

CALLOUS-UNEMOTIONAL TRAITS AND EMOTION PROCESSING IN  
TYPICALLY DEVELOPING YOUTHS

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## ABSTRACT

The aim of this thesis was to investigate whether callous unemotional (CU) traits in typically developing children and adolescents show similar associations with behavioural and neural responses as seen in clinical and forensic populations. Three investigations, presented in Chapters 3-5, focussed on the behavioural and neural correlates of emotion recognition and processing. An exploration of the behavioural recognition of the six basic emotions (happiness, sadness, fear, anger, disgust, and surprise) indicated negative correlations between levels of CU traits and accurate recognition of sadness and disgust (Chapter 3). Based on an examination of neural correlates of emotion recognition during a subliminal emotion processing task, which included angry and fearful faces, it was concluded that activation levels in the bilateral amygdala and insula during fear processing, but not anger processing, were negatively correlated with CU traits (Chapter 4). Finally, based on an investigation of the structural integrity in the bilateral uncinate fasciculus (UF), which is a white matter tract reported to be relevant in psychopathy, it was concluded that fractional anisotropy in the right UF was negatively associated with CU traits, but only in youths aged 16-18 years (Chapter 5). These investigations produced novel findings and advanced the understanding of the dimensional nature of CU traits in typically developing youths.

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## LIST OF ABBREVIATIONS

AB	Antisocial Behaviour
ACC	Anterior Cingulate Cortex
ASPD	Antisocial Personality Disorder
CBCL	Child Behaviour Checklist
CD	Conduct Disorder
CU	Callous-Unemotional (traits)
DTI	Diffusion Tensor Imaging
FA	Fractional Anisotropy
fMRI	Functional Magnetic Resonance Imaging
ICU	Inventory of Callous-Unemotional Traits
K-SADS	Kiddie Schedule of Affective Disorders and Schizophrenia for School Age Children
OFC	Orbitofrontal Cortex
PCL-R	Psychopathy Checklist Revised
RT	Reaction Time
TD	Typically Developing
TE	Echo Time
TR	Repetition Time
UF	Uncinate Fasciculus
WASI	Wechsler Abbreviated Scales of Intelligence



# CHAPTER 1: CALLOUS-UNEMOTIONAL TRAITS IN ADULTS AND YOUTHS WITH AND WITHOUT ANTISOCIAL BEHAVIOUR

## 1.1 Introduction

The aim of this thesis was to investigate the association between callous-unemotional (CU) traits, emotion recognition and functional and structural neuroimaging indices within emotional circuits in typically developing youths without antisocial behaviour (AB). CU traits encompass restricted empathy, shallow affect and using others for one's own gain (Frick & White, 2008). CU traits are closely related to the primary, or interpersonal-affective, factor of psychopathy. High levels of CU traits in childhood are associated with antisocial personality disorder (ASPD) in adulthood, even after controlling for childhood AB and other risk factors (Burke, Loeber, & Birmaher, 2002; Lynam et al., 2007). This chapter introduces the concepts of psychopathy and CU traits, and explores these constructs within individuals with clinically recognised AB and in the non-clinical population.

In this thesis, individuals with AB will include forensic, clinical or incarcerated populations who have committed violent, delinquent and/or antisocial acts. This includes those who have a diagnosis of ASPD, conduct disorder (CD) or conduct problems. The chapter starts with a description of the historical journey of research into psychopathy, including the definitions of relevant terms (Section 1.1.2) and a detailed description of the diagnostic tools (Section 1.2). Findings related to neurocognitive structures and functions of emotional processing in the above adult and youth clinical populations are then reviewed (Section 1.5). The

concept of dimensionality in mental health research (Section 1.6) is then introduced, which provides a rationale for examining the correlates of CU traits in a non-clinical sample. Relevant neurocognitive literature of emotional processing in non-clinical samples is then reviewed (Section 1.7). Finally, the empirical work presented in this thesis is outlined in brief (Section 1.8).

### **1.1.1 History & Prevalence**

Individuals who show callous, unremorseful and manipulative traits were recognised in Ancient Greece as ‘The Unscrupulous’ (Millon & Simonsen, 1998), 1998) and have been documented throughout history and cross culturally (Kiehl & Hoffman, 2011). Hervey Cleckley, considered the modern father of psychopathy, states that “*[the psychopath’s] outer functional aspect masks or disguises something quite different within, concealing behind a perfect mimicry of normal emotion, fine intelligence, and social responsibility, a grossly disabled and irresponsible personality.*” (Cleckley, 1941, p. 385).

Coid, Yang, Ullrich, Roberts and Hare (2009) found the prevalence of psychopathy to be 0.6% in 638 individuals who were selected from a larger sample completing a survey of private households in Great Britain. Participants’ psychopathy scores were higher in males and positively correlated with number of suicide attempts and violent behaviour. The majority of the general adult population (71%) has no evidence of psychopathic traits, whilst a significant proportion has minimal traits (28%) and a small proportion (<1%) meet diagnostic criteria for psychopathy (Coid et al., 2009). A clinical diagnosis of psychopathy is twice as common as bipolar disorder, schizophrenia or anorexia, and approximately as common as

bulimia, panic disorder and obsessive-compulsive personality disorder (American Psychiatric Association, 2013).

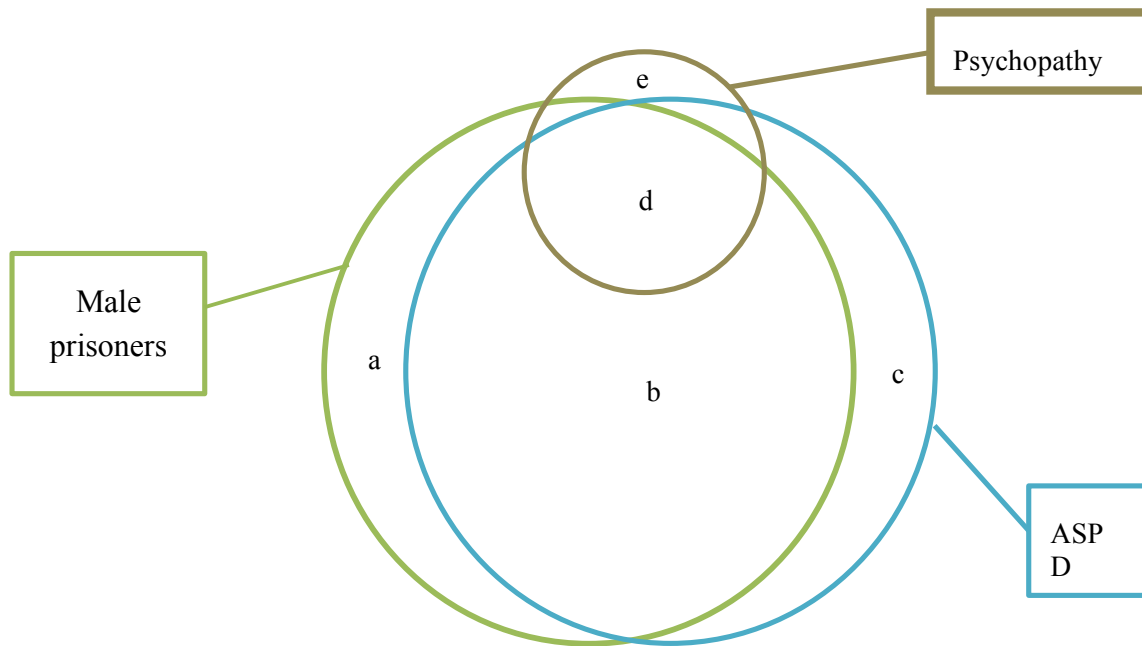
### ***1.1.2 Defining psychopathy and antisocial personality disorder***

It is important to note that ASPD and psychopathy are not interchangeable. As visualized on Figure 1.1, a person can have ASPD without psychopathy, or psychopathy without ASPD. Whilst the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013) recognises ASPD as a personality disorder, psychopathy is not included in the manual, but is instead measured using the Psychopathy Checklist-Revised (PCL-R; Hare, 2003). Since prevalence rates for psychopathy are higher in incarcerated individuals (between 15-25%; Hare, 1996), psychopathy was initially recognised and studied in adults with AB. Incarcerated adults with psychopathy show a more acute pattern of AB than those without psychopathy (Walsh & Walsh, 2006).

Individuals with ASPD are callous, recalcitrant and derisive of others' rights and feelings (De Brito & Hodgins, 2009). They often feel that others are beneath them, tend to show off and appear arrogant. The DSM-5 identifies ASPD as a life-long pattern of AB, including a failure to conform to social norms with respect to lawful behaviour, impulsivity, repeated aggressive behaviour and fights, reckless disregard for safety and a lack of remorse (American Psychiatric Association, 2013). As this polythetic diagnosis focuses mainly on behavioural characteristics, this means that individuals with ASPD are highly heterogeneous (Lykken, 1995); in fact, there are 848 ways in which one can meet criteria for ASPD (Widiger & Trull, 1994), and approximately 2% of the general population is estimated to have ASPD

(American Psychiatric Association, 2013). Comparatively, psychopathy is characterised by a constellation of interpersonal, affective, lifestyle and behavioural features (see Table 1.1; Hare, 2003). Psychopaths seem to lack emotion and are poor at perceiving it in others (Cleckley, 1941).

It is debated whether ASPD and psychopathy reflect comparable or fundamentally dissimilar constructs (Lilienfeld, 1998). The original classification of ASPD in the DSM-I and II described a syndrome corresponding to psychopathy (Patrick, 2007). As the DSM has been developed over time, the DSM diagnostic criteria have moved from describing prototypical descriptions of the disorder to explicit, behaviour-oriented criteria (Patrick, 2007). Thus, it is now understood that ASPD and psychopathy reflect distinct, but overlapping, constructs. As ASPD is highly heterogeneous, an additional diagnosis of psychopathy identifies a more homogenous subgroup within ASPD. The relationship between psychopathy, ASPD and incarceration in males is represented pictorially in Figure 1.1. It can be seen in this figure that one can have psychopathy without ASPD, or ASPD without psychopathy, but they commonly co-occur. It is important to note that psychopathy is not synonymous with criminality; some psychopathic individuals violate society's normative rules, yet avoid conviction (Hare, 1999).



*Figure 1.1. (adapted from Patrick, 2007). Rates of ASPD, psychopathy and incarceration and the relationship between them. The left circle (yellow) represents the male prison population, whilst the right circle (red) represents individuals diagnosed with ASPD and the grey circle (smallest) represents those with psychopathy. a) represents prisoners who do not have APSD; b) represents prisoners with ASPD; c) represents non-incarcerated individuals with ASPD but without psychopathy; d) represents prisoners with ASPD and psychopathy; e) represents non-incarcerated individuals with psychopathy but without ASPD.*

The definition of psychopathy most used in research, and used in this thesis, is operationalised using the Psychopathy Checklist - Revised (PCL-R; Hare, 2003). Those who score  $\geq 30$  in North America or  $\geq 25$  in Europe on the PCL-R are considered psychopaths. It is important to note that psychopathy does not exist purely within the construct of ASPD, but can be recognised in otherwise non-criminal individuals. Whilst psychopathy is more prevalent in those with ASPD

(approximately 32% prevalence; Coid & Ullrich, 2010), it is also recognised in the healthy population (0.6% prevalence, (Coid & Ullrich, 2010).

The PCL-R (see Table 1.1 for items) can be considered a unidimensional construct that is made up of two correlated factors (Hare, 2003). The primary factor indexes the interpersonal-affective aspects of psychopathy and includes flat affect, grandiosity and lack of guilt. The secondary factor taps the social deviance component of psychopathy and includes aggression and violence (Frick, O'Brien, Wootton, & McBurnett, 1994; Livesley, 1998). Whilst high scores on the secondary factor are closely associated with ASPD, scores on the primary factor are not closely related to this disorder, despite a high correlation between factors (Frick et al., 1994). This thesis will include research that has differentiated between the two factors within individuals, although it should be noted that Karpman (1948) postulated that these factors are distinct across individuals. Karpman states that both primary and secondary psychopaths show irresponsible, antisocial and hostile behaviour with no apparent regard for others. However, the two variants differ on the etiology and motivation behind their behaviours; whilst primary psychopaths were born with these tendencies, secondary psychopaths were developed as a conditioned adaptation to harsh factors such as lack of parental warmth and severe punishment.

Recently the PCL-R has been revised as a four facets model, comprising of Interpersonal (Facet 1), Affective (Facet 2), Lifestyle (Facet 3), and Antisocial (Facet 4) facets. The PCL-R is administered by a trained rater using a semi-structured interview and supplementary information. Each of the 20 items are

scored on a three-point scale (0 –2) according to the extent to which it applies to the individual (0 = not at all, 1 = somewhat applies, 2 = applies very well), with a maximum score of 40.

Psychopathy shares similar characteristics with alexithymia with regard to emotional processing deficits. Alexithymia is a clinical disorder where individuals show difficulty identifying and describing their own emotions (Taylor, Bagby, & Parker, 1992) and empathising with others' feelings (Guttman & Laporte, 2002). Deficits in emotion processing, such as difficulties interpreting facial expressions (Dolan & Fullam, 2006) and understanding emotional vocal tones (Herve, Hayes, & Hare, 2003) are seen in both psychopathy and alexithymia. Whilst it seems that alexithymia would have a conceptual overlap with primary psychopathy, recent research with 104 college students found that alexithymia is positively associated to secondary, and not primary psychopathy (Lander, Lutz-Zois, Rye & Goodnight, 2012). This provides additional support for the conceptual difference between primary and secondary psychopathy, and also suggests that primary and secondary psychopathy show different associations with emotion recognition. A further study found that, in a community sample of adults, negative associations between psychopathic traits, alexithymic traits and performance on an empathy task were independent of each other (Lockwood, Bird, Bridge & Viding, 2013). Thus, it is likely that psychopathic traits and alexithymia achieve equifinality, where the same outcome (i.e. poor empathy) is achieved through different mechanisms.

*Table 1.1. Psychopathy Checklist-Revised items*

<b>Factors</b>	<b>Criteria</b>
Primary psychopathy	<ol style="list-style-type: none"> <li>1. Glibness/superficial charm</li> <li>2. Grandiose sense of self-worth</li> <li>3. Pathological lying</li> <li>4. Cunning/manipulative</li> <li>5. Lack of remorse or guilt</li> <li>6. Emotionally shallow</li> <li>7. Callous/lack of empathy</li> <li>8. Failure to accept responsibility for own actions</li> </ol>
Secondary psychopathy	<ol style="list-style-type: none"> <li>9. Need for stimulation/proneness to boredom</li> <li>10. Parasitic lifestyle</li> <li>11. Lack of realistic, long-term goals</li> <li>12. Impulsivity</li> <li>13. Irresponsibility</li> <li>14. Poor behavioural controls</li> <li>15. Early behavioural problems</li> <li>16. Juvenile delinquency</li> <li>17. Revocation of conditional release</li> <li>18. Criminal versatility</li> </ol>
Other items	<ol style="list-style-type: none"> <li>19. Many short-term marital relationships</li> <li>20. Promiscuous sexual behaviour</li> </ol>

### ***1.1.3 Bridging the gap between psychopathy in adults and CU traits in youths***

Like all personality disorders, psychopathy can only be diagnosed in those over the age of 18 years (American Psychiatric Association, 2013). However, there is overwhelming evidence that psychopathic traits do not spontaneously appear in adulthood but develops from childhood (Caspi, Roberts, & Shiner, 2005; Frick &



Viding, 2009; Lynam, Caspi, Moffitt, Loeber, & Stouthamer-Loeber, 2007).

Extending the construct of psychopathy to encompass children and adolescents might aid in the development of causal models for AB in youths (Frick, Marsee, & Patrick, 2006). A PCL-R version designed specifically to assess psychopathic traits in youths (PCL-YV) is described later in this chapter.

Whilst there are many similarities in characteristics between adult psychopaths and youths with AB and high levels of CU (HCU) traits, it is important to note that CU traits in childhood and psychopathy in adulthood are by no means synonymous. The term “*callous-unemotional traits*” was coined in order to avoid the stigma associated with the term “psychopath” (Blair, Leibenluft, & Pine, 2014). Psychopathy in adulthood encompasses two strands; a primary, interpersonal-affective factor and a secondary, antisocial behaviour factor. In contrast, CU traits are only equivalent to primary psychopathy. Thus, psychopathic traits in adults are distinguished from CU traits in children and considering both populations together is not appropriate in this literature review (Dawel, O’Kearney, McKone, & Palermo, 2012).

In line with this, some researchers have criticized the extension of the psychopathy construct to youths (Blair, 1999; Seagrave & Grisso, 2002). For example, PCL-R items including ‘parasitic lifestyle’ and ‘short-term marital relationships’ cannot be validly applied to a juvenile population due to limited work and relationship experiences (Edens, Skeem, Cruise, & Cauffman, 2001).

Despite the concerns that have been expressed regarding this downward extension, many studies have shown that youths with AB/HCU traits are at higher

risk of developing personality disorders in adulthood (Hill, 2003; Robins, 1966). High CU traits are associated with heritable AB, whilst low CU traits are associated with environmentally induced AB; Viding, Jones, Paul, Moffitt and Plomin (2008) showed that, when hyperactivity symptoms were controlled for, genetic factors accounted for 71% of the variance associated with AB in 9-year-old twins exhibiting AB with high CU traits (AB/HCU), but only 36% of the variance in those with AB and low CU traits (AB/LCU). Furthermore, youths with AB/HCU traits show more severe and persistent AB than youths with AB/LCU traits (Fontaine, McCrory, Boivin, Moffitt, & Viding, 2011). Thus, measuring CU traits in youths has significant clinical utility (American Psychiatric Association, 2013), as the traits could be considered a risk factor for psychopathy and ASPD in adulthood.

There has been growing interest in the behavioural and neural correlates of CU traits in typically developing children because recent evidence indicates that some youths present with HCU traits whilst not exhibiting AB (Fontaine et al., 2011; Rowe et al., 2010). In these studies, youths with HCU traits but without AB presented with subclinical levels of AB and “disturbed functioning”. Thus, CU traits may be a useful clinical indicator of mental vulnerability and maladjustment, in addition to their function of subtyping children with AB.

#### ***1.1.4 CU traits in youths with AB and Conduct Disorder***

CU traits are included as a specifier, called *limited prosocial emotions*, within the CD diagnosis in the DSM-5 (American Psychiatric Association, 2013). CD is a behavioural disorder recognised by the DSM since 1968 (American Psychiatric

Association, 1968; referred to as Socialised Aggressive Reaction of Childhood prior to 1991) and can only be diagnosed in those under 18 years old. One needs to have a childhood diagnosis of CD in order to gain a diagnosis of ASPD in adulthood (American Psychiatric Association, 2013). This section explains the primary diagnostic features of CD, then two fictional vignettes describing children with CD and different levels of CU traits are presented. These fictional vignettes were constructed based on the many interviews carried out with youths presenting CD as part of data collection for the FemNAT-CD consortium. The behavioural characteristics of youths with CD with high and low levels of CU traits are reviewed and measures of psychopathic traits and CU traits in children are then explored.

#### ***1.1.4.1 Conduct Disorder***

Whilst ASPD can only be diagnosed in adults, a similar condition called conduct disorder (CD) can only be diagnosed in those under the age of 18. The primary diagnostic features of CD involve a repetitive pattern of severe externalising behaviours, including aggression, deceitfulness and serious violations of rules. To receive a diagnosis of CD, a child must present with three out of 15 symptoms (see Table 1.2) within the past 12 months, with one symptom present within the past six months (American Psychiatric Association, 2013). CD has a prevalence of approximately 5.8% in the UK (Green, McGinnity, Meltzer, Ford, & Goodman, 2005) and 9.5% in the US (Nock, Kazdin, & Hiripi, 2006). Rates of CD are twice as high in males as in females (Maughan, Rowe, & Messer, 2004). Children with CD are often impulsive and regularly show contemptuous and insolent attitudes towards figures of authority, including parents, teachers and police (Loeber, Burke, Lahey, &

Winters, 2000). A diagnosis is made when the disturbance in behaviour causes clinically significant impairment in social, familial, academic, or occupational functioning.

*Table 1.2. DSM-5 Conduct Disorder Diagnostic Criteria*

<b>Symptoms</b>	<b>Criteria</b>
Aggression to People and Animals	1. Often bullies, threatens or intimidates others 2. Initiates physical fights 3. Has used a weapon to cause serious harm to others 4. Has been physically cruel to people 5. Has been physically cruel to animals 6. Has stolen whilst confronting a victim 7. Has forced someone into sexual activity
Destruction of Property	8. Has engaged in fire setting with intention to damage 9. Has deliberately destroyed property (other than fire setting)
Deceitfulness or Theft	10. Has broken into a house, car or building 11. Lies to obtain goods or avoid obligations 12. Has stolen items of non-trivial value without confronting a victim (shoplifting, forgery)
Serious Violation of Rules	13. Stays out at night despite parental prohibitions, beginning before 13 years 14. Has run away from home overnight at least twice, or once having stayed away for a lengthy period of time 15. Often truants from school, beginning before 13 years

## **1.2 Measures of psychopathic and CU traits in youths**

When measuring CU traits, it must be certain that scores are based on the child's characteristic way of relating to others and expressing emotion. The DSM-5 provides clear guidelines to determine whether a child has limited prosocial emotions (i.e. CU traits). These include at least two of the following symptoms: lack of remorse/guilt; callous-lack of empathy; lack of concern about performance; shallow or deficient affect. These symptoms must present for at least 12 months and in multiple relationships/settings. Furthermore, these characteristics must reflect the child's usual manner of interpersonal and emotional functioning, and multiple sources should be considered (American Psychiatric Association, 2013).

CU traits can be measured using a variety of questionnaires, which are described below. All of these measures are designed for youths. Unlike the PCL-R, there are no agreed cut off scores for any of these measures (although some measures have suggested cut off scores based on empirical research).

### ***1.2.1 Hare Psychopathy Checklist: Youth Version***

The Hare Psychopathy Checklist: Youth Version (PCL:YV; Forth, Kosson & Hare, 2003) is adapted for youths from the Hare Psychopathy Checklist-Revised (PCL-R; see Section 1.1.2), which is the most widely used measure of psychopathy in adults. The PCL:YV is aimed at youths aged between 12-18 years old. It is administered by a trained clinician, using a semi-structured interview (lasting between 60-90 minutes) and supplementary information. The clinician rates items on a scale of 0 to 2 indicating whether or not the statement is true. Like the PCL-R,

the PCL:YV can also be considered as a four facets model, comprising of Interpersonal (Facet 1), Affective (Facet 2), Lifestyle (Facet 3), and Antisocial (Facet 4) facets.

### **1.2.2 *Youth Psychopathy Index***

The Youth Psychopathy Index (YPI; Andershed, Kerr, Stattin, & Levander, 2002) uses a four point Likert scale (from 'Does not apply to me well' to 'Applies to me very well') to measure CU traits in youths. It is designed for youths aged 12-18 years old. Parent, teacher and self-report versions are available for this measure. The YPI assesses ten core psychopathy traits through ten subscales (five items each) structured in three factors (Grandiose Manipulative Dimension; Callous-Unemotional Dimension and Impulsive Irresponsible Dimension). Scores on the YPI range from 50 – 200, and Skeem and Cauffman (2003) found that 125 was the optimum cut off in terms of convergent validity with other measures of juvenile psychopathy such as the PCL-YV.

### **1.2.3 *Clinical Assessment of Prosocial Emotions***

The Clinical Assessment of Prosocial Emotions (CAPE; Frick, 2013) is a clinical assessment for youths aged 3 to 21 years, and items are based on the definition of CU traits used by the ICU (Inventory of Callous-Unemotional Traits; Frick, 2003). This measure allows the clinician to obtain richer information than when using the ICU and assists in making diagnostic decisions based on the DSM-5 criteria. The CAPE is designed for input from at least two informants, be that the child himself, a parent and/or a teacher. The rater collects information from multiple sources in

order to decide how well the participant matches the item description from a 0 (Not Descriptive) to 2 (Highly Descriptive) scale.

#### **1.2.4 Antisocial Process Screening Device**

The Antisocial Process Screening Device (APSD; Frick & Hare, 2001) is a downward extension of the PCL-R, and was developed to screen for psychopathy and AB in children aged 6 – 13 years old. It was originally titled the “*Psychopathy Screening Device*”, but the authors altered the name after concerns about using the word psychopathy in regards to children. Versions include self-report, parent- and teacher-rated varieties (a combined score can be derived from more than one informant) on a dimensional scale that examines interpersonal, affective and behavioural symptoms associated with psychopathy. The 20 items on the APSD are scored from 0 (not at all true) to 2 (definitely true). The measure is thought to encompass three clusters of psychopathic symptoms: callous–unemotional traits (“good at keeping promises” (*reverse scored*); six items), narcissism (“Braggs about abilities”; seven items) and impulsivity (“Does not plan ahead”; five items).

#### **1.2.5 Inventory of Callous-Unemotional Traits**

The ICU (Frick, 2003) is based on the CU subscale of the Antisocial Process Screening Device (Frick & Hare, 2001) and consists of 24 items that consider multiple aspects of the affective features of psychopathy. It is designed for youths aged 13-17 years old. Items are rated by either a parent/main caregiver, a teacher or by the youth themselves on a four point Likert scale from 0 (not at all true) to 3 (definitely true). This questionnaire has three subscales: Callousness; Uncaring and Unemotional. Examples from each subscale include, respectively: “*Does not*

*care who he/she hurts to get what he/she wants”; “Tries not to hurt others’ feelings”; and “Is very expressive and emotional”*. This device is used to measure CU traits in each of the following experimental chapters, and is explored in more detail in Chapter 2.

### **1.2.6 Vignettes of CU traits**

#### ***Aidan***

Aidan is 14 years old and lives with his mother and two younger siblings in a council house. His mother is very fond of animals, and they have two dogs and six cats in their three bed home. Aidan’s Mum is on disability benefits as she has agoraphobia and rarely leaves the house. Aidan goes out every night after school, staying out as late as he likes; he has no curfew. If he is in the house, he often fights with his younger brothers and is slapped or yelled at by his Mum. He will sometimes lose his temper and insult his Mum, but he feels bad afterwards and apologises. His Mum says that he is, on the whole, a good boy who means well. Aidan does not do well at school; he often truants lessons or whole days and struggles to understand his work. He is obstreperous in lessons and will punch and kick other boys if they annoy him. He spends a lot of time outside school with close friends, and they graffiti, vandalise and break public property. They once started a fire in the woods, but panicked and put it out when passersby smelled smoke and raised the alarm.

#### ***Amber***

Amber is 14 years old and lives with her parents and older brother in a high rise flat. Her Dad has been in and out of prison throughout Amber’s life, but Amber’s



Mum has a steady job as a shop assistant. They do not have much money because Amber's parents tend to make impulsive purchases. They have a state of the art fridge and television, bought on credit, but struggle to keep up repayments. As a small child Amber preferred to play alone, making up complex imaginary games for herself. When she included others, it was only as accessories. She dislikes joining in with others' games and prefers to be in charge. Amber will take money from other students to buy things and often manipulates others to get her own way. She doesn't have any close friends, but is charming when you first meet her. She will stir up others' emotions and encourage them to fight, but rarely fights herself. Amber is an excellent liar, and her Mum says she never knows what is true and what is false. If her family upset her, she will take revenge, usually breaking their possessions and making it seem like an accident. She rarely feels guilty for her actions.

Whilst both children receive a diagnosis of CD, only Amber would receive the additional specifier of CU traits, due to her callous, manipulative nature. Whilst Aidan has close friends and feels guilty when he insults his Mum, Amber only gets close to people when she can gain from it, for example inducing them to fight with someone she doesn't like.

### **1.3 Suppressor Effects**

CU traits and AB are positively correlated in youths (Pardini, 2006), but these variables have demonstrated contradictory associations with behavioural and neurobiological measures (Crowe & Blair, 2008; Frick, 2012). Thus, AB may act as suppressor for the relationship between CU traits and atypical emotional

processing. The following section explores recent research which has investigated the unique variances associated with CU traits and AB, showing that each variable is associated with behavioural and neuroimaging indices of emotional processing in different ways.

A secondary objective of this thesis was to explore suppressor effects between CU traits and externalising behaviours. Suppression occurs when two interrelated variables have contrasting relationships with the dependent variable; hence including both interrelated variables in a regression increases the strength of the association of each variable with the criterion (Watson, Clark, Chmielewski, & Kotov, 2013). The presence of these suppressor effects indicates that unique aspects of each dimension are associated with distinct variations. Suppressor effects have consistently been observed between conduct problems and CU traits in clinical populations of adolescents (Lozier et al., 2014; Viding et al., 2012), and between externalising behaviours and psychopathic traits in healthy adults (Seara-Cardoso et al., 2012; Seara-Cardoso, Viding, et al., 2015; Vanman, Mejia, Dawson, Schell, & Raine, 2003). However, it is unclear if AB may act as suppressor for the relationship between CU traits and atypical emotional processing in typically developing youths. It is pertinent to differentiate between the individual influences of these constructs on emotion processing, as this allows studies to capture critical distinctions among subpopulations.

Extending these behavioural findings, CU traits were associated with *diminished* startle potentiation when viewing violent films, whereas aggressive tendencies (i.e. AB) were associated with *increased* startle potentiation in a sample of young adults

from the community (Fanti, Kimonis, Hadjicharalambous, & Steinberg, 2016).

Furthermore, a number of recent fMRI studies in adults and youths have identified suppressor effects between AB and CU traits (Hyde, Byrd, Votruba-Drzal, Hariri, & Manuck, 2014; Lockwood, Sebastian, et al., 2013; Lozier, Cardinale, Van Meter, & Marsh, 2014; Seara-Cardoso, Viding, Lickley, & Sebastian, 2015; Sebastian, McCrory, et al., 2012). Seara-Cardoso et al. (2015) found that after controlling for AB, higher CU traits were related to *reduced* neural responsivity to others' pain, whilst higher AB traits were associated with *increased* neural responsivity to others' pain, in the insula, inferior frontal gyrus and midcingulate cortex when controlling for CU traits.

Similarly, Lozier et al. (2014) found that amygdala responses to fearful faces were negatively correlated with CU traits and positively correlated with AB when both variables were modelled simultaneously in youths with AB. In a similar vein, CU traits were negatively correlated with fear conditioning response in the anterior cingulate cortex (ACC), while the impulsive/irresponsible factor of the YPI was positively correlated with brain response in the ACC in a sample of youths with AB who had all been arrested before the age of 12 (Cohn et al., 2013).

In sum, these results suggest that AB and CU traits have inverse relationships with behavioural expression and neural activity. Whereas CU traits were associated with reduced negative feelings and reduced activity in emotion processing areas during viewing of emotional stimuli, AB was associated with experiencing negative emotions and increased neural activity in emotion processing structures. Thus, it is important to differentiate between the individual influences of these constructs on

emotion processing, as studies which do not may have failed to capture critical distinctions among subpopulations. In this thesis, suppressor effects between CU traits and AB are considered in each experimental chapter.

#### **1.4 Behavioural characteristics of antisocial youths with and without CU traits**

Over the past two decades, extensive research has highlighted the theoretical and clinical importance of distinguishing between youths with AB and high CU traits (AB/HCU) and those with AB and low CU traits (AB/LCU; Frick, Ray, Thornton, & Kahn, 2013). Youths with AB/HCU and AB/LCU show distinct temperamental and affective profiles. An early, stable presentation of AB/HCU traits has been associated with greater levels of aggression (Frick, Cornell, et al., 2003), similar to primary psychopathy. In a sample of high-risk males, HCU traits predicted an increased likelihood of violent and aggressive offending in adulthood, even when controlling for age of onset of CD symptoms (Loeber et al., 2005). Furthermore, compared to youths with AB/LCU traits, those with AB/HCU traits displayed more varied and severe patterns of aggressive behaviours at a young age, analogous to those observed in adult psychopathy (Frick, Cornell, et al., 2003; Frick et al., 2006; Frick, Ray, Thornton, & Kahn, 2014). They were less responsive to others' distress (Blair, Colledge, Murray, & Mitchell, 2001; Blair & Frith, 2000; Blair, 1999) and were impervious to punishment but receptive to reward, consistent with a preference for novel and dangerous activities and impulsive behaviour (Blair, 2013; Frick et al., 2006). It should be noted here that CU traits are often measured

with reference to these behaviours, and therefore one should not assume that these behaviours are caused by CU traits.

HCU traits are associated with lower levels of anxiety and fear, especially when controlling for impulsivity and AB (Frick, Lilienfeld, Ellis, Loney, & Silverthorn, 1999; Lynam & Gudonis, 2005; Pardini & Frick, 2013). By contrast, youths with AB/LCU traits are typically less aggressive, habitually displaying reactive aggression in response to threat (Viding & McCrory, 2012), similar to secondary psychopathy. Furthermore, youths with AB/LCU show heightened levels of anger and impulsivity (Frick et al., 2006, 2014), greater sensitivity to negative stimuli (Viding & McCrory, 2012) and are more receptive to others' distress (Jones, Happé, Gilbert, Burnett, & Viding, 2010) compared to those with HCU traits. To revisit the vignettes described previously, Amber (who has high CU traits) does not become upset if she hurts others, whilst Aidan (who has low CU traits) is apologetic and remorseful.

CU traits are predictive of later aggression, AB and psychopathic tendencies (Frick et al., 2014). Parent and teacher-rated levels of CU traits in 500 seven-year-old males predicted criminal behaviour at 25 years old, despite controlling for CD, Attention Deficit Hyperactivity Disorder and ODD (Byrd, Loeber, & Pardini, 2012). However, it should be noted here that the measures for CU traits were taken from archives and did not include items that adequately measured empathy or shallow affect – both key factors in CU traits.

Children and adolescents with AB/HCU traits may be less responsive to treatment and interventions than those with AB/LCU traits (Hawes & Dadds, 2005), and parental intervention may need to be individualised depending on the level of CU traits shown by the child. A recent systematic review concluded that youths with AB/HCU traits *do* show reductions in both their CU traits and AB after behavioural interventions, however they typically begin with poorer levels of functioning and may end the course with higher levels of AB than those with AB/LCU traits (Wilkinson, Waller, & Viding, 2016). Furthermore, those with HCU traits exhibit more severe and stable AB (Frick, Stickle, Dandreaux, Farrell, & Kimonis, 2005) and are more likely to recidivate violently in a two year period after release from jail (Vincent, Vitacco, Grisso, & Corrado, 2003). Thus, the specifier has proven useful in identifying a particularly severe subgroup of youths with CD. This has significant clinical utility, as these youths are more likely to develop APD in adulthood.

The previous sections have described the history, diagnostic criteria and phenotypes of ASPD in adults and CD in children and adolescents, with particular regard to psychopathy and CU traits respectively. This chapter will now go on to discuss research into how these populations' behaviour and brain activity differs from healthy individuals. As this thesis is focussed on emotion recognition, the upcoming sections concentrate on these research topics.

## **1.5 Experimental and neuroimaging findings regarding face processing in antisocial adults and youths with CU traits**

### ***1.5.1 Face processing and emotion recognition***

Prominent psychopathy researchers believe that an affective impairment is fundamental to psychopathy (Blair, 2005; Patrick, 1994). Facial expressions have specific communicatory functions, conveying vital information about the complex social world to the onlooker (Blair, 2003, 2005). The act of recognising facial expressions enables the detection of others' emotional states and provides cues on how to respond (Grossmann & Johnson, 2007).

Basic emotions (including fear, disgust, anger, happiness, sadness and surprise) can be readily perceived and trigger empathic responses. Blair (1995) formulated the Violence Inhibition Model to explain the impairments seen in psychopathy using a developmental perspective. The Violence Inhibition Model states that children learn (through classical conditioning) that an aversive stimulus, such as an action resulting in harm, is paired with an unconditioned stimulus, such as a facial expression depicting fear/distress. Thus, the fearful face becomes a conditioned stimulus associated with pain. Blair and Coles (2000) posit that children with AB/HCU traits do not take advantage of the classical conditioning process during socialisation, so they do not perceive the fearful face as an aversive stimulus. One recent study found that CU traits in youths with AB are negatively associated with activation in brain regions involved in fear processing (including

the insula, amygdala and ACC; Cohn et al., 2013). This may explain the deficient classical conditioning process in youths with HCU traits.

In comparison, youths with AB/LCU traits may be overly distracted by emotional stimuli. Hodson, Lavie & Viding (2014) found that, during an attention task, youths with AB/LCU traits were more distracted by emotional faces than typically developing youths, whilst there was no difference between youths with AB/HCU traits and TD youths. The authors posited that those with AB/HCU traits were able to filter out irrelevant information whilst those with AB/LCU traits were unable to ignore this information. Thus, attention may be a confounding variable when measuring emotion processing with regard to CU traits.

One important motivation for studying the neural basis of empathy in response to others' emotional cues is to better understand conditions that are characterised by difficulties in empathising with other people. For example, boys with AB/HCU reported feeling less empathy for victims of aggression compared to boys with AB/LCU and typically developing controls (Jones et al., 2010). Blair (1995) postulates that children with HCU traits may not perceive sad and fearful expressions as aversive unconditioned stimuli, and therefore may not learn to avoid committing behaviours that cause others harm. On the other hand, youths may not understand the emotional connotations that sad and fear usually elicit. Thus, Blair theorised that CU traits are associated with specific emotion recognition deficits, unlike alexithymia, which is thought to be a general emotion recognition impairment (Grynberg et al, 2012). The following sections review



behavioural, physiological and neuroimaging studies on face processing and emotion recognition in adults and youths with AB.

### ***1.5.2 Experimental findings in emotion recognition and antisocial behaviour***

#### ***1.5.2.1 Adult literature***

A meta-analysis of 26 studies (n= 1376) concluded that adults and youths with AB/HCU have impaired recognition of emotional facial expressions (Dawel et al., 2012), especially fear, happiness, sadness and surprise. A more recent study found that sexual and violent offenders showed reduced discriminability index for all emotions compared to non-offenders, which was most pronounced for fear in both groups, and disgust in sexual offenders only (Gillespie, Rotshtein, Satherley, Beech, & Mitchell, 2015). One study found that, in non-psychopathic samples, fear recognition was impaired in criminals compared to non-criminals. The same study concluded that, in psychopathic samples, fear recognition did not differ between criminals and non-criminals (Stanković, Nešić, Obrenović, Stojanović, & Milošević, 2015). This suggests that psychopathy, rather than AB, is the key factor in determining fear recognition accuracy.

One study not included in Dawel et al.'s meta-analysis purported that the intensity of the presented emotion may influence the strength of the association between psychopathic traits and emotion recognition accuracy. This study found that psychopathy scores in adult offenders were not associated with impairments in emotion recognition when stimuli were presented at an intensity of 100%, but an inverse correlation was observed when stimuli were presented with an intensity of

60% (Hastings, Tangney, & Stuewig, 2008). This suggests that emotion recognition is impaired in psychopathy when emotions are more difficult to recognise. However, a small number of studies included in Dawel et al.'s meta-analysis (i.e. Glass & Newman, 2006) only included emotions at 100% intensity, and visual inspection of their results suggest similar outcomes to Hastings et al. Thus, it is unclear whether the intensity of the emotion does in fact modulate the relationship between psychopathic traits and emotion recognition.

#### ***1.5.2.2 Youth literature***

A meta-analysis by Marsh and Blair (2008) investigated both youths with AB. Whilst the authors observed deficits in fear, sadness and surprise recognition in these youths as a whole, post-hoc analyses found this relationship was not moderated by level of CU traits. However, this analysis included both forensic and community samples of youths and the measures of AB used in each study were not consistent. A more recent meta-analysis improved on Marsh and Blair's research by including more studies and only those with youths with clinically recognised AB or at risk of developing clinically recognised AB ("at risk" terminology was used by the authors to describe community samples from a school for emotional and behavioural difficulties (Blair et al., 2001) and a holiday program in the US in a highly deprived area (Munoz, 2009). Higher CU traits were associated with poorer recognition of anger, fear and sadness (Dawel et al., 2012), with the strongest deficit in fear recognition. However, it should be noted that one study, which found a positive association between fear recognition and CU traits, could not be included in this analysis as the effect sizes could not be calculated. Had this study

ben included, the overall association between fear recognition and CU traits might have been weaker.

Consistent with these findings, a deficit in fear recognition seems to extend to pre-conscious processing. Sylvers, Brennan and Lilienfeld (2011) investigated the time taken for emotional faces to break through to conscious awareness during a continuous flash suppression task in 88 children. High levels of CU traits were associated with longer lag times for fearful faces, and to a lesser extent, disgusted ones, to break into consciousness. This suggests that activity the subcortical visual pathway, which processes subliminal emotions (Pessoa & Adolphs, 2010) and includes the superior colliculus, pulvinar nucleus in the thalamus and amygdala, may be associated with CU traits.

Vasconcellos, Salvador-Silva, Gauer and Gauer (2014) suggest that the amount of time an emotion is present is relevant; this study found that youths with AB/HCU were significantly worse than those with AB/LCU at recognising fear, but only when the faces were presented for 200ms; there were no differences between groups when the faces were presented for 500ms or 1000ms. This suggests that brief or even subliminal facial recognition may be more susceptible to effects of CU traits in clinical populations than facial emotions which are presented for longer. Whilst it is possible that a greater difference is seen between groups with AB/HCU and AB/LCU in brief presentations of emotions, it should also be considered that most other studies (including, but not limited to, Blair & Coles, 2000; Del Gaizo & Falkenbach, 2008; Leist & Dadds, 2009) entered in Dawel's meta-analysis achieved

significant results with longer periods of presentation in their paradigms. Hence, there is insufficient evidence for this argument.

Deficits in emotion recognition are not limited to expression recognition: reaction time (RT) when processing emotional faces is also influenced by CU traits. In a sample of youths at risk of developing AB (often in trouble at home and school), positive associations were found between CU traits and RT when detecting fearful and disgusted (but not happy) faces (Sylvers et al., 2011); those with higher levels of CU traits were slower to recognise emotions. This slower response may reflect a slower cognitive processing speed, which could support Vasconcellos et al.'s claim that, in comparison to those with LCU traits, youths with HCU traits are poorer at recognising briefly presented emotions.

The impairment for detecting emotional information from facial expressions may extend to other sensory modalities; youths with AB/HCU show impaired recognition of sad (Stevens, Charman, & Blair, 2001) and fearful (Blair, Budhani, Colledge, & Scott, 2005) vocal tones compared to those with AB/LCU. Furthermore, a negative association was found between CU traits and accuracy for labelling "afraid" body postures in adolescent males at risk of developing AB (Munoz, 2009).

In sum, adults and children with AB/HCU traits show deficits in recognising emotions, of which fear recognition is most pronounced, compared to those with AB/LCU. The deficit in fear recognition in those with HCU traits may be associated with a failure to attend to the eyes of attachment figures from a very early age and could lead to cascading errors in the development of empathy and conscience

(Dadds, Jambrak, Pasalich, Hawes, & Brennan, 2011). In support of this, Jones et al. (2010) found that boys with AB/HCU traits presented with dysfunctional affective empathy; these participants reported less fear and empathy for victims of aggression compared to those with LCU traits. Interestingly, Dadds et al. (2006) found that by instructing youths with HCU traits to attend to the eyes when recognising fear, their performance improved. It would be interesting for future research to consider whether this eye gaze training also increases empathy levels in youths without AB but with HCU traits. It would also be noteworthy to assess whether CU traits in typically developing populations are associated with reduced emotion recognition abilities, or whether deficits in emotion recognition are limited to populations with AB. It could be that TD populations have developed compensatory mechanisms to overcome deficits in emotion recognition, such as increased eye gaze.

### ***1.5.3 Functional Magnetic Resonance Imaging evidence***

The reduced emotion recognition accuracy discussed above may reflect anomalous activity in emotion processing circuits in the brain. This section focuses on studies which examined the neural correlates of emotional facial expressions using fMRI in adults with psychopathy and youths with AB/HCU traits. The successful processing of affective visual information is reflected in a functionally and structurally modular system. Two paths may exist to allow either conscious affective processing (via the visual cortex) or subliminal processing (via a subcortical pathway; Pessoa & Adolphs, 2010). The conscious pathway travels from the retina via the lateral geniculate nucleus to the visual cortex and on to the amygdala,

whilst the subcortical pathway passes through the superior colliculus and the pulvinar nucleus (in the thalamus) before reaching the amygdala.

#### ***1.5.3.1 Adult literature***

Many fMRI studies have shown that adults with psychopathy present reduced activation in a network of regions central to emotion processing (Anderson & Kiehl, 2012; Blair, 2010; Koenigs, Baskin-Sommers, Zeier, & Newman, 2011; Seara-Cardoso & Viding, 2015). Most of these show that adults with psychopathy/high levels of psychopathic traits show decreased amygdala activity during emotion processing and emotional learning paradigms. Other regions involved in affective behaviours, including the orbitofrontal cortex (OFC) and ventromedial prefrontal cortex (vmPFC), are also reportedly less active in incarcerated adult males scoring high on the PCL-R compared to those with low PCL-R scores.

Participants with high levels of psychopathy showed reduced activity in the inferior occipital gyrus, fusiform gyrus, superior temporal sulcus, inferior frontal gyrus and OFC when they viewed dynamic facial expressions of fear, sadness, happiness and pain (Decety, Skelly, Yoder, & Kiehl, 2014). The authors postulated that this may reflect a pervasive emotion processing deficit across facial emotions in antisocial individuals with psychopathy, although the debate as to whether emotion processing deficits are pervasive or specific to certain emotions is a well-argued one, further explored in Chapter 3.

Blair has consistently argued that psychopathy is linked to amygdala dysfunction (i.e. Blair, 2010), but studies in adult populations are not wholly consistent. This

divergence between studies may be due to the use of different samples and paradigms (Contreras-Rodríguez et al., 2015; Seara-Cardoso, Sebastian, Viding, & Roiser, 2015). A meta-analysis purported that amygdala dysfunction might be more evidenced when a verbal response is given (Wilson, Juodis, & Porter, 2011). Wilson et al. claim that a verbal response taxes the amygdala more, and a meta-analysis of 22 studies ( $N = 1,387$ ) found that studies where participants verbally described the emotional face recorded larger deficits in emotion recognition (which recruits the amygdala) than those where participants responded non-verbally (for example, selecting an option on a screen). However, it should be noted that amygdala activation was not directly measured in this meta-analysis, and so this argument does not have strong support. The research explored above does suggest that psychopathy may be associated with reduced activation in various brain areas, with some evidence for a deficit in amygdala activity.

### **1.5.3.2 Youth literature**

Whilst research involving adults with psychopathy is somewhat inconclusive, evidence of a negative association between CU traits and brain response to faces is clearer in children and adolescents. Youths with high levels of CU traits show amygdala hypoactivity during the processing of conscious (Jones, Laurens, Herba, Barker, & Viding, 2009; Marsh et al., 2008 but see White et al., 2012) and unconscious (Viding et al., 2012) fearful faces. These findings were extended by White et al. (2012), who showed that an atypical amygdala response to consciously processed fearful faces in youths with AB/HCU is not secondary to an attentional deficit (i.e., ameliorated top-down control) but is specifically related to CU traits.

As CU traits are only one facet of psychopathy, the lack of conclusive results in adult psychopathic populations could reflect greater heterogeneity.

In youths, amygdala hypoactivity could partly explain the high propensity for proactive aggression in those with AB/HCU (Blair, 2013). In support of this view, a recent study showed that amygdala response to fearful faces in youths with AB mediated the association between CU traits and proactive aggression (Lozier et al., 2014). In contrast, youths with AB/LCU exhibit hyperactivity in the amygdala when processing both fearful faces (Viding et al., 2012) and fearful eyes (Sebastian et al., 2014), when compared to typically developing youths. These results might partly explain why youths with AB/LCU have emotion regulation difficulties and a propensity towards reactive aggression when feeling threatened (Frick & Viding, 2009).

Studies which measured CU traits in youths with AB using a dimensional approach found similar results to the group analyses reported above. Lozier et al. (2014) reported that right amygdala activity was negatively associated with level of CU traits during a conscious face processing task of neutral, fearful and angry faces, whilst Viding et al. (2012) also found a negative association between CU traits and right amygdala reactivity to fearful facial expressions in youths with AB. It is interesting to note here that there seems to be a lateralization effect to the right amygdala. However, one meta-analysis, which investigated lateralization in the amygdala during processing of emotional stimuli in 385 PET and fMRI studies, did not find any lateralization effects for facial emotions (Costafreda, Brammer, David & Fu, 2008). Nonetheless, the authors did report a left lateralization effect for



stimuli containing language, and a trend towards a right lateralization effect for subliminal stimuli.

#### ***1.5.4 Emotion recognition and empathy***

A lack of empathy (the ability to perceive and understand others' emotions) is a key feature of CU traits (Frick et al., 2014). Previous studies have postulated a close relationship between the ability to detect facial emotions and emotional empathy (Balconi & Canavesio, 2016; Blair, 2005; Dimberg, Thunberg, & Elmehed, 2000). One recent study found that empathic individuals are more skillful in processing facial emotions, with faster RTs when detecting faces (Balconi & Canavesio, 2016). Thus, CU traits may be relevant to the relationship between empathy and emotional face processing.

Empathy deficits in relation to AB in youths have been extensively documented (Stams et al., 2006), with recent fMRI studies examining differences in neural response to perceived pain in others. Lockwood et al. (2013) found that unique variance associated with callous traits was negatively correlated with activity in the ACC and anterior insula in youths with AB. Consistent with these results, Marsh et al. (2013) found that, compared to typically developing youths, those with AB/HCU traits showed reduced response in the ACC and ventral striatum when viewing pain in others. These youths also showed reduced activity in the amygdala and insula when viewing others' pain, but not when imagining that the pain was their own. CU traits were negatively related to the induced brain response in the

amygdala and ACC when perceiving pain in others. This suggests that differing levels of CU traits could be associated with empathy abilities.

A more complex affective processing task found that cartoons requiring the understanding of perceived distress in others within the context of social situations (i.e. emotional empathy) produced reduced amygdala and anterior insula activity in youths with AB, which was negatively correlated with the unique variance associated with CU traits (Sebastian, McCrory, et al., 2012). Using the same task, O’Nions and colleagues found that cartoon scenarios requiring the interpretation of others’ perceived intentions (i.e. theory of mind) did not induce a significantly different brain response in youths with AB/HCU compared to typically developing youths (O’Nions et al., 2014). These results dovetail with behavioural and experimental data (Jones et al., 2010) and highlight the fact that youths with AB/HCU do not have a deficit in understanding the mental state of others, but instead show no emotional response or empathy when others are distressed (Jones et al., 2010). This could explain how youths with high levels of CU traits are able to callously manipulate others for their own benefit.

These results provide emerging evidence of neural vulnerabilities that might hamper successful socialisation of youths with AB/HCU traits, putting them at increased risk of displaying severe AB and proactive aggression without feeling guilt or empathy for their victims. Clinical interventions could look at targeting and improving empathic responding in youths with AB/HCU traits, as this may reduce aggressive and manipulative tendencies.

### ***1.5.5 Functional connectivity***

Emotions are not independently processed by different areas of the brain; some areas feed forward into others, and activation levels in earlier structures may influence responsivity in later structures (Dilgen, Tejeda, & O'Donnell, 2013). For example, reduced activation in the thalamus for subconsciously perceived stimuli may result in reduced activation later on in the subconscious processing circuit the (which travels through the superior colliculus, to the pulvinar nucleus in the thalamus and then the amygdala; Pessoa & Adolphs, 2010). Functional connectivity is acknowledged as a pattern of statistical dependencies between distinct neural areas in the brain. Poor functional connectivity has been recognised in psychopathy during task and rest related fMRI paradigms. For example, Motzkin, Newman, Kiehl & Koenigs (2011) found that psychopathic criminals (i.e. AB/HCU traits) showed reduced functional connectivity between the vmPFC and amygdala as well as between vmPFC and medial parietal cortex. Furthermore, Contreras-Rodríguez et al. (2015) observed a reciprocal decline in functional connectivity between the left amygdala and visual and prefrontal cortices during an emotional face-matching task in adults with AB/HCU traits.

Together with fMRI studies, these results suggest that emotional information does not evoke a customary response in subcortical regions in those with AB/HCU traits. There is also disruption in functional communication between emotion processing areas in psychopathic individuals, suggesting a failure to integrate cognitive information about emotion. In line with behavioural research, CU traits

are negatively associated with neural activation in structures of the brain necessary for emotion processing, including the amygdala, ACC and insula.

#### ***1.5.6 Diffusion Tensor Imaging evidence***

Whilst the previous section outlined functional abnormalities in adults and youths with AB, it is also important to consider structural connections between multiple areas involved in emotion processing. Despite the fact that areas of the brain involved in emotion processing are structurally modular, they are also interdependent and anomalies in one structure on the pathway may cause aberrant processing in additional sites further on (Meyer, Makris, Bates, Caviness, & Kennedy, 1999). It is thought that the information transmission of a given white matter tract can be forecasted by the functions of the grey matter regions it travels between (Passingham, Stephan, & Kötter, 2002). Whilst the function of the uncinate fasciculus (UF) is indistinct, its location and connections associate it with the limbic system and the amygdala, making it a likely candidate for disruption in disorders affecting personality and emotion.

Diffusion tensor imaging (DTI) measures macroscopic axonal organisation in the brain by mapping the diffusion of water (Mori & Zhang, 2006). It allows one to see the spatial location and direction of water diffusion in three dimensions. From the movement of water molecules in the brain (even post mortem), the neuroanatomy and physiology of the brain can be inferred. Mori and Zhang (2006) describe an analogy involving ink stains. A blob of ink on a (wet) piece of paper slowly spreads. If the fibres in the paper are oriented in many different directions, the blob of ink

spreads in a circular shape, reflecting isotropic diffusion. If higher densities of fibres are oriented in the same direction, the blob of ink spreads in an elongated fashion along one axis, reflecting anisotropic diffusion. Isotropic diffusion is seen in cerebral spinal fluid, whilst anisotropic diffusion is seen in white matter tracts.

Fractional Anisotropy (FA) is a summary measure of microstructural integrity and varies between 0 (isotropic diffusion) and 1 (infinite anisotropy) (Le Bihan et al., 2001). FA is the most common measurement reported in DTI studies, as it is highly sensitive to microstructural changes. The extent of anisotropy in white matter increases whilst myelination occurs, meaning that DTI can be used to measure brain maturation in youths (Zimmerman et al., 1998). This section reviews and discusses the studies that have examined structural brain connectivity in emotion processing circuits with particular regard to psychopathy in adulthood and CU traits in youths with AB.

#### ***1.5.6.1 Adult literature***

Research into psychopathy using DTI has found reduced FA in the right UF (the white matter tract connecting ventral frontal and anterior temporal cortices; Craig et al., 2009; Motzkin et al., 2011; Sundram et al., 2012) and the left dorsal cingulum (Sethi et al., 2015) in psychopathic, antisocial offenders when compared to TD controls. The UF is thought to be important in social-affective functioning and emotional empathy as it is located between the amygdala and other structures important in emotion processing (Oishi, Faria, Hsu, Tippet, & Mori, 2015).

To date, only three studies have investigated psychopathy as a continuous variable in relation to DTI. One study with 147 offenders found a negative relationship between psychopathy (total PCL-R score, and also Factors 1 and 2 independently) and FA in the right UF (Wolf et al., 2015), suggesting possible lateralization here. Sundram et al. (2012) found that in a sample of adults with AB, mean FA in the frontal lobe was negatively correlated with Factor 2 and total PCL-R scores. Furthermore, in a different cluster in the frontal lobe, there was a positive correlation between increased mean diffusivity (a sub measure within FA which reports total diffusion within a particular voxel) with Factor 2 scores. A further study which investigated a small group of adult offenders ( $n=11$ ) found a negative correlation between Factor 1 (i.e. CU traits) and FA in an amygdala-prefrontal network (Hoppenbrouwers et al., 2013). Furthermore, the authors report a negative correlation between Factor 2 (i.e. AB) and FA in a striatal network.

#### **1.5.6.2 Youth literature**

Only two studies with youths have examined the association between CU traits and FA and their results have been inconsistent. One found that CU traits were positively correlated with FA in many white matter tracts, including the corticospinal tract, cingulate gyrus, forceps minor, superior longitudinal fasciculus and corpus callosum, but no significant association was observed in the UF (Pape et al., 2015). In contrast, reduced FA in the UF and stria terminalis were both associated with higher levels of CU traits, but not externalising behaviours in a sample of 47 youths with a range of conduct problems and CU traits (Breedén, Cardinale, Lozier, VanMeter, & Marsh, 2015). It is possible that the authors

intended to do group comparisons, but because they did not find anything, they then resolved to carry out dimensional analyses.

The reasons for the inconsistent findings above are unclear, but age or gender differences between the two studies could play a part. Global white matter volume over the entire lifespan follows an inverted U-shaped trajectory, peaking at 37 years of age (Lebel et al., 2012). The UF is one of the last white matter tracts to fully mature, with a peak after 30 years old (Lebel et al., 2012). Asato, Terwilliger, Woo and Luna (2010) postulated that the UF is still developing during adolescence (measured with both chronological age and pubertal status), meaning that age is important to consider when investigating the UF in youths.

Participants in Pape et al.'s study were aged between 12-20 years, with a mean age of 17.6 years, whilst participants in Breeden et al.'s study were aged between 10-17, with a mean age of 14.4 years. Age related changes in white matter microstructure during adolescence and early adulthood are well documented (Peters et al., 2012), and so the three-year difference in mean age might explain the discrepant findings between these two studies. With respect to gender influences, males generally present with higher FA across the brain compared to females (Herting, Maxwell, Irvine, & Nagel, 2012). One-hundred-and-twenty-five participants (85%) in Pape's study, compared to 25 participants (53%) in Breeden's study, were male. As males tend to have higher levels of CU traits compared to females (Essau, Sasagawa, & Frick, 2006), gender differences between the samples could also partly explain the divergence in findings across those studies.

In sum, reduced FA in the UF is associated with increased levels of psychopathy/CU traits in adults and youths with AB. As damage to the UF is associated with reduced emotion processing and empathy (Oishi et al., 2015), this reduced connectivity in adults with psychopathy could be associated with reduced activation in key areas during emotion processing. This hypothesis is supported by Breeden et al. (2015), who found that, among youths with conduct problems, reduced activation in the bilateral amygdalae during a facial emotion processing task was associated with reduced WM integrity in the UF bilaterally.

In conclusion, there is overwhelming evidence across studies using group and dimensional data analytic approaches for reduced structural connections in the UF in adults with AB. However, evidence among antisocial youths with varying levels of CU traits is mixed, so it is unclear whether differences in structural connectivity exist in younger participants, or whether they develop over time.

## **1.6 Mental health is continuous**

There is evidence that many mental health disorders are not discrete taxa, but in fact lie on a continuum (Hudziak, Achenbach, Althoff, & Pine, 2007; Rutter, 2003; Shaw et al., 2011). The nosological system employed by the DSM may fail to account for sources of variance, including gender and age, which could modulate neural systems underlying behaviour (Hudziak et al., 2007). Furthermore, it is postulated that dimensional analyses provide greater statistical power than categorical analyses, assuming that there is a valid linear dimension (Fergusson & Horwood, 1995).



Recently, the DSM-5 renamed “*autism disorder*” as “*autism spectrum disorder*”, in reference to the fact that the personality traits documented in this diagnosis are, to variable extents, recognisable in a large portion of the population (American Psychiatric Association, 2013). Personality traits are considered disordered when they negatively impact on the individual’s life (American Psychiatric Association, 2013). As these traits are continuous, research should also involve participants with lower levels of these personality traits, where they are not severe enough to adversely impact on day to day functioning.

In line with evidence that personality disorders exist on a continuum (Clark, 2007), taxometric analyses suggest that psychopathy in adults (Hare & Neumann, 2008) and CU traits in youths (Murrie et al., 2007) are dimensional constructs. Consequently, individuals diagnosed with psychopathy represent an extreme end of the distribution of psychopathic traits rather than a qualitatively distinct group of individuals. Whilst it is of clear importance to research these traits in their most severe form, it is also of interest to investigate the potential impact of these personality traits on behavioural, social and neurobiological functioning in non-clinical samples. The study of individuals with higher levels of psychopathic traits, but without clinical levels of AB, may lead to enriched comprehension of the pathophysiology of psychopathy and CU traits and facilitate identification of protective factors which prevent these individuals from developing AB (Lilienfeld, 1998).

Rutter (2012) recommended including a syndrome to encompass those with high CU traits, irrespective of whether they present with AB, in the International

Classification System of Diseases (ICD-11). However, it is not known whether it is of clinical importance to recognise CU traits outside of CD in children and adolescents (Herpers, Rommelse, Bons, Buitelaar, & Scheepers, 2012), and HCU traits without AB are rarely recorded in large community samples of youths (Fontaine et al., 2011). Few have investigated the correlates of CU traits in children and adolescents who do not show clinically recognised behavioural difficulties, and more research is required before CU traits outside of AB can be considered a clinical disorder (Frick et al., 2014). This section explores the limited research on CU traits in adults and youths without AB.

## **1.7 Callous-unemotional traits in adults and youths without antisocial behaviour**

### ***1.7.1 Behavioural characteristics***

An increasing number of studies have considered the association between psychopathic traits and behavioural characteristics in adults without AB (Seara-Cardoso & Viding, 2015). High levels of psychopathic traits are associated with reduced caring behaviours towards others, reduced empathy and social confidence and a lower general mood (Fix & Fix, 2015; Ometto et al., 2016), but higher interpersonal functioning and stress management (Fix & Fix, 2015). Higher levels of psychopathic traits also predict delinquent behaviour (Almeida et al., 2015; Fix & Fix, 2015) and aggression (Miller, Wilson, Hyatt, & Zeichner, 2015).

Adults without AB but with HCU exhibit characteristics and behaviour akin to adults with AB/HCU traits (Mullins-Sweatt, Glover, Derefinko, Miller, & Widiger,

2010), but either avoid committing crimes which are likely lead to imprisonment, accomplishing their objective using covert and non-violent methods, or are “successful” criminals who avoid detection (Gao & Raine, 2010). One study investigated individuals with high levels of psychopathic traits using the PCL-R, and divided them into two groups depending on whether they had ever been convicted or not. The authors found that those who had never been convicted (‘successful’; n=16) scored lower overall on the PCL-R compared to those who had been convicted (‘unsuccessful’; n=13), but this was largely driven by lower scores on the second facet, which describes AB. In fact, when only the first factor of the PCL-R (roughly equivalent to CU traits) was considered, the successful psychopaths scored higher than the unsuccessful psychopaths (Ishikawa, Raine, Lencz, Bihrlé, & Lacasse, 2001). This suggests that a range of psychopathic traits can be observed outside of forensic samples. It is interesting that these groups did not differ on IQ score, as one might expect that successful psychopaths were cleverer at hiding their actions than non-successful ones. Successful psychopaths were significantly younger than non-successful psychopaths, however it seems unlikely that age would be a confounding variable here.

### ***1.7.2 Experimental findings in emotion recognition***

A large proportion of research delving into psychopathy, including much of the research included in this thesis, has focussed on emotion processing. High levels of psychopathic traits in the general population have largely been associated with reduced startle responses to aversive stimuli (Benning, Patrick, & Iacono, 2005; Justus & Finn, 2007 but see Ishikawa et al., 2001) and to emotional faces (Ali,

Amorim, & Chamorro-Premuzic, 2009; Seara-Cardoso, Dolberg, Neumann, Roiser, & Viding, 2013; Seara-Cardoso, Neumann, Roiser, McCrory, & Viding, 2012; Sharp, Vanwoerden, Van Baardewijk, Tackett, & Stegge, 2015).

Whilst most studies have found negative associations between emotional processing and psychopathic/CU traits, when specific emotions are individually investigated, results are mixed. With regard to the primary, affective factor of psychopathy, one study found no association with fear recognition (Gordon, Baird, & End, 2004), another reported a positive correlation with fear recognition (with no association reported for the secondary, antisocial facet; Del Gaizo & Falkenbach, 2008) and a third found that both incarcerated and non-criminal psychopaths were poorer at detecting fear compared to incarcerated and non-criminal non-psychopaths (Iria & Barbosa, 2009). The results of that study suggest that the primary rather than the secondary facet is driving these results. The reasons for these inconsistent findings with regards to fear recognition are unclear, but differences in the instruments used to measure psychopathy (Iria & Barbosa used the PCL-R, whilst Gordon, Baird & End and Del Gaizo & Falkenbach used the PPI) and sample characteristics (e.g., size, age range, location) are possible explanations.

A further study found a negative association between psychopathic traits and disgust recognition, although it should be noted that this relationship was largely driven by a correlation between the secondary factor (antisocial behaviour) of the PCL-SV, and so cannot be reliably attributed to CU traits (Acharya & Dolan, 2012). Finally, a recent study in adults without AB found that increasing levels of CU

traits were associated with fewer fixations and reduced dwell time on the eyes relative to the mouth when observing fearful and angry faces, but no association was found between emotion recognition accuracy and level of CU traits (Gillespie, Rotshtein, Wells, Beech, & Mitchell, 2015).

Adults with psychopathic traits are impaired in emotional processing. For example, a recent study found that adults with higher psychopathic traits struggled with emotional perspective taking but not cognitive perspective taking (Lockwood, Bird, Bridge, & Viding, 2013). This suggests that these two processes are distinct, and psychopathic traits are only associated with emotional bluntness, rather than impaired theory of mind. Consistent with research with antisocial adults, high levels of psychopathic traits in the general population are associated with reduced emotional empathy (Benning et al., 2005; Justus & Finn, 2007), as well as with weaker self-reported affective responses to others' emotional faces (Ali et al., 2009; Seara-Cardoso et al., 2013, 2012) and when rating one's own affective response to others' emotional faces (Seara-Cardoso, Sebastian, Viding, & Roiser, 2016).

In a community sample of young adults, participants who scored highly on the primary factor of psychopathy experienced more positive emotions in response to sad faces compared to those with lower levels of primary psychopathy (Ali et al., 2009). The authors concluded that this shows a lack of affective empathy in participants with higher levels of CU traits. Consistent with those results, a more recent study used the same paradigm to investigate affective empathy and found that the primary factor of psychopathy was associated with weaker empathy for

fearful and happy stimuli and reduced proclivity for empathic concern (Seara-Cardoso et al., 2012). Furthermore, individuals with higher levels of CU traits found it easier (i.e. had a shorter RT) when making difficult decisions for moral dilemmas. Similar results were found in a follow up sample of women recruited from the community; high levels of CU traits were associated with reduced empathy to sad and fearful emotions (Seara-Cardoso et al., 2013).

Taken together, these experimental findings suggest that associations between the primary factor of psychopathy and recognition of others' fear are tenuous. In contrast, emotion recognition appears to be weaker in healthy adults and children with higher levels of psychopathic/CU traits. Next, the studies that have examined the neural correlates of emotion processing in healthy adults with varying levels of psychopathic traits are discussed.

### ***1.7.3 Functional Magnetic Resonance Imaging evidence***

A recent review of fMRI research into psychopathic traits in adults without AB concluded that the results mirror those found in clinical and forensic populations (see Seara-Cardoso & Viding, 2015 for a review), supporting the view that psychopathy is a dimensional construct. Gordon et al. (2004) found that when viewing emotional facial expressions, individuals with HCU traits (n=10) showed greater activation in the visual cortex and right dorsolateral prefrontal cortex compared to those with LCU traits (n=10). By contrast, those with LCU traits showed significantly greater activation in the right inferior frontal cortex, right

amygdala and medial prefrontal cortex, a network of regions central to emotion processing, compared to those with HCU traits.

A more recent study with a larger sample (n=200) reported that amygdala activation to fearful faces was negatively correlated to levels of psychopathic traits (Carré et al., 2013). In line with research on adults with AB, suppressor effects (see section 1.3) between psychopathy and externalising behaviours have also been reported in a community sample. For example, Hyde et al. (2014) showed that higher psychopathy scores were associated with lower amygdala reactivity when participants viewed angry or fearful faces, whereas higher ASPD scores were related to greater amygdala reactivity. Importantly, these results were only significant once the statistical model was adjusted for the shared variance between ASPD and psychopathy scores. This suggests that suppressor effects between CU traits and AB are at play in both clinical and community samples.

Together with behavioural research, findings from fMRI studies in healthy adults suggest that links between psychopathy and poor empathic responding extend throughout the continuum of psychopathic traits at both the behavioural and neural levels.

#### ***1.7.4 CU traits in children without antisocial behaviour***

The literature reviewed so far has outlined research which looks at CU traits in adults and youths with AB, and healthy adults. Very little research has focussed on typically developing youths with varying levels of CU traits. This could be because children with high levels of CU traits but without AB are seldom seen in healthy

populations (Fontaine et al., 2011), or that they do not pose a threat to society by indulging in aggressive or antisocial acts.

Understanding CU traits in typically developing youths is important as it may help researchers understand why some youths with high levels of CU traits also present with AB and why some do not. For example, youths subject to early severe deprivation show high CU traits without associated AB (Kumsta, Sonuga-Barke, & Rutter, 2012). Research with healthy populations may also outline risk factors during development that could lead to the development of AB. For example, negative parenting practices, including harsh punishment, psychological aggression and inconsistent discipline have been found to predict CU traits (Waller, Gardner, & Hyde, 2013), while positive parenting was associated with lower CU traits.

Behaviours associated with CU traits may be seen from a very early age. One study found that reduced preferential face tracking in infancy (5 weeks) predicted higher levels of CU traits at 2.5 years, whilst higher maternal sensitivity (i.e. mothers' appropriate, supportive, warm response to infant communication or distress) at 29 weeks predicted lower levels of CU traits in girls only (Bedford, Pickles, Sharp, Wright, & Hill, 2015). This early reduced preference for faces in infancy may reflect a lack of attention for faces, which could be a contributing factor for the reduced recognition of facial expressions of emotions in children with HCU. Dadds et al.'s (2006) intervention, where children are asked to focus on the eyes when recognising an emotion, could be relevant to very young children with high levels



of CU traits; it would be interesting to see if training on how to accurately recognise emotions reduces severity of CU traits in healthy children.

Between 2%-7% of youths without AB from a community sample meet diagnostic threshold for the CU specifier (Kahn, Frick, Youngstrom, Findling, & Youngstrom, 2012). Whilst these youths do not present with clinically recognised levels of difficulties, they may still have difficulties in day to day functioning. High levels of CU traits, whilst controlling for AB, predict behavioural and emotional problems (Frick, Cornell, et al., 2003; Moran, Ford, Butler, & Goodman, 2008; Rowe et al., 2010), behavioural regulation (Frick, Cornell, et al., 2003), impaired emotion recognition (Blair & Coles, 2000; Sharp et al., 2015) and ASPD in adulthood (Burke, Waldman, & Lahey, 2010). HCU traits are associated with risky behaviours including substance misuse (Wymbs et al., 2012). Youths without AB but with HCU traits report that they experience less social support from peers and family members than those with LCU traits; in fact, they are at similar risk as the those with AB/HCU and higher risk than those with AB/LCU to experience minimal social support, demonstrating that CU traits are uniquely associated with low social adjustment (Fanti, 2013).

A further relevant reason for measuring CU traits in typically developing youths is related to the predictive utility of CU traits in the absence of clinically recognised conduct problems. Frick, Cornell, et al. (2003) found that girls without AB but with HCU traits reported higher levels of general delinquency than girls without AB and with LCU traits. This relates to the postulation that traditional CD symptoms

(which include overt behaviours such as fighting, but fewer covert behaviours) may not accurately capture antisocial tendencies as well in girls (Crick, 1996). Thus, CU traits (which do include more covert behaviours that girls are more prone to display) may indicate girls who are at risk for later overt delinquency (Silverthorn & Frick, 1999).

There is also evidence for varying levels of CU traits in clinical samples other than CD. A recent study has looked at CU traits in youths with a diagnosis of autism spectrum disorder (ASD). Using an emotion recognition task, the authors found that whilst there was no association between overall emotion recognition accuracy and CU traits, a negative correlation was observed between CU traits and fear recognition (Carter Leno et al., 2015). This suggests that the negative association between CU traits and emotion recognition is not specific to youths with clinically recognised AB, but a similar pattern of affective difficulties is seen in individuals with ASD and high levels of CU traits.

Taken together, this evidence suggests that high levels of CU traits in samples other than those with severe AB are associated with reduced emotion recognition accuracy and poorer prognosis in adulthood. Thus, it is important to extend current research into CU traits in typically developing populations.

## **1.8 Thesis aims and structure**

This thesis looked at emotion recognition and processing within the field of psychopathy. In all of the experimental chapters, youths aged 9-18 years were

recruited from the FemNAT-CD consortium in Birmingham and Southampton. Participants and their parents were interviewed with the Kiddie-Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (K-SADS - PL; Kaufman et al., 1996) to ascertain that all youths were typically developing (i.e. did not score in the clinical range for any disorders). CU traits were measured with the parent version of the ICU, whilst externalising behaviours were measured with the CBCL. Chapter 2 explored demographics of youths with and without AB with respect to their levels of CU traits and externalising behaviours.

Chapter 3 reported the results of a study using the emotional hexagon task (Calder et al., 1996; Fairchild et al., 2011; Fairchild, Van Goozen, Calder, Stollery, & Goodyer, 2009). There is a negative association between psychopathic/CU traits and recognition of facial emotions in antisocial adults and youths. This chapter explored the association between CU traits and recognition of facial emotion in youths without AB (n = 110, 45 males). Partial correlations accounting for age, intelligence quotient (IQ), gender, site and externalising behaviours revealed negative correlations between CU traits and recognition of sad and disgusted expressions. This supports previous literature with antisocial populations.

Chapter 4 described an fMRI study which assessed activity in areas of the brain central to emotion recognition and processing. Whilst evidence suggests that psychopathy and CU traits are dimensional constructs, to date no fMRI study has examined the neural correlates of affective processing associated with CU traits in typically developing youths. This study addressed this gap in the literature by

investigating the neural correlates of pre-attentive emotion processing in a community sample of youths with varying levels of CU traits. Fifty-six youths (21 males) underwent an fMRI scan where blocks of pre-attentive facial expressions (calm, fearful and angry) were presented, followed by a mask of a calm face. Regressions were conducted looking at the relationship between CU traits and brain response to fearful and angry faces in the amygdala, anterior insula, ACC and OFC. Partial correlations, accounting for age, IQ, gender and externalising behaviours, found negative associations between CU traits and bilateral amygdala and insula activity during fear processing, whilst a positive trend was observed between externalising behaviours and left amygdala activity. This is in line with previous research, and supports evidence that CU traits are associated with reduced activity in emotion processing brain circuits in healthy populations as well as clinical populations.

Finally, in Chapter 5, a study looking at the relationship between CU traits and white matter connectivity is detailed. Adults with psychopathy show reduced white matter integrity in the right UF (Craig et al., 2009; Hoppenbrouwers et al., 2013; Motzkin et al., 2011; Wolf et al., 2015) compared to those without psychopathy. This tract connects the amygdala, insula and vmPFC: structures which are involved in emotion processing and empathy (Blair, 2007, 2008; Marsh et al., 2008; Sebastian, Fontaine, et al., 2012). So far, studies that have examined white matter connectivity in children and adolescents with AB have yielded inconsistent results. This study investigated white matter integrity in the UF in 62 youths (23 males) with a range of CU traits. Results showed that white matter in

the right UF was negatively associated with CU traits in 16-18 year olds, but not in the full sample (which ranged from 9-18 years). This suggests that, as the UF undergoes rapid development over adolescence, CU traits may only be associated with reduced white matter integrity in older youths.

## CHAPTER 2: DEMOGRAPHICS OF YOUTHS WITH AND WITHOUT ANTISOCIAL BEHAVIOUR

### 2.1 FemNAT-CD

The samples used in the following experimental chapters were healthy controls recruited from the FemNAT-CD consortium ([www.femnat-cd.eu](http://www.femnat-cd.eu)); a European multisite study which investigated the environmental and neurobiological factors that may underpin sex differences in CD (Freitag, 2014). Participants were paid for taking part and were recruited from mainstream primary and secondary schools, youth groups and community centres. Exclusion criteria for the subsample of youths in this thesis included: an estimated IQ below 70; inability to speak or understand English; any monogenetic disorder; any genetic syndrome; any chronic or acute neurological disorder; autism spectrum disorder, schizophrenia or bipolar disorder or any current mental health disorder besides learning disorders. Past mental health disorders, excluding disruptive behaviour disorders and psychosis, were acceptable if the participant was in remission (no symptoms for 12 months).

The study required several visits. I carried out all the following steps with participants recruited from Birmingham, whilst colleagues carried out these same steps for participants recruited from Southampton. During the first visit I administered an IQ test and the K-SADS with the child. The parent/main caregiver were separately interviewed with the K-SADS – PL (Kaufman et al., 1996). Next, I ran an fMRI scan, and finally the participants completed questionnaires and

computer tasks. This study was approved by the NHS (NRES Committee West Midlands – Edgbaston; REC reference 13/WM/0483). Children under the age of 16 years gave their assent to participate, whilst their parent or guardian gave consent for their child to take part. Consent was obtained from adolescents aged 16 and above and, in most cases, from their parents/guardians.

## **2.2 Participants**

Whilst all the participants in this thesis come from the large sample of FemNAT-CD, the same participants did not partake in each of the three chapters. In fact, 49 participants took part in all three experiments, whilst an additional 61 participants took part in Chapter 3, seven participants in Chapter 4 and 13 participants in Chapter 5. One of the reasons for this discrepancy was the fact that Southampton collected data for the Hexagon and DTI tasks, whereas I collected data for all three tasks in Birmingham. Furthermore, some participants at both sites were not eligible to enter the scanner, or moved to such a large degree whilst they were in the scanner that their data was rendered unusable. Whilst it would have been preferable to have the same participants in each part of this thesis, this would have been unnecessarily restrictive, causing a lot of data to be disregarded. Whilst the sample sizes differed across chapters, the sample characteristics from each chapter were comparable in terms of age (mean age in Chapter 2 = 13.9; Chapter 3 = 13.9; Chapter 4 = 13.5;  $p = .39$ ), IQ (mean IQ in Chapter 2 = 100.7; Chapter 3 = 101.0; Chapter 4 = 102.5;  $p = .97$ ) and ICU score (mean ICU in Chapter 2 = 17.9; Chapter 3 = 17.7; Chapter 4 = 16.8;  $p = .70$ ; see Table 2.3). There were no statistically significant differences between samples in each chapter. The benefits of having

larger samples in each chapter were thought to outweigh the benefits of having the sample participants in each chapter.

*Table 2.3. Demographics of participants in each experimental task.*

Chapter	2 (Emotion Hexagon)	3 (Subliminal Emotion Processing)	4 (DTI)
Sample size	110	56	62
Age, mean (SD; range)	13.9 (2.7; 9-18)	13.9 (2.5; 9-18)	13.52 (2.7; 9-18)
Male gender (%)	45 (43.2%)	21 (37.5%)	23 (37.0%)
IQ, mean (SD; range)	100.7 (10.8; 72-125)	101.0 (9.4; 83-123)	102.5 (11.6; 73-139)
ICU total, mean (SD; range)	17.9 (9.3; 1-48)	17.7 (7.7; 1-35)	16.76 (7.3; 1-35)
CBCL internalising, mean T score (SD; range)	50.4 (10.8; 33-62)	47.9 (9.9; 33-62)	47.0 (8.6; 33-61)
CBCL externalising, mean T score (SD; range)	46.1 (10.0; 33-62)	44.6 (8.1; 34-62)	45.5 (7.7; 34-61)

*Notes: CBCL = Child Behaviour Checklist; ICU = Inventory of Callous-Unemotional Traits; SD = standard deviation.*

## 2.3 Data analyses

In order to assess whether CU traits are a continuous variable within healthy youths, all of the following experimental chapters use partial correlations rather than a group approach. This is in line with the school of thought stating that CU



traits in youths exist on a continuum (Murrie et al., 2007) and in line with previous studies assessing psychopathy in healthy populations (Del Gaizo & Falkenbach, 2008; Gillespie, Rotshtein, Wells, et al., 2015; Seara-Cardoso et al., 2016).

Age, IQ, site and gender were included as covariates in the partial correlations in each chapter. Past research has shown that age, gender and IQ may influence emotion recognition abilities and white matter connectivity in the brain. Site was included as a covariate where applicable (i.e. Chapters 3 & 5), as different investigators and scanners were present at each site.

Age is positively associated with children's ability to recognise facial expressions, including happiness, surprise, fear and disgust (Lawrence, Campbell, & Skuse, 2015), and negatively correlated with activity in the medial prefrontal cortex when viewing emotional faces (Wu et al., 2016). Age is also positively correlated with white matter connectivity in various brain regions important for attention, motor skills, cognitive ability and memory during childhood and adolescence (Barnea-Goraly et al., 2005; Chiang et al., 2011; Peters et al., 2012).

Gender was included as a covariate, as there is a small female advantage for emotion recognition (Lawrence et al., 2015), and males have greater FA in particular areas of the brain, including the bilateral frontal lobes, the splenium of the corpus callosum and bilateral optic radiations, whilst females have higher FA in the middle and superior occipital gyri (Chiang et al., 2011).

Finally, IQ has also been reported to be positively correlated with emotion recognition (Young & Widom, 2014) and FA in the bilateral frontal and occipito-parietal areas (Schmithorst, Wilke, Dardzinski, & Holland, 2005). Thus, it was considered important for each of the three following chapters to consistently account for the potentially confounding effects of these four variables.

## **2.4 Statistical tests**

This thesis reports Bayes Factors as well as p values from null hypothesis significance tests (NHSTs) throughout. This is because there is growing evidence that Bayes Factor overcomes some of the shortcomings of the ubiquitous p value (Wagenmakers, 2007). NHSTs assume an arbitrary cut off for significance of .05, which may not always be appropriate for a given study (Johnson, 2013).

P values are derived using hypothetical data; they are calculated based on many putative iterations of the same experiment assuming the null hypothesis is true. As these data are theoretical and never actually observed, this may lead to logical errors. Moreover, a p value  $>.05$  in a small sample isn't directly comparable to a similar p value in a larger sample in terms of probability.

In contrast to NHSTs, the Bayesian approach compares the data under both possible hypotheses. The Bayes Factor is a ratio which contrasts the probability of the data fitting under the null hypothesis to the likelihood of fitting under the experimental hypothesis. The more likely the Bayes Factor is under the experimental hypothesis compared to the null hypothesis, the larger the Bayes Factor. Generally, a Bayes Factor below .33 is considered substantial support for

the null hypothesis, whilst a Bayes Factor greater than 3 is considered substantial support for the experimental hypothesis. Any value between these cut offs are considered to be insubstantial evidence for either. Thus, an additional benefit of using Bayes Factors is that one can assess whether there is substantial evidence for the null hypothesis, which cannot be derived from NHSTs. Further, as Bayes Factors are ratios of probabilities, two factors of equal amounts from unequal samples represent the same degree of evidence in favour of the experimental hypothesis.

## **2.5 Interview and Psychometric Measures**

The following interviews were used in each of the following experimental chapters.

### ***2.5.1 Kiddie-Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version***

The K-SADS – PL (Kaufman et al., 1996) is a semi-structured diagnostic interview designed to assess past and current psychopathology (according to the DSM-IV) in youths. This measure is capable of generating 32 child psychiatric diagnoses, which are scored as definite, probable or not present. These diagnoses include, but are not limited to: Major Depression, Mania, Bipolar Disorders, Schizophrenia, Panic Disorder, Separation Anxiety Disorder, Social Phobia, Obsessive-Compulsive Disorder, Attention Deficit Hyperactivity Disorder, CD, Oppositional Defiant Disorder, Anorexia Nervosa, Bulimia and Post-Traumatic Stress Disorder.

This measure consists of a screening section, which asks three questions about every disorder. Each question is scored either 0 (no information), 1 (not at all), 2 (subthreshold) or 3 (above threshold). If a score of 3 is achieved on any items, a supplement is administered, which asks further questions about the disorder. Scores from the screening and supplement are both used to decide whether a psychiatric diagnosis is given. Participants and their parents are interviewed separately by different interviewers, after which summary ratings are created using information from both informants. This interview takes approximately 30 – 45 minutes to administer. Inter-rater reliability was calculated at 92.0% from a subsample of 16 participants from Birmingham (n = 8) and Southampton (n = 8).

### ***2.5.2 Wechsler Abbreviated Scale of Intelligence***

An estimate for the full-scale IQ was obtained using the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999), a nationally standardised measure of general intelligence which has been normed for individuals aged 6 to 89 years. The WASI is linked to both the Wechsler Intelligence Scale for children (WISC-III; Wechsler, 1991) and the Wechsler Adult Intelligence Scale (WAIS-III; Wechsler, 1997) and is usually based on four subtests: Vocabulary; Similarities; Block Design and Matrix Reasoning.

Here, the 2-subtest version (Vocabulary and Matrix Reasoning) was used, lasting approximately 15 minutes. This version highly correlates with longer, in depth measures of IQ, including the four subset version of the WASI and the WISC (Wechsler, 1999). The vocabulary section involves participants explaining the

meaning of various words, which become progressively more advanced. The matrix reasoning involves showing a visual pattern or sequence with a part missing, and five options to fill the gap. The participant is asked to choose which of the five fits the sequence. In both these tests, participants are given as long as they like to answer, although respondents generally answered within 10-30 seconds.

### ***2.5.3 Inventory of Callous-Unemotional Traits***

The ICU (Frick, 2003) was chosen to measure CU traits in this thesis as it specifically taps the callous/unemotional facet of psychopathy and attempts to assimilate the best features from many previous delineations of psychopathy, undersocialised aggression and prosociality in children and adolescents (Frick & Hare, 2001; Kimonis et al., 2008).

This questionnaire is based on the CU subscale of the Antisocial Process Screening Device (Frick & Hare, 2001) and consists of 24 items that tap multiple aspects of the affective features of the psychopathy. The ICU provides a comprehensive inventory of CU traits, and is intended to overcome the limited range of items of the CU subscale of the APSD (Roose, Bijttebier, Decoene, Claes, & Frick, 2010).

Items are rated by a parent/main caregiver on a four point Likert scale from 0 (not at all true) to 3 (definitely true), with a maximum score of 72. This questionnaire has three subscales: Callousness; Uncaring and Unemotional. Examples from each subscale include, respectively: *“Does not care who he/she hurts to get what he/she wants”*; *“Tries not to hurt others’ feelings”*; and *“Is very expressive and emotional”*.

The ICU has been extensively validated across numerous languages and cultures (Essau et al., 2006; Fanti, Frick, & Georgiou, 2009; Kimonis et al., 2008; Roose et al., 2010); a wide age range (Byrd, Kahn, & Pardini, 2013; Ezpeleta, de la Osa, Granero, Penelo, & Domènech, 2013) and both genders (Essau et al., 2006). Furthermore, the operational definition used by the ICU corresponds closely to the one used in the DSM-5 specifier "*With Limited Prosocial Emotions*" (American Psychiatric Association, 2013).

Kimonis, Fanti and Singh (2014) proposed cut off scores between 24-27, dependent on the gender of the child and of the parent, whilst Docherty, Boxer, Huesmann, O'Brien and Bushman (2016) calculated the optimal cut off scores for presence of HCU traits on the ICU as: 28 for youth report; 30 for parent report and 33 for teacher report.

Whilst self-report assessments are particularly useful if parents or teachers are not available or do not have enough contact with their child to provide valuable information (Loney, Frick, Clements, Ellis, & Kerlin, 2003), throughout this thesis the parent rated ICU was used. A parent rated measure was preferred because young children may not be good at recognising some difficulties and personality traits in themselves, and/or may not answer truthfully. In addition, most parents were willing to take part and engaged well with the material. Furthermore, whilst it is recommended that information from child, teacher and parents should be used whenever possible for the ICU, when only one reporter is feasible, parent reports are preferable (Docherty et al., 2016).

### **2.5.3.1 Range of ICU scores**

As all the following chapters use correlational analyses, it was first important to assess whether there is sufficient range of ICU scores in the typically developing population. Therefore, the range of scores in youths with CD and TD youths were compared. Youths (N = 158) and their parents/caregivers were interviewed with the K-SADS semi-structured interview and subsequently divided into those with CD and those who were typically developing (see Table 2.4). There was no difference in the ages of controls and cases ( $t(156) = 1.76, p = .08$ ) or number of controls and cases recruited from each site ( $X^2 = .46, p = .50$ ), but there were significantly more females in the control group than the clinical group ( $X^2 = 15.60, p < .001$ ). Youths with CD ( $n = 46$ ) had a higher average level of CU traits ( $t(156) = 9.72, p < .001$ ) compared to typically developing youths ( $n = 112$ ). Figure 2.2 shows that, while the range of scores in each group overlap greatly, a greater proportion of youths with AB have higher levels of CU traits. This suggests that one cannot accurately categorise whether a youth does or does not present AB solely based on their level of CU traits. Cronbach's alpha for the current sample was .82, suggesting good internal consistency.

*Table 2.4. Demographics of subsample with ICU scores from FemNAT-CD.*

	Conduct Disorder	Typically Developing
N	46	112
Male gender (%)	36 (78.2%)*	61 (43.7%)*
Age, mean (SD; range)	13.9 (2.3; 9 – 18)	13.1 (2.6; 9 – 18)
Site (Soton:Bham)	22:24	47:65
ICU mean (SD; range)	35.9* (13.2; 16 – 66)	17.9* (9.3; 1 – 54)

*\* indicates  $p < .001$ . SD = standard deviation; Soton = Southampton; Bham = Birmingham.*



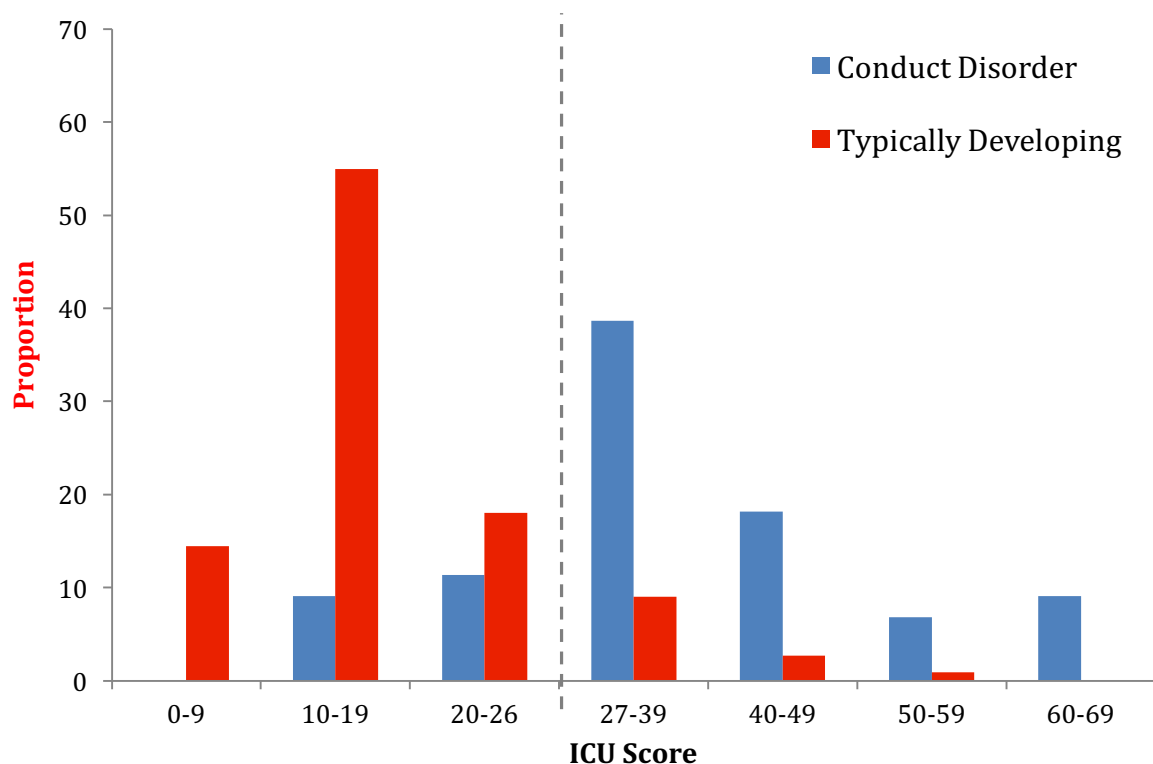


Figure 2.2. Proportion of ICU scores in Conduct Disorder and Typically Developing groups. Dotted line reflects clinical cut off.

#### 2.5.4 Child Behaviour Checklist

Parent/main caregiver reports on the Child Behaviour Checklist (CBCL; Achenbach & Rescorla, 2001) were used to detect more nuanced emotional and behavioural problems in the youths, alongside the K-SADS. The CBCL consists of 120 questions, scored on a three point Likert scale (0=absent, 1= occurs sometimes, 2=occurs often). Scores are divided into eight subscales: anxious/depressed; withdrawn; somatic complaints; social problems; thought problems; attention problems; rule breaking behaviour and aggressive behaviour. It can also be split into internalising (anxious/depressed withdrawn & somatic complaints) and externalising (rule breaking and aggressive behaviour) subscales. T scores below 63 for each of the internalising and externalising subscales are considered in the normal range,

whilst scores between 60 - 63 (inclusive) are considered borderline and those above 63 in the clinical range.

#### **2.5.4.1 Range of CBCL: externalising scores**

As all the following chapters use correlational analyses, it was also important to assess whether there is sufficient range in externalising behaviours in the typically developing population. The same sample as previously described in section 2.5.3.1 was used here. Youths (N = 158) and their parents/caregivers were interviewed with the K-SADS semi-structured interview and subsequently divided into those with CD and those who were typically developing. Youths with CD (n = 46) had a higher average level of externalising behaviours ( $t(156) = 8.71, p < .001$ ) compared to typically developing youths (n = 112). Cronbach's alpha for the current sample was .90, showing good internal consistency for the CBCL measure.

Data from 158 youths from Southampton and Birmingham was analysed (see Table 2.5 for demographics). These were the same youths included above in the ICU analysis. Figure 2.3 shows that, although more youths without AB were in the non-clinical range for externalising behaviours, a small proportion of youths (>1%) in this group showed behaviours in the clinical range. However, a much larger proportion of youths with AB presented with clinical levels of externalising behaviours ( $\chi^2 = 8.70, p = .003$ ).

*Table 2.5. Demographics of subsample with CBCL scores from FemNAT-CD.*

	Conduct Disorder	Typically Developing
N	46	112
Male gender (%)	36 (78.2%)	61 (43.7%)
Age, mean (SD; range)	13.9 (2.3; 9 – 18)	13.1 (2.6; 9 – 18)
Site (Soton:Bham)	22:24	47:65
Externalising mean (SD; range)	65.3 (12.1; 34-82)	47.7 (11.3; 33-84)

*\* indicates  $p < 0.001$ . SD = standard deviation; Soton = Southampton; Bham = Birmingham.*

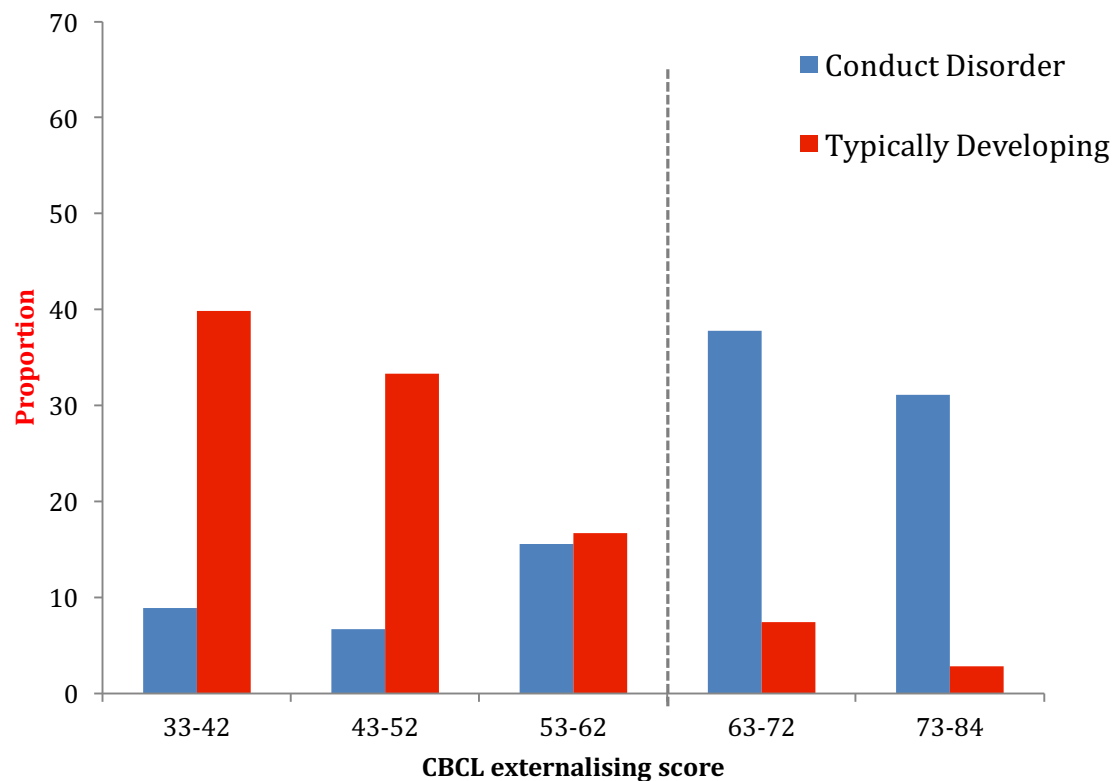


Figure 2.3. Proportion of CBCL externalising scores in Conduct Disorder and Typically Developing groups. Dotted line reflects clinical cut off.

## 2.6 CU traits and Externalising behaviours

Next, data from both CU traits and externalising behaviours measures were correlated. Figure 2.3 shows that there is a moderate positive association between CU traits and levels of externalising behaviours in youths with AB ( $r = .42$ ,  $p = .003$ ), and a weak positive correlations in youths without AB ( $r = .21$ ,  $p = .031$ ). The published cut off scores for clinical levels of externalising behaviours and CU traits, which are overlaid onto Figure 2.4, show that although the majority of youths without AB do not show clinical levels of either variable ( $N = 88$ ), and many youths with AB do show clinical levels of both variables ( $N = 20$ ), there are adolescents in both groups who show clinical levels of one without the other (externalising

behaviours without high levels of CU traits: Control = 9, Case = 7; high levels of CU traits without externalising behaviours: Control = 13, Case =14).

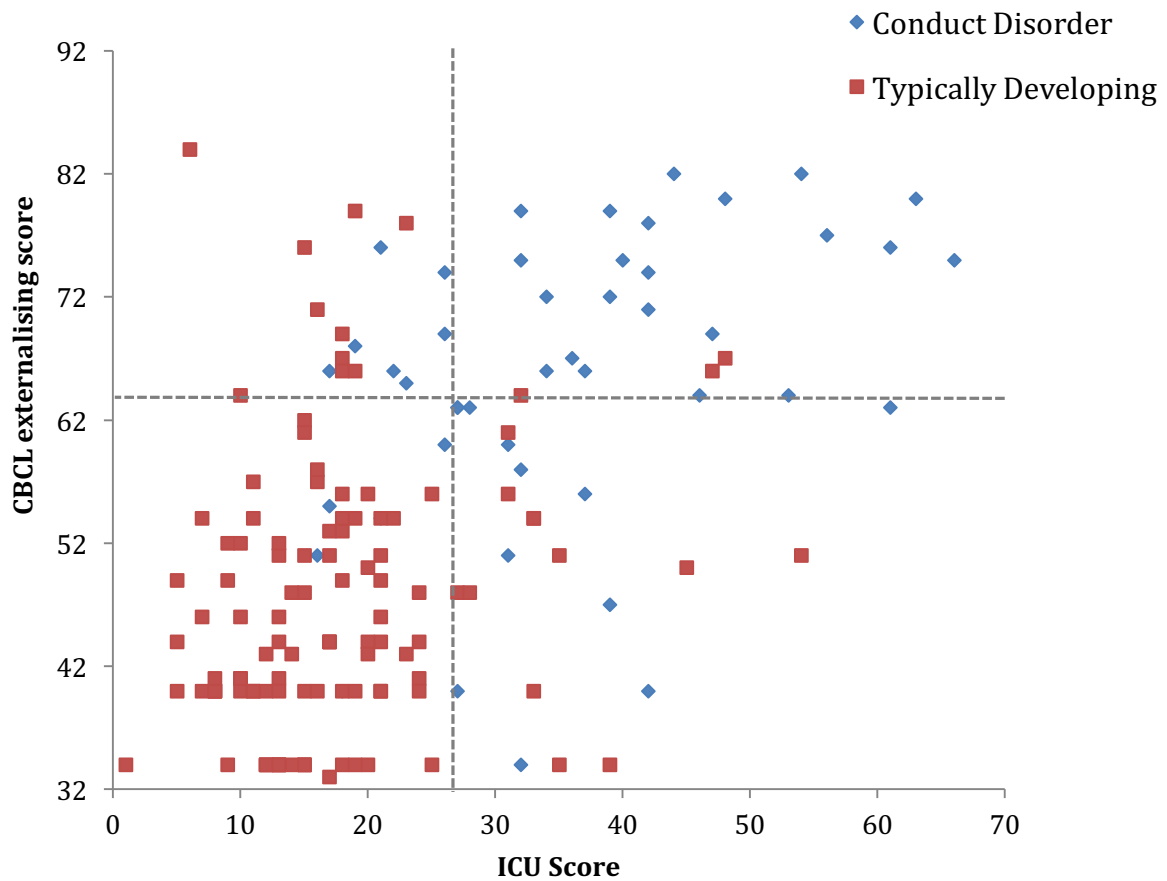


Figure 2.4. Correlation between CU traits and externalising behaviours. Horizontal line denotes clinical cut off for externalising behaviours at the  $t$  value of 63, whilst vertical line denotes clinical cut off for CU traits at a score of 27.

## 2.7 Summary

Typically developing children and adolescents show a range of CU traits and externalising behaviours, with some typically developing youths scoring in the clinical range for either (or, in the case of three youths in the current sample, both)

measures. Similarly, some youths with CD scored in the healthy range for either, or both, measures. This may be a true finding or could reflect a measurement error; some parents may have over- or under-exaggerated their child's behaviours.

Both groups showed positive correlations between CU traits and externalising behaviours, suggesting that these behaviours should not only be researched in the context of CD, but also in the general population. The following chapters will describe three experiments where CU traits and externalising behaviours have been investigated in typically developing youths.

## CHAPTER 3: EMOTION RECOGNITION IN YOUTHS WITHOUT ANTISOCIAL BEHAVIOUR AND VARYING LEVELS OF CALLOUS-UNEMOTIONAL TRAITS

### **3.1 Abstract**

Accurate recognition of emotional expressions is essential for normal social interaction. Among antisocial adults and youths, there is a negative association between psychopathic/CU traits and recognition of facial emotions. It is currently unclear if the same association can be seen in typically developing youths.

The current study included 110 typically developing children and adolescents (aged 9-18 years), who were presented with standardised facial expressions and labelled each emotion as sadness, happiness, anger, disgust, fear or surprise. The propensity to recognise sad and disgusted expressions was inversely correlated with the participant's level of CU traits reported by a parent/caregiver. There was no correlation between the level of externalising behaviours and the ability to accurately categorise emotions, and no suppressor effects between CU traits and externalising behaviours were found. This study thereby provided evidence for negative associations between CU traits and specific emotion recognition deficits, namely sadness and disgust, in typically developing youths.

### **3.2 Introduction**

Chapter 1 reviewed research showing that the levels of psychopathic and CU traits in antisocial populations have a large impact on many behavioural and neurobiological processes. However, to date only two studies have assessed emotion recognition and CU traits in youths without clinically recognised AB, with

inconsistent results. The current chapter will extend this previous research and report the results of a behavioural study examining the association between explicit emotion recognition and levels of CU traits in typically developing youths.

Adults and youths with psychopathy/psychopathic traits consistently show deficits in recognition of facial emotions (Dawel et al., 2012; Marsh & Blair, 2008; but see Gillespie et al., 2015; Gordon et al., 2004) and negative associations have been reported between psychopathic traits and emotion recognition in these populations (Bowen, Morgan, Moore, & Van Goozen, 2014; Hastings et al., 2008; Sharp et al., 2015). There are differing theories as to whether these deficits are pervasive across emotions or whether they are specific to certain emotions. Blair postulated that specific impairments in fear and sadness recognition are contributing factors in the development of psychopathy in adulthood (Blair, Peschardt, Budhani, Mitchell, & Pine, 2006; Blair, 1995). In contrast, Dadds et al., (2011) posited that psychopathy is associated with an attentional deficit to socially relevant cues, leading to a more pervasive emotion recognition impairment.

Whilst one meta-analysis found that AB (including psychopathy) was associated with specific deficits in fear, and to a lesser extent, sadness recognition (Marsh & Blair, 2008), a more recent meta-analysis found evidence for a pervasive deficit across all six basic emotions in psychopathic individuals (Dawel et al., 2012). However, it should be noted that the effect sizes for fear and sadness were larger than for the remaining four emotions. This might reflect that fear and sadness are more difficult to recognise than the other emotions.



When individual emotions were considered, psychopathy was associated with significantly poorer recognition of fear, happiness, sadness and surprise, but not of anger or disgust (Dawel et al., 2012). When only youths were considered, higher CU traits were associated with poorer recognition of anger, fear, and sadness (Dawel et al., 2012). Approximately half of these studies included forensic samples whilst the other half were community dwelling, but the authors did not investigate whether the origin of the sample moderated these results.

To date, there is limited research looking at CU traits and emotion recognition in typically developing adolescents. Similar to psychopathy research, studies investigating CU traits are divided as to whether specific or pervasive emotion recognition deficits are postulated. Blair and Coles (2000) assessed 55 early adolescents aged 11-14 years with the Emotion Hexagon task. In this task, participants identify facial expressions which are morphed between emotions (for example, one morphed stimulus might be 70% happy and 30% surprise). The authors reported that both CU traits and externalising behaviours were negatively correlated with sad and fearful recognition accuracy, but not with happy, angry, disgust or surprise recognition. A more recent study, which included 540 sixth and eighth grade children (mean age 12 years) reported a negative association between CU traits and self-reported emotion recognition skills (Ciucci, Baroncelli, Golmaryami, & Frick, 2015). CU traits were moderately inversely associated with happiness and fear processing (but only in sixth grade children; Ciucci et al., 2015).

Together these studies support the hypothesis of specific, rather than general, emotion recognition impairments. In contrast, another study posited that emotion

deficits in relation to CU traits were pervasive in children aged 10-12 years (Sharp et al., 2015). Sharp et al. reported a stronger association between CU traits and complex emotions (e.g. confusion, boredom) recognition compared to basic emotion recognition (e.g. fear, surprise). However, this study only used pictures of the eye region during this task, whilst Blair & Coles (2000) used whole faces. This could account for the discrepancy between findings, as participants may have found all emotion recognition more difficult when only eyes were visible. It should also be noted here that both Sharp et al. and Blair & Coles studies used adult faces. Whilst the children are clearly able to recognise adult emotions, children may be more adept at recognising emotions from their peers, and so future research could look at replicating these results with age appropriate stimuli.

The current study used the Emotion Hexagon task (Blair & Coles, 2000; Calder et al., 1996; Fairchild, Stobbe, van Goozen, Calder, & Goodyer, 2010; Fairchild et al., 2009) to examine the association between CU traits and recognition of facial emotions in typically developing youths. This study used morphed stimuli of the six basic emotions. These morphs are advantageous because the images are lifelike, control can be exercised over the intensity of the expression and research has found that the percentage that an expression is morphed is proportionate to the viewer's recognition accuracy (Blair, Morris, Frith, Perrett, & Dolan, 1999). Thus, ceiling effects should not be seen in the current, typically developing sample.

The Emotion Hexagon task was chosen as it has been used with youths with varying levels of CU traits in both community (Blair & Coles, 2000) and clinical samples (Fairchild et al., 2010, 2009; Sully, Sonuga-Barke, & Fairchild, 2015). In a

community sample, psychopathic traits were associated with specific deficits in the recognition of negative facial expression of fear and sadness (Blair & Coles, 2000), whilst in a clinical sample, CU traits were negatively associated with fear, sadness and surprise recognition (Fairchild et al., 2010, 2009).

In the current study, accuracy will be computed for 90:10 and 70:30 trials together and also for 70:30 trials on their own. The first measure will be computed in line with previous research (Blair & Coles, 2000; Fairchild et al., 2009), which grouped across these trials. However, this method may cause ceiling effects in typically developing youths and does not allow discernment into whether CU traits are associated with identification of less intense emotions. Therefore, additionally computing the accuracy of just the 70:30 trials will provide greater sensitivity and may reveal subtle associations (Adolphs, Baron-Cohen, & Tranel, 2002; Sharp et al., 2015).

As discussed in Chapter 1, there is mounting evidence that the unique variance associated with AB and CU traits exhibit different associations with behavioural and neurobiological indices (Crowe & Blair, 2008; Frick, 2012). These suppressor effects between AB and CU traits have been observed in both adult and youth populations with AB, but no study has looked at suppressor effects of CU traits and AB in typically developing youths until now.

Based on the above literature, it was hypothesised that high levels of CU traits would be negatively associated with deficits in emotion recognition (i.e. reduced accuracy) in typically developing youths, specifically fear and sadness. This is in

line with Dawel et al. (2012) and Blair and Coles (2000). Further, there was an investigation of whether emotion recognition in typically developing youths is partly influenced by independent, opposing contributions of externalising behaviours and CU traits, as observed in clinical and non-clinical samples (Seara-Cardoso, Sebastian, et al., 2015; Sebastian, Fontaine, et al., 2012).

### **3.3 Methods and Materials**

#### ***3.3.1 Participants***

A subsample of 110 children and adolescents aged 9-18 years took part in this study (see Table 3.6 for demographics). Power calculations ( $\beta = 0.2$ ) based on Blair and Coles (2000) found that a sample size of 45 participants would be sufficient to test the central hypothesis ([www.sample-size.net/correlation-sample-size](http://www.sample-size.net/correlation-sample-size); Hulley, Cummings, Browner, Grady, & Newman, 2013). This study was chosen as it used the Emotion Hexagon task in a community sample of youths. Participants were recruited from mainstream primary and secondary schools, youth groups and community centres in Birmingham (n=74) and Southampton (n=36). The Emotion Hexagon task was administered on a subsequent visit at the University.

*Table 3.6. Socio-demographic and mental health characteristics of the sample (n=110)*

Male gender (%)	45 (43.2%)
Age, mean (SD; range)	13.9 (2.7; 9-18)
IQ, mean (SD; range)	100.7 (10.8; 72-125)
ICU score, mean (SD; range)	17.9 (9.3; 1-48)
CBCL internalising, mean T score (SD; range)	50.4 (10.8; 33-62)
CBCL externalising, mean T score (SD; range)	46.1 (10.0; 33-62)

*Notes: CBCL = Child Behaviour Checklist; ICU = Inventory of Callous-Unemotional Traits; SD = standard deviation.*

### **3.3.2 Interview and Psychometric Measures**

As described in chapter 2, the participants underwent a detailed clinical interview (K-SADS-PL, Kaufman et al., 1996) and IQ test (WASI; Wechsler, 1999) to ascertain whether they were eligible to take part. Parents/caregivers also completed two questionnaires, which measured levels of CU traits (ICU; Frick, 2003) and externalising and internalising behaviours (CBCL; Achenbach & Rescorla, 2001).

### **3.3.3 Experimental Paradigm**

The Emotion Hexagon task was chosen due to its established sensitivity to subtle impairments in emotion recognition (Calder et al., 1996). Stimuli are taken from Ekman and Friesen's (1976) series and include six emotions (happiness, sadness, anger, disgust, fear and surprise), which are consistently recognised cross culturally. Face “JJ” (Ekman & Friesen, 1976) was used throughout this experiment,

and was chosen because all six photographs were of a consistent quality and had similar light levels.

Calder et al. (1996) used norms taken from Ekman and Friesen to arrange each of the six expressions into pairs of their maximum confusabilities. The mean percentage confusabilities for each pair of expressions were: happiness and surprise at 0.8%; surprise and fear at 5.8%; fear and sadness at 2.4%; sadness and disgust at 2.7%; and finally disgust and anger at 6.4%; Calder and colleagues then joined the ends of the sequence (anger and happiness) in order to create a hexagon (see Figure 1a). Five morphed images (90:10; 70:30; 50:50; 30:70; 10:90) were created for the six continua (happiness/surprise, surprise/fear, fear/sadness, sadness/disgust, disgust/anger and anger/happiness). Morphed faces were presented individually on a laptop monitor in a random order. Each face was presented for 5 seconds, after which the stimulus disappeared. Participants then had as long as they needed to select the label that best described the expression they saw. Labels included six options, and participants used the mouse to select their chosen option. No feedback was provided.

Participants completed six blocks, with the first block containing 15 trials and the subsequent five blocks each containing 30 trials. For each emotion, the total score ranged from 0 to 22. This task took between 20 – 30 minutes to complete. Some participants were given a short break in the middle of the task if they became restless.

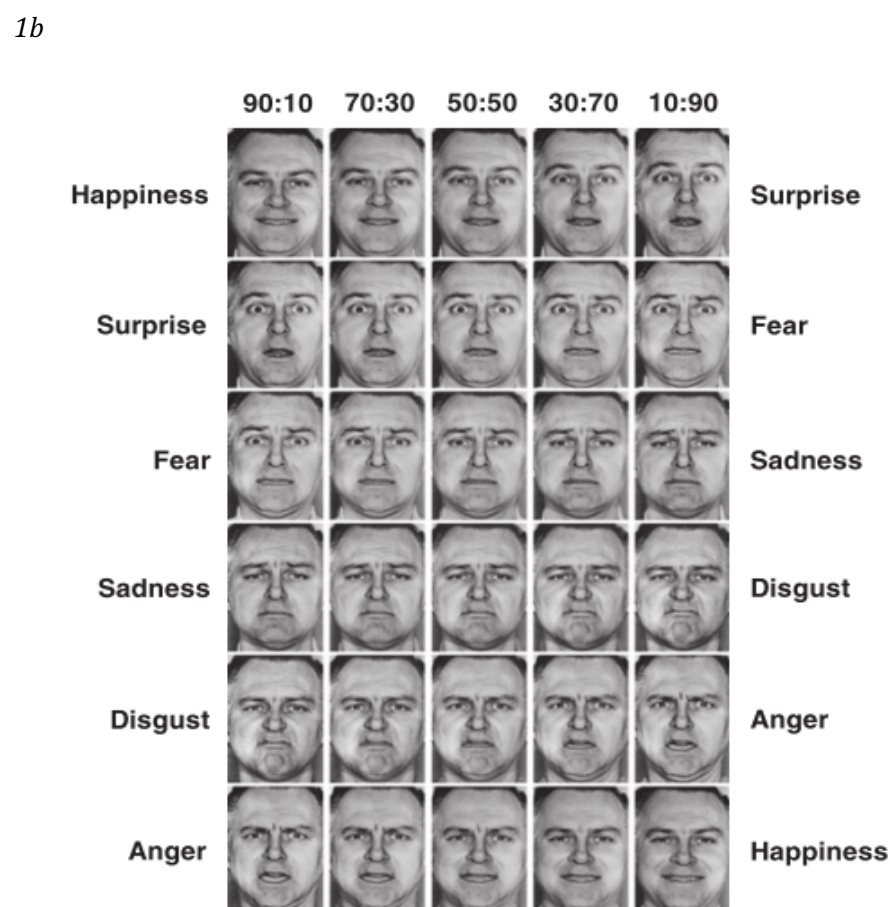
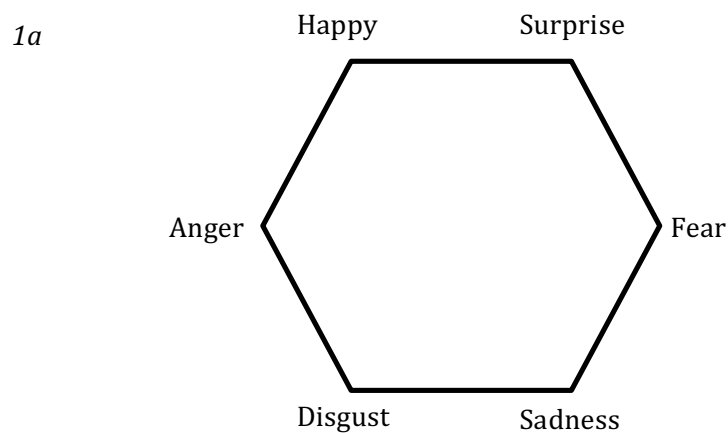


Figure 3.5. 1a: A pictorial representation of the Emotion Hexagon Task. Emotions which are most likely to be confused were placed adjacent on the hexagon. 1b: (taken from Fairchild et al., 2009). Facial expressions used in the task. From top to bottom, the continua are: Happiness to Surprise; Surprise to Fear; Fear to Sadness; Sadness to Disgust; Disgust to Anger; and Anger to Happiness. From left to right, the columns show: 90%:10%; 70%:30%; 50%:50%; 30%:70%; and 10%:90% morphs.

### **3.3.4 Data analyses**

For accuracy data, trials were marked as correct if the participant chose the emotion with the greatest weight (90% or 70%) and for each emotion a score (between 0 and 22) was computed. The accuracy data were not normally distributed (according to Shapiro–Wilk tests of normality; see Appendix 3.1) and followed a negatively skewed distribution. These data could not be transformed into a normal distribution using a log transformation, so, in line with Fairchild et al (2009), these data were analysed using non-parametric alternatives. Two-tailed Mann Whitney U tests were applied to investigate potential site and gender differences between emotion recognition accuracy and the six emotions were individually correlated to the psychometric test scores.

The two psychometric measures were mean scaled in SPSS. Partial correlations were then computed between the six emotions and psychometric measures whilst accounting for age, IQ, site and gender. Following this, partial correlations were computed for all the aforementioned statistical tests to account for potential suppressor effects between CU traits and AB. Finally, the same partial correlations were rerun for the 70:30 continua only to assess whether a stronger effect was seen in less obvious emotions. All analyses were performed using IBM SPSS Statistics for Windows (Version 22).

To assess whether results supporting the null hypotheses were indeed an indicator of non-significance, rather than a lack of power, Bayes Factors for regression were carried out on all results. This measure is a form of statistical inference in which one model is directly compared to another. Bayes Factors fluctuate between 0 and

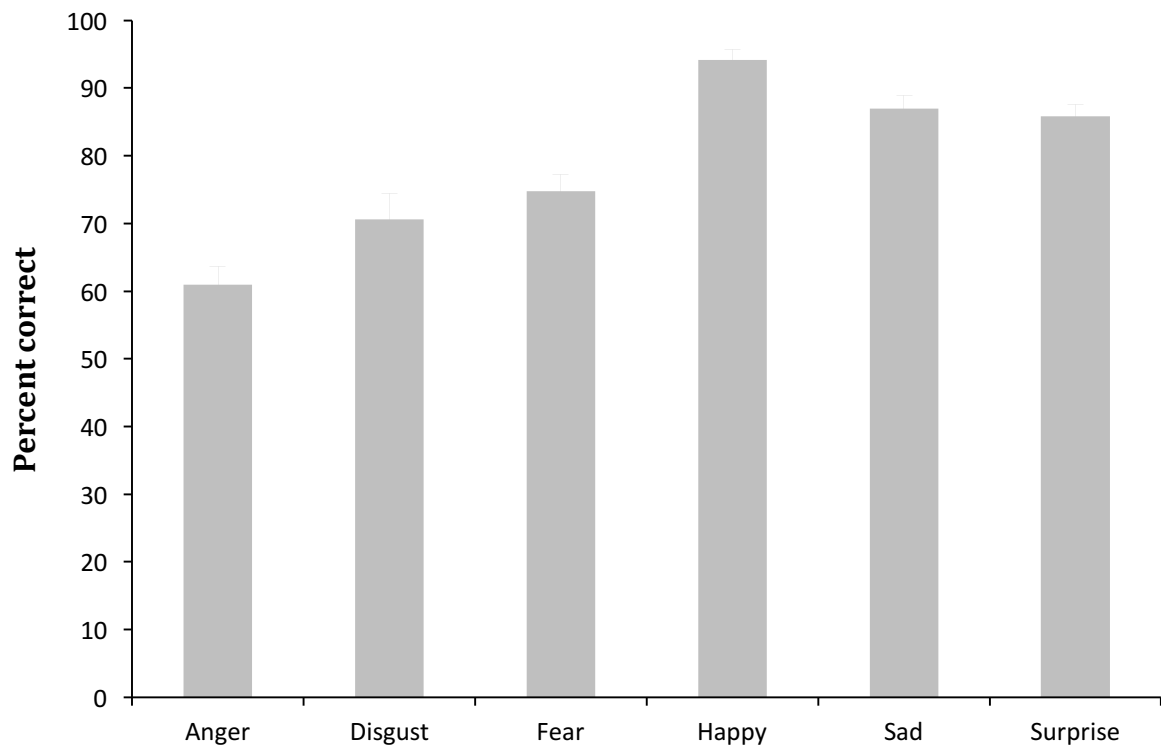


$\infty$  where values less than 1/3 indicate support for the null hypothesis, and values  $>3$  indicate support for the experimental hypothesis. This is more valuable than traditional significance testing using p values. This is because inferring significance from the p value (Fisher, 1935) involves testing a model for the null hypothesis alone, which is then typically used to compare both the null and experimental hypotheses. An online tool was used to calculate Bayes Factors for all analyses ([http://www.lifesci.sussex.ac.uk/home/Zoltan\\_Dienes/inference/Bayes.htm](http://www.lifesci.sussex.ac.uk/home/Zoltan_Dienes/inference/Bayes.htm)). Blair and Coles (2000) correlations were inputted as a plausible maximum effect.

### **3.4 Results**

#### **3.4.1 Site & Gender Effects**

There were no significant differences between sites for IQ ( $t(108) = .37, p = .71$ ), gender ( $X^2(1, N = 110) = 3.6, p = .06$ ), age ( $t(108) = .452, p = .65$ ), CU traits ( $U = 1295.50, N_1 = 69, N_2 = 35, p = .54$ ), CBCL externalising ( $U = 963.00, N_1 = 67, N_2 = 26, p = .43$ ) or overall accuracy ( $U = 1150.00, N_1 = 74, N_2 = 36, p = .25$ ). Males and females did not differ for IQ ( $t(108) = -1.7, p = .10$ ), age ( $t(108) = -.20, p = .85$ ), CU traits ( $U = 1393.00, N_1 = 59, N_2 = 45, p = .67$ ), CBCL externalising ( $U = 879.50, N_1 = 52, N_2 = 41, p = .15$ ) or overall accuracy ( $U = 1597.50, N_1 = 65, N_2 = 45, p = .41$ ). Hence, all participants were considered together in the analyses.



*Figure 3.6. Mean accuracies (90:10 and 70:30 trials) for the six emotions.*

### **3.4.2 Mean accuracy**

Mean accuracy across 90:10 and 70:30 trials for each emotion is presented in Figure 3.6. Spearman's rank correlation coefficients between ICU, both subscales of the CBCL and age, IQ, overall emotion recognition accuracy and individual emotion recognition accuracies are reported in Table 3.7. Externalising behaviours were positively correlated with both CU traits and internalising behaviours, whilst internalising behaviours were negatively correlated with anger recognition. The confusion matrix for this task is reported in Appendix 3.4. When controlling for multiple comparisons, none of these correlations were significant.

*Table 3.7. Zero-order correlations between psychometric measures and overall emotion recognition accuracy.*

	1	2	3
1. CU traits			
2. Internalising behaviours	.17		
3. Externalising behaviours	.34**	.55**	
4. Age	-.03	.001	-.09
5. IQ	-.01	-.10	-.02
6. Overall Accuracy	-.17	-.11	-.06
7. Anger	-.01	-.27**	-.001
8. Disgust	-.19*	-.13	-.05
9. Fear	-.03	-.02	-.08
10. Happy	.01	-.03	-.03
11. Sad	-.05	-.07	-.03
12. Surprise	-.05	-.01	-.02

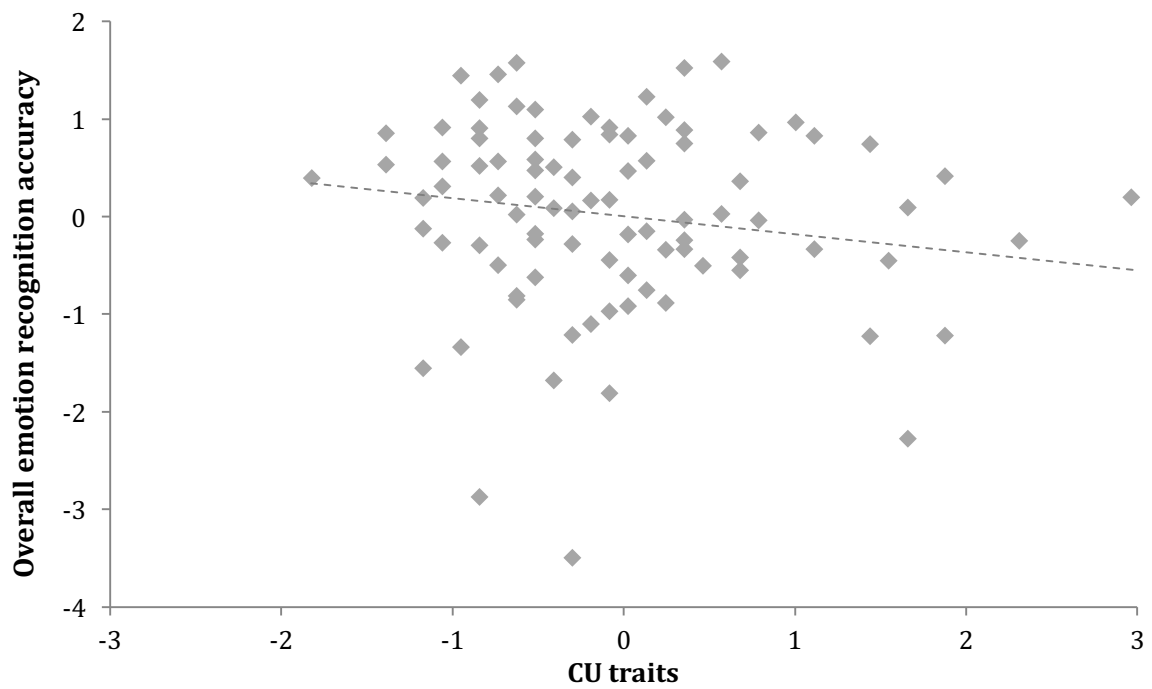
\*  $p < .05$ ; \*\*  $p < .01$

### **3.4.3 Partial Correlations**

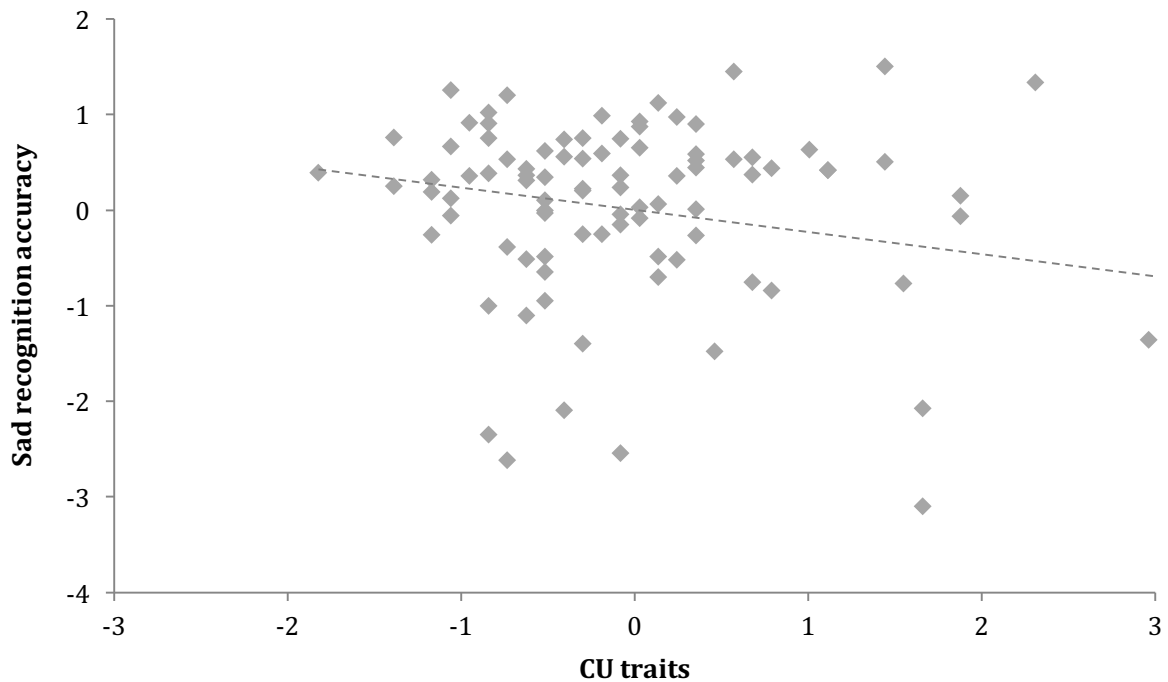
Correlations between emotion recognition and CU traits, when controlling for age, IQ, site and gender, were computed. CU traits were negatively correlated with

sadness recognition ( $r = -.25$ ,  $p = .01$ ,  $BF = 11.11$ ), disgust recognition ( $r = -.20$ ,  $p = .05$ ,  $BF = 3.12$ ) and trended towards a negative association with overall accuracy ( $r = -.16$ ,  $p = .05$ ,  $BF = 2.56$ ). These correlations did not survive an adjustment for multiple comparisons. None of the remaining four emotions reached significance with CU traits (see Appendix 3.2). There were no correlations between externalising behaviours and overall accuracy or any of the six emotions (see Appendix 3.2).

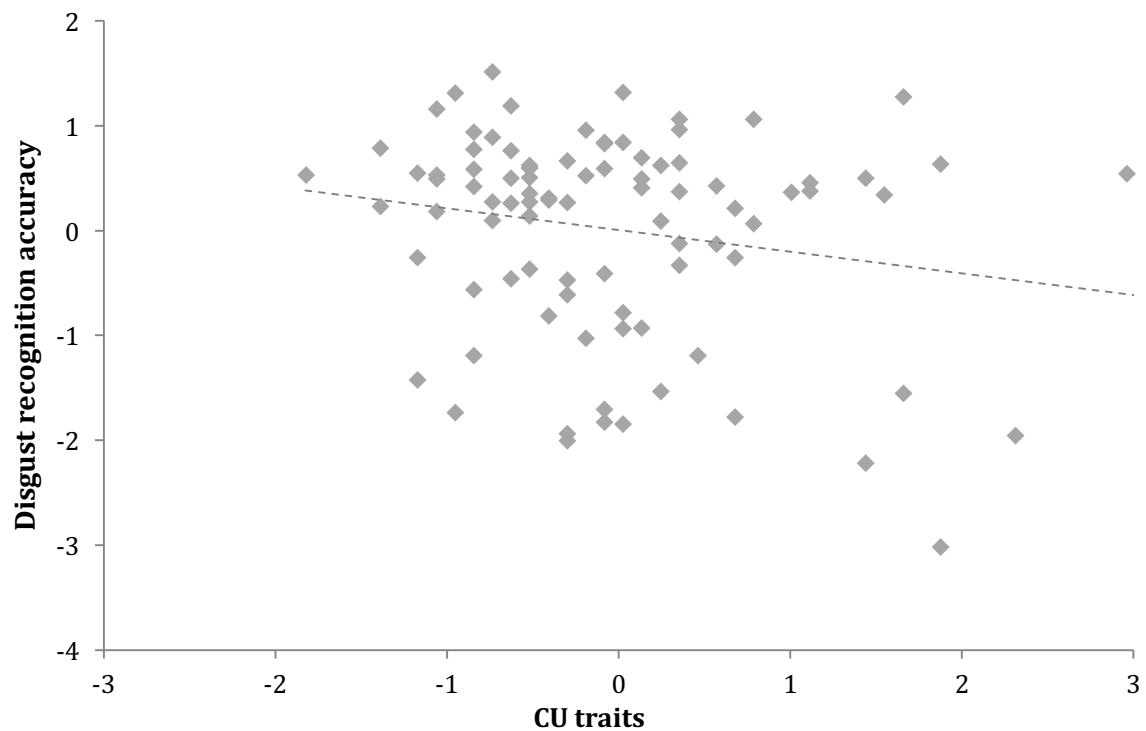
Next, suppressor effects between CU traits and externalising behaviours were examined by including those variables in turn as additional covariates. When controlling for age, IQ, site, gender, and externalising behaviours, CU traits were more strongly correlated with overall accuracy ( $r = -.20$ ,  $p = .03$ ,  $BF = 3.72$ ) which can be pictured on Figure 3.7, sad ( $r = -.25$ ,  $p = .02$ ,  $BF = 10.54$ ; Figure 3.8) and disgust ( $r = -.23$ ,  $p = .03$ ,  $BF = 5.86$ ; Figure 3.9). These correlations remained significant at  $p < .05$  when only 70:30 trials were considered (see Appendix 3.3), although none of these correlations survived adjustment for multiple comparisons. There were no correlations between CU traits and any of the other four emotions, or between externalising behaviours and any of the six emotions. No further correlations reached significance when only 70:30 trials were considered.



*Figure 3.7. Partial correlation between CU traits and overall emotion recognition accuracy. The y axis is standardised for age, IQ, gender, site and externalising behaviours.*



*Figure 3.8. Partial correlation between CU traits and sad recognition accuracy. The y axis is standardised for age, IQ, gender, site and externalising behaviours.*



*Figure 3.9. Partial correlation between CU traits and disgust recognition accuracy. The y axis is standardised for age, IQ, gender, site and externalising behaviours.*

### 3.5 Discussion

This study examined the association between CU traits, externalising behaviours and explicit emotion recognition in typically developing youths. It was predicted that high levels of CU traits would be inversely associated with recognition of fear and sadness. Secondly, we expected to find suppressor effects between CU traits and externalising behaviours in relation to emotion recognition. The current findings, which relate to a large sample of healthy adolescents, found negative correlations between CU traits and overall emotion recognition, sad recognition and disgust recognition, when controlling for gender, age, IQ and externalising behaviours. Whilst the fact that the negative correlation between overall emotion

recognition and CU traits could be considered to support a *general* impairment in emotion processing with respect to CU traits, this correlation seems to be mostly driven by the negative associations between CU traits and sad and disgust recognition. As only two out of the six emotions were found to have significant correlations with CU traits when considered alone, this study could be considered instead to support the hypothesis that only *specific* emotions recognition impairments are associated with CU traits.

The current findings are consistent with previous literature examining youths without AB (Blair & Coles, 2000; Ciucci et al., 2015) and youths with AB (Fairchild et al., 2010, 2009; Woodworth & Waschbusch, 2008). Behavioural deficits associated with CU traits may reflect impaired neural functioning; for example, lesions to the amygdala are associated with reduced ability to recognise sad stimuli (Adolphs et al., 1999; Cristinzio Perrin, Sander, & Vuilleumier, 2007). However, a deficit in fear recognition is more strongly recognised in subjects with amygdala lesions (Adolphs et al., 1999; Cristinzio Perrin et al., 2007), which was not found here.

Interestingly, one study (which included 50 patients with neurodegenerative illnesses) found that grey matter tissue content in the right inferior temporal gyrus (Brodmann's area 20 extending into 21) and the right superior temporal gyrus were negatively correlated with sadness recognition accuracy (Rosen et al., 2006), over and above the other five basic emotions. Rosen et al. concluded that the right temporal neural network is critical for recognition of sad faces; thus,

future research could assess whether functionality in this network is negatively associated with CU traits.

Disgust recognition is associated with activity in the insula (Adolphs, 2002; Papagno et al., 2016), and a recent study found that, in a large sample of youths with AB, CU traits were negatively associated with functional connectivity between the ACC and anterior insula (Yoder, Lahey, & Decety, 2016), whilst observing visual stimuli depicting others' pain. Together, cross modal evidence from the current study and the studies discussed above suggests that activity in the insula may be negatively associated with CU traits, which would be interesting to explore further in healthy youths.

It was hypothesized that the current study would find a negative association between fear recognition accuracy and level of CU traits. One reason that this was not observed here could be that TD youths have developed compensatory mechanisms in order to correctly perceive and recognise fear. I believe it would have been informative to record eye gaze when participants were viewing the stimuli to see whether, like Dadds et al. (2006), those with higher CU traits focused on the eye regions less than those with lower CU traits. On the other hand, it could be that those participants included here without AB but with HCU traits have learned to focus on the eye regions in order to recognize emotions. Future research could compare those with AB/HCU, AB/LCU, without AB/HCU and without AB/LCU to see if AB or level of CU traits is associated with gaze to the eye region during emotion recognition.



Unlike Blair and Coles (2000), the current study did not find any association between emotion recognition accuracy and externalising behaviours. One reason for this could be due to the stringent exclusion criteria applied in this study. Participants were only included if they achieved a score less than 63 on both the internalising and externalising subscales of the CBCL, as this is considered below the clinical threshold. However, Blair and Coles did not impose any such restrictions, meaning that their study could have had a greater amount of variability within their sample.

The current study did not find any evidence for suppressor effects between CU traits and externalising behaviours. This could again be due to the fact that our typically developing sample did not show a sufficient range of externalising behaviours. Similarly, Gillespie, Rotshtein, Wells, et al. (2015), who looked at emotion recognition in a healthy adult sample with a range of psychopathic traits, did not find suppressor effects between primary and secondary psychopathy. Alternatively, the absence of suppressor effects may reflect methodological differences between the present study and previous studies, which mostly used functional imaging paradigms (Hicks & Patrick, 2006; Hyde et al., 2014; Lozier et al., 2014; Seara-Cardoso, Sebastian, et al., 2015; Sebastian, McCrory, et al., 2012).

Blair and Coles (2000) found that CU traits and externalising behaviours were both negatively correlated with anger, sad and fearful emotion recognition in healthy youths, whilst youths and adults with psychopathic traits are deficient in fear recognition (Dawel et al., 2012). The current study did not find associations between fear or anger processing and CU traits; indeed, as Bayes Factor analyses

were below 1/3 for the correlations between CU traits, externalising behaviours and fear recognition (see Appendix 2), there is sufficient evidence for the null hypothesis. There may be several reasons why my study conflicts with these prior findings. Firstly, Blair and Coles used a teacher-rated measure of CU traits and externalising behaviours, whilst in this study, parent rated measures were used. Parents tend to report their offspring as having lower CU traits compared to the teacher's report (Docherty et al., 2016), and so Blair and Coles may have had a different spread of scores in their sample compared to the current study.

Another consideration is that despite the fact that Blair and Coles (2000) recorded IQ scores, these were not taken into account for the main correlations. When the authors controlled for IQ in a post-hoc group comparison (HCU traits vs LCU traits), a significant difference was found in emotion recognition for sadness only. This suggests that, like my study, sadness has the strongest negative association with CU traits.

I found a moderate correlation between age and emotion recognition accuracy, which is consistent with previous research (Lawrence et al., 2015). This suggests that future research should take account of age when using the Emotion Hexagon task. IQ was not correlated with emotion recognition, suggesting that this is not a factor that needs to be accounted for. This is in contrast to Blair and Coles (2000), who found that their findings changed once they accounted for IQ. Many studies have compared clinical populations to typically developing populations using the Emotion Hexagon task (e.g. Fairchild et al., 2010, 2009). As children and adolescents with CD often have lower IQs than typically developing samples

(Fairchild et al., 2009, 2010), it should be further investigated whether IQ does indeed modulate emotion recognition.

Varying levels of CU traits may only be associated with poorer emotion recognition when stimuli are presented at lower intensities (Hastings et al., 2008) or for shorter periods of time (Vasconcellos et al., 2014). However, when only emotions at 70% intensity were considered in the current study, the ensuing negative correlations for sadness and disgust were no stronger than when 90:10 and 70:30 trials were considered together. Further, no correlations for the other four emotions were found in 70:30 trials. These results directly conflict with the above postulation, and instead suggest that the previous paradigms used by Hastings et al. and Vasconcellos et al. may be less sensitive than the Emotion Hexagon task used here.

Deficits in sadness recognition are linked not only to amygdala deficiencies but also to functional connectivity deficits in the right temporal neural network (Rosen et al., 2006). This suggests that CU traits may be associated with more pervasive deficits in neural functioning than previously considered. The fact that the participants in the current sample do not present with clinically recognised disorders suggests that typically developing youths with higher levels of CU traits may have compensatory mechanisms to allow them to function within society. Another possibility is that as only small to moderate negative correlations between sad and disgust recognition and CU traits were found in the current study, these emotion recognition deficits are not severe enough to negatively impact on functioning. It would be interesting to see if sad and disgust recognition deficits in

typically developing youths predicts later aggressive behaviours, or whether these youths with higher levels of CU traits present with more covert delinquent acts than those with lower levels of CU traits.

Despite the fact that this study had a good range of levels of CU traits, a potential limitation is that my measures of CU scores are lower than those reported in control groups in other literature (e.g. De Brito et al., 2009). Whilst many studies take the ICU from two informants, and then use the highest rating as the participant's score (e.g. De Brito et al., 2009), I only collected the ICU from a parent. This is because often only one parent was available, and FemNAT-CD did not work closely with schools in order to get a teacher-rated ICU. This may mean that my ICU scores may be less valid than other studies. Another limitation of the current study is the interpretation of the results, which should be considered with care. Whilst the forced choice paradigm provides a quantifiable measure of emotion recognition ability, it is not known whether consistently misreading one emotion for another does in fact negatively influence one's social communicative ability. Future research could look into the ecological validity of this measure, to assess whether emotion recognition abilities are associated with social communication.

There were various strengths to the current study. First, a thorough clinical assessment (i.e. interview and self-report) process was undertaken in order to ensure that all participants were typically developing. I recruited a large number of participants, which was substantial enough to ensure sufficient power. Studies which also used the Emotion Hexagon task (Blair & Coles, 2000; Fairchild et al.,

2010, 2009) found significant results in groups which were half the size of my sample. Second, both p values and Bayes Factors were reported, which allows one to differentiate between non-significant correlations where there is insufficient power and those where the null hypothesis should be accepted.

The stimuli used in the current experiment were taken from Ekman and Friesen's (1976) series. The choice of stimuli was limited by stipulations by the established consortium, otherwise I would have preferred to use child models. Children may find it easier to recognise emotions in their peers than in adults. It might also be interesting to run the task with both adult and child faces, to see whether there is an interaction between the age of the model (i.e. adult or child) and emotion recognition accuracy; for example, children may be less accurate at recognising disgust in adults, as this is not a common expression for adults to wear. However, children may come across more disgusted expressions in their peers, for example when watching another child try a new food.

It would be interesting to investigate the distractability of typically developing youths with a range of CU traits. Hodson, Lavie & Viding (2014) found that, during an attention task, youths with AB/HCU traits were distracted by emotional faces, whilst youths with AB/LCU traits were not distracted by emotional faces. This suggests that those with AB/HCU traits were able to filter out irrelevant information whilst those with AB/LCU traits were unable to ignore this information. This study looked at attentional capture in youths with AB, and so it would be interesting to see if the same effect is measurable in TD youths. It could be that the hypersensitivity to emotion in youths with AB/LCU is a factor in

explaining their antisocial behaviour, and therefore one would expect that TD youths with LCU traits would not show this hypersensitivity. If they did show this hypersensitivity, it could be that they have developed coping mechanisms which prevent against AB.

Future research should consider why sadness and disgust recognition is influenced by level of CU traits. There may be a fundamental difference in the way that sadness and disgust are processed compared to the other four basic emotions. Adolescents without AB but with high levels of CU traits could be trained on sadness/disgust recognition, to assess whether this has an impact on level of CU traits. An investigation into whether an increase in recognition accuracy for these emotions is associated with a reduction in the level of CU traits warrants further research.

Future research could also investigate whether alexithymia modulates the associations between CU traits and emotion recognition. Previous research has found that alexithymia was associated with difficulties in detection of anger, sadness and fear in 128 adults (Prkachin, Casey & Prkachin, 2009). Alexithymic individuals have difficulty describing emotions and are poor at communicating emotions to others (McDonald & Prkachin, 1990). Alexithymia and primary psychopathy, which is roughly equivalent to CU traits, are not positively associated (Lander, Lutz-Zois, Rye & Goodnight, 2012) and therefore may have independent relationships with emotion recognition. Future research could, therefore, include a measure of alexithymia to assess whether alexithymia modulates the association between CU traits and emotion recognition.

In conclusion, this study found that sadness and disgust recognition accuracies are negatively correlated with CU traits in typically developing youths, whilst general emotion recognition abilities are positively associated with age. This implies that amygdala processing, which is associated with sadness recognition, and insula processing, which is associated with disgust recognition, may be dysfunctional in youths with higher levels of CU traits.

Our results are consistent with prior studies on adolescents with AB (Fairchild et al., 2010; Woodworth & Waschbusch, 2008) and without AB (Blair & Coles, 2000), who found no associations between CU traits and accuracy for anger, happiness and surprise. The small to medium effect size found in the present correlations between CU traits and sadness and disgust recognition are also consistent with previous literature (e.g. Dawel et al., 2012). In addition, the accuracies for each emotion reported in the current study follow a similar pattern to Fairchild et al.'s control group, suggesting that the current results are valid and reliable.

The current study did not find evidence for associations between CU traits or externalising behaviours and the four remaining basic emotions (happiness, surprise, fear and anger) were found. There was a negative association between CU traits and general emotion recognition, but this was mostly generated by significant associations between CU traits and sad and disgust recognition.

This study is novel in that it is the first to suggest that the hypothesis, purported by Blair (Blair et al., 2006; Blair, 1995), that CU traits are associated with specific emotion recognition deficits, rather than a general impairment in emotion recognition, can be extended to typically developing youths. The reported

behavioural associations between emotion processing and CU traits may reflect neural differences associated with CU traits (Adolphs et al., 2002; Gordon et al., 2004; Papagno et al., 2016; Seara-Cardoso & Viding, 2015; Yoder et al., 2016), and so the following chapter will describe the neural activation of a similar population whilst undertaking a subliminal emotion processing task.



## CHAPTER 4: NEURAL RESPONSES TO SUBLIMINAL EMOTIONAL FACES IN YOUTHS WITHOUT ANTISOCIAL BEHAVIOUR AND VARYING LEVELS OF CALLOUS-UNEMOTIONAL TRAITS.

### **4.1 Abstract**

Recent neuroimaging studies with children and adolescents with CD reported negative associations between CU traits and neural activation during emotion processing. Studies with community samples of adults have also reported negative correlations between psychopathic traits and activation in the amygdala and insula when viewing fearful and angry faces. The current study is, to my knowledge, the first to investigate whether these associations between CU traits and emotion processing are present in typically developing youths. A subliminal face processing task, in which fearful and angry faces were presented for 17ms followed by backwards masking of a calm face, was employed to assess 63 typically developing youths aged 9-18 years. Partial correlations accounting for age, IQ and gender found negative associations between CU traits and bilateral amygdala and insula activity during fear processing, whilst a positive correlation was observed between externalising behaviours and left amygdala response to angry faces in males. No suppressor effects were found. This supports evidence that CU traits are associated with reduced activity in emotion processing brain circuits in typically developing populations as well as in clinical populations. This provides further evidence that CU traits in typically developing youths are associated with emotion processing deficits.

## **4.2 Introduction**

The previous chapter examined the association between CU traits and behavioural measurements of emotional processing. This chapter will focus on threatening emotions, namely fear and anger, and examine neural response to these emotions presented subliminally. As stated earlier in this thesis, conscious emotion processing recruits brain areas including the lateral geniculate nucleus, visual cortex and amygdala, whilst subliminal emotion processing recruits a different neural network, namely the superior colliculus, the pulvinar nucleus and the amygdala (Pessoa & Adolphs, 2010).

Whilst fear is construed as an indirect threat, anger is considered a direct threat (Blair, 2012). Previous literature has focussed on neural activity associated with fear processing in psychopathy, as there is mounting evidence that fearful facial expression processing deficits are associated with amygdala dysfunction in psychopathic individuals (Blair, 2007). Amygdala activity during processing of angry faces was also reported to be negatively associated with CU traits in adults (Waller et al., 2016). This chapter will investigate whether brain responses to masked subliminal threatening emotional faces are associated with varying levels of CU traits in typically developing youths.

In adult forensic samples, there is ample evidence of a negative association between CU traits and neural activity to fearful faces (Seara-Cardoso & Viding, 2015). Decety et al. (2014) found that activation in the left insula, right vmPFC, OFC and right supplementary motor area in adults were negatively correlated with the primary factor of psychopathy (roughly equivalent to CU traits) while viewing

dynamic facial expressions of fear, sadness, happiness and pain. Similarly, CU traits in youths with AB were associated with reduced amygdala, ACC, insula, IFG and vmPFC activity during conscious fear processing (for a review see Baker, Clanton, Rogers, & De Brito, 2015; see also Jones et al., 2009; Marsh et al., 2008).

Research using subliminally presented emotions found similar results. Subliminal stimuli are presented for a very short time (e.g. 17ms), and are below participants' threshold for conscious perception. Subliminally presented emotions recruit a different neural pathway to supraliminal presented emotions, which was described earlier in Chapter 1. A negative association between CU traits and amygdala reactivity to fearful facial expressions was observed in youths with AB (Viding et al., 2012). In sum, activation in the amygdala, ACC and insula is consistently negatively correlated with the primary facet of psychopathy/CU traits when processing fearful faces subliminally and supraliminally.

To date, substantially fewer neuroimaging studies on psychopathy and CU traits have considered brain responses to angry faces. One study with an adult clinical sample reported a negative correlation between activation in the right amygdala in response to angry faces and the primary facet of psychopathy, whilst activation in the right ACC was negatively correlated with the antisocial behaviour facet (Dolan & Fullam, 2009). Reduced OFC response to angry faces was reported in a small group of adults with intermittent explosive disorder and high psychopathy scores compared to controls (Coccaro, McCloskey, Fitzgerald, & Phan, 2007). The OFC is thought to be involved in other behaviours (including instrumental learning) which are impaired in individuals with psychopathy (Lapierre, Braun, & Hodgins,

1995). Taken together, this research suggests that response in the amygdala and OFC is reduced in adults with high levels of the primary facet of psychopathy (roughly equivalent to CU traits) when viewing angry faces.

Whilst these studies are informative, a clear limitation is that the authors focussed on participants at the extreme end of the psychopathy and CU traits continua (e.g., clinical or forensic samples). This does not address whether CU traits are associated with altered brain function in healthy populations (Seara-Cardoso & Viding, 2015). Despite evidence that psychopathic traits are present to differing degrees across the general population (Hare & Neumann, 2008), few studies have examined whether these patterns of associations between psychopathic/CU traits and brain response to facial expressions extend to community samples. This emerging body of literature concerning psychopathic/CU traits, where participants are representative of the general population and the data is analysed continuously, is discussed next.

The neuroimaging literature suggests that the findings in community samples with varying levels of psychopathic traits mirror those reported in forensic and clinical (Seara-Cardoso & Viding, 2015). For example, Carré et al. (2013) contrasted fearful faces > shapes and angry faces > shapes during a conscious emotion recognition task. Adults saw three faces and matched the emotion of a target face with the correct emotion displayed on one of two faces presented simultaneously.

Amygdala response to fearful facial expressions was *negatively* associated with the primary facet of psychopathy, whereas activation in the amygdala to angry expressions was *positively* associated with the secondary facet of psychopathy.

Gordon et al. (2004) found that university students with high levels of psychopathic traits (n=10) present reduced activation in frontal areas and the amygdala when viewing fearful faces compared to low scorers (n=10). However, it should be noted that the sample size in this study was small and effect sizes were weak. In a large community sample of adults (n=406), psychopathic traits in men (n=193) were negatively associated with amygdala reactivity to angry faces, whilst no relationship was observed in women or when either gender viewed fearful faces (Waller et al., 2016).

When externalising behaviours were considered, a positive association between bilateral amygdala activity to angry faces and self-reported AB was reported for men, whilst no association was reported for women (Waller et al., 2016). The OFC is known to be activated by angry faces (Blair et al., 1999) and reactivity of the OFC to angry faces was negatively related to aggression in a community sample of adults (Beyer, Münte, Göttlich, & Krämer, 2015). Interestingly, Seara-Cardoso et al. (2016) found negative correlations between both facets of psychopathy and amygdala and anterior insula activity for all conditions (sad, fearful, angry, happy and neutral) > baseline, but not for emotional faces > neutral faces. This suggests that neural activity to faces themselves, rather than the emotions, may be the source for differences observed along the psychopathic/CU traits continua.

In sum, previous literature suggests that CU traits are negatively associated with brain activity in the amygdala during processing of fearful and angry faces, a pattern of result that is strikingly consistent despite differences in paradigms and data analytic strategy. By contrast, the evidence for externalising behaviours has

been less consistent (Waller et al., 2016). Studies reported both positive and negative associations between externalising behaviours and brain activity in the amygdala during the processing of fearful and angry faces. This could be due to the wide range of externalising behaviours; one person who shows overt aggressive behaviours is not necessarily equivalent to one who steals covertly, but both may score equally on a measure of externalising behaviours. The heterogeneity within externalising behaviours renders it a less favourable subtyping approach within clinically recognised behavioural disorders than CU traits (Frick et al., 2014).

Suppressor effects have been found in previous neuroimaging studies with both adults and youths with AB (e.g. Seara-Cardoso, Viding, et al., 2015). One study with male prisoners found that the primary facet of the PCL-R (roughly equivalent to CU traits) was negatively associated with amygdala activation, whereas the secondary facet was positively associated with amygdala activation (Hyde et al., 2014). Similarly, amygdala responses to fearful faces and stimuli eliciting empathy were negatively correlated with CU traits and positively correlated with AB when both variables were modelled simultaneously in youths with AB (Lozier et al., 2014; Sebastian, McCrory, et al., 2012).

More recently, suppressor effects were reported in community samples of adults. In particular, Seara-Cardoso, Viding, et al. (2015) found that after controlling for the other variable, higher CU traits were related to *reduced* neural responsivity to others' pain, while higher AB traits (roughly equivalent to externalizing behaviours) were associated with *increased* neural responsivity in the bilateral anterior insula, inferior frontal gyrus, ACC and midcingulate cortex. Finally, Waller

et al. (2016) found that suppressor effects did not generalise across gender and were only present for certain facial expressions. Specifically, the researchers reported a positive association between externalising behaviours and amygdala response and a negative association between CU traits and amygdala activity in men during processing of angry faces. However, these suppressor effects were not observed for females, or when males viewed fearful faces. I will explore suppressor effects in the current study, to assess whether the opposing relationships between externalizing behaviours, CU traits and amygdala activation during emotion processing are also present in TD youths.

Chapter 1 discussed how subliminal and supraliminal emotion processing recruits different brain areas (see Section 1.5.3). Sylvers et al. (2011) posited that subliminal emotion processing impairments are characteristic of CU traits, and that threat processing deficits in youths with HCU traits are not a product of overt attentional factors. Evidence suggests that there is a temporal double dissociation between supraliminal versus subliminal perception of fear (Liddell, Williams, Rathjen, Shevrin, & Gordon, 2004). Brain activity in response to subliminal fearful faces enhanced the N2 “excitatory” component of an event-related potential, which is believed to represent automatic aspects of face processing. Distinct to this, supraliminal fear perception was accompanied by enhanced responsivity to the later P3 “inhibitory” component, which is implicated in attention and integration of emotional processes (Liddell et al., 2004). The previous chapter did not find associations between CU traits and conscious recognition of fear and anger, suggesting that overt attentional factors are unlikely to be associated with CU

traits in typically developing youths. Therefore, a subliminal emotion processing task (rather than a supraliminal task requiring attention) may be more sensitive to neural correlates in this specific population.

Currently, no fMRI study has looked at the association between CU traits and brain response to emotional faces in a sample of typically developing youths.

Furthermore, no research has yet investigated suppressor effects in community samples of youths without AB. In the present study I used a subliminal emotion processing task involving fearful, angry and calm faces to address this gap in the literature. Fearful and angry emotions were chosen because of substantial evidence from clinical, forensic, and community samples of adults and youths indicating that psychopathic and CU traits are associated with impaired processing of facial expressions conveying threat (Dawel et al., 2012). Calm (rather than neutral) faces were used as a baseline measure of brain activity, as children with higher levels of CU traits may infer hostility from neutral faces (Dadds et al., 2006).

Four regions of interest (ROIs), comprising of the bilateral amygdala, insula, OFC and ACC, were investigated here. These regions are robustly activated by subliminal faces (Brooks et al., 2012; Öhman, 2005). Decreased activation in these regions has been associated with elevated levels of psychopathic and CU traits in previous literature (Dolan & Fullam, 2009; Jones et al., 2009; Marsh et al., 2008; Seara-Cardoso & Viding, 2015; Viding et al., 2012). However, it should be noted that only the amygdala has been consistently activated by subliminal emotional faces (Brooks et al., 2012).



The current study measured externalising behaviours alongside CU traits to examine whether these measures contributed individually to variance in activation in the ROIs or whether shared variance was associated with neural response during fear and anger processing. Specifically, the current study aimed to assess whether inter-individual variability in CU traits is associated with brain response in the bilateral amygdala, ACC, OFC and insula when viewing fearful and angry faces. It was predicted that CU traits would be negatively correlated with the responses of the region of interests to fearful faces. Whilst there is much less evidence for anger processing and CU traits, it was also posited that CU traits would be inversely associated with the neural processing of angry faces in the ROIs. It was additionally predicted that externalising behaviours would be associated with fear and anger processing, but given the mixed evidence reviewed above no predictions regarding the direction of this association were postulated. As a previous study reported gender differences for the relationship between externalizing behaviours and anger processing (Waller et al, 2016), I will finally assess males and females separately in this correlation.

## **4.3 Methods**

### **4.3.1 Participants**

Sixty-three typically developing youths from Birmingham were recruited for this study. Further details of recruitment methods and inclusion/exclusion criteria are detailed in Chapter 2. Two youths were excluded due to excessive motion (>3mm in at least 50% of slices) during scanning, whilst five were excluded due to achieving a score in the clinical range on the CBCL, leaving a final sample of 56

(Table 4.1). Power calculations ( $\beta = 0.2$ ) using the correlation coefficient of  $R = -.53$  from Viding et al. (2012), who used the same task in boys with conduct problems and varying levels of CU traits) found that a sample size of 26 participants is sufficient to test the central hypothesis ([www.sample-size.net/correlation-sample-size](http://www.sample-size.net/correlation-sample-size); Hulley et al., 2013). This study was chosen as it used the same task in a clinical sample of youths and found a negative correlation between CU traits and right amygdala activity.

*Table 4.1: Socio-demographic and mental health characteristics of the sample*

	All (n = 56)	Males (n = 23)	Females (n = 39)
Age, mean (SD; range)	13.9 (2.5; 9-18)	14.3 (2.5; 9-18)	13.1 (2.66; 9-17)
IQ, mean (SD; range)	101.0 (9.4; 83-123)	102.3 (9.9; 90-123)	100.1 (12.6; 83-118)
ICU total, mean (SD; range)	17.7 (7.7; 1-35)	19.0 (7.1; 8-35)	15.4 (7.1; 1-33)
CBCL internalising, mean T score (SD; range)	44.6 (8.1; 34-62)	43.3 (7.1; 34-59)	45.8 (8.9; 34-62)
CBCL externalising, mean T score (SD; range)	47.9 (9.9; 33-62)	45.4 (6.2; 34-61)	45.6 (8.7; 34-61)

*Notes: CBCL = Child Behaviour Checklist; ICU = Inventory of Callous-Unemotional Traits; SD = standard deviation.*

### **4.3.2 Psychometric measures**

The psychometric measures described in chapter 2 were completed by all participants.

### **4.3.3 Experimental task**

This task is based on Viding et al. (2012). Participants passively observed subliminal emotional facial expressions posed by male or female actors followed by backwards masking of a calm face from the same actor (see Figure 4.1). A calm mask was chosen because it those with high levels of CU traits may infer hostility from neutral faces (Dadds et al., 2006). Stimuli included 18 expressions from six actors (3 males, 3 females) who each portrayed fear, anger and calm. Five participants also observed six faces portraying sadness, but these data are not considered here.

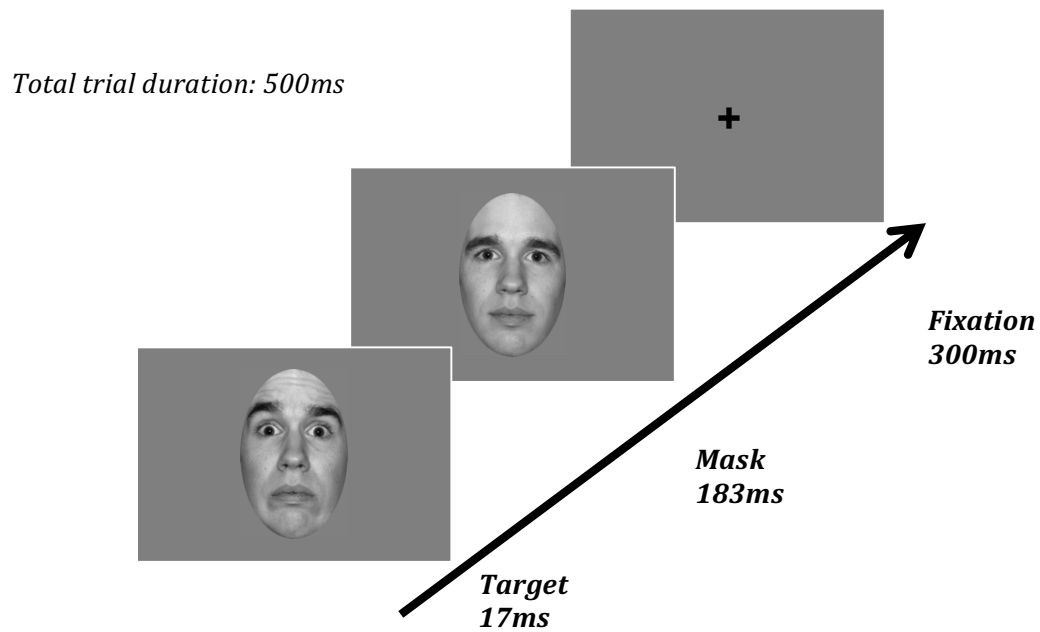
Stimuli were taken from the NimStim set of facial expressions (Tottenham et al., 2009). The same actors who were used in Viding et al. (2012) were included in the current study. Viding et al. informally chose actors from the NimStim set who had as few extraneous features as possible (e.g. beards, moles, hair covering the forehead). These faces were then ranked best to worst exemplars of fear and calm. These rankings were then taken into account when choosing the final stimuli.

Stimuli were of a standard size and presented in greyscale, with hair removed, on a mid-grey background. The target face was presented for 17ms, followed by a calm mask for 183ms. The subjective experience is of seeing a calm face. A grey cross interstimulus interval was presented for 300ms, with the centre of the cross at the

same place as the nose of the target and mask faces. Each trial lasted 500ms, and each block consisted of 30 trials of one emotion. The only difference between blocks was that the subliminally presented faces were fearful, angry or calm.

Participants pressed a button when they saw a white fixation cross at the beginning of each rest block, in order to ensure that attention was maintained throughout the task. The total task duration was 9 minutes, which consisted of 24 experimental blocks of 15s and 12 rest blocks of 15s.

To ensure that exposure duration meant that participants did not consciously see the masked emotional faces, 11 participants (mean age 14.27 years) were shown 10 blocks of emotional faces and asked to label the emotion as fear, sadness or anger. Average accuracy was 14.39%, with the highest score being 33% (chance level; two participants) and the lowest score being 0% (four participants). When this task was previously used by Viding et al., the authors asked all of their participants what they had seen. Out of Viding et al.'s 46 participants, only three mentioned seeing emotion (although fear, which was the only emotion included in the task, was not mentioned by any participants). Removing their data did not change Viding et al.'s results.



*Figure 4.10. A fear trial of the subliminal face processing task.*

#### **4.3.4 MRI acquisition parameters**

A 3T Phillips Achieva MRI scanner at the Birmingham University Imaging Centre acquired  $T_2^*$ -weighted echo planar imaging (EPI) volumes using a 32-channel head coil. These data were acquired in a single run of 9 minutes, with 198 task volumes and 5 dummy volumes. The following acquisition parameters were applied: 41 slices; TE=30ms; TR=2500ms; matrix size=64×64; voxel size=3×3×3; flip angle=83°; field of view=192mm; slice thickness=2mm. A high resolution, sagittal, 3D T1-weighted dataset, with an in-plane resolution of 1×1×1mm and lasting six minutes, was obtained for DARTEL normalisation. This scan consisted of 192 slices, with TE=3.7ms; TI = 900ms; TR=8ms, flip angle = 9° and matrix size=256×256. Finally, field maps were collected to remove distortion caused by

magnetic field inhomogeneity. The following acquisition parameters were applied for the FieldMap, which lasted approximately one minute: 46 slices; TE 1=4.6ms; TE 2 = 6.9ms; TR=500ms; matrix size=64×64.

## **4.4 fMRI data analyses**

### **4.4.1 Pre-processing**

Data were pre-processed following a standard procedure in SPM12 ([www.fil.ion.ucl.ac.uk/spm](http://www.fil.ion.ucl.ac.uk/spm)). The first five functional volumes were discarded to allow for T1 equilibrium. A FieldMap from each participant was processed using the FieldMap toolbox to produce a voxel displacement map (VDM). The EPI image was then co-registered with the VDM. The EPI was corrected for movement using the VDM with distortions interaction. Next, the Template-O-Matic (Wilke, Holland, Altaye, & Gaser, 2008) toolbox was used to create a standardised a priori tissue probability map (TPM) based on the age and the sex of the 56 participants. The structural images were segmented with reference to the TPM into grey matter and white matter, based on a multi-channel approach using the New Segment tool.

The segmented grey and white matter images generated a template using the Diffeomorphic Anatomical Registration Through Exponentiated Lie Algebra toolbox (DARTEL; Ashburner, 2007). This template was used to normalise the grey and white matter segmented images by iteratively warping the images into a common space using non-linear registration. Finally, the DARTEL template and EPI images were normalised to Montreal Neurological Institute (MNI) standard space (Evans et al., 1993) and smoothed using a Gaussian kernel of full width at half maximum resolution of 6 x 6 x 6mm to account for residual inter-subject

differences and to comply with the continuity assumption of random field theory (Brett, Penny, & Kiebel, 2003).

For two participants, two regressors were created to model corrupted images resulting from excessive motion (i.e. between-scan motion of  $>1.5\text{mm}$  or  $1.5^\circ$ ). In these participants, two images were removed and the adjacent images interpolated in order to prevent distortion of the between-subjects mask.

#### ***4.4.2 First-level analysis***

First-level analyses included three regressors, each including eight 15s blocks of fear, anger and calm, modelled as boxcar functions and convolved with a canonical haemodynamic response function and its temporal derivative. The six realignment parameters were modelled as covariates of no interest.

Blocks where there was no registered behavioural response (three participants; one with one block unregistered, one with three blocks unregistered and one with five blocks unregistered out of a total of eight blocks) were excluded. Whilst none of the participants fell asleep during this scan, the fact that no behavioural response was registered suggested that they stopped paying attention. General linear models were used to estimate the responses for fear, anger and calm conditions. The resulting beta maps were carried forward to subsequent second-level random-effects analyses.

#### **4.4.3 Second-level ROI analyses**

The a priori ROIs included the bilateral amygdala, OFC, ACC and insula. These areas are visualised on a standard MNI brain (see Figure 4.2). I defined these ROIs anatomically using masks from the automated anatomical labelling atlas, provided by the Wake Forest University PickAtlas (Maldjian, Laurienti, Kraft, & Burdette, 2003).

I extracted the representative response (Eigenvariate) of each participant in the three conditions (fear, anger and calm) for each ROI using the pre-specified anatomical mask in SPM12. I then computed residual variables (which accounted for age, sex and IQ score) for fear > calm and anger > calm by running a regression in SPSS. ICU and CBCL scores were mean scaled. Pearson correlations tested the relationship between the standardised responses in each ROI and the ICU. Because I hypothesised negative associations between fear and anger responses in each ROI and ICU scores, one-tailed p values were used. These correlations were then repeated with CBCL externalising scores in place of ICU scores. I had no directional predictions regarding the relations between CBCL and fear/anger response, and so two-tailed p values were applied for these analyses.

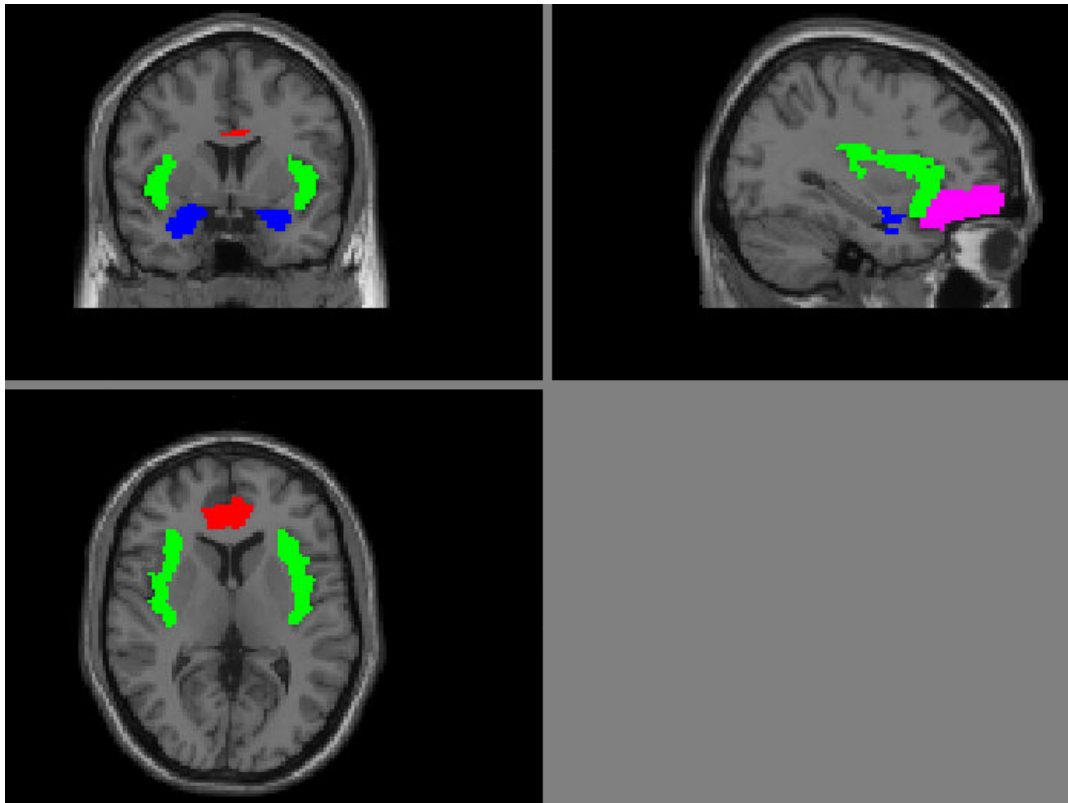
As the data were normally distributed according to the Shapiro-Wilk Test, the False Discovery Rate adjustment (Yekutieli & Benjamini, 1999) was applied to control for the likelihood of making a Type I error on multiple comparisons. In line with previous research (Lockwood, Seara-Cardoso, & Viding, 2014; Seara-Cardoso et al., 2013), corrected p values are reported here. As with the previous chapter, an



online tool was used to calculate Bayes Factors for all analyses

([http://www.lifesci.sussex.ac.uk/home/Zoltan\\_Dienes/inference/Bayes.htm](http://www.lifesci.sussex.ac.uk/home/Zoltan_Dienes/inference/Bayes.htm);

Dienes, 2014) based on Viding et al. (2012). The reason for using Bayes Factors as well as traditional statistical tests in my thesis was outlined in section 2.4. Waller et al.'s (2016) correlations were inputted as a plausible maximum effect for the anger>calm correlation with externalising behaviours when the current correlations were split by gender.



*Figure 4.11. Regions of interest overlaid onto a standard MNI brain. The red block indicates ACC, the green indicates insula, the blue indicates amygdala and the pink indicates OFC.*

## 4.5 Results

Participants pressed a button when they saw a white fixation cross before every rest block. Across all participants there was a mean response time of 605ms (SD = 162ms).

### 4.5.1 Correlations between psychometric measures

ICU scores were positively correlated with externalising behaviours, whilst internalising behaviours were also positively correlated with externalising behaviours (see Table 4.2).

Table 4.2. Zero-order correlations between psychometric measures

	1	2	3
1. ICU score			
2. CBCL (internalising)	.03		
3. CBCL (externalising)	.42**	.35**	
4. Age	-.001	-.11	-.10
5. IQ	-.02	-.14	-.06

\*. Correlation is significant at .05 level

\*\*. Correlation is significant at .001 level

Notes: CBCL = Child Behaviour Checklist; ICU = Inventory of Callous-Unemotional Traits.

### 4.5.2 Fear > Calm

The correlations between ICU and CBCL externalising scores and activation in the fear>calm condition were examined (see Table 4.3), controlling for age, IQ and

gender. CU traits were negatively associated with bilateral amygdala (Figures 4.3-4.4; left amygdala  $BF = 6.03$ ; right amygdala  $BF = 30.33$ ) and insula (Figures 4.5-4.6; left insula  $BF = 18.16$ ; right insula  $BF = 30.33$ ). There was a trend towards a negative association between externalising behaviours and right amygdala activity, but this did not survive FDR correction. Interestingly, however, the Bayes Factor for this relationship was considered significant ( $BF = 4.86$ ). There were no significant associations between OFC and ACC activity and either of the psychometric measures (see Appendix 4.3 for Bayes Factors).

*Table 4.3. Correlates between CU traits, externalising behaviours and neural activity in ROIs during fear condition.*

		ICU		CBCL	
		r	p	r	p
Amygdala	L	<b>-.30*</b>	.04	-.17	.61
	R	<b>-.37*</b>	.01	-.35	.08
Insula	L	<b>-.35*</b>	.03	-.15	.56
	R	<b>-.37*</b>	.01	-.23	.40
ACC	L	-.08	2.32	-.04	.87
	R	-.10	.32	-.003	7.84
OFC	L	-.08	.32	-.05	1.14
	R	-.18	.16	-.04	0.99

*Abbreviations: ICU – Inventory of Callous-Unemotional traits, CBCL – Child Behaviour Checklist (externalising behaviours), L – left hemisphere, R – right hemisphere, ACC – anterior cingulate cortex, OFC – orbitofrontal cortex.*

*\*significant at  $p < .05$*

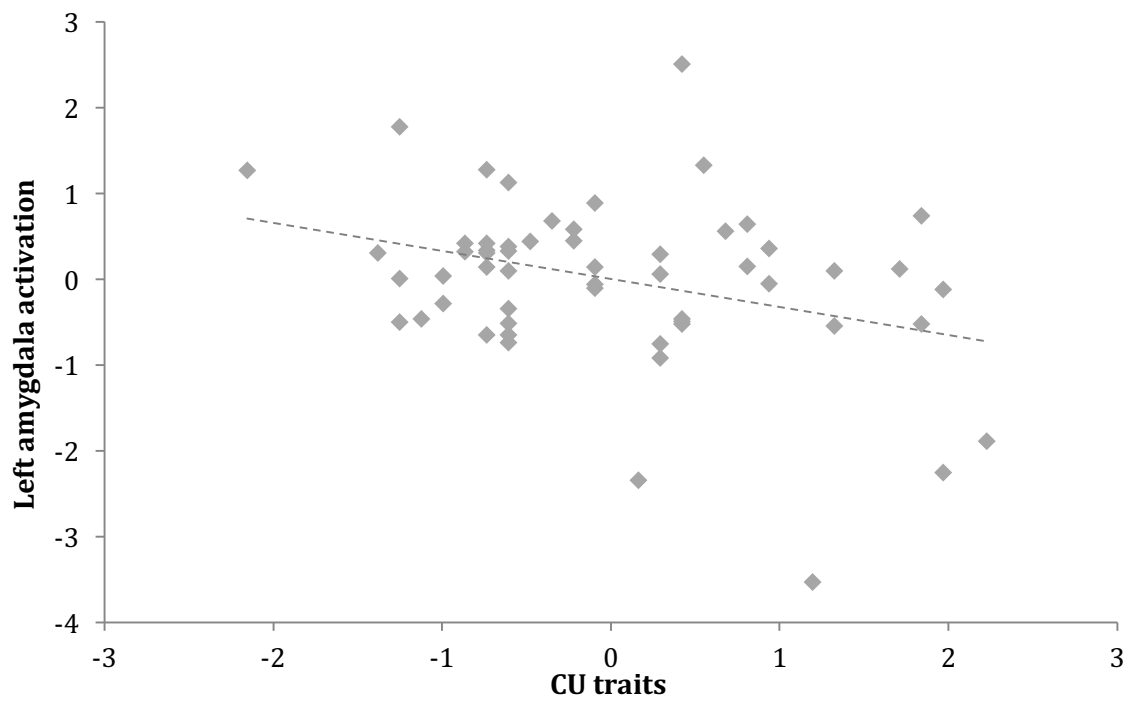


Figure 4.12. Residuals of the left amygdala activation for fear>calm faces as a function of CU traits, after controlling for age, IQ and gender.

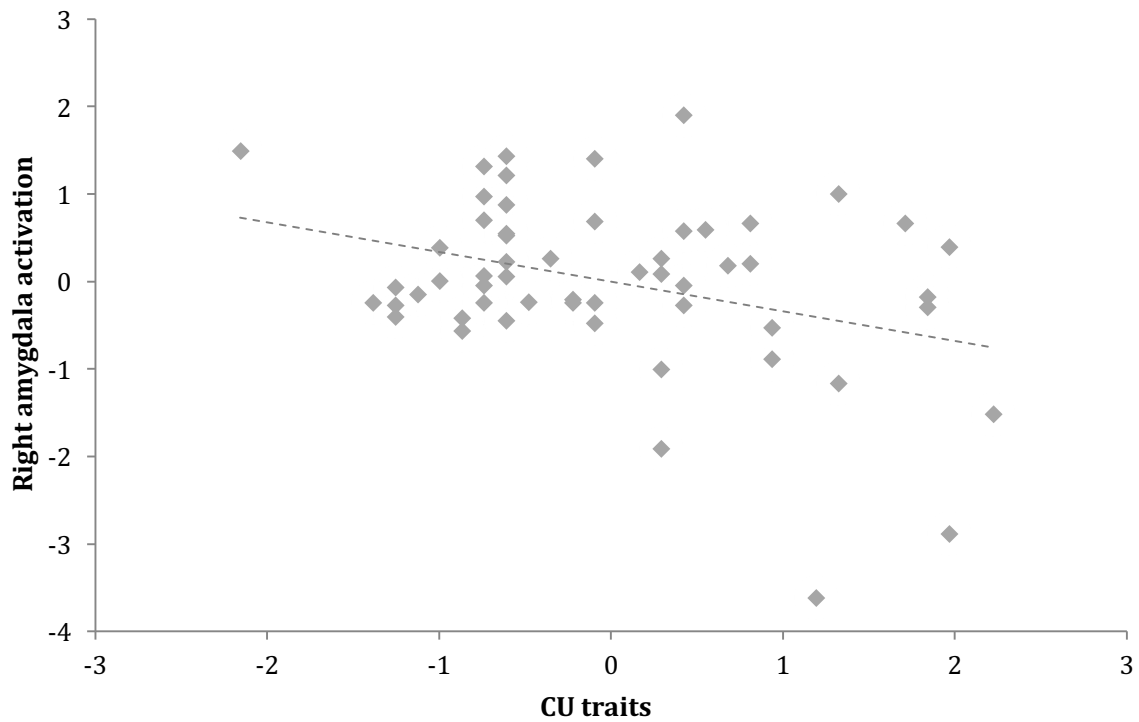


Figure 4.13. Residuals of the right amygdala activation for fear>calm faces as function of CU traits, after controlling for age, IQ and gender.

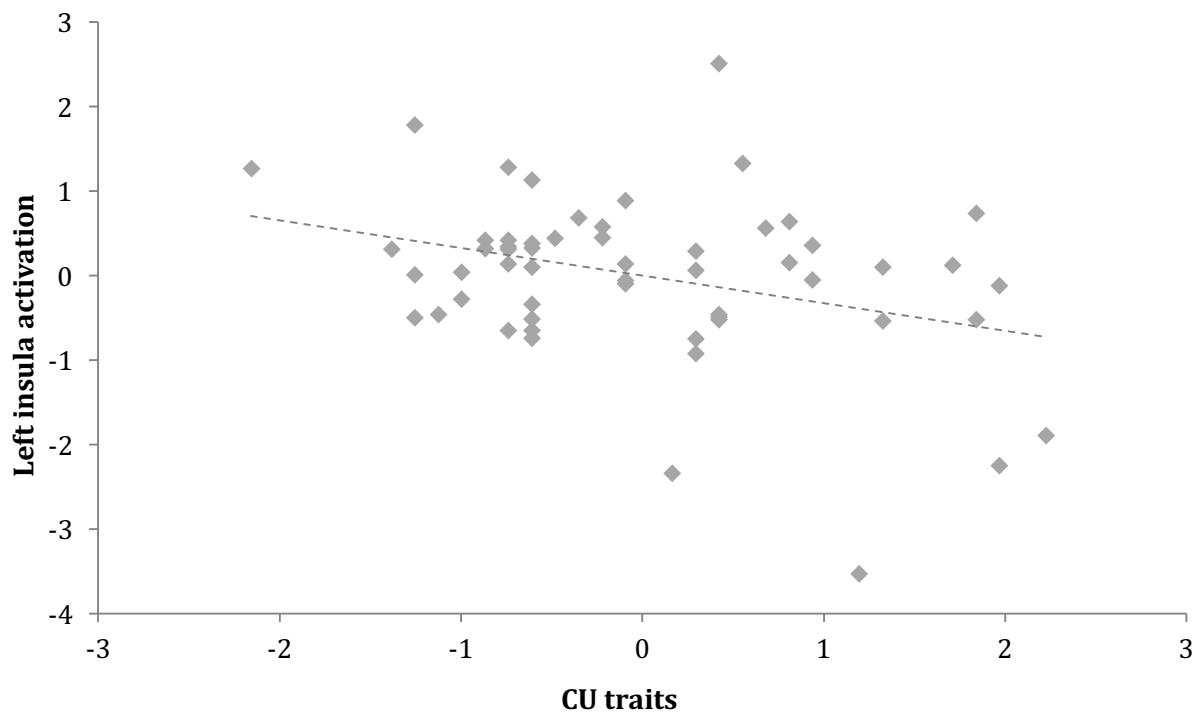


Figure 4.14. Residuals of the left insula activation for fear>calm faces as a function of CU traits, after controlling for age, IQ and gender.

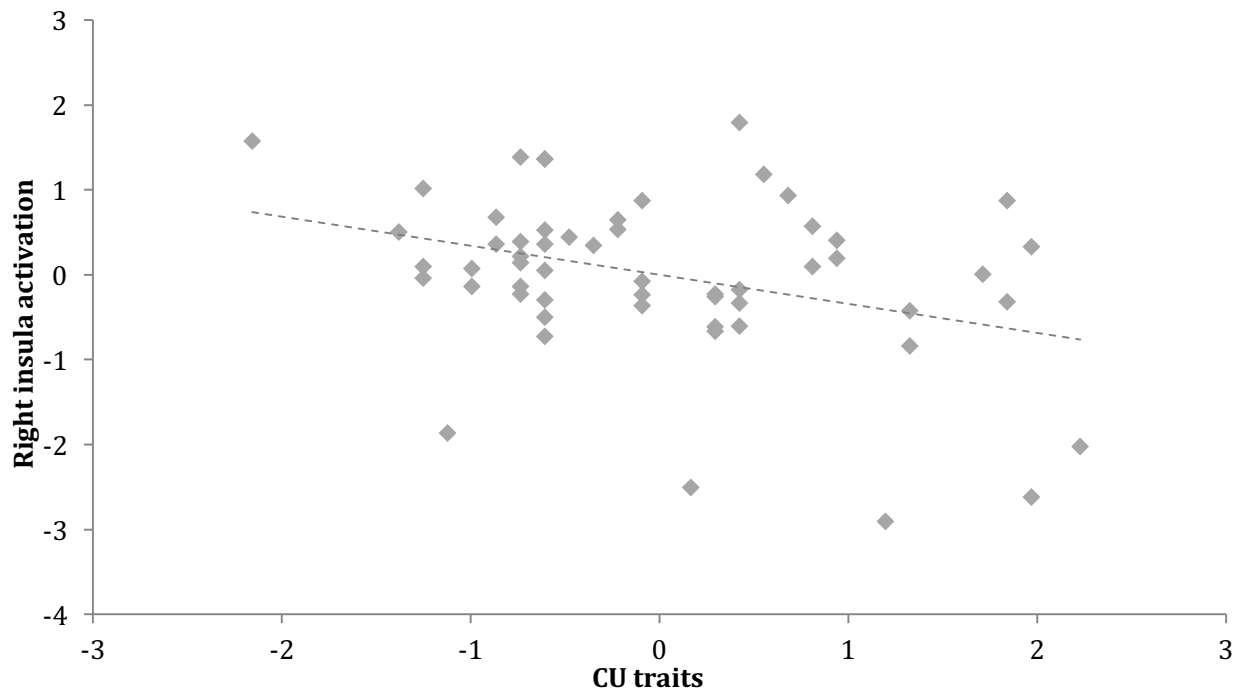


Figure 4.15. Residuals of the right insula activation for fear>calm faces as a function of CU traits, after controlling for age, IQ and gender.

### 4.5.3 Anger > Calm

ICU and CBCL externalising scores were correlated with activation in the anger>calm condition, controlling for age, gender and IQ (see Table 4.4). No significant correlations were found in any of the ROIs (see Appendix 4.4 for Bayes Factors).

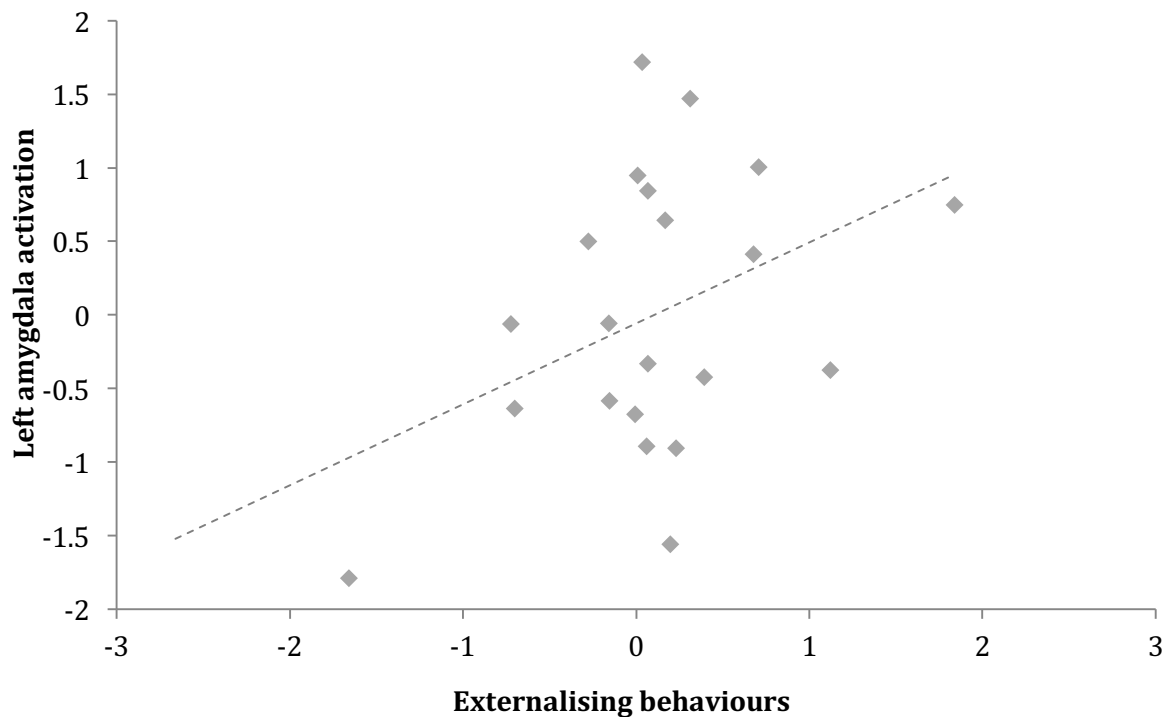
*Table 4.4. Correlations between CU traits, externalising behaviours and neural activity in ROIs during anger condition*

		ICU		CBCL	
		r	p	r	p
Amygdala	L	.12	.21	.07	.61
	R	.03	.43	.09	.52
Insula	L	.19	.08	.03	.82
	R	.11	.21	.01	.96
ACC	L	.05	.36	-.05	.74
	R	.07	.31	-.09	.53
OFC	L	.20	.08	.06	.68
	R	.03	.41	-.01	.95

*Abbreviations: ICU – Inventory of Callous-Unemotional traits, CBCL – Child Behaviour Checklist (externalising behaviours), L – left hemisphere, R – right hemisphere, ACC – anterior cingulate cortex, OFC – orbitofrontal cortex.*

As previous research has found negative associations between CU traits/externalising behaviours when only men were considered (Waller et al., 2016), the correlations between amygdala activation and psychometric measures were also run separately for males (n=21). This analysis revealed a significant

positive association between externalising behaviours and left amygdala activity ( $r = .45$ ,  $p = .03$ , Bayes Factor = 3.72; see *Figure 4.16*). When females only ( $N = 41$ ) were considered, there were no significant associations between amygdala activation and psychometric measures (left amygdala:  $r = -.14$ ,  $p = .42$ , Bayes Factor = .42; right amygdala:  $r = .05$ ,  $p = .76$ , Bayes Factor = .30).



*Figure 4.16. Residuals of the left amygdala activation for angry > calm faces (males only,  $n=21$ ) as a function of externalising behaviours, after controlling for age and IQ.*

#### **4.5.4 Shared variance between CU traits and externalising behaviours**

Finally, we investigated whether these associations were driven by shared variance between CU traits and externalising behaviours or whether they reflect unique variance specific to the individual measures. When each measure was mean scaled and entered as an additional covariate of the other, the correlations became



weaker for both fear (Appendix 4.5) and anger (Appendix 4.6) conditions, with none of them surviving FDR adjustment. Similarly, when males only were considered and CU traits accounted for, the association between externalising behaviours and left amygdala activity when viewing angry faces became non-significant. Taken together, these results suggest that variance shared by CU traits and externalising behaviours is likely to drive the correlations reported in this study.

## **4.6 Discussion**

This study is, to our knowledge, the first to investigate the association between CU traits and brain response to subliminally presented emotional faces in typically developing children and adolescents. We hypothesised that level of CU traits would be negatively associated with neural activity in the bilateral amygdala, ACC, OFC and insula during subliminal fear processing. This hypothesis was partially supported, as we found the predicted association with CU traits in the bilateral amygdala and insula. We hypothesised that externalising behaviours would also be associated with activation in the four ROIs, but we did not speculate a direction. We found a negative correlation between right amygdala activity and externalising behaviours, which generated a significant Bayes Factor but did not survive the False Discovery Rate adjustment (Yekutieli & Benjamini, 1999). Interestingly, and in line with Waller et al. (2016), we also found that externalising behaviours were positively associated with left amygdala response to angry faces in males only. There was no association between angry faces and amygdala response in females. Finally, we examined whether CU traits and externalising behaviours contributed

separately to variance in activation in the ROIs, or whether shared variance was associated with neural response during fear and anger processing. Despite evidence of a positive relationship between externalising behaviours and amygdala activity in males, the current study did not find evidence of suppressor effects in the overall sample. This suggests that shared, rather than individual, variance between CU traits and externalising behaviours is likely to drive the significant correlations observed here.

The negative correlation between CU traits and the neural response to fearful faces in the amygdala and insula is consistent with several previous studies which examined brain response in adults and youths at the extreme of the CU traits continuum (Jones et al., 2009; Lozier et al., 2014; Marsh et al., 2008; Viding et al., 2012). Viding et al. (2012) found a negative correlation between CU traits and amygdala activity with an almost identical task, whilst Lozier et al. (2014) found a negative association between amygdala activity and CU traits during a conscious emotion processing paradigm. However, it should be noted that Lozier et al. (2014) reported results from a fear>baseline comparison, rather than a fear>calm comparison, leaving the possibility that those results are associated with face processing in general rather than emotion processing *per se*. My results are also consistent with those reported in violent adults (Dolan & Fullam, 2009) and typically developing adults (Seara-Cardoso, Sebastian, et al., 2015). I extended these findings to show that a negative association between CU traits and activity in the amygdala and insula is also apparent in typically developing youths.

The insula is also involved in empathy processing (Singer, Critchley, & Preuschoff, 2009). Low empathy can lead to a turbulent lifestyle and has been linked to violent criminal behaviour (Jolliffe & Farrington, 2004). Psychopathic traits (derived from measures of CU traits and AB) were negatively associated with empathy skills in community samples of 2760 youths (Dadds et al., 2009) and adults (Mullins-Nelson, Salekin, & Leistico, 2006; Seara-Cardoso, Viding, et al., 2015). Youths with AB/HCU showed less heart rate change from baseline than youths with AB/LCU when viewing two film clips which elicit empathic sadness (de Wied, van Boxtel, Matthys & Meeu, 2012). The current study could suggest that this relationship between empathy and CU traits is influenced by insula activation. Further research could investigate whether insula activity modulates the association between empathic sadness and CU traits.

Whilst I found that the negative correlation between right amygdala activation and externalising behaviours did not survive FDR correction, a Bayes Factor of 4.86 was achieved, which suggests that this correlation was significant. However, this result should be heeded carefully, as the Bayes Factor calculated was based on previous results between CU traits and amygdala activity (Viding et al., 2012). To my knowledge, there are no previous significant results between externalising behaviours and amygdala activity that could be applied here to assess the statistical likelihood of the current finding, and so a replication of this finding would be reassuring.

I found a positive correlation between externalising behaviours and anger processing in the left amygdala when males only were considered. This is in line

with Waller et al. (2016), who did not find an association between externalising behaviours and bilateral amygdala reactivity to angry faces when men and women were considered together, but did observe a positive relationship when only men were considered. When only females were considered, the current result generated a Bayes Factor  $\leq 1/3$ . This suggests that there is no association between externalising behaviours and anger processing in females.

This difference in findings between genders may reflect sex-related differences in oxytocin signalling (Waller et al., 2016) as well as evolutionary effects (Kret & De Gelder, 2012). Aggression is historically seen as more socially acceptable in men than women (Serbin, Marchessault, McAffer, Peters, & Schwartzman, 1993). This can become maladaptive in the long term, for example with male violent offenders whose biological predispositions of aggressiveness were overly expressed in the childhood environment (Lansford et al., 2007). The current result advances the field of research by suggesting that gender differences in threat processing are associated with amygdala reactivity from childhood. This could be due to reinforcement of aggression-related gender stereotypes from an early age (Serbin et al., 1993).

No associations between CU traits and neural activity in the ACC or OFC were seen during fear and anger processing, despite previous evidence suggesting that these areas are impaired in psychopathy (Decety et al., 2014). Bayes Factors of less than 3 were achieved for these correlations (apart from left OFC during anger processing; see Appendix 4.4). This suggests that the results reflect a lack of associations rather than insensitivity. The reason for the insignificant results could

be that the current paradigm did not sufficiently recruit the OFC and ACC. Adolphs et al. (2002) suggested that the OFC is recruited after 170ms or viewing the stimulus, which would mean that the current presentation time of 17ms would be too quick for the OFC. Furthermore, Morris, Öhman and Dolan (1999) found that connectivity between the right amygdala and the OFC was actually reduced during subliminal fear processing. This would suggest that the activation in the amygdala suppressed activation in the OFC (Morris et al., 1999). The ACC is reliably recruited in the subliminal processing of pain (Brooks et al., 2012) and so the current stimuli may not have activated this region sufficiently. Future research could look at specific pain stimuli, rather than threatening faces, to assess whether there is an association between the ACC and CU traits in a different paradigm.

Neurobiological deficits may be exacerbated by lifestyle choices seen in adults with psychopathy, for instance substance misuse. Prolonged amphetamine misuse was shown to cause disturbances in functions mediated by the OFC (Rogers, 1999), and adults with high levels of psychopathic traits were impaired on a response reversal task thought to require the OFC (Budhani, Richell & Blair, 2006), whereas youths with high levels of psychopathic traits were not impaired on this task (Blair et al., 2001). The fact that in the present study typically developing youths with no history of drug misuse were sampled could also be a factor in why associations between CU traits and OFC function were not found.

The current study did not find any associations between subclinical levels of externalising behaviours and subliminal fear or anger processing in the insula, OFC or ACC. This is in agreement with Carré et al. (2013), who also did not find any

correlations between the antisocial facet of psychopathy and amygdala reactivity during fear processing in a large community sample of young adults. On the other hand, limited research with clinical samples found contrasting results, which are explored next.

Decety et al. (2014) found that, during fear processing, activation in the right insula was negatively correlated with the antisocial factor of psychopathy (roughly equivalent to externalizing behaviours), and Seara-Cardoso et al. (2016) reported a negative association between the antisocial facet of psychopathy and bilateral anterior insula response to all faces relative to baseline in a community sample of adults. However, these two studies may not be very informative with regards to emotion processing; Decety et al.'s paradigm contrasted individual emotions to a low level, scrambled face, rather than a calm face used in the current study. Seara-Cardoso et al. did not report correlations for individual emotions, but rather reported for all emotional faces over rest. These paradigms are therefore not as informative about emotion processing as the paradigm used in the current study. The disparate results explored above might suggest that externalising behaviours are not reliably associated with a consistent pattern of neural responses to emotional stimuli, or instead they could reflect the heterogeneity within the construct of externalising behaviours.

Finally, we assessed whether CU traits and externalising behaviours contributed individually to variance in activation in the ROIs, or whether shared variance was associated with neural activity. We found that when these measures were entered together in the analysis, their association with BOLD response in the ROIs were

weaker; this is in line with Seara-Cardoso, Sebastian, et al. (2015) and suggests that variance shared by both dimensions is likely to drive the results.

The presence of suppressor effects can outline critical distinctions among subpopulations; the lack of any suppressor effects seen here may infer that CU traits and externalising behaviours are not embedded within a unitary measure within typically developing youths. However, it may also be that these suppressor effects are not visible in the current task, or that the task was not sensitive enough to infer suppression in typically developing youths; it is difficult to reliably report suppressor effects as the phenomenon can be masked by sample fluctuations, experimental paradigms and the direction in which variables have been scaled (Maassen & Bakker, 2001).

There are several limitations to this study that should be noted. First, we only included fear and anger. This is because the task was already designed by the FemNAT-CD consortium, and I was unable to adapt the task. Chapter 3 concluded that sadness and disgust recognition were negatively correlated with CU traits in typically developing youths, and so it would have been interesting to assess whether neural responses to these emotions are also associated with CU traits. However, time limitations in the MRI scanner meant that only two emotions could be assessed, and as fear and anger have the greatest research body with respect to psychopathy and CU traits, these were deemed most appropriate. Fear and anger correspond to different facets of threat, and so they are also often considered to be the most conceptually interesting in relation to CU traits. Future research could look at the other four emotions, particularly sadness and disgust, to assess

whether neural activity during subliminal processing of these emotions is associated with CU traits in typically developing youths. Second, we did not use eye tracking, which would have been useful to determine which aspects of the face were viewed in those with differing levels of CU traits. Finally, as this study was cross-sectional, we are unable to explore possible changes in patterns of neural activity associated with CU traits across time.

This study is also characterised by a number of strengths. First, these findings mirror those from clinical samples (i.e. Viding et al., 2012), suggesting a dimensional nature to CU traits and amygdala response to fearful faces. Secondly, multiple sources of information combining categorical (K-SADS) and dimensional (CBCL) approaches ascertained that all participants were typically developing. Six participants, who were deemed healthy using the K-SADS, scored in the clinical range on the CBCL for internalising or externalising behaviours and were removed from analyses. This is more conservative than other studies, which only excluded participants if they presented with certain (opposed to any) disorders on the K-SADS. Marsh et al.'s (2008) exclusion criteria for healthy controls only included psychosis, pervasive developmental disorders, Tourette's syndrome, mood or anxiety disorders, neurologic disorders, IQ <80, or medical illness severe enough to require treatment), or do not assess overall mental health at all (Gordon et al., 2004).

This study extends our current understanding of CU traits in typically developing youths in a number of ways. First, we showed that bilateral amygdala and insula activation during viewing of subliminally presented fearful faces was negatively



associated with level of CU traits. When only males were considered, there was a positive correlation between externalising behaviours and activation in the left amygdala in response to angry faces. Finally, suppressor effects between CU traits and externalising behaviours were not seen in this study.

Chapter 3 suggests that CU traits are not associated with reduced fear recognition abilities, whilst the current chapter showed that there is a negative association between CU traits and amygdala and insula activity to fearful faces in typically developing youths. This suggests that protective factors may be at play in youths without AB but with HCU traits, which allows them to attend to and accurately recognise fearful faces.

## CHAPTER 5: WHITE MATTER INTEGRITY IN YOUTHS WITHOUT ANTISOCIAL BEHAVIOUR AND VARYING LEVELS OF CALLOUS-UNEMOTIONAL TRAITS

### 5.1 Abstract

CU traits are associated with structural and functional brain abnormalities in the amygdala, insula and ventromedial prefrontal cortex. These regions are connected via the uncinated fasciculus (UF) white matter tract. Adults with psychopathy and psychopathic traits show reduced white matter integrity in the UF, but evidence from clinical populations of adolescents has provided mixed findings. It is currently unclear if an association between CU traits and structural integrity in the UF can be seen in typically developing youths. The current study examined whether there is an association between CU traits and FA using tract-based spatial statistics in 63 typically developing youths aged 9-18 years. An association between CU traits and UF was not observed across the entire sample, but CU traits were negatively associated with FA in the right UF in adolescents aged 16-18 years. This suggests that higher levels of CU traits are associated with reduced structural connectivity in the UF in typically developing adolescents, similar to findings from clinical samples of adults. The fact that the UF undergoes rapid development as typically developing children age may have meant that correlates with CU traits were not yet notable in younger children, or that the relationship between CU traits and UF development is not linear.

## 5.2 Introduction

The previous chapter described how CU traits were negatively associated with bilateral insula and amygdala responsivity to fearful faces during a subliminal emotion face processing task. As well as being associated with reduced neural response, CU traits may also be associated with reduced structural connectivity (Motzkin et al., 2011). The UF is a hook-shaped white matter tract which links the anterior temporal lobe with the frontal lobe, passing the amygdala, hippocampus, insular cortex and vmPFC (Kier, Staib, Davis, & Bronen, 2004). These brain areas are involved in a multitude of social, cognitive, and affective functions such as empathy (Bzdok et al., 2012; Morelli, Rameson, & Lieberman, 2014; Sebastian, Fontaine, et al., 2012), decision making (Gupta, Kosciak, Bechara, & Tranel, 2011; Rodrigo, Padrón, de Vega, & Ferstl, 2014) and aversive classical conditioning (Hooker, Verosky, Miyakawa, Knight, & D'Esposito, 2008; Tzschoppe et al., 2014): processes shown to be impaired in psychopathy (Blair, 2007, 2008; Fontaine, Barker, Salekin, & Viding, 2008; Marsh & Blair, 2008; Sebastian, Fontaine, et al., 2012). The fact that the UF connects brain areas relevant to psychopathy research means that the UF is often explored in psychopathic populations (Von Der Heide et al., 2013). This chapter will explore structural connectivity in the UF in typically developing youths with a range of CU traits.

The structural integrity of white matter tracts in the brain are commonly measured using FA. FA represents the proportion of diffusion in the direction parallel to the axonal bundle (axial diffusivity) relative to perpendicular diffusion (radial diffusivity) (Le Bihan et al., 2001). FA is highly sensitive to microstructural

changes and fibre coherence, and DTI is used to measure brain maturation and myelination (Zimmerman et al., 1998). A number of studies on psychopathy have looked at FA across the whole brain (e.g. Asato et al., 2010; Haney-Caron, Caprihan, & Stevens, 2013; Motzkin et al., 2011), whilst others have focussed on ROIs within specific tracts (e.g. Breeden et al., 2015).

Recent research has investigated the structural integrity of the UF in antisocial adults and youths. Male offenders with psychopathy showed reduced white matter integrity in the right UF compared to offenders without psychopathy (Craig et al., 2009; Hoppenbrouwers et al., 2013; Motzkin et al., 2011). As well as reduced structural integrity of the UF, Motzkin and colleagues (2011) also found reduced functional connectivity between the amygdala and vmPFC. This implies that white matter tracts connecting prefrontal and temporal regions are of particular interest with respect to psychopathy. Wolf et al. (2015) found that, in a large sample of adult offenders, there was an overall negative association between FA in the right UF and PCL-R score. When the PCL-R score was parsed into the two factors of psychopathy, primary and secondary, this relationship was found to be mostly driven by the primary factor (roughly equivalent to CU traits). In contrast, the secondary factor (roughly equivalent to externalizing behaviours) trended towards a negative relationship.

An emerging body of literature has examined the UF among children and adolescents with AB, but these studies have yielded conflicting results. Whilst some studies have reported no differences in white matter integrity in the UF between youths with and without AB (Finger et al., 2012; Haney-Caron et al., 2013;

Li, Mathews, Wang, Dunn, & Kronenberger, 2005), others have observed increased FA in youths with AB (Passamonti et al., 2012; Sarkar et al., 2013, 2016; Zhang et al., 2014). Studies which have looked specifically at CU traits in youths with AB have found that these traits were *positively* associated with FA in the corpus callosum, corticospinal tract and superior longitudinal fasciculus, but not the UF (Pape et al., 2015; Sarkar et al., 2016). Pape and colleagues did, however, find a positive correlation between FA in the UF and grandiose/manipulative traits. One should bear in mind that this sample comprised of youths who had all been arrested before the age of 12 for a range of deeds that would be prosecutable above this age, and therefore are not representative of all youths with AB. The current study will expand on these results, whilst accounting for important confounding variables such as current mental health. Disorders such as Attention Deficit Hyperactivity Disorder (Tamm, Barnea-Goraly, & Reiss, 2012) and emotion dysregulation disorders (Versace et al., 2015) have been reported to be associated with aberrant white matter integrity in the UF in youths, thereby emphasising the importance of accounting for these factors.

In line with results from forensic adult samples (Wolf et al., 2015), a negative association between right UF FA values and CU traits had also been reported in healthy adult males aged 18-21 years (Sobhani, Baker, Martins, Tuvblad, & Aziz-Zadeh, 2015). The authors found this association when scores from two measures of psychopathy - the APSD and PCL:YV - were individually considered, suggesting that this finding is robust across psychometric measures. It should be noted that Sobhani et al. did not assess whether participants had any mental health

diagnoses, but rather assumed that they were healthy as they were recruited from the community. Therefore, it is unknown whether any mental health diagnoses within the sample could have confounded results. In sum, there is currently evidence for a negative association between the structural integrity of the UF and CU traits in adults.

The UF is one of the last white matter tracts to fully mature, with a peak after 30 years old (Lebel et al., 2012). Asato et al. (2010) postulated that the UF is still developing during adolescence (measured with both chronological age and pubertal status), meaning that age is important to consider when investigating the UF in youths. Studies which have looked specifically at CU traits in youths with AB have had a wide range of ages in their samples; for example, Sarkar et al. (2013) had a sample ranging from 12-19 years, whilst Pape et al. (2015) sample ranged from 12-20 years. These studies both controlled for age in their analyses, and in fact Sarkar et al. reported no correlation between age and FA in the UF.

Additionally, it is noteworthy to consider gender in DTI analyses. Males have higher overall FA (Herting et al., 2012) and higher levels of CU traits (Essau et al., 2006) compared to females, so it is especially important to account for gender in order to avoid Type I errors.

Inconsistent findings are reported in adolescent samples. Breeden et al. (2015) modelled AB and CU traits individually in youths with and without AB ( $n = 47$ ). The authors reported that white matter integrity in both the bilateral UF and the right stria terminalis/fornix were negatively associated with both AB and CU traits. However, when both variables were modelled together, the unique variance

associated with CU traits was driving the correlations in all three brain areas. The negative association between white matter integrity and CU traits in the left UF was also present when only the youths with AB (n=26) were included. In contrast, Sarkar et al. (2013) reported that the increase in FA observed in their study was in fact unrelated to CU traits, and reported no correlation between age and FA in the left UF. Finger et al. (2012) found no differences in FA in youths with AB and high CU traits compared to typically developing controls, despite finding differences in functional connectivity. However, this study did not look at CU traits specifically, but rather looked at AB and CU together, somewhat muddying results.

The current study will investigate white matter integrity in typically developing youths with a range of CU traits. In their recent review, Olson, Heide, Alm and Vyas (2015) emphasised the utility of taking a dimensional approach when assessing psychopathy in the UF. Based on past literature, average FA across the whole brain was firstly assessed with respect to age. I hypothesized that age would be positively correlated with whole brain FA. Following this, average FA in the bilateral UF was considered. I hypothesised that FA in the bilateral UF would be negatively correlated with CU traits. Further, I investigated whether structural integrity in the UF in youths without AB is partly influenced by independent, opposing contributions of externalising behaviours and CU traits, as observed for other metrics in clinical and non-clinical samples (Seara-Cardoso et al., 2016; Sebastian, McCrory, et al., 2012).

## 5.3 Methods

### 5.3.1 Participants

Sixty-two typically developing youths were recruited from advertising in schools and youth groups in the local community (*Table 5.8*) in Birmingham ( $n = 40$ ) and Southampton ( $n = 22$ ). I recruited those from Birmingham, and further recruitment techniques are discussed in Chapter 2. Power calculations ( $\beta = 0.2$ ) based on Breeden et al. (2015) found that a sample size of 55 participants would be sufficient to test the central hypothesis ([www.sample-size.net/correlation-sample-size](http://www.sample-size.net/correlation-sample-size); Hulley et al., 2013). This study was chosen as it investigated CU traits and externalising behaviours in a similar age range (10-17 years) of youths with and without conduct problems, and found that both of these measures were negatively correlated with structural integrity in the bilateral UF. Participants had no current or past history of any psychiatric illnesses. All participants over the age of 16 gave written informed consent, whilst participants under the age of 16 gave assent and a parent gave written informed consent.



*Table 5.8. Socio-demographic and mental health characteristics of the sample (n=62)*

	All	Males (n = 23)	Females (n = 39)
Age, mean (SD; range)	13.52 (2.67; 9-18)	14.30 (2.49; 9-18)	13.05 (2.66; 9-17)
IQ, mean (SD; range)	102.47 (11.63; 73-139)	102.35 (9.85; 90-123)	102.54 (12.56; 73-139)
ICU total, mean (SD; range)	16.76 (7.31; 1-35)	19.00 (7.13; 8-35)	15.44 (7.01; 1-33)
CBCL internalising, mean T score (SD; range)	47.0 (8.61; 33-61)	47.62 (7.01; 34-61)	46.96 (8.56; 33-61)
CBCL externalising, mean T score (SD; range)	45.52 (7.74; 34-61)	45.50 (6.31; 34-61)	45.56 (8.52; 34-61)

*Notes: CBCL = Child Behaviour Checklist; ICU = Inventory of Callous-Unemotional Traits; SD = standard deviation.*

### **5.3.2 Psychometric measures**

These measures and collection techniques are described fully in Chapter 2.

### **5.3.3 MRI acquisition parameters**

DTI data were acquired using a Philips Achieva 3T (Birmingham) or Siemens Tim Trio 3T (Southampton) scanner. Both sites underwent a site qualification procedure prior to data collection, and scanning parameters were adjusted according to a physicist's recommendations until the protocols were comparable. EPI volumes covering the whole brain (UOB: TE/TR = 87ms/8000ms, bandwidth = 19.3Hz, field of view (FOV) = 256mm; 62 axial slices, 2mm slice thickness; UoS = TE/TR = 92/8800, bandwidth = 1776Hz, field of view (FOV) = 256mm; 62 axial

slices, 2mm slice thickness) were acquired using a 32 channel head coil. Diffusion weighted images were sensitized for diffusion along 64 different directions with a b-value of 1000 s/mm<sup>2</sup>. An additional T2-weighted b=0 volume was also acquired to aid with eddy correction (achieved using FSL and FMRIB's Diffusion Toolbox; <http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FDT>).

#### **5.3.4 Data analyses**

Data were analysed using FSL ([www.fmrib.ox.ac.uk/fsl/](http://www.fmrib.ox.ac.uk/fsl/)). Firstly, we estimated distortions in the magnetic field using an algorithm detailed by Andersson, Graham et al. (2016). Subject specific b-vectors were used during pre-processing of the Southampton data to aid eddy correction as angulation was applied during acquisition in this site. No angulation was applied at Birmingham.

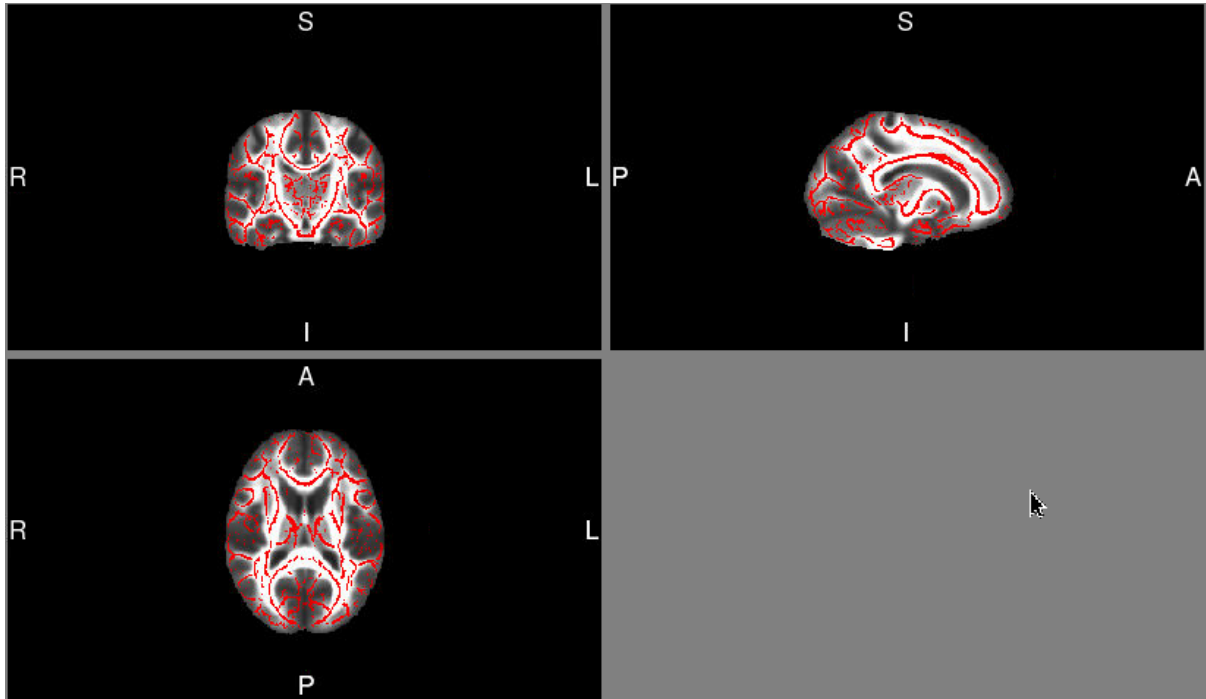
A susceptibility-induced off-resonance field as estimated from a pair of b=0 volume acquired with reversed PE-polarities (Andersson, Skare, & Ashburner, 2003), where one b=0 volume was the first volume of the diffusion data set, and one b=0 was acquired afterwards. The estimated field was subsequently used together with all the diffusion data to estimate eddy current-induced distortions and subject movement (Andersson & Sotiropoulos, 2016). In addition, movement induced signal dropout was identified and the lost signal was replaced by a non-parametric Q-space interpolation (Andersson, Graham, Zsoldos, & Sotiropoulos, 2016).

Tract-based spatial statistics (Smith et al., 2006) were then computed using an automated method from the FSL software library

([fsl.fmrib.ox.ac.uk/fsl/fslwiki/TBSS/UserGuide](http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/TBSS/UserGuide)). TBSS uses a non-linear approach to account for issues with standard registration processes. This approach includes a skeletonisation step that improves residual image misalignment and removes the need for data smoothing (Bach et al., 2014).

A subject specific mean FA image was calculated for each of the 62 participants, after which a subject specific white matter skeleton was created. The mean FA skeleton was thresholded at 0.2 with the resulting binary mask used for voxelwise comparison of FA statistics. The mean FA was then projected onto the common skeleton, which was averaged from the entire sample and transformed into MNI space (see Figure 5.16).

From this, the mean FA for each participant was extracted for the whole brain and the bilateral UF using binary masks from the JHU white matter tractography atlas (Hua et al, 2008). These values were then exported to SPSS, where they were mean scaled and correlated to psychometric measures. As with both previous experimental chapters, an online tool was used to calculate Bayes Factors for all analyses ([www.lifesci.sussex.ac.uk/home/Zoltan\\_Dienes/inference/Bayes.htm](http://www.lifesci.sussex.ac.uk/home/Zoltan_Dienes/inference/Bayes.htm); Dienes, 2014), where current data was compared to significant correlations reported in Breeden et al. (2015).



*Figure 5.17. Mean skeletonised FA visualised on MNI brain.*

## 5.4 Results

### 5.4.1 Site & Gender Effects

There were no significant differences between sites for IQ ( $t(60) = -.19, p = .85$ ), gender ( $X^2 = .13, p = .72$ ), age ( $t(60) = -1.4, p = .18$ ), CU traits ( $t(60) = -.56, p = .58$ ), CBCL externalising ( $t(60) = .58, p = .57$ ) or overall FA ( $t(60) = .25, p = .81$ ).

Southampton recruited 15 girls and 7 boys, whilst Birmingham recruited 26 girls and 14 boys. Males and females did not differ for IQ ( $t(60) = .06, p = .95$ ) or CBCL externalising ( $t(60) = .06, p = .95$ ), but there was a trend for boys to be older ( $t(60) = -1.8, p = .08$ ) and have higher levels of CU traits ( $t(60) = -1.88, p = .07$ ). Males showed significantly greater whole brain FA than females ( $t(60) = -3.23, p < .001$ ),

which is consistent with previous literature (Herting, Maxwell, Irvine & Nagel, 2011).

#### **5.4.2 Age Effects**

On the basis of previous studies showing that age is positively correlated to whole brain FA in youths (Asato et al., 2010; Lebel et al., 2012), one-tailed correlations between age and FA was carried out (see Figure 5.18). When males and females were considered together, there was a significant positive correlation between age and whole brain FA ( $r = .29$ ,  $N = 62$ ,  $p = .01$ ). This association remained significant when females ( $r = .42$ ,  $N = 40$ ,  $p = .01$ ) were considered separately, but when males alone were considered the association was non-significant ( $r = .25$ ,  $N = 22$ ,  $p = .26$ ). This could be due to the fact that there were fewer males than females in the current sample.

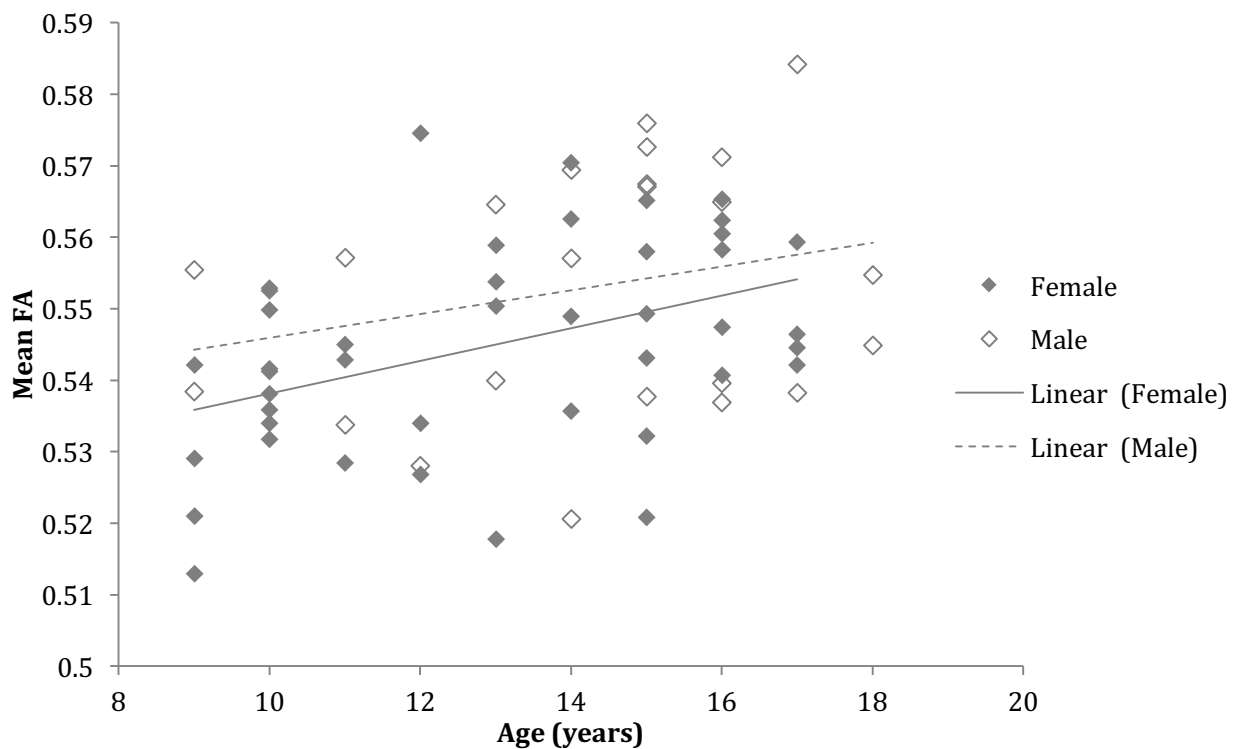


Figure 5.18. Correlation between whole brain fractional anisotropy and age.

#### 5.4.3 Correlations between psychometric measures

To assess whether the sample in the current chapter matches previous chapters, we computed correlations across the various relevant behavioural measures. Two-tailed zero-order correlations between age, IQ, ICU and both subscales of the CBCL are reported in *Table 5.9*. Consistent with the results of the previous chapters, externalising behaviours were positively correlated with both CU traits and internalising behaviours.

Table 5.9. Zero-order correlations between psychometric measures.

	1	2	3
1. CU traits			
2. Internalising behaviours	.01		
3. Externalising behaviours	.36**	.41**	
4. Age	-.04	-.03	-.23
5. IQ	.05	-.14	-.05

\*\* $p < .01$

\* $p < .05$

#### 5.4.4 Correlations with FA

Next, partial correlations between average FA of the right and left UF, whole brain FA and the two psychometric measures were computed, controlling for age, IQ, site and gender. They presented a negative pattern of correlation for both CU traits and externalising behaviours with FA in the UF and across the whole brain, but none of these correlations were significant (see Table 5.10).

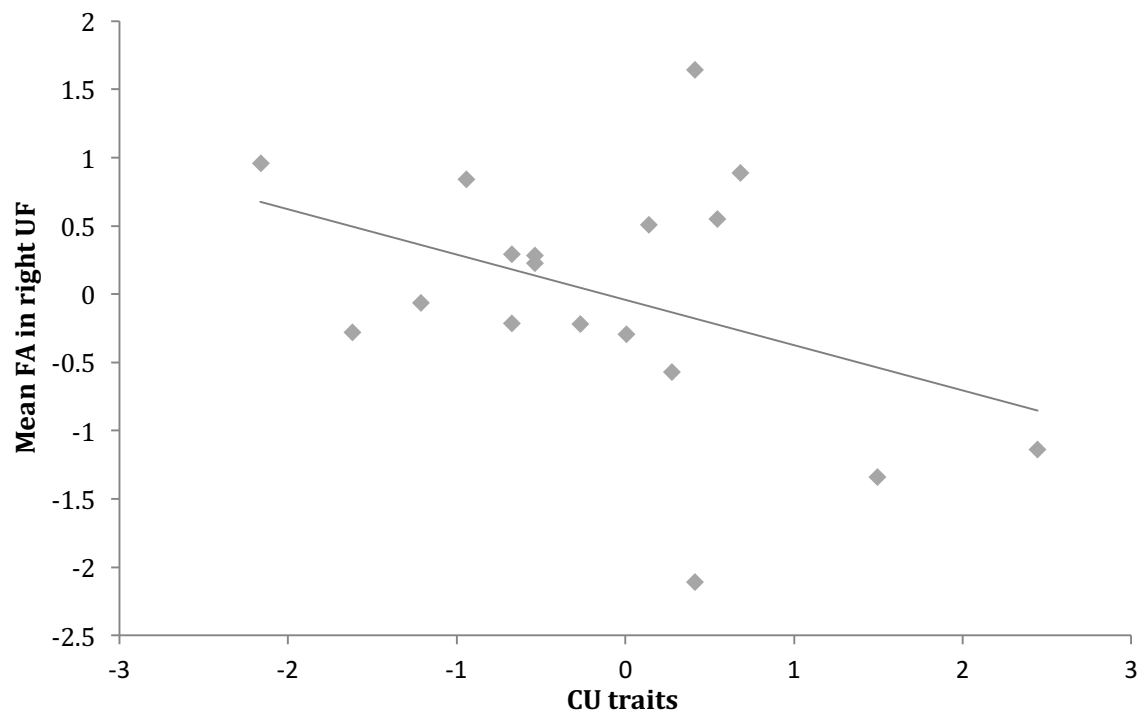
*Table 5.10. Correlations between psychometric measures and white matter integrity, standardised for age, IQ, gender and site.*

	CU traits		Externalising behaviours	
	r	p	r	p
Whole brain	-.06	.33	-.18	.19
Left UF	-.039	.39	-.15	.25
Right UF	-.077	.28	-.13	.33

*Note: Correlations controlled for age, IQ, site and gender.*

As previous research has found correlations between CU traits and the FA of the right UF in young adults (aged 18-21 years), we also reran correlations using only the older participants in the current sample (N = 18, aged 16-18 years). When controlling for site, gender and IQ, there was a significant negative correlation between CU traits and structural integrity in the right UF ( $r = -.49$ ,  $p = .03$ ;  $BF = 6.19$ ; see Figure 5.3), but not the left UF ( $r = -.25$ ,  $p = .19$ ,  $BF = 1.10$ ) or whole brain ( $r = -.27$ ,  $p = .16$ ,  $BF = 1.23$ ). The Bayes Factor ( $BF > 3$ ) suggest strong evidence supporting the negative correlation in the right UF, but inconclusive evidence ( $BF > 1/3$ ) regarding the association between CU traits and FA in the left UF and whole brain FA.





*Figure 5.3. Residuals of structural integrity in right UF as a function of CU traits, after controlling for site, gender and IQ, in youths aged 16-18 years.*

When youths aged 9-15 years were considered in a partial correlation controlling for site, gender and IQ, there were no significant correlations between CU traits or FA in the right UF ( $r = -.01$ ,  $p = .48$ ;  $BF = .30$ ), but not the left UF ( $r = -.01$ ,  $p = .50$ ,  $BF = .29$ ) or whole brain ( $r = -.03$ ,  $p = .41$ ,  $BF = .33$ ). As these Bayes Factors were  $\leq 1/3$ , there evidence for the null hypothesis in these youths.

#### **5.4.5 Shared variance between CU traits and externalising behaviours**

Finally, we investigated whether these patterns were strengthened when controlling for the shared variance between CU traits and externalising behaviours. Suppressor effects between CU traits and externalising behaviours were examined. Partial correlations between average FA of the right and left UF,

whole brain FA and CU traits, controlling for age, IQ, site, gender and externalising behaviours were computed. Following this, partial correlations between average FA of the right and left UF, whole brain FA and externalising behaviours, controlling for age, IQ, site, gender and CU traits were computed. All correlations remained non-significant. (Table 5.11). Additionally, we assessed whether there were suppressor effects in 16-18 year olds only, but none of the correlations were significant.

*Table 5.11. Correlations between psychometric measures and white matter integrity, standardised for age, IQ, gender, site and the additional variable.*

	CU traits <sup>1</sup>		Externalising behaviours <sup>2</sup>	
	r	p	r	p
Whole brain	-.06	.32	-.18	.19
Left UF	-.04	.38	-.15	.25
Right UF	-.08	.28	-.13	.33

<sup>1</sup> Correlation controlled for age, IQ, site, gender and externalising behaviours.

<sup>2</sup> Correlation controlled for age, IQ, site, gender and CU traits.

## 5.5 Discussion

The present study investigated whether there is an association between CU traits and white matter integrity in typically developing youths. We hypothesised that FA in the bilateral UF would be negatively correlated with CU traits. Furthermore, we investigated whether structural integrity in the UF in youths without AB is partly influenced by independent, opposing contributions of externalising

behaviours and CU traits, as observed for other metrics in clinical and non-clinical samples (Seara-Cardoso et al., 2016; Sebastian, McCrory, et al., 2012). We found that age was positively correlated with whole brain FA, which is in line with current literature (Barnea-Goraly et al., 2005; Chen, Zhang, Yushkevich, Liu, & Beaulieu, 2016). We found an unreliable negative association between CU traits and FA in the ROI across the whole sample. FA in the right UF was associated with CU traits in a subsample of 16-18 year olds only, whilst there was no association between CU traits and FA in the UF in youths aged 9-15 years. Unlike Breeden et al. (2015), the current study found no association between externalising behaviours and FA in the UF.

The current finding of an association between CU traits and structural integrity in the right UF in youths aged 16-18 years supports previous literature with a community sample of young adults (aged 18-21 years), which found a negative association between CU traits and structural integrity in the right UF only (Sobhani et al., 2015). Sobhani et al. (2015) found this association when scores from both the APSD and PCL:YV were individually considered, suggesting that the finding is robust across psychometric measures. However, Sobhani et al. specifically chose the 500 participants for their level of CU traits; half of the sample had low levels of CU traits (0th–25th percentiles) and half had high levels of CU traits (75th–100th percentiles) of a composite psychopathy score. Thus, the range of psychopathy scores was purposefully chosen to be particularly disparate. It is encouraging that the current study replicated these findings using a full range of available scores rather than an extreme group approach.

Both the current study and Sobhani et al. (2015) found associations in the right UF only. This suggests that either there is hemispheric lateralisation with respect to CU traits, or that there is a stronger association between FA and CU traits in the right UF than the left. The previous chapter found stronger correlations between subliminal fear processing and CU traits in the right amygdala and insula compared to the left amygdala and insula, although all four correlations were significant. This could suggest that CU traits have a stronger association with brain areas in the right hemisphere than the left. However, a recent study reported different lateralization patterns of five subcomponents of the UF using advanced particle filtering tractography (Hau et al., 2016), which suggests that there may in fact be a lateralisation effect here. My sample size of 16-18 year olds reported here was only 18 participants, which is under the 55 recommended by the power calculations. Future research could gather a larger sample of 16-18 year olds to ascertain whether this additional power allows an association between FA in the left UF and CU traits to be observed, or whether this association is indeed restricted to the right UF only.

The current study found no association between FA in the UF and CU traits when participants aged 9-15 years were considered. Whilst other studies did not report correlations between structural integrity in the UF and CU traits (Pape et al., 2015; Sarkar et al., 2016), this is the first study to our knowledge to report evidence for no association between these measures. The lack of association seen here could be influenced by the development trajectory of the UF; it is one of the last white matter tracts to fully mature (Lebel et al., 2012). This finding therefore suggests

that CU traits are not associated with reduced FA in the UF from childhood, but develop during adolescence.

It is relevant at this point to consider that this study did not find a positive association between age and whole brain FA in males only, which is unexpected (see Simmonds, Hallquist, Asato, & Luna, 2014 but also Menzies, Goddings, Whitaker, Blakemore, & Viner, 2015). This could be taken to suggest that the current sample of males are not representative, which could have impeded our investigations of FA in the UF. Conversely, it should also be considered that Simmonds et al. (2014), who conducted a longitudinal study into white matter development in 128 individuals, found that the UF underwent an interim period during adolescence with no significant growth and no differences between males and females. Therefore, the males in this sample could reflect this period of stagnation. Whilst males and females in the current sample had similar age ranges, males were on average 1.25 years older than females. Therefore, it could be that some males had entered the interim period of stagnation. This research, together with mixed results reported above, suggests that adolescence is a difficult time to assess development in the UF, as there are many factors which could influence results.

Unlike Breeden et al. (2015) the current study did not find any association between structural integrity in the UF and externalising behaviours. One reason for this could be due to the stringent exclusion criteria applied in this study.

Participants were only included if they achieved a score less than 63 on both the internalising and externalising subscales of the CBCL, as this is considered below

the clinical threshold. Whilst it could be claimed that their sample had a greater degree of variability as the authors did not impose any such restrictions, post-hoc analyses found that externalising behaviours were not related to WM integrity after CU traits were controlled for (Breedén et al., 2015). Therefore, both the current study and Breedén et al. found that CU traits are related to FA in the UF, whereas externalising behaviours are not likely to be related.

We did not find any evidence for suppressor effects between CU traits, externalising behaviours and structural integrity in the UF. This could be due to the fact that our typically developing sample did not show a large enough range of externalising behaviours, or it could reflect previous findings which did not find any association between externalising behaviours and FA in the UF when CU traits were controlled for (Breedén et al., 2015). To the best of our knowledge, suppressor effects have not been reported in DTI studies investigating psychopathy or CU traits. Therefore, the current results may reveal methodological differences between the present study and fMRI studies which reported suppressor effects in these populations (Hyde et al., 2014; Lockwood, Sebastian, et al., 2013; Lozier et al., 2014; Seara-Cardoso, Viding, et al., 2015; Sebastian, McCrory, et al., 2012). On the other hand, the unique variance presented by CU traits and externalising behaviours may be more closely linked to variations in brain activity rather than brain structure.

The current study may have found divergent results in our whole sample compared to Breedén et al. (2015) and Sobhani et al. (2015) due to the fact that we looked at the whole UF, whereas Breedén et al. and Sobhani et al. specified pre-

defined ROIs within the centre of the left and right UF. Our method may therefore have diluted our results in the younger participants. In comparison, the fact that the UF undergoes rapid development as healthy children age may have meant that the relationship between CU traits and FA was not yet notable in younger children.

FA is derived from the difference between two absolute values: axial diffusivity (rate of diffusion along the fibre tract) and radial diffusivity (rate of diffusion perpendicular to the fibre tract). FA could reflect several different factors, including the degree of orientation of axonal membranes, the compactness of myelin sheaths, or the amount of branching or crossing of fibres (Giorgio et al., 2010). It would have been beneficial in this chapter to break down FA measurements into axial and radial diffusivity measures, or tractography measures, which could provide further evidence on which aspect of structural connectivity drives the negative association between CU traits and FA in the UF.

The DTI technique used in this chapter is poor at modelling areas where fibre pathways cross paths, which could be an issue for the UF due to its high anatomical curvature (Olson et al., 2015). It would be interesting to replicate this study with a more powerful technique which does not pose such technical limitations, such as probabilistic tractography. Future research could also account for pubertal maturation as well as age, as pubertal status is associated with increases in FA in frontal white matter when controlling for age (Herting et al., 2012).

A strength of the current study was the thorough screening that participants underwent to ensure that they were not taking any kind of drugs or medication.

This is particularly relevant to DTI studies which focus on the UF, as opiate use is associated with reduced FA within this white matter tract (Upadhyay et al., 2010). Other studies (such as Sobhani et al., 2015) did not carry out such thorough screening. Sobhani et al. also did not account for externalising behaviours, which could mean that their participants might have been eligible for a research diagnosis of oppositional defiant disorder or CD.

The findings from this study provided novel evidence that CU traits were negatively correlated with right UF FA in typically developing participants aged 16-18 years, whilst there is no relationship between CU traits and UF FA in those aged 9-15 years. The magnitude of neural activity in regions such as the amygdala and insula, which are connected via the UF, may be influenced by alterations to the quality of structural connections within the UF (Ford & Kensing, 2014).

Therefore, the negative relationship between CU traits and FA in the UF reported in 16-18 year olds here may help to explain the negative association between amygdala and insula activity and CU traits reported in Chapter 4. Consistent with previous literature, age was positively correlated with whole brain FA. There was insufficient evidence for a negative association between CU traits and FA in the UF in the entire sample (9-18 years) despite indications that a relationship exists between psychopathy and structural integrity in the UF in adulthood. Finally, suppressor effects between CU traits and externalising behaviours were not seen in this study. Future research could look at whether the association between FA in the right UF and CU is present at a young age (CU traits are recognizable in children as young as two and a half years old; Bedford et al., 2015). It would also be



interesting to investigate whether this association is stable across time, which could be achieved with a longitudinal design.

## CHAPTER 6: SUMMARY AND CONCLUSIONS

The main aim of this thesis was to advance understanding of CU traits in typically developing youths. This was achieved via behavioural and neuroimaging techniques, including fMRI and DTI. This final chapter summarises and critically appraises the main results and statistical methods from the previous experimental chapters. Following this, strengths, limitations and directions for future research are discussed.

### **6.1 Summary of Results**

The main research aim was to investigate whether CU traits in typically developing children and adolescents show similar associations with behavioural and neural responses to those seen in individuals within clinical and forensic populations. In clinical and forensic populations, higher levels of CU traits have been found to be associated with poorer recognition of anger, fear and sadness (Dawel et al., 2012), with the strongest deficit observed in fear recognition. Negative associations have also been reported between CU traits and amygdala activity during processing of fearful faces (Lozier et al., 2014; Viding et al., 2012) and FA in the UF (Breedén et al., 2015; Wolf et al., 2015) in clinical populations. Whilst most research has investigated CU traits in clinical and forensic populations, there is growing evidence that these traits fall along a continuum across clinical and non-clinical samples.

Psychopathy in adults (Hare & Neumann, 2008) and CU traits in youths (Murrie et al., 2007) are dimensional constructs present in both clinical and healthy

populations. Consequently, individuals diagnosed with psychopathy represent an extreme end of the distribution of psychopathic traits rather than a qualitatively distinct group of individuals. Whilst it is of clear importance to research these traits in their most severe form, only a small body of research has investigated these traits in non-clinical samples. This thesis was novel in that it addressed this gap in the literature by assessing the behavioural and neural correlates of CU traits and emotion processing in typically developing youths.

Research with individuals with varying levels of CU traits but without antisocial tendencies may lead to a clearer understanding of the pathophysiology of CU traits and help identify protective factors that may prevent these individuals from developing AB (Lilienfeld, 1998). My thesis has found that different levels of CU traits in youths without AB are indeed continuous and should be considered on a spectrum rather than discrete taxa. As CU traits in TD youths are inversely associated with emotion recognition and neural response during emotion processing, this provides evidence for the argument that CU traits should be considered to be clinically independent to Conduct Disorder (Rutter, 2012).

This thesis focussed on three main research areas with respect to emotion processing. Firstly, the association between CU traits and the recognition of the six basic emotions was investigated. Among those with AB, higher levels of psychopathic/CU traits have been shown to be associated with poorer recognition of facial emotions, specifically fear and sadness (Dawel et al., 2012). In Chapter 3, the investigation into whether this was also the case in 110 typically developing

youths is detailed. Results showed that sadness and disgust recognition accuracy was inversely correlated with CU traits.

The results presented in Chapter 3 support the theory that CU traits are related to impairments when recognising specific emotions, rather than a general impairment in emotional facial expression recognition (Blair et al., 2006). These impairments may mirror reduced attention to the eyes of emotional faces.

Evidence suggests that sad faces are recognised by focussing on the eye region (Schurgin et al., 2014). A recent study with a community sample of adult males found that primary psychopathic traits (equivalent to CU traits) were negatively correlated with the number of fixations on the eyes relative to the mouth when viewing the six basic emotions (Gillespie, Rotshtein, Wells, et al., 2015). This would support the premise that diminished sadness recognition reported in Chapter 3 could be caused by reduced attention to the eyes. However, since disgusted faces are recognised by focussing on the mouth region (Schurgin et al., 2014), this theory does not neatly correspond with the emotions found to be associated with CU traits (i.e. sadness and disgust) in Chapter 3.

It would have been interesting to measure eye gaze and fixations in this chapter; these techniques are more sensitive than accuracy measures (Prinzmetal, McCool, & Park, 2005) and may call attention to more nuanced discrepancies associated with CU traits. If CU traits in typically developing youths are in fact associated with longer RTs and reduced eye gaze fixations, this would suggest that emotions are processed less effectively. Future work in this area could also investigate whether instruction on focussing on the eye regions leads to increased accuracy in TD

youths with higher levels of CU traits, seeing as this instruction led to increased accuracy in emotion identification in youths with conduct problems and HCU traits (Dadds et al., 2006).

My second experiment (Chapter 4) detailed an investigation into activity in brain areas known to be relevant for emotion processing in a subliminal emotion processing paradigm. A recent neuroimaging study in children with conduct problems reported a negative association between CU traits and amygdala activity during subliminal fear processing (Viding et al., 2012). Chapter 4 described a similar subliminal processing task in typically developing youths, where negative associations between CU traits and bilateral amygdala and insula activity during fear processing, and a positive correlation between externalising behaviours and left amygdala response to angry faces in males only, were found. These results support evidence that CU traits are associated with reduced activity in emotion processing brain circuits in typically developing populations, whilst externalising behaviours are associated with increased activity. Interestingly, the amygdala is involved in processing of sad faces (Blair et al., 1999), whilst the insula is involved in the processing of disgusted faces (Wicker et al., 2003). Therefore, the results from this chapter dovetail with those reported in Chapter 3, where CU traits were negatively associated with sad and disgust processing.

The results reported in Chapter 4 suggest a dissociation between amygdala activity and externalising behaviours in males and females. A positive correlation between externalising behaviours and anger processing in the left amygdala was reported in males, whilst evidence supported a lack of any association between

externalising behaviours and amygdala reactivity to angry faces in females. This is not down to any differences in externalising scores between the genders (see Table 5.8). This neural response pattern might suggest that males attend more to cues of aggression (Schienle, Schäfer, Stark, Walter, & Vaitl, 2005) and could be a factor in why CD is more often seen in males than females (Maughan et al., 2004).

As a Bayes Factor of less than 1/3 was found in the female sample in this study, I can state that there was no relationship between externalising behaviours and amygdala activity during anger processing in the amygdala in females. This finding is a novel and important contribution to the field of AB, as it suggests that males and females show different neural patterns in response to threat stimuli. Males may show greater amygdala activity due to the fact that anger is often seen as more socially acceptable in men rather than women (Serbin et al., 1993). In fact, women leaders who showed anger were judged as less effective than when they did not show anger, whilst men were judged as equally effective whilst showing anger and neutral affect (Lewis, 2000). It would be interesting to assess whether the same dissociation reported in Chapter 4 is seen within populations with AB; previous research has considered amygdala activation during anger processing in male samples with AB (e.g. Passamonti et al., 2010), but to my knowledge no research has looked at anger processing and externalising behaviours in females with AB.

The last experimental chapter (Chapter 5) described a study which examined the association between CU traits and the structural integrity of the UF: a white matter tract in the brain that is important for emotion processing. CU traits are associated

with structural and functional brain abnormalities in the amygdala and ventromedial prefrontal cortex, two regions of the brain that are connected via the UF (Von Der Heide et al., 2013). These areas are involved in various social, cognitive, and affective functions (Bzdok et al., 2012; Gupta et al., 2011; Hooker et al., 2008; Morelli et al., 2014; Sebastian, Fontaine, et al., 2012; Tzschoppe et al., 2014) that are known to be impaired in psychopathy (Blair, 2007, 2008; Fontaine et al., 2008; Marsh et al., 2008; Sebastian, McCrory, et al., 2012). Chapter 5 described diffusivity in the UF using TBSS. To my knowledge, no previous research has looked dimensionally at CU traits in typically developing youths with respect to FA. This study found CU traits were negatively associated with FA in the right UF, but only among adolescents aged 16-18 years. This suggests that CU traits are associated with reduced structural connectivity in the UF in typically developing older adolescents, consistent with findings from clinical samples of adults (Craig et al., 2009; Hoppenbrouwers et al., 2013; Motzkin et al., 2011).

Chapter 5 suggested that white matter changes as a function of CU can be seen in older, but not in younger, youths. This study reported a negative association between CU traits and structural integrity in the right UF in youths aged 16-18 years, whilst there was sufficient evidence to support the null hypothesis in those aged 9-15 years. These results suggest that CU traits are not associated with reduced FA in the UF from childhood, but develop during adolescence. As parent-reported CU traits are considered to be a stable characteristic (Frick, Kimonis, Dandreaux, & Farell, 2003), it is interesting that these traits are not associated with FA in the UF from a younger age. This suggests that CU traits may be

associated with the *development* of the UF during late puberty. It is currently unknown whether these findings mirror those from clinical samples, as no research has looked at CU traits dimensionally in the UF. It would be interesting for future research to assess whether the same pattern of results is present in clinical samples. Overall, these key findings suggest that age is a highly relevant factor in DTI studies that concentrate on the UF.

## **6.2 Overall considerations**

It was recently recommended that a syndrome including high CU traits, irrespective of AB, should be included in the International Classification System of Diseases (ICD-11) (Rutter, 2012). This adaptation was suggested because there are several distinctions between CU traits and AB, including: CU traits are more highly heritable than AB (Viding et al., 2008); participants with AB/HCU traits respond more poorly to treatment for AB than those with AB/LCU traits (Hawes & Dadds, 2005). Furthermore, CU traits are moderately stable over time and HCU without AB is associated with a host of problems (Lynam et al., 2007). The current thesis has shown that CU traits are associated with behavioural and neurobiological correlates in typically developing youths. This could be considered as support for Rutter (2012)'s argument that CU traits should be considered as an independent variable to AB.

Youths in the current sample were stringently chosen to be typically developing using the K-SADS and CBCL. However, these measures do not identify problematic behaviours such as poor peer relations, passive aggressive behaviours or reduced



empathy. It is entirely possible that my participants might have shown these behaviours and they were undetected by my instruments. Even if a child is not considered a proactive bully, he or she may play a significant role when witnessing bullying of another student, for example laughing and encouraging the bully, holding a victim still, or encouraging others to watch whilst a peer is victimized (Salmivalli et al., 1996). Therefore, it would be interesting to determine if CU traits in typically developing youths are associated with broader bullying behaviours. If this is indeed the case, a controversial idea is that schools could therefore identify which children are more likely to become bullies (or accessories to bullying) and put extra effort into rehabilitation.

It is also possible that HCU traits in typically developing youths are associated with impairments in cognitive functions such as empathy (Jones et al., 2010). One study found that typically developing children with HCU traits to be low in affective empathy and high in bullying behaviours compared to those with LCU traits (Munoz, Qualter & Padgett, 2010). Therefore, CU traits in children could outline stable behavioural characteristics that may be useful in later life. For example, some careers may be more suited to people who have low levels of emotional empathy but do not show antisocial behaviour, such as making redundancies or working in the stock market. This may help channel children into suitable careers, or away from unsuitable jobs.

Studies examining CU traits in youths with conduct problems have usually relied on male only or predominantly male samples (i.e. Fairchild et al., 2009; Viding et al., 2012). This is because conduct problems are more prevalent in males

(Maughan et al., 2004). However, conduct problems are not solely restricted to the male sex, and so research should include mixed samples of participants. This thesis, where similar associations to those seen in male clinical samples were produced despite the reliance on samples predominantly composed of female participants, is therefore an important contribution to this field. The novel results highlighted in this thesis support the view that emotional deficits associated with psychopathy may generalise across genders (Sutton, Vitale, & Newman, 2002). A recent study investigated the relationship between CU traits and gender in a community sample of adolescents. This study reported that gender was not correlated with CU traits, but gender did moderate the relationship between CU traits and physical aggression (Nwafor, Onyeizugbo, & Anazonwu, 2015); girls with HCU traits showed less physical aggression than males with HCU traits. Therefore, the fact that participants in this thesis were mostly female could have meant that gender acted as a protective factor against high levels of overt externalising behaviours.

Instead of showing overt, externalising behaviours, females with high levels of CU traits may show more covert, manipulative behaviours. O'Keefe, Carr, & McQuaid, (1998) found that females with CD had a significantly higher ratio of covert to overt behaviour problems than males with CD. Furthermore, CD symptoms in females showed a unique pattern, including deviant peer group membership, lying and running away. It would be illuminating to investigate whether typically developing females with higher levels of CU traits show more covert AB than females with lower levels of CU traits. If this were the case, I may not have picked

up on these traits in my assessment criteria, as the participants could have concealed such behaviours from their parents and from the investigators.

Callous-unemotional traits depict a stable personality feature, thought to be unchanging over time (Frick & Ellis, 1999). However, one study with 1,443 adolescents found that 15 and 16-year-old youths had significantly higher ICU scores than their peers aged 13-14 years and 17-18 years (Essau, Sasagawa & Frick, 2006). This pattern of age-associated differences suggests that the normative level of CU traits may in fact vary over the course of pubertal development (Edens, Skeem, Cruise, & Cauffman, 2001). My thesis included youths aged between 9-18 years, and I did not look at whether CU traits varied across these age groups. However, I did control for age in all of my three experimental chapters, and so age should not have confounded the current results.

### **6.3 Suppressor Effects**

In this thesis, suppressor effects between CU traits and AB were considered in each experimental chapter. Unlike previous studies, we did not find any evidence of suppressor effects. There are several reasons that may explain why these effects were not apparent. Firstly, I was very stringent with inclusion criteria and excluded any participants who scored in the clinical range for internalising or externalising behaviours on the CBCL. This could mean that I did not have the range of externalising behaviours that other studies possessed since no other published studies have applied the same rigorous criteria. It could also be the case that suppressor effects are less noticeable in healthy populations or with the tasks

used here. Finally, unlike claims from many studies (e.g. Lozier et al, 2014; Viding et al., 2012; Seara-Cardoso et al., 2012) suppressor effects may not exist between these two measures.

#### **6.4 Strengths and Limitations**

A key strength of this thesis is that the behavioural and neuroimaging correlates of CU traits used across the three experimental chapters were similar to those used in existing studies on clinical samples to allow for direct comparisons to be made between typically developing and clinical samples. Typically, studies into CU traits use group comparisons to compare those with HCU traits to those with LCU traits. A fundamental strength of the current thesis is the evidence across the three chapters that CU traits are not binary, but can be considered as a continuous variable.

A further strength of this thesis is the inclusion of Bayes Factors and NHSTs. Bayes Factors allow one to assess whether there is substantial evidence either for or against a hypothesis or whether there is insufficient evidence. This is in contrast to NHSTs, which only report whether there is substantial or insubstantial evidence for the hypothesis. Further, as Bayes Factors are ratios of probabilities, two factors of equal amounts from unequal samples represent the same degree of evidence.

If Bayes Factors had not been reported in this thesis, the NHSTs would have had to be adjusted for multiple comparisons. For example, in Chapter 3, 12 statistical tests were calculated. According to Bonferroni corrections, this would have meant that only p values less than .004 ( $.05 \div 12$ ) could be considered significant. Neither

of the correlations reported in Chapter 3 would be regarded as significant under these stringent guidelines. The issue of correction for multiple comparisons is not pertinent from a Bayesian perspective (Gelman, Hill, & Yajima, 2012), meaning that the results reported in Chapter 3 can be considered significant.

One limitation of this thesis is that socio-economic status (SES) was not measured in these youths. Low SES is associated with reduced working memory and executive functioning abilities (Piccolo et al., 2016) and diminished brain surface area (Noble et al., 2015) in children. Furthermore, SES is negatively associated with CU traits and low SES is a predictor of stable, high levels of CU traits over time (Frick, Kimonis, et al., 2003). It would be interesting to assess whether SES influences the relationship between CU traits and brain activity during emotion processing in typically developing youths.

A final limitation of this thesis is that I was not able to design the tasks myself. As I joined the FemNAT-CD consortium after its inception and development, I carved out my thesis to include tasks which had already been designed. Therefore, I was unable to make adaptations (such as using child actors in the Emotion Hexagon task, or including additional emotions in the subliminal face processing task). However, this limitation could also be seen as a strength; as the sites included exactly the same tasks, this meant I was able to include data from both Birmingham and Southampton safe in the knowledge that the tasks were identical in each site.

## **6.4 Future directions**

Unlike previous studies, the current thesis did not find any evidence of suppressor effects. In order to assess whether the stringent inclusion criteria denied the presence of suppressor effects here, it would be pertinent to replicate the current studies with a male only sample of typically developing youths to be in line with previous clinical studies (e.g. Viding et al., 2012). However, it should be noted that Viding et al. (2012) also did not find suppressor effects in their sample of males with conduct problems. Furthermore, one could also replicate a variety of paradigms in which clear suppressor effects were found in a clinical sample (e.g. Seara-Cardoso et al., 2016; Sebastian, Fontaine, et al., 2012) with the current, typically developing sample of youths.

There are a number of aspects that this thesis did not examine in relation to CU traits in typically developing youths. First, I did not address whether levels of CU traits are predictive of psychiatric and social outcomes. It would be interesting to follow up with the current samples to see whether the same associations in each of the experimental chapters are present in the current sample later in life. Second, it will be important to investigate whether youths with high levels of CU traits present with any factors that are protective against AB, such as proficient parenting or resource-rich surroundings (Fanti, Colins, Andershed, & Sikki, 2016). This could lead to the development of treatment or preventative measures against AB in clinical cases. For example, one study found that youths without AB but with HCU traits showed less risky decision making than those with AB/HCU traits,

which could reflect a potential protective factor against the development of AB (Fanti, Kimonis, et al., 2016).

Further, it would be interesting to investigate whether there are any shared neurocognitive characteristics during emotion processing between typically developing youths with high levels of CU traits and those with CD and high levels of CU traits. This could be achieved using the current tasks in the FemNAT-CD consortium.

The current thesis did not look cross-sectionally at whether levels of CU traits were associated with other behavioural traits or lifestyle factors, such as peer problems. One study has reported a positive correlation between levels of CU traits and number of peer problems in a clinic-referred sample (Andrade, Sorge, Djordjevic, & Naber, 2015). Furthermore, CU traits moderated the relationship between impulsive behaviours and peer problems. Future research should address this gap by investigating whether CU traits in typically developing youths are associated with maladaptive relationships.

Some of the youths included in my thesis had ICU scores (which measure CU traits) above the proposed clinical cut off of 26 (Kimonis, Fanti & Singh, 2014). The fact that these children did in fact meet criteria to be considered typically developing could suggest that this cut off is too strict. On the other hand, these children may have a higher risk of developing antisocial behaviour, which could be triggered by a stressor. It would be interesting to follow these children for the next 5 years to

see if they do indeed develop antisocial behaviour, or if they channel their behaviours into societally acceptable, yet dangerous, activities such as sky diving.

Previous research has found a positive association between psychopathic traits, RT and eye gaze in healthy adults (Gillespie, Rotshtein, Wells, et al., 2015), whilst positive associations were found between CU traits and RT when detecting fearful and disgusted faces in youths “at risk” of developing AB (Sylvers et al., 2011). It would be informative to record RT and eye gaze when participants viewed the stimuli in the Emotion Hexagon (chapter 3) and subliminal emotion processing (chapter 4) tasks. This addition in the Emotion Hexagon task would assess whether fixation dwell time is negatively associated with CU traits in adolescents, and whether this pattern is seen across emotions (as Gillespie, Rotshtein, Wells, et al., 2015 found), or whether it is specific to sadness and disgust (as found in this thesis). Measuring eye gaze in the subliminal emotion processing task would elucidate whether those who presented with reduced amygdala activation viewed the eyes first, potentially gathering more information about the subliminally presented emotion and activating the subconscious emotion processing network, or whether these youths viewed another aspect of the face first and missed the preconscious fear cue.

In Chapter 4, activation in emotion processing areas of the brain in response to subliminal processing of anger and fear were correlated against CU traits. In light of findings from Chapter 3, where only sadness and disgust were found to be negatively correlated with CU traits, it would be of interest for future research to assess whether similar negative associations between CU traits and neural



activation during sadness and disgust processing are present. To build on this, one could look at negative emotions (i.e. fear, anger, sadness and disgust) across behavioural indices, and conscious and subliminal fMRI to see if there are similar associations across modalities.

It would be interesting to assess whether alexithymia modulates the associations between CU traits and emotion recognition/processing. Alexithymia is associated with difficulties in detection of anger, sadness and fear, and reduced activation in the amygdala during the processing of negative stimuli (van der Velde et al., 2013). However, to my knowledge no research has looked at whether alexithymia is associated with FA in the right UF. As CU traits and alexithymia present as behaviourally similar characteristics, but are not associated with one another (Lander, Lutz-Zois, Rye & Goodnight, 2012), it would be interesting to assess whether there are differences in the relationships between structural connectivity and each of the two clinical measures. On the other hand, similarities between neural patterns of activation associated with CU traits and alexithymia could suggest that the two disorders present similar cognitively, but have different behavioural outcomes.

The current thesis found a clear negative association between CU traits and structural integrity of the UF when 16-18 year olds only were considered, but support for the null hypothesis was generated in 9-15 year olds. Adolescence is a period of rapid brain growth and maturity, particularly in areas accountable for emotion regulation (Ernst, Pine, & Hardin, 2006). Thus, future research in the field of DTI should take into account that age could be a confounding factor among

youths with CU traits. Future research could also investigate whether radial or axial diffusivity are specifically underlying the association between FA and CU traits in the UF.

## **6.5 Conclusion**

This thesis represents a novel piece of work into the dimensional nature of CU traits in typically developing youths. The main objective of my thesis was to assess whether there is a relationship between behavioural and neural correlates of CU traits and emotion processing in typically developing youths. CU traits, whilst typically studied within the context of clinically recognised behavioural disorders, are also present to varying degrees in healthy children.

The current thesis is the first to use paradigms previously applied in research with antisocial youths to assess the dimensional nature of CU traits across a typically developing cohort. The first study demonstrated that accurate recognition of sadness and disgust was negatively associated with CU traits. The second study revealed that neural activation in the bilateral amygdala and insula were negatively correlated with CU traits when viewing subliminally presented fearful faces. A positive association between amygdala response to anger and externalising behaviours was also found in males only. The final study found that CU traits were negatively associated with structural integrity in the right UF in youths aged 16-18 years.

This research shows that CU traits should not be solely considered within the construct of antisocial behaviour, and provides evidence that CU traits should be

considered independently in future clinical descriptions. This research is a building block on which clinical understanding of callous personality traits can be developed. Future research should assess whether levels of CU traits are predictive of psychiatric and social outcomes in typically developing youths. If so, assessments of CU traits in children could be used to identify those who have the right characteristics for certain careers where a callous nature is beneficial, i.e. the military.

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## APPENDICES

### **Appendix 3.1. Shapiro-Wilk Test of normality for performance on the emotion recognition task and psychometric tests.**

		Statistic	df	Sig.
Emotion Recognition Task	Happy	.510**	110	.000
	Sad	.721**	110	.000
	Anger	.913**	110	.000
	Disgust	.834**	110	.000
	Surprise	.838**	110	.000
	Fear	.909**	110	.000
	Overall Accuracy	.896**	110	.000
Psychometric tests	CU traits	.912**	93	.000
	Internalising behaviours	.962**	93	.008
	Externalising behaviours	.928**	93	.000

**\*\* significant at the 0.01 level**

## Appendix 3.2. Bayes Factor analyses for correlations between psychometric measures and emotion recognition accuracy.

*3.2.1. Correlations between psychometric measures and accuracy of the six emotions, controlled for age, IQ, site and gender.*

		Overall accuracy	Anger	Disgust	Fear	Happy	Sad	Surprise
CU traits	Correlation Coefficient	-.16	-.1	<b>-.19*</b>	-.01	-.02	<b>-.25*</b>	-.05
	Sig. (2- tailed)	.05	.32	.05	.92	.88	.01	.65
	Bayes Factor	2.56	.88	3.12	.22	.30	11.11	.40
Externalising behaviours	Correlation Coefficient	.004	.01	-.01	-.05	.06	-.09	.05
	Sig. (2- tailed)	.99	.90	.91	.62	.56	.39	.62
	Bayes Factor	.28	.29	.29	.32	.33	.40	.32

3.2.2. Correlations between psychometric measures and accuracy of the six emotions, controlled for age, IQ, site, gender and the additional variable.

		Overall Accuracy	Anger	Disgust	Fear	Happy	Sad	Surprise
CU traits <sup>1</sup>	Correlation	<b>-.20*</b>	-.14	<b>-.23*</b>	.01	-.02	<b>-.25*</b>	-.10
	Sig. (2-tailed)	.03	.18	.03	.95	.87	.02	.37
	Bayes Factor	3.72	.79	5.86	.22	.30	10.54	.46
Externalising behaviours <sup>2</sup>	Correlation	.04	.06	.07	-.05	.06	.002	.08
	Sig. (2-tailed)	.64	.56	.53	.63	.55	.99	.44
	Bayes Factor	.30	.43	.50	.22	.35	.29	.36

<sup>1</sup> Correlation controlled for age, IQ and externalising behaviours.

<sup>2</sup> Correlation controlled for age, IQ and CU traits.

Notes: These correlations were computed using Blair and Coles (2000) reported correlations as plausible maximum effects. For the Anger, Fear and Sad conditions, the significant correlations reported in the Blair and Coles study were used. As this study reported non-significant results for Happy, Disgust and Surprise conditions, following advice from Zoltan Dienes we instead used an average of the three significant conditions in order to run Bayes Factor analyses on Happy, Disgust and Surprise.

### Appendix 3.3. 70:30 continua only

#### 3.3.1 Correlations between psychometric measures and accuracy of the six emotions for 70:30 continua only.

		Anger	Disgust	Fear	Happy	Sad	Surprise
CU traits	Correlation	-.061	-.236*	-.145	-.022	-.244*	-.082
	Sig. (2-tailed)	.582	.032	.192	.841	.026	.464
	df	104	104	104	104	104	104
Externalising Behaviours	Correlation	.05	-.064	.008	.058	-.05	.005
	Sig. (2-tailed)	.655	.566	.941	.602	.656	.963
	df	93	93	93	93	93	93

\* significant after Bayes Factor analysis

Note: Correlations controlled for age and IQ.

#### 3.3.2. Correlations between psychometric measures and accuracy of the six emotions for 70:10 continua only, when controlling for suppressor effects.

		Anger	Disgust	Fear	Happy	Sad	Surprise
CU traits <sup>2</sup>	Correlation	-.087	-.229*	-.16	-.048	-.244*	-.09
	Sig. (2-tailed)	.436	.038	.151	.666	.027	.419
	df	86	86	86	86	86	86
Externalising Behaviours <sup>3</sup>	Correlation	.079	.029	.069	.072	.049	.039
	Sig. (2-tailed)	.478	.794	.535	.519	.663	.725

df	86	86	86	86	86	86
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*\* significant after Bayes Factor analysis*

*<sup>1</sup> Correlation controlled for age and IQ.*

*<sup>2</sup> Correlation controlled for age, IQ and externalising behaviours*

*<sup>3</sup> Correlation controlled for age, IQ and CU traits.*

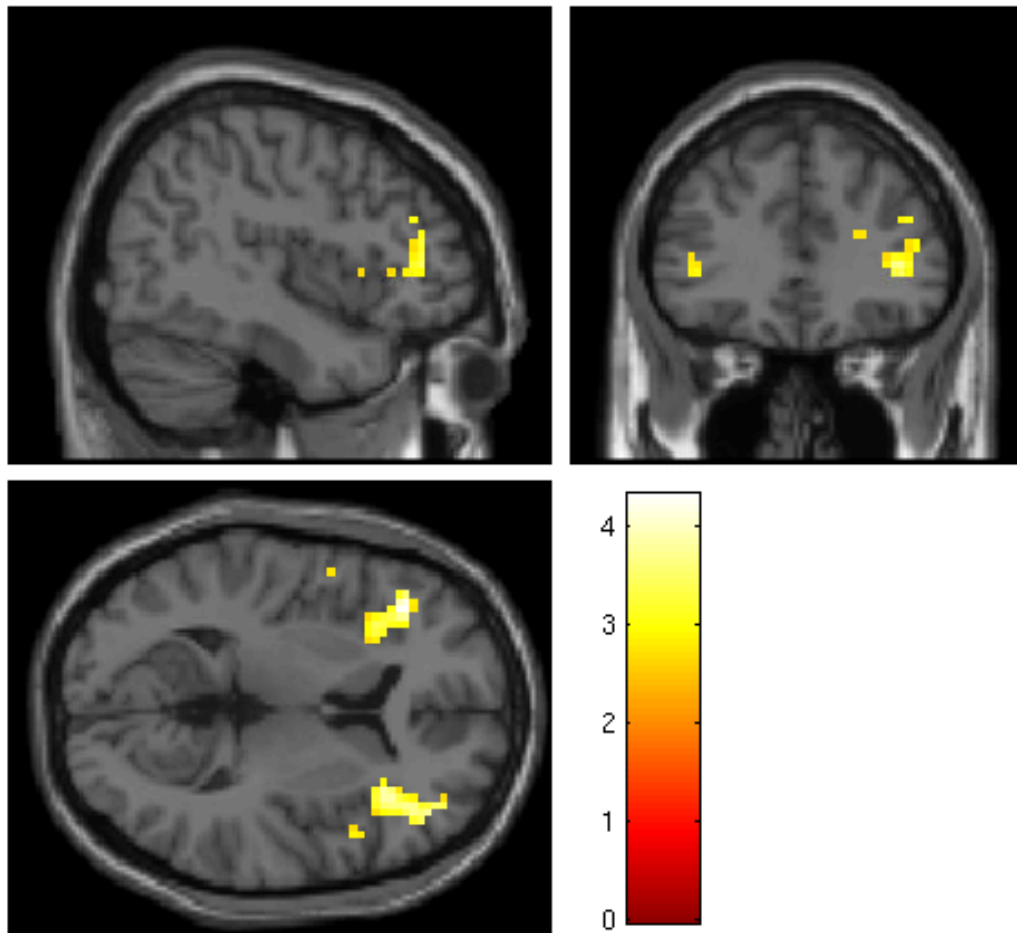


### Appendix 3.4. Confusion Matrix

The confusion matrix indicates that overall participants most commonly confused anger with disgust, and fear with surprise (Table 5), which is consistent with a previous study (Fairchild et al., 2009). Next, correlations between these data and ICU and CBCL scores were examined, but these did not yield any significant correlations.

Identified as (%)	Actual expression depicted					
	Anger	Disgust	Fear	Happy	Sad	Surprise
Anger	<b>61.9</b>	14.7	1.7	1.5	1.2	1.2
Disgust	22.1	<b>73.4</b>	3.3	1.0	6.4	1.6
Fear	4.6	1.5	<b>74.7</b>	1.0	3.3	6.8
Happy	0.6	0.6	0.8	<b>94.2</b>	0.8	3.4
Sad	2.1	8.9	3.1	1.0	<b>87.4</b>	1.2
Surprise	8.5	0.9	16.4	1.3	1.0	<b>85.8</b>

#### Appendix 4.1. Neural activity for threat > calm



Stimuli in threatening (fearful and angry) conditions elicited significantly stronger neural responses than the calm condition in several clusters, which can be visualised on a standard brain (see Appendix 1). These areas, which showed a main effect at  $p < .005$  uncorrected at the peak level, with a cluster size  $\geq 10$ , included the left inferior frontal lobe, right middle frontal lobe, bilateral putamen and bilateral insula.

**Appendix 4.2. Regions showing a main effect at  $p < .005$  uncorrected at the peak level, with a cluster size  $\geq 10$ , for threat (fear and anger) > calm faces.**

Brain region	L/R	Peak voxel (MNI)			Cluster size	z-value
		x	y	z		
Inferior Frontal Lobe	L	-39	33	6	141	4.19
Insula	R	33	24	9	154	3.92
Rolandic Operandi	L	-54	6	12	134	3.53
Inferior Parietal Lobe	R	54	-33	51	17	3.14
Insula	L	-39	9	0	13	3.05

### Appendix 4.3 Bayes Factor analyses for correlations between psychometric measures and ROI activation during fear>calm.

		ICU	CBCL
Amygdala	L	6.03	1.40
	R	30.33	4.86
Insula	L	18.16	1.06
	R	30.33	1.91
ACC	L	.21	.65
	R	.19	.62
OFC	L	.21	.66
	R	.14	.65

*Abbreviations: ICU – Inventory of Callous-Unemotional traits, CBCL – Child Behaviour Checklist (externalising behaviours), L – left hemisphere, R – right hemisphere, ACC – anterior cingulate cortex, OFC – orbitofrontal cortex.*

*Notes: These correlations were computed using Viding et al (2012) reported correlations for the ICU column, and Waller et al (2016) for the CBCL column.*

#### Appendix 4.4 Bayes Factor analyses for correlations between psychometric measures and ROI activation during anger>calm.

		ICU	CBCL
Amygdala	L	.46	.69
	R	.21	.74
Insula	L	1.06	.64
	R	.41	.63
ACC	L	.24	.66
	R	.28	.74
OFC	L	1.22	.67
	R	.21	.63

*Abbreviations: ICU – Inventory of Callous-Unemotional traits, CBCL – Child Behaviour Checklist (externalising behaviours), L – left hemisphere, R – right hemisphere, ACC – anterior cingulate cortex, OFC – orbitofrontal cortex.*

*Notes: These correlations were computed using Viding et al (2012) reported correlations for the ICU column, and Waller et al (2016) for the CBCL column.*

**Appendix 4.5. Correlations between CU traits, externalising behaviours and neural activity in ROIs during fear condition, when controlling for suppressor effects.**

		ICU <sup>1</sup>		CBCL <sup>2</sup>	
		r	p	r	p
Amygdala	L	-.25	.04	-.04	.76
	R	-.25	.04	-.23	.10
Insula	L	-.32	.01	.01	.99
	R	-.31	.01	-.08	.56
ACC	L	-.07	.33	-.01	.94
	R	-.11	.21	.05	.71
OFC	L	-.07	.32	-.02	.90
	R	-.18	.10	.04	.79

*Abbreviations: ICU – Inventory of Callous-Unemotional traits, CBCL – Child Behaviour Checklist (externalising behaviours) L – left hemisphere, R – right hemisphere, ACC – anterior cingulate cortex, OFC – orbitofrontal cortex.*

<sup>1</sup> = correlation controlling for age, IQ, gender and externalising behaviours

<sup>2</sup> = correlation controlling for age, IQ, gender and CU traits

**Appendix 4.6. Correlations between CU traits, externalising behaviours and neural activity in ROIs during anger condition, when controlling for suppressor effects.**

		ICU <sup>1</sup>		CBCL <sup>2</sup>	
		r	p	r	p
Amygdala	L	.09	.26	.03	.86
	R	-.01	.46	.09	.54
Insula	L	.20	.07	-.06	.67
	R	.12	.20	-.05	.74
ACC	L	.08	.28	-.08	.58
	R	.12	.19	-.13	.35
OFC	L	.19	.09	-.03	.83
	R	.04	.39	-.03	.86

*Abbreviations: ICU – Inventory of Callous-Unemotional traits, CBCL – Child Behaviour Checklist (externalising behaviours) L – left hemisphere, R – right hemisphere, ACC – anterior cingulate cortex, OFC – orbitofrontal cortex.*

*<sup>1</sup> = correlation controlling for age, IQ, gender and externalising behaviours*

*<sup>2</sup> = correlation controlling for age, IQ, gender and CU traits*

### Appendix 5.1. Bayes Factor analyses for correlations between psychometric measures and emotion recognition accuracy.

		Whole brain	Left UF	Right UF
Table 3 Correlations	CU traits	.36	.31	.41
	Externalising	1.38	.99	.84
Table 4 Correlations	CU traits	.37	.31	.41
	Externalising	1.38	.99	.85

*Notes: These correlations were computed using Breeden (2015) reported correlations as plausible maximum effects. For the whole brain condition, an average of the bilateral UF was used, following advice from Zoltan Dienes. As Breeden et al did not finding significant correlations for the externalising behaviours when CU traits were controlled for (row 4), we instead used the plausible maximum effects from the original externalising correlations.*