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Response inhibition and impulsivity: an fMRI study

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Abstract

Aggressive, suicidal and violent behaviour have been associated with impulsive personality and difficulty in inhibiting responses. We used functional magnetic resonance imaging (fMRI) of the whole brain to examine the neural correlates of response inhibition in 19 normal subjects as they performed a Go/NoGo task. Subjects completed Eysenck's Impulsivity Scale, Barratt's Impulsivity Scale (BIS) and behavioural impulsivity tasks. Associations between blood oxygen level dependent (BOLD) response, trait impulsivity, task performance and National Adult Reading Test (NART) IQ were investigated. Neural response during response inhibition was most prominent in the right lateral orbitofrontal cortex. Responses were also seen in superior temporal gyrus, medial orbitofrontal cortex, cingulate gyrus, and inferior parietal lobule, predominantly on the right side. Subjects with greater scores on impulsivity scales and who made more errors had greater activation of paralimbic areas during response inhibition, while less impulsive individuals and those with least errors activated higher order association areas. Exploratory factor analysis of orbital activations, personality measures and errors of commission did not reveal a unitary dimension of impulsivity. However, the strong association between posterior orbital activation and Eysenck's impulsivity score on a single factor suggests that greater engagement of right orbitofrontal cortex was needed to maintain behavioural inhibition in impulsive individuals. Lower IQ was more important than impulsivity scores in determining errors of commission during the task. Neuroimaging of brain activity during the Go/NoGo task may be useful in understanding the functional neuroanatomy and associated neurochemistry of response inhibition. It may also allow study of the effects of physical and psychological interventions on response inhibition in clinical conditions such as antisocial personality disorder.

Keywords: Go/NoGo; Impulsivity; Functional magnetic resonance imaging; Orbitofrontal cortex; Frontal lobe; Antisocial personality disorder

1. Introduction

Impulsivity is a multidimensional concept that incorporates failure of response inhibition, rapid processing of information, novelty seeking, and inability to delay gratification (Barratt, 1985, 1994). Impulsivity is one of the defining characteristics of a number of psychiatric diagnoses, particularly borderline and antisocial personality disorders (Stein, Hollander, & Liebowit 1995; Stein, Towney, & Hollander, 1995). Poor impulse control correlates significantly with suicidal, violent and aggressive behaviour (Plutchik & Van Praag, 1989, 1995) and is an increasingly important aspect of risk assessment in a variety of clinical situations, including assessment of dangerousness (Monahan et al., 2000). Most attempts to measure impulsivity rely on psychometric self-report trait measures. Some behavioural impulsivity tasks have been developed, measuring preference for a smaller more immediate reward over a delayed larger reward, and impaired motor inhibition, however, psychometric and behavioural impulsivity measures do not correlate well with each other (Barratt & Patton, 1983; Barratt, Stanford, Kent, & Felthous, 1997). Behavioural impulsivity tasks tend to have low test–retest reliability, apart from the Go/NoGo task, which has reasonable temporal stability (Kindlon, Mezzacappa, & Earls, 1995).

Impulsivity is a feature of damage to the frontal lobe and an "acquired sociopathic" syndrome has been described following ventromedial frontal lobe lesions (Damasio, Tranel, & Damasio, 1990; Grafman et al., 1996; Paradiso, Chemerinski, Yazici, Tartaro, & Robinson, 1999). This has lead to suggestions that impaired ventromedial frontal lobe function may contribute to poor impulse control in antisocial personality disorders (Damasio, 2000). In support of this notion a variety of neuropsychological deficits have been reported in antisocial populations (Morgan & Lilienfeld, 2000). Neuroimaging studies in this population report a reduction in prefrontal metabolism (Raine, Buchsbaum,

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& LaCasse, 1997), and reduced prefrontal grey matter volumes (Raine, Lencz, Bihrle, La Casse, & Colletti, 2000).

Positron emission tomography (PET) (Kawashima et al., 1996; Krams, Rushworth, Deiber, Frackowiak, & Passingham, 1998; Nobre, Coull, Frith, & Mesulam, 1999) and functional Magnetic Resonance Imaging (fMRI) studies (Casey et al., 1997; Garavan, Ross, & Stein, 1999; Hager et al., 1998; Konishi, Nakajima, Uchida, Sekihara, & Miyashita, 1998) of response inhibition and processing novel stimuli suggest a role for the prefrontal cortex, especially the right lateral frontal cortex, and a network of associated regions in response inhibition. It is not clear to what extent these inhibition-related activations may depend on subjects' impulsivity. Garavan, Ross, Murphy, Roche, & Stein (2002) have reported greater reliance on anterior cingulate cortex during Go/NoGo in subjects who are more absent-minded, using a cognitive measure that they have found to be correlated with Barrett's Impulsivity Scale (BIS). The key novel aspect of the present study is the direct investigation of the relationship between trait impulsivity measures and blood oxygen level dependent (BOLD) response.

We hypothesized that: (1) orbitofrontal cortex would be activated during response inhibition, (2) low scores on psychometric (trait) impulsivity measures would be associated with greater activation in orbitofrontal cortex during response inhibition, (3) low error-rates on the Go/NoGo response inhibition task would be associated with greater activation in the orbitofrontal cortex during response inhibition, (4) psychometric (trait) impulsivity scores would correlate positively with error-rate on response inhibition tasks.

2. Methods

2.1. Subjects

Twenty-one subjects were recruited by advertisement at their work-places. All subjects were male, right-handed, aged 18–50 years, and employed by the National Health Service or the University of Manchester. The Local Research Ethics Committee granted ethical approval. Subjects participated in a Structured Clinical Interview (SCID-NP) (Spitzer, Williams, Gibbon, & First, 1990) administered by a psychiatrist. Exclusion criteria were: current DSM III-R psychiatric axis I disorder, neurological disorder, currently (within 72 h) taking psychotropic medication or illicit substances, previous serious head injury, and any contraindication to MRI.

2.2. Assessment of impulsivity and neuropsychological test performance

Trait impulsivity was assessed using the impulsivity subscale of Eysenck's impulsivity, venturesomeness and empathy inventory (IVE-I) (Eysenck & Eysenck, 1991), and the Barratt's Impulsivity Scale (BIS) (Barratt, 1994). Both were used as they differ in their conceptual basis (for a review see Parker & Bagby, 1997). The computerised behavioural tests of impulsivity were adaptations of the Go/NoGo task used by Casey et al. (1997) (see below) and Newman's card playing task (CPT) (Newman, Patterson, & Kosson, 1987). CPT was scored on the amount of money won and number of cards played. Intelligence was estimated using the National Adult Reading Test (NART) (Nelson & Willison, 1991). Data were analysed using SPSS v10.0 (SPSS Inc., Chicago, IL). Correlations between psychometric and behavioural measures of impulsivity were examined using Spearmann's rank-order correlations. Partial correlations were computed controlling for NART scores.

2.3. Scanning procedure

Images were acquired on a 1.5-T Philips Gyroscan ACS NT (Philips, Hamburg) scanner with Powertrack 6000 gradients operating at a software level of 6.1.2 using a quadrature headcoil as a radiofrequency receiver. Functional images were acquired using a single shot echo planar imaging (EPI) sequence (relaxation time = 3100 ms, echo time = 50 ms, field of view = 230 mm^2, flip angle = 90°, voxel dimension = 1.8 mm × 1.8 mm × 7 mm and 128 × 64 matrix) to prescribe the functional slice locations. Seventy-two volumes were acquired, each comprising 14 contiguous transverse slices (7 mm thick with no slice skip, in plane resolution = 1.8 mm) aligned with the corpus callosum, covering the entire brain. (The corpus callosum was defined on scout images in the sagittal plane before EPI acquisition.) The T-2 weighted images depicted blood oxygen level dependent contrast. To facilitate later registration of individual fMRI data sets in standard space, a T-1 weighted EPI data set (relaxation time = 6850 ms, echo time = 18 ms, field of view = 230 mm^2, voxel dimension = 0.89 mm × 0.89 mm × 3.5 mm) was acquired in the same session in 28 contiguous transverse planes (3.5 mm thick, no slice skip, in plane resolution = 0.89 mm), parallel to the corpus callosum.

2.4. Activation paradigm

A simple Go/NoGo paradigm was developed to probe response inhibition without unduly loading working memory. It was based on a modification of the task described by Casey et al. (1997). Subjects were shown a continuous series of 120 letters and instructed to respond, by pressing a pneumatic bulb with their right hand, to any letter except V (V was used as the non-target instead of X because X may be associated with meanings such as "Stop!"). Seventy-five percent of the trials were targets (i.e. letters other than V). There were two conditions: Block A—the Go condition had 20 targets, and Block B—the NoGo condition had 10 targets and 10 non-targets. Because it is not possible to control for the effects of manual response frequency in a simple Go/NoGo analysis, Casey et al. used a motor control block. They found that data from the motor control block did not alter their