Neurocognitive differences in children with or without CU-traits

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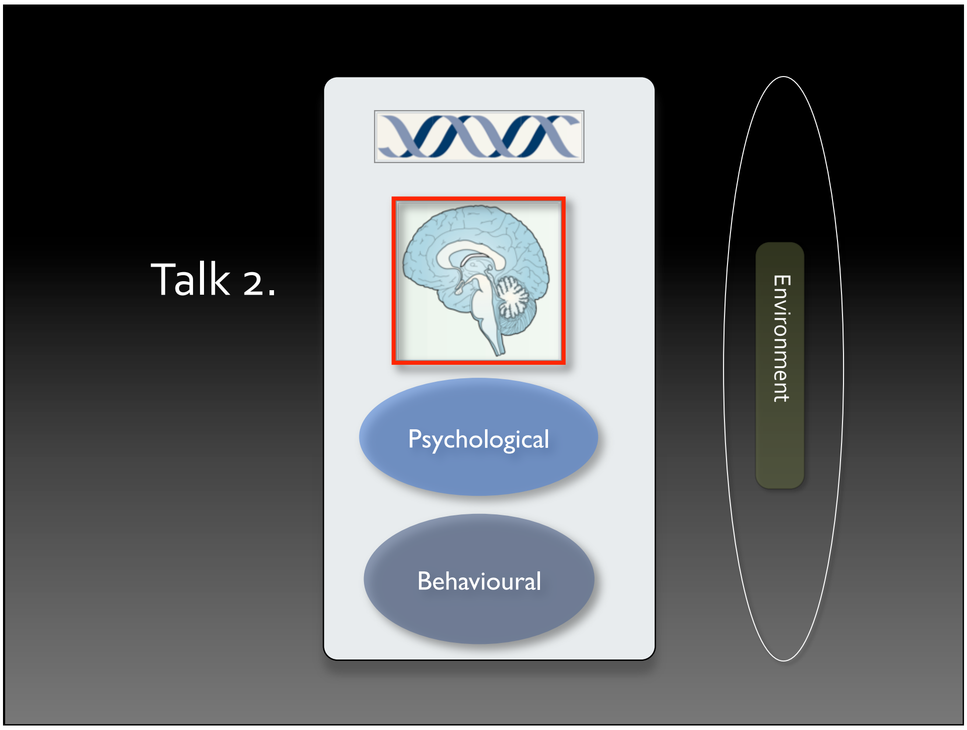

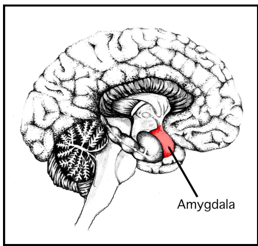

- Adults with psychopathy have structural and functional abnormalities in several brain areas implicated in the processing of salient/affective information and empathy (e.g. amygdala and insula) and reinforcement learning (e.g. orbitofrontal and ventromedial prefrontal cortex)

- Do children with CP and high CU (CP/HCU) show structural and functional abnormalities resembling those seen in adult psychopaths?
- Do CU traits and CP have distinct contributions to neural activity in affect/empathy processing areas of the brain?
- Do children with CP/HCU and CP/LCU look different in terms of their neural function?

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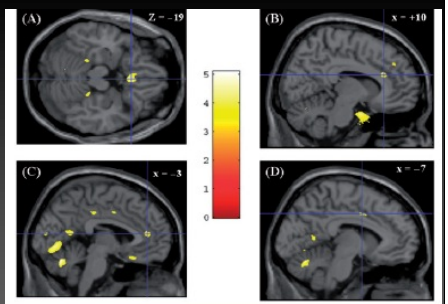
BRAIN
A JOURNAL OF NEUROLOGY

Size matters: Increased grey matter in boys with conduct problems and callous–unemotional traits

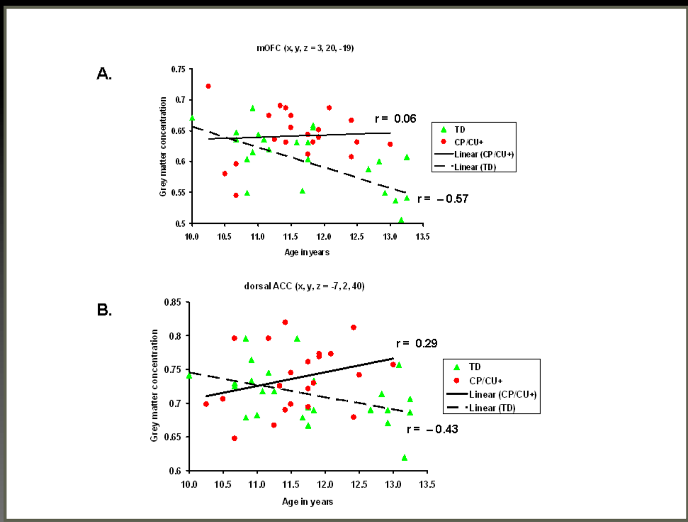
Stéphane A. De Brito,[1] Andrea Mechelli,[2] Marko Wilke,[3] Kristin R. Laurens,[1] Alice P. Jones,[4] Gareth J. Barker,[5] Sheilagh Hodgins[1] and Essi Viding[4,6]



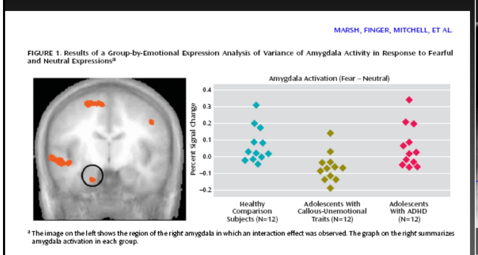
- Increased grey matter in boys with CP/HCU in several brain areas implicated in social and moral cognition; reinforcement learning
  - e.g. orbitofrontal cortex (OFC), anterior cingulate cortex (ACC), posterior cingulate cortex (PCC), and parahippocampal gyrus (PGH)

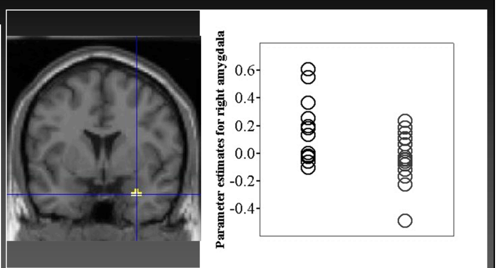
(2009)

Aberrant maturation?



Compared with typically developing children or those with ADHD, children with CP/HCU show lower amygdala activation to other people's fear





Marsh et al., 2008

Jones et al., 2009

- Compared with typically developing children or those with ADHD, children with CP/HCU also show atypical activation of ventromedial , orbitofrontal and striatal areas when processing reinforcement information (punishments, rewards, expected value processing; Finger et al., 2008; 2010; White et al., 2013)

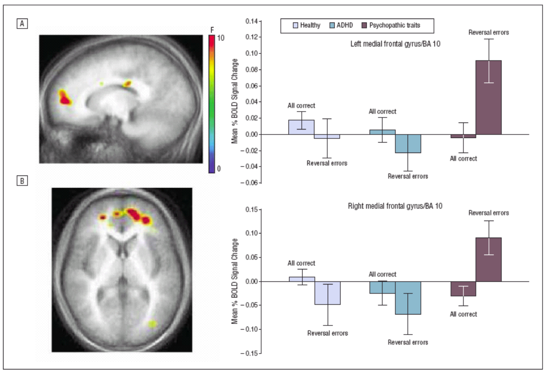


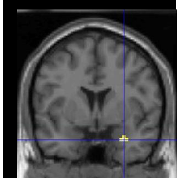
Figure 2. Diagnosis × response type interaction. In the left (A) and right (B) ventromedial prefrontal cortex/Brodmann area (BA) 10, healthy children and children with attention-deficit/hyperactivity disorder (ADHD) demonstrated decreased blood oxygenation level–dependent (BOLD) responses during punished reversal errors compared with correct rewarded responses. In contrast, patients with psychopathic traits showed increased BOLD responses during punished reversal errors in this region. Error bars represent standard errors.

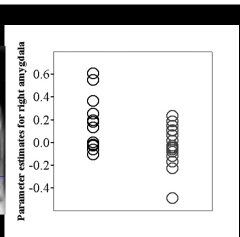
Finger et al., 2008

Summary

- Structural and functional differences in many of the areas that have been implicated in studies of adult psychopaths
- Brain imaging findings in line with what cognitive experimental studies have shown
- However, the majority of studies to date have not investigated the unique contributions of CU and CP to neural activity or compared CP/HCU vs. CP/LCU groups

- Do children with CP and high CU (CP/HCU) show structural and functional abnormalities resembling those seen in adult psychopaths?
- Do CU traits and CP have distinct contributions to neural activity in affect/empathy processing areas of the brain?
- Do children with CP/HCU and CP/LCU look different in terms of their neural function?





- Compared with typically developing children or those with ADHD, children with CP/HCU show:
  - lower amygdala activation to other people's fear (Jones et al., 2009; Marsh et al., 2008)
- Some studies have reported more amygdala reactivity to affective stimuli (faces, scenes) in children with CP than in typically developing children (e.g. Decety et al., 2009; Herpertz et al., 2008; Passamonti et al., 2010).

Sebastian, McCrory, Cecil, Lockwood, DeBrito, Fontaine & Viding, 2012, AGP

Aim 1:

We wanted to expand the currently small neuroimaging literature in CP by comparing CP and TD children with fMRI on a complex affective processing task requiring understanding of emotions.

Aim 2:

We wanted to explore conflicting findings regarding amygdala activation in CP by investigating unique contributions of CP and CU to variance in amygdala response.

- Behavioural studies have shown positive associations between CP and emotional reactivity and negative associations between CU and emotional reactivity (e.g. Frick et al., 1999; Kimonis et al., 2005).

Participant Demographics

	TD Controls (n=16)	CPs (n=31)	*p*-value
Age	13.51 (1.65)	14.34 (1.75)	.125
F-IQ	105.94 (12.37)	100.84 (11.51)	.167
V-IQ	56.13 (10.61)	51.55 (8.19)	.108
P-IQ	50.13 (8.61)	48.29 (9.53)	.522
Socio-Economic Status	2.69 (.87)	3.20 (1.03)	.104
Ethnicity	14 White, 1 Black, 1 Mixed	20 White, 5 Black, 6 Mixed	.288
Handedness	12 Right, 3 Left, 1 Ambidextrous	26 Right, 5 Left	.492

TD and CP groups matched on age, IQ, socio-economic status, ethnicity and handedness

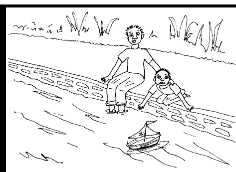
Participants: Questionnaire measures

	TD Controls (n=16)	CPs (n=31)	*p*-value
Inventory of Callous-Unemotional Traits (ICU)	23.88 (5.91)	45.10 (11.09)	.001
Child and Adolescent Symptom Inventory (CASI-4R)			
Conduct Disorder	.51 (.75)	10.95 (6.14)	.001
ADHD	9.88 (6.20)	25.82 (11.37)	.001
Generalised Anxiety Disorder	3.75 (3.19)	7.43 (6.18)	.01
Major Depressive Episode	2.63 (1.75)	4.61 (2.86)	.02
Alcohol Use and Disorders	1.13 (1.78)	4.61 (6.57)	.044
Drug Use and Disorders	0 (.00)	1.77 (4.27)	.105

TD and CP groups differed on key variables of interest (CU traits and conduct disorder symptoms)

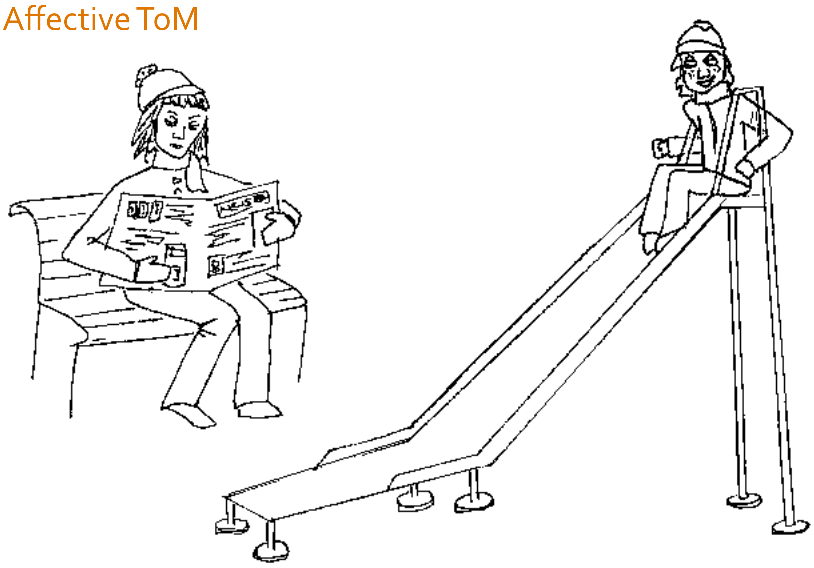
Groups also differed on symptom counts for conditions commonly co-morbid with conduct problems

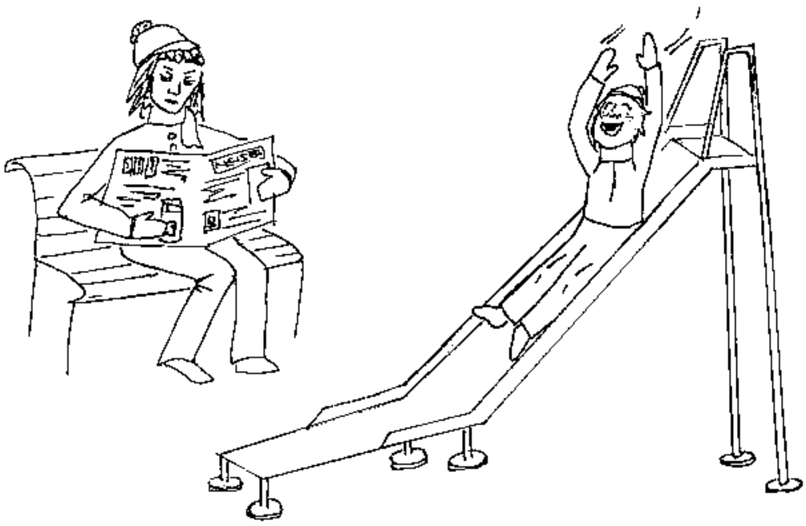
Cartoon Task

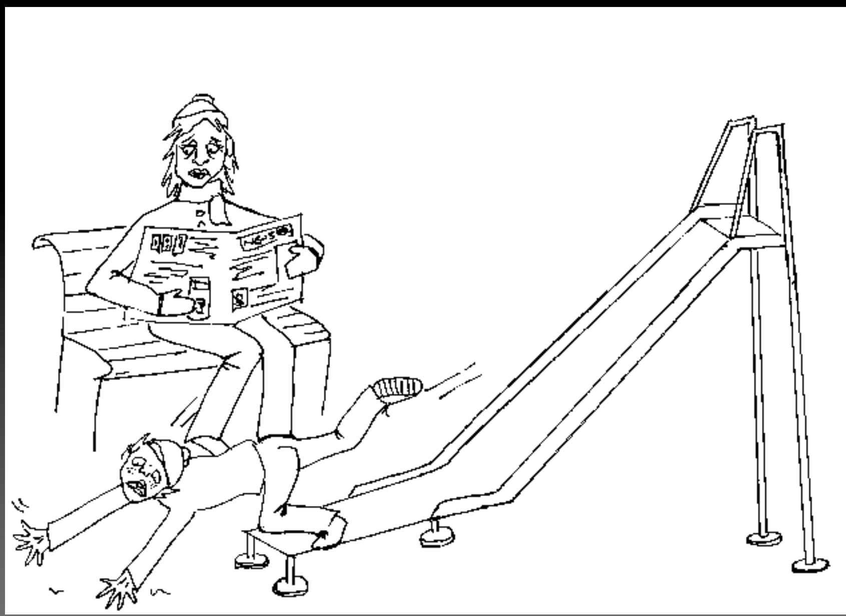


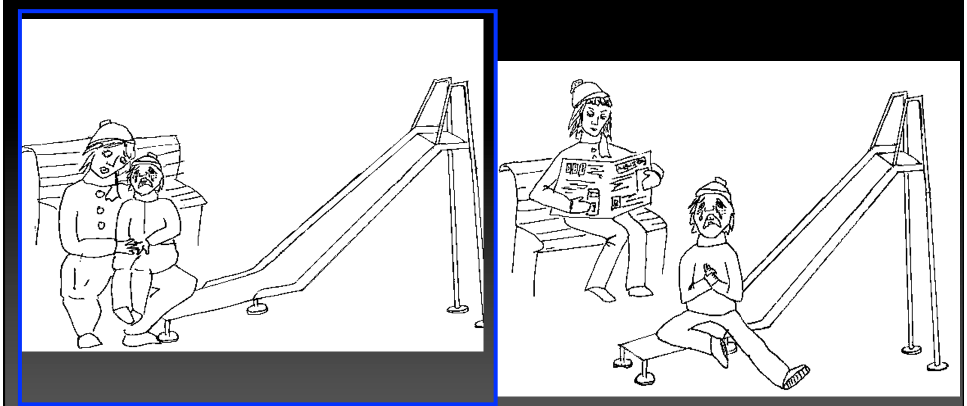
- Participants viewed cartoon vignettes and were asked to decide **'What happens next?'**
  - Affective ToM (decision based on how characters feel)
  - Cognitive ToM (decision based on what characters think)
- Cartoons matched for social content and story complexity. Based on Völlm et al. (2006) and Sebastian et al. (in press).
  - Physical causality cartoons (cause and effect reasoning) were used in main effect analyses to ensure that both Affective and Cognitive ToM cartoons activated the ToM network
- Participants completed 30 cartoons (10 from each condition) in a 9 minute 1.5T fMRI scan. Data were analysed in blocks.

Affective ToM

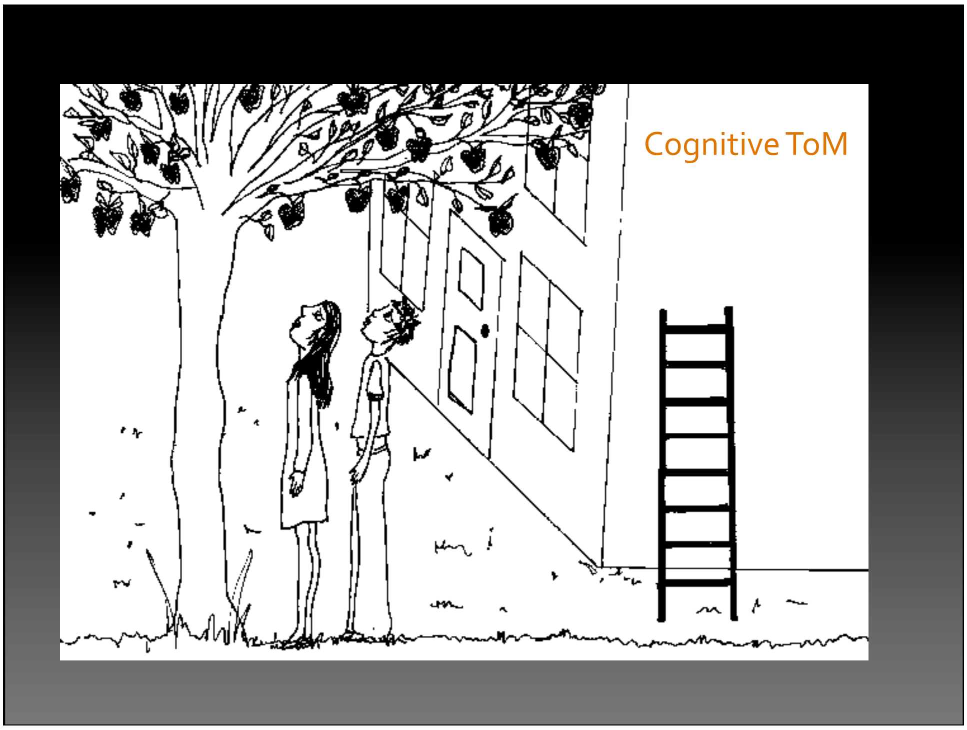


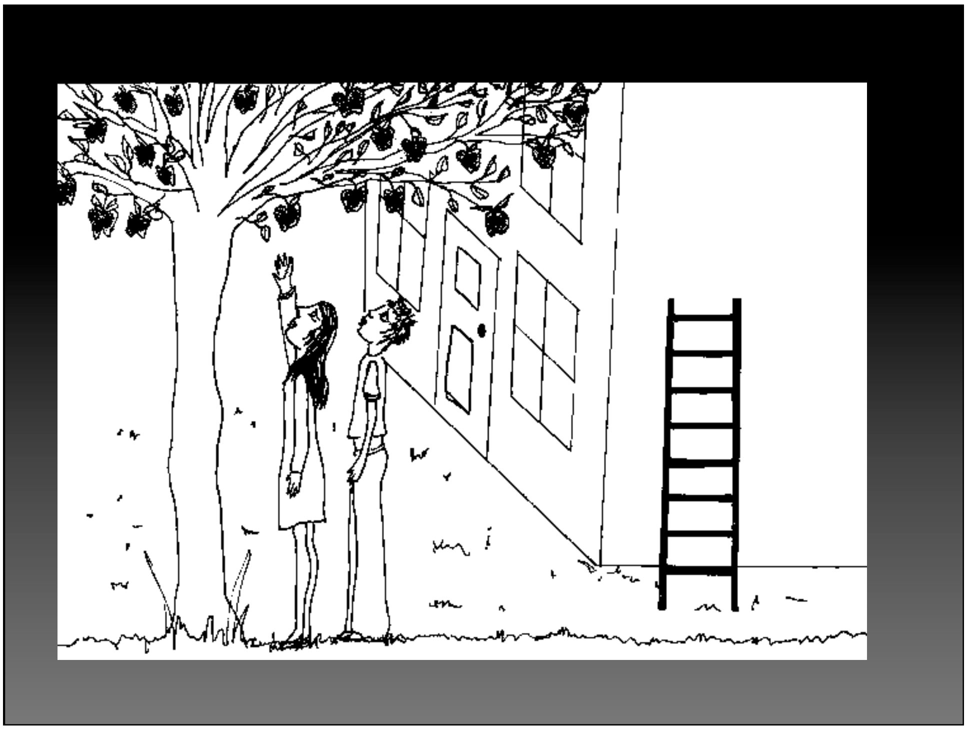


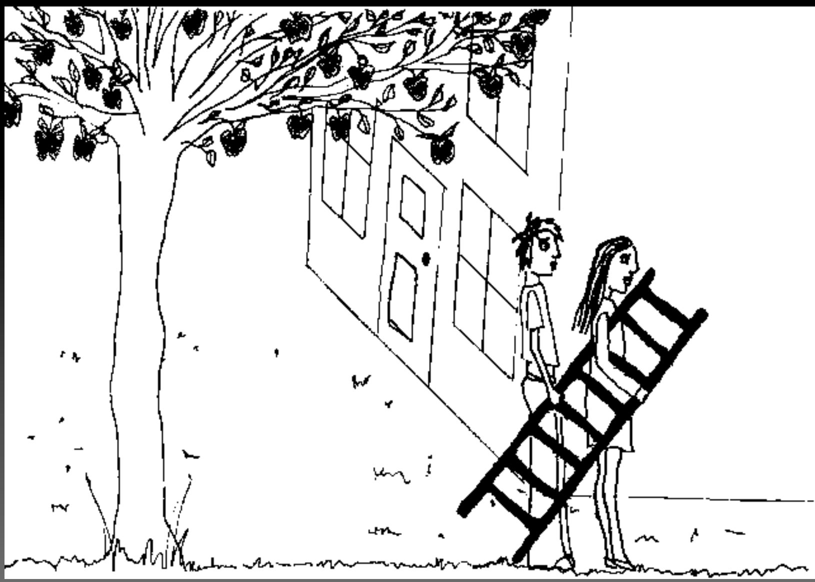




‘Correct’ answer involves understanding emotions (affective ToM)


Cognitive ToM



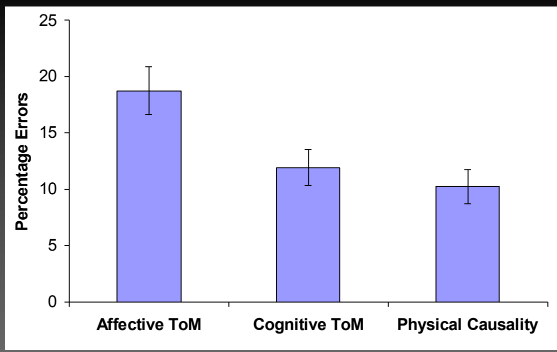


‘Correct’ answer involves understanding intentions

Main Effects of the Task

Behavioural Data

- RT: No main effect of Group or Condition, or interaction.
- Errors: No main effect of Group or interaction. Main effect of Condition:

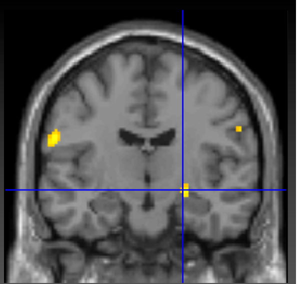


Importantly, lack of an interaction between Group and Condition means that behavioural data do not complicate interpretation of fMRI group comparisons.

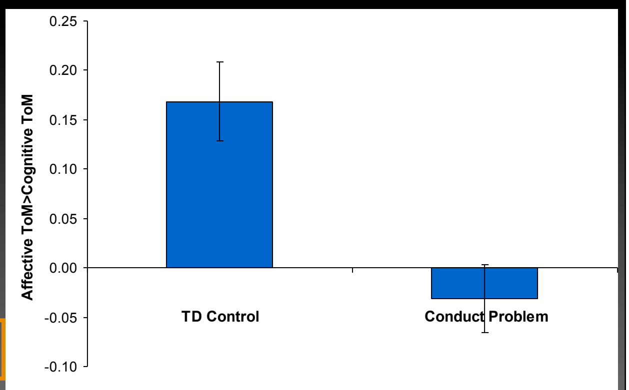
TD>CP: Group Comparison

Right amygdala [24 -12 -10]

Affective > Cognitive ToM contrast



p<.05 FWE (SVC). At *p*<.001, *k*=6. Display: *p*<.005



*$p \leq .001$

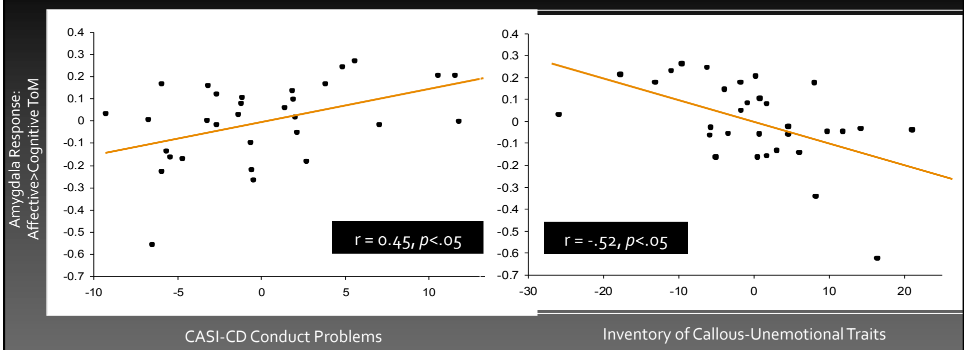
ROI co-ordinates defined on the basis of previous studies investigating empathy in developmental samples

Dimensional Variables in CP group

Amygdala

Positive correlation between amygdala response and conduct problems, controlling for CU traits

Negative correlation between amygdala response and CU traits, controlling for conduct problems



Results remained after controlling for hyperactivity, depression, anxiety and alcohol use

- CP adolescents show reduced amygdala response during complex affective processing (affective ToM)
- Positive correlation between amygdala activity and CP; negative correlation between amygdala activity and CU, in the CP group
  - Findings in line with previous behavioural data (e.g. Frick et al., 1999; Hicks & Patrick, 2006; Kimonis et al, 2006).
- Highlights possible heterogeneity of emotional responsivity in children with CP; those with highest levels of CU are least responsive to other people's distress – at neural, as well as behavioural level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Report

Association of Callous Traits with Reduced Neural Response to Others' Pain in Children with Conduct Problems

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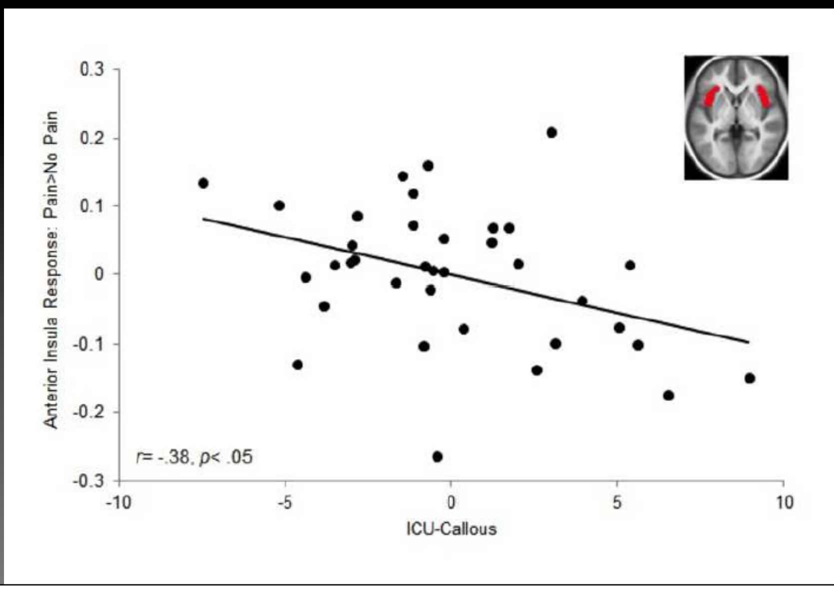
One method for investigating neural processing of empathy is to measure responses to others' pain [4]. Delineating these responses in children with CP is of particular interest because this group often inflicts pain on others [1]. fMRI studies in healthy populations have identified a network of brain regions activated by both the experience and observation of pain. This network includes sensory regions such as somatosensory cortex, affective-motivational regions (linked to processing emotional responses to pain), such as anterior insula (AI) and anterior cingulate cortex (ACC), and cognitive-regulatory regions, such as inferior frontal gyrus (IFG) [7, 8, 10, 15, 16].

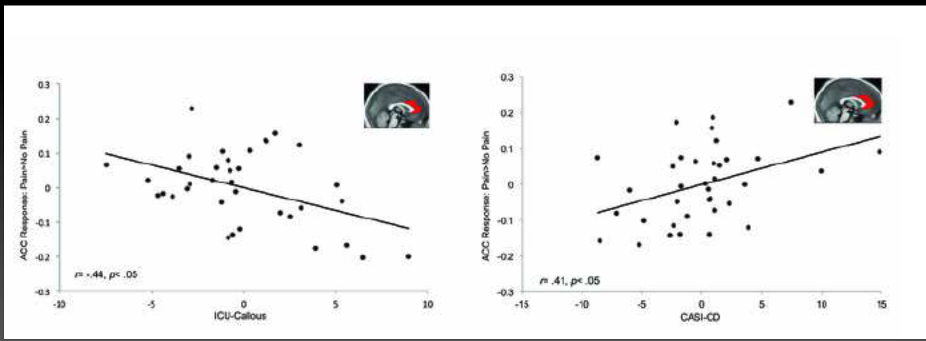
Atypical function and structure in several of these regions, including AI, ACC, and prefrontal cortex, have been implicated

Focus on brain areas associated with 'empathy for pain', e.g. Insula and ACC

Anterior Insula
Contrast: Pain > No Pain
Controls > Children with CP (p=0.02)



Anterior Cingulate Cortex
Contrast: Pain > No Pain
Controls > Children with CP (p=0.05)

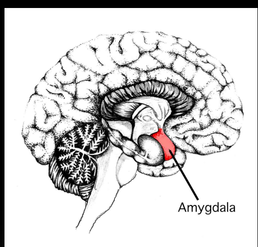


- CP adolescents show reduced insula and anterior cingulate response when processing other people's pain

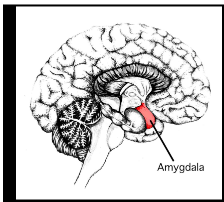
- Positive correlation between ACC activity and CP; negative correlation between insula and ACC activity and callousness, within the CP group

- Further highlights possible heterogeneity of emotional responsivity in children with CP; those with highest levels of callousness are least responsive to other people's distress – at neural, as well as behavioural level

- Do children with CP and high CU (CP/HCU) show structural and functional abnormalities resembling those seen in adult psychopaths?
- Do CU traits and CP have distinct contributions to neural activity in affect/empathy processing areas of the brain?
- Do children with CP/HCU and CP/LCU look different in terms of their neural function?



- fMRI studies of children with CP have reported atypical activation of the amygdala to emotional stimuli
  - Reports of amygdala hypo- and hyperactivity
  - (e.g. Decety et al., 2009; Herpertz et al., 2008; Jones et al., 2009; Marsh et al., 2008; Passamonti et al., 2010; Sterzer et al., 2005)
- Mixed findings
  - Possible explanations include paradigm differences between the studies [emotional stimuli are not equivalent in what they index] ; variation in the levels of CU traits across different samples

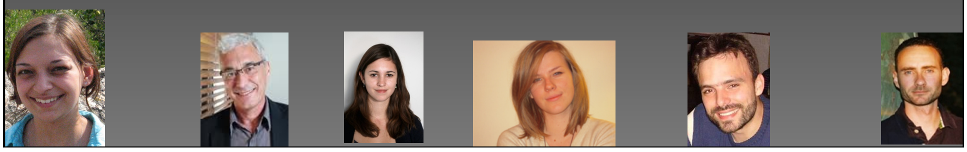


- To date, fMRI studies of children with conduct problems have focused on affective stimuli presented under prolonged viewing conditions.
- The amygdala also responds to salient stimuli when stimuli are presented pre-attentively (i.e., before reaching conscious awareness or attention).
- This is consistent with the amygdala's role as part of a functional network engaged in triggering an orienting response to salient stimuli, including emotional facial expressions, so that appropriate processing of and behavioral responses to such stimuli can be prioritized.

- Do subtypes of children with CP and high vs. low CU traits differ in their pre-attentive amygdala response to fearful faces?
  - Fearful faces signal distress and potential threat in the surroundings
    - Children with CP and high CU traits are fearless and insensitive to other people's distress
    - Children with CP and low CU traits are hypersensitive to perceived threat

Amygdala response to pre-attentive masked fear in children with conduct problems

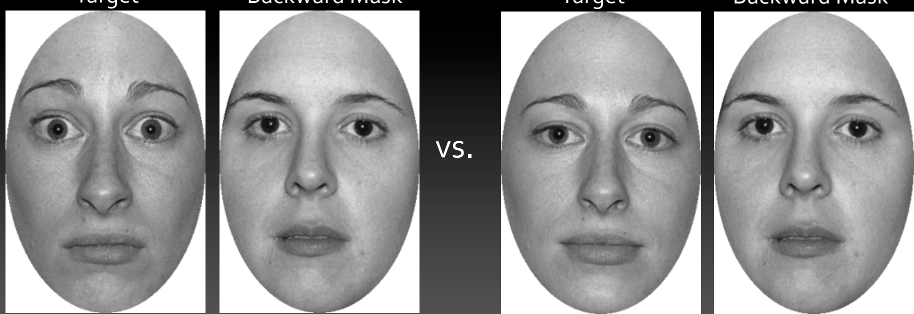
Viding/Sebastian, Dadds, Lockwood, Cecil, de Brito, & McCrory, 2012, AJP



Masked Fear Task

Fear Condition | Calm Condition

Target | Backward Mask | Target | Backward Mask



17ms | 183ms | 300ms ISI | 17ms | 183ms | 300ms ISI

- Identity of target and mask always differed. Equal male and female faces.
- Based on series of papers by the Whalen group.

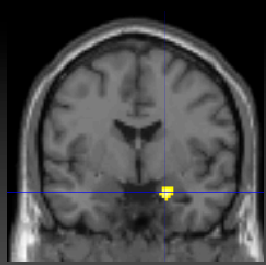
Participants

	CP/HCU N=15	CP/LCU N=15	TD Controls N=16	
Age	14.22	14.69	13.73	ns.
Full-IQ	98.73	103.87	107.69	ns.
SES	3.35	2.99	2.77	ns.
				ns.
Conduct Problems	13.88	7.85	0.38	*p*<.01, all groups
CU Traits	53.00	35.13	24.50	

- CU groups determined by median split on ICU measure of CU traits
- Groups also matched on ethnicity and handedness
- Symptoms of commonly comorbid disorders (ADHD, GAD, MDE) were also taken to assess their possible contributions to results

CP(low CU) > Comparison > CP(high CU)

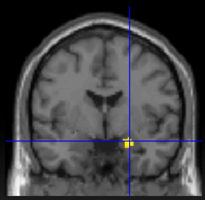
Right amygdala [20 -2 -22]

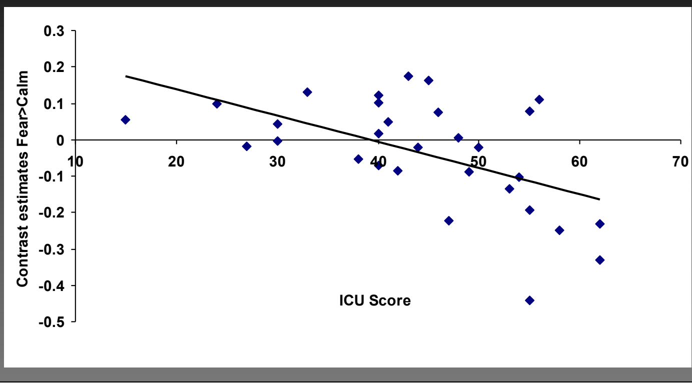


p<.05, FEW-SVC

Findings were not explained by group differences in conduct disorder, ADHD, anxiety, depression or substance use symptoms.

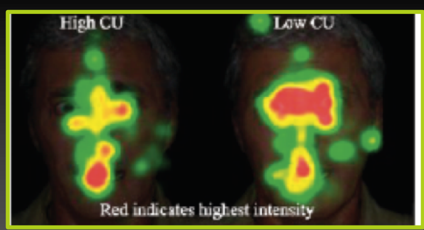
- Regression analysis across CP group
- Continuous relationship between right amygdala [24 -2 -18] response to masked fear and ICU score ($p<.05$, FWE-SVC)





Summary

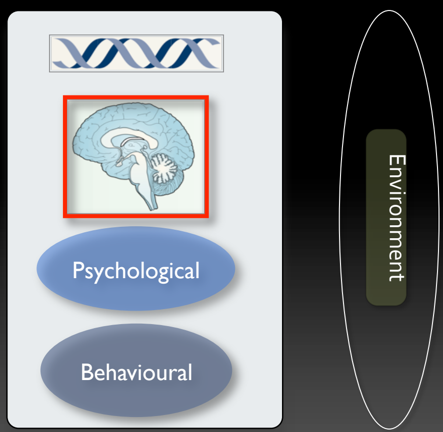
- Deficit in detecting and representing fear is present at the earliest levels of processing in children with CP and high levels of CU
  – This may explain why these children orient less to other people's distress cues (Dadds et al., 2008)?



- Heterogeneity of emotional responsivity in children with CP
  – Those with high levels of CU show lowest amygdala response to other people's distress/potential threat

Conclusions

- CP/HCU and CP/LCU appear to have different patterns of atypical brain function, former associated with low and the latter with exaggerated amygdala activity to fearful faces – at least under some task conditions
- Challenge to devise ecologically valid task conditions under which the amygdala functioning and its degree of malleability, can be investigated in each CP subtype



Conduct Problems with CU

- Abnormally unresponsive to threat/ distress, at neural, as well as behavioural level

Conduct Problems without CU

- Increased neural activity to threat/ distress
- Similar to what is seen in maltreated children (McCrory et al., 2011; 2013)

Implications

- Neurocognitive research essential when we want to know why children behave the way they do and what we might want to do about it
- Some treatment strategies may work both for children with CP/HCU and CP/LCU, but both groups will also benefit from specific approaches tailored to their individual problems