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DOES ISOLATING CRITICAL FACIAL FEATURES MODULATE ACTIVITY IN EMOTION-RELATED BRAIN REGIONS FOR INDIVIDUALS WITH HIGH COLDHEARTEDNESS?

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ABSTRACT

Psychopathy, a developmental disorder characterized by profound behavioural disturbance, is associated with impaired recognition of distress cues. Previous studies indicate that this impairment can be improved by redirecting attention to critical cues (the eyes for fearful faces), although the associated functional neuroanatomy remains unknown. fMRI was used on a community sample of individuals with high vs. low scores on the Coldheartedness (CH) subscale of the Psychopathic Personality Inventory (N=32). Participants identified emotional expressions consisting of whole, or partial faces that isolated critical portions of each expression. Contrasting functional activity between the least-informative (eyes removed) and the most-informative (eyes only) portion of fearful faces revealed reduced activity in neural regions associated with emotion (amygdala and medial prefrontal cortex) and attention (fronto-parietal network), in the high CH group relative to the low CH group. Individuals with high CH traits exhibit abnormalities in neurocognitive systems responsible for orienting attention to critical emotional cues.

Keywords: psychopathy, coldheartedness, fMRI, empathy, facial expression recognition, amygdala, medial prefrontal cortex

CO-AUTHORSHIP

All experimental and written work for this thesis was performed by Thida Han, with the exception of the following:

As supervisor, Dr. Derek Mitchell contributed to all aspects of this thesis project. This included: conceptualization, experimental design, data analysis, interpretation, and editing of written work.

Dr. Richard Neufeld was a collaborator on this project. His involvement included conceptualization of the project, experimental design, consultation on statistical analyses, and interpretation of the data.

Gesine Alders conducted a pilot project that also utilized the Partial Face Encoding task. She collaborated in formatting the stimuli, programming the task, and assisted in the initial collection of participant imaging data.

Steven Greening was the primary fMRI technologist for the Partial Face Encoding task. He also assisted with some aspects of data analysis and interpretation.

Kim Krueger also acted as an fMRI technologist for the Partial Face Encoding task.

Betsy Schaefer assisted in participant recruitment and collection of behavioural data.

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LIST OF ABBREVIATIONS

AFNI	Analysis of Functional NeuroImages
ANOVA	Analysis of variance
BOLD	Blood oxygen level dependent
CH	Coldheartedness
fMRI	Functional magnetic resonance imaging
IES	Integrated emotion systems
MNI	Montreal Neurological Institute
PCL-R	Psychopathy Checklist – Revised
PCL	Psychopathy Checklist
PFE	Partial Face Encoding
PPI-R	Psychopathic Personality Inventory – Revised
ROI	Region of interest
SCID	Structured Clinical Interview of the DSM-IV-TR
SRP-II	Hare Self-Report Psychopathy Scale – II
VIM	Violence inhibition mechanism

CHAPTER 1

1 Introduction

1.1 The construct of psychopathy

Psychopathy is a developmental disorder marked by profound emotional and behavioural disturbance. Individuals with this disorder are characterized by a callous, manipulative interpersonal style, superficial charm, egocentricity, and poor impulse control (Cleckley, 1976; Hare, Hart, & Harpur, 1991). Psychopathic individuals commit a disproportionate amount of crime and violence (Hare, 1978), and fail to comprehend the severity of their actions even when confronted (Mitchell, Richell, Leonard, & Blair, 2006). These individuals have shown poor responses to traditional forms of treatment (Ogloff, Wong, & Greenwood, 1990), and high rates of recidivism (Hemphill, Hare, & Wong, 1998). Research examining the construct of psychopathy has suggested that psychopathic traits exist on a continuum, and levels of these traits can be measured in the general population (Lilienfeld, 1994; Widiger & Lynam, 1998). Studies have provided evidence that non-clinical individuals with high psychopathic traits exhibit some of the abnormalities seen in their clinical counterparts. Abnormalities have even been observed in children with high psychopathic traits (R. J. Blair, 1999; R. J. Blair, Budhani, Colledge, & Scott, 2005; R. J. Blair, Colledge, & Mitchell, 2001; R. J. Blair, Colledge, Murray, & Mitchell, 2001; Finger et al., 2008; Marsh et al., 2008). The persistence of these traits across cultures (Murphy, 1976), their early emergence in development (Lynam, Caspi, Moffitt, Loeber, & Stouthamer-Loeber, 2007), and resistance to treatment (Ogloff, Wong, & Greenwood, 1990) have motivated researchers to examine

psychopathic traits at a neurocognitive level. Studying psychopathic traits in the general population can lead to a broader understanding of aggressive and antisocial behaviours.

1.2 Assessing psychopathic traits in clinical and community samples

Clinical psychopathy has been systematically described as a constellation of 16 personality features, including superficial charm, lack of empathy, dishonesty, self-centeredness, failure to form strong emotional bonds, and failure to learn from punishment (Cleckley, 1976). The most extensively validated measures of psychopathy are the Psychopathy Checklist-Revised (PCL-R; Hare, 1991a) and its predecessor, the Psychopathy Checklist (PCL; Hare, 1985). These instruments facilitated the proliferation of research with incarcerated samples (Malterer, Lilienfeld, Neumann, & Newman, 2010). However, the PCL-R consists of semi-structured interviews that require extensive formal training for adequate inter-rater reliability, are extremely time consuming, and incorporate high-quality file data that is usually derived from correctional files (Lilienfeld & Widows, 2005). These extensive administration requirements suggest the PCL-R may not be the most efficient instrument for measuring psychopathic traits in non-institutionalized persons, who can provide a more accessible and mild variant of the neurocognitive deficits that present in the clinical disorder.

The current study will utilize the Psychopathic Personality Inventory – Revised (PPI-R; Lilienfeld & Widows, 2005), which was developed as a tool to assess levels of psychopathic traits in non-clinical samples (Lilienfeld & Andrews, 1996; Poythress, Edens, & Lilienfeld, 1998). The PPI-R is a self-report instrument that offers a less

expensive and less time-intensive way of capturing both the affective/interpersonal and impulsive/irresponsible components of psychopathy (Benning, Patrick, Hicks, Blonigen, & Krueger, 2003). Significant correlations have been found between the PPI-R and an array of both personality and psychopathy measures (Benning, Patrick, Blonigen, Hicks, & Iacono, 2005; Benning, et al., 2003; Lilienfeld & Andrews, 1996). Evidence for the construct validity of the PPI-R has been obtained based on significant correlations with two other self-report measures that have emerged in recent years: the Hare Self-Report Psychopathy Scale-II (SRP-II; Hare, 1991b) and Levenson's Self-Report Psychopathy Scale (Levenson, Kiehl, & Fitzpatrick, 1995). Several previous findings lead to the selection of the PPI-R over these other two measures. Unlike the SRP-II or the Levenson scale, the PPI-R provides a separate index of core psychopathic traits, including a lack of empathy (Lilienfeld & Widows, 2005). Although both the SRP-II and the Levenson scale demonstrate good internal consistency, the PPI-R shows stronger convergent and discriminant validity (Falkenbach, Poythress, Falki, & Manchak, 2007). For these reasons, the PPI-R has received greater support in studies that investigate psychopathic traits in non-clinical and non-forensic samples (Falkenbach, et al., 2007).

In the current study we will use functional neuroimaging to examine the brain activity associated with emotion recognition in individuals identified by high versus low scores on a specific subscale of the PPI-R. Previous studies have successfully used the PPI-R in conjunction with neuroimaging to compare cognitive and emotional processes between community samples of individuals with different levels of psychopathic traits (Fullam, McKie, & Dolan, 2009; Gordon, Baird, & End, 2004; Harenski, Kim, & Hamann, 2009; Nunez, Casey, Egner, Hare, & Hirsch, 2005). The PPI-R consists of

eight subscales, and participants in our study will be grouped based on extreme high or low scores on the Coldheartedness subscale.

The Coldheartedness (CH) subscale measures a propensity towards callousness, guiltlessness, and an absence of sentimentality (Lilienfeld & Widows, 2005). CH is one of four PPI subscales that are substantially correlated with the PCL-R (Poythress, et al., 1998). CH scores are shown to be correlated with Factor 1, but not Factor 2, of the PCL-R (Poythress, et al., 1998), suggesting a specific association with psychopathic characteristics rather than general behavioural deviance (Viding, 2004). Research on the outcome of children with high Factor 1 scores, which include callousness and lack of empathy, has indicated that their propensity toward antisocial behaviours is influenced by genetics (Viding, Blair, Moffitt, & Plomin, 2005), as opposed to environmental markers such as quality of parenting (Devita, Forth, & Hare, 1990; Wootton, Frick, Shelton, & Silverthorn, 1997). Previous studies have shown that individuals with high versus low CH scores exhibit differences that are observable at the psychophysiological level (Fecteau, Pascual-Leone, & Theoret, 2008).

1.3 Neurocognitive abnormalities associated with psychopathy

Recent research on psychopathy has focused on examining the neural basis of this disorder, and how functional and structural abnormalities might contribute to the personality traits exhibited. Much of the evidence collected has identified the medial prefrontal cortex and the amygdala as two areas that are likely to be involved in the pathophysiology of this disorder.

1.3.1 Evidence for prefrontal cortex abnormalities in psychopathy

Individuals with psychopathy are impaired on cognitive tasks that are thought to reflect orbital/ventromedial prefrontal cortex functioning. For example, patients with damage to the orbitofrontal cortex are impaired on reversal learning tasks, which require a participant to change their strategy when a previously advantageous response becomes unfavourable (Rahman, Sahakian, Hodges, Rogers, & Robbins, 1999; Rolls, 2000; Rolls, Hornak, Wade, & McGrath, 1994). Patients with lesions of the ventromedial prefrontal cortex are also impaired on tasks that involve complex decision making, such as the Iowa Gambling Task (Bechara, Tranel, & Damasio, 2000). Additional evidence draws from research indicating that individuals with trauma to the orbitofrontal cortex present with abnormalities in aggressive behaviour (Zald & Kim, 1996) and a callous disregard for others known as 'acquired sociopathy' (R. J. Blair & Cipolotti, 2000).

Psychopathy is associated with similar abnormalities in fundamental decision making processes. Behavioural evidence indicates that individuals with psychopathy are impaired at response reversal (R. J. Blair, Colledge, & Mitchell, 2001; Mitchell, Colledge, Leonard, & Blair, 2002; Mitchell et al., 2006). Deficits in complex decision making tasks, such as the Iowa Gambling Task, are also seen in adults (Mitchell, et al., 2002; van Honk, Hermans, Putman, Montagne, & Schutter, 2002) and youths (R. J. Blair, Colledge, & Mitchell, 2001) with high psychopathic traits. In addition to these behavioural impairments, neuroimaging has associated high psychopathic traits with functional abnormalities in the medial prefrontal cortex. Individuals with high psychopathic traits exhibit abnormal activity in the medial prefrontal cortex during tasks involving reversal learning (Finger, et al., 2008), fear conditioning (Birbaumer et al.,

2005), and passive avoidance (Finger et al., 2011; Newman & Kosson, 1986). The convergence of findings produced by lesion studies, behavioural measures, and neuroimaging has suggested that dysfunction in the medial prefrontal cortex is likely to be involved in psychopathy.

1.3.2 Evidence for amygdala dysfunction in psychopathy

The amygdala is known to be involved in many of the processes impaired in psychopathy (R. J. Blair, 2003b), and is suggested to be one of the core neural systems involved in this disorder (Patrick, 1994). For example, reduced amygdala volume has been found in individuals with psychopathy (Yang & Raine, 2009), and evidence from lesion studies has suggested that striking parallels exist between psychopathy and patients with amygdala damage. Individuals with psychopathy exhibit deficits in startle reflex (Patrick, Bradley, & Lang, 1993), fear conditioning (Flor, Birbaumer, Hermann, Ziegler, & Patrick, 2002; Lykken, 1957), and instrumental learning (Mitchell, Fine, et al., 2006). Similarly, patients with lesions of the amygdala also present with deficits in startle reflex (Angrilli et al., 1996), fear conditioning (LaBar, LeDoux, Spencer, & Phelps, 1995), and instrumental learning (LeDoux, 1998).

Amygdala dysfunction is known to cause cognitive impairments that have clear implications for social behaviour. One of the most critical areas of impairment is in the recognition of emotional expressions. Knowledge of this deficit comes from extensive testing of patient S.M., a woman who suffers from nearly complete bilateral amygdala damage (Adolphs, Tranel, Damasio, & Damasio, 1994), and has been the human subject

with the most selective amygdala damage to date (Adolphs et al., 2005). Although her recognition of identity was preserved, patient S.M. presented with an inability to recognize fearful facial expressions. This suggests that the amygdala plays an integral and specific role in the recognition of fear (Adolphs, et al., 1994). Other studies examining patients with amygdala lesions report that deficits in the recognition of fear are observed most frequently (Adolphs, et al., 1994; Adolphs, Tranel, Damasio, & Damasio, 1995; Adolphs et al., 1999; Broks et al., 1998; Calder et al., 1996; Scott et al., 1997; Sprengelmeyer et al., 1999), with impairments in the recognition of sadness and anger also occasionally reported (Adolphs, et al., 1999; Broks, et al., 1998; Scott, et al., 1997; Sprengelmeyer, et al., 1999).

Neuroimaging studies provide additional evidence that psychopathy is likely associated with abnormal amygdala activity. One of the main lines of evidence comes from studies examining the functional abnormalities associated with emotional expression recognition in psychopathy. Individuals with high psychopathic traits show reduced activation of the amygdala (Gordon, et al., 2004) and limbic system (Kiehl et al., 2001) during facial affect recognition.

The long list of commonalities between the impairments observed in psychopathy and patients with amygdala damage has provided compelling evidence that abnormal amygdala dysfunction likely plays a prominent role in psychopathy. Abnormalities in functional connectivity may also be involved, since interactions between the amygdala and medial prefrontal cortex are critical for a variety of the cognitive functions impaired in this group, ranging from decision making to emotional learning and processing of emotional stimuli. In-vivo diffusion tensor imaging has shown that relative to matched

controls, psychopaths have significantly reduced fractional anisotropy (an indirect measure of microstructural integrity) in the uncinate fasciculus, a white-matter tract linking the amygdala with medial prefrontal cortex (Craig et al., 2009).

1.4 Distress cue processing in individuals with high psychopathic traits

The ability to process emotional expressions in psychopathy has received considerable focus as one route of research that could help delineate the neurocognitive dysfunction associated with this disorder. Studies using behavioural measures have shown a selective deficit for the recognition of sad and fearful faces (R. J. Blair & Coles, 2000; Stevens, Charman, & Blair, 2001) fearful vocal affect (R. J. Blair, Budhani, et al., 2005; R. J. Blair et al., 2002), and reduced sensitivity to fearful and sad facial expressions (R. J. Blair, Colledge, Murray, et al., 2001). Insensitivity to distress cues is thought to put these individuals at heightened risk for aggression and maladaptive social functioning (R. J. Blair, 2005b).

1.5 The repercussions of impaired distress recognition

Impaired recognition of distress cues can be detrimental to social functioning for several reasons. Processing the emotional signals of our peers is a fundamental component of human social interaction. Facial expressions are a form of non-verbal communication that rapidly transmit information about the valence of an object or a situation (R. J. Blair, 2003a). Consequently, facial expressions can modulate the

probability that a specific behaviour will be repeated by an observer. For example, happy facial expressions can increase the probability that an associated behaviour will be performed by an observer (Matthews & Wells, 1999), while aversive stimuli like expressions of fear (Mineka & Cook, 1993), sadness, and disgust (R. J. Blair, 2003a) convey to an observer that a novel object should be avoided. In social animal species, ethologists have shown that signs of submission can terminate the aggressive behaviour of an attacker (Lorenz, 2002). In humans, non-verbal cues of distress can activate a violence inhibition mechanism (R. J. Blair, 1995), which is a cognitive response that initiates withdrawal of an assailant (R. J. Blair, 1995). The VIM model has recently been extended into the computationally tractable integrated emotion systems (IES) model, which suggests that the symptoms seen in psychopathy involve a neurocognitive system of regions including the medial prefrontal cortex and the amygdala (R. J. Blair, 2004, 2005a). In addition to inhibiting aggressive behaviour, expressions of fear and sadness can act as effective distress cues to stimulate prosocial behaviour, such as compassionate responses and the elicitation of care (Marsh & Ambady, 2007; Marsh, Kozak, & Ambady, 2007). Abnormalities in the processing of emotional expressions have the potential to disrupt this mechanism, which could result in maladaptive social functioning.

1.6 Improving distress cue recognition and rationale for the current study

Recently, eye-tracking techniques have been applied in conjunction with behavioural testing to further investigate the emotional expression recognition deficits seen in amygdala lesion patients. This approach revealed that individuals with amygdala

lesions view facial expressions differently than individuals who are neurologically intact. Amygdala lesion patients appear to neglect the eye region when viewing emotional faces (Adolphs, et al., 2005). Importantly, once they were explicitly instructed to attend to the eye region, the recognition deficit reversed, and their accuracy returned to the level of controls. This pattern of findings suggests that information from the eye region may be critical for the recognition of fear, and that the fear recognition impairment seen in amygdala lesion patients is a consequence of ineffective viewing behaviours.

Following this revelation, a similar approach was applied to youth with high versus low psychopathic traits (Dadds et al., 2006). When allowed to free gaze, individuals with high psychopathic traits showed poor recognition accuracy for fearful faces. When instructed to attend to the eye region, their accuracy also improved to the level of matched controls. Neglect of the most emotionally salient aspect of facial expressions may drive impaired distress recognition, and the consequent empathic dysfunction seen in psychopathy. Simply manipulating the way these individuals inspected faces was sufficient to attain normal levels of recognition for fearful faces. However, the functional neuroanatomy associated with this type of manipulation still remains unknown.

Manipulating how emotional faces are viewed could provide a useful tool for improving distress recognition. The current study will examine the impact of isolating facial features on empathic responding in individuals high and low on a core facet of psychopathy scores: the CH subscale. Individuals with high CH scores are characterized by a lack of empathy. Attention could potentially provide a mechanism to arouse empathy in individuals with empathic dysfunction by boosting the salience of emotional

details (R. J. Blair & Mitchell, 2009). However, it is unknown whether the improvements seen behaviourally (Dadds, et al., 2006) are due to the activation of the same emotion network used by typically-developing individuals, which might suggest a route to elicit empathic responding and subsequently prosocial behaviour. Alternatively, the improvement observed in previous studies may be due to a compensatory strategy using an alternate neural network. This latter explanation would raise questions about whether improved emotion recognition accuracy is associated with genuine or artificial empathic responding. Although accurate recognition of facial expressions is associated with violence inhibition (R. J. Blair, 1995), these findings may depend on the activation of neural regions associated with normal recognition. If improved emotion recognition is associated with activation of alternate neural regions in individuals with empathic dysfunction, it is unknown whether these routes will have the same positive implications for prosocial behaviour.

The neurocognitive deficits seen in psychopathy are relatively focal in nature. Consequently, other regions are likely to be recruited to compensate for the core deficits. Research has demonstrated that psychopathy is not associated with impairments in memory, language (Hart, Forth, & Hare, 1990), or generalized executive dysfunction (LaPierre, Braun, & Hodgins, 1995; Mitchell, et al., 2002). For example, individuals with psychopathic traits show intact performance on attentional set shifting, such as the intradimensional/extradimensional shift task (Mitchell, et al., 2002). While individuals with psychopathy are impaired at processes that involve the orbitofrontal cortex in conjunction with the amygdala, such as reversal learning (LaPierre, et al., 1995; Mitchell, et al., 2002), the ventrolateral prefrontal cortex does not appear to be impaired (Finger, et

al., 2008). The ventrolateral prefrontal cortex is involved in a host of emotion-related functions (for a review, see Mitchell, 2011), including negative emotion encoding, emotional response modulation, and attention to emotionally significant stimuli. These factors suggest that the ventrolateral prefrontal cortex may be a prime candidate for a contributor to the compensatory neural network that individuals with high CH traits could use to identify emotional expressions.

1.7 Neural regions implicated in the recognition of emotional expressions

Cross-cultural studies have indicated that the emotions of fear, happiness, sadness, anger, disgust, and surprise are accompanied by facial expressions that are innate and universally recognized (Darwin, 1872; Ekman & Friesen, 1971; Ekman et al., 1987). The stimuli in the current study included facial expressions of fear, disgust, anger, and happiness, as well as neutral faces. Though researchers once believed that all emotions were processed using shared neural networks, there has been a recent increase in the investigation of distinct substrates responsible for processing different emotions (Adolphs, Baron-Cohen, & Tranel, 2002; Morris et al., 1996; Phillips et al., 1997). Studies examining the neural pathways involved in empathy have indicated that viewing emotional expressions in others activates the same neural regions as when we experience that emotion ourselves (Carr, Iacoboni, Dubeau, Mazziotta, & Lenzi, 2003; Pfeifer, Iacoboni, Mazziotta, & Dapretto, 2008). Knowing which neural regions are typically associated with the emotions in our study will suggest where neural activity may be seen and whether individuals in our study are likely to show functional abnormalities.

1.7.1 Fear

Fearful facial expressions are easily detectable, aid in the identification of potential threats, and allow for the rapid formulation of a behavioural response (Hardee, Thompson, & Puce, 2008). Fearful faces play a role in aversive and appetitive conditioning as well as instrumental learning (Everitt, Cardinal, Hall, Parkinson, & Robbins, 2000; Killcross, Robbins, & Everitt, 1997). Specifically, fearful facial expressions can act as social aversive unconditioned stimuli, which convey to others that an object or situation should be avoided (Mineka & Cook, 1993). Lesion studies indicate that damage to the amygdala can selectively impair the ability to recognize fearful facial expressions (Adolphs, et al., 1994; Adolphs, et al., 1995; Adolphs, et al., 1999; Broks, et al., 1998; Calder, et al., 1996; Sprengelmeyer, et al., 1999). Neuroimaging studies also report that the presentation of a fearful face is associated with activation of the amygdala in neurologically healthy individuals (Fusar-Poli et al., 2009; Gamer & Buchel, 2009; Morris, et al., 1996). Although most studies have utilized visual fear-related stimuli, activation of the amygdala has also been associated with vocal expressions of fear (Phillips et al., 1998). The amygdala activates more strongly and preferentially to fear relative to neutral faces (Breiter et al., 1996), and has even been shown to activate in response to fearful faces that are not consciously perceived (Whalen et al., 1998).

Neuroimaging has indicated that individuals with high psychopathic traits exhibit reduced amygdala activity relative to controls when processing fearful faces (Jones, Laurens, Herba, Barker, & Viding, 2009; Marsh, et al., 2008). These findings converge with findings of fear recognition impairments in amygdala lesion patients and

neuroimaging of fear-related stimuli, suggesting that the amygdala is a strong candidate for the processing of fearful faces.

1.7.2 Disgust

Facial expressions of disgust are produced as an innate response to repulsive stimuli in the environment (Darwin, 1872) or a distasteful social situation, including moral transgressions (Chapman, Kim, Susskind, & Anderson, 2009). Impaired ratings of disgusted expressions have been seen in patients with lesions of the right (Anderson & Phelps, 1997) and left (Anderson & Phelps, 1998) amygdala. Studies of patients with focal lesions have also reported that deficits specific to, or most severe for disgust are associated with damage to the left insula and basal ganglia (Calder, Lawrence, & Young, 2001), or insula and temporal lobes (Adolphs, et al., 2002). These findings are corroborated by reports of severe or selective disgust recognition deficits in patients with diseases characterized by atrophy or neuronal loss in the insula or basal ganglia, including Huntington's disease (Hayes, Stevenson, & Coltheart, 2007; Wang, Hoosain, Yang, Meng, & Wang, 2003), Parkinson's disease (Kan, Kawamura, Hasegawa, Mochizuki, & Nakamura, 2002; Suzuki, Hoshino, Shigemasu, & Kawamura, 2006), and Wilson's disease (Wang, et al., 2003). Similarly, neuroimaging studies examining the recognition of disgusted facial expressions have implicated the insular cortex (Calder, Keane, Manes, Antoun, & Young, 2000; Phillips et al., 2004; Phillips, et al., 1998; Phillips, et al., 1997; Sprengelmeyer, Rausch, Eysel, & Przuntek, 1998; Wicker et al.,

2003) and the basal ganglia (Phillips, et al., 1998; Phillips, et al., 1997; Sprengelmeyer, et al., 1998) in the processing of disgust.

Of the studies that have examined emotion processing in psychopathy, few have incorporated expressions of disgust. Only one study of facial expression processing in psychopathy is known to have detected impairments in the classification of disgusted expressions (Kosson, Suchy, Mayer, & Libby, 2002). Other studies have not detected impaired recognition of disgust in facial expressions (R. J. Blair & Coles, 2000; Dolan & Fullam, 2006) or vocal affect (R. J. Blair, et al., 2002) to be associated with psychopathy. No studies have examined disgust processing in psychopathy using neuroimaging.

1.7.3 Anger

Displays of anger are important signals that can be used to exert dominance and modulate the behavioural response of others (R. J. Blair & Cipolotti, 2000; Keltner & Anderson, 2000). As we have noted, lesions of the orbitofrontal cortex are associated with emotion recognition deficits that are most severe for angry (Lough et al., 2006; Mitchell, Avny, & Blair, 2006) and disgusted expressions (R. J. Blair & Cipolotti, 2000).

Although relatively few neuroimaging studies have used angry facial expressions as stimuli, meta-analyses have revealed the lateral orbitofrontal cortex to be the region most consistently activated during the presentation of anger (Phan, Wager, Taylor, & Liberzon, 2002). Angry facial expressions have also been linked to the posterior right cingulate gyrus and left medial temporal gyrus (Sprengelmeyer, et al., 1998). In addition, the orbitofrontal cortex and anterior cingulate cortex have also been linked to encoding

the intensity of angry faces (R. J. R. Blair, Morris, Frith, Perrett, & Dolan, 1999). Although some neuroimaging studies have reported amygdala activity in response to angry faces, the findings are inconsistent, and the relative activity is typically smaller than that produced by fearful faces (Ewbank et al., 2009; Whalen et al., 2001).

Although psychopathy has been linked to dysfunction of the orbitofrontal cortex, anger recognition impairments are not typically observed in individuals with psychopathy (Mitchell, Avny, et al., 2006). In addition, the neurocognitive dysfunction that is associated with anger recognition impairment is believed to be dissociable from the neurocognitive abnormalities evident in individuals with high psychopathic traits (R. J. Blair & Cipolotti, 2000; Mitchell, Avny, et al., 2006)

1.7.4 Happy

Happy facial expressions are produced in the initial stage preceding laughter, and encompass the smile as an integral part of the expression (Darwin, 1872). Impaired recognition of happy faces has been seen in patients with lesions of the orbitofrontal cortex (R. J. Blair & Cipolotti, 2000; Mitchell, Avny, et al., 2006), and occasionally in patients with damage of the amygdala and ventromedial prefrontal cortices (Lough, et al., 2006; Rosen et al., 2002).

Neuroimaging studies examining the neural correlates associated with viewing happy faces have produced highly varied findings. Some studies have reported increased activation in the amygdala (Breiter, et al., 1996; Derntl et al., 2009; Fusar-Poli, et al., 2009). Others have reported increased activity in areas of the prefrontal cortex, including

the orbitofrontal or medial frontal cortex (Kesler-West et al., 2001), the ventromedial prefrontal cortex and rostral anterior cingulate (Fusar-Poli, et al., 2009). A meta-analysis of 55 neuroimaging studies of emotion processing reported that activation of the basal ganglia was found in nearly 70% of studies that induced happiness (Phan, et al., 2002).

Although individuals with psychopathy are not typically associated with impaired recognition of happy faces (R. J. Blair, Colledge, Murray, et al., 2001) or happy vocal tones (R. J. Blair, et al., 2002; Stevens, et al., 2001), one neuroimaging study has indicated that individuals with psychopathy show reduced activity in the fusiform and extrastriate cortices when processing happy faces (Deeley et al., 2006).

1.8 Hypotheses

In the current study, we will examine whether individuals with high versus low scores on the CH subscale of the PPI-R (Lilienfeld & Widows, 2005) exhibit differences in functional neuroanatomy when viewing more versus less informative portions of emotional faces. Two dissociable sets of hypotheses can be formulated based on traditional and emerging views of amygdala function.

1.8.1 Hypotheses based on the traditional perspective of amygdala function

The traditional view of the amygdala has suggested that this substrate is involved in the encoding or processing of distress (R. J. Blair, 1995, 2003a; LeDoux, 1998). In line with this view, studies have used neuroimaging to show that the amygdala responds

specifically to fearful faces, and that this response is modulated by the intensity of the fearful face during a gender discrimination task (Morris, et al., 1996). In our study, the traditional view of amygdala function might predict that amygdala responsiveness should be largest during the most informative condition of distress (fear eyes only) relative to the least informative condition (fear eyes removed) for individuals with low CH scores. In accordance with this view, we would expect the high CH group to show reduced activity relative to the low CH group on whole fearful faces. Other studies have successfully demonstrated that functional brain abnormalities can be observed in community samples of individuals with high psychopathic traits that are similar to the abnormalities exhibited by clinical populations (Gordon, et al., 2004; Rilling et al., 2007). Clinical populations with high psychopathic traits show significant between group differences in amygdala activity (Jones, et al., 2009; Marsh, et al., 2008), but it remains unknown whether this deficit may be present in a community sample that is presumably less impaired and may not show differences that can be observed behaviourally. Finally, we anticipate that no significant between-group differences in functional amygdala activity will be seen during fearful faces with the eyes isolated, or with the eyes removed. Since psychopathy is thought to be associated with a selective impairment in distress processing, no significant differences are expected between the high and low CH groups on facial expressions of happiness, anger, disgust, and neutral, regardless of the portion condition.

1.8.2 Hypotheses based on the recent "emotion-orienting" perspective of amygdala function

Recently, a new formulation has suggested that the amygdala directs attention toward the most salient region of a stimulus in order to resolve ambiguity (Adolphs, 2010). Findings from recent neuroimaging studies have provided some support for this account (Asghar et al., 2008; Gamer & Buchel, 2009), and have led to speculation that that the mechanism by which the amygdala orients attention to code salience might engage even more when the eyes (the most informative region of fearful faces) are covered in an attempt to glean whatever information possible from the missing region (Adolphs, 2010). If this emotional-orienting account of amygdala function is true, different predictions can be made regarding our task. Individuals with low CH scores will show greater amygdala activity relative to the high CH group when viewing whole faces of any emotion. This group difference should be heightened when the most informative region of each emotional face is missing. We expect that contrast will provide the most sensitive index of dysfunction, because the system will be taxed as it searches for cues in the most ambiguous recognition condition. This contrast may also be necessary to extract between-group differences in our community sample of individuals with psychopathic traits, who likely show less severe neurocognitive deficits than a clinical population. No significant differences in amygdala activity between the high and low CH groups will be seen when the most informative region of each emotional face is isolated.

1.9 Significance

Functional magnetic resonance imaging (fMRI) methods have revealed associations between psychopathic traits, characteristic impairments, and abnormal structure or function of the fronto-temporal network, hippocampus, and amygdala. Given that the Partial Face Encoding Task involves affect recognition and directing attention via the isolation of facial features, findings from previous neuroimaging studies suggest involvement of the amygdala or fronto-temporal network might be seen depending on the depth of processing in our participants. If amygdala activity can be rescued by manipulating attention, these findings could have important implications for clinical psychopathy. Reinstatement of activity in the amygdala would suggest that genuine empathy can be harnessed by behavioural means, and points to a potential route to develop early intervention strategies to curb maladaptive social behaviour. If compensatory networks are shown to be active, higher cognitive functions may be responsible for decoding social cues without arousing genuine empathic responding. Finally, findings that reflect Adolphs' (2010) predictions will suggest that the amygdala plays a very different role than purely distress recognition, as was traditionally thought. Completion of this study will facilitate a greater understanding of the neural networks associated with face processing in individuals with high and low levels of CH traits.

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CHAPTER 2

Isolating Critical Facial Features and the Associated Neural Activity in Individuals with High vs. Low Coldheartedness

2.1 Introduction

Psychopathy is a developmental disorder associated with profound behavioural and emotional disturbance (Cleckley, 1976). Psychopaths commit a disproportionate amount of crime and violence (Hare, 1978), and exhibit a callous-unemotional and manipulative interpersonal style (Hare, Hart, & Harpur, 1991). Cardinal features of the disorder include reduced sensitivity to the emotional signals of others, and reduced empathic responding to victims (Blair, 2005; Hare, et al., 1991). One prominent neurocognitive model of psychopathy suggests that this disorder is associated with dysfunction in the amygdala and functionally connected regions of ventromedial frontal cortex (Blair, Peschardt, Budhani, Mitchell, & Pine, 2006). At the cognitive level, these functional abnormalities are associated with impaired stimulus-reinforcement learning (Blair et al., 2004; Mitchell et al., 2006; Newman & Kosson, 1986), and reduced sensitivity to emotional cues in others (Blair, Colledge, Murray, & Mitchell, 2001). In combination, these deficits are thought to disrupt the development of moral socialization, leaving individuals with psychopathic tendencies at greater risk of using antisocial patterns of behaviour to achieve their goals (Blair, et al., 2006). In support of this model, functional neuroimaging has demonstrated abnormalities in a network involving orbital/ventromedial prefrontal cortex or the amygdala in clinically diagnosed psychopathic adults (Birbaumer et al., 2005; Kiehl et al., 2001; Muller et al., 2003), children with callous and unemotional traits (Finger et al., 2008; Marsh et al., 2008), and even in non-psychiatric individuals with high levels of psychopathic traits identified through self-report (Gordon, Baird, & End, 2004; Rilling et al., 2007).

One aspect of social cognition that has received considerable interest with regard to psychopathy is emotional expression recognition. To most humans, the presentation of distress cues such as fearful or sad facial expressions is aversive (Bandura & Rosenthal, 1966). Facial expressions of distress are thought to act as social reinforcers by communicating the negative valence that actions have on others (Blair, 2003). Accordingly, the viewing of distress has been linked with the interruption of aggression (Perry & Perry, 1974), and the initiation of prosocial behaviour (Hoffman, 1975). Relative to healthy controls, individuals with psychopathic tendencies have been found to display a selective deficit in the recognition of distress cues, particularly fearful faces (Blair & Coles, 2000; Blair, et al., 2001; Stevens, Charman, & Blair, 2001), and fearful vocal affect (Blair, Budhani, Colledge, & Scott, 2005; Blair et al., 2002). Neuroimaging has revealed that this recognition impairment is associated with functional brain abnormalities, including reduced amygdala activity in response to fearful faces (Jones, Laurens, Herba, Barker, & Viding, 2009; Marsh, et al., 2008), and general affective stimuli (Gordon, et al., 2004; Kiehl, et al., 2001). Since distress recognition and moral socialization are closely linked, uncovering techniques to help these individuals recognize distress has the potential to improve empathic responding. This could suggest a route for early intervention and rehabilitation approaches for psychopathic individuals, who respond poorly to available therapeutic treatment (Ogloff, Wong, & Greenwood, 1990).

Attention may be one means of improving distress recognition. Evidence for this route was recently demonstrated in a patient with focal lesions of the bilateral amygdala, and later in children with callous and unemotional traits. Using eye-tracking and behavioural manipulations of attention, Adolphs et al. (2005) showed that the fear

recognition impairment observed in a patient with an amygdala lesion is associated with a failure to attend to the eye region of faces. When the patient was instructed to attend to the eyes, her expression recognition performance improved to the same level as healthy controls. An identical pattern was observed in children with callous and unemotional traits. They too showed a failure to attend to the eye region and concomitant recognition impairment that was alleviated once these children received instructions to gaze at the eyes (Dadds et al., 2006). Although these studies suggest that directing attention to specific facial features can be a potent tool to alleviate emotional expression recognition deficits, the impact this manipulation may have on neural activity in emotion-related brain regions remains unclear.

Recently, a new formulation concerning the functional contribution of the amygdala to fearful face recognition has been developed. According to this view, the amygdala directs attention toward the most salient elements of a stimulus in order to resolve ambiguity (Adolphs, 2010). Recent neuroimaging evidence has supported this formulation. For example, the amygdala is shown to be activated differentially to fearful faces relative to neutral faces, even when the eye region of fearful faces is masked (Asghar et al., 2008). Furthermore, in a recent study, Gamer and Buchel (2009) varied the location that participants initially fixated on emotional facial expressions. They found that participants with the largest activity in the right amygdala showed the most prominent gaze shifts toward the eye region of fearful faces (Gamer & Buchel, 2009). Taken together, these findings have led to speculation that the mechanism by which the amygdala orients attention to code salience might engage even more when the eyes are

covered, in an attempt to glean any information possible from the missing region (Adolphs, 2010). However, this hypothesis has not yet been tested empirically.

The current study examines the impact that isolating distinct regions of the face has on the functional neuroanatomy of emotional expression recognition in a community sample of individuals with high versus low scores on a core subscale of psychopathic traits: Coldheartedness (CH). This study features a novel task which isolates the most and least informative regions of emotional faces (e.g., fearful faces with the eyes isolated and fearful faces with the eyes removed, respectively). While previous functional neuroimaging studies have examined emotional expression recognition in psychopathy used passive viewing or gender discrimination tasks (Jones, et al., 2009) involving two or three emotions, our study asks participants to identify which of five emotional expressions (fear, happy, angry, disgust, and neutral) are seen. Participants were selected based on extreme high or low scores on the CH subscale of the Psychopathic Personality Inventory - Revised (PPI-R; Lilienfeld & Widows, 2005), a widely-used and valid self-report measure that has good reliability and construct validity in community samples (Lilienfeld & Widows, 2005). In at least two previous fMRI studies, higher levels of psychopathic traits as indexed by the PPI have been associated with functional brain abnormalities, particularly in region-of-interest analyses (Gordon, et al., 2004; Rilling, et al., 2007). Prior studies have also demonstrated that individuals with high versus low CH scores show differences at the psychophysiological level (Fecteau, Pascual-Leone, & Theoret, 2008).

A series of dissociable predictions can be made based on traditional and emerging conceptions of amygdala function. One possibility is that individuals with high relative

to low CH scores show generalized amygdala dysfunction that is apparent to fearful faces but will be alleviated when the eyes are isolated. Alternatively, isolating the eyes could result in compensatory engagement of other neural regions implicated in social cognition, such as anterior regions of orbitofrontal cortex that might be unaffected in individuals with high CH traits, as has been speculated in psychopathy (Mitchell, Avny, & Blair, 2006). Another possibility is that the amygdala directs processing resources toward the most salient elements of a stimulus in order to resolve ambiguity (Adolphs, 2010). According to this perspective, amygdala activity should be greatest when the most ambiguous facial features are present. Thus, on the basis of this view, the prediction can be made that any existing functional amygdala abnormalities associated with high relative to low CH traits should be most apparent when viewing fearful faces with the eyes removed (i.e., when the mechanism for orienting should be most taxed) (c.f., Adolphs, 2010). The current study tests these dissociable predictions.

2.2 Methods

2.2.1 The Psychopathic Personality Inventory – Revised

The PPI-R (Lilienfeld & Widows, 2005) is a 154-item self-report personality measure that includes 8 subscales: Machiavellian Egocentricity, Rebellious Nonconformity, Blame Externalization, Carefree Nonplanfulness, Social Influence, Fearlessness, Stress Immunity, and Coldheartedness. Participants in the current study were grouped based on their scores on the Coldheartedness subscale (CH; e.g., "I look

out for myself before I look out for anyone else."), which is described as 'a propensity towards callousness, guiltlessness, and unsentimentality' (Lilienfeld & Andrews, 1996). Traits captured by the CH subscale are thought to best reflect trait-empathy (Blair, 2005), as this subscale has been correlated with a measure of emotional empathy (see Fecteau, et al., 2008) as well as Factor 1 of the Psychopathy Checklist – Revised (PCL-R; Hare, 1991; Poythress, Edens, & Lilienfeld, 1998). Items are rated on a four-point scale and yield acceptable internal consistency (Cronbach's alpha > 0.80), good composite reliability (> 0.90), and good test-retest reliability ($r = 0.82$ for coldheartedness; Lilienfeld & Widows, 2005). The PPI-R has been standardized and validated for use with men and women aged 18 – 86, and can be used to examine the continuum of psychopathic personality traits present in clinical or non-clinical settings (Lilienfeld & Widows, 2005). Although most imaging studies using psychopathic individuals have utilized the Psychopathy Checklist (PCL; Hare, 1985) or the PCL-R (Hare, 1991) these studies have typically involved incarcerated populations (Kiehl et al., 2004; Muller et al., 2008; Muller, et al., 2003; Raine et al., 2004; Yang et al., 2005; Yang, Raine, Narr, Colletti, & Toga, 2009) and require access to collateral information. The PPI-R is a comparable measure for examining psychopathic traits in non-incarcerated populations: it has been shown to correlate positively (0.54) with the PCL-R (Poythress, et al., 1998) and exhibits a dual-factor structure (Benning, Patrick, Hicks, Blonigen, & Krueger, 2003) similar to that of the PCL-R.

All participants had been administered the PPI-R at an earlier assessment, and were recruited for this study based on their CH scores. Age- and gender-matched normative data for all subscales is included in the PPI-R manual (Lilienfeld & Widows,

2005), and was used to group participants. Subjects whose scores fell in the top 33% of normative data for their age and gender were categorized as the high CH group, while subjects whose scores fell in the bottom 33% of normative data for their age and gender were placed in the low CH group.

2.2.2 Participants

Thirty-four subjects participated in the current study. Data from two subjects were excluded due to scanner malfunction or inability to follow instructions, leaving 32 participants who were categorized in one of two groups: a high CH group ($N = 16$) and a low CH group ($N = 16$) (see Table 1). Participants were recruited from the University of Western Ontario and the general London community through flyers posted around campus and advertisements in the local newspaper. All participants were between the ages of 17 and 35, were in good health, and were screened using the Structured Clinical Interview of the DSM-IV-TR (SCID; First, Spitzer, Williams, & Gibbon, 1995) to exclude any history of Axis-I disorders or neurological injury. One participant in the high CH group had been diagnosed with conduct disorder. All subjects had normal or corrected-to-normal vision, and were right-handed as determined by the Edinburgh Handedness Inventory (Oldfield, 1971). Groups did not differ significantly in terms of age ($t(30) = 0.48$, *ns*) or IQ ($t(30) = -0.75$, *ns*). This study was performed in accordance with standards of the University of Western Ontario Research Ethics Board. Participants received monetary compensation for participation in this study.

Table 1. Participant demographic information

Group	Gender	Age	IQ	CH score percentile
	Female, Male	M(SD)	M(SD)	M(SD)
High CH	10, 6	24.44(5.15)	113(6.54)	89.94(6.24)
Low CH	9, 7	25.25(4.49)	110(11.31)	15.50(10.84)

2.2.3 fMRI Data Acquisition

Subjects were scanned while performing the task in a 3.0 Tesla Siemens MRI scanner with a 32-channel head coil at Robarts Research Institute. A high resolution, T1-weighted anatomical scan was acquired at the beginning of each session (repetition time = 2300 ms; echo time = 4.25 ms; 192 axial slices; voxel size = 1 mm isovoxels; 256 x 256 matrix; field of view = 25.6 cm). Six functional MRI runs followed, in order to measure changes in BOLD. Functional images were acquired with a T2*-gradient echo-planar imaging (EPI) sequence (repetition time = 3000 ms; echo time = 30 ms; 120 x 120 matrix; flip angle 90°; field of view = 24cm). Coverage was obtained with 45 axial brain slices (thickness 2.5 mm; 2 x 2 mm in-plane resolution). Slices were acquired in an interleaved fashion. For each experimental run, 147 volumes were acquired.

2.2.4 Experimental Task

Participants completed the Partial Face Encoding (PFE) task, a novel emotion recognition task in which they viewed grayscale images of actors depicting realistic emotional faces and identified the emotion seen. Stimuli for the PFE were constructed using the empirically-validated Karolinska Directed Emotional Faces (Lundqvist, Flykt, & Ohman, 1998). All faces were photographs of college-aged actors (balanced for gender), facing straight ahead at the viewer, and making one of five emotional expressions: fear, anger, happiness, disgust, and neutral. Using Adobe Photoshop Elements 4.0, all stimuli were converted to grayscale images on a black background, realigned 1 to 2°, resized to fit the computer screen, with the hair and the ears cropped out

so that only the face remained. Three portion conditions were also used for each of the five emotions: a "whole face" condition that allowed the subject to free gaze, an "eyes only" condition which was cropped so that only the eye region and eyebrows could be seen, and an "eyes removed" condition in which the eye and eyebrow region was cropped out, and only the remaining portions of the face could be seen (see Figure 1). To construct the eyes only and eyes removed faces, 12% above and below the nasion were used as upper and lower boundaries, respectively. Inter-rater reliability was highly correlated for all nasion estimates ($r = 0.91, p < .01$). If nasion estimates differed by greater than 4% between raters, the mean estimate was used as the nasion.

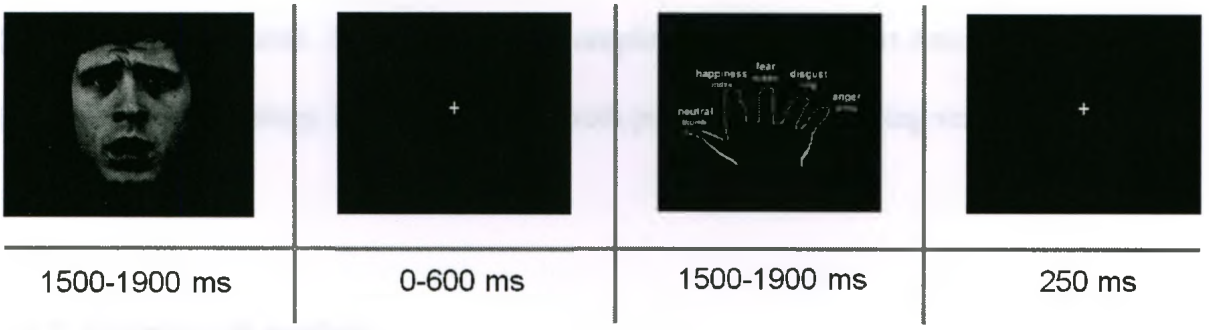
A response screen was also constructed, during which participants would be asked to choose which emotion they had seen. The response screen was comprised of a simple outline of a right hand, with the name of the five emotions above the five fingers, indicating which button press corresponded to which emotion (see Figure 2).

Figure 1. Example of whole face, eyes only, and eyes removed stimuli across 5 emotions

Figure 2. Example of response screen

The PFE task consisted of 6 full runs (7 min 21 s per run). Stimuli were presented through a data projector onto a screen that was visible to a subject in the scanner using a mirror positioned above the coil in the MRI. Instructions were projected on the screen at the beginning of each run to ensure that their administration was standardized across participants. Each run began with a fixation cross (1200 ms). Each trial consisted of a face (1500, 1700, or 1900 ms), followed by a fixation point (0, 300, or 600 ms), then a response screen (1500, 1700, or 1900 ms), and a fixation cross (250 ms; see Figure 3). Variable stimulus durations were pseudo-randomly assigned by portion and emotion. Each run consisted of 90 images, balanced for emotion (fear, anger, happiness, disgust, and neutral), portion of face (whole face, eyes only, or eyes removed) and gender. Each run ended with a final fixation point (18 s). Run order and response screens were varied across all participants, but each participant viewed the same response screen for all trials. Responses were recorded using a 5-button response box (Current Designs, Pennsylvania) held in the right hand of the participant. While in the scanner, participants also completed two practice versions of the task prior to administration of the 6 test runs. Practice A was an abbreviated version of the PFE task, in which the name of the emotion was projected on the screen in place of an emotional face and feedback was provided following their response on each trial ("Correct!", "Incorrect.", or "No response detected."). Practice B was identical to the actual PFE task (emotional faces were used and no feedback was provided), though its duration was shorter than an actual test run. Completion of these practice tasks ensured that all participants understood the objectives and were able to respond proficiently.

Figure 3. Partial Face Encoding task structure



The PFE program was constructed and run using E-Prime software (Psychology Software Tools, 2002), which allowed for the acquisition of accuracy and response time (ms) data for each trial. Participants also completed the State-Trait Anxiety Inventory (Consulting Psychology Press Inc., 1977) both prior to and following scanning.

2.2.5 Behavioural analysis

Statistical analysis of behavioural recognition accuracy data was conducted using the PASW statistical package (2008). A 2 (Group: high CH scorers, low CH scorers) by 3 (Portion: whole, eyes only, eyes removed) by 5 (Emotion: anger, disgust, fear, happy, neutral) analysis of variance (ANOVA) was performed. Only correct responses made during the response screen were included in the analysis. The threshold for significance was set at $p < .05$. Subsequent post-hoc t-test comparisons were also performed at a significance threshold of $p < .05$.

2.2.6 fMRI analysis

Individual and group analyses were conducted using Analysis of Functional NeuroImages software (AFNI; Cox, 1996). The first four volumes collected before magnetization equilibrium was reached in each of the six runs were discarded from analysis. Six regressors were included in the analysis that accounted for baseline drift. Motion correction was achieved by registering all blood oxygen level dependent (BOLD) data in each run of the task to the first volume of the first experimental run, which was

collected immediately following the anatomical image. Each volume was spatially smoothed using an isotropic 4 mm full-width half-maximum Gaussian kernel to reduce the influence of individual differences in anatomy before creating group maps. All runs for each subject were concatenated, forming one complete data file per subject. To normalize the time series data, the signal intensity of a given voxel at each time point was divided by the mean signal intensity of that voxel for each run, and multiplied by 100. The resulting regression coefficients represented the percent signal change from the mean activity. Regressors were created by convolving the stimulus events with a gamma-variate basis function to account for the slow hemodynamic response. Regressors were created for each of the 15 face stimuli conditions: 5 emotions (neutral, happy, angry, fear, and disgust) and 3 portions (whole, eyes only, eyes removed), by taking into account the onset and duration of each trial that participants correctly identified the given emotion. Trials in which the participant inaccurately labelled the given emotion, or responded outside of the response screen presentation, were categorized as incorrect trials. Four regressors of no interest were also modelled.

The BOLD response was fitted to each of these 19 regressors to perform linear regression modelling. To account for voxel-wise correlated drifting, a baseline plus linear drift and quadratic trend were modeled to the time series of each voxel and regressor. This produced a beta coefficient and a t-value for each voxel and regressor. Additional motion correction was applied during deconvolution, by regressing out volumes that were identified as having excessive motion, even after the motion correction described above. Threshold for acceptable motion was set at 4 mm. To perform group analyses, each participant's data was transformed into the standard space of Talairach and

Tournoux (1988). This was followed by primary analyses of the regression coefficients, described below.

2.2.6.1 Whole brain analysis

Contrast tests were performed on 3-dimensional data, by comparing BOLD activity between the two groups on the 15 regressors of interest. Regions significantly active at a threshold of $p < .001$ were examined. To reduce the probability of Type I error, we corrected for multiple comparisons using AlphaSim, an AFNI spatial clustering operation with 1000 Monte Carlo simulations taking into account the entire echo-planar imaging matrix. Clusters that survived correction were significant at $p < .05$.

2.2.6.2 ROI approach to amygdala activity

Based on predictions about the amygdala's role in emotion processing (Adolphs, 2010) and dysfunction associated with psychopathy (Jones, et al., 2009; Marsh, et al., 2008), a region of interest (ROI) analysis was justified to investigate activity in this substrate at a more liberal threshold ($p < .01$, with small volume correction at $p < .05$).

2.3 Results

2.3.1 Behavioural Results

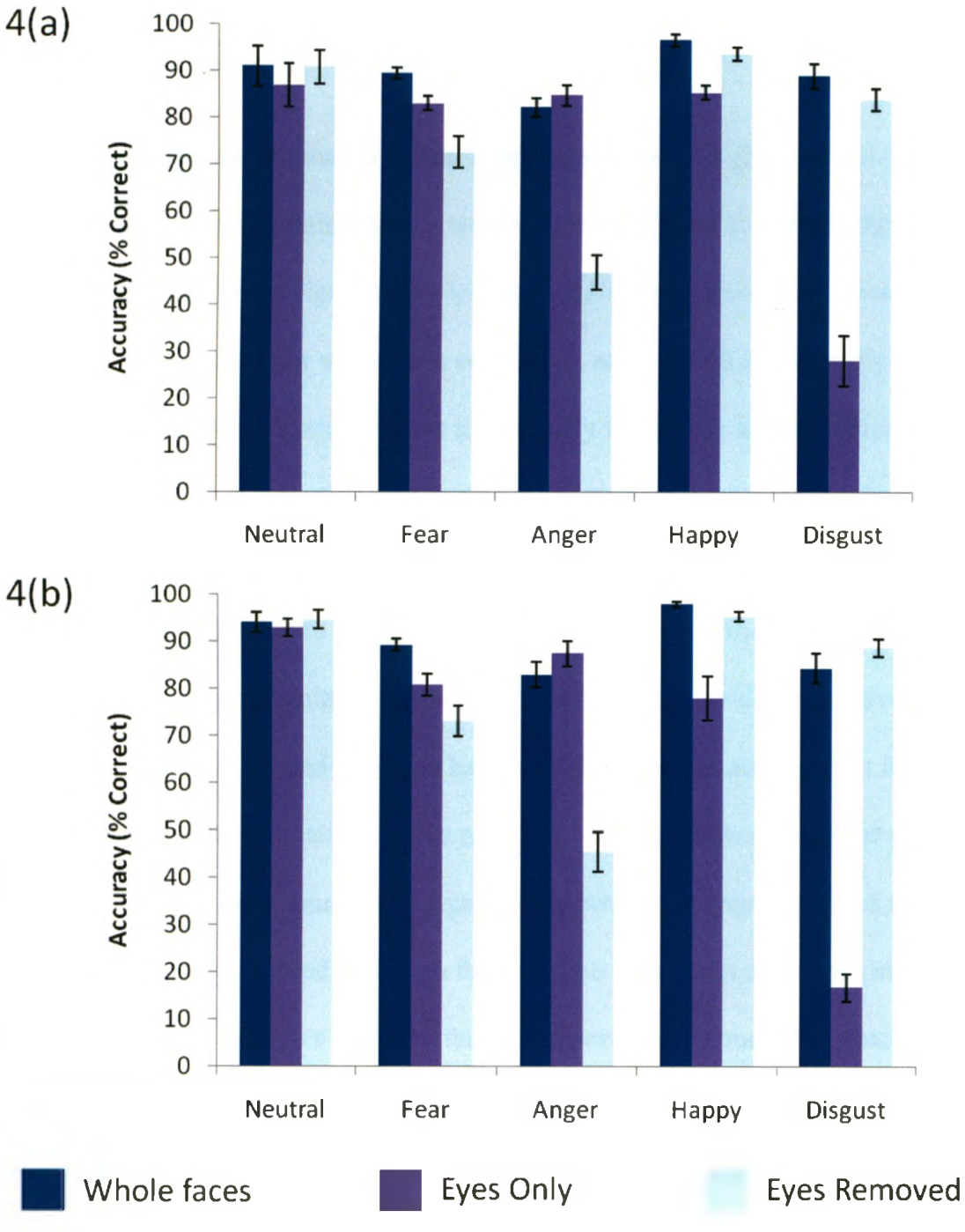
A 2 (Group: high CH, low CH) by 3 (Portion: whole, eyes only, eyes removed), by 5 (Emotion: fear, happy, anger, disgust, neutral) repeated measures ANOVA was performed on participants' accuracy data from the PFE task. Since Mauchly's test for sphericity was significant for the main effect of Emotion ($W(9) = 0.27, p < .001$), for the main effect of Portion ($W(2) = 0.75, p < .05$), and for the Emotion by Portion interaction ($W(35) = 0.03, p < .001$), the more conservative Greenhouse-Geisser correction was applied. The behavioural data yielded a significant main effect of Emotion ($F(2.65, 79.41) = 61.96; p < .001$) and a significant main effect of Portion ($F(1.60, 48.04) = 141.19; p < .001$). The ANOVA also revealed a significant Emotion by Portion interaction ($F(4.79, 143.62) = 197.9; p < .001$) and a significant Emotion by Portion by Group interaction ($F(8, 240) = 2.36; p < .05$).

To delineate the nature of the emotion by portion by group interaction, two sets of follow-up ANOVAs were conducted. First, a 2 (Group) by 5 (Emotion) ANOVA run separately for each portion condition yielded a significant main effect of Emotion for whole face ($F(2.7, 82.42) = 12.43, p < .001$), eyes only ($F(2.74, 82.12) = 171.38, p < .001$), and eyes removed ($F(2.77, 83.08) = 109.52, p < .001$). No significant main effect of Group, or Group by Emotion interaction emerged for any of these contrasts. Following this, a 2 (Group) by 3 (Portion) ANOVA was conducted separately for each emotion, which revealed a significant main effect of Portion for fear ($F(1.5, 46.18) = 36.58, p < .001$), neutral ($F(2, 60) = 4.01, p < .05$), happy ($F(1.14, 34.23) = 32.57, p <$

.001), anger ($F(1.50, 44.94) = 185.92, p < .001$) and disgust ($F(1.45, 43.56) = 379.02, p < .001$), but only a significant Group by Portion interaction for disgust ($F(1.45, 43.6) = 4.56, p < .05$).

This combination of results suggests that the Group by Portion by Emotion interaction was driven by this effect which existed only for disgusted faces (see Figure 4). The Group by Portion interaction for disgust was explored further using a series of independent-samples t-tests, which showed that the two groups did not significantly differ in their recognition accuracy of whole, eyes only, and eyes removed faces of disgust ($p > .05$ in each case). A series of paired-samples t-tests were then performed within each group. Individuals with low CH scores were significantly more accurate at recognizing disgust when presented with whole faces relative to when they viewed eyes only ($t(15) = 11.65, p < .001$) or eyes removed ($t(15) = 2.95, p < .05$) faces, and were also significantly more accurate when given eyes removed relative to eyes only stimuli ($t(15) = -10.34, p < .001$). Individuals with high CH scores were significantly more accurate at recognizing disgust from whole faces relative to eyes only stimuli ($t(15) = 20.52, p < .001$), and for eyes removed stimuli relative to eyes only stimuli ($t(15) = -25.08, p < .001$). However, accuracy for whole relative to eyes removed faces of disgust was not found to be significantly different in the high CH group ($t(15) = -1.51$, *ns*).

Figure 4. Recognition accuracy on Partial Face Encoding task for (a) low CH group and (b) high CH group. Follow-up comparisons revealed that Group by Portion by Emotion interaction was driven by significantly greater recognition accuracy for the low CH group in the whole face condition of disgust relative to the eyes removed condition ($p < .05$), whereas the high CH group did not significantly differ in recognition accuracy for whole vs. eyes removed conditions of disgust (*ns*). Groups did not significantly differ in comparison tests of any other conditions.



Analysis of the group by portion by emotion interaction revealed that this effect was driven by how accurately the two groups recognized facial expressions of disgust across the three portion conditions. However, our analyses also indicated that the two groups exhibited the same pattern of recognition accuracy when viewing the most informative (eyes removed) versus the least informative (eyes only) portion of disgust. This finding, in conjunction with the non-significant main effect of group for the other emotion conditions validated a closer examination of the emotion by portion interaction.

To delineate the emotion by portion interaction, the two groups were collapsed for post hoc tests. A series of paired t-tests were conducted (Table 1). When viewing fearful faces, all participants were significantly less accurate in the eyes removed condition than they were in the eyes only or whole face conditions, and showed significantly greater accuracy for whole fearful faces relative to eyes only faces. For anger, participants' recognition accuracy was significantly worse when viewing eyes removed faces relative to eyes only and whole faces, and was significantly better when recognizing anger from eyes only stimuli compared to whole face stimuli. However, participants were significantly worse at recognizing happiness in the eyes only condition relative to eyes removed and whole faces, and they also had significantly better accuracy for happiness when shown whole faces relative to eyes removed. Disgust showed a similar pattern, with recognition accuracy found to be significantly worse for eyes only faces relative to whole faces and eyes removed, although there was no significant difference in accuracy between whole faces and eyes removed faces. However, since our initial analyses showed that only the high CH group is characterized by this pattern, this latter result appears to drive the 3-way interaction and should therefore be interpreted with caution.

Table 2. Partial Face Encoding Task: post-hoc tests of Emotion by Portion interaction

Comparison	**df**	**t**	***p***
Fear			
whole > eyes only	31	5.63	< .001
whole > eyes removed	31	8.08	< .001
eyes only > eyes removed	31	4.06	< .001
Anger			
whole < eyes only	31	-3.31	< .05
whole > eyes removed	31	15.41	< .001
eyes only > eyes removed	31	14.56	< .001
Happy			
whole > eyes only	31	6.19	< .001
whole > eyes removed	31	3.76	< .005
eyes only < eyes removed	31	-4.96	< .001
Disgust			
whole > eyes only	31	20.74	< .001
whole > eyes removed	31	0.19	*ns*
eyes only < eyes removed	31	-19.4	< .001

These findings indicate that the eye region contains critical information used to accurately identify anger and fear in facial expressions. Conversely, the lower region of the face, which is isolated in the eyes removed stimuli, appears to contain critical information used for the accurate recognition of happiness and disgust.

2.3.2 fMRI Results

2.3.2.1 Between-Group Contrasts of Least vs. Most Informative Portion of Emotional Faces

In conjunction with results from a recent pilot study (Alders & Mitchell, 2010) the above behavioural findings guided our subsequent analysis of the neuroimaging data collected during Partial Face Encoding. Contrast tests were performed between the conditions of each emotional face that were the most or least informative (contained or did not contain information critical for accurate recognition, respectively).

Fear: Eyes Removed – Eyes Only

When the least informative portion of fearful faces (eyes removed) was contrasted with the most informative portion (eyes only), individuals with low, relative to high CH scores showed significantly greater activity in the bilateral medial frontal gyrus, bilateral inferior parietal lobule, bilateral superior frontal gyrus, bilateral middle frontal gyrus, and right cingulate gyrus ($p < .001$; .05 corrected, see Table 2 and Figures 5 – 7). In addition, an ROI analysis revealed that individuals with low CH scores also showed significantly

greater activity than individuals with high CH scores in the left amygdala ($p < .01$, small-volume corrected).

Figure 5. The low CH group showed significantly greater activity relative to the high CH group in (a) left amygdala ($p < .01$; small-volume corrected), and (b) medial prefrontal cortex ($p < .001$; .05 corrected), when the least informative portion of fearful faces (eyes removed) was contrasted with the most informative portion (eyes only). Follow-up comparisons revealed greater activity in these regions for the low CH group when viewing the least informative condition of fear relative to the most informative condition, whereas the high CH group shows greater activity in these regions for the most informative condition relative to the least.

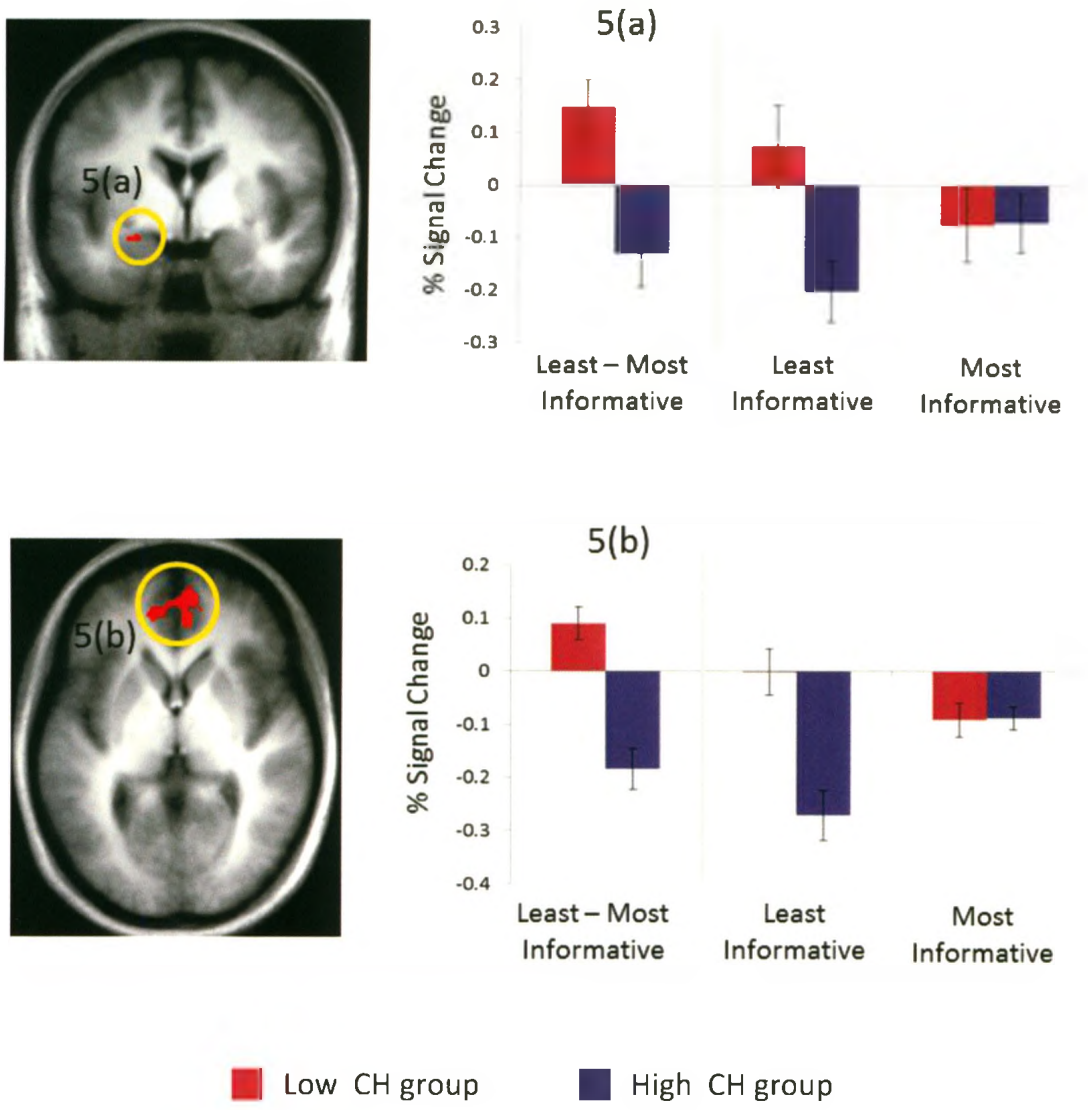
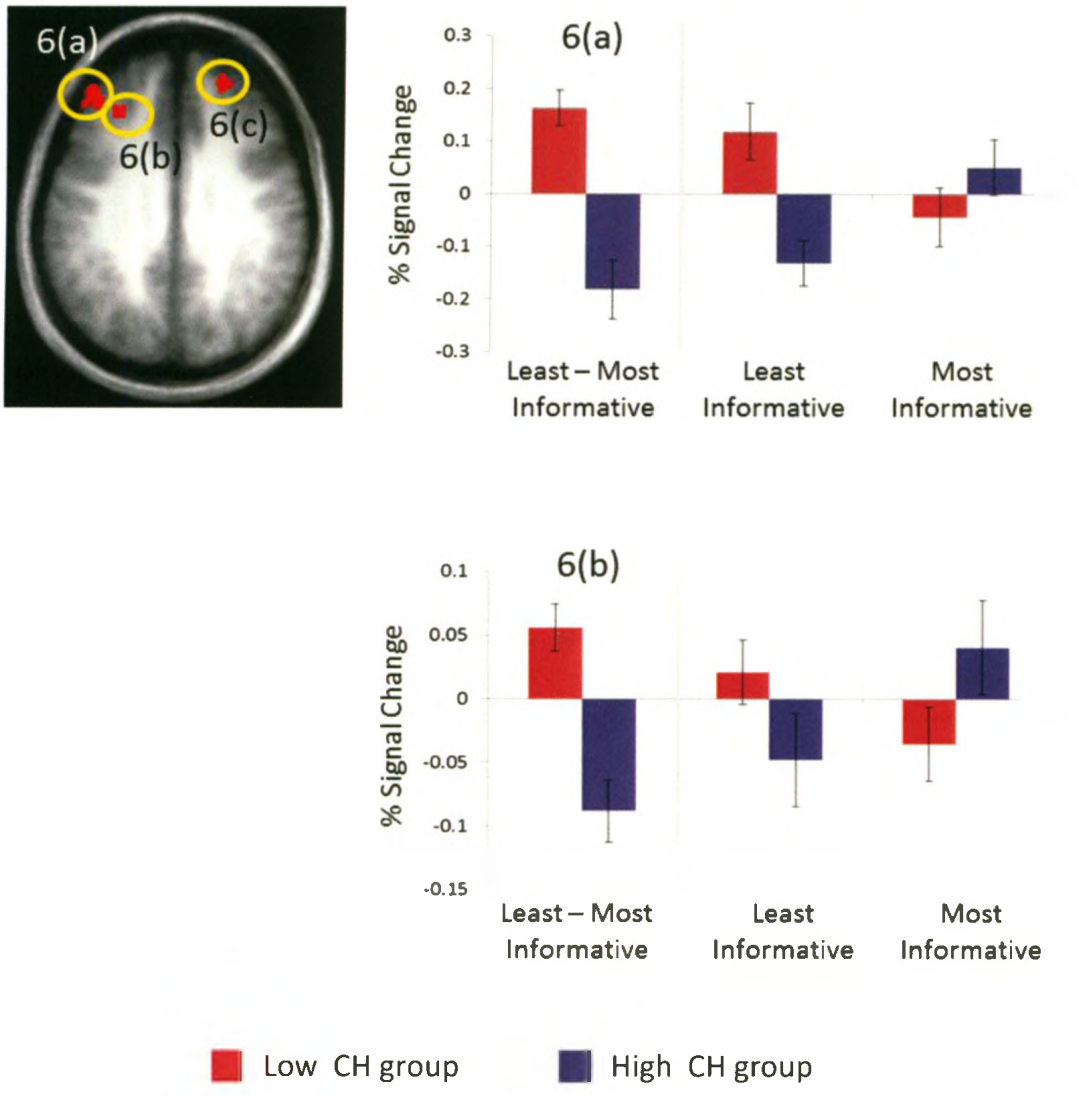
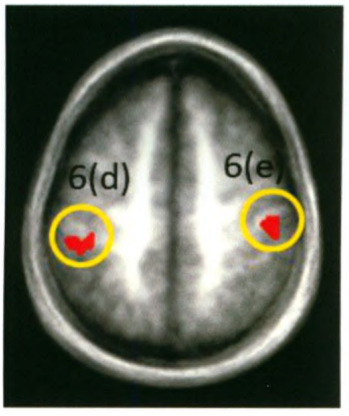


Figure 6. The low CH group also showed significantly greater activity relative to the high CH group in (a) left superior frontal gyrus, (b) left middle frontal gyrus, (c) right superior frontal gyrus, and right middle frontal gyrus, (d) left inferior parietal cortex, and (e) right inferior parietal cortex ($p < .001$; .05 corrected), when the least informative portion of fearful faces (eyes removed) was contrasted with the most informative portion (eyes only). Follow-up comparisons revealed greater activity in these regions for the low CH group when viewing the least informative condition of fear relative to the most informative condition, whereas the high CH group shows greater activity in these regions for the most informative condition relative to the least.

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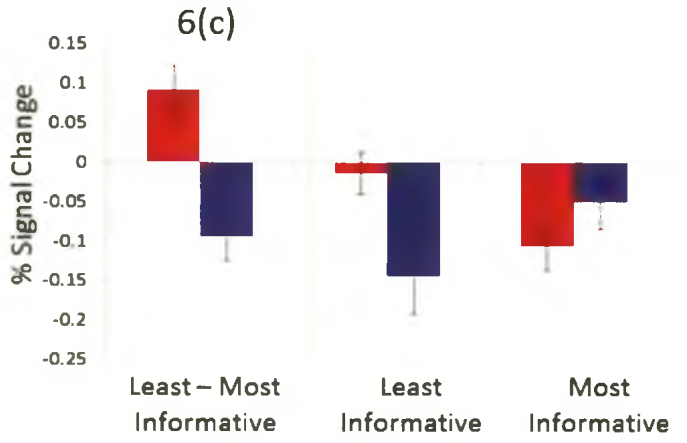
6(c)
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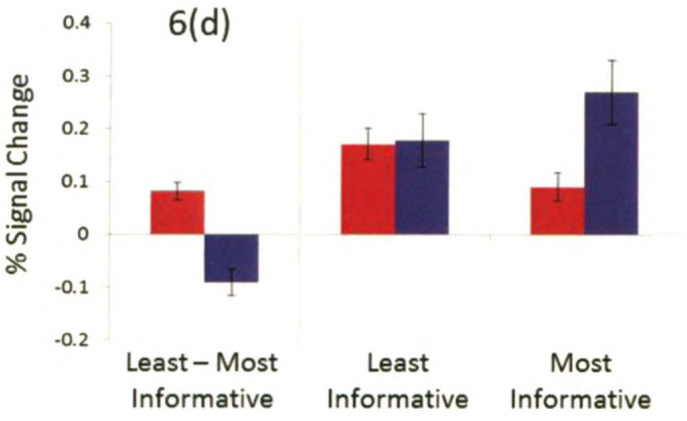
0.15
0.1
0.05
0
-0.05
-0.1
-0.15
-0.2
-0.25
Least – Most Informative
Least Informative
Most Informative


6(d)
% Signal Change
0.4
0.3
0.2
0.1
0
-0.1
-0.2
Least – Most Informative
Least Informative
Most Informative

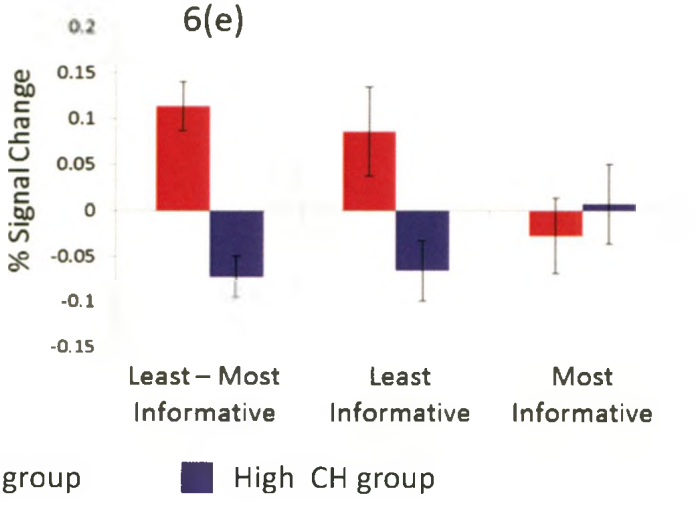
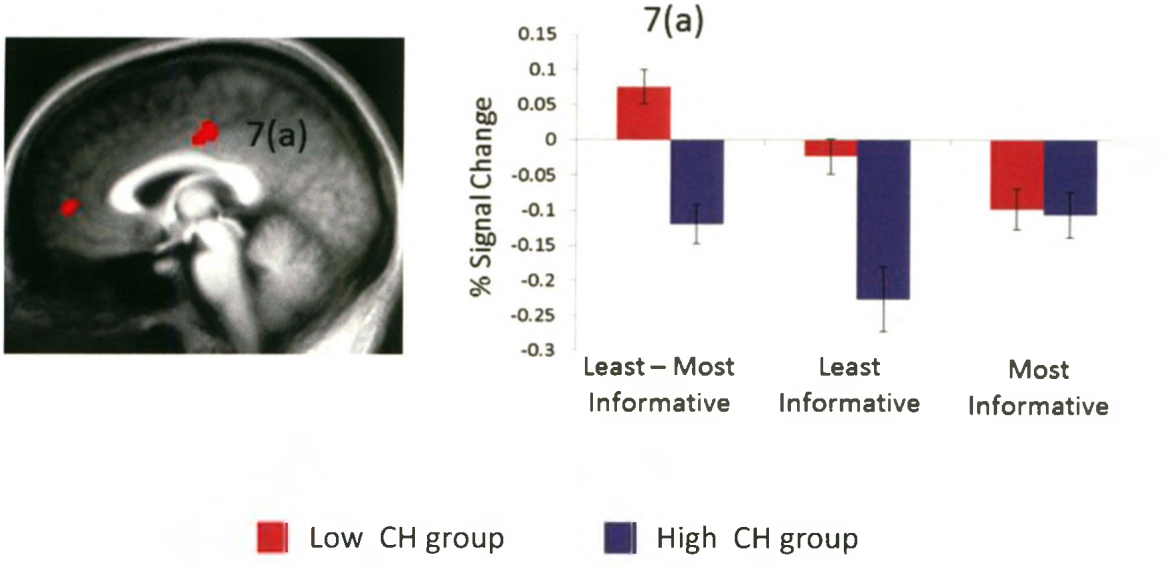

6(e)
% Signal Change
0.2
0.15
0.1
0.05
0
-0.05
-0.1
-0.15
Least – Most Informative
Least Informative
Most Informative
Low CH group
High CH group

Figure 7. The low CH group also showed significantly greater activity relative to the high CH group in (a) right cingulate gyrus ($p < .001$; .05 corrected), when the least informative portion of fearful faces (eyes removed) was contrasted with the most informative portion (eyes only). Follow-up comparisons revealed greater activity in these regions for the low CH group when viewing the least informative condition of fear relative to the most informative condition, whereas the high CH group shows greater activity in these regions for the most informative condition relative to the least.



Happy: Eyes Only – Eyes Removed

Relative to the high CH group, individuals with low CH scores showed significantly greater activity in the left fusiform gyrus, and left middle temporal gyrus when viewing the least informative portion (eyes only) of happy faces ($p < .001$; .05 corrected, see Table 2 and Figure 9). In addition, ROI analysis using this contrast showed that individuals with low CH scores also showed significantly greater activity in bilateral amygdala relative to the high CH group ($p < .01$; small-volume corrected, see Table 2 and Figure 8).

Other Emotions

Between group contrasts were also performed on the least vs. most informative portions of anger (eyes removed vs. eyes only), and disgust (eyes only vs. eyes removed). These contrasts revealed no significant clusters of activation in a corrected whole-brain contrast, or ROI analysis of the left and right amygdala.

Figure 8. The low CH group showed significantly greater activity relative to the high CH group when the least informative portion of happy faces (eyes only) was contrasted with the most informative portion (eyes removed), including (a) right amygdala and (b) left amygdala ($p < .01$; small-volume corrected). Follow-up comparisons revealed greater activity in these regions for the low CH group when viewing the least informative condition of fear relative to the most informative condition, whereas the high CH group shows greater activity in these regions for the most informative condition relative to the least.

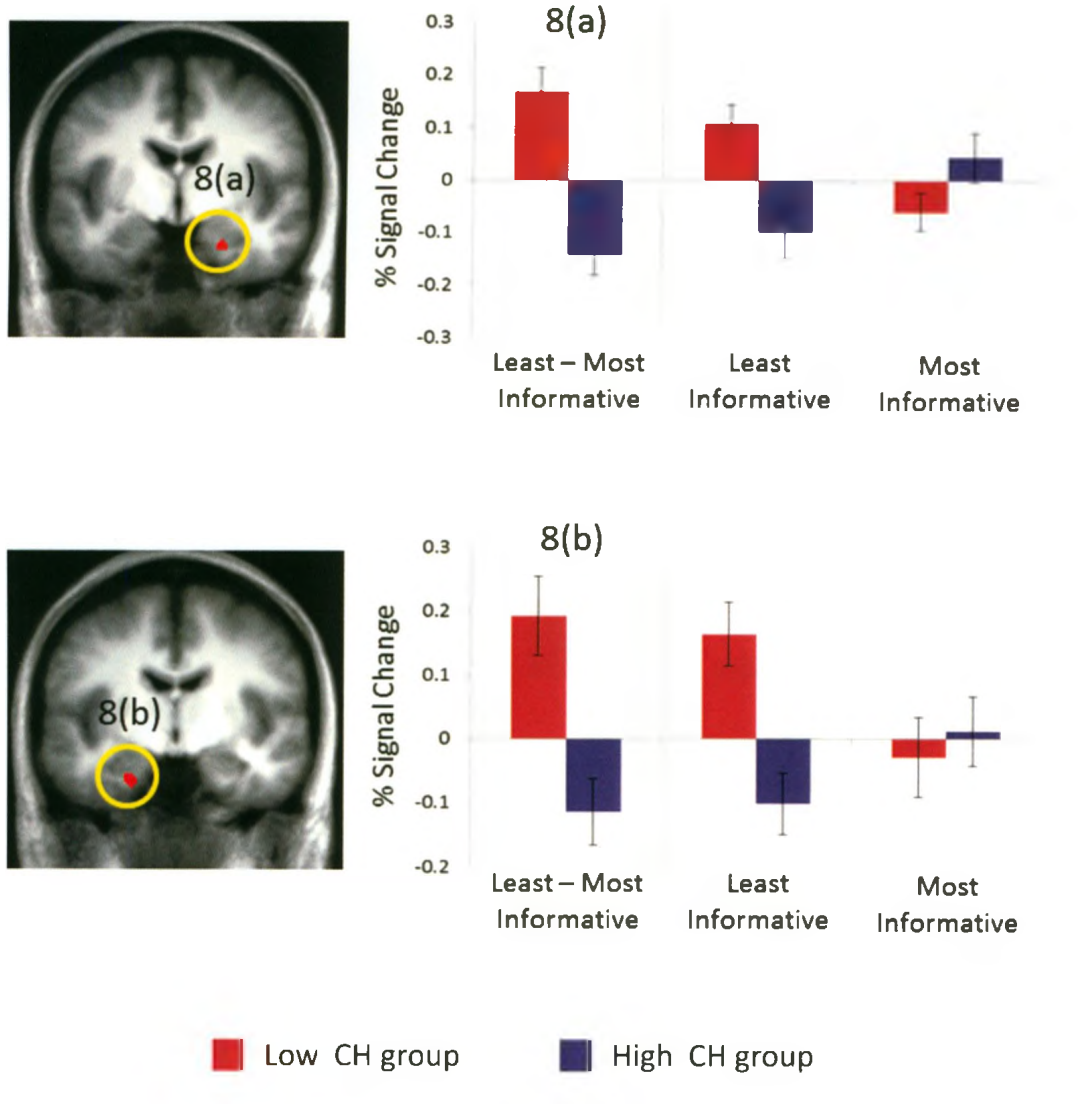


Figure 9. The low CH group showed significantly greater activity relative to the high CH group when the least informative portion of happy faces (eyes only) was contrasted with the most informative portion (eyes removed), including (a) left fusiform gyrus and (b) left middle temporal gyrus ($p < .001$; .05 corrected). Follow-up comparisons revealed greater activity in these regions for the low CH group when viewing the least informative condition of fear relative to the most informative condition, whereas the high CH group shows greater activity in these regions for the most informative condition relative to the least.

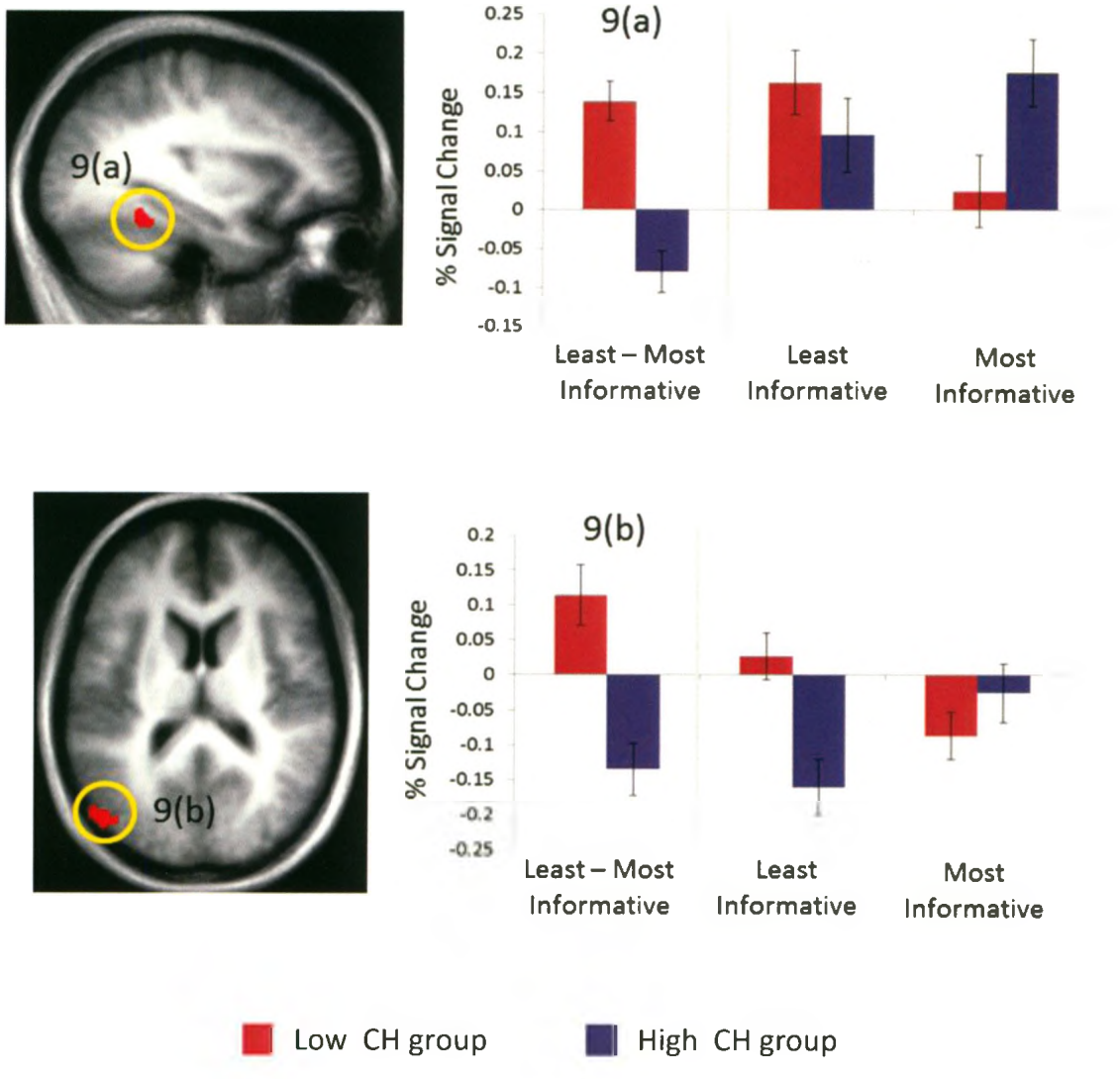


Table 3. Areas showing significantly greater activity in individuals with low relative to high CH scores when the least informative portion of an emotional face was contrasted with the most informative portion. Table displays the anatomical location, hemispheric location (left = L, right = R), Brodmann's Area (BA), MNI coordinates (x, y, z), and the maximum neural activity for the peak of that cluster (t-value).

Anatomical Location	**L/R**	**BA**	**x**	**y**	**z**	**t-value**
Fear (Eyes Removed > Eyes Only)						
Medial frontal gyrus/anterior cingulate	L/R	10, 32	6.3	55.3	4.3	5.7
Inferior parietal lobule	L	40	-39.1	-31.9	45.9	4.9
Superior frontal gyrus	L	9	-41.7	35.8	33.2	4.7
Inferior parietal lobule/postcentral gyrus	R	2	46.7	-26.7	46.2	5.9
Middle frontal gyrus	L	9	-26.5	30.3	41.0	4.4
Middle frontal gyrus	R	8	24.0	30.2	43.8	4.7
Cingulate gyrus	R		1.3	-18.9	43.9	5.2
Superior frontal gyrus	R	9	21.5	43.3	39.0	4.6
Amygdala*	L		-24.0	-0.7	-13.4	3.5
Happy (Eyes Only > Eyes Removed)						
Fusiform gyrus	L	37	-31.6	-46.9	-19.1	5.7
Middle temporal gyrus	L	19/39	-49.2	-76.8	13.6	4.4
Amygdala*	R		18.9	-0.2	-25.3	5.0
Amygdala*	L		-26.5	4.7	-19.1	3.6

Thresholded at $p < .001$; $p < .05$ corrected

* Thresholded at $p < .01$; $p < .05$, small volume corrected

2.3.2.2 Covariate Analysis of Least Informative vs. Most Informative Contrast

To examine the effect that CH scores had on the differences in neural activity between the least informative (eyes removed) and most informative (eyes only) conditions of fearful faces, we used AFNI 3dttest ++ to perform this contrast with each participants' percentile score on this subscale entered as a covariate. The results of this analysis corroborated the original contrasts, indicating that lower CH scores were associated with a larger differential effect of the least informative versus the most informative conditions for fearful faces in bilateral medial frontal gyrus, left superior frontal gyrus, and bilateral inferior parietal lobule (see Table 3).

Figure 10. Covariate analyses revealed that lower CH scores were associated with larger differential effects of the least informative versus the most informative conditions for fearful faces in (a) right medial frontal gyrus and (b) left medial frontal gyrus ($p < .001$; .05 corrected).

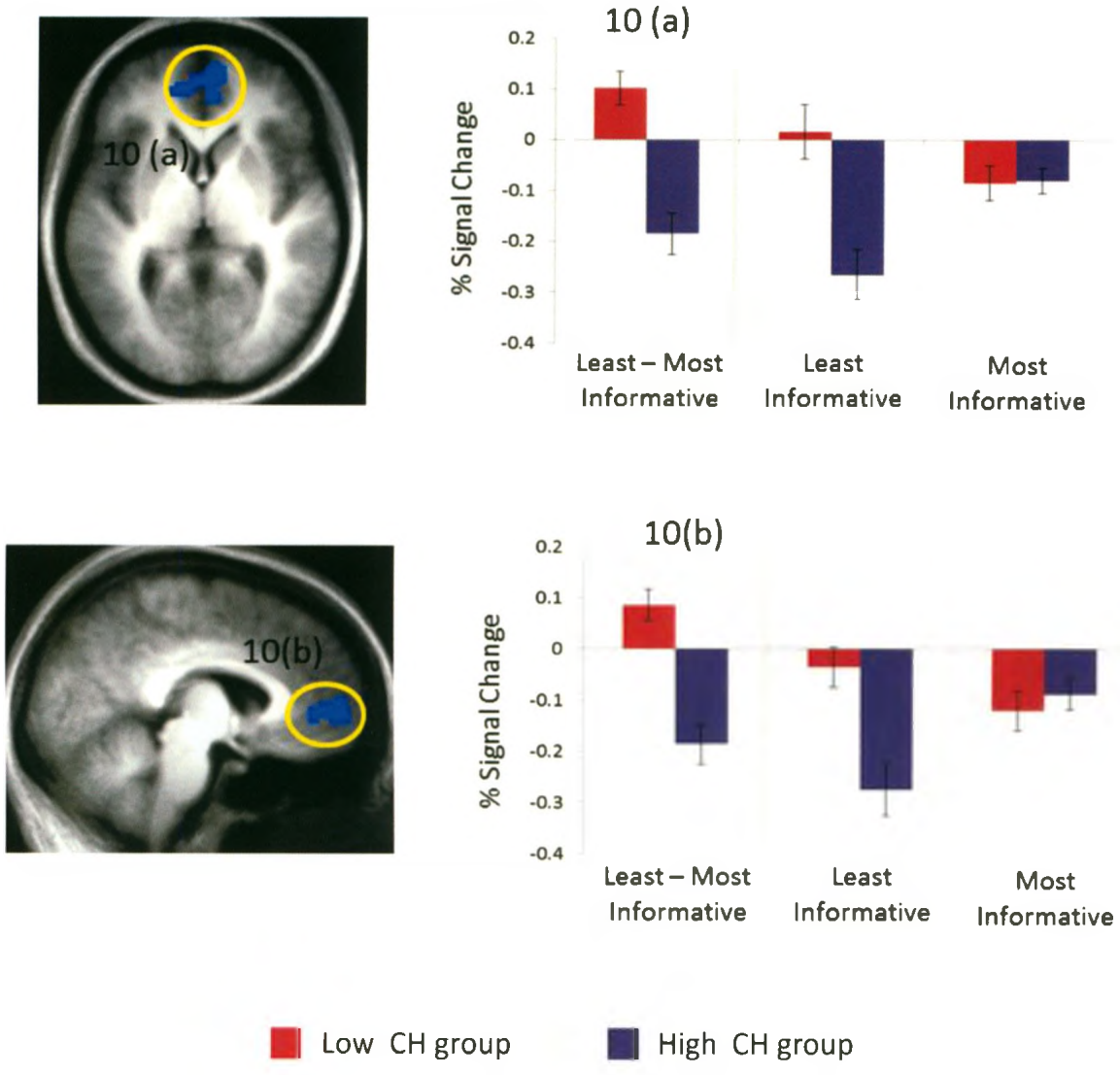


Figure 11. Covariate analyses also revealed that lower CH scores were associated with larger differential effects of the least informative versus the most informative conditions for fearful faces in (a) left superior frontal gyrus, (b) left inferior parietal lobule, and (c) right inferior parietal lobule ($p < .001$; .05 corrected).

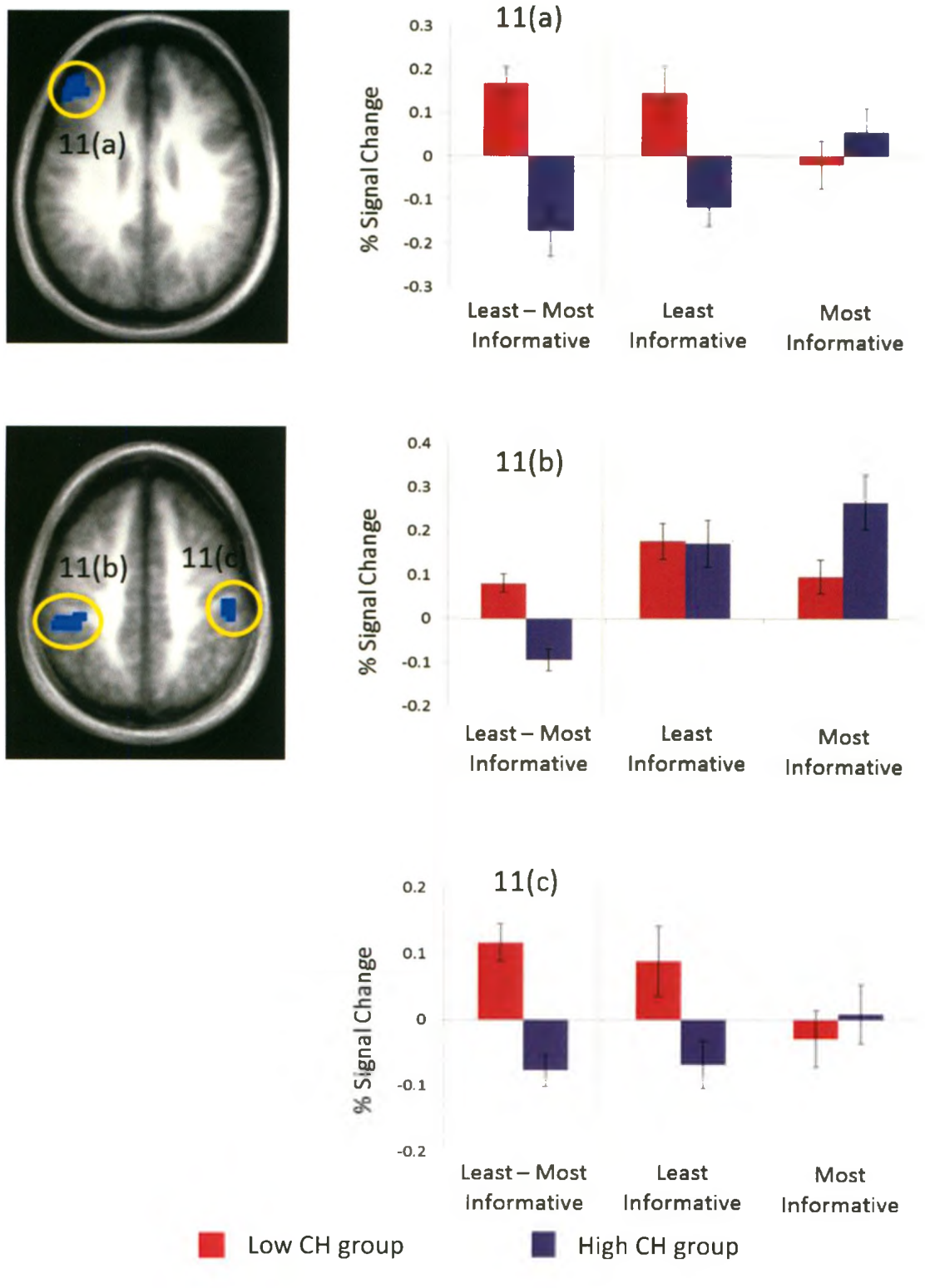


Table 4. Areas where neural activity was amplified by low CH scores when the least informative portion of fear was contrasted with the most informative portion.

Anatomical Location	L/R	BA	x	y	z	t-value
Fear (Eyes Removed > Eyes Only)						
Medial frontal gyrus/anterior cingulate	R	10, 32	6.3	55.1	7.0	-5.2
Superior frontal gyrus/middle frontal gyrus	L	9	-41.7	35.8	33.2	-5.0
Inferior parietal lobule/postcentral gyrus	L	40, 2	-39.1	-31.9	45.9	-4.5
Medial frontal gyrus	L	10	-11.4	44.9	6.4	-4.9
Inferior parietal lobule/postcentral gyrus	R	2	46.7	-26.7	46.2	-5.2

Thresholded at $p < .001$; $p < .05$ corrected

2.3.2.3 Between-Group Contrasts of Emotional Faces vs. Neutral Faces

Previous studies have observed functional abnormalities in individuals with high psychopathic traits relative to comparison groups when fear is contrasted with neutral, using whole face stimuli (Jones, et al., 2009; Marsh, et al., 2008). To determine whether similar abnormalities were evident in our community sample of participants with high vs. low CH scores, additional contrasts were performed comparing whole emotional faces with whole neutral faces.

Fear Whole – Neutral Whole

Individuals in the high CH group showed significantly greater activity in the precuneus when fear whole faces were contrasted with neutral whole faces, relative to the low CH group ($p < .001$; .05 corrected). No significant clusters of activation survived correction for the ROI analysis of the amygdala.

Anger Whole – Neutral Whole

The whole brain analysis revealed no significant differences in activity between the low and high CH groups. However, ROI analysis of the amygdala showed that individuals with low CH scores had significantly greater activity in the amygdala when angry whole faces were contrasted with neutral whole faces, relative to individuals with high CH scores ($p < .01$; .05 small-volume corrected).

Other Emotions

Individuals with high vs. low CH scores were not found to significantly differ in our whole-brain analysis of functional activity shown during the presentation of happy or disgusted whole faces relative to neutral whole faces. ROI analysis of the amygdala also showed no significant between-group differences using the same contrasts.

Table 5. Areas that yielded significant between group differences when emotional whole faces were contrasted with neutral whole faces.

Anatomical Location	**L/R**	**BA**	**x**	**y**	**z**	**t-value**
Fear Whole – Neutral Whole						
Precuneus	L/R	31	1.3	-72.1	24.8	-4.3
Anger Whole – Neutral Whole						
Amygdala/parahippocampal gyrus*	R		18.9	-5.7	-16.7	3.5

Thresholded at $p < .001$; $p < .05$ corrected

* Thresholded at $p < .01$; $p < .05$, small volume corrected

2.4 Discussion

2.4.1 Summary of findings

Accurate processing of facial expressions is implicated in regulating aggression and initiating prosocial behaviour (Hoffman, 1975; Perry & Perry, 1974). Previous studies involving clinical populations indicate that individuals with high psychopathic traits exhibit abnormalities in the processing of emotional expressions, particularly for fearful faces (Dadds, et al., 2006; Jones, et al., 2009; Marsh, et al., 2008). At the behavioural level, fear recognition deficits have been alleviated in individuals with amygdala lesions (Adolphs, et al., 2005) and psychopathic traits (Dadds, et al., 2006) by directing attention to the eyes; the area that contains information that is critical for the identification of fear. However, previous studies have not investigated the functional neuroanatomy that is associated with this type of attentional manipulation. Consequently, it remains unclear whether the behavioural recognition accuracy improvement observed in psychopathy is accompanied by a concomitant normalization of activity in brain regions linked to emotional expression recognition and prosocial behaviour. In the current study, fMRI was used to examine how individuals with high versus low scores on the CH subscale of the PPI-R responded at the neural level to a novel emotion recognition task that isolated distinct components of emotional expressions. At a behavioural level, our sample of individuals with high versus low CH scores did not differ significantly in their recognition accuracy of fearful, happy, angry, disgusted, and neutral expressions. In both groups, the recognition accuracy for fearful and angry faces was lowest when the eyes were occluded, consistent with the idea that that the eye region is the "most informative" portion for recognizing these emotions. Happy and disgusted faces showed

the opposite pattern; recognition accuracy was lowest when participants were presented with the eyes only portion, suggesting that information outside this region is the "most informative" for the recognition of these emotions. At a functional level, differences between the high and low CH groups were most pronounced when participants had to identify the emotion without critical cues available, relative to when the same cues were isolated. When asked to identify fearful faces with the most informative cues occluded, individuals with low relative to high CH scores showed significantly greater activity in regions previously implicated in emotion and attention, including the amygdala, medial frontal gyrus (BA 10, 32), middle frontal gyrus (BA 8, 9), superior frontal gyrus (BA 9), inferior parietal lobule (BA 2, 40), and cingulate gyrus (BA 9). A similar pattern of activity was seen in response to happy faces, in the amygdala, fusiform gyrus (BA 37), and middle temporal gyrus (BA 13, 39) for individuals with low relative to high CH scores. Community samples of individuals with high scores on the CH subscale exhibit emotion-related functional brain abnormalities relative to their low CH peers. We discuss the implications of these findings in terms of the amygdala's role in emotional face processing and current neurocognitive models of psychopathy.

2.4.2 Implications for views on the role of the amygdala and emotional empathy

These findings have important implications for two views concerning the amygdala's involvement in emotional empathy. The traditional view has been that the amygdala's role in emotion processing is to encode distress (Blair, 2003; LeDoux, 1998). Several predictions can be generated from this model. First, one possibility is that

amygdala activity in individuals with low CH scores should be greatest in conditions where distress is the most apparent (e.g. fear eyes only relative to eyes removed). Second, given evidence that focusing attention on the eyes alleviates fear recognition impairments in clinical populations, individuals with high CH scores might show either normalized amygdala activity or the recruitment of a compensatory network of brain regions when eyes are isolated. Our primary results were not consistent with this model. Individuals with low CH scores showed enhanced amygdala activity when the most diagnostic region of a distressed facial expression was missing (fear eyes removed). Individuals with high CH scores showed the opposite pattern, with increased amygdala activity when fearful eyes were isolated. However, it is noteworthy that although the level of amygdala activity was increased in this condition for the high CH group, activity remained below baseline levels. In addition, the level of activity was less than that elicited by the least informative condition in the low CH group.

Adolphs (2010) has recently proposed an alternate view of amygdala function that implicates this substrate in orienting attention to the "most salient" portion of a stimulus, or the area that contains information critical for disambiguating the emotion seen. According to this theory, when the most salient portion is missing, this mechanism will become more engaged in an attempt to gather as much information as possible from that stimulus. In line with this perspective, we found that the individuals with low CH scores in our study showed greater amygdala activity when viewing fearful and happy faces with the most salient region missing, relative to when that region was isolated. In sharp contrast, individuals with high CH scores showed greater amygdala activity when the most salient region of fearful and happy faces were isolated relative to when these

regions were missing. The finding of increased amygdala activity in response to happy faces implies that an updated model of amygdala function should also include responses to biologically salient positive affect in the environment.

It is important to note that although this perspective offers a specific model of amygdala function for emotional expression recognition, a similar pattern of activity was observed in other neural regions in the low CH group including prefrontal cortex, parietal cortex, and fusiform gyrus. One possibility is that these areas work in concert with the amygdala to direct attention towards the emotionally salient features of a stimulus. Although the relative importance of these neural regions in performing this function remains unclear, the data elicited from lesion studies (e.g. Adolphs, Tranel, Damasio, & Damasio, 1995) suggest the amygdala is crucial for performing this function. Nevertheless, the medial prefrontal cortex has been linked to emotion processing (Adolphs, 2002; Mattavelli, Catteneo, & Papagno, 2011). It has dense connections with the amygdala, and plays a role in regulating limbic function (for a review, see Mitchell, 2011). The medial prefrontal cortex and anterior cingulate are also associated with cognitive control (Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004), and might provide top-down assistance to the amygdala when the disambiguation of a stimulus is particularly challenging, such as the least informative conditions of our PFE task. Enhanced activity in the fusiform gyrus was also associated with amygdala activity in response to the least informative condition of happy faces. Previous studies have indicated that this region is associated with emotion perception (Haxby, Hoffman, & Gobbini, 2000), that it has substantial connections with and is influenced by the amygdala (Fairhall & Ishai, 2007; Vuilleumier & Pourtois, 2007). Based on this line of evidence,

perhaps the amygdala augments representations in the fusiform gyrus to assist in deciphering which emotion is present when given the most challenging stimulus condition.

2.4.3 Implications for neurocognitive models of psychopathy

Although the pattern of results observed in the low CH group was consistent with newly emerging theories of the role of the amygdala in emotional expression processing, a strikingly divergent pattern was observed in the high CH group. Consistent with previous studies involving clinical populations, we observed functional abnormalities in amygdala and medial prefrontal cortex during facial expression processing in our community sample of individuals with high CH scores. These findings are broadly consistent with current neurocognitive perspectives of psychopathy, particularly the Integrated Emotion Systems model (Blair, 2004). However, our findings have potentially important implications for extending these models. For example, the high CH group in our study showed an inverse pattern of activity relative to the low CH group, with greater activity in the amygdala and prefrontal cortex for the most informative condition of fearful and happy faces, relative to the least informative. This pattern suggests that individuals with high CH scores are not utilizing this amygdala-medial prefrontal system properly to orient attention to critical components of emotional cues when most needed. Furthermore, our experimental manipulation also revealed reduced activity in the inferior parietal lobule, for the high CH group relative to the low CH group, although most studies have indicated that these regions are functionally intact in psychopathy (Blair & Mitchell, 2009; Blair, Mitchell, & Blair, 2005). One possibility is that the functional

abnormalities observed in frontoparietal areas may be downstream effects of a primary amygdala dysfunction. The low CH group could be identifying the emotion when the least informative region is shown by utilizing both bottom-up (amygdala) and top-down (parietal cortex) interactions. Although speculative, one possibility is that, in the low CH group, attention areas like inferior parietal cortex are recruited in response to frustrated attempts of the amygdala and medial prefrontal cortex to locate the key disambiguating information. This idea is supported by studies showing that similar regions of medial prefrontal cortex respond to unexpected processing conflict caused by salient emotional stimuli (Bishop, Duncan, Brett, & Lawrence, 2004). In contrast, the high CH group may not have generated these subcortical and prefrontal signals in response to the least informative conditions, and the abnormalities observed in other attention-related (dorsal prefrontal and parietal cortices) and ventral visual system areas (fusiform gyrus) are secondary to dysfunction of the amygdala-medial prefrontal network. In fact, the activity seen in the parietal cortex was opposite in the high CH group, and appeared to harness attention only when the most informative portion of fearful faces was shown.

2.4.4 Detecting between-group differences in a community sample

Since participants in this study were taken from a community sample, we anticipated that neuroimaging may provide a more sensitive measure of between-group differences that were not discernable behaviourally. Functional differences were more subtle and elusive using a community sample of individuals with high and low CH scores. For example, contrasts performed between fearful and neutral whole faces was

not sufficient to detect differences in amygdala activity between the high and low CH groups in our study, although these contrasts have been used to detect differences in clinical samples of individuals with high psychopathic traits (Jones, et al., 2009; Marsh, et al., 2008). However, differences emerged using the least informative versus most informative portion contrast, a test that may be more sensitive to subtle between-group functional abnormalities. The least informative fearful face condition may have acted as a "stress-test" which challenged the neurocognitive system for emotion recognition, and provided a higher level of difficulty required to uncover the abnormalities associated with high psychopathic traits in a community sample.

2.4.5 Limitations and future directions

A possible caveat of our study is that the functional differences seen might be explained by a "time-on-task" effect; driven by one group requiring longer time to complete the given task. This explanation is unlikely because it suggests that individuals in the high CH group, who showed reduced activity, were faster at identifying happy and fearful faces in the least informative condition. In addition, the Partial Face Encoding task instructed participants to identify the emotion only when the response screen was presented, so that the BOLD response associated with viewing the emotional stimuli did not overlap with the motor planning, motor response, or other elaborative processes during identification. As a consequence, response times were not included in our analysis because they were not accurate representations of the time participants needed to identify the emotion. To empirically compare reaction times between the groups, a modified

version of our study could be replicated, which allows participants to make responses free of time constraints. The reaction time data could then be subjected to stochastic mathematical modelling approaches that have been used to great effect to clarify the nature of a cognitive process or its deficit in other studies (as described in Neufeld, Boksman, Vollick, George, & Carter, 2010).

Our findings raise several additional questions that will guide future research. Although behavioural differences in recognition accuracy were not seen in the high and low CH groups, our findings did not include direct evidence that individuals with high CH scores were using a compensatory network to perform the task. As a consequence, the mechanism by which our high CH group were able to perform the task in the presence of the observed functional abnormalities is unclear. An additional unanswered question concerns how the amygdala determines which portion of the facial expression is "salient". Another neural structure may be responsible for coding salience and communicate this information to the amygdala, although such a structure was not identified by our manipulations. Finally, our findings are consistent with the idea that the amygdala is not the substrate responsible for labelling affect. Another substrate, not yet identified, may label affect but was not uncovered by our experimental manipulation. Future studies can help disentangle these issues by applying functional neuroimaging in conjunction with lesion studies. Future work that applies similar attentional manipulations in combination with eye tracking could also be useful, particularly in a clinical population.

2.4.6 Conclusions

This study investigated whether individuals with high versus low Coldheartedness exhibit differences in functional neuroanatomy on an emotion recognition task that strategically isolated the most and least informative portions of facial expressions. Neuroimaging provided a more sensitive measure of between-group differences in a community sample of individuals with high and low CH scores that were not discernable via behavioural measures. In line with recent accounts of amygdala function that emphasize orienting to cues necessary to disambiguate a stimulus, individuals with low CH scores showed increased amygdala activity in the most ambiguous conditions of fearful and happy faces. In sharp contrast, individuals with high CH scores were characterized by reduced amygdala activity in the most ambiguous recognition condition, and increased or normalized activity in the least ambiguous condition. The findings of our study also extend current theories of emotional orienting, suggesting that regions outside of amygdala may also contribute to this process. Specifically, medial areas of the prefrontal cortex and fronto-parietal attention network were activated when the most versus least informative conditions of fearful faces were contrasted in individuals with low CH scores. High scores on the CH subscale of the PPI-R are associated with functional abnormalities in this network. Future studies that utilize a combined neuroimaging and eye tracking approach in populations with clinical psychopathy may help delineate how these impairments are linked to the social dysfunction associated with this disorder.

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CHAPTER 3

3 General Discussion and Conclusions

3.1 Summary of major findings

This study demonstrated that processing emotional faces can be associated with functional abnormalities in a community sample of individuals with high Coldheartedness (CH) scores on the Psychopathic Personality Inventory – Revised (Lilienfeld & Widows, 2005) relative to their low CH peers. Scores on the CH subscale are thought to represent a lack of empathy (R. J. Blair, 2005; Lilienfeld & Widows, 2005), which is one of the core features of psychopathy (Hare, 1996). Participants in our study were tested on a novel emotion recognition task that isolated different portions of fearful, happy, angry, disgusted, and neutral faces. Neuroimaging measures successfully detected subtle between-group differences in the functional neuroanatomy of the high versus low CH groups that were not otherwise discernable by behavioural measures. Group differences were the most pronounced when contrasts were performed between the neural activity associated with the most and least informative conditions of fearful and happy faces.

Individuals with low CH scores showed significantly greater activity in networks involved in emotion and attention, specifically, the amygdala, fusiform gyrus (BA 37), medial frontal gyrus (10, 32), superior frontal gyrus (BA 9), middle frontal gyrus (BA 8, 9), and inferior parietal lobule (BA 2, 40), when viewing the most ambiguous condition of fearful and happy faces. In contrast, the high CH group showed abnormal activation in this network, and showed the greatest activity during the most informative condition of

fearful and happy faces, relative to the least informative. Since our task did not identify an alternate neural network that compensates to successfully perform this strategy in the high CH group, this suggests a potential direction for future studies.

3.2 Implications of the current study on theories on amygdala function

The traditional view of amygdala function posits that the amygdala is responsible for encoding or representing distress (R. J. Blair, 1995, 2003; LeDoux, 1998). This view suggested that the greatest amygdala activity would be seen in the low CH group when the eyes of fearful faces were isolated, as this condition would be expected to most clearly communicate distress. However, this pattern of findings was not reflected in our study. Instead, the pattern of activity seen in our low CH group supported the recent proposal that the amygdala orients attention in order to disambiguate a stimulus (Adolphs, 2010). As predicted by this view, individuals with low CH scores showed the greatest amygdala activity when the least informative portion of fearful (and happy) faces was viewed, relative to the most informative portion. A major finding of this study was that the prediction that was made regarding amygdala functioning was not limited to this substrate. Other regions that have been implicated in emotion processing and attention also appear to assist the amygdala in orienting attention toward emotional salience in the environment.

3.3 Distributed brain networks for processing ambiguous emotional faces

Our findings suggest that a network of brain regions in the prefrontal and parietal cortices may work in concert with the amygdala to orient attention. These emotion and attention regions may be recruited downstream by the amygdala to assist in disambiguating challenging stimuli. One possibility is that medial prefrontal cortex recruits attentional assistance from the inferior parietal lobules when presented with a highly ambiguous and biologically relevant stimulus. Although speculative, this idea is supported by evidence that the medial prefrontal cortex possesses dense connections with the amygdala (Mitchell, 2011), is associated with cognitive control (Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004), and responds to processing conflict in the presence of salient emotional stimuli (Bishop, Duncan, Brett, & Lawrence, 2004). Amygdala and/or medial prefrontal cortex abnormalities, similar to those seen in clinical psychopathy populations (R. J. Blair, 2007b; Marsh et al., 2008) could render the high CH group unable to recruit assistance from the emotion and attention network when it is most needed for disambiguation.

3.4 Implications of the current study on neurocognitive models of psychopathy

Individuals with high CH scores exhibit a very different pattern of neural activity than individuals with low CH scores when viewing portions of emotional faces that isolate or occlude critical features. While the low CH group utilized a network of regions implicated in emotion and attention during the least informative condition of fearful and happy faces, the high CH group showed greater activity across these regions when the

most informative portion of fearful and happy faces was isolated, relative to the least informative portion.

Although reduced amygdala activity was seen in the high CH group relative to the low CH group, it is important to note that the amygdala activity of the high group did vary across different conditions. Increased amygdala activity was shown in this group during the most informative portion of fearful and happy faces, relative to the least informative. This suggests that individuals with high CH scores are characterized by amygdala function that is abnormal, but still susceptible to modification via behavioural manipulations. An important caveat of this finding is that the level of amygdala activity still remained below baseline levels, so the functional significance of this modification remains unclear.

In our community sample of individuals with high CH scores, abnormalities in neural activity were also seen in regions of the frontal and parietal cortices. The abnormal frontal cortex activity seen in our high CH group is consistent with reports from previous studies suggesting that psychopathy may be associated with dysfunction in regions of the orbitofrontal cortex and the ventrolateral prefrontal cortex (K. S. Blair et al., 2006; R. J. Blair, 2007a, 2007b; R. J. Blair, Colledge, & Mitchell, 2001; Finger et al., 2008). In contrast, abnormal functioning of the parietal cortex is a novel finding. Since parietal cortex abnormalities are not typically associated with psychopathy, the abnormalities seen in our study may be downstream effects of amygdala dysfunction. The inferior parietal lobules are known to be involved in attention, and as we have mentioned, activity in these regions may be produced in response to heightened conflict-

related activity in the amygdala and medial prefrontal cortex when presented with a stimulus that is highly ambiguous.

3.5 Clinical implications

Community samples of individuals with high psychopathic traits, such as the high CH group in the current study, may possess neurocognitive abnormalities that are similar (though less severe) to those observed in forensic or clinical samples of individuals with psychopathy. Performing research on community samples has the potential to illuminate our understanding of the aggression and antisocial behaviours often associated with clinical psychopathy, without the confounds of criminality or institutionalization (Hare & Neumann, 2009). Ultimately, gaining a more thorough understanding of psychopathic traits could help develop early intervention strategies for children who display emotional difficulties, to lower the risk of those children developing offending behaviours. Increasing our knowledge of this area may also suggest strategies for instilling empathy in healthy populations of developing children.

Prior research indicates that individuals with clinical psychopathy do not benefit from prison treatment programs that are based on emotions, talk-therapy, psychodynamic, or those aimed at developing empathy, conscience and interpersonal skills (R. J. Blair, 2008; Harris & Rice, 2007a, 2007b; Wong & Burt, 2007). Our findings raise the possibility that the amygdala dysfunction and fear recognition deficits associated with psychopathy may stem from impaired orientation of attention towards biologically relevant stimuli in the environment, similar to that exhibited by our high coldheartedness

group. Perhaps improving distress cue recognition via these means could provide an alternate route for early intervention strategies for youth at risk of antisocial and aggressive behaviours. It is important to emphasize that our findings were obtained from a community sample of individuals identified as high scorers on a subscale of psychopathic traits that reflect a lack of empathy. Whether these findings can be extended to clinical psychopathic and severely conduct disordered individuals remains to be tested. Further validation of these findings should be obtained by performing additional studies of partial face encoding in children and adults with clinical psychopathy, using an approach that combines neuroimaging with measures of eye-tracking.

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Use of Human Subjects - Ethics Approval Notice

Principal Investigator: Dr. D. Mitchell

Review Number: 13616 **Revision Number:** 7

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Department and Institution: Psychiatry, London Health Sciences Centre

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Ethics Approval Date: July 27, 2009 **Expiry Date:** August 31, 2012

Documents Reviewed and Approved: Additional Co-Investigator, Study Instruments

Documents Received for Information:

This is to notify you that The University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced revision(s) or amendment(s) on the approval date noted above. The membership of this REB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the UWO Updated Approval Request Form.

During the course of the research, no deviations from, or changes to, the protocol or consent form may be initiated without prior written approval from the HSREB except when necessary to eliminate immediate hazards to the subject or when the change(s) involve only logistical or administrative aspects of the study (e.g. change of monitor, telephone number). Expedited review of minor change(s) in ongoing studies will be considered. Subjects must receive a copy of the signed information/consent documentation.

Investigators must promptly also report to the HSREB:

a) changes increasing the risk to the participant(s) and/or affecting significantly the conduct of the study;
b) all adverse and unexpected experiences or events that are both serious and unexpected;
c) new information that may adversely affect the safety of the subjects or the conduct of the study.

If these changes/adverse events require a change to the information/consent documentation, and/or recruitment advertisement, the newly revised information/consent documentation, and/or advertisement, must be submitted to this office for approval.

Members of the HSREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the HSREB.

Chair of HSREB: Dr. Joseph Gilbert

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