blair et al., 2006 Journal of Child Psychology and Psychiatry)
Conduct Disorder (CD)

- CD is characterized by "a repetitive and persistent pattern of behavior in which the basic rights of others or major age-appropriate societal norms or rules are violated“, resulting in a clinically significant impairment in functioning.

- Includes:
  - Aggression to people and animals
  - Destruction of property
  - Deceitfulness and theft
  - Violation of rules

*Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM; 5) APA, 2013*
DSM-5 Diagnostic Criteria for CD

Aggression to people and animals
1. often bullies, threatens, or intimidate others
2. often initiates physical fights
3. has used a weapon that can cause serious physical harm to others
4. has been physically cruel to people
5. has been physically cruel to animals
6. has stolen while confronting a victim
7. has forced someone into sexual activity

Destruction of property
1. has deliberately engaged in fire setting with the intention of causing damage
2. has deliberately destroyed others’ property (other than by fire setting)

Deceitfulness or theft
10. has broken into someone else’s house, building, or car
11. often lies to obtain goods or favours or to avoid obligations
12. has stolen items of nontrivial value without confronting a victim

Serious violations of rules
13. often stays out at night despite parental prohibitions, beginning before age 13
14. has run away from home overnight at least twice
15. often truant from school, beginning before age 13
DSM-5 Diagnostic Criteria for CD: Subtypes and specifiers

- **Childhood-Onset Type:** at least one problem with conduct before age 10
- **Adolescent-Onset Type:** no problems with conduct before age 10
- **Severity:** Mild, Moderate, Severe
- **New specifier- With Limited Prosocial Emotions**
  - lack of remorse or guilt,
  - callous-lack of empathy,
  - lack of concern about performance in important activities, and
  - shallow or deficient affect

*Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM; 5) APA, 2013*
Disorders Co-Morbid with CD

- Children with CD frequently display other types of problems
  
  - Between 8.7% and 45.4% of boys and between 1.2% and 61.4% of girls with CD also present **ADHD**
  
  - In community samples, the prevalence of co-morbid **anxiety disorders** ranges from 22% to 33%, while among children with CD who have sought treatment 60% to 75% present anxiety disorders
  
  - Co-morbidity estimates ranging from 12 to 17.6 % have been found for **depressive disorders**

De Brito and Hodgins, 2009 in McMurrnan & Howard Eds.
Conduct Disorder as risk factor for Psychiatric Disorders in Adulthood

- Conduct Disorder is Associated with Many Psychiatric Outcomes in Adulthood

Presence of Conduct Disorder by Age 15

Kim-Cohen et al, Arch. Gen Psychiatry., 2003
CD as risk factors for problems in adolescence and adulthood

- Mental health
- Legal
- Educational
- Social
- Occupational
- Physical health

E.g., even in a sample of young children (ages 4 and 5), CD predicted significant behavioural and educational difficulties 5 years later (Kim-Cohen et al., 2009)
### Costs of Conduct Disorder

<table>
<thead>
<tr>
<th></th>
<th>No problems</th>
<th>Conduct problems</th>
<th>Conduct disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Education</td>
<td>£1508</td>
<td>£7524</td>
<td>£12478</td>
</tr>
<tr>
<td>Foster care</td>
<td>£1320</td>
<td>£3412</td>
<td>£7647</td>
</tr>
<tr>
<td>Health</td>
<td>£247</td>
<td>£1237</td>
<td>£2178</td>
</tr>
<tr>
<td>Crime</td>
<td>£2541</td>
<td>£8604</td>
<td>£44821</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>£7423</strong></td>
<td><strong>£24324</strong></td>
<td><strong>£70179</strong></td>
</tr>
</tbody>
</table>

*Scott et al, BMC, 2001*
The high societal costs of childhood conduct problems: evidence from administrative records up to age 38 in a longitudinal birth cohort

Joshua G. Rivenbark, Candice L. Odgers, Avshalom Caspi, HonaLee Harrington, Sean Hogan, Renate M. Houts, Richie Poulton, and Terrie E. Moffitt

adulthood. They found, perhaps not surprisingly, that those with childhood CP evidenced far higher levels of service utilization than all other individuals in the sample. What was staggering though was the sheer volume of service utilization. Although those with childhood CP represented only 9% of the sample, they accounted for a whopping 50% of criminal convictions, 15% of all hospital bed nights, 16% of all emergency department visits, 21% of all prescription fills, 13% of all injury claims, and 25% of all welfare benefit months. Similar results have been reported
Two subgroups of childhood onset conduct disorder

- Two subtypes based on levels of callous-unemotional (CU) traits:
  - Lack of guilt and empathy
  - Callous use of others
- Included as specifier in DSM-5
- There is evidence for distinct neurocognitive profiles and differing aetiologies
- CD+CU subtype = Lack of emotional responsiveness to negative emotional stimuli
- CD-CU traits = ↑ emotional reactivity/poor emotion regulation

(Frick and Viding, 2009; Blair, 2013)
Assessment of callous-unemotional traits

Antisocial Process Screening Device
Self-report, parent-, teacher-report (Frick & Hare, 2001)

Inventory of Callous-Unemotional Traits
Self-report, parent-, teacher-report (Frick, 2004)

Youth Psychopathic Traits Inventory
Self-report, parent-, teacher-report (Hendershed et al. 2002)

Psychopathy Checklist: Youth Version
Semi structured interview + File information (Forth, Kosson, & Hare, 2003)

Callous-Unemotional Traits
• Emotions are fake
• Feels bad when does something wrong
• Concerned about others’ feelings
• Insincere charm/manipulative

Antisocial-impulsive domain
• Gets angry/frustrated
• Gets bored easily
• Acts without thinking
• Does risky things
Childhood-onset CD with high callous-unemotional traits

- Show a more severe, stable, and aggressive pattern of behaviour
- Deficits in the processing of negative emotional stimuli
- Less sensitive to punishment cues
- Show more positive outcome expectancies in aggressive situations with peers (bullying)
- Fearless and thrill seeking and show lower levels of anxiety

→ Temperamental features which can interfere with the normal development of conscience
Childhood-onset CD with low callous-unemotional traits

- Typically do not show problems in empathy and guilt
- High rates of anxiety and they appear to be highly distressed by the effects of their behavior on others
- Show a hostile attribution bias in social situations
- More likely to come from families with high rates of hostile and inconsistent parenting practices
- Less aggressive and more reactive aggression

Aggressive behaviour here involves deficits in the cognitive or emotional regulation of behaviour
Amygdala Response to Preattentive Masked Fear in Children With Conduct Problems: The Role of Callous-Unemotional Traits

Viding et al. (2012) American Journal of Psychiatry
Conduct disorder: Sex matters!

Getting the phenotypes right: an essential ingredient for understanding aetiological mechanisms underlying persistent violence and developing effective treatments

Sheilagh Hodgins¹*, Stephane de Brito¹,², Emily Simonoff³, Timo Vloet⁴ and Essi Viding²

The present article discusses five challenges confronting scientists who aim to advance understanding of the neurobiological mechanisms associated with persistent violence. These challenges are: (1) to develop evidence-based hypotheses and to design studies that test alternate hypotheses; (2) to recruit samples that are homogeneous with respect to variables that may be linked to neurobiological mechanisms underpinning violent behaviour; (3) to use reliable and valid measures in order to fully characterize participants so that the external validity of the results is evident; (4) to restrict the range of age of participants so as not to confuse developmental change with group differences; and (5) to take account of sex. Our goal is to
Recent evidence suggests that the prevalence of CD in females has increased.

There are pronounced sex differences in:
- The development and course of the disorder
- Patterns of comorbidity, particularly for internalising disorders (e.g., PTSD, depression)

Despite this body of evidence, the majority of neuroimaging studies on CD have focused on male subjects only.

(Collishaw et al., 2004; Afifi et al., 2011; Berkout et al., 2011; Meier et al., 2011; Kerekes et al., 2014)
Conduct disorder in adolescent females: current state of research and study design of the FemNAT-CD consortium

Christine M. Freitag¹ · Kerstin Konrad² · Christina Stadler³ · Stephane A. De Brito⁴ · Arne Popma⁵ · Sabine C. Herpertz⁶ · Beate Herpertz-Dahlmann⁷ · Inga Neumann⁸ · Meinhard Kieser⁹ · Andreas G. Chiocchetti¹ · Christina Schwenck¹,¹⁰ · Graeme Fairchild¹¹
The FemNAT-CD Project

● **Overall Aims:** To Improve our understanding of the role of complex genetic and environmental risk factors implicated in the development of different subtypes of CD and their underlying neurobiology, and, for the first time, examine sex differences in the development of CD

● FemNAT-CD consortium comprised of 17 partners that provide clinical and scientific knowledge.

● Funded by EC’s 7th Framework Programme.

● Study is supported by the Violence and Injury Prevention Program of the WHO
Domains of emotion dysfunction in CD

- **Deficient emotion recognition** (i.e., reduced responsiveness to aversive and distress cues as well as to positive social cues)
- **Deficient emotional learning** (i.e., impaired learning from and decision-making based on aversive cues, like punishment, particularly in the context of competing rewards)
- **Deficient emotion regulation** (i.e., heightened threat response and impulsive reactions to triggers of stress and frustration)

---

Neurocognitive profile of youths with Conduct Disorder

Gregor Kohls

Kerstin Konrad
Model-based neurocognitive battery

HEXAGON

Reward stimuli:
- Button press: You have WON 700 points.
- No press: You have 10700 points total.

Ommission error:
- Correct response: You have 10000 points total.

Punishment stimuli:
- Button press: You have LOST 700 points.
- No press: You have 9300 points total.

Correct avoidance:
- Correct avoidance: You have 10000 points total.

GO/NOGO

Emotion regulation:
- Neutral
- Happiness
- Neutral
- Fear

Cognitive control:
- Neutral
- Happiness
- Neutral
- Fear
## Sample characteristics (preliminary)

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Controls</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=907 (f/m)</td>
<td>399 (58% / 42%)</td>
<td>508 (65% / 35%)</td>
<td>.043</td>
</tr>
<tr>
<td>Early-Onset vs. Late-Onset</td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>CD\textsubscript{f} (n=233)</td>
<td>CD\textsubscript{m} (n=166)</td>
<td>HC\textsubscript{f} (n=330)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>14.6</td>
<td>13.7</td>
<td>14.0</td>
</tr>
<tr>
<td>Estimated IQ</td>
<td>93.3</td>
<td>96.7</td>
<td>105.0</td>
</tr>
<tr>
<td>CD severity (KSADS)</td>
<td>4.7</td>
<td>5.1</td>
<td>0.05</td>
</tr>
<tr>
<td>CU traits (ICU parent)</td>
<td>34.4</td>
<td>35.1</td>
<td>15.9</td>
</tr>
<tr>
<td>+ODD</td>
<td>72%</td>
<td>78%</td>
<td></td>
</tr>
<tr>
<td>+ADHD</td>
<td>34%</td>
<td>58%</td>
<td></td>
</tr>
<tr>
<td>+MDD</td>
<td>25%</td>
<td>15%</td>
<td></td>
</tr>
<tr>
<td>+SUD</td>
<td>15%</td>
<td>12%</td>
<td></td>
</tr>
<tr>
<td>+ANX</td>
<td>16%</td>
<td>13%</td>
<td></td>
</tr>
<tr>
<td>+PTSD</td>
<td>10%</td>
<td>3%</td>
<td></td>
</tr>
</tbody>
</table>
Emotional HEXAGON Task

HEXAGON: Emotion recognition accuracy

Sign. Group effect (HC > CD):  p = 0.008

HOWEVER:
- No sign. Group by Sex interaction
- CDf > CDm for Disgust & Sadness
- No sign. differences between CD onset types or ICU/YPI subgroups
- No sign. association with CD symptom severity (KSADS; CBCL)
- Sig. negative correlation with ADHD symptom severity in cases (r = -.26, p < .001), but Group effect remains significant with ADHD symptoms as covariate.
Passive AVOIDANCE Learning Task

**Reward stimuli**
- **Button press**
  - You have WON 700 points.
  - You have 10700 points total.
- **No press**
  - You have 10000 points total.

**Punishment stimuli**
- **Button press**
  - You have LOST 700 points.
  - You have 9300 points total.
- **No press**
  - You have 10000 points total.

Correct response
- Correct response

Omission error
- Ommission error

Passive avoidance error
- Passive avoidance error

Correct avoidance
- Correct avoidance


FemNAT-CD is funded by the European Commission within the 7th Framework Programme.
AVOIDANCE: Reinforcement learning accuracy

Sign. Condition x Group effect: $p=0.008$

HOWEVER:
- No sign. interaction with factor Sex
- No sign. differences between CD onset types or ICU/YPI subgroups
- Not correlated with CD or ADHD symptom severities (KSADS)

(FANCOVA with age, IQ, and center as covariates, followed by univariate ANCOVAs)
Emotional GO/NOGO Task

<table>
<thead>
<tr>
<th>Go</th>
<th>Nogo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutral</td>
<td>Happiness</td>
</tr>
<tr>
<td>Neutral</td>
<td>Fear</td>
</tr>
<tr>
<td>Happiness</td>
<td>Neutral</td>
</tr>
<tr>
<td>Fear</td>
<td>Neutral</td>
</tr>
<tr>
<td>Fear</td>
<td>Happiness</td>
</tr>
<tr>
<td>Happiness</td>
<td>Fear</td>
</tr>
</tbody>
</table>

Emotion regulation
(i.e., ability to maintain cognitive control when confronted with interfering emotion information)

Hare et al. 2005, *Biol Psychiatry.*
GO/NOGO:
Emotion regulation accuracy (error rates)

Group effect (CD > HC): $p<.001$
Sex effect (M > F): $p<.001$

HOWEVER:
- No sign. Group by Sex interaction
- No sign. differences between CD onset types or CU subgroups
- Sign. correlated with ADHD symptom severity in CDm (KSADS), but Group effect remains significant with ADHD symptoms as covariate.
CD cases with an emotion deficit (cut-off based on lowest 10% of age- and IQ-corrected scores in controls)

**Emotion recognition:** 31%
(n=124)  
\[ z = -1.6 \]

**Unimpaired cases:** 49% (n=194)  
\[ z = 0.2 \]

[Unimpaired controls: 75% (n=383)  
\[ z = 0.4 \]]

- **Emotion recognition:** 31% (n=124)  
  \[ z = -1.6 \]

- **Emotional learning:** 21% (n=82)  
  \[ z = -1.4 \]

- **Emotion regulation:** 21% (n=82)  
  \[ z = -1.7 \]

**Group comparisons (p ≤ .05):**
- IQ: 0 = 1 > 2 > 3
- High CU: 0 < 3 (p=0.069)

(ADHD: Nigg et al. 2005; Sonuga-Barke et al. 2010; Sjöwall et al. 2013)
Summary and discussion

Neurocognitive impairments in emotion recognition, emotional learning and emotion regulation are shared by girls and boys with CD (as a group):

- No unique sex-specific profile of emotion dysfunction in CD.
- CD age of onset subtype as well as callous-unemotional traits did not contribute to differential emotional profile dysfunction.
- ADHD symptoms need to be considered as an influential factor for emotional profile impairment severity in CD.
- Very heterogeneous neurocognitive profile, with even a subgroup of cases showing no dysfunction (at least in our neurocognitive test battery).

Clinical implications:

- Emotion recognition, learning and regulation as integral parts of intervention programs in female and male CD (e.g., “Start Now”), with individually different foci.
- Future: Normalizing neurocognitive dysfunction through neurofeedback or transcranial direct current stimulation (tDCS) to improve emotion processing?
Functional MRI Correlates

Emotion Processing
Brain response to facial expressions in male and female youths with conduct disorder

Jack Rogers
<table>
<thead>
<tr>
<th>Variable</th>
<th>Female CD (N=74)</th>
<th>Female TD (N=142)</th>
<th>Male CD (N=87)</th>
<th>Male TD (N=108)</th>
<th>F group (p)</th>
<th>F sex (p)</th>
<th>F Gr X sex (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>14.66 (2.27)</td>
<td>14.10 (2.78)</td>
<td>13.61 (2.49)</td>
<td>13.58 (2.67)</td>
<td>0.67 (p=0.41)</td>
<td>7.35 (p=0.01)</td>
<td>3.21 (p=0.02)</td>
</tr>
<tr>
<td>Estimated IQ</td>
<td>94.79 (13.00)</td>
<td>103.61 (10.98)</td>
<td>94.82 (13.32)</td>
<td>105.32 (11.71)</td>
<td>31.58 (p&lt;0.001)</td>
<td>0.53 (p=0.47)</td>
<td>11.30 (p&lt;0.001)</td>
</tr>
<tr>
<td>Lifetime CD symptoms</td>
<td>5.30 (2.53)</td>
<td>0.14 (0.39)</td>
<td>5.29 (2.55)</td>
<td>0.19 (0.48)</td>
<td>979.07 (p&lt;0.001)</td>
<td>3.71 (p=0.06)</td>
<td>324.81 (p&lt;0.001)</td>
</tr>
<tr>
<td>ICU total (parent)</td>
<td>33.05 (11.49)</td>
<td>15.99 (7.48)</td>
<td>34.67 (12.24)</td>
<td>19.49 (7.13)</td>
<td>293.86 (p&lt;0.001)</td>
<td>13.57 (p&lt;0.001)</td>
<td>102.99 (p&lt;0.001)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No. with Current DSM-IV diagnoses</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>$X^2$ group (p)</th>
<th>$X^2$ sex (p)</th>
<th>$X^2$ Gr X sex (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ODD</td>
<td>57</td>
<td>0</td>
<td>62</td>
<td>0</td>
<td>259.31 (p&lt;0.001)</td>
<td>1.54 (p=0.22)</td>
<td>259.95 (p&lt;0.001)</td>
</tr>
<tr>
<td>ADHD</td>
<td>32</td>
<td>0</td>
<td>48</td>
<td>0</td>
<td>153.72 (p&lt;0.001)</td>
<td>6.41 (p=0.01)</td>
<td>157.34 (p&lt;0.001)</td>
</tr>
<tr>
<td>GAD</td>
<td>17</td>
<td>0</td>
<td>11</td>
<td>0</td>
<td>46.48 (p&lt;0.001)</td>
<td>0.78 (p=0.38)</td>
<td>53.18 (p&lt;0.001)</td>
</tr>
<tr>
<td>MDD</td>
<td>18</td>
<td>0</td>
<td>9</td>
<td>0</td>
<td>44.70 (p&lt;0.001)</td>
<td>2.27 (p=0.13)</td>
<td>57.41 (p&lt;0.001)</td>
</tr>
<tr>
<td>PDS: Pre/Early</td>
<td>5</td>
<td>17</td>
<td>32</td>
<td>35</td>
<td>0.90 (p=0.64)</td>
<td>36.76 (p&lt;0.001)</td>
<td>36.91 (p&lt;0.001)</td>
</tr>
<tr>
<td>Mid/ Late/ Post</td>
<td>69</td>
<td>125</td>
<td>55</td>
<td>72</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
fMRI emotion processing task

Gender discrimination task with fearful, angry and neutral faces presented in epochs of five stimuli (plus null events)
Conduct Disorder group show lower amygdala response to faces

- **Main effect of diagnosis** (both males and females with CD) found in the contrast ‘all faces > fixation’

- (CD<TD) reflecting reduced activation in right amygdala
Conduct Disorder group show lower amygdala response to faces
Males and females with CD show different response to anger

- **Sex-by-diagnosis** interaction in **left amygdala**
Males and females with CD show different response to anger

This interaction reflects reduced amygdala response to angry faces compared to neutral faces for females with CD whilst males with CD showed an increased response to angry faces compared to neutral faces.
Dimensional analyses in youth with CD

Association with CD symptoms and CU traits
Fear-neutral
Negative correlation with Unemotional traits

- Whole brain
- Left Fusiform gyrus (BA 18)

Unemotional traits

1. I am very good at concealing my emotions.
19. I even fool my friends. (Chamorro-Premuzic et al., 2001)
6. I do not show my emotions to others.
22. I hide my feelings from others.
14. It is easy for others to tell how I am feeling. (Rapaport, 1980)

Unemotional traits

Fear neutral Peak voxel in left Fusiform [-18, 66, -3]
Discussion

- **Neural response to emotions**
  - *Sex-by-group* interaction for *left amygdala* response to *angry faces*
  - Consistent with behavioural evidence that both males and females with CD are impaired are recognising angry faces
  - **BUT** these data suggest that neurobiological basis of emotion processing in CD may be partly different for males and females
  - In healthy males evidence for increased amygdala response to faces in general (Fusar-Poli) and angry faces in particular (Schneider)

- **Neural response to faces**
  - Main effect of group (CD < TD) in the *right amygdala*
  - Region central for salience detection
  - Data might explain previous data showing general impairment recognising facial expressions
Discussion con’t

- Dimensional analyses in the CD group
- Neural response to emotions
- CU traits
  - **Whole-brain**: Negative association between ICU unemotional dimension and fusiform response to fear-neutral
  - **Fusiform** gyrus is key for processing of fearful faces (meta-analysis Fusar-Poli). Evidence of structural (Rogers & De Brito) and functional (Noordermeer et al.) abnormalities in CD
Discussion con’t

● **Limitations**
  • Cross-sectional design
  • Sex of the stimuli was not included as factor in the analyses

● **Next steps**
  • Systematically examine the influence of comorbidities, medication, and childhood adversity
  • Connectivity analyses (e.g., vmPFC – amygdala)
  • Investigate the functional significance of those differences (e.g., instrumental vs. reactive aggression, neurocognitive measures) (see Lozier et al., 2014)
General Discussion and conclusions

- Overall, we found some similarities in functional abnormalities between males and females with CD
- BUT sex matters!
- Our findings indicate that the relationship between CD and brain response partly *differs by sex*
  - Neurobiological basis of CD differs between males & females

- Therefore combining small numbers of males and females in the same sample runs the risk of cancelling out CD-related effects that are either *specific to one sex* or operate in *opposite directions* in males and females
Future directions

- Longitudinal studies are needed to test whether main effects of diagnosis and sex-by-diagnosis interactions are stable over time or reflect maturational differences between the sexes or groups.

- Future studies should also systematically investigate the functional consequences of functional brain abnormalities by linking MRI with clinical and neuropsychological data in same sample.
Implications for clinical assessment

● Need to carefully assess the level of severity of the child or adolescent’s behaviour:
  
  • *Mild*—with few symptoms beyond the diagnostic threshold and behavior that causes relative minor harm to others (e.g., lying, truancy)
  
  • *Moderate*—the number of symptoms and amount of harm to others are intermediate to those specified as “mild” or “severe”
  
  • *Severe*—many symptoms beyond the diagnostic threshold that cause considerable harm to others (e.g., rape, use of a weapon)

● Need to identify the age of onset
  
  • Ideally, use multiple sources (youth’s self-report, parent reporting and official records) and use the youngest age across sources

● Need to assess the level of CU severity
  
  • Ideally use multiple sources and total CU scores

### Implications for clinical assessment

- Assess for as many risk factors as possible associated with CD across the different developmental pathways
  
  - **Adolescent-onset**: some personality traits (e.g., attitudes rejecting traditional status hierarchies) and environmental factors (e.g., poor parental supervision, association with a deviant peer group) ⇒ exaggerated rebelliousness
  
  - **Child-onset + low CU traits**: certain dispositional (e.g., high levels of emotional reactivity, low verbal intelligence) and contextual (e.g., harsh and inconsistent parenting) factors ⇒ impaired behavioural and emotional regulation
  
  - **Child-onset + high CU traits**: dispositional (e.g., low levels of emotional reactivity to distress in others) and contextual (e.g., low parental warmth) factors can contribute to low levels of empathy and guilt

Implications for treatment

● **Prevention is key!!!**
  - Youths with CD who are most aggressive and who are most likely to continue their antisocial behavior into adulthood often start exhibiting mild conduct problems very early in childhood
  - CU behaviours, fearless temperament, poor emotional regulation

● **Interventions need to be comprehensive and target multiple risk factors**
  - No gene, no temperamental risk factor, and no environmental risk factor operate in isolation
  - Most effective interventions for antisocial behavior involve multiple components, rather than targeting only a single risk factor
    - Social skills training, educational tutoring, contingency management training to teachers in the classroom, and social cognitive interventions focused perspective-taking and emotion regulation

Conduct disorders and psychopathy in children and adolescents: aetiology, clinical presentation and treatment strategies of callous-unemotional traits

Simone Pisano¹, Pietro Muratori², Chiara Gorga³, Valentina Levantini², Raffaella Iuliano⁴*, Gennaro Catone³, Giangennaro Coppola¹, Annarita Milone² and Gabriele Masi²

Table 1 Currently available psychotherapeutic treatments for children with conduct disorder and high CU traits

<table>
<thead>
<tr>
<th>Name</th>
<th>Age range</th>
<th>Treatment target</th>
<th>Time range</th>
<th>Directed to (children, parents, teachers etc.)</th>
<th>Main references</th>
</tr>
</thead>
<tbody>
<tr>
<td>CARES Module</td>
<td>3.5–8</td>
<td>Improvement of emotion recognition and labelling; enhancement of pro-social and empathic behaviour; increase of child’s frustration tolerance.</td>
<td>6 weeks</td>
<td>Children</td>
<td>Datyner et al., 2016</td>
</tr>
<tr>
<td>ERT</td>
<td>6–16</td>
<td>Enhancement of emotion recognition and interpretation; improvements of empathic abilities.</td>
<td>4 sessions (90 min each)</td>
<td>Children</td>
<td>Dadds et al., [94]</td>
</tr>
<tr>
<td>Mental Models</td>
<td>Adolescents</td>
<td>Increase positive emotion and reduce negative affect; improvement of decision-making skills; reduction of psychopathic features.</td>
<td>12 weeks</td>
<td>Children</td>
<td>Salekin et al., [96]</td>
</tr>
<tr>
<td>CP Program</td>
<td>7–14</td>
<td>Improvement of emotion recognition, especially anger; increase of child’s ability to cope with anger arousal; enhancement of perspective taking ability and problem solving skills; improvement of parenting skills.</td>
<td>12 months</td>
<td>Children and parents</td>
<td>Lochman and Wells, [97]; Muratori et al., [98]</td>
</tr>
</tbody>
</table>

Legend: CARES coaching and rewarding emotional skills, ERT emotion recognition training, CP coping power
Implications for treatment

- Interventions need to be individualized and based on the behavioural, affective and neurocognitive profile of the different developmental pathways
  - **Adolescent-onset**: Focusing on enhancing identity development in adolescents and increasing contact with prosocial peers, such as mentoring programs or programs that provide structured after-school activities
  - **Child-onset + low CU traits**: Focusing on anger control or reducing harsh and ineffective parenting
  - **Child-onset + high CU traits**: Intervention that focused on teaching parents methods of using positive reinforcement to encourage prosocial behaviour, consistent with the reward-oriented response style. Intensive treatment program that utilize reward-oriented approaches, targeted the self-interests of the adolescent

ENIGMA Antisocial Behavior

What is ENIGMA?

The ENIGMA Network brings together researchers in imaging genomics to understand brain structure, function, and disease, based on brain imaging and genetic data. We welcome brain researchers, imagers, geneticists, methods developers, and others interested in cracking the neuro-genetic code!
Locations of ENIGMA Members Across the World

Member: Christoph Lenglet
Working Group: Ataxia
Institution: 
Latitude: 45.0
Longitude: -93.3
Tänan teid tähelepanu eest!
Kas küsimusi on?
s.a.debrito@bham.ac.uk