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White matter microstructural abnormalities in the frontal lobe of adults with antisocial personality disorder

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ABSTRACT

Antisocial personality disorder (ASPD) and psychopathy involve significant interpersonal and behavioural impairments. However, little is known about their underlying neurobiology and in particular, abnormalities in white matter (WM) microstructure. A preliminary diffusion tensor magnetic resonance imaging (DT-MRI) study of adult psychopaths employing tractography revealed abnormalities in the right uncinate fasciculus (UF) (Craig et al., 2009), indicating fronto-limbic disconnectivity. However, it is not clear whether WM abnormalities are restricted to this tract or are or more widespread, including other tracts which are involved in connectivity with the frontal lobe.

We performed whole brain voxel-based analyses on WM fractional anisotropy (FA) and mean diffusivity (MD) maps acquired with DT-MRI to compare 15 adults with ASPD and healthy age, handedness and IQ-matched controls. Also, within ASPD subjects we related differences in FA and MD to measures of psychopathy.

Significant WM FA reduction and MD increases were found respectively in ASPD subjects relative to controls. FA was bilaterally reduced in the genu of corpus callosum while in the right frontal lobe FA reduction was found in the UF, inferior fronto-occipital fasciculus (IFOF), anterior corona radiata and anterior limb and genu of the internal capsule. These differences negatively correlated with measures of psychopathy. Also in the right frontal lobe, increased MD was found in the IFOF and UF, and the corpus callosum and anterior corona radiata. There was a significant positive correlation between MD and psychopathy scores.

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Conclusions: The present study confirms a previous report of reduced FA in the UF. Additionally, we report for the first time, FA deficits in tracts involved in interhemispheric as well as frontal lobe connectivity in conjunction with MD increases in the frontal lobe. Hence, we provide evidence of significant WM microstructural abnormalities in frontal brain regions in ASPD and psychopathy.

1. Introduction

1.1. *The frontal lobe theory of antisocial personality disorder (ASPD) and psychopathy*

The importance of the frontal lobes to social behaviour was first recognised in the 19th century following the case of Phineas Gage, in whom frontal lobe damage resulted in profound personality change associated with markedly inappropriate social behaviour [Harlow, 1993 (1869)]. A 'frontal lobe' syndrome was subsequently delineated based on clinical observations of the behaviour of patients with frontal lobe damage (Lishman, 1998) where symptoms included apathy, emotional lability, a lack of social awareness, unconcern for social rules, impulsivity, and reactive aggression.

It is currently recognised that there is much overlap between frontal lobe syndrome and 'functional' or 'non-organic' personality disorders (PDs), particularly ASPD and psychopathy (Damasio, 2000). The definition of psychopathy has changed little since Hervey Cleckley published *The Mask of Sanity* in 1941 where he described the psychopath as a charming, callous, superficial individual, lacking conscience and genuine emotion (Cleckley, 1941). The *Psychopathy Checklist* (PCL, Hare, 1980) and the later *Psychopathy Checklist – Revised* (PCL-R, Hare, 1991) were designed to operationalise Cleckley's concept of psychopathy as a basis for diagnosing the disorder. The PCL-R consists of 20 items characterised broadly by two dimensions: Factor 1 items are primarily interpersonal or emotional traits such as remorselessness, deception, shallow affect and callousness, whereas Factor 2 items assess behavioural symptoms such as violence, criminality, and dysfunctional lifestyle. For a diagnosis of psychopathy, attributes from both of these factors need to be present. While PCL-R scores $\geq$30 have traditionally been used to classify an individual as having psychopathy (Hare, 2003), more recent studies have argued for a score of $\geq$25 as sufficient for diagnosis (Edens and Petrila, 2006; Edens et al., 2010; Rutherford et al., 1999).

While the related construct of ASPD in *DSM-IV-TR* (Diagnostic and Statistical Manual Fourth Edition – Text Revision, American Psychiatric Association, 2000) includes several traits present in psychopathy (e.g., lack of guilt/remorse, and impulsivity), diagnostic criteria can be met based entirely on antisocial behaviours (e.g., violation of social norms, irresponsibility, and criminality). Hence, the emotional deficits fundamental to psychopathy are not necessary for a diagnosis of ASPD, even if these are present in some cases. Estimates of the prevalence of the two disorders also differ, suggesting that these are non-equivalent diagnoses. While most adult psychopathic offenders meet criteria for ASPD, only approximately one third of those with ASPD are psychopathic (Hart and Hare, 1997). Psychopathy has therefore been postulated to be a particularly severe subtype of ASPD (Dolan and Doyle, 2007). Psychopathy and ASPD are however distinguished from behaviours secondary to frontal lobe lesions by high levels of both reactive (elicited by frustration) and instrumental (goal-directed) violence (Blair, 2001; Glenn and Raine, 2009). Nevertheless, overlaps between traits of both psychopathy and ASPD, and frontal lobe syndrome, have led to the suggestion that both PDs may result from frontal lobe abnormality (Damasio, 2000). Neuroimaging studies of both people with ASPD, and of individuals with psychopathy, have provided evidence of abnormalities of frontal lobe structure and function relative to control populations, together with deficits in temporal, limbic, and other brain regions (see Table 1).

For example, neuroimaging studies of adult psychopaths examining the frontal cortex have reported reduced grey matter volume in conjunction with reduction in the superior temporal gyrus (Muller et al., 2008), and in the prefrontal cortex (PFC) of 'unsuccessful' (caught) psychopaths, versus healthy controls (Yang et al., 2005). Furthermore, higher total and subfactor PCL-R scores (arrogant/deceptive, affective, and impulsive/unstable) were associated with reduced prefrontal grey matter volume (*ibid*). Similarly, prefrontal and temporal cortical grey matter thinning was found in psychopathic individuals, with right hemisphere reductions related to elevated PCL-R Factor 1 'Affective' facet scores (Yang et al., 2009b).

Other studies have identified associations between psychopathic traits and specific subregions of the PFC. In particular, the association found in brain injured patients between ventromedial PFC (vmPFC) damage and reactive aggression (Blair and Cipolotti, 2000; Grafman et al., 1996) is mirrored by vmPFC structural and functional impairments in psychopaths (Tiihonen et al., 2008). Functional neuroimaging studies of people with psychopathy have also provided evidence of abnormal frontal lobe perfusion and abnormalities of task-related activation in prefrontal and other brain regions on reversal learning paradigms (Table 1). Individuals with ASPD have shown similar structural and functional prefrontal abnormalities to psychopaths – for instance reduced prefrontal grey matter volume has been found in both antisocial adults (Raine et al., 2000) and conduct disordered children (Huebner et al., 2008), compared with healthy controls. Also, cortical thinning of the medial frontal lobe has been found in ASPD (Narayan et al., 2007).

Nevertheless, structural and functional abnormalities in people with psychopathy and ASPD are not restricted to the frontal lobe. For example, abnormal amygdala structure and function have each been found to correlate with the emotion processing deficits observed in ASPD and psychopathic individuals (Gordon et al., 2004; Kiehl et al., 2001; Yang et al., 2009a), as well as in regions (such as fusiform–extrastriate cortices) known to be modulated by the amygdala (Deeley