

Impulsivity, time perception, emotion and reinforcement sensitivity in patients with orbitofrontal cortex lesions

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Summary

Damage to the orbitofrontal cortex (OFC) in humans has been associated with disinhibited or socially inappropriate behaviour and emotional changes. Some of the changes may be related to difficulty in responding correctly to rewards and punishers, in that these patients have difficulty in learning to correct their choice of a visual stimulus when it is no longer associated with reward. We extend this fundamental approach by investigating the relationship between frontal dysfunction and impulsive behaviour, the behavioural, emotional and personality changes seen in patients with prefrontal cortex damage, and thus in addition illuminate the cognitive and biological processes that are impaired in impulsive people. OFC patients ($n = 23$) performed more impulsively on both self-report and cognitive/behavioural tests of impulsivity, reported more inappropriate 'frontal' behaviours, and performed worse on a stimulus–reinforcement association reversal task, than non-OFC prefrontal cortex lesion control ($n = 20$) and normal control ($n = 39$) participants. Further, OFC patients experienced more subjective anger than non-OFC and normal participants, and less subjective happiness than normals; and had a faster subjective sense of time (overestimated and

underproduced time intervals) than normal controls, while non-OFC patients did not differ from normals. Finally, both OFC and non-OFC patients were less open to experience than normal participants. There were no differences between OFC patients, non-OFC lesion patients and normal controls on all other personality traits, most notably extraversion. In a spatial working memory task, the non-OFC group, most of whom had dorsolateral prefrontal cortex lesions, were impaired in that they repeatedly returned to previously chosen empty locations ('within errors'), whereas OFC patients were not impaired on this measure. Thus there is a dissociation between the effects of OFC damage which does not affect this measure of spatial working memory but does affect impulsive and inappropriate behaviour, reversal, personality, time perception and emotion; and dorsolateral prefrontal cortex damage which does affect this measure of spatial working memory, but not impulsive and inappropriate behaviour, reversal, personality, time perception and emotion. The effects of OFC damage on impulsive and related behaviours described here have implications for understanding impulsive behaviour.

Keywords: impulsivity; time perception; emotion; personality; orbitofrontal cortex

Abbreviations: ACA = anterior communicating artery; BIS = Barrat Impulsiveness Scale; DLFC = dorsolateral prefrontal cortex; MCA = middle cerebral artery; MFFT = Matching Familiar Figures Test; OFC = orbitofrontal cortex; PFC = prefrontal cortex; SWM = spatial working memory

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Introduction

Damage to the ventral prefrontal cortex (PFC) has been associated with disinhibited or socially inappropriate behaviour and misinterpretation of peoples' moods (Damasio,

1994; Rolls *et al.*, 1994; Hornak *et al.*, 1996). Some of the changes may be related to difficulty in responding correctly to rewards and punishers, in that these patients have difficulty in

Table 1 Lesion sites (classified according to the three main subdivisions of PFC) and aetiology

Patient	Orbital	Medial	Dorsolateral	Aetiology of lesion
	BA: 10, 11, 12, 25	BA: 8, 9, 10	BA: 9, 46	
Patients with OFC damage				
R.M.	++			ACA aneurysm and subarachnoid haemorrhage
J.A.	++	++		Meningioma
S.R.*	++	R	R	TBI
C.B.*	++	++	++	TBI
AL*	++	++	++	TBI
M.A.	++	++	++	ACA aneurysm and subarachnoid haemorrhage
E.O.*	++	++	++	TBI
R.Q.	R			ACA aneurysm and subarachnoid haemorrhage
T.R.	R			Meningioma
O.I.	R	R		ACA aneurysm and subarachnoid haemorrhage
B.Q.	R	R		Epileptic focus
R.R.	L	L		ACA aneurysm and subarachnoid haemorrhage
R.U.	L	++		ACA aneurysm and subarachnoid haemorrhage
G.I.	L	L		MCA aneurysm and subarachnoid haemorrhage
R.Q.	R		R	ACA aneurysm and subarachnoid haemorrhage
P.O.	R	R	R	MCA aneurysm and subarachnoid haemorrhage
S.N.*	R	R	R	TBI
L.B.*	R	R	R	TBI
Q.G.	R	R	R	Meningioma
D.B.	L	L	L	Astrocytoma
L.S.	L	L	L	Epileptic focus
R.K.	L	L	L	Epileptic focus
V.F.	L	L	L	Epileptic focus
Patients with non-OFC damage				
V.O.		(++) Fr.pole		Contusions: focal head injury
Q.O.		L		Oligodendroglioma
O.F.		L		Epileptic focus
I.M.*		++	++ (some T)	TBI
U.C.		R	R	Epileptic focus
G.E.		R	R	Oligodendroglioma
G.D.		R	R	Epileptic focus
B.R.		R	R	Epileptic focus
O.R.		R	R	Epileptic focus
A.G.		L	L	Malignant ependymoma
R.C.			R	Epileptic focus
G.F.			R	ACA aneurysm and subarachnoid haemorrhage
S.O.*			R (some BG)	MCA aneurysm and subarachnoid haemorrhage
H.D.			R (some BG)	MCA aneurysm and subarachnoid haemorrhage
F.L.			R (some P+T)	MCA aneurysm and subarachnoid haemorrhage
O.L.			R (some P+T)	MCA aneurysm and subarachnoid haemorrhage
V.I.			R (some P+T)	MCA aneurysm and subarachnoid haemorrhage
E.L.			R (some T)	MCA aneurysm and subarachnoid haemorrhage
B.O.			L (some P+T)	MCA aneurysm and subarachnoid haemorrhage
A.L.			L (some T)	MCA aneurysm and subarachnoid haemorrhage

BA = Brodmann area; BG = basal ganglia; P = parietal; T = temporal; R = right-sided unilateral lesion; L = left-sided unilateral lesion; ++ = bilateral lesion; ACA = anterior communicating artery; MCA = middle cerebral artery; TBI = traumatic brain injury; patient initials in bold = King's College surgical lesion patients; * = Oxford Centre for Enablement patients; all other patients are from the Radcliffe Infirmary (International Subarachnoid Aneurysm Trial)

learning to reverse their choice of a visual stimulus when it is no longer associated with reward (Rolls *et al.*, 1994; Hornak *et al.*, 2004; see Fellows and Farah, 2003). Indeed, investigations in macaques have shown that orbitofrontal cortex (OFC) neurons represent rewards and punishers (produced by taste, olfactory and visual stimuli), that the neurons in this region reverse their visual and olfactory responses during

reversals (Rolls, 1999a, b, 2000, 2004), and that lesions of this region impair reversal (Iversen and Mishkin, 1970; Jones and Mishkin, 1972; Dias *et al.*, 1996). Consistent with this, in a human functional MRI study, the OFC was activated by monetary rewards and punishments, and the magnitude of the activation was related to the magnitude of the reinforcers (O'Doherty *et al.*, 2001).

There is a potential link of OFC function to impulsive behaviour in that impulsive people are less sensitive to punishment and more sensitive to reward than non-impulsive people (Wallace and Newman *et al.*, 1990; Corr *et al.*, 1995; Pickering and Gray, 1999), approaching reward situations even when punishers make restraint more appropriate (Gray, 1973). Impulsive people show poor passive avoidance (in that they do not withhold a response to avoid a stimulus associated with punishment) (Corr *et al.*, 1995). Evidence from studies of human personality and monkeys suggests that impulsivity may be made up of several independent factors (Evenden, 1999). Accordingly, impulsivity was tested in this study using different measures, including both cognitive/behavioural and self-report methods.

One aim was therefore to perform direct investigations of impulsiveness in patients with OFC damage, and to relate any deficits found to performance on a reversal task. Further, as sensitivity to reward and punishment may be an important factor in determining personality (Gray, 1973), we also measured their personality traits (using the Big Five Inventory (John *et al.*, 1991). Because cognitive tempo (as measured in time estimation and time production tasks) may be related to impulsiveness (Barratt, 1983; Barratt and Patton, 1983; Stanford and Barratt, 1996), time perception tests were also given to the subjects. In particular, the internal clocks of impulsive individuals may run faster than those of non-impulsive individuals (Barratt and Patton, 1983), so an impulsive individual would be likely to overestimate and under-produce time intervals (Van den Broek, 1992). Previous imaging and lesion studies have suggested the involvement of the PFC in time perception (Harrington and Haaland, 1999; Mimura *et al.*, 2000), but there is no clear evidence on the relative contributions of the OFC versus other parts of the PFC. To investigate whether impulsivity, personality, reinforcement sensitivity and time perception are closely linked to other changes that follow OFC damage, the inappropriate and related behaviour, and the changes in subjective emotion, that are often found in OFC patients (Rolls *et al.*, 1994; Hornak *et al.*, 1996, 2003), were also measured. A comparison group of patients, with PFC lesions outside the OFC [the non-OFC group, most of whom had damage in the dorsolateral prefrontal cortex (DLFC)], and a spatial working memory (SWM) task, sensitive to damage in the DLFC (Ungerleider *et al.*, 1998; Levy and Goldman-Rakic 2000), were also included in the design, to investigate possible dissociations between functions of different parts of the PFC.

This investigation aims to increase our understanding of the association between frontal dysfunction and impulsive behaviour, the behavioural changes seen in patients with PFC damage, and the cognitive and biological processes that are impaired in impulsive people.

Methods

Participants

Ethics approval was obtained from the Department of Experimental Psychology (University of Oxford), the Ethical Committee (Research) of the Institute of Psychiatry (King's College London) and the Oxfordshire Psychiatric Research Ethics Committee. All participants gave written informed consent before testing began.

Normal control participants

A total of 39 participants (10 male; 29 female) were included in this group, ranging in age from 18 to 71 years (mean = 40.3, SD = 20.5). Participants were excluded if they had disturbed vision, had a history of or current neurological illness, a current major psychiatric illness, or current substance or alcohol abuse.

Prefrontal lesion participants

The 43 frontal lesion patients included in this study were recruited from the Department of Neurosurgery, King's College Hospital, London (19); the International Subarachnoid Aneurysm Trial (ISAT) at the Radcliffe Infirmary, Oxford (16); and the Oxford Centre for Enablement, Oxford (eight). Some patients received their lesion as a result of a surgical excision of a brain tumour (seven) or severe epilepsy (10), 18 patients had a subarachnoid haemorrhage and a coiling or clipping of a ruptured anterior communicating artery (ACA; eight) or middle cerebral artery (MCA; 10) aneurysm, which resulted in ischaemia or infarction in the ventral prefrontal cortex, and eight received their lesion as a result of traumatic brain injury. The time since the patients sustained their lesion varied from 6 months to 20 years (mean = 5.0, SD = 4.8). Clinical information for each lesion patient is listed in Table 1.

The site of the lesion, indicated in Table 1, was ascertained by acquiring MRI or CT scans and/or neurosurgeons' reports and brain maps. Patients were classified according to the prefrontal sectors' functional significance, as shown by earlier investigations (Rowe *et al.*, 2001; Hornak *et al.*, 2003), into which the lesions encroached. This classification was useful in that major differences including double dissociations between the groups on the tests utilized here were found. These areas were defined anatomically as orbital [Brodmann areas (BA) 10, 11, 12, 13 and 25], medial (BA 8, 9 and 10) and dorsolateral (BA 9 and 46) PFC. Figure 1 shows illustrations of the neurosurgeons' drawings of the location of lesions of the subset of patients in this study who were referred from King's College Hospital. Exclusion criteria included damage outside of the PFC (some minor exceptions, see Table 1), disturbed vision, current psychiatric illness, and substance or alcohol abuse.

OFC lesion participants

Twenty-three (15 male; eight female) patients, ranging in age from 30 to 63 (mean = 48.7, SD = 10.0), were included in the OFC lesion group. The criterion for inclusion in this group was that the patient had damage including or restricted to the OFC (areas F11, F12 and/or F13 denoted by Damasio and Damasio, 1989) (either bilaterally or unilaterally). Of these patients, regardless of whether or not they had DLFC or medial damage, seven had bilateral OFC damage, nine had damage to the right OFC, and seven had damage to the left OFC. In total, three patients had OFC damage alone, one had OFC and DLFC damage, six had OFC and medial PFC damage, and 13 had OFC, medial PFC and DLFC damage (see Table 1). It was a feature of the

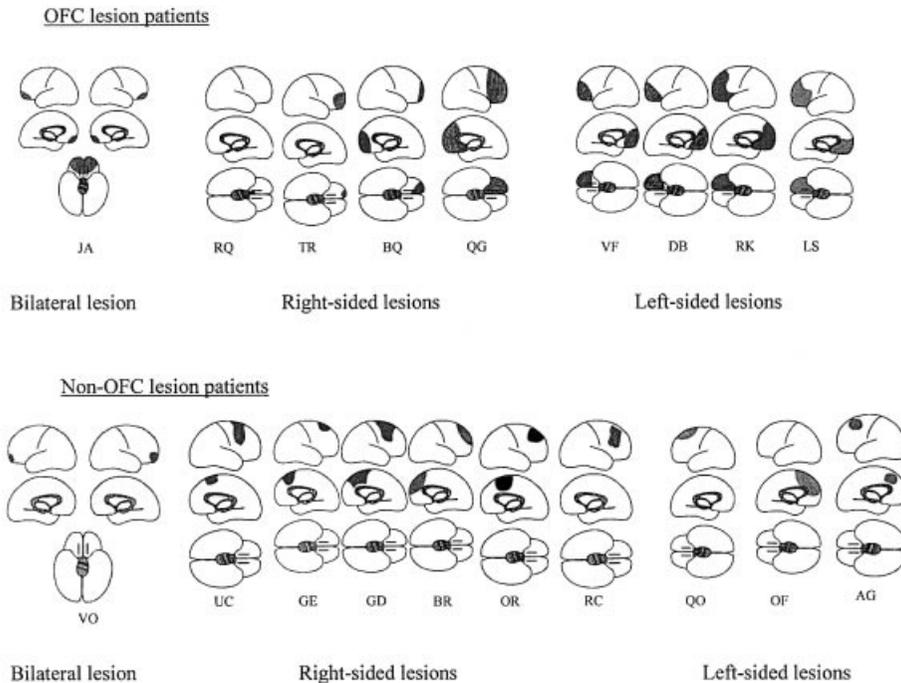


Fig. 1 Lesion sites of King's College neurosurgical patients (lesion sites are shown and the patients' encoded initials are below each brain diagram). This figure can be viewed in colour as supplementary material at Brain Online.

design of this investigation that it included many patients with clearly circumscribed neurosurgical lesions (see Fig. 1), and that all other patients were included only if the MRI or CT scan revealed a localized lesion. Moreover, it was an OFC lesion that was the common lesion across this patient group, and this allows the inference that it is a lesion of the OFC that leads to the effects found in this patient group. This inference was supported by analysis of the data from the patients with surgically circumscribed lesions shown in Fig. 1 and by the findings of Hornak *et al.* (2003, 2004).

Control participants with PFC damage outside of the OFC

Twenty (eight male; 12 female) patients, ranging in age from 19 to 71 (mean = 46.0, SD = 15.1), included in this lesion control group had PFC damage outside the OFC (non-OFC group). DLFC damage (with or without medial PFC damage) was the main site of damage for inclusion in this group, with three patients having medial damage alone (see Table 1).

Materials and procedures

Questionnaires

Self-report impulsivity measure: Barratt Impulsiveness Scale. The Barratt Impulsiveness Scale, version 11 (BIS-11) (Patton *et al.*, 1995) is a 30-item, 4-point Likert scale questionnaire that assesses long-term patterns of behaviour by asking subjects questions about the way they think and act without relation to any specific time period. It is used as a trait measure of impulsivity. The BIS-11 is made up of three subscales: non-planning impulsivity (attention to details); motor impulsivity (acting without thinking); and cognitive impulsivity (future-oriented thinking and coping stability).

Personality questionnaire: the Big Five Inventory. The Big Five Inventory (John *et al.*, 1991) is a 44-item 5-point Likert scale questionnaire designed to measure the five scales or broad domains of the five factor personality model (McCrae and Costa, 1996). (i) Extraversion: talkative, energetic, enthusiastic, adventurous, outgoing (versus introversion). (ii) Agreeableness: helpful, trusting, forgiving, considerate, cooperative (versus antagonism). (iii) Conscientiousness: thorough, reliable, persevering, efficient, organized (versus lack of direction/careless). (iv) Neuroticism: gloomy, tense, worrying, moody, nervous, unstable (versus emotionally stable/relaxed). (v) Openness to experience: wide interests, original, curious, artistic, imaginative, inventive, idealistic (versus closed to experience).

Frontal behaviour questionnaire. We developed this self-report 20-item, 5-point Likert scale (0, 0.25, 0.5, 1.0 and 1.5) questionnaire from the informant-report behavioural questionnaire designed by Rolls *et al.* (1994) to measure types of behavioural problems generally believed to result from frontal damage such as disinhibition, social inappropriateness, perseveration and uncooperativeness.

Subjective emotion questionnaire. This questionnaire measures, on a 4-point Likert scale, how often participants experience each of the following emotions in their current daily life: sadness, anger, fear, happiness and disgust. This questionnaire was developed based on a verbal subjective emotion test in Rolls *et al.* (1994) where participants were questioned about any change they experienced in the intensity or frequency of each of the above-mentioned five emotions since their brain injury. The total subjective emotion score as well as the subjective sadness, anger, fear, happiness and disgust subscores were recorded.

Tests

The probabilistic reversal test

The task consisted of a visual (object) discrimination learning and reversal test for probabilistic monetary reward and loss (described in detail by O'Doherty *et al.*, 2001; Hornak *et al.*, 2004). This test is formed in two stages: an 'acquisition' task where participants learn to touch one of two patterns on the computer screen and to avoid touching the other; and a 'reversal' task where they then learn to reverse their selection based on 'monetary' rewards and punishers being received. The rewards and losses, which could be obtained for a choice of a stimulus, were distributed probabilistically. The frequency ratio of rewards to losses for the 'good' stimulus (S+) was 70 : 30, whereas for the 'bad' stimulus (S-) it was 40 : 60. The magnitude of the rewards varied according to a uniform random distribution as follows: for the S+, the rewards ranged from £80 to £250 (of artificial money), and the losses ranged from £10 to £60. For the S-, the rewards ranged from £30 to £65, and the losses ranged from £250 to £600. The following measures were obtained. (i) Number of trials to reach criterion on the acquisition task: the number of trials taken to acquire the positive stimulus; the criterion was reached by selecting the S+ on 16 out of the previous 18 consecutive trials. (ii) Total pounds accumulated after 100 trials on the reversal task. (iii) Number of trials until the first reversal on the reversal task: the number of trials taken to achieve the first reversal; marked by the trial in which the participant started consecutively touching the new S+. (iv) Total number of reversals achieved by 100 trials: a reversal was considered successful when the new S+ was chosen on nine out of the previous 10 trials. (v) Punishment insensitivity on the reversal task: the total number of consecutive touches to a stimulus after having lost a minimum of £250. This measures the extent to which participants fail to switch immediately from a stimulus on the next trial following a large loss (£250 corresponds to the lower bound of the money that can be lost by touching the S-). (vi) Reward insensitivity on the reversal task: the total number of times a participant touched a stimulus and won a minimum of £80 but did not touch the same stimulus again on the next trial. This measures the extent to which participants fail to stick to a stimulus following a large gain on that stimulus (£80 corresponds to the lower bound of the amount that can be won on the S+).

Matching Familiar Figures Test

This standard cognitive behavioural measure of impulsivity, created by Kagan (1966), measures reflection impulsivity, operationally defined as a composite of two dimensions: latency to first response and accuracy of choice or total errors, which are combined in the Matching Familiar Figures Test (MFFT). Each participant selects (points to), from the set of highly similar pictures, the one that is exactly the same as the standard picture. Participants were given 12 trials with eight variants each to choose from, with a different target object for each trial. Mean time latency of the participants' first response across all trials and number of errors made before choosing the correct item were recorded.

SWM task

This task was from the Cambridge Neuropsychological Test Automated Battery (CANTAB; CeNeS Ltd, Cambridge).

Participants were asked to find a blue token in each of the boxes displayed and use them to fill up an empty column on the right hand side of the screen, whilst not returning to boxes where a blue token had been found previously. Subjects were given four trials with four boxes, four trials with six boxes, and four trials with eight boxes. The following variables were measured. (i) Between errors: the number of times the subject revisits a box in which a token has already been found. (ii) Within errors: the number of times a subject revisits a box already found to be empty during the same search. (iii) Strategy: Owen *et al.* (1990) have suggested that an efficient strategy for completing this task is to follow a predetermined sequence by beginning with a specific box and then, once a blue token has been found, to return to that box to start the new search sequence. An estimate of the use of this strategy is obtained by counting the number of times the subject begins a new search with the same box. A high score denotes poor use of this strategy.

Time perception task

Time estimation. Participants estimated time intervals (10, 30, 60 and 90 s; each presented twice in a random sequence), during which they were distracted by reading aloud randomized numbers (1–9) from a computer screen, that ranged in presentation time from 100 to 2900 ms, in order to prevent subvocal counting. Stimuli were presented at random times to prevent participants using pacing as a marker for time. The number of seconds estimated after each interval, averaged across two runs, and the total time estimated [sum of the average times estimated at each interval divided by 190 (the total number of seconds that actually passed)] were recorded. For one retrospective 10 s interval (the first interval presented), participants were not told it was a time estimation task until they were asked at the end of the interval how much time they thought had passed.

Time production. The participants read aloud randomized numbers and said stop when they thought a set number of seconds had passed. For each time interval, the time produced was compared with the actual time interval participants were asked to produce. The number of seconds produced at each interval, averaged across two runs, and the total time produced [sum of the average times produced at each interval divided by 190 (the total number of seconds participants were asked to produce)] were recorded.

Time pacing. Participants counted out loud starting from 1 going upward consecutively at what they felt was a one per second rate and stopped when the experimenter said 'stop'. No distracter task was used. Time intervals were the same as for the time estimation and production tasks, but each interval was presented only once in a random sequence. Participants counted from 1 at the beginning of each trial. The total number of seconds that actually passed across all four time intervals (190) divided by the total number of seconds counted by the participant across all four time intervals (the average concept of a second) was recorded.

Long-term time estimation. At the end of the entire time perception experiment (~20 min), participants were asked 'How much time do you think has passed from the moment we started the time task until now?' Their response was recorded and compared with the actual time that had passed.

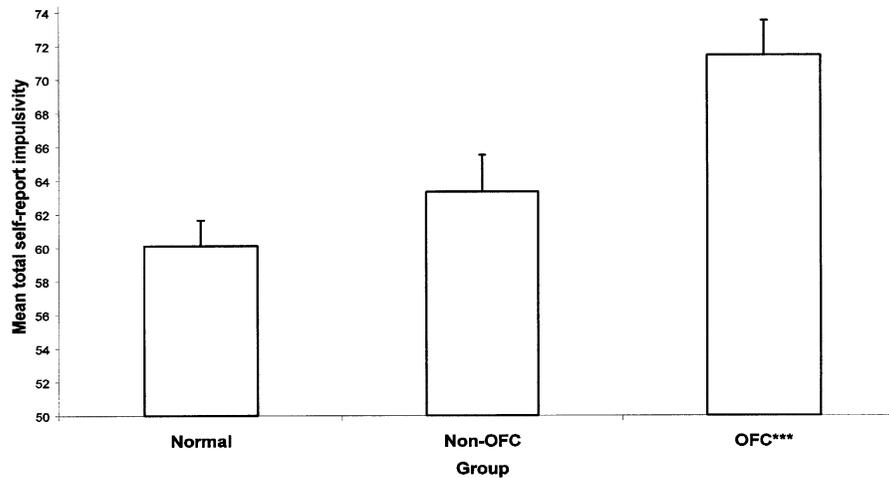


Fig. 2 Self-report impulsivity. Histogram of the mean total score on the self-report impulsivity questionnaire across all three groups. OFC participants reported significantly more self-report impulsivity than non-OFC and normal participants.

Statistical analyses

A one-way analysis of variance (ANOVA) was performed on each of the variables to determine if the mean scores differed significantly by group. If an ANOVA yielded a significant F value, a Fisher's least significant difference *post hoc* test was performed to identify the specific source of the difference. For all histograms presented, based on ANOVAs, error bars represent the SEM, and $*P < 0.05$, $**P < 0.01$, and $***P < 0.001$ with respect to normals. An alpha level of 0.05 was used for all statistical tests.

Kruskal–Wallis non-parametric tests were performed on variables that were not normally distributed. If the Kruskal–Wallis test yielded non-significant results, no results were reported for that variable.

As ANOVAs revealed between-groups differences in terms of gender [$F(3,79) = 5.13$, $P < 0.01$], analyses of covariance (ANCOVAs) with gender identified as the covariate were performed. Also, although ANOVAs revealed no age differences between groups, ANCOVA with age identified as the covariate was performed, as a double check. ANCOVA revealed that none of the significant differences between groups was due to the effect of age or gender.

The King's College Hospital patients completed the questionnaire measures, but were not given the behavioural tests (i.e. the reversal, MFFT, SWM and time perception tasks) due to testing time constraints, or the Borderline Personality Disorder questionnaire due to sensitivity issues. In a small number of instances, other participants did not complete all the tasks due to testing time constraints.

Results

Main analysis

Impulsivity questionnaire

A one-way ANOVA revealed a significant difference in participants' total impulsivity score [$F(2,79) = 9.98$, $P < 0.001$], and, as illustrated in Fig. 2, *post hoc* analyses revealed that the OFC patients' ($n = 23$) total impulsivity was greater (mean = 71.4, SD = 9.9) than that of non-OFC

(mean = 63.3, SD = 9.8, $P < 0.01$, $n = 20$) and normal (mean = 60.1, SD = 9.5, $P < 0.001$, $n = 39$) participants.

A one-way ANOVA confirmed that there was a significant difference in participants' motor impulsivity subscore [$F(2,9) = 3.91$, $P < 0.05$], and *post hoc* analyses revealed that motor impulsivity was greater in OFC (mean = 24.8, SD = 3.9) than in non-OFC (mean = 21.9, SD = 5.2, $P < 0.05$) and normal (mean = 22.1, SD = 3.5, $P < 0.05$) participants. Also, OFC participants' non-planning impulsivity subscore (mean = 29.1, SD = 6.2) was significantly higher than that of non-OFC (mean = 25.4, SD = 6.0, $P < 0.05$) and normal (mean = 22.4, SD = 4.6, $P < 0.001$) participants [omnibus $F(2,79) = 11.12$, $P < 0.001$]. Finally, there were no significant differences between groups in terms of the cognitive impulsivity subscore. No significant differences between the non-OFC and normal groups were found for any of the impulsivity questionnaire measures.

Behavioural impulsivity

The interesting differences in impulsivity revealed by the impulsivity questionnaire were elucidated further by the results found in the behavioural impulsivity task.

As Fig. 3 illustrates, analysis of the number of errors made per time latency to respond on the MFFT indicated that participants in the OFC group were more impulsive, i.e. made significantly more errors and were quicker to respond (mean = 1.2, SD = 1.2, $n = 12$) than both non-OFC (mean = 0.54, SD = 0.32, $P < 0.05$, $n = 9$) and normal participants (mean = 0.27, SD = 0.48, $P < 0.001$, $n = 39$) [omnibus $F(2,57) = 9.35$, $P < 0.001$].

Analysis of the number of errors made on the MFFT showed that OFC (mean = 21.0, SD = 10.0, $P < 0.001$) and non-OFC (mean = 18.2, SD = 7.3, $P < 0.001$) participants both made significantly more errors than did normal partici-

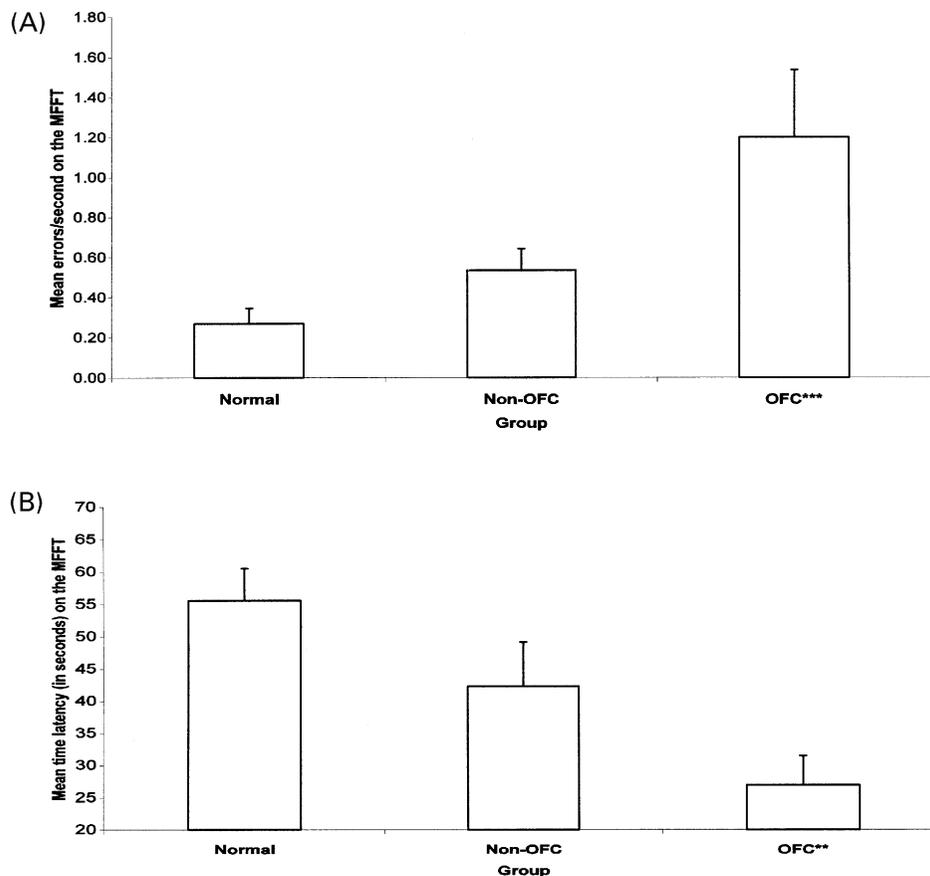


Fig. 3 Behavioural impulsivity. (A) Histogram of mean total errors made divided by the average number of seconds taken to make the first choice of a stimulus on the MFFT across all groups. The higher the score, the more behaviourally impulsive (i.e. the more errors made and the less time taken to choose a stimulus). OFC patients were significantly more impulsive than non-OFC and normal participants. (B) Histogram of mean time latency (in seconds) to choose the first stimulus on each trial on the MFFT across all groups. A short time corresponds to being more behaviourally impulsive. OFC patients had significantly lower time latencies than normal participants.

pants (mean = 8.2, SD = 6.0) [omnibus $F(2,57) = 8.48$, $P < 0.001$].

Finally, as Fig. 3 illustrates, OFC patients' time latency (mean = 26.9, SD = 15.8) was significantly lower than that of the normal group (mean = 55.6, SD = 30.7, $P < 0.005$) [omnibus $F(2,57) = 5.37$, $P < 0.01$], indicating that the OFC patients responded more quickly (impulsively) on the MFFT task than did participants in the normal group. The DLFC patients did not have longer than average latencies.

Time perception

Of the time perception variables, a significant group difference was found in participants' time estimation in total, $F(2,57) = 2.71$, $P < 0.05$, and at 90 s, $F(2,57) = 3.87$, $P < 0.05$, and time production at 90 s, $F(2,57) = 5.17$, $P < 0.01$.

As Fig. 4 illustrates, *post hoc* analysis revealed that OFC participants (mean = 1.5, SD = 1.4, $n = 13$) estimated that significantly more time had passed in total [time estimated across all intervals/actual time passed (190)] than normal

participants (mean = 0.72, SD = 0.35, $P < 0.005$, $n = 39$), and OFC participants (mean = 109.2, SD = 87.7) estimated that significantly more time had passed at the 90 s interval than normal participants (mean = 65.0, SD = 33.4, $P < 0.05$). While OFC patients overestimated time in both cases, indicating a faster subjective sense of time, normal participants underestimated time. Further, OFC participants' produced significantly less time at 90 s (mean = 3.9, SD = 45.3) than normal participants (mean = 124.2, SD = 39.5, $P < 0.005$). While OFC patients under-produced the time interval, indicating a faster subjective sense of time, both control groups overproduced the time interval. There were no significant group differences in their average concept of a second, but counting aloud may not accurately measure cognitive pace.

Reversal

ANOVAs performed on each of the reversal variables indicated that there were significant group differences for the total pounds accumulated by the 100th trial, total number

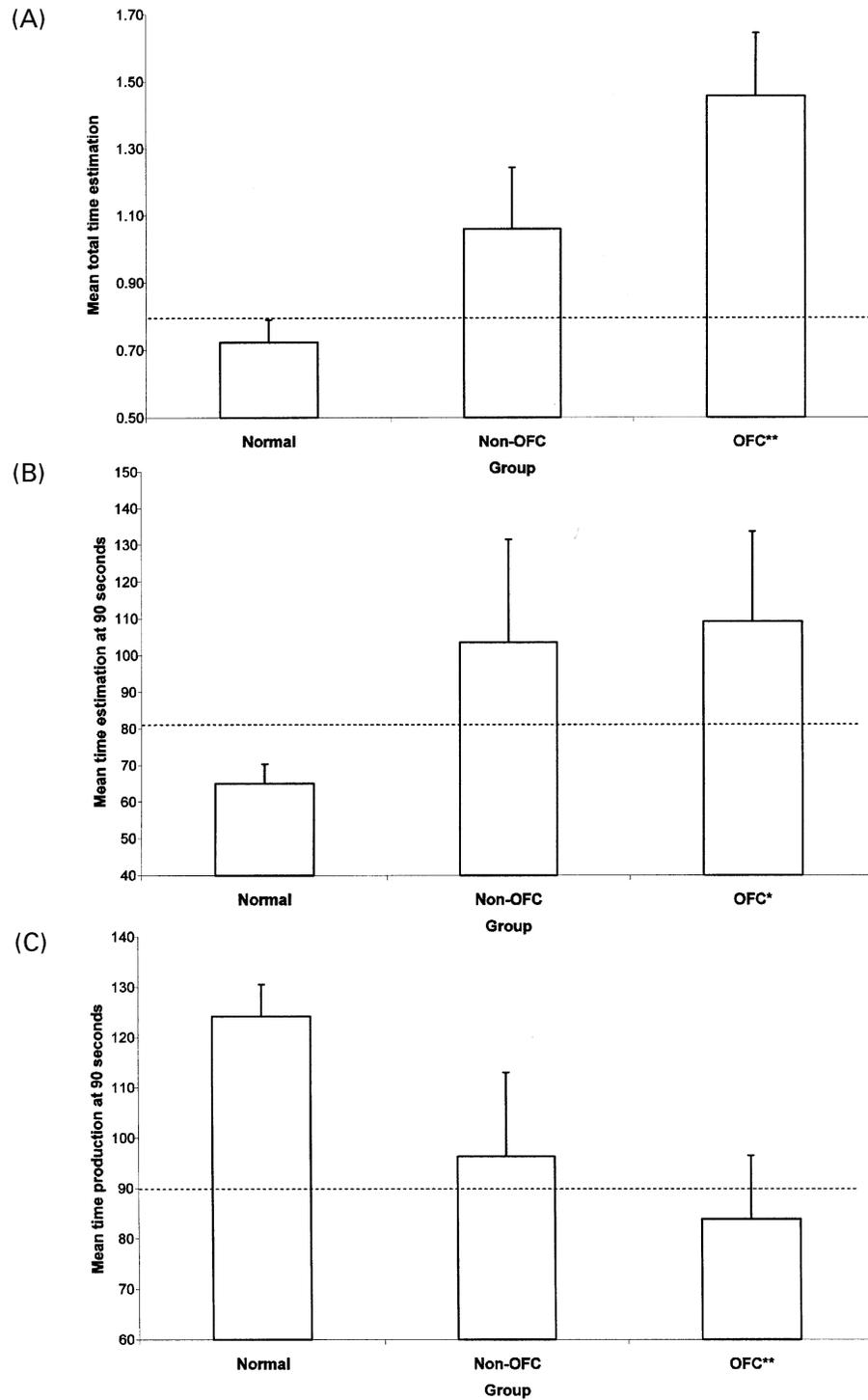


Fig. 4 Timing. **(A)** Histogram of participants' mean total time estimation score [total number of seconds estimated across all time intervals divided by 190 (total number of seconds actually passed)] by group. OFC participants estimated that significantly more time had passed than did normal participants. OFC patients overestimated time (had a faster subjective sense of time), while normal participants underestimated time. **(B)** Histogram of participants' mean time production at 90 s by group. OFC participants produced a significantly lower amount of time at the 90 s interval than did normal participants. While OFC patients under-produced the time interval, indicating faster subjective sense of time, both control groups overproduced the time interval.

of reversals achieved by 100 trials, punishment insensitivity, and reward insensitivity variables [$F(3,58) = 21.37, P < 0.001, F(3,58) = 17.17, P < 0.001, F(3,58) = 8.06, P < 0.005$ and $F(3,58) = 10.85, P < 0.001,$] [respectively. (The King's College neurosurgical patients are not included in the analysis of reversal, as their data have been published elsewhere (Hornak *et al.*, 2004)].

As Fig. 5 illustrates, OFC patients earned significantly less money (mean = -4308, SD = 4268, $n = 13$) than both non-OFC (mean = -2.9, SD = 2925, $P < 0.01, n = 9$) and normal (mean = 2093, SD = 2604, $p < 0.001, n = 39$) participants. While the OFC group lost money, normal patients gained money. *Post hoc* analyses indicated that the OFC group completed fewer reversals (mean = 1.3, SD = 1.4) than non-OFC (mean = 3.0, SD = 1.3, $P < 0.005$) and normal (mean = 3.5, SD = 1.0, $P < 0.001$) participants. Further, *post hoc* tests revealed that the OFC group (mean = 12.5, SD = 8.8) was significantly more insensitive to punishment than the normal group (mean = 3.9, SD = 6.2, $P < 0.005$) and OFC patients were significantly more insensitive to reward (mean = 6.9, SD = 5.3) than normal participants (mean = 3.9, SD = 6.2, $P < 0.005$). In all cases, there was no significant difference between normal and non-OFC participants.

Frontal behaviour questionnaire

As Fig. 6 illustrates, OFC participants' total scores (mean = 11.3, SD = 3.8, $n = 23$) were significantly higher, implying more maladaptive behaviours, than those of both non-OFC (mean = 8.9, SD = 1.9, $P < 0.005, n = 20$) and normal (mean = 9.3, SD = 2.0, $P < 0.005, n = 39$) participants [omnibus $F(3,79) = 6.14, P < 0.005$]. Non-OFC and normal participants did not differ significantly on this measure. Analyses of participants' responses to individual questions are given in Table 2, and show that the OFC patients were different from controls in that on average they were impulsive, inappropriate, aggressive/violent, angry or irritable, lacked self-concern, and were reward insensitive, listless and uncooperative.

Groups did not differ in terms of how often they misinterpret others' moods, stick to their point when they feel they are right, try something else when they do not get an expected reward, feel full of energy, show their emotions in their facial expressions, can predict someone else's mood from their facial expression, stop to help someone who looks upset, stop to think before making a decision, such as gambling, and take risks when they gamble (questions 6, 7, 9, 12, 14, 15, 16, 18, 19 and 20).

Subjective emotion

As Fig. 7 illustrates, OFC patients (mean = 1.4, SD = 0.89) reported experiencing significantly more anger than non-OFC (mean = 0.74, SD = 0.56, $P < 0.005$) and normal (mean = 0.74, SD = 0.55, $P < 0.001$) participants [omnibus $F(2,78) = 7.84, P < 0.005$], and OFC participants (mean = 1.7, SD = 0.77)

reported experiencing significantly less happiness than normal participants (mean = 2.1, SD = 0.52, $P < 0.01$) [omnibus $F(2,78) = 3.87, P < 0.05$]. There were no significant group differences in participants' total subjective emotion score, or sadness, fear or disgust subscores.

Personality

On the Big Five personality questionnaire, only participants' openness to experience differed significantly by group, $F(2,79) = 7.03, P < 0.005$, with results showing that OFC (mean = 32.8, SD = 8.5, $P < 0.005, n = 23$) and non-OFC (mean = 32.5, SD = 7.8, $P < 0.005, n = 20$) participants were significantly less open to experience than normal participants (mean = 38.7, SD = 9.3, $n = 39$) (see Fig. 8).

SWM task

ANOVAs performed on each of the SWM variables (between errors, within errors and strategy) indicated that participants' scores differed significantly by group on all three measures, $F(2,59) = 24.59, P < 0.001; F(2,59) = 3.63, P < 0.05$; and $F(2,59) = 10.29, P < 0.001$, respectively.

As depicted in Fig. 9, *post hoc* analysis revealed that participants in the OFC group (mean = 65.8, SD = 29.5, $P < 0.001, n = 14$) and the non-OFC group (mean = 64.2, SD = 29.0, $P < 0.001, n = 9$) made significantly more between errors than did normal participants (mean = 23.1, SD = 18.3, $n = 39$), that non-OFC participants (mean = 11.4, SD = 23.4, $P < 0.05$) made significantly more within errors than did normal participants (mean = 2.0, SD = 3.2), and that OFC (mean = 37.2, SD = 5.0, $P < 0.005$) and non-OFC (mean = 38.7, SD = 2.3, $P < 0.005$) participants made significantly more strategy errors than normal participants (mean = 31.2, SD = 6.3).

Correlations between measures

To investigate the relationships between the different measures, Pearson correlations (two-tailed) were performed across all participants, for the total score or main variable of each measure (all variables within each measure were significantly correlated with each other). A Bonferroni correction was applied in order to allow for the number of comparisons being performed, and resulted in the critical alpha level for any one correlation being lowered to 0.004 from 0.05. Some correlations are mentioned where $P < 0.01$ if they were deemed *a priori* to be interesting. Table 3 shows the correlation matrix.

Discussion

The new findings described herein include the following, each of which is discussed below. OFC patients performed more impulsively as shown by both self-report (total score on the BIS-11, and non-planning and motor impulsivity subscale scores), and cognitive/behavioural (errors per second on the

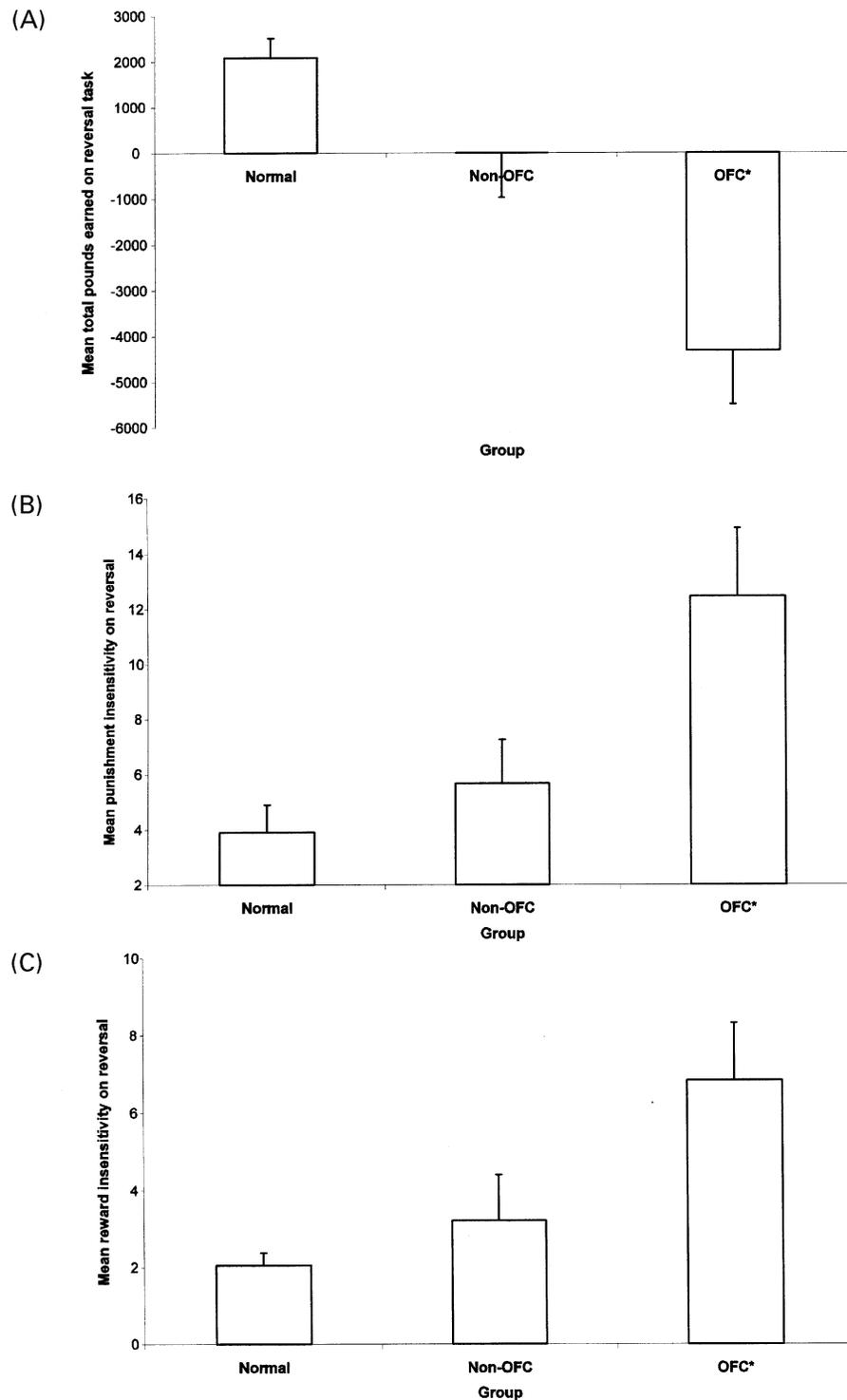


Fig. 5 Reversal performance. **(A)** Histogram of participants' mean total pounds accumulated by the 100th trial on the reversal task by group. OFC participants earned significantly less 'money' than did participants in all other groups. While normal participants earned 'money', OFC participants lost 'money'. **(B)** Histogram of participants' punishment insensitivity (the number of times a consecutive response is made to a stimulus following a monetary loss \geq £250) on the reversal task by group. OFC participants showed significantly higher punishment insensitivity than participants in both control groups. **(C)** Histogram of participants' reward insensitivity (the number of times a participant failed to choose a stimulus following a monetary gain \geq £80) on the reversal task by group. OFC participants showed significantly higher reward insensitivity than normal and non-OFC participants.

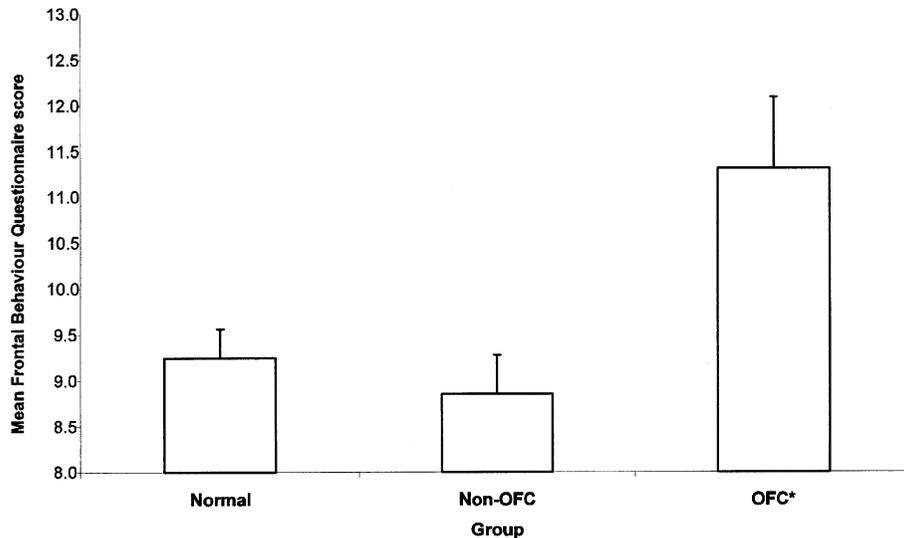


Fig. 6 Histogram of participants' mean Frontal Behavioural Questionnaire total score by group. OFC participants' mean total scores were significantly higher than those of both normal and non-OFC participants.

Table 2 Means, SD, and *F* and *P* values of individual questions on the Frontal Behaviour Questionnaire that revealed significant between-group differences

Question	Mean = SD			<i>F</i> value	<i>P</i> <
	OFC	Non-OFC	Normal		
1. Do you ever feel that you do or say things but would rather stop yourself?	0.67 ± 0.38**	48 ± 0.21	0.42 ± 0.31	4.73	0.05
2. Do you ever do things in the company of other people that they find somewhat inappropriate?	0.49 ± 0.44	0.20 ± 0.22*	0.38 ± 0.27	4.58	0.05
3. Do you ever feel like acting violently when you don't get what you want?	0.47 ± 0.42**	0.15 ± 0.24	0.23 ± 0.28	6.11	0.005
4. Do you ever find yourself saying things in an aggressive or abusive fashion to other people?	0.59 ± 0.43**	0.33 ± 0.37	0.20 ± 0.24	9.48	0.001
5. Do you ever get angry or irritable?	0.79 ± 0.34**	0.49 ± 0.21	0.48 ± 0.22	11.86	0.001
8. If you don't get an expected reward that you want do you try harder to get it?	0.67 ± 0.42	0.41 ± 0.27**	0.84 ± 0.45	7.34	0.005
10. Do you ever worry about yourself?	0.43 ± 0.31*	0.43 ± 0.30*	0.69 ± 0.42	5.45	0.01
11. Do you ever feel listless?	0.83 ± 0.44**	0.66 ± 0.38	0.47 ± 0.29	7.38	0.005
13. Are there occasions when you do not feel like cooperating when asked to?	0.66 ± 0.38	0.40 ± 0.27	0.57 ± 0.35	3.24	0.05
17. Do you stop to think before you act?	0.61 ± 0.46*	0.41 ± 0.34	0.36 ± 0.29	3.62	0.05

***P* < 0.001; **P* < 0.05 from normals; Bold = *P* < 0.05 from non-OFC patients; for all *F* values, degrees of freedom = 2, 79.

MFFT) measures of impulsivity, reported more inappropriate 'frontal' behaviours as assessed by the Frontal Behaviour Questionnaire, and performed worse on the reversal task, than non-OFC and normal controls. Further, OFC patients experienced more subjective anger than non-OFC patients, and less subjective happiness than normals; and had a faster subjective sense of time (more time estimated in total and at 90 s and less time produced at 90 s) than normal controls, while non-OFC patients did not differ from normals. Finally, both OFC and non-OFC patients made significantly more between-SWM errors, and were less open to experience than normal participants. There were no differences between OFC patients, non-

OFC lesion patients and normal controls on all other personality traits, most notably extraversion. In sum, OFC patients were impulsive, reported inappropriate behaviours, were angry, unhappy, closed to experience, insensitive to punishment and reward (demonstrated by their poor reversal performance), had fast cognitive tempos and poor SWM.

Self-report impulsivity

OFC patients were more impulsive than normal and non-OFC lesion controls on both the self-report and the cognitive behavioural task measures of impulsivity. This shows that not

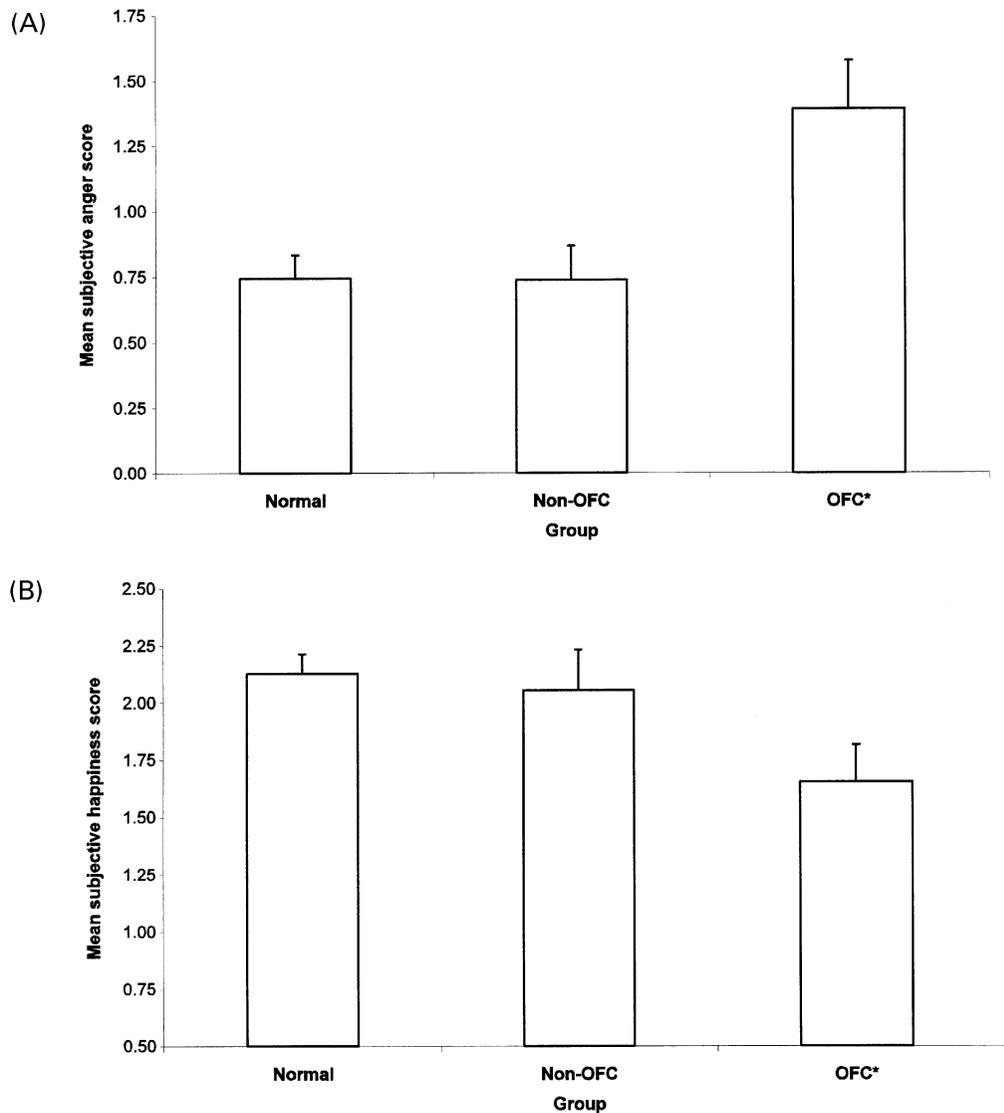


Fig. 7 Subjective emotion. (A) Histogram of participants' mean subjective anger score on the subjective emotion questionnaire by group. OFC participants reported experiencing significantly more anger than normal and non-OFC participants. (B) Histogram of participants' mean subjective happiness score on the subjective emotion questionnaire by group. OFC participants reported experiencing significantly less happiness than normal participants.

only were the OFC patients impulsive, but they also had considerable insight into their condition. Moreover, this impulsiveness appears to be specifically related to the OFC, in that the non-OFC patients (who mainly had DLFC damage) were not impaired on both measures.

Interestingly, impulsivity was related to time perception problems. OFC patients had a faster subjective sense of time than normal controls (and than non-OFC patients for total time estimation) in terms of more time estimated in total and at 90 s, and less total time produced at 90 s. Further, the non-planning subcategory of the self-report impulsivity questionnaire (the BIS-11) was positively correlated with increased time estimation (in total and at each time interval), and decreased time production (in total and at the 30, 60 and 90 s

intervals). In the behavioural impulsivity task, OFC patients also made significantly faster responses than normals. This suggests that impulsivity may be at least partly due to a fast cognitive pace (see Barratt, 1983; Barratt and Patton, 1983), which may lead to impatience or the inability to stop and think before acting.

Part of the reason that OFC patients are impulsive could also be related to a tendency to respond rapidly to rewards and punishers without assessing the consequences sufficiently. This could contribute to the OFC patients' poorer performance on the reversal task, as considered below. OFC patients may act without giving themselves enough time to think about their behaviours and to modify them accordingly.

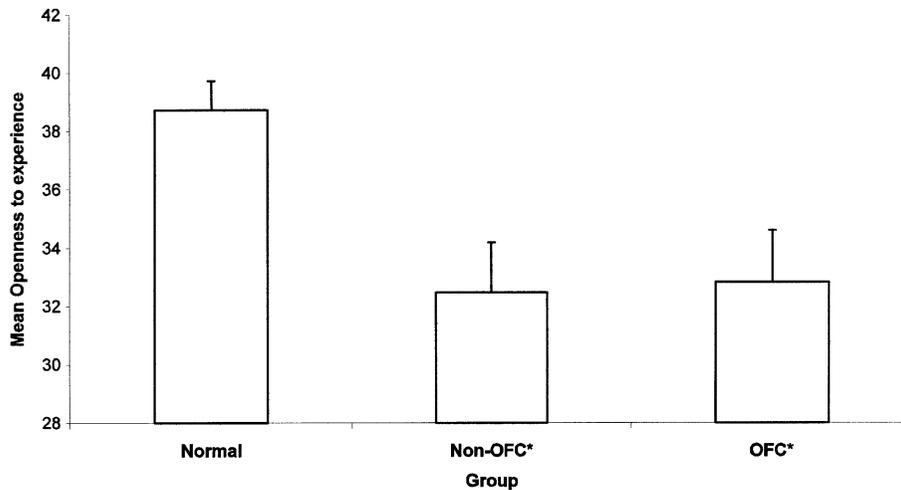


Fig. 8 Openness to experience. Histogram of participants' mean openness to experience score on the Big Five Inventory by group. Both OFC and non-OFC patients were significantly less open to experience than normal participants.

Behavioural impulsivity

On the MFFT, a cognitive/behavioural test of impulsivity, the main difference was that OFC patients had shorter response latencies than the non-OFC patients and normals. This was the most sensitive measure of a difference in the behavioural impulsivity task, in that the number of errors did not differ between lesion groups.

Impulsive behaviour, in terms of lower response latency and increased errors on the MFFT, could be due at least in part to OFC patients' desire for an immediate reward (getting the correct answer) despite the consequences (making the wrong choice by choosing too quickly). Thus, they fail to wait even though it would be beneficial to take more time to think about the task before acting. This could be related to their poor performance on the reward reversal task, as discussed below. In fact, behavioural impulsivity correlated negatively with pounds earned on the reversal task across all subjects.

The finding that the non-OFC lesion patients made a greater number of errors on this task than normals could be due to other cognitive deficits such as failure to pay attention. Indeed, all non-OFC patients who participated in this task had DLFC damage ($n = 9$), which is associated with attention (Iba and Sawaguchi, 2003; Hornak *et al.*, 2004).

Time perception

The intolerance of delay or inability to delay responding on impulsivity tasks may be related to a faster cognitive tempo in OFC patients. It has been noted previously that impulsive individuals without brain damage tend to overestimate and underproduce time intervals (Van den Broek, 1992). We found that OFC patients also overestimated and underproduced time intervals.

One possible explanation for our finding is that OFC patients have a faster cognitive pace (their internal clocks

may run faster). Other possible explanations are that they are less sensitive to the implied punisher of ending the trial too early, and/or they may become frustrated with delay of reward (waiting for the time interval to end), making time intervals feel subjectively longer than they actually are. A fast cognitive tempo may cause or simply exacerbate the frustration of non-reward and intolerance of delay of reward (the ending of the time task) that is demonstrated by OFC patients on time perception tasks. Whatever the underlying cause, it appears that OFC participants have a problem with evaluating the passage of time, which may be related to the behavioural deficits (e.g. impulsivity and inappropriate 'frontal' behaviours) identified in these patients.

Time perception difficulties cannot be attributed to DLFC damage in this study, in that non-OFC patients (all nine given these tests had DLFC damage) did not differ from normal controls. The finding that non-OFC patients were impaired at SWM (and that there was no correlation between time production or time estimation and SWM) indicates that SWM and time perception rely on different brain processes.

Probabilistic reversal

There were no significant differences between groups in terms of the 'number of trials until the first reversal', and the 'number of trials completed to acquire a positive stimulus'. Further, the acquisition task was completed successfully by all participants. This indicates that all the participants understood the task demands and were able to follow the task instructions, and that their reversal impairments (discussed next) are related to a failure to change behaviours in response to changed reinforcers, rather than a failure simply to learn stimulus-reinforcement associations (acquisition of the task).

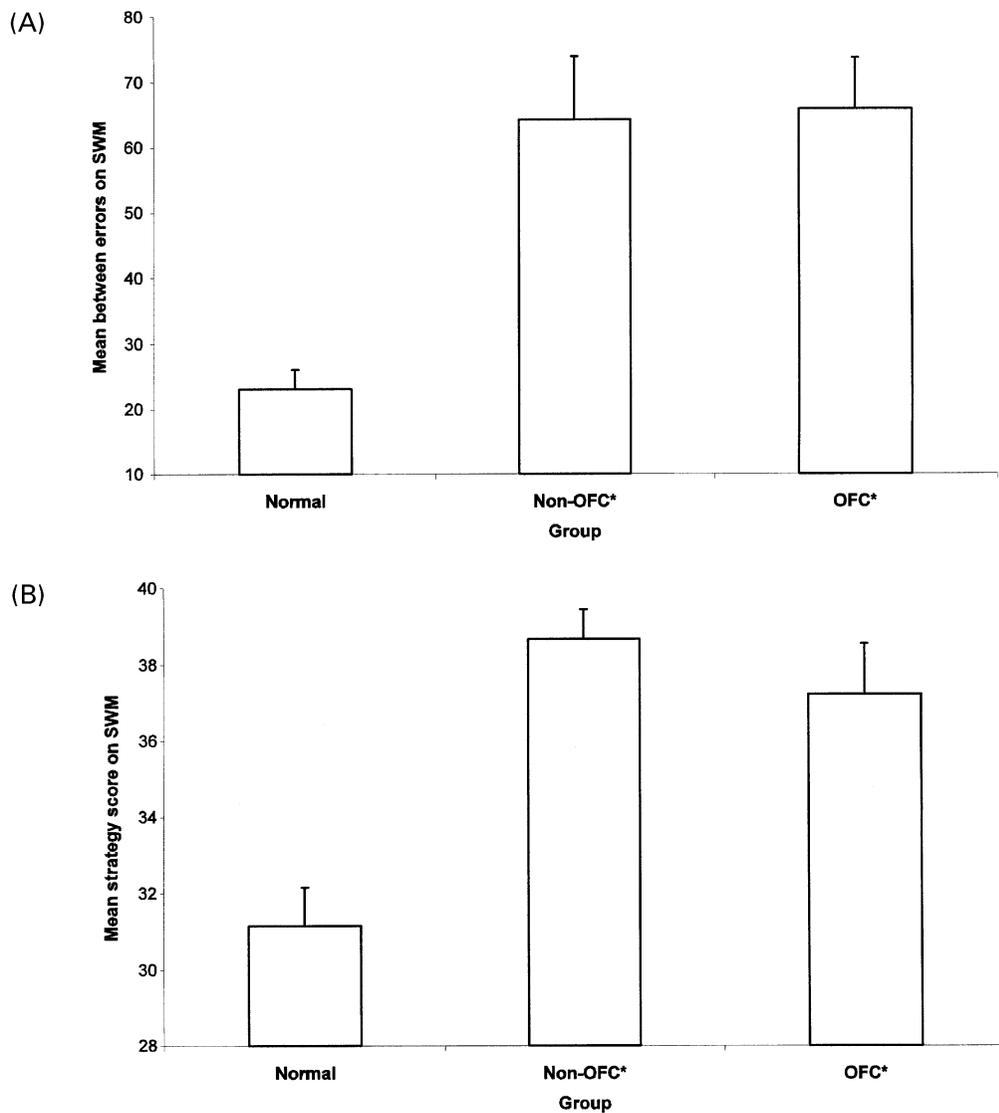


Fig. 9 Spatial working memory. **(A)** Histogram of participants' mean number of between errors on the SWM task by group. Both non-OFC and OFC patients (most of whom had DLFC damage) made significantly more 'between' SWM errors than normal participants. **(B)** Histogram of participants' mean strategy score on the SWM task by group. Both non-OFC and OFC patients (most of whom had DLFC damage) had a significantly higher strategy score, indicating a worse strategy used, than normal participants.

OFC patients, compared with non-OFC and normal controls, were significantly impaired on the reversal task. Their impairment was not related to motor perseveration (i.e. a failure of inhibitory control of the arm/hand with which patients reached out to the now incorrect stimulus) as a response was required and made on every trial and the position of the old S+ was constantly changing. So the continued selection of the old S+ must reflect OFC patients' difficulty in forming new stimulus–reward associations when reinforcement contingencies are reversed (see further Rolls, 1999b; Hornak *et al.*, 2004). The current results are consistent with the hypothesis that one important function of the OFC is representing the reward and punishment value of stimuli and,

more specifically, since all of the OFC patients succeeded in the acquisition stage of the reversal task (before the first reversal), in updating the associations between stimuli and reinforcers when the associations change. The clear instructions explaining that reversals will occur and that the subject was to alter his/her choice of stimulus accordingly, and the fact that the patients made a selection on every trial, excludes an interpretation in terms of lack of initiative or failure to understand the task requirements.

In the reversal task, not only did OFC patients fail to switch their choice of stimulus following a large punishment (punishment insensitivity), continuing to choose a previously rewarded but now punished stimulus, but they also failed to

Table 3 Correlations of the most salient variables of each test/questionnaire across all subjects

		SRI	E	A	N	O	FBQ	SE	BI	Total £s	BtSWM	TE total
C	<i>r</i>	-0.510										
	<i>P</i>	0.000										
N	<i>r</i>		-0.383	-0.230								
	<i>P</i>		0.000	0.038								
O	<i>r</i>	-0.372										
	<i>P</i>	0.001										
FBQ	<i>r</i>			-0.342	0.251							
	<i>P</i>			0.002	0.023							
SE	<i>r</i>			-0.238	0.400		0.367					
	<i>P</i>			0.032	0.000		0.001					
BI	<i>r</i>	0.325*			0.266		0.295					
	<i>P</i>	0.002			0.040		0.022					
Total £s	<i>r</i>	-0.295					-0.267	-0.389	-0.419			
	<i>P</i>	0.011					0.021	0.001	0.001			
BtSWM	<i>r</i>	0.325				-0.387	0.311		0.452	-0.544		
	<i>P</i>	0.010				0.002	0.014		0.000	0.000		
TE total	<i>r</i>	0.290				-0.463					0.319	
	<i>P</i>	0.025				0.000					0.013	
TP total	<i>r</i>	-0.327				0.361*	-0.281					-0.500
	<i>P</i>	0.011				0.005	0.030					0.000

Bold font = correlation significant at $P < 0.004$ (two-tailed); * = correlation significant at $P < 0.01$ (two-tailed); all other correlations are significant at $P < 0.05$; SRI = total self-report impulsivity score; E = extraversion; A = agreeableness; C = conscientiousness; N = neuroticism; O = openness to experience; FBQ = Frontal Behaviour Questionnaire score; SE = total subjective emotion score; BI = errors/second on the MFFT (behavioural impulsivity); total £s = total pounds earned on the reversal task; BtSWM = between errors on the SWM task; TE total = total time estimation; TP total = total time production.

continue choosing a stimulus following a large reward (reward insensitivity) (see Fig. 5), implying a difficulty in learning to respond to (or acquiring) the now rewarded stimulus. This set of results thus shows that not only can we reject a response inhibition hypothesis of OFC damage, but also that the deficit is not just a failure of 'inhibition' to a previously rewarded stimulus (Roberts and Wallis, 2000). (Consistent with this, what Aron *et al.*, 2003 described as a deficit in stop-go inhibition was associated with damage to the lateral right inferior gyrus.) The reward and punishment insensitivity effects we describe in patients with OFC lesions directly complement the functional MRI finding of loci in the human OFC where the magnitude of the monetary reward, and separately the magnitude of the monetary loss, in the same task, are represented (O'Doherty *et al.*, 2001). Although bilateral but not unilateral surgical OFC lesions led to reversal impairments in the same task (Hornak *et al.*, 2004), when the patients in this study were classified on the basis of surgical notes and structural MRI as having unilateral damage, a deficit on the reversal task was found (unilateral OFC $n = 8$; mean = £-3831 won, SEM = 1355; $P < 0.05$, compared with the non-OFC control group $n = 8$, mean = £146 won, SEM = 1540).

Interestingly, while OFC patients were making the wrong choices on this task, they often showed a strong affective response such as sighing or wincing. Thus, they are aware that they have chosen disadvantageously, yet are unable to stop themselves making a similar disadvantageous choice on the next trial. Their explicit system seems to be monitoring and

reacting to a failure of their implicit system to make adjustments to changing stimulus-reinforcement associations. This is consistent with the finding that OFC patients report being impulsive on the self-report impulsivity questionnaire yet, despite being aware of their impulsive behaviours, continue to act impulsively as demonstrated by their impulsive behaviour on the MFFT.

Overall, these findings suggest that the impairments at emotion-related reversal learning in OFC-lesioned humans are best characterized as being due to a fundamental difficulty in processing rewards and punishments or in reversing stimulus-reinforcer associations, rather than being attributed simply to a difficulty in inhibiting previously relevant responses. Further, some of the reasons for the behavioural and emotional changes experienced by people following OFC damage may be related to deficits in decoding the reward and punishment value of stimuli and using the results of the decoding to modify behaviour and emotional state (Rolls *et al.*, 1994; Rolls, 1999a, 2000).

Frontal Behaviour Questionnaire

OFC patients reported significantly more inappropriate social behaviours than both non-OFC lesion and normal controls on the (self-report) Frontal Behaviour Questionnaire. Since OFC patients also scored significantly worse than both control groups on the reversal task, this suggests that the difficulty shown by OFC patients in rapidly altering stimulus-reinforcement associations may at least be partly responsible

for their disinhibited and inappropriate behaviour. Interestingly, the self-report and expanded version of the Frontal Behaviour Questionnaire used here was able to reveal deficits similar to those found with the questionnaire used elsewhere in which independent raters reported on the frontal behaviour (Rolls *et al.*, 1994; Hornak *et al.*, 2004). The implication is that patients with OFC lesions do have some insight into their behavioural changes.

Inappropriate 'frontal' behaviours are also linked to impulsivity in that OFC patients behaved and reported being significantly more impulsive in addition to reporting significantly more 'frontal' behaviours than both control groups. Further, self-report impulsivity and Frontal Behaviour Questionnaire scores were positively correlated across all subjects. OFC patients' impulsivity in terms of increased response times on the MFFT and faster cognitive tempos on the time perception tasks could contribute to their failure to interact with others appropriately. OFC patients may be too impatient to wait for appropriate feedback or to learn new stimulus–reinforcement associations and therefore fail to cooperate or respond appropriately in social situations. As such, the results of the present study have implications for the treatment of the problems OFC lesion patients are likely to face both within the family and when they return to work.

Subjective emotion (anger and happiness)

OFC patients reported experiencing more anger and less happiness than both lesion and normal control groups but there was no difference in sadness, fear and disgust. This may be attributed to a frustration from not getting appropriate social feedback because of their impulsive and inappropriate behaviours, or to their explicit awareness of their implicit deficits exemplified by their answers on the Frontal Behavior Questionnaire and their awareness that they are behaving impulsively and inappropriately, but inability to stop themselves. The relationship between emotionality and inappropriate behaviour is supported further by the fact that subjective emotion and 'frontal' behaviour scores were positively correlated across all subjects. Also, OFC patients' insensitivity to positive reinforcers, demonstrated by their performance on the reversal task, may cause them to be less happy and more angry.

Finally, perhaps the OFC patients' lesions were not large enough to affect all of their emotions (16 out of 23 OFC patients had only unilateral lesions). Consistent with the hypothesis that larger OFC lesions may affect emotion more, Hornak *et al.* (2003) found that bilateral but not unilateral discrete surgical OFC lesions produced significant changes in social behaviour and in subjective emotional state. Also, across all subjects, total subjective emotion score was positively correlated with 'frontal' behaviour, neuroticism and poor reversal performance. Thus OFC patients' emotional abnormalities could be a result of, a cause of or intricately related to their inappropriate behaviours.

Personality

Extraversion

OFC patients differed from both non-OFC and normal control groups in terms of impulsivity, but not extraversion. The concept of impulsivity has developed from being considered a facet of extraversion (Eysenck, 1981) to being considered a trait in its own right that is highly correlated with extraversion. In the current study, there was no significant correlation between extraversion and behavioural or self-report impulsivity. The implication of these findings is that there may be no essential relationship between impulsivity and extraversion, and that the OFC is related to impulsivity and not extraversion.

Openness to experience, and behavioural flexibility

OFC patients did not differ from non-OFC patients and normals on any of the personality dimensions except openness to experience, where both OFC and non-OFC lesions groups were significantly less open to experience than normal controls. A factor that may contribute to the reduced openness to experience of the OFC group is their deficit in stimulus–reinforcement association reversal, in that they do not change their behaviour appropriately when the reinforcement contingencies change. A factor that may contribute to the reduced openness to experience of the non-OFC group (most of whom had DLFC damage) is the difficulty DLFC patients have with processing novel stimuli, which may make decisions, and reasoning, difficult (see Krawczyk, 2002).

SWM task

Although both the non-OFC and the OFC group (14 out of 23 of whom had some DLFC damage) were impaired in that they made more between errors and used poorer strategies, only the OFC lesion group acted impulsively, had a faster cognitive tempo, failed to reverse stimulus–reinforcement associations, were more emotional and reported significantly more 'frontal' behaviours compared with normals. This single dissociation supports the notion that this latter set of deficits shown by OFC patients is unique to OFC damage and is not related to DLFC deficits or SWM (see Owen, 1997; Deco *et al.*, 2004).

There was some indication of a double dissociation, in that non-OFC patients made more 'within errors' in the SWM task than the OFC patients, whereas the OFC patients were impaired more than the non-OFC patients on the tests described above. Given that 'within errors' are the number of times that a subject revisits a box already found to be empty during the same search, the DLFC deficit can be easily related to short-term memory. In contrast, OFC patients may make more 'between errors', revisiting a box more often in which a token has already been found, because they associate that box with a reward and cannot relearn the new reinforcement

contingency. Once a token has been found in a box, one can never be found in there again. This implies that OFC patients may have a problem in the SWM task because of their difficulty in relearning new reinforcement contingencies, consistent with the evidence implicating the OFC in impulsivity, time perception, stimulus–reinforcement reversal, subjective emotion and inappropriate behaviour.

Overall implications for OFC function

The evidence strongly supports the view that the OFC is involved in representing the reward and punishment value of primary (unlearned) and secondary (learned) reinforcers, and in reversing by learning stimulus–reinforcement associations (Rolls, 1999a, b). The results described herein extend these ideas in relation to impulsivity, time perception and personality as well as the closely associated changes in subjective emotion, and social and emotional behaviour.

One of the fascinating new findings in this study was the increase in impulsivity (measured by both the BIS-11 questionnaire and the MFFT task) of patients with OFC lesions. Comparison with the other tests performed suggests that one contributing factor to the impulsivity of the OFC group may be their insensitivity to reward and punishment revealed in the reversal task (behavioural impulsivity and reversal performance were negatively correlated, $r = -0.42$, $P < 0.01$). Another contributing factor may be related to their overestimation and underproduction of time. These changes could be due to a fast cognitive tempo, or giving in to the frustration of waiting despite the negative consequences of not performing the task well. These findings suggest that impulsivity, expressed in both normal and psychiatric populations, may be related to functions taking place in brain regions that include the OFC. Further, the impulsivity reported by OFC patients was closely related to the Frontal Behaviour Questionnaire score ($r = 0.30$, $P < 0.01$, across all subjects).

Interestingly, most personality traits (extraversion, neuroticism, conscientiousness and agreeableness) were not affected by OFC lesions.

With respect to subjective emotion, the only effects attributed to OFC damage were higher frequency of anger and lower frequency of happiness, which may be attributed to frustration from not getting appropriate social feedback because of their impulsive and inappropriate behaviours. Indeed, across all subjects, total subjective emotion score was positively correlated with Frontal Behaviour Questionnaire score, and negatively with reversal performance.

The range of deficits just summarized in the OFC patients could not be attributed to deficits in SWM, in that these deficits were not present in the DLFC group (who had SWM impairments). Although there was a deficit in SWM in the OFC group, this could have been because of their difficulty in relearning new reinforcement contingencies, as discussed above.

In relation to earlier work, we note that although previous investigators have not measured impulsiveness, time perception or personality traits with the Big Five personality questionnaire, Tranel *et al.* (2002) have found deficits in a gambling task, and of emotion and personality after right but not left ventromedial PFC lesions; Sanfey *et al.* (2003) have shown that some patients with ventromedial PFC lesions make risky decisions in a gambling task; and that the results described here may be relevant to understanding fronto-temporal dementia in which changes in reversal learning and decision making may occur early (Rahman *et al.*, 1999). Further, Stuss and Alexander (2000) have emphasized that the functions of the frontal lobes in executive function are related in part to the affective changes, and the alteration in impulsiveness that we describe here that can be produced by OFC lesions elucidates one way in which the frontal lobes are involved in executive functions.

Therapeutic implications for OFC patients

OFC patients' significantly high impulsivity could be related to their inappropriate behaviour in social situations, as measured by the Frontal Behaviour Questionnaire, and their experience of more anger and less happiness compared with both control groups. OFC patients may be in a vicious cycle of impulsive behaviour that leads to negative social feedback and feelings of anger and decreased happiness. Perhaps if patients were taught to use alternative measures to cope, they would improve. For example, if they were taught to stop and explicitly evaluate situations before implicitly acting or taking decisions, perhaps they would act less impulsively and inappropriately, get better social feedback and feel better about themselves.

Also, if OFC patients are in fact impaired at learning changing reinforcement associations, perhaps they would be able to learn changes in reinforcement contingencies if they took more time before simply responding based on the old reinforcement contingency. They may have two deficits, one being a failure to alter their behaviour in response to changing reinforcement contingencies, and the other being a propensity to act without thinking owing to frustration (i.e. impatience due to wanting a reward immediately despite the costs involved or a fast cognitive pace). Each type of deficit may exacerbate the other, intensifying behavioural impairments. However, if OFC patients were encouraged to wait before responding, perhaps they could override the desire for an immediate reward and respond in the most efficient way. Thus, OFC patients might be encouraged to use their explicit system before implicitly responding.

Further, in emotional and social interactions, there is a continuous process of exchanging reinforcers (any reward or punishment) and reinforcing signals (such as smiling or a disapproving look). Failure to respond normally to reinforcers may be a fundamental deficit that underlies impulsiveness, disinhibition and misinterpretation of other peoples' moods. A fast cognitive tempo may also exacerbate OFC patients'

inappropriate responses to environmental reinforcers as patients respond too quickly to allow for ample time to evaluate reinforcement contingencies properly and respond appropriately. Recognition of this could help with management of these patients. Explanation of these problems to OFC patients may help them to identify situations in which their behaviour may be inappropriate and then to take corrective measures. Given their ability to describe what responses should be made on the reversal task, patients could be encouraged to verbalize their intentions and then given explicit training in carrying them out. Training in a wide range of extinction and reversal situations may also be beneficial, as this might enable patients to produce more appropriate behaviours in a wide range of emotional and social situations in which such alteration of behaviour by learning normally occurs.

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