

# Brain abnormalities in antisocial, psychopathic individuals

Yaling Yang and Adrian Raine

Since the 19th century it has been speculated that structural and functional impairment of the prefrontal cortex predisposes to antisocial, psychopathic behaviour, but it is only in the last few years that brain imaging research has been utilised to scientifically test this hypothesis. This review summarises findings from brain imaging research on antisocial, psychopathic, and aggressive individuals. It is concluded that impairments in a frontal-temporal circuit (i.e. the ventral and lateral regions of the prefrontal cortex, superior temporal gyrus, amygdala-hippocampal complex, and the anterior cingulate cortex) may be associated with antisocial personality disorder and psychopathy. It is hypothesised that abnormalities in frontal-temporal-subcortical circuits may contribute, at least in part, to antisocial and psychopathic features including poor inhibitory control, reward dominance, lack of remorse, fearlessness, shallow affect, and impaired moral judgment. Studies with larger and more homogeneous antisocial groups are needed to further examine this hypothesis. (*Netherlands Journal of Psychology*, 63, 156-165.)

Keywords: Antisocial; psychopathy; brain imaging

Before Partridge introduced the term ‘sociopathy’ in the 1930s, the concept of psychopathy had been characterised as ‘derangement of the moral faculties’ (Rush, 1812) and ‘moral insanity’ (Pritchard, 1835). Such descriptions remain today as the most vivid portraits of those individuals who suffer from psychopathy. Although many social and behavioural studies have been devoted to the understanding of psychopathic and antisocial

behaviour, the search for the biological foundation of psychopathy only began after a tragic accident happened over 150 years ago. Phineas Gage was a railway construction worker who was viewed as trustworthy, responsible, and well-liked until an accident damaged his prefrontal cortex. He almost completely recovered from the accident physically and had little trouble ambulating and communicating. However, his personality underwent a radical change and became psychopathic-like, irresponsible, profane, and indifferent to social situations, so much so that his family and friends described him as ‘no longer Gage’. After his death, a careful examination of his skull revealed damage to several pre-

Department of Psychology and Neuroscience Programme,  
University of Southern California, USA

Correspondence to: A. Raine, Department of Psychology and  
Neuroscience Programme, University of Southern California,  
USA, e-mail: araine@sas.upenn.edu

Submitted 12 April 2007; revision accepted 30 July 2007.

frontal regions, including the ventromedial prefrontal and orbitofrontal cortices (Damasio, 1994).

Since then, the study of the human brain has moved beyond the clinical arena and into the experimental laboratory. Functionally, positron emission tomography (PET) is used to measure brain glucose metabolism, single photon emission computerised tomography (SPECT) assesses regional blood flow, and functional magnetic resonance imaging (fMRI) measures real-time blood flow and blood oxygenation level changes in response to external stimuli. In terms of structural imaging, anatomical MRI (aMRI) is employed most commonly to detect regional volumetric abnormalities. In the past few years, accumulating knowledge supports the existence of a relationship between brain deficits and psychopathic behaviour. While prefrontal deficits seem to be the most replicable finding in antisocial psychopathic individuals (i.e. Dolan, Deakin, Roberts & Anderson, 2002; Raine, Lencz, Bihrlé, LaCasse & Colletti, 2000; Yang, Raine, Lencz, Bihrlé, LaCasse & Colletti, 2005), recent studies have begun to reveal the involvement of several localised brain regions (ventral and lateral prefrontal areas, the superior temporal cortex, the amygdala-hippocampal complex, corpus callosum, anterior cingulate) that may represent risk factors for psychopathy (i.e. Laakso, Gunning-Dixon, Vaurio, Repo, Soininen & Tiihonen, 2002; Kiehl et al., 2001; Kiehl, Smith, Mendrek, Forster, Hare & Liddle, 2004; Kruesi, Casanova, Mannheim & Johnson-Bilder, 2004; Völlm et al., 2004). It is also worth clarifying that psychopathy and antisocial personality disorder (APD) are different but related constructs; the majority of psychopaths have APD, but not everyone with APD is psychopathic. To provide a more comprehensive review, this article will outline empirical findings on individuals with antisocial, psychopathic features to illustrate how structural and functional brain abnormalities may predispose to one to these disorders. Throughout this review article, if not otherwise stated, these individuals have either a diagnosis of APD and/or psychopathy or have antisocial-related features (e.g. aggression). The term 'antisocial, psychopathic individuals' will be used to refer to this broad group.

### **Ventral prefrontal regions - orbitofrontal and ventromedial prefrontal cortex**

The ventral regions of the prefrontal cortex include the orbitofrontal (OFC) and ventromedial prefrontal cortex (VMPFC, also known as the rectal gyrus), and are densely connected with many brain regions including associated prefrontal areas, the amygdala, and the basal ganglia. Such connectivity allows these regions to receive inputs on emotional information and assign these inputs with reward values. The

reward-tagged information is then output from the ventral prefrontal regions to the dorsolateral and ventrolateral prefrontal cortices for final decision-making (Goldman-Rakic, 1995; Fuster, 1997). Lesion studies have found that patients with damage to the ventral prefrontal regions demonstrate a significant alteration in personality described as the 'acquired sociopathic syndrome', a syndrome that includes social disinhibition, shallow affect, decreased empathy, and poor ability to predict the future consequences of their actions (Bechara & Damasio, 2000; Bechara, Dolan & Hindes, 2002; Damasio, 1994). Although patients with adult-acquired lesions to the ventral prefrontal regions show no disruption in moral reasoning, those with similar damages acquired early in life fail to learn factual knowledge about accepted standards of moral behaviour, leading to both severely impaired social behaviour and defective social and moral reasoning (Anderson, Bechara & Damasio, 1999).

With the increasing use of brain imaging in cognitive psychological research, evidence collected from healthy subjects has begun to confirm the involvement of the OFC and VMPFC in a complex chain of cognitive processes beginning with information receiving, followed by reward coding and ending with ultimate decision-making. Recent fMRI studies have shown that the ventral prefrontal regions, particularly the VMPFC, are activated during tasks in which participants are asked to attribute the mental states of others and make ethical decisions. For example, Greene, Sommerville, Nystrom, Darley and Cohen (2001) found that reasoning about emotionally engaging ethical dilemmas (compared with dilemmas that are less emotionally engaging) activates the medial prefrontal, posterior cingulate, and posterior superior temporal cortices. Similar findings were reported by Moll et al. (2002) showing activation in the OFC and posterior superior temporal gyrus during passive viewing of scenes that evoke moral emotions (emotions involving the interests or welfare of either society or others). Heekeren, Wartenburger, Schmidt, Schwintowski and Villringer (2003) showed activation in bilateral VMPFC, left lateral PFC, and temporal cortex during simple moral decisions compared with semantic decisions. One conclusion that could be drawn from these functional imaging studies is that the functions of the OFC and VMPFC are most directly involved in the moral decision-making process, particularly when it involves affective cues.

Only one study has been published to date examining localised structural deficits in antisocial psychopathic individuals within the prefrontal cortex. Laakso et al. (2002) found reduced grey matter volumes in the OFC and left dorsolateral prefrontal cortex in antisocial individuals with alcoholism compared with controls. The authors argued that the effects were abolished after con-

trolling for duration of alcoholism. However, due to the fact that this covariate (alcoholism duration) correlated very strongly with group membership (i.e. all controls had zero onset age, all antisocial participants had some onset age), this argument does not seem entirely warranted. The finding of reduced OFC volume is consistent with several studies which tested the relationship between widespread prefrontal grey matter volume and antisocial, psychopathic individuals (Laakso et al., 2002; Raine et al., 2000; Yang et al., 2005). Several fMRI studies on psychopaths have also revealed OFC and/or VMPFC dysfunction such as inability to inhibit responses and abnormal affective information processing. One study showed different patterns of activation between antisocial individuals and normal controls during an inhibition task; the control group showed right DLPFC and left OFC activation, while individuals with APD showed a more bilateral and extended activation pattern across frontal regions (Völlm et al., 2004). Another study showed greater activation of the OFC during response inhibition in impulsive individuals, and suggested that this region is required in order to sustain behavioural inhibition, and that greater engagement of the right OFC was needed to maintain inhibition in impulsive individuals (Horn, Dolan, Elliott, Deakin & Woodruff, 2003).

Regarding abnormal affective information processing in psychopathy, Müller et al. (2003) reported increased activation in right prefrontal regions and the amygdala when viewing negative pictures and the left OFC during viewing of positive pictures in psychopathic individuals. Using a fear-conditioning task, Birbaumer et al. (2005) also showed deactivation in the OFC and anterior cingulate cortex in psychopathic individuals compared with controls. Overall, these studies indicate that functional and structural deficits to the OFC and VMPFC may play a crucial role in psychopathic features such as impulsivity, shallow affect, and indifference to moral rules.

#### **Lateral prefrontal regions - dorsolateral and ventrolateral prefrontal cortex**

The lateral section of the prefrontal cortex contains two major functional areas – the dorsolateral and ventrolateral prefrontal regions. Anatomically, the dorsolateral prefrontal cortex (DLPFC) covers most of the superior and middle frontal cortices while the ventrolateral prefrontal cortex (VLPFC) overlaps with the inferior frontal cortex. The importance of the roles they may play in predisposing to antisocial psychopathic behaviour remains debatable due to the fact that lesions localised to these specific regions have been argued by some to not predispose to antisocial, psychopathic personality

(Dolan & Park, 2002). However, these regions, especially the DLPFC, have been shown to be linked to executive functions which have been found to be impaired in antisocial individuals as reported in several studies and reviews (Brower & Price, 2001; Morgan & Lilienfeld, 2000; Giancola & Mezzich, 2000; Fishbein, 2000; Stevens, Kaplan & Hesselbrock, 2003; Dolan & Park, 2002). Debate does remain, though, as to whether executive functions are impaired specifically in psychopathic antisocial individuals.

In order to investigate the possible involvement of the DLPFC and VLPFC in antisocial, psychopathic behaviour, information gathered from functional imaging studies on healthy subjects is essential in order to better understand the functional properties of these regions. First, several studies have tested the cognitive function of inhibitory control, speculated to be influenced by these lateral prefrontal regions. Using fMRI, Konishi, Nakajima, Uchida, Schihara and Miyashita (1998) suggested that the right DLPFC constitutes the neural underpinnings of response inhibition. A more complicated neural network was revealed by Garavan et al. (1999) who showed involvement of the DLPFC and VLPFC in response inhibition. Again, Liddle, Kiehl and Smith (2001) showed significant activation in the DLPFC and VLPFC during response inhibition trials. A similar result was found in a more recent study showing increased activation in the DLPFC, the lateral OFC, anterior-medial prefrontal cortex, superior temporal gyrus and cingulate gyrus during the response inhibition (Horn et al., 2003). These are among the many studies that indicate a strong connection between the inhibition control and the lateral prefrontal regions.

Another new perspective has associated the DLPFC and VLPFC to a more complex cognitive function commonly seen in human interaction and communication: deception (the act of lying, cheating and manipulating others). This assumed connection is supported by several recent fMRI studies using healthy individuals to perform deception tasks. For example, Spence, Farrow, Herford, Wilkinson, Zheng and Woodruff (2001) showed that lying about autobiographical events was associated with increased activation in the bilateral VLPFC. Similarly, by asking the participants to fake memory loss, Lee et al. (2002) found a frontal-parietal-subcortical circuit including the DLPFC to be activated during the deception task. Phan, Magalhaes, Ziemlewicz, Fitzgerald, Green and Smith (2005) demonstrated to subjects before scanning that their performance and brain activity would be monitored in real time to evoke performance anxiety about generating lies. In this study, they found strong associations between increased activation in the DLPFC and VLPFC, as well as the dorso-medial prefrontal and superior temporal cortices

when subjects provided false answers. Again, Nunez, Casey, Egner, Hare and Hirsch (2005) reported increased activation in the DLPFC, anterior cingulate cortex, caudate, and thalamic nuclei during deception. Overall, the above studies provided some initial evidence supporting the association between the lateral prefrontal regions and deception.

Although it represents an intriguing issue, very few studies have attempted to explore the structural or functional integrity of the lateral prefrontal regions in psychopathic individuals. Structurally, only one aMRI has been conducted on antisocial personality disorder (Laakso et al., 2002). As described above, the results indicated reduced grey matter volume in the left DLPFC and the OFC in alcoholics with antisocial personalities compared with controls. Regarding function, one recent fMRI study showed that patients found to have APD activated a different neural network involving the DLPFC, VLPFC and anterior cingulate cortex during a response inhibition task compared with normal controls who instead activated the right DLPFC and OFC (Völlm et al., 2004). Several studies have also found a link between dysfunction in the lateral prefrontal regions and impairments in processing affective stimuli in psychopathy. Schneider, Habel, Kessler, Posse, Grodd & Müller-Gartner (2000) found increased activation in the DLPFC in individuals with APD during aversive classical conditioning compared with decreased activation in normal controls. Gordon, Baird & End (2004) showed increased activation in the right DLPFC but decreased right VLPFC activation in individuals with high psychopathy scores compared with those with low scores during an affect recognition task. However, inconsistent conclusions have also been raised in several neuropsychological studies on the existence of the DLPFC and VLPFC dysfunction in psychopathic individuals (Hart, Forth & Hare (1990); Lapierre, Braun & Hodgins (1995); Gorenstein, 1982). It is worth mentioning that the absence of normal controls in some of these studies (i.e. Hart et al., 1990) makes it difficult to interpret whether DLPFC and VLPFC functioning is indeed associated with psychopathic behaviour. Most of the above functional imaging results support the hypothesis that the core personality features of psychopathy may be a result of OFC dysfunction, but that the additional involvement of DLPFC dysfunction may additionally contribute to the externalising behaviour problems seen in antisocial, psychopathic individuals such as poor planning, disorganisation, and difficulty keeping in mind future consequences (Dinn & Harris, 2000).

### Superior temporal gyrus

The superior temporal gyrus (STG), including Brodmann areas 41/42 (the primary auditory cortex) and 22 (Wernicke's area), is closely connected with frontal, parietal, occipital and limbic regions. Not surprisingly, therefore, this region has long been considered a key structure for processing auditory information and comprehending sound-based language presentation. More recently, however, researchers have also discovered another functional role of the STG. It is a major player in the brain circuits that function as the 'social brain' along with the amygdala and the OFC (Zilbovicius, Meresse, Chabane, Brunelle, Samson & Boddaert, 2006). It has been proposed that the STG is involved in facial expression processing, while the amygdala and the OFC link sensory representation of stimuli to their motivational value (Adolphs, 2003). Working together, these regions facilitate efficient performance in social behavior such as cooperative and altruism as well as coercion, deception and manipulation towards others (Adolphs, 1999, 2003; Byrne & Whiten, 1988; Dunbar, 2003).

An increasing number of functional studies on healthy individuals are starting to provide evidence confirming the involvement of the STG in several social cognition functions, including moral decision-making and 'theory of mind' (see Frith & Frith, 1999; Greene & Haidt, 2002; Allison, Puce, & McCarthy, 2000 for reviews). For example, Heekeren, Wartenburger, Schmidt, Prehn, Schwintowski and Villringer (2005) found increased activation in the posterior STG, several frontal regions, and the amygdala during moral decision-making compared with semantic decisions. Similarly, Moll et al. (2002) observed elevated activation in the STG as well as the OFC and medial prefrontal regions during the viewing of scenes that evoke moral emotions. Robertson et al. (2007) again demonstrated that sensitivity to moral issues is associated with increased activation in the posterior STG, medial prefrontal region and posterior cingulate cortex. On the other hand, 'theory of mind' (ToM) has been referred to as the ability to attribute mental states (e.g. desires, intentions, and beliefs) to others, and is another function linked to the STG as well as several other brain regions (e.g. the medial prefrontal cortex, temporal poles). Völlm et al. (2006) revealed increased activation in the STG, lateral OFC, and middle frontal gyrus in response to ToM stimuli. Brunet, Sarfati, Hardy-Bayle and Decety (2000) showed increased blood flow in the STG and prefrontal regions during the attribution of intention to others. Castelli, Happe, Frith and Frith (2000) reported similar results, showing that increased activation in the STG and medial prefrontal cortex is associated with mental state attribution. Vogeley et al. (2001) again reported increased STG and anterior

cingulate cortex activation during modelling the mental states of others. Therefore, it may be concluded from these functional imaging studies that this region may contribute crucially to social cognition in general and to efficient interpersonal communication in particular.

Early computed tomographic studies of antisocial psychopathic adults found temporal lobe abnormalities in some cases, although methodological limitations and inconsistent findings make drawing conclusions difficult (Bassarath, 2001). Since then, studies conducted mainly on aggressive and violent patients and offenders have observed reduced temporal lobe volumes (Volkow et al., 1995; Amen, Stubblefield, Carmichael & Thisted (1996), Wong et al., 1997; Hirano, Mega, Dinov, Mishkin & Cummings (2000); Dolan, Deakin, Roberts & Anderson (2002). One structural MRI study observed a significant and widespread reduction in temporal grey matter volume in early onset conduct disorder (Kruesi et al., 2004). However, no study to date has revealed localised abnormalities in the superior portion of the temporal lobe in antisocial psychopathic individuals. Functionally, one study found increased bilateral blood flow in the frontotemporal regions during the processing of emotional words (Intrator et al., 1997). Alternatively, significant negative correlations were found between psychopathy (particularly the Factor 1 interpersonal features) and frontotemporal perfusion (Soderstrom, Hultin, Tullberg, Wikkelso, Ekholm & Forsman, 2002). Using a working memory task, Raine et al. (2001) found reduced activation in the right temporal lobe in violent offenders who had suffered child abuse compared with non-violent but abused individuals and normal controls. Another fMRI study conducted on psychopaths found that psychopathic individuals fail to show the appropriate neural differentiation between abstract and concrete stimuli in the right STG, left VLPFC, middle temporal cortex, and anterior cingulate cortex during a semantic task (Kiehl et al., 2004). Most of the above studies that reported temporal lobe structural and functional abnormalities have also found co-existing frontal deficits. Therefore, it is plausible that the findings of temporal lobe deficits in antisocial psychopathic individuals may in part reflect frontotemporal dysfunction. Still, the possibility remains that additional structural or functional deficits to the temporal lobe, especially the superior section, may be present in psychopathic individuals.

### **Amygdala-hippocampal complex**

The amygdala is located adjacent to the hippocampus in the medial temporal lobe and is densely interconnected with the hippocampus, forming the amygdala-hippocampal complex. The amygdala, particularly the basolateral sec-

tion, receives inputs from the temporal cortex, the OFC and the hippocampus, and the central part of the amygdala, and sends efferents back to the surrounding projection sites. Patients who have isolated lesions to the amygdala usually show symptoms such as the inability to recognise fear from facial expressions and poor recollection of emotional events (i.e. Adolphs, Tranel & Denburg, 2000). On the other hand, the hippocampus receives inputs from the prefrontal cortex, amygdala, and the cingulate cortex, and outputs information to several regions including the fornix and the hypothalamus. When the hippocampus is damaged, patients usually show symptoms such as profound memory disturbance and impaired aversive classical conditioning (Holscher, 2003; Otto & Poon, 2006).

As mentioned above, the amygdala and hippocampus have long been considered part of the brain circuitry implicated in processing, storing and recollecting affective information. More specifically, the amygdala is particularly responsive to affective stimuli such as threat, fear and anxiety (Davidson & Irwin, 1999), while the hippocampus is thought by some to play an important role in the processing of moral cognition (Moll, de Oliveira-Souze & Eslinger, 2003) and may facilitate conscious recollection of memories that allow past events to influence current decisions (Casebeer, 2003). Recent fMRI studies using more specific affective stimuli have provided confirmation indicating that the amygdala and the hippocampus are associated with negative emotions such as fear and threat in healthy subjects. For example, Whalen et al. (1998) first showed significantly increased amygdala activation in response to masked fearful faces (which the subjects were unaware of consciously) and a decrease in amygdala activation when viewing masked happy faces. Using threatening pictures, increased activation in the bilateral amygdala was found when the pictures induced subjects' fearful responses (Hariri, Mattay, Tessitore, Fera & Weinberger, 2002). Similarly, by using fear-inducing pictures, Schienle et al. (2005) found a similar activation pattern including the amygdala, the right hippocampus, and the right DLPFC in phobic patients compared with controls. Kuchinke, Jacobs, Grubich, Vo, Conrad and Herrmann (2005) also showed a distinct activation pattern including the hippocampus, the cingulate cortex, and lingual gyrus during presentation of negative words. In conclusion, the amygdala-hippocampal complex is likely to be responsible for the processing of emotion information such as threat-related emotional responding, fear conditioning, the appraisal of fearful facial expressions (Hariri et al., 2002; Wehner et al., 1997), remembering the declarative facts of negative stimuli, and the establishment of their context (Schienle et al., 2005; Wehner et al., 1997).

Relationships between abnormalities in the amygdala-hippocampal complex and individuals with antisocial, psychopathic behaviour have been found in several imaging studies. Laakso, Vaurio, Savolainen, Repo, Soininen and Tiihonen (2000) demonstrated reduced right hippocampal volume reductions in violent offenders with APD who were also early-onset alcoholics compared with controls. Again, in 2001, Laakso et al. found reduced posterior hippocampus volumes to be associated with increased psychopathy scores in antisocial alcoholics. Raine et al. (2004) found that unsuccessful (caught) psychopaths showed an exaggerated anterior hippocampal asymmetry (right > left) relative to both successful psychopaths (not caught) and controls. Regarding the amygdala, one abstract has reported reduced volume in this structure to be associated with increased psychopathy scores within a sample of violent offenders (Tiihonen, Hodgins & Vaurio, 2000). Functionally, one study on murderers found abnormal asymmetries of functioning, with murderers showing lower left and increased right functioning in both the amygdala and hippocampus compared with controls (Raine, Buchsbaum & LaCasse, 1997). Similarly, Soderstrom et al. (2000) also found bilaterally reduced hippocampal functioning in a group of violent offenders. More recently, by using affective pictures as stimuli, a growing number of fMRI studies have found abnormal amygdala activation in psychopathic individuals and adolescents with conduct disorders compared with normal controls (Schneider, Habel, Kessler, Posse, Grodd & Müller-Gartner, 2000; Kiehl, et al. 2001; Müller et al., 2003; Veit et al., 2002; Sterzer, Stadler, Krebs, Kleinschmidt & Poustka, 2005). These findings from functional imaging studies suggest that while prefrontal deficits may play a major role in psychopathy traits such as poor inhibition control and chronic lying, impairments in the amygdala-hippocampal complex may contribute crucially to key antisocial, psychopathic personality traits such as lack of empathy and shallow affect.

#### **Other brain areas - corpus callosum and anterior cingulate cortex**

Although the majority of studies on antisocial, psychopathic individuals have been focusing on the prefrontal cortex and the temporal regions (the STG and the amygdala-hippocampal complex in particular), several studies have also revealed additional brain deficits in other brain regions in psychopathic individuals such as the corpus callosum and the anterior cingulate cortex. Regarding the corpus callosum, Raine et al. (1997) found that murderers exhibited decreased metabolic activity in the corpus callosum compared with normal controls. Again, in a group of psychopathic antisocial individuals, Raine et al. (2003) found significant increased callosal white

matter volume, increased callosal length, and increased functional interhemispheric connectivity compared with controls. The authors also argued that larger callosal volumes were associated with affective and interpersonal deficits and low spatial ability.

Anterior cingulate cortex (ACC) dysfunction has been linked to antisocial and psychopathic behaviour in several functional imaging studies. Kiehl et al. (2001) found that criminal psychopaths showed significantly less affect-related activity in the ACC, posterior cingulate cortex, amygdala, hippocampus, and parahippocampus gyrus. Similarly, Sterzer et al. (2005) observed reduced activation in the right dorsal ACC and left amygdala during viewing of negative pictures in adolescents with severe conduct disorder. Recently, Kumari et al. (2006) revealed reduced activation in the ACC in patients with APD compared with controls during a working memory task. Although these studies on the ACC have provided some initial evidence for impairments in this region in antisocial individuals, more studies are needed to thoroughly examine the involvement of other brain regions in predisposing antisocial psychopathic behaviour.

#### **Limitations**

This review inevitably has several limitations. Due to the fact that all studies conducted to date are cross-sectional, the causal relationship between the brain pathology and antisocial, psychopathic behavior remains in question. Although it is possible that the observed structural and functional deficits in these individuals represent a consequence of their antisocial, psychopathic features, it is likely that brain impairment is a key risk factor that could lead to the development of APD or psychopathy. Another limitation concerns the heterogeneity in the antisocial and psychopathic groups reviewed. In the literature, individuals with multiple antisocial behavioural patterns and psychopathic features are often mixed together to form one subject group. In addition, many of the antisocial, psychopathic individuals studied have comorbid psychiatric disorders such as alcohol or drug abuse, which may contribute to the brain deficits found. These factors may influence the findings of these studies. Thus, future studies using well-defined antisocial or psychopathic groups for which comorbidities are carefully controlled are needed for a more in-depth understanding of the biological pathologies underlying these disorders.

#### **Conclusions**

Psychopathic and antisocial individuals have been found to have abnormalities in the prefrontal cortex, superior temporal cortex, the

amygdala-hippocampal complex, the corpus callosum, and the anterior cingulate cortex. The functional significance of impairments in these regions can be best understood by considering findings from imaging studies on healthy individuals. Regarding the prefrontal cortex, the ventral prefrontal regions (the OFC and VMPFC) are involved in decision-making processing that involve reward or moral values, while the lateral regions (the DLPFC and VLPFC) mediate executive function including response inhibition and deception. The superior temporal gyrus is more involved in social cognition such as moral decision-making and 'theory of mind'. Sub-cortically, the amygdala-hippocampal complex plays a central role in processing and recollecting affective information, while the corpus callo-

sum facilitates interhemispheric communication. Surrounding the corpus callosum, the anterior cingulate cortex is centrally involved in emotional processing and social behaviour. Given the evidence reviewed in this article, it is hypothesised that the structural and functional abnormalities in the frontal-temporal circuit may contribute, at least in part, to antisocial and psychopathic features including poor inhibition control, reward dominance, lack of remorse, fearlessness, shallow affect, and impaired moral judgment. Future research investigating localised structural and functional deficits in these areas on a larger and more homogeneous sample of antisocial, psychopathic individuals is needed to examine this hypothesis.

## References

- Allison, T. Puce, A. & McCarthy, G. (2000). Social perception from visual cues: role of the STS region. *Trends in Cognitive Sciences*, 7, 267-278.
- Adolphs, R. (1999). Social cognition and the human brain. *Trends in Cognitive Sciences*, 3, 469-479.
- Adolphs, R. (2003). Cognitive neuroscience of human social behavior. *Nature Reviews Neuroscience*, 4, 165-178.
- Adolphs, R., Tranel, D. & Denburg, N. (2000). Impaired emotional declarative memory following unilateral amygdala damage. *Learning and Memory*, 7, 180-186.
- Amen, D.G., Stubblefield, M., Carmichael, B. & Thisted, R. (1996). Brain SPECT findings and aggressiveness. *Annals of Clinical Psychiatry*, 8, 129-37.
- Anderson, S.W., Bechara, A., Damasio, H., Tranel, D. & Damasio, A.R. (1999). Impairment of social and moral behavior related to early damage in human prefrontal cortex. *Nature Neuroscience*, 2, 1032-1037.
- Bassarath, L. (2001). Neuroimaging studies of antisocial behavior. *Canadian Journal of Psychiatry*, 46, 728-32. Review.
- Bechara, A., Damasio, H. & Damasio, A.R. (2000). Emotion, decision making and the orbitofrontal cortex. [Review]. *Cerebral Cortex*, 10, 295-307.
- Bechara, A., Dolan, S. & Hindes, A. (2002). Decision-making and addiction (part II): myopia for the future or hypersensitivity to reward? *Neuropsychologia*, 40, 1690-705.
- Birbaumer, N., Veit, R., Lotze, M., Erb, M., Hermann, C., Grodd, W. & Flor, H. (2005). Deficient fear conditioning in psychopathy. *Archives of General Psychiatry*, 62, 799-801.
- Brower, M.C. & Price, B.H. (2001). Neuropsychiatry of frontal lobe dysfunction in violent and criminal behavior: a critical review. *Journal of Neurology, Neurosurgery, and Psychiatry*, 7, 720-6.
- Brunet, E., Sarfati, Y., Hardy-Bayle, M.C. & Decety, J. (2000). A PET investigation of the attribution of intentions with a nonverbal task. *Neuroimage*, 11, 157-166.
- Byrne, R.W. & Whiten, A. (1988). *Machiavellian Intelligence*. Oxford University Press, Oxford.
- Casebeer, W.D. (2003). Moral cognition and its neural constituents. *Nature Review Neuroscience*, 4, 840-846.
- Castelli, F., Happe, F., Frith, U., & Frith, C. (2000). Movement and mind: a functional imaging study of perception and interpretation of complex intentional movement patterns. *Neuroimage*, 12, 314-325.
- Damasio, A.R. (1994). Descartes' error and the future of human life. *Scientific American* 271, 144.
- Davidson, R.J. & Irwin, W. (1999). The functional neuroanatomy of emotion and affective style. *Trends in Cognitive Sciences* 3, 11-21.
- Dinn, W.M. & Harris, C.L. (2000). Neurocognitive function in antisocial personality disorder. *Psychiatry Research* 97, 173-90.
- Dolan, M.C., Deakin, J.F., Roberts, N. & Anderson, I.M. (2002). Quantitative frontal and temporal structural MRI studies in personality-disordered offenders and control subjects. *Psychiatry Research*, 116, 133-49.
- Dolan, M. & Park, I. (2002). The neuropsychology of antisocial personality disorder. *Psychological Medicine*, 32, 417-27.
- Dunbar, R.I.M. (2003). The social brain: mind, language, and society in evolutionary perspective. *Annual Review of Anthropology*, 32, 163-181.
- Fishbein, D. (2000). Neuropsychological function, drug abuse, and violence: A conceptual framework. *Criminal Justice & Behavior*, 27, 139-159.
- Frith, U. & Frith, C.D. (2003). Development and neurophysiology of mentalizing. *Philosophical Transactions of the Royal Society of London*, 358, 459-473.
- Fuster, J.M. (1997). The prefrontal cortex. Anatomy physiology and neuropsychology of the frontal lobe, 3rd ed. New York: Raven.

- Garavan, H., Ross, T.J. & Stein, E.A. (1999). Right hemispheric dominance of inhibition control: An event-related functional MRI study. *Proceedings of the National Academy of Science*, *96*, 8301-8306.
- Giancola, P.R. & Mezzich, A.C. (2000). Executive cognitive functioning mediates the relation between language competence and antisocial behavior in conduct-disordered adolescent females. *Aggressive Behavior*, *26*, 359-375.
- Goldman-Rakic, P.S. (1995). Architecture of the prefrontal cortex and the central executive. *Annals of the New York Academy of Sciences*, *94*, 1612-1614.
- Gordon, H.L., Baird, A.A. & End, A. (2004). Functional differences among those high and low on a trait measure of psychopathy. *Biological Psychiatry*, *56*, 516-521.
- Gorenstein, E.E. (1982). Frontal lobe functions in psychopaths. *Journal of Abnormal Psychology*, *91*, 368-379.
- Greene, J. & Haidt, J. (2002). How (and where) does moral judgment work? *Trends in Cognitive Sciences*, *6*, 517-523.
- Greene, J.D., Sommerville, R.B., Nystrom, L.E., Darley, J.M. & Cohen, J.D. (2001). An fMRI investigation of emotional engagement in moral judgment. *Science*, *293*, 2105-2108.
- Hariri, A.R., Mattay, V.S., Tessitore, A., Fera, F. & Weinberger D.R. (2002). Neocortical modulation of the amygdala response to fearful stimuli. *Biological Psychiatry*, *53*, 494-501.
- Hart, S.D., Forth, A.E., Hare, R.D. (1990). Performance of criminal psychopaths on selected neuropsychological tests [Review]. *Journal of Abnormal Psychology*, *100*, 391-398.
- Heekeren, H.R., Wartenburger, I., Schmidt, H., Schwintowski, H. & Villringer, A. (2003). An fMRI study of simple ethical decision-making. *Neuroreport*, *14*, 1215-1219.
- Heekeren, H.R., Wartenburger, I., Schmidt, H., Prehn, K., Schwintowski, H.P. & Villringer, A. (2005). Influence of bodily harm on neural correlates of semantic and moral decision-making. *Neuroimage*, *24*, 887-897.
- Hirono, N., Mega, M.S., Dinov, I.D., Mishkin, F. & Cummings, J.L. (2000). Left frontal-temporal hypoperfusion is associated with aggression in patient with dementia. *Archives Neurology*, *57*, 861-866.
- Holscher, C. (2003). Time, space and hippocampal functions. *Reviews in the Neurosciences*, *14*, 253-284.
- Horn, N.R., Dolan, M., Elliott, R., Deakin, J.F.W. & Woodruff, P.W.R. (2003). Response inhibition and impulsivity: an fMRI study. *Neuropsychologia*, *41*, 1959-1966.
- Intrator, J., Hare, R., Stritzke, P., Brichswein, K., Dorfman, D., Harpur, T., Bernstein, D., Handelsman, L., Schaefer, C., Keilp, J., Rosen, J. & Machac, J. (1997). A brain imaging (Single Photon Emission Computerized Tomography) study of semantic and affective processing in psychopaths. *Biological Psychiatry*, *42*, 96-103.
- Kiehl, K.A., Smith, A.M., Hare, R.D., Mendrek, A., Forster, B.B., Brink, J., Brink, J. & Liddle, P.F. (2001). Limbic abnormalities in affective processing by criminal psychopaths as revealed by functional magnetic resonance imaging. *Biological Psychiatry*, *50*, 677-84.
- Kiehl, K.A., Smith, A.M., Mendrek, A., Forster, B.B., Hare, R.D. & Liddle, P.F. (2004). Temporal lobe abnormalities in semantic processing by criminal psychopaths as revealed by functional magnetic resonance imaging. *Psychiatry Research Neuroimaging*, *130*, 27-42.
- Konishi, S., Nakajima, K., Uchida, L., Schihara, K., & Miyashita, Y. (1998). No-go dominant brain activity in human inferior prefrontal cortex revealed by functional magnetic resonance imaging. *The European Journal of Neuroscience*, *10*, 1209-1213.
- Kruesi, M.J.P., Casanova, M.F., Mannheim, G. & Johnson-Bilder, A. (2004). Reduced temporal lobe volume in early onset conduct disorder. *Psychiatry Research Neuroimaging*, *132*, 1-11.
- Kuchinke, L., Jacobs, A.M., Grubich, C., Vo, M.L., Conrad, M., & Herrmann, M. (2005). Incidental effects of emotional valence in single word processing: an fMRI study. *Neuroimage*, *28*, 1022-32.
- Kumari, V., Aasen, I., Taylor, P., Ffytche, D.H., Das, M., Barkataki, I., Goswami, S., O'Connell, P., Howlett, M., Williams, S.C.R. & Sharma, T. (2006). Neural dysfunction and violence in schizophrenia: An fMRI investigation. *Schizophrenia Research*, *84*, 144-164.
- Laakso, M.P., Vaurio, O., Savolainen, L., Repo, E., Soininen, H. & Tiihonen, J. (2000). A volumetric MRI study of the hippocampus in type 1 and 2 alcoholism. *Behavioral Brain Research*, *109*, 177-186.
- Laakso, M.P., Vaurio, O., Koivisto, E., Savolainen, L., Eronen, M., Aronen, H.J., Hakola, P., Repo, E., Soininen, H. & Tiihonen, J. (2001). Psychopathy and the posterior hippocampus. *Behavioral Brain Research*, *118*, 187-193.
- Laakso, M.P., Gunning-Dixon, F., Vaurio, O., Repo, E., Soininen, H. & Tiihonen, J. (2002). Prefrontal volume in habitually violent subjects with antisocial personality disorder and type 2 alcoholism. *Psychiatry Research Neuroimaging*, *114*, 95-102.
- Lapierre, D., Braun, C.M. & Hodgins, S. (1995). Ventral frontal deficits in psychopathy: Neuropsychological test findings. *Neuropsychologia*, *33*, 139-151.
- Lee, T.M.C., Liu, H., Tan, L., Chan, C.C.H., Mahankali, S., Feng, C., Hou, J., Fox, P.T. & Gao, J. (2002). Lie detection by functional magnetic resonance imaging. *Human Brain Mapping*, *15*, 157-164.
- Liddle, P.F., Kiehl, K.A. & Smith, A.M. (2001). Event-related fMRI study of response inhibition. *Human Brain Mapping*, *12*, 100-109.
- Moll, J., de Oliveira-Souza, R., Eslinger, P.J., Bramati, I.E., Mourao-Miranda, J., Andreiuolo, P.A. & Pessoa, L. (2002). The neural correlates of moral sensitivity: A functional magnetic resonance imaging investigation of basic and moral emotions. *The Journal of Neuroscience*, *22*, 2730-2736.
- Moll, J., de Oliveira-Souza, R. & Eslinger, P.J. (2003). Morals and the human brain: a working model. *Neuroreport*, *13*, 299-305.

- Morgan, B.A. & Lilienfeld, O.S. (2000). A meta-analytic review of the relation between antisocial behavior and neuropsychological measures of executive function. *Clinical Psychology Review*, 20, 113-136.
- Müller, J.L., Sommer, M., Wagner, V., Lange, K., Taschler, H., Roder, C. H., Schuierer, G., Klein, H. E. & Hajak, G. (2003). Abnormalities in emotion processing within cortical and subcortical regions in criminal psychopaths: Evidence from a functional magnetic resonance imaging study using pictures with emotional content. *Biological Psychiatry*, 54, 152-162.
- Nunez, J.M., Casey, B.J., Egner, T., Hare, T & Hirsch, J. (2005). Intentional false responding shares neural substrates with response conflict and cognitive control. *Neuroimage*, 25, 267-277.
- Otto, T. & Poon, P. (2006). Dorsal hippocampal contributions to unimodal contextual conditioning. *Journal of Neurosciences*, 26, 6603-9.
- Phan, K.L., Magalhaes, A., Ziemlewicz, T.J., Fitzgerald, D.A., Green, C. & Smith, W. (2005). Neural correlates of telling lies: A functional magnetic resonance imaging study at 4 Tesla. *Academic Radiology*, 12, 164-172.
- Pritchard, J.C. (1835). *A treatise on insanity and other disorders affecting the mind*. Sherwood, Gilbert and Piper: London.
- Raine, A., Buchsbaum, M. & LaCasse, L. (1997). Brain abnormalities in murderers indicated by positron emission tomography. *Biological Psychiatry*, 42, 495-508.
- Raine, A., Lencz, T., Bihrlé, S., LaCasse, L. & Colletti, P. (2000). Reduced prefrontal gray matter volume and reduced autonomic activity in antisocial personality disorder. *Archives of General Psychiatry*, 57, 119-127.
- Raine A., Lencz, T., Taylor K., Hellige J.B., Bihrlé, S., LaCasse, L., Lee M., Ishikawa S. & Colletti, P. (2003). Corpus callosum abnormalities in psychopathic antisocial individuals. *Archives of General Psychiatry*, 160, 1627-35.
- Raine, A., Ishikawa, S.S., Arce, E., Lencz, T., Knuth, K.H., Bihrlé, S., LaCasse, L. & Colletti, P. (2004). Hippocampal structural asymmetry in unsuccessful psychopaths. *Biological Psychiatry*, 55, 185-191.
- Raine, A., Park, S., Lencz T., Bihrlé, S., LaCasse, L., Widom C.S., Dayeh, L. & Singh, M. (2001). Reduced right hemisphere activation in severely abused violent offenders during a working memory task: An fMRI study. *Aggressive Behavior*, 27, 111-129.
- Robertson, D., Snarey, J., Ousley, O., Harenski, K., Dubois, B.F., Gilkey, R. & Kilts, C. (2007). The neural processing of moral sensitivity to issues of justice and care. *Neuropsychologia*, 45, 755-766.
- Rush, B. (1812). *Medical inquiries and observations, upon the diseases, of the mind*. Philadelphia: Kimber and Richardson.
- Schienle, A., Schafer, A., Walter, B., Stark, R., & Vaitl, D. (2005). Brain activation of spider phobics towards disorder-relevant, generally disgust- and fear-inducing pictures. *Neuroscience Letter*, 388, 1-6.
- Schneider, F., Habel, U., Kessler, C., Posse, S., Grodd, W., & Müller-Gartner, H. (2000). functional imaging of conditioned aversive emotional responses in antisocial personality disorder. *Neuropsychobiology*, 42, 192-201.
- Soderstrom, H., Hultin, L., Tullberg, M., Wikkelso, C., Ekholm, S., & Forsman, A. (2002). Reduced frontotemporal perfusion in psychopathic personality. *Psychiatry Research Neuroimaging*, 114, 81-94.
- Spence, S.A. Farrow, T.F., Herford, A.E., Wilkinson, I.D. Zheng, Y. & Woodruff, P.W. (2001). Behavioral and functional anatomical correlates of deception in humans. *Neuroreport*, 12, 2849-2853.
- Sterzer, P., Stadler, C., Krebs, A., Kleinschmidt, A. & Poustka, F. (2005). Abnormal neural responses to emotional visual stimuli in adolescents with conduct disorder. *Biological Psychiatry*, 57, 7-15.
- Stevens, M.C., Kaplan, R.F. & Hesselbrock, V.M. (2003). Executive-cognitive functioning in the development of antisocial personality disorder. *Addictive Behaviors*, 28, 285-300.
- Tiihonen, J., Hodgins, S. & Vaurio, O. (2000). Amygdaloid volume loss in psychopathy. *Society for Neuroscience Abstracts*, 2017.
- Veit, R., Flor, H., Erb, M., Hermann, C., Lotze, M., Grodd, W. & Birbaumer, N. (2002). Brain circuits involved in emotional learning in antisocial behavior and social phobia in humans. *Neuroscience letters*, 328, 233-236.
- Vogeley, K., Bussfeld, P., Newen, A., Herrmann, S., Happe, F., Falkai, P., Maier, W., Shah, N.J., Fink, G.R. & Zilles, K. (2001). Mind reading: neural mechanisms of theory of mind and self-perspective. *Neuroimage*, 14, 170-181.
- Volkow, N.D., Tancredi, L.R., Grant, C., Gillespie, H., Valentine, A., Mullani, N., Wang, G.L. & Hollister, L. (1995). Brain glucose metabolism in violent psychiatric patients: a preliminary study. *Psychiatry Research*, 61, 243-253.
- Völlm, B., Richardson, P., Stirling, J., Elliott, R., Dolan, M., Chaudhry, I., Del Ben, C., McKie, S., Anderson, I. & Deakin, B. (2004). Neurobiological substrates of antisocial and borderline personality disorders: preliminary result of a functional fMRI study. *Criminal Behavior and Mental Health*, 14, 39-54.
- Völlm, B. A., Taylor, A.N., Richardson, P., Corcoran, R., Stirling, J., McKie, S., Deakin, J. F. & Elliott, R. (2006). Neuronal correlates of theory of mind and empathy: a functional magnetic resonance imaging study in a nonverbal task. *Neuroimage*, 29, 90-8.
- Wehner, J.M., Radcliffe, R.A., Rosmann, S.T. Christensen, S.C., Rasmussen D.L., Fulker, D.W. & Wiles, M. (1997) Quantitative trait locus analyses of contextual fear conditioning in mice. *Nature Genetics*, 17, 331-334.
- Whalen, P.J., Bush, G., McNally, R.J., Wilhelm, S., McInerney, S.C., Jenike, M.A. & Rauch, S.L. (1998). The emotional counting stroop paradigm: A functional magnetic resonance imaging probe of the anterior cingulate affective division. *Biological Psychiatry*, 44, 1219-1228.

- Wong, M. T., Fenwick, P. B., Lumsden, J., Fenton, G. M., Maisey, M. N., Lewis, P. & Badawi, R. (1997). Positron emission tomography in male violent offenders with schizophrenia. *Psychiatry Research*, 68, 111-123.
- Yang, Y., Raine, A., Lencz, T., Bihrlle, S., LaCasse, L. & Colletti, P. (2005). Volume reduction in prefrontal gray matter in unsuccessful criminal psychopaths. *Biological Psychiatry*, 57, 1103-1108.
- Zilbovicius, M., Meresse, I., Chabane, N., Brunelle, F., Samson, Y. & Boddaert, N. (2006). Autism, the superior temporal sulcus and social perception. *Trends in Neuroscience*, 29, 359-366.