



## Neural and behavioural responses to threat in men with a history of serious violence and schizophrenia or antisocial personality disorder

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### ABSTRACT

**Background:** Contemporary theories and evidence implicate defective emotion regulation in violent behaviour. The two psychiatric illnesses most implicated in violence are schizophrenia and antisocial personality disorder (APD). This study examined behavioural and brain abnormalities in violent men with schizophrenia or APD during anticipatory fear.

**Method:** Fifty-three men [14 non-violent healthy controls, 13 with schizophrenia and a history of serious violence (VSZ), 13 with schizophrenia without a history of violence (SZ), 13 with APD and a history of serious violence] underwent blood-oxygenation-level-dependent fMRI during an experiment involving repeated presentations of 'safe' and 'threat of electric shock' conditions and provided ratings of shock anticipation and fear. Schizophrenia patients did not have co-morbid APD.

**Results:** VSZ participants reported the highest, and APD participants the lowest, level of shock anticipation and fear, with intermediate ratings by SZ and healthy participants. The violent, relative to non-violent, groups showed altered activity modulation in occipital and temporal regions, from early to latter parts of threat periods. Additionally, VSZ patients displayed exaggerated whereas APD patients showed attenuated thalamic-striatal activity during latter threat periods.

**Conclusions:** Aberrant activity in occipital and temporal regions when exposed to sustained visual threat cues is associated with a predisposition to violence in both schizophrenia and APD. This common biological deficit, however, appears to arise from dissimilar behavioural mechanisms related to differences in the strength of aversive conditioning and behavioural response to sustained threat cues (enhanced in VSZ; attenuated in APD), also reflected in opposite patterns of alternations in thalamic-striatal activity, in these two disorders.

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## 1. Introduction

Violent behaviour is associated with certain mental disorders, most markedly schizophrenia (Arseneault et al.,

2000) and antisocial personality disorder (APD) (Hodgins, 1992). Although positive symptoms may drive inpatient violence, several other factors contribute on their own or in interaction with symptoms to persistent violence in the community shown by schizophrenia patients (Krakowski, 2005).

Dysfunction within a neural circuit implicated in emotion regulation is considered to constitute the neural substrates of violence (Davidson et al., 2000). This circuit includes several

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regions of the prefrontal cortex, amygdala, hippocampus, hypothalamus, anterior cingulate (AC), striatum and other interconnected structures (Davidson et al., 2000). Behaviourally, schizophrenia patients with a history of violent behaviour show a better ability to identify facial emotional expressions but a poorer ability to discriminate between intensity of emotions compared to non-violent schizophrenia patients (Silver et al., 2005). Schizophrenia patients with high psychopathy scores show impaired recognition of sadness at low intensity compared to those with low psychopathy scores (Fullam and Dolan, 2006). Despite the vast literature showing cortico-limbic abnormalities during processing of affective information (e.g. Gur et al., 2002; Williams et al., 2004), previous studies have not examined functional brain abnormalities using an affective processing paradigm in association with persistent violent behaviour in schizophrenia.

There is reliable evidence of impaired ability to anticipate punishment, reduced psychophysiological responsiveness to threatening events, and reduced experience of aversive states in individuals with high psychopathic traits who form part of a wider group of people with APD (review, Herba et al., 2004). Studies of psychopathic/APD individuals suggest that altered functions mainly of regions located within the frontal and temporal lobes, that are implicated in response inhibition, modulation of aggressive or submissive behaviour, recognition of expressions of fear and anger, and fear conditioning, are involved in mediation and expression of psychopathy and antisocial behaviour (reviews, Herpertz and Sass, 2000; Dolan, 2002; Herba et al., 2004; Kumari and Taylor, *In press*). Event-related potentials and imaging studies of psychopathic individuals by Kiehl and colleagues have shown paralimbic dysfunction and associated behavioural abnormalities in psychopathy (review, Kiehl, 2006).

In this study we examined neural dysfunctions, measured with functional magnetic resonance imaging (fMRI), associated with a history of serious physical violence during an anticipatory fear paradigm (Chua et al., 1999; Kumari et al., 2007) in schizophrenia. We also studied a group with APD and a history of similar level of violence to that in patients with schizophrenia to elucidate common and distinct brain correlates of violence in these two disorders. We hypothesized, albeit with limited confidence given the lack of relevant imaging data in schizophrenia, that both violent groups would show altered fronto-temporal activity. We also predicted that our experimental manipulation involving an aversive procedure would be the least effective in violent APD individuals.

## 2. Materials and methods

### 2.1. Participants and design

We used a cross-sectional design, involving four groups: (i) 14 healthy men (HC) with no history of violence or a mental disorder, (ii) 13 men with schizophrenia with no history of violence (SZ), (iii) 13 men with schizophrenia and a history of serious violence (VSZ), and (iv) 13 men with APD and a similar history of violence to that of VSZ.

VSZ and APD patients were recruited from specialist high and medium security hospitals which provide treatment and security for people with mental disorders who are subject to compulsory detention because of their dangerous, violent or

criminal propensities. Most of them had extensive violence histories before admission to a secure hospital. SZ patients were recruited from local hospitals or outpatient clinics and included only if they did not have a history of violent behaviour, verified at interview and by clinical record screen. HC were recruited via local advertisements and screened for a history of mental illness (Spitzer et al., 1990). The sample was recruited as part of a larger project (Kumari et al., 2006; Narayan et al., 2007).

All included participants were aged between 18 and 55 years, free of substance abuse (confirmed by urine analysis), neurological conditions or head injury, and spoke English as their first language. SZ and VSZ patients had a diagnosis of schizophrenia (First et al., 1995) but no co-morbid diagnosis of APD (First et al., 1997). APD patients had a diagnosis of APD (cluster B, DSM IV) but no co-morbid diagnosis of schizophrenia. Among the schizophrenia groups, diagnosis included paranoid (9 SZ, 10 VSZ), undifferentiated (2 SZ, 3 VSZ), disorganised (1 SZ) and residual (1 SZ) subtypes. Within the APD group, 8 patients had co-morbid antisocial and borderline personality disorders, 3 had co-morbid antisocial, borderline and paranoid personality disorders, 1 had antisocial, borderline and histrionic personality disorders, and 1 had antisocial personality disorder without other co-morbid disorders. All VSZ and APD had been free of alcohol and substance misuse for a minimum of two years (confirmed by regular random urine screens in secure hospitals).

The study procedures were approved by relevant local ethics committees. All participants provided written informed consent.

### 2.2. Assessment of violence

The history of violence (or a lack of it) was established using clinical and forensic records (where appropriate). It is sometimes a matter of chance whether criminal proceedings are pursued; the level of harm done to the victim of an assault can also depend on a range of factors other than the nature of the assault itself. In order to minimise these distortions, research ratings of violence were made according to the Gunn–Robertson scale (score range 0–8) (Gunn and Robertson, 1976) based on the frequency of serious violence over lifetime (score 0–4) and the severity of the most recent violence act (score 0–4). A cut-off of 5 was used for inclusion in the violent groups, indicative of an index fatal or near fatal act of violence against another and at least one other episode of at least moderately serious violence. Any evidence of actual violence against another person, whether or not it had led to a criminal conviction was taken as an exclusion criterion for HC and SZ groups.

### 2.3. Other assessments

In all patients with schizophrenia, symptoms were rated using the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987). The PANSS is a popular semi-structured interview consisting of a 30-item, 7-point severity scale [1 (absence of psychopathology) to 7 (extremely severe)]. It assesses a wide range of symptoms of schizophrenia, yielding 'positive', 'negative' and 'general psychopathology' symptom sub-scales. The 5-factor model of PANSS (Lindenmayer et al., 1995) examines 'positive', 'negative', 'cognitive', 'excitement' and 'depression' syndromes.

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