

EDITORIAL

Neuropsychological investigations of the impulsive personality disorders¹

BACKGROUND

There has been revived interest within the last few years in neuropsychological investigations of personality disorders (PDs) associated with impulsive and/or anti-social behaviour. Neuropsychological studies of such PDs offer two potential benefits: (i) an improving characterization of the cognitive and emotional difficulties experienced by individuals diagnosed with these disorders and, in particular, borderline PD and anti-social PD; (ii) the development of more precise hypotheses about the role of brain dysfunction in the aetiology and behavioural problems associated with these conditions. The most recent neuropsychological studies of impulsive PD have been interpreted against a background of accumulating evidence for structural (Driessen *et al.* 2000; Raine *et al.* 2000; Dolan *et al.* 2001), neurochemical (Coccaro & Siever, 1995; Steinberg *et al.* 1997; Leyton *et al.* 2001) and functional brain abnormalities (Donegan *et al.* 2003). Future studies of impulsive PDs will be able to exploit advances in structural imaging (e.g. diffusion tensor imaging/tract mapping, e.g. Hoptman *et al.* 2002), as well as pharmacological and behavioural genetics (McGuffin & Thapar, 1992; Lesch *et al.* 1996; Skodol *et al.* 2002).

Against these emerging opportunities need to be set the obstacles. Like similar research in psychiatric illnesses (e.g. Rogers & Robbins, 2001), neuropsychological investigation of PD is complicated by significant clinical factors. First, there is the continuing debate about the validity of the diagnostic criteria used to identify particular PDs (e.g. Tyrer, 1999), as well as variability between samples that probably arises through different methods of diagnosis (Kaye & Shea, 2000). Recently, dimensional approaches to specifying personality disturbances have identified dysfunctional traits as part of a continuum of normality personality and also demonstrated that higher order clustering of these traits converges on several domains of impaired function specified by conventional categorical systems (Livesley *et al.* 1992, 1998). However, in general, neuropsychological studies in this area have continued to identify clinical samples in terms of DSM-III-R or DSM-IV Axis II (American Psychiatric Association, 1994), but supplemented this information with a dimensional measure of impulsivity.

Secondly, impulsive PDs tend to have markedly high rates of co-morbid AXIS I psychopathology (Skodol *et al.* 1999) as well as other forms of DSM-IV PDs (Skodol *et al.* 1999; Becker *et al.* 2000). Some of these disorders, e.g. depression (Elliott *et al.* 1996) and substance dependence (Rogers *et al.* 1999), are themselves associated with cognitive and emotional impairments that can be difficult to separate from those associated with the index PD. Finally, psychotropic medication and situational factors such as clinical samples interviewed in detention and control samples interviewed in the community have uncertain effects on motivation and neuropsychological task performance. It is unlikely that any one study could 'cover all of these bases'; as with investigations in other neuropsychiatric populations, comparison groups need to be selected to control factors of relevance to the particular cognitive or emotional functions targeted by investigators. Of course, these technical difficulties also affect methodologies used to investigate other biological factors in PD but they limit the interpretation of emerging neuropsychological data and will continue to do so even as

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neuropsychological approaches are integrated more fully with brain imaging and pharmacological protocols.

In this commentary, I consider three studies recently published in *Psychological Medicine*. Two describe investigations involving samples of hospitalized offenders with antisocial traits (see Dolan & Park, 2002; Dolan *et al.* 2002*a*) while the third study describes an investigation involving a sample characterized by borderline PD (see Bazanis *et al.* 2002). All three studies involve patient samples that are characterized by high levels of impulsivity chiefly manifested as either self-directed or outwardly directed aggression. In their different ways, these studies exemplify current trends in neuropsychological research with impulsive/antisocial PDs but point to important directions in which this kind of research needs to be developed over the next few years.

FRONTAL LOBE/‘EXECUTIVE FUNCTION’ IN ANTISOCIAL PERSONALITY DISORDERS

One continuing controversy is whether the antisocial PDs are associated with impairments in the so-called ‘executive functions’. ‘Executive functions’ collectively mediate the dynamic organization of behaviour and permit us to use our cognitive resources in different ways to realize changing behavioural objectives. These functions include the ability to manipulate information in short-term memory, reorient our attention, and plan sequences of action to attain distal goals. There is convincing evidence that these functions depend, in large part, upon the integrity of the frontal lobes (Stuss, 2002). While there is little evidence that psychopathy – involving a propensity to an antisocial lifestyle combined with an emotional shallowness and absence of guilt (as characterized by the Psychopathy Checklist-Revised (Hare, 1991)) – is associated with impaired ‘executive function’ (Hart *et al.* 1990; see Blair & Frith, 2000 for review), there have been reports of impairments in antisocial groups more broadly defined (e.g. Dinn & Harris, 2000). One recent review concluded that ‘executive function’ is impaired in antisocial PD, with an estimated effect size of 0.62 (medium to large) (see Morgan & Lilienfeld, 2000).

To examine the relationship between impaired ‘executive function’ in antisocial PD and impulsivity, Dolan *et al.* (2001*a*) administered a battery of neuropsychological tests focusing on predominantly frontal lobe tasks and also tested post-synaptic 5-hydroxytryptamine function as measured by the hormonal (prolactin) response to a D-fenfluramine challenge (Goodall *et al.* 1993). Personality disordered offenders from maximum-security psychiatric hospitals were characterized using the Special Hospital Assessment of Personality and Socialisation (SHAPS) (Blackburn, 1986) into those who were high impulsive and those who were low impulsive. The neuropsychological task performance and prolactin responses of these groups were compared with that of a group of non-offender controls. All participants were screened for DSM-III-R Axis I illness, neurological illness or head injury, illicit drug use within the last 5 years, physical illness and prescribed psychoactive medication. Consistent with several previous studies (e.g. Coccaro *et al.* 1997), high impulsive offenders showed blunted prolactin responses to the D-fenfluramine challenge compared to low impulsive offenders, suggesting that increased impulsivity is associated with 5-HT abnormalities; in this study, the difference in prolactin response between the high impulsive offenders and the non-offender controls was not significant. High impulsive offenders showed impaired ‘executive function’ (as measured by differences in composite *z* scores of task performance) compared to both low impulsive offenders and controls. Memory function was not markedly affected. However, while impulsivity was associated with aggression, impulsivity itself was most closely associated with both level of performance on frontal lobe tasks and prolactin response. Therefore, these results suggest that impulsivity in anti-social individuals may be mediated by both impaired neuropsychological function – in particular, ‘executive function’ – and reduced 5-HT activity; as previously found, there also appears to be a rather more direct association between impaired neuropsychological function and aggression, probably also involving lowered IQ (Heilbrun, 1982).

More precise information about the nature of neuropsychological function in antisocial groups is provided by the second study considered here (Dolan & Park, 2002). This study specifically involved

offenders diagnosed with DSM-IV antisocial PD but no other AXIS II PD and who had been screened for current AXIS I disorder, previous drug or alcohol dependence, learning disability, medication and neurological damage. The tasks were selected as being putatively associated with both dorsolateral and ventromedial frontal lobe function, and included the Tower of London planning test (Owen *et al.* 1990) and a visual discrimination learning paradigm that tests the ability to shift an attentional bias or 'set' on the basis of feedback information (Owen *et al.* 1991). Both these cognitive activities are believed to depend upon activity within predominantly dorsolateral portions of the prefrontal cortex (Rogers *et al.* 2000). The battery also included a Go/No Go task in which participants were required to respond to 70% of visually presented stimuli but withhold responding to the remaining 30% of stimuli. It is likely that the inhibitory aspects of such tasks depend upon inferior portions of the frontal lobes (e.g. Aron *et al.* 2003). The final task was a delayed-matching-to-sample paradigm in which participants are shown a visual stimulus and, after a variable delay in which the stimulus is absent, required to select it from a display of four test stimuli (the target stimulus + three distractors). Delay-dependent deficits on this task are thought to indicate problems with recognition mnemonic processing mediated by inferior and medial temporal cortex (Mishkin, 1982; Owen *et al.* 1995).

Comparison with non-offender controls matched for age and IQ demonstrated that the antisocial PD offenders were impaired at formulating sequences of actions to solve problems on the Tower of London planning test, and that they were impaired at shifting a learnt attentional bias in visual discrimination learning. These two deficits are consistent with the proposal that antisocial PD involves dysfunction of circuitry encompassing the dorsolateral prefrontal cortex. The offenders also exhibited problems in the performance of the Go/No Go task, making consistently more errors of commission than the non-offender controls, and suggesting dysfunction in more inferior frontal areas as well. Finally, the antisocial PD offenders were consistently less accurate than controls at the delayed-matching-to-sample test. Since the deficit was as great at short delays as at long delays, it seems unlikely that this represents a purely mnemonic deficit and may instead represent some kind of attentional problem or difficulty with encoding the visual stimuli. Overall, these data demonstrate that a stringently screened sample of offenders identifiable as having diagnoses of DSM-IV antisocial PD but no other PD have a pattern of relatively widespread deficits on tasks involving predominantly frontal lobe function. They strengthen the evidence base for the proposal that antisocial PDs may involve alterations in frontally mediated cognition.

IMPAIRED CHOICE ASSOCIATED WITH IMPULSIVITY IN BORDERLINE PERSONALITY DISORDER

Our third paper examines neuropsychological function in the context of borderline PD. In contrast to antisocial PD, neuropsychological studies of borderline PD samples has been sporadic and limited in focus (O'Leary, 2000). There is some limited evidence that patients diagnosed with borderline PD exhibit a range of neuropsychological impairments. Specifically, deficits have been demonstrated on tasks involving attention, memory, visuospatial function, and emotional processing (O'Leary *et al.* 1991; Burgess, 1992; Judd & Ruff, 1993; van Reekum, 1993; Kurtz & Morey, 1999). However, these deficits have not been consistently replicated (see Driessen *et al.* 2000; Sprock *et al.* 2000). More recently, the focus has shifted to areas of cognition that appear most directly related to the specific symptomology of borderline PD. Dougherty *et al.* (1999) observed that female patients with borderline PD had difficulties tolerating delayed rewards compared to a non-psychiatric controls. As described above, several studies have shown that antisocial groups are impaired at tasks that require some form of behavioural inhibition, and Leyton *et al.* (2001) have reported similar problems in borderline PD patients compared to healthy controls.

In the third paper considered here, Bazanis *et al.* (2002) investigated the performance of patients identified as having a history of impulsive aggression in the context of a diagnosis of borderline PD on a decision-making task involving choices between uncertain rewards and punishments. The task required participants first to predict which of two probabilistic events would occur and then, to

decide how much they wished to gamble of their previously acquired reward on their prediction being correct. The task was structured in such a way as to separate risk-hunting *versus* risk-averse strategies of gambling and to discriminate both strategies from fast, premature responding that might reflect motor disinhibition. Previous research had shown that this task is impaired following focal damage to orbitofrontal areas but not dorsolateral or dorsomedial frontal areas (see Rogers *et al.* 1999). The patients were screened for current AXIS I psychopathology, current or previous psychotic illness, history of head injury, alcohol dependence or abuse within the previous 2 months.

Compared with healthy controls, borderline PD patients exhibited a pattern of delayed and maladaptive choices when choosing between probabilistic events, but markedly disinhibited responding when gambling on the outcome of their decisions. Notably, the delayed maladaptive choices of the borderline PD patients suggests that impulsivity in the context of these PDs is not always manifest as 'actions that appear poorly conceived, prematurely expressed ...' (Daruna & Barnes, 1993) but may reflect a deeper cognitive deficit associated with resolving between competing courses of action. Similar effects have been observed in healthy volunteers selected for high levels of self-report impulsivity (Dickman, 1985). Bazanis *et al.* (2002) also administered a version of the Tower of London planning task (Owen *et al.* 1995) and found that the performance of the borderline PD patients was significantly impaired compared with controls and that, like the patients studied by Dolan & Park (2002), the magnitude of impairment increased with problem complexity. Together, these data suggest that borderline PD is associated with brain dysfunction in orbitofrontal and dorsolateral regions of the frontal lobes, consistent with similar reports in individuals with the highly co-morbid antisocial PD (Dinn & Harris, 2000; Dolan & Park, 2002).

CONCLUSION

Collectively, these findings suggest that neuropsychological investigations can, in the context of careful clinical assessment, provide insights into altered cognitive and emotional processes associated with impulsive PDs. However, future research needs to meet two related challenges. First, it must demonstrate patterns of deficits that are specific to particular PDs. Currently, while there is increasing evidence that impulsive PDs are associated with neuropsychological deficits, there are virtually no data concerning whether these deficits are distinctive to one PD (or cluster of PDs) compared with other PDs (or cluster of PDs). Indeed, it is noteworthy that the clearest evidence of impairment in the three papers considered above involved comparisons between PD offenders/patients and non-psychiatric healthy controls. Thus, demonstrating convincing differences between different clusters of PDs, or between different PDs and samples with relevant AXIS I illnesses (e.g. mood disorders in the case of borderline PD), and helping to delineate appropriate endophenotypes for other biological perspectives on PD (Siever *et al.* 2002), represents a rather stronger test for future research.

Secondly, future research needs to specify the relationships between cognitive and emotional deficits on the one hand and the symptomology of the PDs on the other hand. One way to meet this challenge will be to integrate properly different kinds of methodologies in order to establish how cognitive deficits in these disorders interact with other aspects of their pathophysiology. For example, recent research has suggested that altering 5-HT function in healthy volunteers can alter performance of the decision-making task used in Bazanis *et al.* (2002). Since there is now increasing evidence that 5-HT function is compromised in borderline PD (including the neuromodulation of the prefrontal cortex; Soloff *et al.* 2000), we can test the hypothesis that the impaired decision-making associated with borderline PD involves altered neuromodulation of cognitive processes mediated by the prefrontal cortex. Currently, several international groups of PD researchers are now using brain-imaging technology to test such approaches formally.

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