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Decision-making processes following damage to the prefrontal cortex

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Summary

Recent work has suggested an association between the orbitofrontal cortex in humans and practical decision making. The aim of this study was to investigate the profile of cognitive deficits, with particular emphasis on decision-making processes, following damage to different sectors of the human prefrontal cortex. Patients with discrete orbitofrontal (OBF) lesions, dorsolateral (DL) lesions, dorsomedial (DM) lesions and large frontal lesions (Large) were compared with matched controls on three different decision-making tasks: the Iowa Gambling Task and two recently developed tasks that attempt to fractionate some of the cognitive components of the Iowa task. A comprehensive battery including the assessment of recognition memory, working memory, planning ability and attentional set-shifting was also administered. Whilst combined frontal patients were impaired on several of the tasks employed, distinct profiles emerged for each patient group. In contrast to previous data, patients with focal OBF lesions performed at control levels on the three decision-making tasks (and the executive tasks), but showed some evidence of prolonged deliberation. DL patients showed pronounced impairment on working memory, planning, attentional shifting and the Iowa Gambling Task. DM patients were impaired at the Iowa Gambling Task and also at planning. The Large group displayed diffuse impairment, but were the only group to exhibit risky decision making. Methodological differences from previous studies of OBF patient groups are discussed, with particular attention to lesion laterality, lesion size and psychiatric presentation. Ventral and dorsal aspects of prefrontal cortex must interact in the maintenance of rational and 'non-risky' decision making.

Keywords: prefrontal cortex; decision making; risk taking; orbitofrontal; executive function

Abbreviations: AcoA = anterior communicating artery; BA = Brodmann area; CANTAB = Cambridge Neuropsychological Test Automated Battery; DL = dorsolateral; DM = dorsomedial; EDS = extra-dimensional shift; ID-ED = intra-dimensional/extra-dimensional shift; IDS = intra-dimensional shift; OBF = orbitofrontal; PFC = prefrontal cortex

Introduction

Patients with damage involving orbitofrontal (OBF) cortex have been reported to display severe impairments in real-life decision making, despite remaining unimpaired intellectually and on traditional neuropsychological measures (Eslinger and Damasio, 1985; Shallice and Burgess, 1991). This syndrome has been labelled 'acquired sociopathy', and is characterized by repeated engagement in high-risk behaviours that are rewarding in the short term but have likely negative consequences for the patient's well-being. The engagement in such behaviours has been proposed to arise from impaired decision making between various response options on the basis of faulty 'somatic marking' (Damasio, 1994; Bechara *et al*., 2000). These behaviours may be quantifiable using neuropsychological measures derived from everyday decision making. Bechara *et al*. (1994) developed a task (the Iowa Gambling Task) where subjects must make a series of card

selections resulting in winning and losing money. The four card decks are characterized by different reward–punishment profiles, such that decks A and B offer high rewards but higher penalties, resulting in overall loss, whereas decks C and D offer smaller rewards but minimal penalties, resulting in overall profit. Healthy controls developed a preference for the 'safe' decks by about trial 40 (of 100 choices). However, a small group of frontal patients, with damage including the medial OBF cortex, typically preferred the riskier decks for the duration of the task, and also failed to develop anticipatory skin responses prior to risky decisions (Bechara *et al*., 1994, 1996). The deficit cannot be readily explained in terms of working memory impairment, as these patients were capable of performing a delay task, sensitive to more dorsal prefrontal damage (Bechara *et al*., 1998).

Although the working memory component of the Iowa Gambling Task may have been controlled for, 'risky' decision making on the task could still be associated with a number of potentially dissociable mechanisms, including reduced deliberation, poor learning of outcome probabilities, genuine preference for risky outcomes, and deficits in strategy acquisition and maintenance. We have developed a task with the aim of dissecting these components further (Rogers *et al*., 1999*a*). In the 'Gamble' task, subjects must initially make a fairly simple probabilistic decision, and must then gamble points on their confidence in this decision. A strength of the task is that all the information needed to make the decision and place the bet is visually presented on the screen, and each trial is relatively independent of the last; hence, working memory and learning processes are minimized. The task also aims to dissociate motor impulsivity from genuine risk-taking behaviour: the bets are presented in both ascending and descending series, and therefore in the ascending condition, subjects must suppress their response to place a higher bet. Using the 'Gamble' task we have demonstrated that patients with OBF cortex damage show impaired quality of decision making (choosing the likely outcome on fewer trials), deliberate for longer about their decisions and bet reduced amounts (Rogers *et al*., 1999*a*). Patients with dorsolateral (DL) and dorsomedial (DM) prefrontal lesions behaved similarly to controls on the task (Rogers *et al*., 1999*a*).

The Bechara *et al*. and Rogers *et al*. investigations of decision-making cognition in frontal patients have both been limited in several ways. In particular, patient groups with damage including OBF cortex rather than restricted to OBF cortex have been studied. In the case series examined by Bechara *et al*. (1994, 1996, 1998), the lesion overlap between patients was greatest in the medial orbitofrontal region, but lesions extended in several patients to anterior dorsolateral cortex, cingulate gyrus and temporal pole. In the Rogers *et al*. (1999*a*) study, 10 patients with frontal damage including OBF cortex were compared with 10 patients with damage restricted to the DL and DM prefrontal cortex (PFC). To confirm the involvement of OBF cortex in decision making it is necessary to study patients with more focal lesions. The effect of lesion laterality has also been inadequately assessed: the Bechara group case series had mostly bilateral lesions, whilst the Rogers group had a mixture of unilateral and bilateral damage. A recent abstract from Tranel *et al*. (2000) has indicated that right-lateralized damage may preferentially affect decision-making processes. Finally, previous studies have overlooked the potentially confounding effects of psychiatric symptoms. Secondary mood disturbance (both depression and mania) is well-documented following frontal cortex damage (e.g. see Robinson *et al*., 1988) and may modulate decision-making processes independently of the organic damage, e.g. see Murphy *et al*., 2001).

The 'Gamble' task was subsequently adapted for use in functional neuroimaging. In the modified 'Risk' task (Rogers *et al*., 1999*b*), the subject must again choose between two mutually exclusive options, but the decision making and betting responses are now combined, and the level of reward associated with each bet is systematically pitted against the likelihood of reward. The larger reward is always associated with the least likely outcome to ensure an element of conflict, which was not an original feature of the Gamble task. A PET investigation in healthy subjects revealed significant activations associated with resolution of reward conflict in three foci in inferior frontal cortex: the anterior part of the middle frontal gyrus [Brodmann area (BA) 10], in the orbital gyrus (BA 11) and in the anterior portion of the inferior frontal gyrus (BA 47) (Rogers *et al*., 1999*b*).

The impetus for the present investigation was to compare decision-making cognition on the three tasks described above, in patients with unilateral lesions restricted to specific subregions of the prefrontal cortex. The modified Risk task (Rogers *et al*., 1999*b*) has not previously been used in brain-damaged patients. In order to refine the measurement of decision-making cognition, it is critical to compare directly the sensitivity and specificity of the tasks currently in use. The present study examined the effects of restricted OBF, DL and DM lesions on decision-making performance. A fourth group of patients with large frontal lesions involving both dorsal and ventral aspects of PFC was also examined. Patients with bilateral lesions or lesions extending outside of the frontal lobe were specifically excluded.

The second objective of the present study was to examine the effects of discrete damage to prefrontal subregions on other aspects of executive function. This would enable comparison of the OBF deficit profile with the impairments traditionally seen following frontal lobe damage, and also permit investigation of the relationship between decision making and other forms of executive function. Human lesion studies have robustly implicated PFC in the mediation of working memory (Owen *et al*., 1990, 1999; D'Esposito and Postle, 1999), planning (Owen *et al*., 1990; Morris *et al*., 1997), attentional set-shifting (Milner, 1963; Owen *et al*., 1991; Stuss *et al*., 2000) and verbal fluency (Borkowski *et al*., 1967; Stuss *et al*., 1998), and whilst neuroimaging research has suggested focal (and dissociable) activations within the PFC (e.g. Baker *et al*., 1996), there is a paucity of data on the

Table 1 *Characteristics of individual patients*

Subjects	Age (years)	Sex	Aetiology	Side	Years post-onset	Medication
Orbitofrontal						
C.E.	61	M	Excs. oligodendroglioma	L	12	Carbamazepine
M.B.	47	M	Haemorrhage	L	5	Phenytoin, folic acid
E.H.	44	F	Excs. meningioma	L	6	Carbamazepine
E.T.	49	F	Haemorrhage (AcoA)	R	3	Phenytoin
S.D.	39	F	Haemorrhage (AcoA)	L	2	Phenytoin
Dorsolateral						
A.D.	63	F	Infarct	L	5	Aspirin
S.H.	44	F	AVM	R	8	Phenytoin, lamotrigine
C.G.	52	F	Excs. oligodendroglioma	R	40	Aspirin, atenolol, oestrogens, carbamazepine
K.G.	64	F	Haemorrhage (AcoA)	R	2	None
Dorsomedial						
P.P.	59	F	Excs. meningioma	L	3	None
G.D.	46	F	Excs. oligodendroglioma	L	14	Phenytoin
S.J.	73	M	Infarction	L	4	Aspirin
D.T.	69	M	Infarction	R	4	Warfarin, simvastatim
J.T.	58	M	Excs. meningioma	L	5	None
Large						
M.M.	46	M	Haemorrhage (AcoA)	L	2	None
J.K.	53	F	Haemorrhage (AcoA)	R	3	Carbamazepine
D.R.	55	M	Excs. meningioma	R	2	None
M.K.	59	F	Excs. oligodendroglioma	R	2	None
C.P.	37	F	Haemorrhage (AcoA)	R	8	Sodium valproate

Table 2 *Subject characteristics [mean (SEM)]*

Group	*n*	Gender (M : F)	Age (years)	NART IQ
Orbitofrontal	5	2 : 3	47.8 (8.5)	119 (4.6)
Dorsolateral	4	0 : 4	55.7 (9.5)	120 (4.6)
Dorsomedial	5	3 : 2	61.0 (10.6)	111 (9.9)
Large lesion	5	2 : 3	50.0 (8.7)	115 (9.0)
Controls	13	6 : 7	52.7 (10.9)	116 (9.6)

effects of lesions to PFC subregions on these tasks (for recent exceptions, see Stuss *et al*., 1998, 2000). Neuroimaging research is unable to demonstrate the necessary involvement of an activated brain region for task performance, and whilst repetitive transcranial magnetic stimulation may have the capacity to induce highly localized 'transient lesions' in healthy subjects during cognitive task performance, repetitive transcranial magnetic stimulation is at present only effective at regions lying near the scalp and therefore cannot be used to stimulate inferior PFC. Human lesion research therefore remains particularly valuable as a means of assessing the role of PFC in cognition, and moreover, provides direct information useful for diagnosis and rehabilitation after brain damage.

Methods

Subjects

Patients were recruited from the CCNRP (Cambridge Cognitive Neuroscience Research Panel) at the MRC Cognition and Brain Sciences Unit (n = 18) and from the King's College Hospital in London (n = 1). The CCNRP is an accumulating database of volunteers with focal brain lesions. The study was approved by the Cambridge Local Research Ethics Committee and patients gave informed consent to participate. All patients had a single focal lesion, verified by MRI, confined to frontal structures. Lesion aetiology was mostly cerebrovascular haemorrhage or tumour resection (Table 1). Exclusion criteria were current/previous psychiatric diagnoses, colour blindness, neurological disease other than that determining inclusion in the study and history of diffuse brain damage.

Healthy control volunteers from the Cambridge area were obtained through an advertisement in the local newspaper and were paid. Controls were closely matched with patients for age and National Adult Reading Test (NART) (Nelson, 1982) estimate of premorbid verbal IQ (Table 2). There were no differences between frontal subgroups and controls in terms of age [$F(4,27) = 1.48$, $P = 0.235$] or NART score [$F(4,27) = 0.966$, $P = 0.442$].

Neuroradiological assessment

Eighteen patients received MRI scans of the brain, with 3D set acquisition in the coronal plane using a SPGR (spin gradient echo) T_1-weighted sequence and a T_2-weighted axial sequence. One subject had his lesion location determined from a previous MRI scan. MRI scans were interpreted by a neurologist with experience in structural neuroimaging (F.M.) and a senior neuroradiologist (N.A.) who were both blind to the experimental results. Lesions were traced using

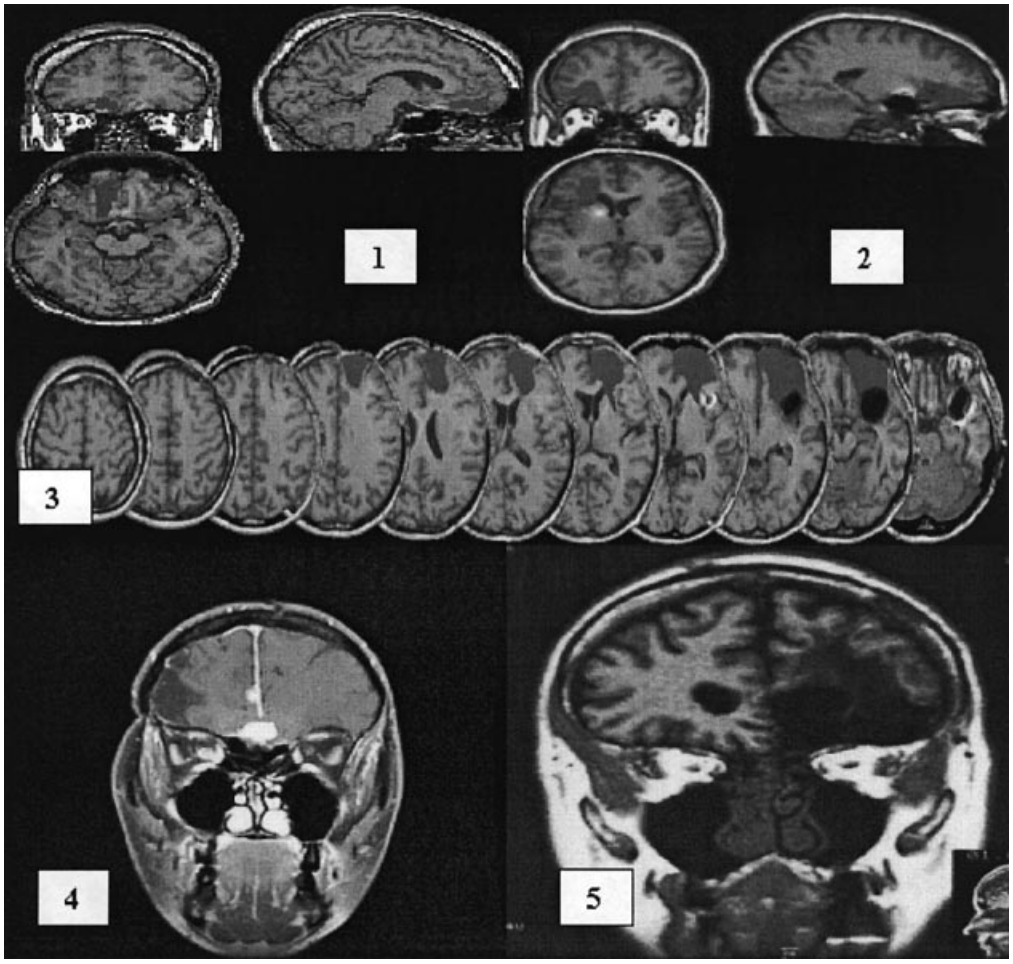

Fig. 1 Location of lesions in patients included in the OBF group. Patient 1: limited damage involving the left medial orbital surface, including the gyrus rectus. Patient 2: damage to the left inferior orbital PFC, including the orbital gyrus. Patient 3: cortical loss involving most of inferior right PFC including the gyrus rectus and orbital gyrus, but sparing the middle frontal gyrus in the middle surface and the cingulate gyrus on the medial surface. Patient 4: damage involving the left lateral orbital surface and extending laterally. Patient 5: damage involving the left orbital surface and extending along the centrum semiovale.

MRIcro v. 1.25 (available at http://www.psychology.nottingham.ac.uk/staff/cr1/mricro.html) and normalized to a standard template using SPM96 (statistical parametric mapping) (Friston *et al*., 1995) with cost function masking (Brett *et al*., 2002) to mask the lesion from the calculation of the normalization parameters. Lesions were then localized with standard atlases (Talairach and Tournoux, 1988; Damasio, 1995) and four groups were identified: five patients with discrete OBF lesions, four patients with discrete DL lesions, five patients with discrete DM lesions and five patients with lesions involving the ventral and dorsal areas of the prefrontal cortex (Large lesions group) (see Figs 1–4).

Neuropsychological testing

With the exception of verbal fluency, neuropsychological testing was computerized and run on a Datalux 486 PC with a 26.7 cm touch-sensitive monitor. Several tasks were taken from the Cambridge Neuropsychological Test Automated Battery (CANTAB) (CeNeS PLC, Cambridge, UK; Robbins *et al*., 1994, 1998). Testing lasted 3–4 h and was consequently split over two sessions at least 1 week apart. Patients were tested at home. Testing was administered in a fixed order, with the exception that the order of the Gamble and Risk tasks was counterbalanced across subjects.

Verbal fluency (Benton and Hamsher, 1976)

This is a traditional neuropsychological assessment in which subjects are required to generate as many words as possible beginning with the letters F, A and S, each in 1 min. Scores are summed across the 3 min. In the second part of this test subjects are asked to produce as many exemplars as they can from the semantic category 'Animals' in a period of 90 s.

Spatial span (CANTAB; Owen et al.*, 1990)*

This is a visuospatial short-term memory test based upon the Corsi Block Tapping Task (Milner, 1971). Subjects are shown a series of white boxes in a spatial array that change

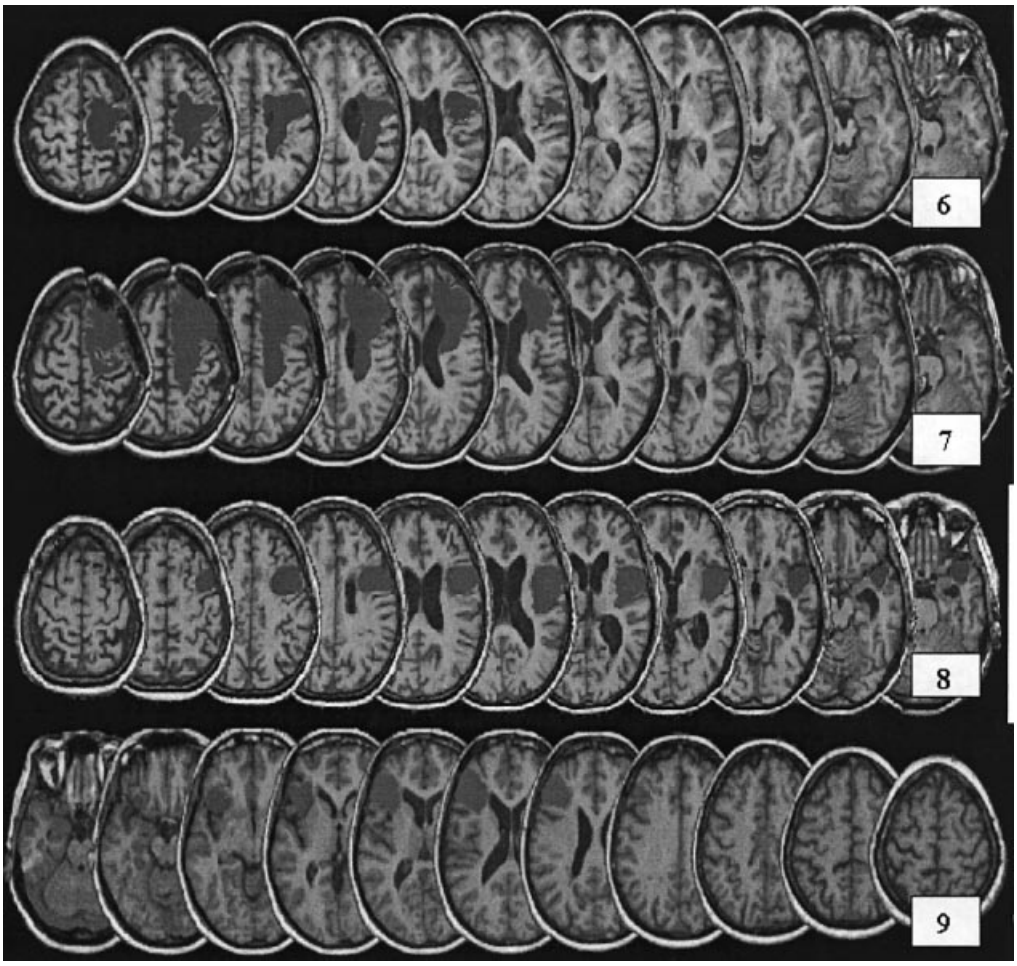

Fig. 2 Location of lesions in patients included in the DL group. Patient 6: area of cortical loss involving the right superior DL PFC. Medial areas are spared. Patient 7: large area of cortical loss involving the right superior DL PFC. Medial and polar areas are spared. Patient 8: limited damage to the right DL PFC. Patient 9: limited damage to the left DL PFC.

colour one by one. They must reproduce the sequence by touching the boxes in the same order that they changed colour. Sequence length increases from two to nine boxes; the task terminates if subjects make three errors at any one level. Dependent variables are the final level at which the subject correctly reproduces a sequence (i.e. the spatial span), and numbers of errors.

Pattern/spatial recognition memory (CANTAB) (Sahakian et al.*, 1988)*

In the pattern recognition task, two sets of 12 geometric patterns are displayed in a box in the centre of the screen for 3 s each. Subjects must look carefully at the patterns and try to remember them. In the test phase each pattern is presented alongside a novel pattern, and the subject must touch the recognized pattern. In the spatial recognition task, four sets of five white boxes are displayed at various positions on the screen, one box at a time. Subjects must remember the place on the screen where each box appeared. In the test phase, the boxes are presented again together with other boxes in novel locations; subjects must touch the box in the recognized location. Percentage correct responses and response latencies constitute the performance indices on both tasks.

Spatial working memory (CANTAB) (Owen et al.*, 1990)*

In this self-ordered working memory task, subjects must search through a series of boxes to find coloured tokens. Boxes yielding tokens must be marked mentally and avoided on subsequent trials. The task becomes more difficult as the number of boxes increases from three to four, six and eight. Dependent variables are between search errors (returning to boxes which have yielded tokens on previous trials) and a strategy score derived from the number of search patterns started from each box (where a low score indicates good use of strategy).

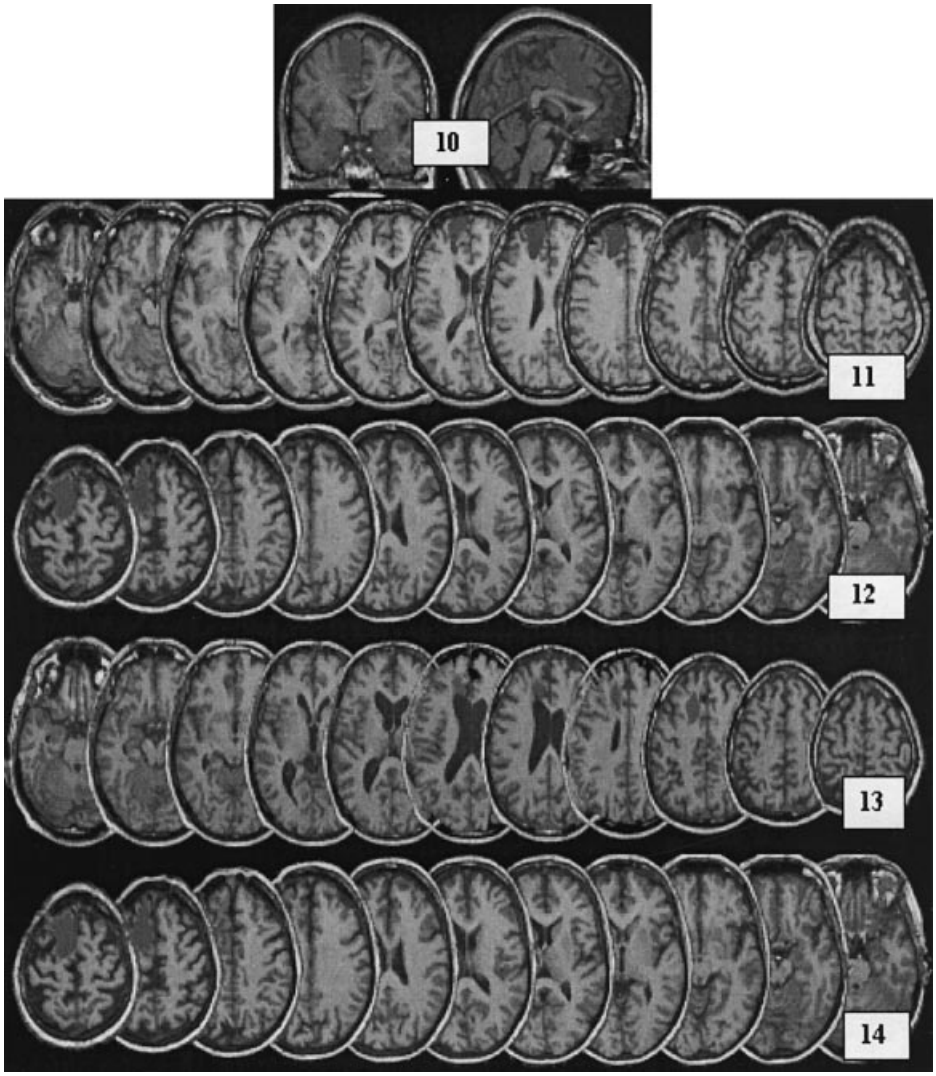

Fig. 3 Location of lesions in patients included in the DM group. Patient 10: damage involving the left superior frontal gyrus and cingulate gyrus. Patient 11: limited damage to the right cingulate gyrus. Patient 12: cortical loss involving the left superior frontal gyrus and the cingulate gyrus. Patient 13: limited damage involving the left cingulate gyrus. Patient 14: damage to the left superior frontal gyrus.

One-touch Tower of London (Owen et al.*, 1995)*

This is a test of planning in which subjects are presented with two arrangements of coloured balls, and must calculate how to move the balls in one arrangement to form the second arrangement. Problems vary in level of difficulty from one move up to five moves. Subjects are initially trained on the CANTAB version of the task where they must move the balls on the screen, one at a time. Then, in the 'one-touch' version of the task, they must calculate the number of moves in their head and then touch one of the boxes (numbered 1 to 5) at the bottom of the screen. The 'one-touch' version places higher demands on the forward-planning element of the task as subjects are forced to plan ahead. Performance indices are the number of problems solved at the first attempt, the mean number of attempts taken at each level of difficulty (1–5), and the latency to respond (deliberation time).

Three dimensional attentional-set shifting

This modified version of the intra-dimensional/extra-dimensional shift (ID-ED) task from the CANTAB battery (Downes *et al*., 1989) incorporates an additional (third) dimension (Rogers *et al*., 2000). Subjects make a series of visual discriminations passing through eight stages. Six consecutively correct responses advances the subject to the next stage, whilst failure to reach the criterion within 50 trials causes task termination. The task deconstructs components of the Wisconsin Card Sort Test, but is fundamentally similar in that subjects must discriminate stimuli on the basis of colour, shape or number of components. At reversal stages (stages 2, 4, 6, 8), subjects must shift responding to the other exemplar within a dimension (e.g. red to blue within the dimension of colour). At the intra-dimensional shift (IDS) stage, new stimuli are introduced but the correct dimension (e.g. colour)

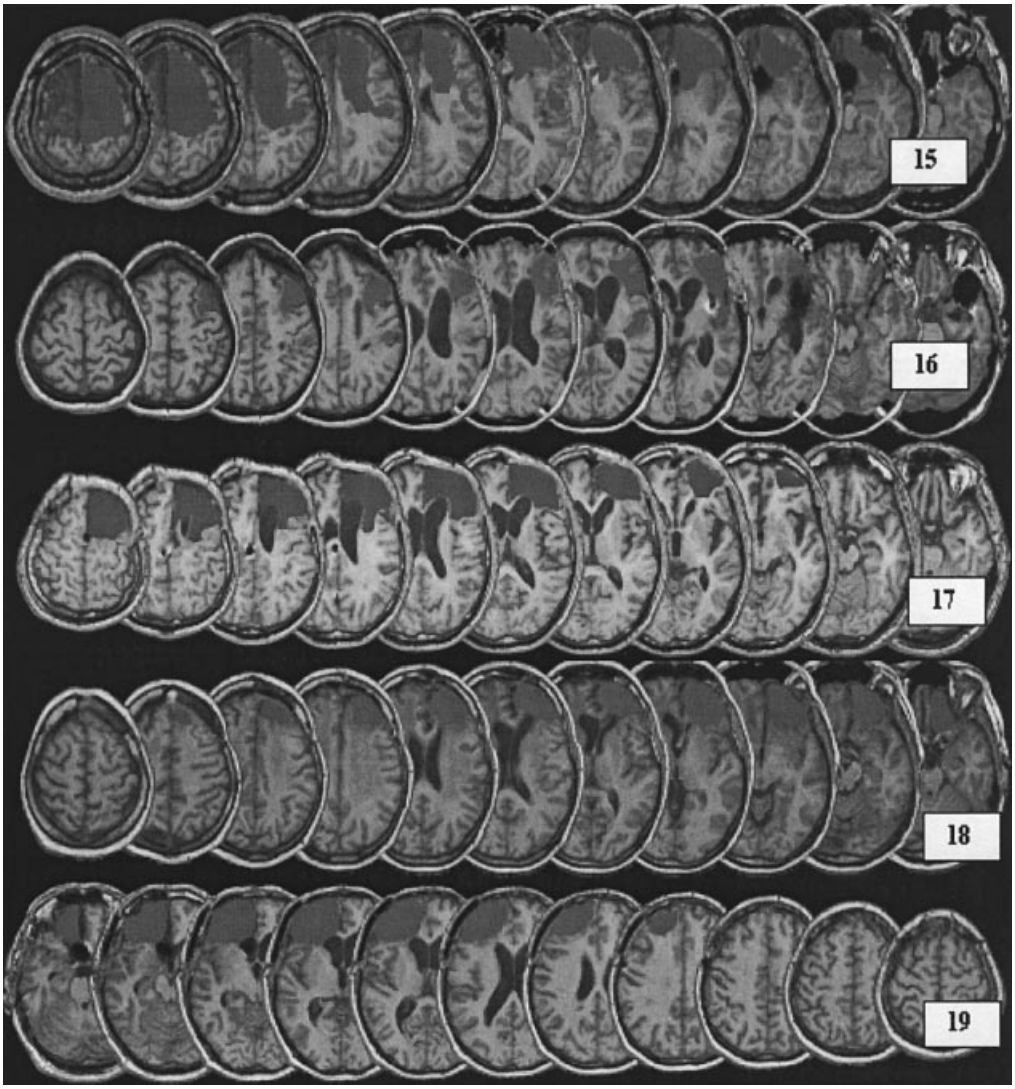

Fig. 4 Location of lesions in patients included in the large frontal lesions group. All patients have lesions involving ventral and more posterior areas of the prefrontal cortex.

remains the same. At the extra-dimensional shift (EDS) stage, new stimuli are introduced and subjects must shift responding to a new dimension (e.g. colour to shape). Dependent variables are the number of stages passed, and the number of errors at reversal stages (combined), IDS and EDS.

Decision making tasks

Iowa Gambling Task (Bechara et al.*, 1994)*

Here the subject is required to sample repeatedly from four decks of cards (A–D). Each card selection results in the subject winning an amount of money, while after some selections subjects also lose an amount of money. Decks A and B are characterized by large wins ($100 on each trial) but occasional large punishments (e.g. $1250 on deck B), such that subjects lose money over repeated choices. Decks C and D are associated with smaller wins (only $50 per trial) but smaller losses, so that subjects make a profit over repeated choices. The main dependent variable on the task is the number of choices from decks A and B, the risky decks.

Gamble task (Rogers et al.*, 1999*a*)*

Subjects are presented with a display of a mixture of 10 red and blue boxes, and must decide whether they think a yellow token is hidden under a red box or a blue box. This is a relatively simple probabilistic decision, and the ratio of red to blue boxes (9 : 1, 8 : 2, 7 : 3, 6 : 4) varies from trial to trial in a randomized manner. Token location is pre-specified and pseudo-randomized; hence the probability of the subject choosing correctly is independent on each trial. The subject indicates his decision by touching a response panel marked either ‘red’ or ‘blue’. After making this initial choice the subject attempts to increase a points score by placing a bet on

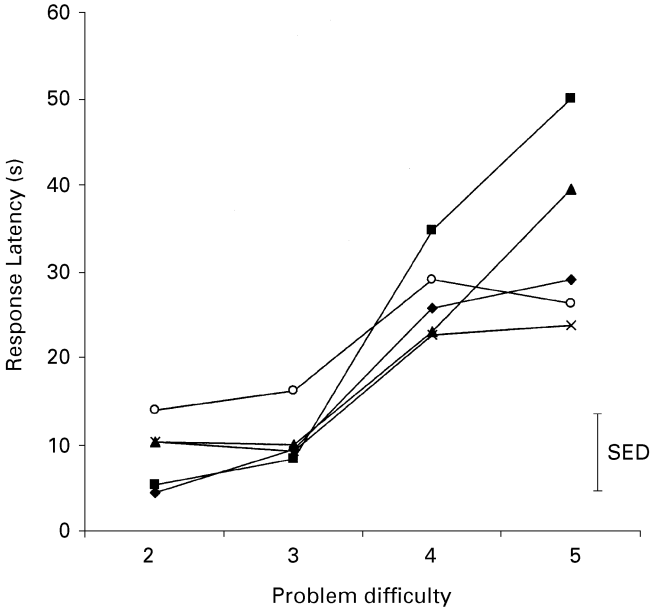

Fig. 5 Deliberation times on the One-touch Tower of London task in frontal subgroups, by level of difficulty (two to five move problems), in controls (filled diamonds), OBF (filled squares), DL (filled trianges), DM (crosses) and Large lesion groups (open circles). SED = standard error of the difference between means.

their confidence in their decision being correct. Possible bets are presented by the computer in a sequence (either ascending or descending) of 5, 25, 50, 75 and 95% of the points available at the time of the decision. Each bet is displayed for a period of 5 s before being replaced by its successor, and subjects must touch the box when they feel the displayed amount is an appropriate bet. Following bet selection, the token location is revealed, accompanied by either a 'You win!' message and a short rising musical scale, or a 'You lose!' message and a low tone. Correct choices increase the points total by the amount bet whilst incorrect choices decrease the points total by the amount bet.

The task enables the probabilistic element of decision making to be dissected from the risk-taking element, as the choice and bet responses are separate. Deliberation times (to make the decision) are also assessed as a third dependent variable. The three variables may each interact with the ratio of red to blue boxes: at the 9 : 1 ratio, subjects should pick the likely outcome more consistently, be more confident in their decisions and hence bet more, and may deliberate less, in comparison with trials at the 6 : 4 ratio. Furthermore, comparison of ascending and descending conditions enables impulsive behaviour to be separated from genuine risk-taking behaviour (genuine risk takers must inhibit motor responding for many seconds in the ascending condition).

Risk task (Rogers et al.*, 1999*b*)*

This task is similar to the Gamble task described above, with the core difference being that there is a fixed bet available with each choice of box colour, and these bets vary with the box ratio across trials. The subject is told that the computer has hidden a token inside one of six red or blue boxes and the subject must decide whether the token is hidden inside a red box or a blue box. The gamble is now intrinsic to the decision made; for example, there may be a 4 : 2 ratio of red to blue boxes, with a gamble of 10 points for choosing red and 90 points for choosing blue (the gamble is displayed in each response panel). If the subject correctly chose red he would win only 10 points but a wrong decision would only lose 10 points. Correct choice of blue would win the subject 90 points whereas a wrong decision would lose 90 points. Whilst the token is more likely to be hidden under a red box, will the subject be tempted into choosing blue by the higher reward at stake? It is emphasized to subjects that choices might involve either conservative or risk-taking behaviour, and that they should try to maximize profits from an initial loan of 100 points. The ratio of coloured boxes (5 : 1, 4 : 2 and 3 : 3) and the balance between the associated rewards (10 vs 90, 20 vs 80, 30 vs 70, 40 vs 60 and 50 vs 50) varies independently from trial to trial according to a fixed pseudo-random sequence. This sequence ensures that each balance of reward and ratio of coloured boxes co-occurs an equal number of times, with the restriction that on all trials with an unequal ratio of red and blue boxes (i.e. 5 : 1 or 4 : 2), the larger reward was always associated with the least likely outcome (i.e. the colour with the fewest number of boxes), thus capturing the conflict inherent in risk-taking situations. Speed of decision making and percentage choice of most likely outcome were assessed at each reward value, for the 4 : 2 and 5 : 1 ratios only (the 3 : 3 ratio is not analysed as neither choice is more or less likely).

Statistical analysis

Test scores in Tables 3 and 4 are presented as means with standard errors of the mean. Effects were considered significant at $P < 0.05$, using two-tailed tests. Raw data were tested for conformity to the normal distribution using the Kolmogorov–Smirnov test. Scores were transformed to reduce skewness where normality was violated {latency scores were subjected to the logarithmic transformation [log 10 (latency)] and proportion scores to the arcsine transformation [2arcsine (proportion score)]; see Howell, 1997}. Core dependent variables for each task were subjected to two sets of analyses. First, an independent samples *t*-test was used to compare the combined frontal patient group with controls, to examine the comparability of the present study group with the traditional literature on frontal lesions. Secondly, a one-way ANOVA (analysis of variance) (unweighted means) compared the five groups (four frontal subgroups and controls). Assessment of performance on Gamble and Risk tasks was based on published work (Rogers *et al.*, 1999*a*, *b*), thus all comparisons were regarded as 'planned' and investigated using Helmert orthogonal linear contrasts, in addition to *post hoc* tests. Simple effects were examined on the other tasks

Table 3 *Neuropsychological performance on executive and mnemonic tasks in the frontal subgroups and controls [mean (SEM)]*

	Controls	OBF	DL	DM	Large
Verbal fluency (F, A, S)	45.6 (1.64)	40.6 (3.79)	37.3 (12.5)	30.2 (3.57)	31.8 (7.32)
Spatial span					
Span score	5.22 (0.36)	5.50 (0.50)	4.67 (0.88)	4.20 (0.37)	5.00 (0.45)
Total errors	12.8 (1.79)	10.0 (1.00)	11.3 (2.60)	10.2 (1.85)	14.6 (1.81)
Pattern recognition (%)	79.6 (5.70)	95.0 (1.56)	73.6 (13.2)	80.8 (3.39)	79.2 (3.73)
Spatial recognition (%)	78.3 (3.23)	80.0 (2.74)	73.3 (1.67)	78.0 (6.04)	53.0 (8.31)
Spatial working memory					
Between search errors	28.1 (5.15)	19.6 (8.12)	54.3 (9.41)	36.6 (8.42)	58.4 (2.04)
Strategy score	34.3 (0.71)	29.8 (2.52)	38.8 (0.85)	32.8 (2.08)	40.6 (1.44)
One-touch Tower of London					
Optimal solutions	13.8 (0.62)	13.8 (0.49)	10.0 (1.78)	9.80 (1.62)	9.20 (0.97)
Mean attempts (four move problems)	1.25 (0.095)	1.30 (0.15)	1.63 (0.22)	1.80 (0.24)	1.80 (0.24)
Mean attempts (five move problems)	1.25 (0.095)	1.25 (0.14)	2.25 (0.40)	2.00 (0.21)	2.20 (0.14)
ID-ED task					
IDS errors	1.00 (0.13)	2.20 (2.20)	0.67 (0.33)	0.40 (0.24)	1.25 (0.25)
EDS errors	4.18 (0.85)	3.60 (1.25)	2.67 (0.67)	3.00 (1.26)	13.5 (3.50)
Reversal errors (summed)	5.18 (0.46)	9.60 (4.41)	5.00 (0.58)	13.6 (4.50)	10.8 (6.45)

using *post hoc* comparisons (Tukey's HSD), where the main effect of group was significant. In the figures, the index of variation used is not the standard error of the mean, but the standard error of the difference of the means, which is appropriate when one is interested in the (within-subjects) relationship between variables rather than the variables themselves. This is calculated by the formula from Cochran and Cox (1957):

$$(\mathrm{MSe}/n_1) + (\mathrm{MSe}/n_2) + (\mathrm{MSe}/n_3). \ldots,$$

where MSe is the mean square error of the interaction term, and n is the number of subjects per group.

Results

Neuropsychological tests

Verbal fluency

The combined frontal group was significantly impaired at letter fluency (F, A, S) [$t(26) = 2.13$, $P = 0.046$] but not category fluency (Animals) [$t(26) = 1.46$, $P = 0.156$]. There was no statistically significant difference among the four frontal subgroups and controls on letter fluency [$F(4,23) = 1.63$, $P = 0.201$] or category fluency [$F(4,23) = 1.36$, $P = 0.277$].

Pattern and spatial recognition

Pattern recognition performance (percentage correct) was not significantly impaired in either the combined frontal group [$t(25) = 0.600$, $P = 0.558$] or the five subgroups [$F(4,22) = 1.61$, $P = 0.208$]. There was similarly no effect on pattern recognition response latency (both $P > 0.10$). On spatial recognition (percentage correct), the combined frontal group were unimpaired relative to controls [$t(25) = 1.26$, $P = 0.219$] but subgroup effects were apparent [$F(4,22) = 4.76$, $P = 0.06$] due to poor performance of the Large group compared with the controls ($P = 0.007$), OBF group ($P = 0.011$) and DM group ($P = 0.021$). Both the OBF and DM subgroups performed very well, thus masking differences between controls and all frontals combined. Spatial recognition response latency was similar between frontals and controls ($P > 0.10$) and across subgroups [$F(4,22) = 2.36$, $P = 0.09$].

Spatial span

There were no significant differences between controls and combined frontals in their spatial span [frontal group mean 4.82 (SD 1.07), control mean 5.22 (SD 1.09); $t(24) = 0.895$, $P = 0.380$] or total number of errors [frontal mean 11.6 (SD 4.0), control mean 12.8 (SD 5.36); $t(24) = 0.38$, $P = 0.546$]. There were similarly no apparent differences across subgroups, [$F(4,21) = 1.08$, $P = 0.392$] and [$F(4,21) = 0.917$, $P = 0.472$], respectively (see Table 3).

Spatial working memory

The combined frontal group made more between search errors than the controls, but this was not significant because of the large variability in the data [frontals mean 41.6 (SD 21.7), control mean 28.1 (SD 15.4); $t(26) = 1.67$, $P = 0.108$]. When the five groups were compared (see Table 3) there was a significant difference between groups [$F(4,23) = 5.67$, $P = 0.003$]. *Post hoc* comparisons showed that the Large lesion group made more errors overall than controls ($P = 0.018$) and the OBF group ($P = 0.006$). The DL group also made more errors than the OBF group ($P = 0.026$).

There was no significant group difference between controls and the combined frontals for the strategy score [$t(26) =$

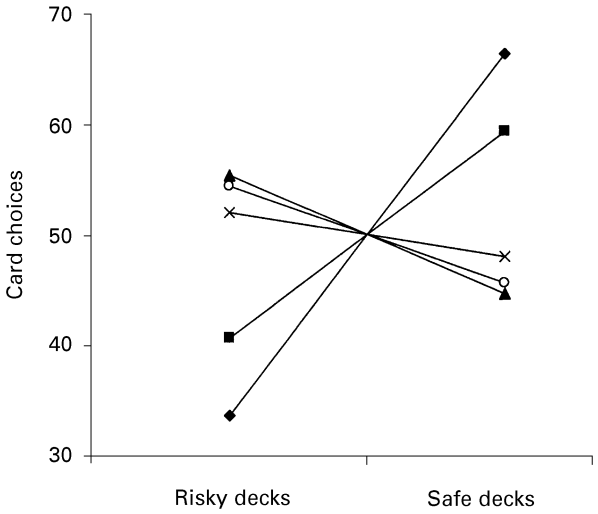

Fig. 6 Iowa Gambling Task performance in controls (filled diamonds), OBF (filled squares), DL (filled trianges), DM (crosses) and Large lesion groups (open circles).

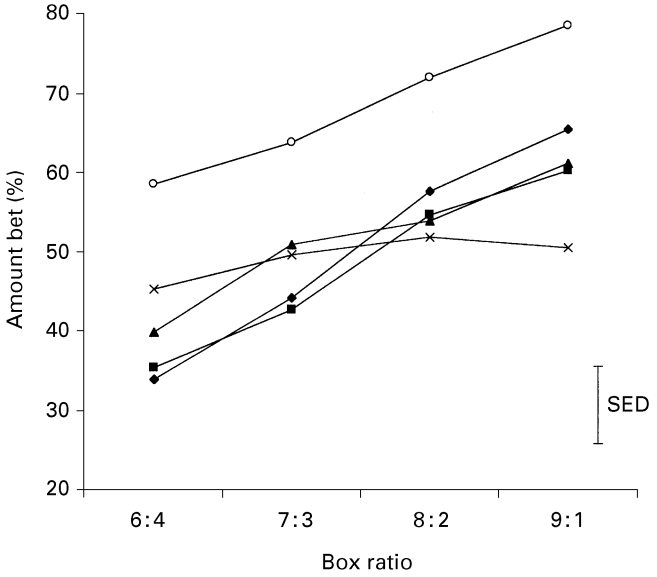

Fig. 7 Risk adjustment (percentage of current points total bet on each decision) on the Gamble task in controls (filled diamonds), OBF (filled squares), DL (filled trianges), DM (crosses) and Large lesion groups (open circles). Across all groups, subjects place higher bets with increasing box ratio. Patients with large frontal lesions place higher bets at all box ratios than the other groups. SED = standard error of the difference between means.

0.478, $P = 0.636$], but there was a significant difference between the five subgroups [$F(4,23) = 7.23$, $P = 0.001$), obscured in the combined frontal group because of the superior performance of the OBF and DM groups. The DL group were impaired relative to OBF group ($P = 0.009$), while the Large group were impaired relative to controls ($P = 0.036$), the OBF group ($P = 0.001$) and the DM group ($P = 0.018$).

One-touch Tower of London

The combined frontal group solved significantly fewer problems on the first attempt relative to controls [frontal mean 10.7 (SD 3.16), controls 13.8 (SD 1.75); $t(25) = 2.52$, $P = 0.018$], and this effect was also significant for the comparison across frontal subgroups and controls [$F(4,22) = 4.71$, $P = 0.007$] (see Table 3). The Large lesion group were impaired relative to controls ($P = 0.030$). Group by level of difficulty interaction terms were significant for both sets of analyses, [$F(4,100) = 3.72$, $P = 0.007$] for combined frontals, [$F(16,88) = 2.29$, $P = 0.008$] for subgroups, due to particular impairment in three frontal groups on the four and five move problems, which place greatest demands on forward planning. The mean number of attempts taken on five move problems was greater in the DL group relative to controls ($P = 0.008$), DM group relative to controls ($P = 0.041$) and Large group relative to controls ($P = 0.006$). The OBF group performed accurately on the task, and were significantly better than DL ($P = 0.017$) and Large ($P = 0.016$) subgroups on the most difficult problems. However, the OBF group specifically showed longer deliberation times on the task relative to the other groups (see Fig. 5). They took nearly twice as long as controls to solve the five move problems (50 s compared with 29 s), whilst the DM and Large groups performed similarly to controls (24 s and 26 s, respectively). The subgroup ANOVA was significant [$F(4,22) = 3.31$, $P = 0.029$] and the OBF group were impaired relative to controls ($P = 0.078$) and DM patients ($P = 0.039$).

Three-dimensional ID-ED set shifting

Four frontal patients failed to complete the task: one DL patient and three Large patients. The DL patient failed at compound discrimination, and the Large lesion patients failed at compound reversal, EDS and extra-dimensional reversal. The two patients failing the task prior to the EDS stage were excluded from analysis of errors at each stage (see Table 3). The combined frontal group were not significantly impaired at IDS [$t(26) = 0.221$, $P = 0.827$], EDS [$t(26) = 0.743$, $P = 0.464$] or summed reversal trials [$t(26) = 1.74$, $P = 0.093$]. However, analysis by location did reveal a significant difference across the frontal groups at the EDS stage [$F(4,23) = 6.73$, $P = 0.001$]: the Large group were impaired relative to all other subgroups ($P < 0.005$ for each comparison). There was no difference among the five groups at the IDS stage [$F(4,23) = 0.525$, $P = 0.718$] or at combined reversal stages [$F(4,23) = 1.36$, $P = 0.278$].

Decision making tasks

Iowa Gambling Task

The combined frontal group made significantly more selections from the risky decks than controls [$t(28) = 3.88$, $P <$

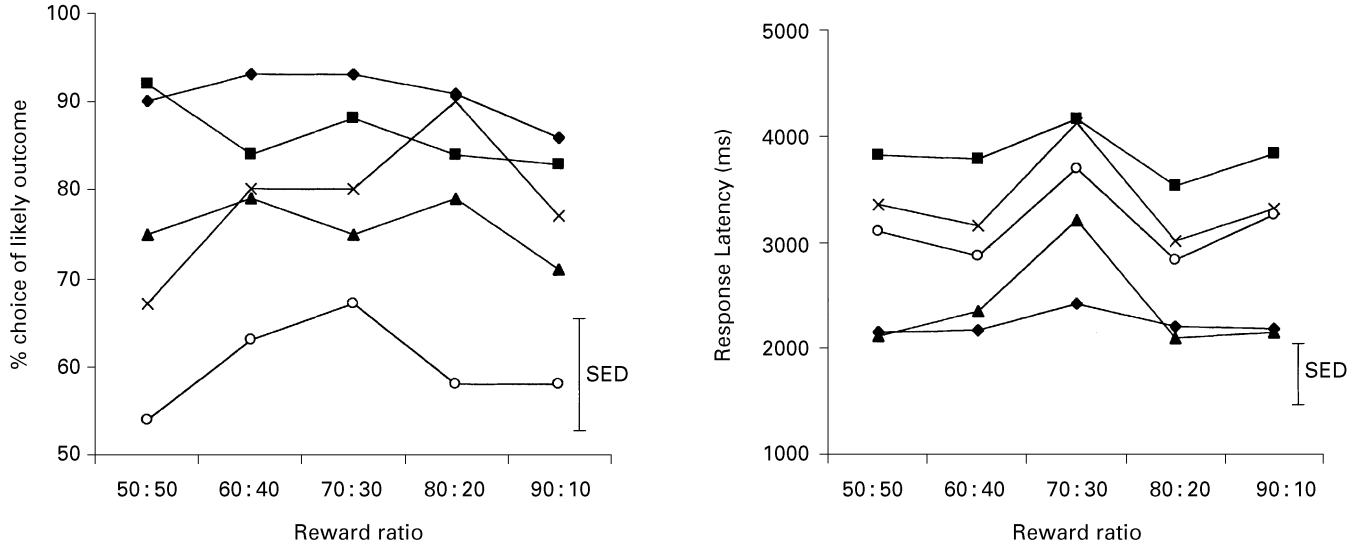

Fig. 8 Performance on the Risk task in controls (filled diamonds), OBF (filled squares), DL (filled trianges), DM (crosses) and Large lesion groups (open circles), at the 5 : 1 box ratios. Error bars represent standard error of the difference between means.

0.001] and there was a significant effect across the five subgroups [$F(4,25) = 5.42$, $P = 0.003$]. Three subgroups were impaired relative to controls: the DL group ($P = 0.037$), the DM group ($P = 0.030$) and the Large group ($P = 0.012$). These three groups made, on average, more choices from the risky decks than from the safe decks. The OBF group, in contrast, performed similarly to controls (see Fig. 6).

Gamble task

(i) Quality of decision making. The combined frontal group did not show poorer decision making than controls [$F(1,27) = 0.894$, $P = 0.353$], and there were no significant differences among the five subgroups [$F(4,24) = 0.636$, $P = 0.642$], although the DL and DM groups showed a tendency to make optimal choices less often than the OBF and Large groups (see Table 3). The main effect of ratio on the quality of decision making approached significance [$F(3,72) = 2.57$, $P = 0.07$], such that subjects were more likely to pick the likely outcome at higher ratios (i.e. 9 : 1 over 6 : 4), but there was no interaction of group by ratio.

(ii) Risk adjustment. There was a highly significant effect of ratio on the amount bet [$F(3,72) = 21.9$, $P < 0.001$], with larger ratios generally producing higher bets. There were no significant differences for either the combined frontals compared with controls, or among the five separate subgroups (both $P > 0.10$). There was also no significant interaction of group with ratio. However, the Large lesion group placed significantly higher bets than the other patient subgroups [Helmert contrast: $t(24) = 2.07$, $P = 0.049$] (see Fig. 7). All subjects placed larger bets in the descending compared with the ascending condition [$F(1,84) = 40.7$, $P < 0.001$], but group by condition (ascend versus descend) interaction terms were not significant for either analysis (both $P > 0.10$), thus impulsivity of responding did not differ between groups.

(iii) Speed of decision making. Deliberation time was marginally slower in the combined frontal group than controls [$F(1,27) = 3.42$, $P = 0.076$], but there were no differences among frontal subgroups [$F(4,24) = 0.810$, $P = 0.531$]. Deliberation time was only weakly affected by ratio ($P = 0.07$) such that subjects took longer to decide at lower ratios, but there was no interaction of group by ratio.

Risk task

A three-factor ANOVA model with box ratio as a two-level (5 : 1 vs 4 : 2, within-subjects) factor, reward proportion as a five-level (50 : 50, 60 : 40, 70 : 30, 80 : 20, 90 : 10, within-subjects) factor, and group as between subjects factor, revealed no differences between subgroups [$F(4,26) = 2.08$, $P = 0.112$] but a number of significant interaction terms: box ratio $\times$ group [$F(4,26) = 3.12$; $P = 0.032$]; box ratio $\times$ reward proportion [$F(4,104) = 2.81$; $P = 0.029$]; and group $\times$ reward proportion [$F(16,104) = 1.73$, $P = 0.05$]. Because subjects performed differently at the two box ratios [$F(1,26) = 3.32$, $P = 0.08$], separate ANOVAs for each ratio condition were conducted to elucidate the nature of the interaction effects. For the 5 : 1 box ratio, the combined frontal group was impaired relative to controls [$F(1,29) = 5.73$, $P = 0.023$], and there was an effect of subgroup [$F(4,26) = 2.79$, $P = 0.047$] due to the Large lesion group choosing the likely outcome less than controls ($P = 0.029$). There were no significant main effects of reward proportion or group by reward proportion interactions. For the 4 : 2 ratio, the combined frontal group chose the likely outcome less often [$F(1,29) = 4.78$, $P = 0.037$], but there were no differences among frontal subgroups [$F(4,26) = 1.51$, $P = 0.229$]. Although the choice

Table 4 *Cognitive performance on the decision-making tasks in frontal subgroups and controls [mean (SEM)]*

	Controls	OBF	DL	DM	Large
Iowa Gambling Task					
Choices from risky decks (A and B)	33.6 (3.51)	40.6 (5.30)	55.3 (6.96)	52.0 (2.72)	54.4 (4.32)
Gamble task					
% likely choice	90.6 (14.2)	92.2 (8.17)	81.5 (24.6)	81.5 (11.4)	89.1 (9.55)
% bet (of total)	50.3 (14.5)	48.2 (11.5)	51.4 (17.6)	49.2 (14.1)	68.2 (6.43)
Decision latency (ms)	2517 (1023)	3245 (1222)	3057 (860)	3165 (509)	3384 (1721)
Risk task					
4 : 2 ratio—% likely choice	86.3 (3.04)	77.5 (11.7)	67.5 (11.8)	78.1 (6.81)	67.6 (12.4)
4 : 2 ratio—decision latency (ms)	2563 (333.9)	4091 (1541)	2432 (715.8)	3570 (546.6)	3379 (1268)
5 : 1 ratio—% likely choice	90.5 (3.29)	85.9 (7.22)	75.9 (11.0)	78.7 (8.82)	60.0 (12.6)
5 : 1 ratio—decision latency (ms)	2220 (239.6)	3822 (1063)	2384 (605.2)	3388 (403.9)	3150 (827.9)

of the most likely outcome was reduced in the Large and DL compared with OBF and DM groups (see Fig. 8), these differences were not significant. There were no significant main effects of reward or group by reward interactions. The combined frontal group also deliberated longer before making decisions on the 5 : 1 box trials [frontals mean 3198 ms (SD 1455 ms), controls mean 2220 ms (SD 896 ms); $F(1,29) = 4.81$, $P = 0.037$], but this effect was not significant for the 4 : 2 box trials ($P = 0.199$), and there were no differences between the five subgroups on deliberation (both $P > 0.10$), although the OBF group deliberated longest at both box ratios (see Table 4).

Summary of findings on decision making tasks

Patients in the dorsomedial, dorsolateral, and large lesion groups selected more cards from risky decks than controls on the Iowa Gambling Task. This effect was also seen in the combined group of frontal patients. On the Gamble task, the group with large frontal lesions placed higher bets than the other groups, and the combined frontal group deliberated for longer. Quality of decision making did not significantly differ among the groups. On the Risk task, the Large lesion group again showed risk taking behaviour, choosing the less likely, but higher rewarding, outcome more often than controls. This effect was also seen in the combined frontal group, who also deliberated for longer over decisions.

Discussion

The present investigation is the first to compare directly three decision-making tasks in patients with focal damage to prefrontal subregions. One, the Iowa Gambling Task, has well-established sensitivity to medial orbitofrontal cortex damage. Two further tasks developed in this laboratory attempt to fractionate the component processes of the Iowa Gambling Task, and control for the working memory and learning processes inherent in that task by employing a visual format where all the information required to make the decisions is explicitly presented to subjects. A group of patients with large lesions to frontal cortex was impaired on all three decision-making tasks: they selected more cards from risky decks on the Iowa Gambling Task, they placed higher bets on simple probabilistic decisions on the Gamble task and they chose the less likely, but more rewarding, option more frequently on the Risk task. However, a surprising and important finding was that a group of patients with unilateral lesions restricted to orbitofrontal cortex performed similarly to controls on all three tasks.

Neuroradiological assessment of lesion location in the 19 patients tested identified four groups: an OBF group, a DM PFC group, a DL PFC group and a group with large frontal pathology involving both ventral and dorsal cortex. Performance on a neuropsychological battery including executive and mnemonic measures as well as the three decision-making tasks was examined across the frontal subgroups, but a second analysis of the combined frontal patients was also performed to assess comparability with previous data on frontal damage. Our combined frontal group was significantly impaired on verbal fluency and One-touch Tower of London, consistent with previous findings (Borkowski *et al*., 1967; Shallice, 1982). The combined group also showed impaired decision making on the Iowa Gambling Task and the Risk task, and deliberated for longer on both the Gamble and Risk tasks. The OBF group was remarkably unimpaired on this wide-ranging test battery. Indeed, the superior performance of the OBF group appears to have masked effects in the combined frontal group on spatial recognition memory and spatial working memory. The only cognitive abnormality seen in the OBF group was lengthened deliberation times on several tasks. While this effect was relatively specific to the OBF group on the One-touch Tower of London task (where the other groups, if anything, deliberated less than controls), lengthened deliberation times on the Gamble and Risk tasks were seen in all frontal subgroups.

Patients with selective dorsomedial damage chose more cards from risky decks on the Iowa Gambling Task than controls, but no deficits were revealed on the Gamble or Risk tasks. The DM group was also impaired at forward planning on the One-touch Tower of London task, but performed well on spatial recognition, spatial span and spatial working

memory tasks. Patients with DL PFC lesions displayed Iowa Gambling Task and One-touch Tower of London impairments, but additional deficits were apparent on spatial working memory and a novel task measuring attentional set-switching. Finally, the group with large prefrontal lesions showed impairment across a broad range of the tasks, including spatial recognition memory, spatial working memory, One-touch Tower of London and ID-ED attentional set-shifting, as well as the three decision-making tasks. Effects in the large lesion group included those not apparent in the combined frontal analysis, as subjects with discrete lesions performing the tasks adequately would dilute effects in a combined group. This clearly highlights a potential confound in previous studies using mixed groups of frontal patients with varying lesion foci and lesion aetiologies, and could explain inconsistencies across reports.

Prefrontal contributions to decision making

The patients with large lesions were the only group to show impaired decision making on the Gamble and Risk tasks. Their profile of performance on the Gamble task resembled that of patients with fvFTD (frontal variant frontotemporal dementia) (Rahman *et al*., 1999) and aneurysmal subarachnoid haemorrhage of the anterior communicating artery (AcoA) (Mavaddat *et al*., 2000). Both of these groups also typically have rather diffuse frontal pathology, albeit preferentially affecting the ventral aspects. The Large lesion, fvFTD and AcoA patients all placed higher bets under both ascending and descending conditions, thereby demonstrating genuine risk-taking behaviour. Our finding that patients with selective damage either to OBF or to DL or DM PFC did not also behave like this suggests that the size of the lesion may be critical, and that damage to both dorsal and ventral prefrontal systems is necessary to disrupt decision making. The Large lesion group was also impaired at the Iowa Gambling Task, but so too were the DL and DM patients. The Iowa Gambling Task requires a number of extraneous cognitive processes that are not involved in the Gamble task, for example, working memory for the bad decks, and the assimilation of reward–punishment information into a successful response strategy. Whereas Bechara *et al*. (1998) demonstrated gambling task impairments in the presence of intact working memory, our DL patients were impaired at a specific test of working memory, which may contribute to their deficit on the Iowa Gambling Task task. Likewise, the DM group were deficient at the One-touch Tower of London task, which may resemble the Iowa Gambling Task in requiring prospective consideration of the outcomes of responses. In conclusion, we do not consider the evidence for a localized dorsolateral or dorsomedial PFC contribution to decision making to be compelling.

While an intuitive explanation of the present data might be in terms of lesion size or 'mass action' (e.g. the OBF group showed mainly intact performance due to having the smallest lesions), it can be seen from Figs 1–4 that this was clearly not the case. The DM group, which showed clear cognitive impairment, had the smallest lesions. The only effect seen in the OBF group was lengthened deliberation times in planning and a tendency towards longer response latencies on the Gamble and Risk tasks. Rogers *et al*. (1999*a*) reported that OBF patients show lengthened deliberation time on the Gamble task, although in the presence of altered quality of decision making and betting. Murphy *et al*. (2001) also showed that manic patients deliberated longer on difficult decisions. Although it is difficult to interpret precisely, increased deliberation clearly indicates that OBF damage is not merely associated with motor impulsivity, which would be expected to reduce deliberation. The role of OBF cortex in inhibitory control is likely to be multifaceted. One possibility that we are unable to rule out is that the retarded latencies reflect an incipient deficit in decision making, which is compensated by lengthened deliberation.

Our finding that patients with selective OBF lesions displayed intact quality of decision making and appropriate risk-taking behaviour across three tasks assessing such performance was unexpected, and apparently contrasts with previous reports by Bechara *et al*. (1994) and Rogers *et al*. (1999*a*). While the group sizes in the present study were admittedly small, patients with discrete OBF damage are unusual, and our group sizes are comparable with the other studies in the field (Bechara *et al*., 1994, 1996; Stuss *et al*., 2000). Impairments were detected on the tasks in at least one of the other frontal groups, and thus lack of test sensitivity or statistical power does not seem the most obvious explanation. To reconcile our data with the previous studies, it should first be noted that on the basis of the stringent inclusion criteria in the present study, many of the patients used in the studies by Bechara *et al.* and Rogers *et al.* would have been categorized in our Large lesion group, for which significant decision-making impairments were evident. For example, Damasio's patient (E.V.R.) with acquired sociopathy had a large bilateral lesion involving the entire right OBF and extending to medial and dorsolateral areas. In the Bechara *et al*. case series, the medial OBF cortex represented only the area of lesion overlap between all the patients. Similarly, of the 10 OBF patients studied by Rogers *et al*. (1999*a*), six also had damage extending outside OBF.

Secondly, laterality of the lesion may be crucial: whilst the Bechara *et al.* patient series had bilateral lesions, four of the five patients in the OBF group in the present study had a left-sided lesion, whilst four of the five patients in the Large group, with decision-making deficits, had right-sided lesions. A recent abstract by Tranel *et al*. (2000) also highlights the importance of laterality in patients with unilateral damage: Iowa Gambling Task impairment was observed in patients with right, but not left, ventromedial PFC damage. Whilst our single patient with a right-sided OBF lesion did not seem anomalous compared with the rest of the group, a laterality effect is also consistent with the PET imaging study by Rogers *et al*. (1999*b*), which demonstrated predominantly right-sided OBF activation associated with resolution of

reward conflict on the Risk task. In the Rogers *et al*. (1999*a*) lesion study, which also demonstrated OBF-associated decision-making impairments, one patient had a bilateral lesion, while four of the unilateral lesions were right sided. Patients with selective OBF damage are very unusual and a multi-centre or meta-analytic approach may be required to confirm the laterality effect suggested by these data.

There are at least two further factors that may contribute to differences between the present data and the previous studies. In the Bechara *et al*. investigations, patients were only included if they demonstrated real-life decision-making deficits. The extent to which their findings generally apply to the cognitive sequelae of OBF damage therefore remains unclear. Finally, in the present study subjects were screened for psychiatric symptomatology which, if present, led to exclusion. The emergence of affective syndromes secondary to lateralized frontal pathology is well documented: left-sided lesions are associated with depressive symptomatology and right-sided lesions are (less commonly) associated with secondary mania (Robinson *et al*., 1988). Decision-making deficits (on the Gamble task) have been demonstrated as state effects in patients with ('primary') mania and depression (Murphy *et al*., 2001). In neurological patients, although one may argue that the decision-making impairment and mood disorder may both be the result of the frontal pathology, it is equally possible that the mood disorder itself has caused the decision-making impairment. Previous studies have not reported psychiatric status in the frontal patients and may consequently be confounded by affective syndromes.

Other executive function deficits in patients with focal prefrontal damage

Investigation of the effects of frontal lesions on other neuropsychological measures enables the specificity of the decision-making deficits to be assessed. The Iowa Gambling Task in particular has working memory, contingency learning and possible set-shifting components, which are tapped separately by the present test battery. The self-ordered spatial working memory and One-touch Tower of London tests both require strategic choice among different candidate response sequences, although each sequence or 'search' is associated with only a single goal, rather than the need to evaluate the balance between probabilistic outcomes and variable reward magnitudes as in the three decision-making tasks. Large frontal lesions significantly impaired spatial working memory strategy scores and One-touch Tower of London performance, as well as performance on the Iowa Gambling Task. The more focal DL and DM lesions also impaired One-touch Tower of London performance, but only the DL lesion affected self-ordered spatial working memory. Thus, only a limited dissociation from the Iowa Gambling Task was found. However, these findings do not necessarily contradict the data of Bechara *et al*. (1998), which show a dissociation between their task and spatial working memory performance, as performance on the spatial span task was intact in our Large, DL and DM groups. The greater sensitivity of the self-ordered spatial working memory task, which has been associated with ventrolateral and DL PFC foci from a PET study (Owen *et al*., 1996), is probable because it contains an additional strategic element (Owen *et al*., 1990; Robbins, 1996), which was not a major component of the delay tasks used by Bechara *et al*. (1998). However, the findings do raise the possibility that (impaired) executive processes may contribute to performance on tasks with decision-making cognition. This would be at least partly consistent with the conclusions of a recent meta-analytical review of functional imaging data, implicating a network of mid-dorsolateral PFC, mid-ventrolateral PFC and anterior cingulate foci that contribute to a broad range of cognitive functions including working memory, problem solving, episodic memory, control processes and response selection (Duncan and Owen, 2000). Finally, only the patients with large frontal lesions were also impaired at attentional set-shifting. The deficit was specific to the extra-dimensional shift stage of the ID-ED task, which is fully consistent with previous findings that frontal patients with regionally heterogeneous lesions were significantly impaired in their ability to shift response set to a previously irrelevant dimension (EDS), but not in shifting attention to novel exemplars of the same dimension (IDS) (Owen *et al*., 1991). From our data, there is clearly no reason to link the Iowa Gambing Task deficit to a shifting impairment *per se*, and this is consistent with a previous report of dissociated performance on the Iowa Gambling Task and the Wisconsin Card Sort Test in Patient E.V.R. (Damasio, 1994).

Conclusions

Patients with restricted, predominantly left-sided, OBF cortex damage performed at control levels on a range of cognitive tasks assessing decision making, working memory, planning and attentional shifting. These results seem to contradict previous findings using decision-making tasks, but may be explained by possible laterality effects and the focal nature of these lesions compared with those of previous studies. In contrast, patients with large frontal lesions and selective DL lesions were impaired across a range of tasks requiring working memory, planning, and attentional shifting. Patients with large frontal lesions placed higher bets and made less rational decisions on two recently developed decision-making tasks. Of the three decision-making tasks employed in the present study, the Iowa Gambling Task appears to be the most sensitive, but may detect impairment on the basis of its extra load on working memory and associative learning in addition to its capacity for measuring decision making that involves risk taking.

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