Emotion-related learning in patients with social and emotional changes associated with frontal lobe damage

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Abstract
A group of patients with damage to the ventral part of the frontal lobes was severely impaired relative to a group of patients without damage in this area (the non-ventral group) in the reversal and in the extinction of simple visual discrimination tests. In these tests they continued to make responses to a previously rewarded stimulus. Patients often reported verbally that the contingencies had changed, but were unable to alter their behaviour appropriately. These impairments occurred independently of IQ or verbal memory impairments. The perseverative touching of a previously rewarded stimulus is consistent with work on non-human primates showing impaired reversal and extinction after orbitofrontal lesions. Performance on these reversal and extinction tests was highly correlated with scores obtained on a behaviour questionnaire, which reflected the degree of disinhibited and socially inappropriate behaviour exhibited by patients. It is suggested that a difficulty in modifying responses, especially when followed by negative consequences, as manifested in these simple laboratory tests, may contribute to the inappropriate behaviour shown in daily life by patients with frontal lobe damage.

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Patients with frontal lobe brain damage, produced, for example, by closed head injury or cerebrovascular accident, may show altered emotion and social behaviour, such as disinhibited or socially inappropriate behaviour, impulsiveness, and misinterpretation of people's moods. In humans, there is little understanding of the processing that normally takes place in the affected region, or even of exactly which part of the frontal lobe is crucial for the changes. On the other hand, there have been many advances in the past few years in understanding the neural basis of emotion in non-human primates, and the location, connections, and functions of the frontal region involved in emotion. The research described here aims to take this fundamental research and to investigate whether it has implications for understanding and treating the symptoms in these patients, and in their rehabilitation.

The analysis of one part of the frontal cortex, the orbitofrontal cortex, suggests that one way that it is important in emotions is because it is involved in emotion-related learning. For example, the learning deficits associated with damage to the orbitofrontal cortex in non-human primates include impaired extinction and impaired visual discrimination reversal. Extinction is the normal reduction in behaviour when rewards are no longer given. The impairment in extinction produced by orbitofrontal damage consists of continued responding for the previously rewarded stimulus. In a visual discrimination task, responses to one stimulus are associated with reward, and to the other with no reward (or punishment). In the reversal of the task, the stimulus previously associated with reward becomes, after the reversal, associated with non-reward and vice versa. The deficit in reversal produced by damage to the orbitofrontal cortex also consists of continued responding to the previously rewarded stimulus. These two deficits can be understood as a failure to break, or adjust, previously learned associations between stimuli and primary reinforcers (for example, reward or punishment). In modern approaches to emotion, emotions are often considered to be states elicited by rewarding and punishing stimuli. For example, the emotion of fear is a state elicited by stimuli learned to be associated with punishment, and joy is a state associated with rewarding stimuli. Because emotions are related to rewarding and punishing (reinforcing) events (which alter the probability of behaviour occurring), any failure to correct behaviour when the reinforcement value of environmental stimuli changes will lead to inappropriate emotional and social behaviour. Thus the main aim of this investigation was to determine whether patients with altered social and emotional behaviour after frontal lobe damage have deficits in this type of learning, as such a deficit could provide a fundamental explanation for at least some of the symptoms found.

It should be noted that visual or object discrimination reversal is different from spatial reversal or alternation, in which the dorsolateral prefrontal cortex is implicated. This spatial short term memory processing may have little to do with emotion, by contrast with learning associations between environmental stimuli and rewards.

The evidence that the orbitofrontal cortex is involved in processing and learning about rewards is extensive. For example, it is now known that the orbitofrontal cortex receives
information about primary reinforcers (such as taste, smell, and touch), and indeed contains the secondary taste and olfactory cortices. The orbitofrontal cortex also receives visual and auditory inputs (from the temporal lobe visual and auditory cortical areas), and rapid association learning and unlearning of these inputs in terms of their ability to influence neurons that respond to primary reinforcers occurs. The same regions contain neurons that respond to emotion-provoking stimuli, such as faces, and indeed damage to the orbitofrontal cortex in non-human primates affects not just stimulus-reinforcement learning, but also emotional responses to objects.

In some previous studies deficits on tasks such as pattern reversal and object alternation have been reported in patients with Korsakoff's syndrome or Alzheimer's disease, in whom there is often some frontal involvement. It is also well known that patients with frontal lobe damage may have impairments on the Wisconsin card sorting task, but this task involves considerable cognitive processing—for example, categorisation of stimuli by colour, number, or shape. We wished to test the stimulus-reinforcement learning hypothesis directly, and therefore designed a much simpler test than the Wisconsin task, in which the main element was the extinction or reversal of stimulus-reinforcement associations. We also sought to relate difficulties with reversal or extinction, or similar tasks, to social and behavioural problems that the patient might also show in daily life, in which a difficulty with inhibition might also be involved.

Methods

PATIENTS

Twenty patients attending the Rivermead Rehabilitation Centre, Oxford, as either inpatients or outpatients, were studied. Most had had head injury or stroke (table 1). Patients were included if they agreed to enter the study, which had local ethics committee approval, if they were thought to have frontal lobe damage (see later) or if they were thought to show behavioural changes consistent with frontal lobe damage. Other patients were included in a non-frontal group (see later) if the above criteria were not met. No patient was included unless their language comprehension was adequate for understanding the instructions for the tests and their expressive language was adequate for answering questions about their emotions and behaviour. For this reason there was a preponderance of patients with right-sided damage. Pilot studies on a group of normal subjects (recruited from the staff of the Rivermead Rehabilitation Centre) were performed to provide information on normal performance in the reversal and extinction tests.

The sites of the brain damage in these patients were determined by MRI whenever possible, and when not possible, by CT, and are indicated, together with clinical details, in table 1. Localisation was taken from the formal radiological reports, and patients were divided into two groups on the basis of identified location of damage. Twelve had lesions that included damage relating to the ventral (inferior) parts of the frontal lobes (ventral frontal group), and eight did not have damage to this region (non-ventral group). The damage in the non-ventral group was either outside the frontal lobes, or, in two patients (cases 18 and 20) whose results were similar to the other members of the non-ventral group, in the dorsolateral frontal region, as shown in table 1. The ventral frontal group here thus refers to a group of patients with damage related to the ventral part of the frontal lobes. The time since the brain damage varied from a few months to many years in some cases.

All the patients included in this study had severe disability as evidenced by the need to be at the Rivermead Rehabilitation Centre. The aetiology of the brain damage was varied, as were the disabilities of the patients. None of the patients in either group had any general cognitive deterioration as shown by their performance on standard neuropsychological tests.

REVERSAL

In this test the patient learned to touch one of two simple patterns that appeared one at a time on a touch screen. The stimuli were highly discriminable coloured fractal images displayed on a video monitor fitted with a touch screen of a 386 AT computer. The patients gained one point for touching the correct pattern, and lost one point for touching the incorrect pattern. (They also gained a point for not touching the incorrect pattern and lost a point for not touching the correct pattern.)

Patterns remained on the screen for seven seconds if not touched (regardless of whether it was correct not to touch them). They
behaviours or characteristics were assessed: disinhibition or social inappropriateness; violence; verbal aggressiveness; anger or irritability; misinterpretation of people's moods; inflexibility; perseveration; unconcern about condition; lack of initiative; uncooperativeness; flat affect, on the following scale: 1-5 = very much/all the time; 1-0 = characteristic or behaviour was present; 0-5 = sometimes/a little; 0-0 = never/not at all.

SUBJECTIVE EMOTIONAL CHANGES
Patients completed a questionnaire (J Hornak, ET Rolls, D Wade, unpublished data), which related to changes in the experience of positive and negative emotions (sadness, anger, fear, disgust, and excitement/enjoyment) since their illness or injury.

OTHER NEUROPSYCHOLOGICAL TESTS
To determine whether the alterations found in the patients with ventral frontal damage were selective, or were part of a general cognitive deterioration, performance on a number of standard clinical tests, including tests for the performance of other memory systems, was evaluated. The tests included paired associate learning (from the Wechsler memory test), verbal IQ (from the WAIS-R), for some patients story recall (from the Wechsler memory test), and for three patients the Tower of London task, which tests planning and the memory for planned actions.  

Results

REVERSAL AND EXTINCTION

Comparison of ventral frontal and non-ventral groups

In the learning of the visual discriminations that were the preliminary parts of the reversal and extinction test, all patients in both groups reached the criterion with a minimum of errors once they had understood what was required of them. When the contingencies were altered, the patients in the ventral frontal group tended to touch the previously rewarded stimulus, and in this way performed poorly both in extinction and reversal. Patients in the non-ventral group, like normal subjects, generally made only a few errors before achieving the criterion of nine correct out of the preceding 10 trials. In the reversal test, patients in the non-ventral group, like normal subjects, successfully reversed a second (and third) time with very few or only a single error at each new reversal (table 2). In this way, in the first 30 trials, the non-ventral group achieved a median of two (mean of 1-9) reversals. By contrast, the ventral frontal group achieved a median of 0 (mean of 0-56) reversals (see table 2).

In reversal, table 2 shows the median trial on which the last error was made in achieving the criterion on the first reversal for the two groups. Where a patient failed to reach criterion within 30 or more trials, the trial on which the last error was made before the test ended was used instead. On a Mann-Whitney test, the difference between the groups on this

EXTINCTION

This test used two other highly discriminable fractal images as stimuli, but otherwise it started in the same way, with the same instructions. After criterion had been reached, it became, without warning, incorrect to touch either pattern. Points could only be won by refraining from touching both of the patterns, and were lost by touching either of them. As in the reversal test, the patient advanced each new trial himself by pressing the space bar on a keyboard. In both the reversal and extinction tests, comments made by the patient during the tests were recorded, as were responses to questioning directly after each test. The extinction test was run after the reversal task, with a gap of at least five minutes between the tests.

POST-TEST INTERVIEW

Directly after each test, the patient was asked to explain what the task had involved, how he could gain and lose points, and which stimulus had been correct initially. He was then asked what had happened later in the test (when contingencies were altered), and how he had responded.

BEHAVIOUR QUESTIONNAIRE

A member of staff involved in each patient's care or rehabilitation was asked to complete a questionnaire designed to reflect the types of behavioural problems generally believed to result from frontal damage. The following...
measure was significant at $p = 0.019$ ($U = 9.5$, two tailed tests except where stated).

In extinction, (table 2), there was also a large difference between the ventral frontal and non-ventral groups on the last error score ($p = 0.0035$, $U = 3.0$).

Of the 10 patients in the ventral frontal group, all performed poorly relative to the non-ventral group in terms of the last error trial or either the reversal, or the extinction test, or both.

Performance of severely impaired patients with ventral frontal damage

The performance on the first 30 trials of those patients with ventral frontal damage who failed to reach criteria within 25 trials on either reversal or extinction was further analysed. Six of the 10 tested fell into this category in reversal, and six (which included three different patients) in extinction.

In reversal, these patients made some correct responses, so that they gave themselves the opportunity to discover how points could be won in reversal, although their performance remained close to the chance level of 50% (table 3). The maximum runs of consecutive correct responses show, however, that they were never close to reaching the criterion.

Table 3 also shows, for reversal, the group mean percentages of all old S+ (previously correct stimuli) touched (commission errors) and of all the old S− (previously incorrect stimuli) not touched (omission errors). The patients with ventral frontal damage clearly found it harder to refrain from touching the old S + than to learn to touch the old S −. (The percentage of commission errors was 76%, compared with 33% of omission errors.) Patients generally followed an incorrect touch of the old S + with another touch on its next appearance, despite the fact that they lost a point each time they did so. Similarly, on the few occasions when they refrained from touching the old S +, and were rewarded with a point, they failed to repeat this correct response on the next occurrence of that stimulus. The perseveration of touch responses to the old S + stimulus was in fact the major obstacle to the patient's reaching the criterion. There were few errors of either type in the non-ventral group.

Table 4 shows a similar pattern for correct responses and error types in extinction, with the percentage of old S + touched in error (70%) being greater than that for old S − (40%). There were few errors of either type in the non-ventral group.

Verbal comments of patients with ventral frontal damage during reversal and extinction

On the first reversal trial patients generally made some objection or comment that clearly showed their awareness that the contingencies had changed (for example, "they're switched!"), and the same was true when extinction began. Some patients seemed to try to instruct themselves to respond in a way that would yield points, but without success. Case 8, for example, in extinction, announced at trial 24 that she would not touch any more stimuli. She restrained herself for a few trials, but then touched the next seven stimuli in succession, whereupon the test was ended. Similarly, case 2 bemoaned the fact that he always touched the old S + "wrongly", but continued to do so for a total of a further seven trials before the test was ended. Case 4 often said "No!" to himself, but then touched the stimulus, and commented, "I knew I was wrong". On one occasion he was asked whether it would be correct to touch a stimulus. He correctly answered "No", hesitated, and then did so.

Post-test interview

All patients described the two stimuli accurately and remembered which stimulus had been correct at the beginning of the test. They explained how points could be gained and lost, and how the contingencies switched in reversal—namely, that it was no longer correct to touch the original S+, and that doing so lost points. They described how the original S− became correct instead. They also explained how both stimuli became incorrect to touch in extinction. They were all able to describe the fact that they had nevertheless continued touching the old S + in both tests. For example, case 8, when asked whether she had continued to touch the S + after it had become incorrect in the reversal test, answered "a few times... I lost a lot of
points. I didn't learn from my mistakes—I went on touching it”.

When asked why they had continued to touch the old S+ if it was incorrect to do so, some were at a loss. Case 7, for example, said “I don’t know... something in there (indicating his head) told me to touch it and try to get a point”. Others gave somewhat confabulatory justifications, claiming, for example, that they had hoped that the S+ might have become positive again if they kept on touching it. This claim was made despite the fact that the patient had discovered that not touching it could gain points, and despite their avowed aim to gain as many points as possible.

**BEHAVIOUR**

Table 2 shows that on the behaviour questionnaire the group median for the ventral frontal group was 6.0 (mean 5.7 (SD 1.8)), whereas the group median for the non-ventral group was 8.0 (mean 1.0 (SD 0.8)). There was no overlap between the scores of individual patients within the two groups (Mann-Whitney U = 0, p = 0.003).

The five commonest types of behaviour abnormality in the ventral frontal group, present in nine or more of the 12 patients, were: disinhibited or socially inappropriate behaviour (extreme for five patients) (mean = 1.0, non-ventral group = 0.0); misinterpretation of people’s moods (mean = 0.7, non-ventral group = 0.06); impulsiveness (mean = 0.7, non-ventral group = 0.3); unconcern about or underestimation of the seriousness of his condition (mean = 0.7, non-ventral group = 0.2); lack of initiative (mean = 0.8; non-ventral group = 0.3).

No patient in the non-ventral group was disinhibited or socially inappropriate.

Examples of disinhibited or inappropriate behaviour shown by patients with ventral frontal damage

Sexually explicit references, suggestive comments, or actual sexual advances were made to staff by cases 3, 8, and 10. Case 10 had also exhibited himself in the town centre. Cases 2 and 7 were overfriendly (case 7 swept a member of staff off her feet to hug and kiss her because he was in a good mood), case 3 was boastful, claiming he was more handsome and that his humour had improved since his accident (in fact his humour was childish and repetitive). Case 3 also tactlessly told a member of staff she was much less pretty than someone else. Case 4 practised karate kicks in the canteen and mimed the savage blows he would inflict on anyone who crossed him. Case 5 planned to kill the driver of the car that had hit him and asked the police to help him carry out his plan. Case 1 upset his wife by buying her a piece of cheap jewellery she would never have considered wearing.

Disinhibited or inappropriate behaviour was present in patients with unilateral as well as bilateral lesions.

**Correlation between behaviour and emotional change**

Patients who scored highly on the behavioural questionnaire also reported considerable changes in their experience of emotion since their accident or injury. Using a score based on overall change (increase and decrease in positive or negative subjective emotion; J Hornak, ET Rolls, D Wade, unpublished data) there was a strong positive correlation between these subjective emotional change scores and the behaviour scores (Spearman rank correlation (r = 0.764, p = 0.002, one tailed)).

**Correlation between behaviour and performance on reversal and extinction**

A significant correlation was found between scores on the behaviour questionnaire and the percentage of errors of commission in the reversal test (% of old S+ touched) (Spearman r = 0.69, p = 0.007 (two tailed)) (see figure (A)). Data are shown for, and the correlation was calculated across, all patients in both groups.

In the extinction test a significant correlation was also found between scores on the behaviour questionnaire and the percentage of old S+ touched (Spearman r = 0.61, p = 0.023 (two tailed)) (see figure (B)).
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BEHAVIOUR
Table 2 shows that on the behaviour questionnaire the group median for the ventral frontal group was 6-0 (mean 5-7 (SD 1-8)), whereas the group median for the non-ventral group was 0-8 (mean 1-0 (SD 0-8)). There was no overlap between the scores of individual patients within the two groups (Mann-Whitney U = 0, p = 0-003).

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- disinhibited or socially inappropriate behaviour (extreme for five patients) (mean = 1-0, non-ventral group = 0-0; misinterpretation of people’s moods (mean = 0-7, non-ventral group = 0-06); impulsiveness (mean = 0-7, non-ventral group = 0-9); uncernt about or undervestimation of the seriousness of his condition (mean = 0-7, non-ventral group = 0-2); lack of initiative (mean = 0-6; non-ventral group = 0-5).

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CORRELATION BETWEEN BEHAVIOUR AND PERFORMANCE ON REVERSAL AND EXTINCTION
A significant correlation was found between scores on the behaviour questionnaire and the percentage of errors of commission in the reversal test (% of old S+ touched) (Spearman ρ = 0-69, p = 0-007 (two tailed)) (see figure (A). Data are shown for, and the correlation was calculated across, all patients in both groups.

In the extinction test a significant correlation was also found between scores on the behaviour questionnaire and the percentage of old S+ touched (Spearman ρ = 0-61, p = 0-023 (two tailed)) (see figure (B)).
RELATION BETWEEN NEUROPSYCHOLOGICAL TESTS AND PERFORMANCE ON REVERSAL AND EXTINCTION

In those patients who were tested (which included seven of the 10 patients with ventral frontal damage), verbal IQ was within the average range, and in all cases scores were within 1 SD of the mean. Two patients in the ventral frontal group obtained scores above 110, placing them in the high average range. As shown in Table 2, the median score (—0.4) for both groups on the paired associate learning test was well within 1 SD of the mean. On a Mann-Whitney test there was no significant difference between the two groups (p = 0.67).

Importantly, there was no correlation between either verbal IQ scores or paired associate learning scores and performance on either reversal or extinction, as measured by the percentage of old S+ (previously rewarded stimuli) touched. Four Spearman rank correlations were performed, giving nonsignificant results in all cases as follows: reversal and verbal IQ ρ = 0.00; extinction and verbal IQ ρ = 0.06; reversal and paired associate learning ρ = 0.23; extinction and paired associate learning ρ = 0.15.

All of the patients in the ventral frontal group who were tested (cases 1, 8, and 9) on the Tower of London task performed normally, achieving scores within 1 SD of the mean for normal subjects.

Discussion

In this study it was shown that performance on reversal, extinction, or both, in which previously learned associations between environmental stimuli and rewards must be altered, was impaired in patients with damage to the ventral parts of the frontal lobes. This learning deficit was separable from other types of learning and memory problems, in that there was no correlation with paired associate learning performance (which is more related to temporal lobe damage). The ventral frontal learning deficit was also separable from the effects of a general disturbance in brain function, in that there was no correlation with verbal IQ. This learning deficit may contribute to the emotional and social problems that can occur in patients with ventral frontal damage, because the ability to respond appropriately to reinforcing stimuli and to learn when their reinforcement associations change is of central importance in emotion, and in social and behavioural responses to emotional stimuli.21

Another new finding of this study, which supports this hypothesis, was that scores on the behaviour questionnaire, which was designed to quantify the social-behavioural abnormalities associated with frontal damage, were positively correlated with performance on the reversal and extinction tests, using the percentage of previously correct stimuli touched in error as an index of performance on both tests. This suggests that the difficulty shown by the ventral frontal group in rapidly altering stimulus-reinforcement associations may be at least partly responsible for their disinhibited and inappropriate behaviour.

In the tests of reversal and extinction, the patients with ventral frontal damage had difficulty in learning from their mistakes or benefiting from their correct responses. The major obstacle to reaching the criterion in both tests was the perseveration of touching the old S+. Although most of the patients were reported as showing some degree of impulsiveness on the questionnaire, all were able to refrain from touching the old S+ for the first three trials during initial learning of the tasks (before the contingencies were altered). The difficulty for these patients therefore consists particularly in refraining from touching a once correct stimulus after it becomes incorrect, even though doing so consistently lost them points, and resulted, to their dismay, in increasingly large negative running score totals. Performance on these reversal and extinction tests may capture rather directly one of the fundamental learning difficulties that may underly poor performance in the Wisconsin card sorting task—a more complicated task that involves other cognitive capacities than reinforcement-related learning.

The perseveration of touch responses to the old S+ is consistent with what has been described in the literature for non-human primates with lesions of the orbitofrontal cortex,21 an area likely to be damaged in severe head injury (which half of the ventral frontal group had had). Magnetic resonance imaging did in fact show that damage included this ventral frontal area in the ventral frontal group, but never did so in the non-ventral group. The performance of the ventral frontal group on reversal and extinction is also consistent with studies on patients with frontal damage using other tests in which patients are required to inhibit a response (in go or no-go, and object-alternation, tasks). The present study is, however, the first to relate performance on such a test to the patients' social behaviour in daily life. The present results also provide further striking evidence of the dissociation, described in the literature, between what patients with frontal damage say and what they do.11-14 Because patients with ventral frontal damage commented on the changing contingencies when they occurred, and described both the tests and their own performance accurately afterwards, their impairment cannot be attributed to a general failure of comprehension or to an inability to retain the instructions given at the beginning long enough to achieve success.

Additionally, the three patients with ventral frontal damage who were also tested on the Tower of London task all performed normally, although severely impaired at either reversal, extinction, or both. This normal performance on a test of planning is consistent with a generally held view15-16 that lesions of the dorsolateral frontal lobe are more likely to affect planning and other higher cognitive functions, whereas lesions of the orbitofrontal cortex, with its connections to the limbic system, have a greater effect on social behaviour.
and emotion. Preliminary evidence consistent with such a double dissociation of function within the frontal lobe is in fact already provided by cases 18 and 20 in the present study in both of whom the lesions were confined to the dorsolateral part of the frontal lobe. Neither patient had shown any appreciable alteration in their social behaviour or in their experience of emotion and both also performed normally on reversal and extinction. Both were, however, reported in the assessments made by clinical psychologists to show impaired planning on a number of different tasks.

The present results have implications for rehabilitation. They suggest that one of the fundamental problems for the type of patient described here is in altering behavioural responses when environmental reinforcers change. 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 expression). Failure to respond normally to reinforcers may be a fundamental deficit that underlies impulsiveness, disinhibition, and misinterpretation of other people’s moods. Recognition of this should help with management of these patients. Explanation of these problems to such 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, 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 might also be of benefit, as this might enable such patients to produce more appropriate behaviour in the wide range of emotional and social situations in which such alteration of behaviour by learning normally occurs.

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