An fMRI investigation of empathic processing in boys with conduct problems and varying levels of callous-unemotional traits

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\textbf{ABSTRACT}

The ability to empathise relies in part on using one’s own affective experience to simulate the affective experience of others. This process is supported by a number of brain areas including the anterior insula (AI), anterior cingulate cortex (ACC), medial prefrontal cortex (mPFC), and the amygdala. Children with conduct problems (CP), and in particular those with high levels of callous-unemotional traits (CP/HCU) present with less empathy than their peers. They also show reduced neural response in areas supporting empathic processing when viewing other people in distress. The current study focused on identifying brain areas co-activated during affective introspection of: i) One’s own emotions (‘Own emotion’); ii) Others’ emotions (‘Other emotion’); and iii) One’s feelings about others’ emotions (‘Feel for other’) during fearful vs neutral scenarios in typically developing boys (TD; \( n = 31 \)), boys with CP/HCU (\( n = 31 \)), and boys with CP and low levels of CU (CP/LCU; \( n = 33 \)). The conjunction analysis across conditions within the TD group revealed significant clusters of activation in the AI, ACC/mPFC, and occipital cortex. Conjunction analyses across conditions in the CP/HCU and CP/LCU groups did not identify these areas as significantly activated. However, follow-up analyses were not able to confirm statistically significant differences between groups across the whole network, and Bayes-factor analyses did not provide substantial support for either the null or alternate hypotheses. Post-hoc comparisons indicated that the lack of conjunction effects in the CP/HCU group may reflect reduced affective introspection in the ‘Other emotion’ and ‘Feel for other’ conditions, and by reduced affective introspection in the ‘Own emotion’ condition in the CP/LCU group. These findings provide limited and ultimately equivocal evidence for altered affective introspection regarding others in CP/HCU, and altered affective introspection for own emotions in CP/LCU, and highlight the need for further research to systematically investigate the precise nature of empathy deficits in children with CP.

\textbf{1. Introduction}

Empathy is the capacity to understand and resonate with the affective experience of another (Singer and Lamm, 2009; Lockwood, 2016). Empathy plays a key role in inhibiting aggression and promoting prosocial behaviour (Eisenberg et al., 2005; Decety et al., 2016). Empathy processing is thought to be a risk factor for the development of psychopathy (Blair et al., 2014). Atypical empathic processing is thought to be a risk factor for the development of psychopathy (Blair et al., 2014). The ability of individuals with psychopathy to hurt and manipulate other people without concern for their welfare, suggests an atypical empathic/vicarious response to other people’s distress (Viding and McCrory, 2015; Lockwood, 2016). Although it would be entirely inappropriate (and indeed erroneous) to diagnose children with psychopathy, a subgroup of children with conduct problems (CP) who also present with callous-unemotional (CU) traits present with atypical empathic responses to other people’s suffering (Blair et al., 2014; Viding and McCrory, 2015). Such a pattern is similar to that seen in adults with psychopathy (Blair et al., 2014; Seara-Cardoso and Viding, 2015). Children with CP and high levels of CU traits (CP/HCU) are at a substantially increased risk of developing persistent antisocial behaviour compared with both typically developing (TD) peers and peers with CP and lower levels of CU traits (CP/HCU) (Frick et al., 2014; Viding and McCrory, 2015). There have been considerable efforts in recent years to understand the neurocognitive basis of empathy problems observed in these children (Blair et al., 2014; Viding and McCrory, 2015).

Empathic processing in typically developing children is supported by a number of brain regions that have been implicated in...
understanding and resonating with the affective experience of others (Singer and Lamm, 2009; Lockwood, 2016). Across both animal and human studies two brain areas, the anterior insula (AI) and anterior cingulate cortex (ACC), have been robustly associated with empathic processing/vicarious processing of emotions (Singer and Lamm, 2009; Lockwood, 2016). Other areas, such as inferior frontal gyrus and amygdala, have also been implicated in empathic processing (Singer and Lamm, 2009; Lockwood, 2016).

Neuroimaging studies have shown that children with CP, in particular those with CP/HCU, show atypical response to others' pain and distress in regions implicated in empathic processing (e.g. Lockwood et al., 2013; Marsh et al., 2013; Michalska et al., 2016; Yoder et al., 2016). For example, Marsh et al. (2013) reported reduced amygdala and ACC responses to photographs of pain-inducing injuries in children with CP, with those with HCU reporting the most pronounced differences compared with typically developing (TD) children. Lockwood et al. (2013) reported reduced AI and ACC responses to photographs of hands and feet in painful situations in boys with CP, with the degree of activation correlating negatively with the level of CU traits. Michalska et al. (2016) studied youth with CP as they viewed video clips of intentional and unintentional harm and reported that both CP and CU traits were negatively associated with AI and anterior midcingulate responses to intentional harm. Finally, Yoder et al. (2016) reporting on the same sample and task showed that HCU was associated with disrupted connectivity between ACC and AI and ACC and amygdala. They concluded that HCU is characterized by the disruption to cortical networks involved in detecting and appropriately responding to salient environmental cues, such as other people's distress.

This pattern of findings is in line with data from adults with high levels of psychopathic traits or diagnosed psychopathy. In several studies probing neural response to expressions of pain or distress, and other people's body parts experiencing pleasant or painful touch, adults with psychopathic traits/diagnosed psychopathy show lower AI activity (but see Decety et al., 2013 for a study reporting greater AI activity in incarcerated psychopaths in response to facial expressions of pain), and lower ACC response to these stimuli (e.g. Decety et al., 2013; Meffert et al., 2013; Seara-Cardoso et al., 2015, 2016). Interestingly, Meffert et al. (2013) report that when individuals with psychopathy are instructed to “empathize” whilst observing other people's hands receiving pleasant or painful touch, the group differences between neural responses in AI, ACC and IGF seen between individuals with psychopathy and typically developing controls are reduced, i.e. the neural response in those with psychopathy is no longer significantly lower than that which is seen in controls.

We wanted to further investigate the neural basis of empathy in children with CP/HCU, as contrasted with CP/LCU and TD children who were matched for age, SES and ability. We were particularly interested in isolating those brain areas that support processes thought to be critically involved in introspection about one's own emotions and thinking about others' emotions, which are thought to be involved in empathic responses to others (de Vignemont and Singer, 2006; Bird and Viding, 2014). We therefore sought to investigate regions co-activated during these processes. To achieve our aim we used a task that incorporated conditions requiring: (i) introspection about one's own feelings when picturing oneself in a fear-inducing situation; (ii) thinking about what another person is feeling when picturing him in a fear-inducing situation; and (iii) introspection about one's own feelings in response to hearing about another person in a fear-inducing situation. We reasoned that common brain areas activated across all of these conditions would be particularly important for resonating with and understanding others' emotions and using one’s own affective state to guide these processes.

Our task enabled us to first identify those brain areas that are commonly activated during all these processes in typically developing (TD) children using conjunction analyses. Based on previous research we hypothesised that the AI and ACC should activate across all the task conditions. We then assessed whether such a network observed in TD children was also consistently activated by children in CP/HCU and CP/LCU groups across conditions. We further examined whether there were differences in activity in any of these core affective introspective regions specifically, by directly comparing groups across these conditions using a functional ROI approach informed by the previous conjunction analyses. We hypothesised that, compared to TD children, children with CP/HCU would show significantly reduced activation of AI and ACC.

No directional hypothesis was made for CP/LCU children as previous work has primarily indicated that affective resonance/empathy deficits are more robustly associated with the children with CP/HCU rather than their peers with lower CU traits (Jones et al., 2010; Schwenck et al., 2012; but see Martin-Key et al., 2016), but this group was also compared with TD children on an exploratory basis.

2. Methods

2.1. Participants

Boys aged 11–16 years were recruited from the community via newspaper advertisements, and local mainstream and specialist provision schools. Screening questionnaires were administered to parents of 360 boys and teachers of 215 boys whose families expressed an interest in taking part and provided informed consent. The screening measures provided a research diagnosis of current conduct problems; dimensional assessment of CU traits; an overall screen for psychopathology; demographic data for group-matching purposes (i.e. socioeconomic status, parent-defined ethnicity, and handedness); and information regarding previous neurological or psychiatric diagnoses.

Current conduct disorder symptoms were assessed using the Child and Adolescent Symptom Inventory–4R (CASI-4R) Conduct Disorder (CASI-CDS) subscale (Gadow and Sprafkin, 2009). CU traits were assessed using the Inventory of Callous-Unemotional Traits (ICU) (Essau et al., 2006). Both were scored by taking the highest ratings from either the parent or the teacher questionnaire for any given item (Piacentini et al., 1992). For the CASI-CDS scale, inclusion in the conduct problem group required that the score met either parent or teacher severity cutoff (parent report: cut-off = 4+ [ages 10–12] and 3+ [ages 12–16]; teacher report: cut-off = 3+ [ages 10–12], 4+ [ages 12–14], and 6+ [ages 15–16]). These scores are associated with a clinical diagnosis of conduct disorder (Sprafkin and Gadow, 1998). Typically developing participants were required to score in the normal range for this measure, and below the cut-off for total difficulties on the Strengths and Difficulties Questionnaire (Goodman, 1997).

Automatic exclusion criteria for both conduct problems and typically developing groups included a previous diagnosis of any neurological or psychotic disorder, or current psychiatric medication. To recruit a representative group of children with conduct problems, common comorbidities (ADHD, generalized anxiety disorder [GAD], depression, and substance/alcohol abuse) were not used as exclusion criteria, but current parent-reported symptom counts were obtained during scanning sessions, so that their possible contribution to the findings could be systematically assessed.

On the basis of the screening information, one hundred participants took part in the fMRI scanning session. Participants were provided with a complete description of the study. Informed consent was obtained from parents and written assent from all participants. All aspects of the study were approved by the University College London Research Ethics Committee (Project ID number: 0622/001) and was conducted in accordance with the Declaration of Helsinki.

Three participants (one with CP and two typically developing) withdrew from the session prior to collection of the task data due to poor tolerance of the scanner environment. Of the sample who completed scanning (66 participants with CP, 31 typically developing participants), data from 2 participants (both CP/HCU) were excluded due to image artifacts and poor registration. The remaining boys in the CP
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