What neuroimaging tells us about psychopathic disorders

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The concept of psychopathy and its neurobiological basis are discussed. Structural (computed tomography, magnetic resonance imaging) and functional (positron emission tomography, functional magnetic resonance imaging, single photon emission tomography) studies in antisocial and psychopathic samples are reviewed in this article.

In England and Wales, the legal concept of psychopathic disorder is defined in the Mental Health Act 1993 'as a persistent disorder or disability of mind (whether or not including significant impairment of intelligence) which results in abnormally aggressive or seriously irresponsible conduct on the part of the person concerned'. The term 'psychopathic' originated in 19th century Germany to cover all disorders of the personality. Hare (1998) criticized many of the early typologies and concluded that psychopathy was a distinct clinical entity which could be diagnosed using a 20-item checklist (the *Hare Psychopathy Checklist – Revised*) with a cut-off score of >30 for the diagnosis of prototypical psychopathy (*Table 1*).

The prototypical Hare's psychopath exhibits a constellation of affective, interpersonal and behavioural characteristics, including deceitfulness, egocentricity, manipulativeness, callousness and socially deviant behaviour. Psychopaths account for approximately one quarter of the 75% of the prison population that meet the criteria for antisocial personality disorder (APD) (Hare, 1998).

Research also shows that while most psychopaths meet the criteria for APD, a significant proportion also meet the criteria for other axis II disorders, particularly paranoid, narcissistic and borderline personality disorders (BPD) (Blackburn, 1998). As psychopathy is associated with a number of axis II disorders, it is best understood in terms of its key interpersonal and behavioural components, i.e. viewed as a combination of impulsive behaviour and deficient emotional responses which lead to a failure to refrain from antisocial behaviours.

THE NEUROBIOLOGY OF PSYCHOPATHY AND ANTISOCIAL BEHAVIOUR

The biological and environmental factors responsible for the development and maintenance of psychopathy remain poorly understood. Psychophysiological and neuropsychological research, however, suggests psychopaths exhibit a variety of information and emotional processing deficits (Blair, 1995; Hare, 1998; Newman, 1998) which can be theoretically linked to neural

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TABLE 1.
Items in the *Hare Psychopathy Checklist – Revised*

Factor 1: interpersonal/affective	1. Glibness/superficial charm
	2. Grandiose sense of self-worth
	4. Pathological lying
	5. Conning/manipulative
	6. Lack of remorse or guilt
	7. Shallow affect
	8. Callous/lack of empathy
	16. Failure to accept responsibility for own actions
Factor 2: social deviance	3. Need for stimulation/proneness to boredom
	9. Parasitic lifestyle
	10. Poor behavioural controls
	12. Early behavioural problems
	13. Lack of realistic, long-term goals
	14. Impulsivity
	15. Irresponsibility
	18. Juvenile delinquency
	19. Revocation of conditional release
Additional items	11. Promiscuous sexual behaviour
	20. Criminal versatility
	17. Many short-term marital relationships

From Hare (1990)

circuits involving prefrontal and temporo-limbic brain regions.

The prefrontal cortex, with its rich and widespread brain interconnections, is important in impulse control and the processing and integration of both emotional and unemotional information (Damasio, 1994). As psychopaths and patients with 'acquired sociopathy' secondary to ventromedial brain lesions also display similar attenuation of anticipatory electrodermal response to noxious stimuli (Damasio, 1994), the ventromedial prefrontal cortex is likely to be a particularly important brain area in the aetiology of psychopathy and antisocial behaviour.

The amygdala plays a significant role in the modulation of aggressive or submissive behaviours in social contexts and is implicated in fear conditioning, the ability to recognize facial expressions of fear and anger, and memory for emotional material. Brain lesioning studies (Damasio, 1994; Murphy et al, 2001) indicate that the amygdala and ventromedial prefrontal cortex have similar functions and that disruption of the amygdala–ventromedial prefrontal cortical circuit results in deficits in emotional learning in its broadest sense. However, they differ in their bias towards the positive or negative rewards, and the amygdala may be particularly associated with the processing of more basic information on emotions than the ventromedial cortex, which has a monitoring and evaluating role. The amygdala appears to be a relevant substrate for the study of the callous-unemotional dimension of the APD and psychopathy given its prominent role in fear conditioning and emotional processing.

Two key theories to explain psychopathy have emerged in the academic literature. The 'somatic marker hypothesis' by Damasio (1994) suggests psychopaths show deficits in decision making which reflect an inability to activate autonomic somatic states linked to the anticipation of rewards and punishments, and the deficit lies primarily in the ventromedial prefrontal cortex. The 'violence inhibition mechanism' proposed by Blair (1995) suggests psychopaths fail to display the submission cues that normally inhibit aggressive responses, and this results in difficulties with empathy. The amygdala is believed to be the key neural substrate for the latter functions.

STRUCTURAL STUDIES IN IMPULSIVE-AGGRESSIVE PERSONALITY DISORDERS

There have been remarkably few structural brain studies on impulsive-aggressive personality disorders and psychopaths despite reports that damage to the prefrontal cortex results in a 'pseudo-psychopathic syndrome' (Meyers, 1992; Damasio, 1994). Much of the available literature focuses on the prevalence of brain abnormalities in personality-disordered or violent populations rather than on quantitative structural neuroimaging studies, and the findings are inconsistent.

Woods et al (1995) reported evidence of ventricular enlargement and periventricular hyperintensities on magnetic resonance imaging (MRI) in patients with a primary diagnosis of personality disorder (PD) compared with healthy controls. Several computed tomography (CT) studies, however, have failed to find any evidence of ventricular enlargement or prefrontal abnormalities in BPDs (which are generally characterized as highly impulsive) compared with healthy controls (reviewed by Kemperman et al, 1997). The lack of control for confounds, such as axis I pathology, and the lower spatial resolution of CT may account for the discrepant findings.

In one of the few quantitative MRI studies examining total prefrontal brain volumes in aggressive APD offenders, the author found no evidence of reduced volumes in a comparison with healthy controls (Dolan, 1998). A more recent study using higher resolution MRI scanners to assess gray matter volume report an 11% reduction in prefrontal gray matter in men with a diagnosis of APD compared with normal men or with drug- or alcohol-dependent men without APD (Raine et al, 2000). The latter findings suggest that subtle structural deficits in the prefrontal cortex gray matter are apparent in antisocial populations.

It is also noteworthy that the same study suggested that APD subjects who had prefrontal gray matter volume reductions also had lower skin conductance activity during a stress task than those without reduced prefrontal gray volume. As the prefrontal cortex is a key component of the neural circuit involved in fear conditioning and stress responsivity, the findings suggest prefrontal deficits may account for the reported difficulties in fear conditioning and autonomic responsiveness in antisocial populations.

To date, there have been no structural neuroimaging studies comparing psychopathic with non-psychopathic groups, and such work is needed to clarify whether similar prefrontal gray matter volume reductions are apparent in constitutional psychopaths who do not have a history of head injury. As the ventromedial prefrontal cortex is specifically implicated in anticipatory

autonomic responses and risk-taking behaviour (Damasio, 1994), future studies need to examine gray and white matter volume reductions in the subregions of the prefrontal cortex.

STRUCTURAL NEUROIMAGING STUDIES ON VIOLENT/CRIMINAL POPULATIONS

There are several CT studies on offender samples, but many fail to report significant evidence of brain abnormalities in specific subgroups of criminals. In the majority of cases where brain abnormalities have been reported, it has been the temporal rather than prefrontal areas that have been cited as abnormal, particularly in violent and sexually aggressive offenders (Raine, 1993). At present, it is difficult to draw definite conclusions from available studies on violent offenders, as almost all published reports come from the same research group and few include a healthy control group. The low spatial resolution of CT also limits its utility in assessing prefrontal abnormalities because of partial volume effects. MRI studies on violent psychiatric samples are limited, but most show an increased prevalence of anterior temporal lobe lesions in violent compared with non-violent patients (reviewed by Raine, 1993).

Overall, there seems reasonable evidence that temporal abnormalities are present in aggressive or violent personality-disordered samples, but future morphological studies are needed to examine specific structural volumes in the amygdala and hippocampus. In support of this notion, Laasko et al (2001) reported a negative correlation between dorsal hippocampal volume and psychopathy score in repetitively violent alcoholics with APD. As the hippocampus is also implicated in fear conditioning, the finding again points to a neural circuit involving prefrontal and temporo-limbic brain regions in the aetiology of psychopathic and antisocial behaviour.

FUNCTIONAL NEUROIMAGING STUDIES ON IMPULSIVE-AGGRESSIVE AND PSYCHOPATHIC SAMPLES

There are a limited number of functional neuroimaging studies in BPDs, APDs, psychopaths and violent offenders, but the findings generally point to dysfunction in the brain regions involved in emotional and learning processes. For example, Goyer et al (1994) used positron emission tomography to examine regional cerebral metabolic rates of glucose metabolism (rCMRG) in the frontal lobes of PD patients and normal controls. Patients with BPD showed a significant decrease in frontal metabolism in the inferior frontal lobes and an increase in the more superior prefrontal areas. Regardless of diagnosis, lifetime history of aggressive impulse difficulties correlated negatively with rCMRG in the prefrontal cortex during an auditory activation task, suggesting a significant relationship between impulsive aggression and frontal cortical functioning.

Raine et al (1994) also reported a selected reduction in prefrontal rCMRG in murderers compared with an age- and sex-matched healthy control sample using a similar methodology. The reduction was most marked in the ventromedial brain regions and primarily apparent in those from stable backgrounds, which suggests that the observed deficits are better accounted for by genetic than environmental influences (Raine et al, 1998).

In one of the few functional MRI (fMRI) studies in psychopathic populations, Smith (2000) reported that psychopaths had attenuated left dorsolateral prefrontal activations during the performance of response inhibition tasks compared with healthy controls. The findings suggest that the disinhibition observed in psychopathy may be related to a deficit in processing information in this brain region. However, future fMRI studies need to specifically activate the ventromedial cortex, as this brain region is implicated in both impulse control and emotional learning in psychopathic and antisocial populations.

There is a small number of functional imaging studies addressing affective information processing and learning in psychopathic samples. Intrator et al (1997) used single photon emission computed tomography (SPECT) to examine responses to neutral and emotional words in psychopathic and non-psychopathic substance abusers and community controls during a lexical decision task. Contrary to initial expectations, psychopaths showed greater relative activation in emotional than neutral conditions than the non-psychopathic groups. The data were interpreted as evidence that psychopaths had difficulties in processing emotional information, which resulted in greater activation in the cortical regions involved in adding affect to language. Additionally, the group found that psychopaths activated more posterior brain regions than non-psychopaths, suggesting that psychopaths have anomalies in the way they process semantic and affective information.

In subsequent fMRI studies from a related group, Kiehl (2000) also reported that psychopaths exhibited an unusual pattern of activation of prefrontal and limbic regions in the

processing of emotional words compared with controls undertaking a similar task. Schneider et al (2000), using an olfactory aversive classical conditioning paradigm in fMRI, have reported that people with APDs who meet the criteria for psychopathy show a differential conditioning effect in the amygdala and in the dorsolateral prefrontal cortex compared with controls despite both groups indicating similar subjective conditioning. Psychopaths showed greater brain activity in these regions, suggesting a need for greater effort in the performance of the aversive conditioning task, but also showed an insensitivity of the amygdala to the aversive character of the unconditioned stimulus during the habituation phase. The findings point to the importance of the amygdala in emotional learning processes and our understanding of the interpersonal deficits seen in psychopathy.

CONCLUSIONS

Brain imaging studies in antisocial and psychopathic populations are limited in number and require replication using larger sample sizes, better characterized samples and more region-specific cognitive activation paradigms. Available studies do, however, point to evidence of subtle structural and functional deficits in the neural circuits implicated in impulse control and emotional information processing, i.e. the prefrontal and temporo-limbic brain regions. As yet, the significance of the findings remains unclear, and causal associations between the observed deficits and the development and maintenance of psychopathic and antisocial behaviours have yet to be established.

Future scanning studies are likely to use combined methodologies to assess the impact of specific pharmacological agents in 'normalizing' brain activation patterns and to evaluate associated cognitive, emotional and behavioural changes in this difficult to treat group of disorders. HM

KEY POINTS

- Psychopathic disorder is best conceptualized in terms of a variety of personality disorders associated with impulse control problems and antisocial behaviour.
- Psychopathy assessed using the *Hare Psychopathy Checklist – Revised* measures a distinct clinical construct.
- The prefrontal cortex and temporo-limbic brain regions are involved in impulse control and emotional regulation.
- The prefrontal cortex and temporo-limbic brain regions are theoretically dysfunctional in psychopathy.
- Neuroimaging studies confirm that psychopathic patients have subtle structural and functional deficits in the prefrontal cortex and amygdala/hippocampal brain regions.

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