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Anatomy of the dorsal default-mode network in conduct disorder: Association with callous-unemotional traits☆

Arjun Sethi[a,b,c,*], Sagari Sarkar[d], Flavio Dell'Acqua[d], Essi Viding[c], Marco Catani[a,b], Declan G.M. Murphy[b,1], Michael C. Craig[a,b,e,1]

[a] Natbrainlab, Department of Forensic & Neurodevelopmental Sciences, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK
[b] Sacker Institute for Translational Neurodevelopment, Department of Forensic & Neurodevelopmental Sciences, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK
[c] Developmental Risk & Resilience Unit, University College London, London, UK
[d] Natbrainlab, Department of Neuroimaging, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK
[e] National Autism Unit, Bethlem Royal Hospital, SLAM NHS Foundation Trust, Kent, UK

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ABSTRACT

We recently reported that emotional detachment in adult psychopathy was associated with structural abnormalities in the dorsal 'default-mode' network (DMN). However, it is unclear whether these differences are present in young people at risk of psychopathy. The most widely recognised group at risk for psychopathy are children/adolescents with conduct disorder (CD) and callous-unemotional (CU) traits. We therefore examined the microstructure of the dorsal DMN in 27 CD youths (14-with/13-without CU traits) compared to 16 typically developing controls using DTI tractography. Both CD groups had significantly ($p < 0.025$) reduced dorsal DMN radial diffusivity compared to controls. In those with diagnostically significant CU traits, exploratory analyses (uncorrected for multiple comparisons) suggested that radial diffusivity was negatively correlated with CU severity (Left: $rho = -0.68$, $p = 0.015$). These results suggest that CD youths have microstructural abnormalities in the same network as adults with psychopathy. Further, the association with childhood/adolescent measures of emotional detachment (CU traits) resembles the relationship between emotional detachment and network microstructure in adult psychopaths. However, these changes appear to occur in opposite directions – with increased myelination in adolescent CD but reduced integrity in adult psychopathy. Collectively, these findings suggest that developmental abnormalities in dorsal DMN may play a role in the emergence of psychopathy.

1. Introduction

Psychopathy is characterized by persistent antisocial behaviour and emotional detachment. The most commonly used instrument to measure these traits is the Psychopathy Checklist Revised (PCL-R), which quantifies emotional detachment ('factor 1') and antisocial behaviour ('factor 2') along separate dimensions (Hare, 2003). The underlying cause for psychopathy is most likely complex but there is compelling evidence that adults with psychopathy have differences in brain anatomy and function. For example we, and others, have previously reported that factors 1 and 2 are associated with microstructural abnormalities, consistent with reduced myelination, in a dorsal component of the default-mode network (DMN) (Sethi et al., 2015) and an amygdala–orbitofrontal limbic network (Craig et al., 2009; Motzkin et al., 2011; Passamonti et al., 2012) respectively. The dorsal DMN is of particular interest in the development of psychopathy due to the functions associated with it. Specifically, whilst the ventral component of the DMN (connecting the medial temporal lobe and posterior cingulate cortex (PCC)) is linked to autobiographical memory and spatial orientation (Catani and Thiebault de Schotten, 2012), the dorsal DMN, and the regions it connects (the medial prefrontal cortex and PCC), underpin affective (Kiehl et al., 2001; Maddock et al., 2003), social (Buckner et al., 2008; Völlm et al., 2006) and moral (Greene et al., 2001; Harrison et al., 2008) processing. In adult psychopathy,

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* Corresponding author at: Natbrainlab, Department of Forensic & Neurodevelopmental Sciences, Institute of Psychiatry, Psychology & Neuroscience, King's College London, SE5 8A, UK.
E-mail address: arjun.sethi@kcl.ac.uk (A. Sethi).

[1] Joint authorship.

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microstructural abnormalities within the dorsal DMN are linked to the affective and interpersonal differences that define the disorder (Sethi et al., 2015). However, the aetiology of these differences remains unclear.

Contemporary views suggest that adult psychopathy is the endpoint of a heritable neurodevelopmental disorder with its origins in early childhood (Frick and Viding, 2009). Indeed studies report that children with psychopathic traits display behavioural and neurocognitive differences that are similar to those found in adult psychopaths (Blair, 2013; Viding and McCrory, 2015). These psychopathic traits can be assessed using the Antisocial Process Screening Device (APSD; Frick and Hare, 2001), where emotional detachment is captured by the quantitative measurement of callous and unemotional (CU) traits. Importantly, interpersonal callousness and psychopathy measures in adolescence appear to predict adult psychopathy even when controlling for severity of adolescent antisocial behaviour (Burke et al., 2007; Lynam et al., 2007). Understanding whether dorsal DMN abnormalities previously described in adults with psychopathy are also related to CD and CU traits in childhood is therefore critical to characterising the developmental basis of the disorder.

Initial findings suggest this network may indeed be important for the development of psychopathy. Firstly, a recent twin study using the same tractography methods as our prior work (Sethi et al., 2015) revealed that the microstructure of the dorsal cingulum had moderate to high heritability, whilst the microstructure of the ventral cingulum was mostly determined by environmental factors (Budisavljevic et al., 2016). This indicates that the differences associated with this network appear to be heritable, and may reflect a basis for the heritability of psychopathy. This is further supported by findings that show that the grey matter of the PCC – which is one of the contributing nodes of the dorsal DMN – confers the heritability of CU traits (Rijsdijk et al., 2010). Secondly, recent studies have shown reduced functional connectivity within the DMN in CD (Broulidakis et al., 2016; Zhou et al., 2016). However, whether these changes reflect an underlying structural network deficit in those at risk of developing psychopathy has yet to be determined.

Therefore, in the current study we performed DTI tractography of the dorsal and ventral cingulum in 27 youths with conduct disorder (CD), 14 with and 13 without CU traits, as determined by DSM-V (Frick and Moffitt, 2010; Kahn et al., 2012), and 16 age and IQ matched typically developing controls. We hypothesised that, compared to controls, children with CD would have microstructural abnormalities in the DMN consistent with reduced myelination. Further, these abnormalities would be most severe in individuals with heightened levels of CU traits.

2. Methods

2.1. Participants

Twenty-seven right-handed male participants (aged 12–17) with CD were recruited from an Institute of Psychiatry database, Youth Offending Teams, Pupil Referral Units, youth projects and mainstream educational institutions as described in (Sarkar et al., 2013). These included 14 with, and 13 without, clinically significant CU traits. Sixteen right-handed controls from the same age range and inner city areas were also recruited through schools and youth services. Age, full scale IQ (FSIQ), ethnicity, substance use history, and ADHD diagnosis or hyperactive symptomatology did not differ significantly between groups, with two control, one CD-CU and one CD + CU youths having a prior diagnosis of ADHD. Aside from ADHD and CD, both cases and controls were medication free and neither group suffered from any other mental health problems. All participants fulfilled MRI safety criteria, spoke English as their first language, and had a FSIQ of 80–120. Participants gave full informed consent, with additional consent gained from parents/guardians when aged < 16. This study was approved by the Joint South London and Maudsley Research Ethics Committee (243/00).

2.2. Questionnaires

Parent and self-report versions of the Strengths and Difficulties Questionnaire (SDQ; (Goodman, 1997)) were used to obtain measures of conduct problems and hyperactivity, and parent and self-report measures of the Antisocial Process Screening Device (APSD; (Frick and Hare, 2001)) were used to obtain measures of CU traits. Accepted subscales for both measures comprised the highest raters' items (Jones et al., 2009; Sarkar et al., 2013). Postal versions of parental measures were used when parents did not accompany older participants. IQ was measured with the Wechsler Abbreviated Scale of Intelligence (WASI; (Wechsler, 1999)), and handedness by the Edinburgh Handedness Inventory (Oldfield, 1971).

2.3. Interviews and research diagnoses

Research diagnoses of CD were obtained using the CD and oppositional defiant disorder (ODD) subsections of the Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime Version (K-SADS-PL; (Kaufman et al., 1997)). Screening interviews were given to all participants, with those meeting CD or ODD criteria given complete interviews for both disorders. No participants met the criteria for ODD in the absence of CD. Interviews were conducted by a research psychologist (SS) and supervised by a psychiatrist (QD). Further information about antisocial behaviour was gained from teachers, social workers, parents and youth club workers. The CD group contained boys who had histories of serious, violent antisocial behaviour, including grievous bodily harm, sexual assault, robbery and burglary.

Research diagnosis of CD + CU was determined using proposed DSM specifier questions of the APSD (Frick and Moffitt, 2010; Kahn et al., 2012). These questions consist of four (lack of remorse or guilt, lack of empathy, unconcerned about performance, and shallow or deficient affect) of six questions from the callous-unemotional trait scale of the APSD. As recommended, answers of 'Definitely True' to at least two of these questions was taken as sufficient specification for the presence of callous-unemotional traits (Frick and Moffitt, 2010; Kahn et al., 2012).

2.4. Diffusion MRI acquisition

Diffusion MRI data were acquired using a GE Signa HDx 3.0T MR scanner (General Electric, USA), with actively shielded gradients (max amplitude 40 mT/m). The body coil was used for RF transmission, and eight-channel headcoil for signal reception, with a parallel imaging (Array Spatial Sensitivity Encoding Technique; ASSET) speed up factor of two. Head movement was minimised with extra padding, and a cardiac gated acquisition was used to minimise pulsatile cardiac artefacts in the parenchyma. Data were acquired using a multi-slice doubly refocused spin-echo echo planar imaging (EPI) sequence, optimised for parenchymal diffusion tensor measurement. Each volume consisted of 60 contiguous near-axial slices with a voxel size of $1.85 \times 1.85 \times 2.4$ mm. TE was 104.5 ms with a TR varying between 12 and 20 RR intervals. Thirty-two diffusion weighted volumes were acquired with gradient directions distributed uniformly in space and a maximum B-value of 1,300 mm^2/s, as well as four volumes with no diffusion weighting (Jones et al., 2002). The scanning sequence lasted approximately 15 min.

2.5. Diffusion MRI data processing

Data underwent extensive quality control checks, with all B0 and diffusion weighted volumes visually inspected for image corruption, motion artefacts and signal drop out. Datasets with more than two motion artefacts in different volumes on the same slice were removed