Social reasoning, emotion and empathy in frontotemporal dementia

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Abstract

Introduction:: Social cognition is crucial for human interaction, and is markedly impaired in the frontal variant of frontotemporal dementia (fvFTD). The relationship of various aspects of social functioning, however, remains controversial in this group.
Methods:: Patients with fvFTD ($n = 18$), and matched controls ($n = 13$), were tested using tasks designed to assess their Theory of Mind (ToM), moral reasoning, emotion recognition and executive function. Caregivers documented changes in empathy compared to premorbid functioning.
Results:: We found marked impairments in the abilities of fvFTD patients, relative to controls, in ability to mentalise (ToM), which was evident on a cartoon test, but not on a story-based ToM task. Knowledge of social rules was intact, but moral reasoning was defective, and was due, in part, to an inability to rate the seriousness of moral and conventional transgressions appropriately. Executive function was impaired in this group, and compromised aspects of moral reasoning, but ToM performance was independent of this. Emotion recognition was globally impaired in fvFTD, but was particularly so for anger and disgust which may partly explain the difficulty these patients have with identifying social violations. Empathy, as rated by carers, was also shown to be abnormal.
Conclusion:: It appears that social reasoning is disrupted in a number of ways in fvFTD, and the findings provide a basis for the understanding and further study of abnormal behaviour in this disease. The results are discussed in light of neuroimaging findings in studies of social cognition and the locus of pathology in fvFTD.
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1. Introduction

It is now widely acknowledged that changes in interpersonal behaviour such as loss of empathy, disinhibition, impaired social awareness and loss of insight are hallmarks of the frontal or behavioural variant of frontotemporal dementia (fvFTD) (Lund & Manchester Groups, 1994; Mendez & Perryman, 2002; Neary et al., 1998).

A key aspect of social cognition is the ability to infer other peoples' mental states, thoughts and feelings. This is referred to as Theory of Mind (ToM) or mentalising ability. Gregory et al. (2002) proposed that assessment of performance on ToM tasks in patients with fvFTD may be relevant in understanding the genesis of the change in social interaction in these patients and may assist in earlier diagnosis. This hypothesis was supported by findings in a study comparing groups of patients with fvFTD, Alzheimer's disease and healthy controls who were administered a range of ToM tasks. FvFTD patients were specifically impaired on tests of ToM, but only one of the tasks (the faux pas test) was particularly sensitive to impairment in ToM. The specificity of the faux pas test is however questionable since it depends on knowledge of social norms and rules and perhaps emotional responses to violations of these norms, in addition to ToM (Berthoz, Armony, Blair, & Dolan, 2002; Blair & Cipolotti, 2000). The ability to appreciate, and respond to, the normal social conventions of society has been explored in subjects with psychopathy and acquired sociopathy but has not been examined in fvFTD (Blair & Cipolotti, 2000).

Another of the tasks employed by Gregory et al. (the Mind in the Eyes Task), held to be an advanced test of ToM, involves

recognition of complex emotions rather than purely mental states. Recognition of emotional expression in faces and voices was shown to be impaired in a small group of patients with fvFTD (Keane, Calder, Hodges, & Young, 2002), but an in depth study of a single fvFTD patient showed very poor performance on the faux pas test, with a normal level on the Mind in the Eyes Test (Lough, Gregory, & Hodges, 2001), suggesting that recognition of emotion and ability to mentalise may be separable. Indeed, several authors have stressed a distinction between different aspects of social cognition: particularly between the representation of mental states (e.g., thoughts or beliefs; classic Theory of Mind) and the representation of or response to emotional states (inferred from facial and vocal expressions as well as body gestures) (Blair & Cipolotti, 2000; Joseph & Tager-Flusberg, 2004).

There is now a growing body of evidence concerning the neural basis of the representation of mental states (ToM). Within frontal cortex, a critical region appears to be ventromedial prefrontal cortex (Frith & Frith, 2003). Recent imaging studies suggest that this region undergoes degeneration in fvFTD (Williams, Nestor, & Hodges, 2005).

In this study, we aimed to take a broader perspective on the issue of deficits in social cognition in a large group of patients with fvFTD. In particular, we aimed to explore the relationship between deficits in Theory of Mind, social norm processing, emotional responsiveness, and the ability to empathise and to reason morally Interestingly, recent fMRI imaging work has stressed the importance of ventromedial prefrontal cortex in moral decision making (Greene & Haidt, 2002; Moll, Oliveira-Souza, Bramati, & Grafman, 2002). A well-established social situations task (Dewey, 1991) was employed to assess the ability to recognise violations of social norms. A moral/conventional distinction task (Blair, 1995) was used to assess moral and social reasoning. In order to detect any changes in ability to empathise over time, a care-givers questionnaire (Davis, 1980; Perry et al., 2001) was employed. Based upon previous work we predicted that patients with fvFTD would show deficits in ToM, emotion recognition and the ability to empathise (Blair & Cipolotti, 2000; Gregory et al., 2002; Keane et al., 2002; Lough et al., 2001). Moral reasoning and the ability to recognise violations in socially acceptable behaviour have not been examined in fvFTD.

2. Methods

2.1. Ascertainment of patients

A total of 31 participants were included in the study: 18 patients with frontotemporal dementia (16 males and 2 females, age range 47–74 years, mean 61.1 ± 6.7) and 13 healthy control volunteers (9 males and 4 females, age range 43–75 years, mean 57.0 ± 9.1) chosen to match the patients for premorbid IQ based on the National Adult Reading Test (NART). A professor of behavioural neurology (JRH), and a consultant clinical psychologist (SL) assessed all of the patients, who were seen at the Early Onset Dementia Clinic at Addenbrooke's Hospital, Cambridge between 2000 and 2002. A history was taken from the patient and from a close relative/carer. Patients underwent routine haematology, biochemistry, tests of thyroid function, screening tests for syphilis, examination of the CSF and a physical examination. Structural neuroimaging, either CT or MRI scan, was obtained in all cases to exclude other causes of dementia.

All patients presented with a corroborated history of progressive decline in social interpersonal conduct and behaviour with emotional blunting and loss of insight. All fulfilled the Lund-Manchester consensus criteria for frontotemporal dementia (Neary et al., 1998) plus our locally developed criteria applied in previous studies (Bozeat, Gregory, Ralph, & Hodges, 2000). Patients presenting primarily with language complaints (progressive non-fluent aphasia or semantic dementia), or those showing a significant degree of semantic impairment that might interfere with their comprehension of tasks were excluded.

2.2. Theory of Mind and social reasoning tasks

Three aspects of social cognition were assessed:

(1) the ability to represent the internal mental states of others (ToM);
(2) the ability to appreciate the appropriateness of behaviour in different social contexts;
(3) sensitivity to moral and conventional rules.

2.2.1. Theory of Mind tasks
2.2.1.1. Theory of Mind cartoons. This task was similar to that employed by Corcoran, Cahill, and Frith (1997). Two sets of cartoon jokes were used. The jokes in one set (physical) could be understood in physical terms, while the jokes in the other set (ToM) required the participants to perceive the mental state of the main character. The two sets were intermixed in a randomised order and given in a single test session. Participants were required to explain the joke using the question "Why might someone find this funny?" In explaining the ToM jokes, patients had to use language which indicated that they had correctly perceived the mental state inferred in the cartoon for the interpretation of the joke to be accepted as correct (e.g., "thought that", "did not know", "believed that"). In the other set of jokes, a physical explanation of the cartoon was acceptable, but not simple naming or identification of parts/actions. Explanations were recorded verbatim and scored by two independent raters who, after training, achieved >90% concordance. Each set was scored from a total of 10 with one point awarded for each acceptable explanation.

2.2.1.2. Theory of Mind stories. The task consisted of participants reading 16 stories describing naturalistic social situations and being asked why the characters behaved as they did (Happe, 1994). Half of the stories required ToM accounts (i.e., appropriate references to mental states) to give a correct explanation, while the other eight required a physical explanation (i.e., a reasonable behavioural account). Each set of eight was scored with one point awarded for each acceptable explanation (modified from Happe (1994) which had a 2, 1, 0 comprehension score and then a 1 or 0 for correct identification of mental or physical state).

2.2.2. The moral/conventional distinction task
This task was based on the distinction between two classes of social rules: moral (i.e., victim based) and conventional (i.e., minor social-disorder). Moral transgressions are typically judged more serious than conventional transgressions and they continue, unlike conventional transgressions, to be judged as non-permissible even in the absence of prohibiting rules. Eight scenarios containing moral transgressions and eight scenarios containing conventional transgressions from Blair and Cipolotti (2000) were presented to the participants in a randomised order. Four questions, presented in a fixed order after each scenario had been read, were used to assess the moral/conventional distinction. Examples of the transgression stories used and the four questions are described in Appendix A.1.

Participants scored either 0 or 1 according to whether they answered the permissibility question "Was it right for X to do Y?" as right or wrong, respectively. Thus, if all eight moral and eight conventional transgressions were correctly considered impermissible, the participant would score the maximum of 8 for both the moral and conventional transgressions (permissibility score). For transgressions correctly identified as non-permissible, the participants were asked to rate the seriousness of the transgression on a scale of 1–10. The maximum seriousness score for both types of transgression was thus 80. The number of transgressions judged as non-permissible in the absence of rules was calculated from answers to the final two questions outlined in Appendix A.1(3). The transgression was

countered firstly with consensus opinion and secondly with permission from authority. On each occasion the participant did not yield to the counter argument, a score of 1 leading to a potential maximum score of 16 for both moral and conventional transgressions (absent rules score).

2.2.3. Social situations task

This task (Dewey, 1991) was designed to investigate participants' ability to judge the appropriateness of behaviours, for which there are no formal societal prohibitions, but which nonetheless may induce irritation or anger in observers. Nine short stories, each incorporating behaviours that were either normative or a violation were read by each participant. At various points in each story, the participant was asked to comment on how appropriate the behaviour was, giving a score from 1 to 4. A score of 1 indicated the situation to be judged as socially normal. Scores from 2 to 4 indicated a judged violation of normal social behaviour with 2 being mild and 4 being serious. Three scores were obtained for this task: behaviours identified as normative, behaviours identified as violations and an appropriateness score reflecting severity of rating of violations. The task instructions and an example story are given in Appendix A.2.

2.3. Recognition of facial emotion expression

2.3.1. Facial emotion expression processing task

This task was based on a paradigm originally described by Calder, Young, Perrett, Hodges, and Etcoff (1996) and modified by Blair and Cipolotti (2000). Recognition of six emotion expressions was assessed: surprise, happiness, anger, disgust, sadness and fearfulness. The stimuli were morphed black and white images of faces ranging in sequence from neutral to full expression of an emotion. Each face was presented on a computer screen for 23 s with 40 successive frames from a neutral expression to a target emotion. Trials ($n = 36$) consisted of images of 6 different people morphing to each of the 6 emotions. Participants were required to name the target emotion as soon as possible. The score for each emotion was a maximum of 6 correct. Although the number of frames to decision about the nature of the expressed emotion was recorded on each trial as many in the patient group performed at ceiling this data was not collated.

2.4. Assessment of empathy

2.4.1. Interpersonal Reactivity Index (IRI)

The IRI (Davis, 1980; Perry et al., 2001) has been developed primarily as an assessment of empathy. It consists of four subscales: empathic concern, perspective taking, personal distress and fantasy. Each subscale consists of 28 statements. Following the procedure of Perry et al. (2001), two versions of the IRI were administered to the caregiver of each participant in the fvFTD group. In the first version, the relative was asked to rate on a Likert scale from 0 to 4 how well each of the 28 statements described the patient prior to the onset of the disease. In the second version, the exact same procedure was repeated, however this time the relative was to rate the patient's current status on each statement. By this method any perceived changes over time in the patient's empathy could be quantified.

2.5. Frontal/executive tasks

2.5.1. The Hayling and Brixton tests

These tests were administered and scored following the procedure outlined by Burgess and Shallice (1997). In the Hayling test, subjects have to complete several sentences with either an expected or an unrelated word. The two conditions are felt to measure initiation or inhibition, respectively. The Brixton test is a spatial rule detection task testing the ability to detect and adapt to rules in a series of stimuli.

2.6. Statistical analysis

Statistical analyses were performed using SPSS. Group comparisons employed analysis of variance (ANOVA). Parametric statistics were used since an initial exploration of the data set suggested an acceptable distribution (skewness < 1.00, kurtosis < 3.00), except for the IRI data where the Wilcoxon sign test was employed.

3. Results

3.1. Matching on age and NART error score

Comparison of the two groups' mean scores showed no significant difference for age (fvFTD = 61.1 ± 6.7, controls = 57.0 ± 9.1; p = ns) or for NART error score (fvFTD = 17.9 ± 7.2, controls = 16.5 ± 6.9; p = ns), indicating good matching for age and premorbid IQ. The mean mini-mental state examination (MMSE) score for patients was 28 (± 2.8) and for the Addenbrooke's Cognitive Examination (ACE) was 86.5 (± 8.4).

3.2. Frontal/executive tests—Hayling and Brixton tasks (Table 1)

One-way ANOVAs indicated that fvFTD patients performed significantly worse than controls on both the Hayling and Brixton tasks ($F(1, 29) = 23.89$ and 6.14, $p < 0.001$ and 0.05, respectively). Given these group differences and previous suggestions that social cognition and executive function may not be entirely dissociable, the score on the Hayling task (the task with the greatest group difference) was consistently initially entered as a covariate in the following analysis. On the occasions when the score on the Hayling task had no significant relationship with the specific task performance, the data were re-analyzed with ANOVAs.

3.3. Theory of Mind tests (Fig. 1; ToM, Table 2)

3.3.1. Cartoons task

A two-way 2 (group: fvFTD and controls) × 2 (cartoon type: ToM and physical) ANCOVA with score on the Hayling as the covariate was performed. This revealed a main effect of group ($F(1, 28) = 4.92$, $p < 0.05$); fvFTD patients showed more difficulty with the task than controls. There was also a main effect of cartoon type ($F(1, 28) = 11.22$, $p < 0.005$); the ToM cartoons were more difficult than the physical cartoons. Importantly, the group by cartoon type interaction was highly significant ($F(1, 28) = 13.64$, $p < 0.001$) (see Fig. 1). Planned follow-up univariate ANCOVAs, indicated that while fvFTD patients found the ToM cartoons significantly more difficult than controls ($F(1, 28) = 12.15$, $p < 0.005$), this was not the case for the physical cartoons ($F(1, 28) < 1$, ns). The covariate, score on the Hayling task, had a significant relationship with performance on the cartoons task ($F(1, 28) = 5.40$, $p < 0.05$), although there was no significant interaction with cartoon type. In short, participants with lower

Table 1

Performance on Hayling and Brixton tests by frontal variant FTD (fvFTD) and control subjects showing mean (±standard deviation) scores and one-way ANOVA results with degrees of freedom of 1, 29

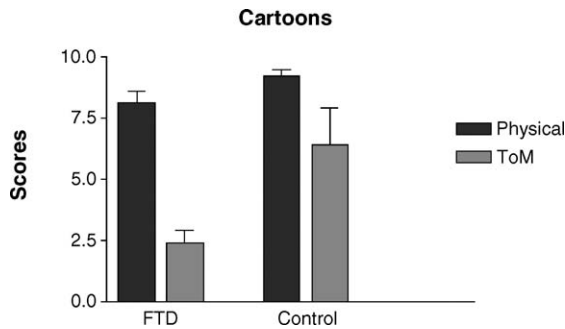|	FvFTD	Controls	ANOVA F-value
Hayling scaled score	2.7 (2.0)	5.6 (0.8)	23.90[***]
Brixton scaled score	4.3 (2.3)	6.2 (2.0)	6.14[*]

[*] $p < 0.05$.
[***] $p < 0.001$.

Fig. 1. Patient vs. control performance on ToM and physical cartoons (mean ± S.E.M.).

scores on the Hayling performed worse on the cartoons task, but this relationship was with the general ability to successfully process the cartoons rather than with the specific processes involved in the representation of the mental states of others. The analysis was then performed using the results from the Brixton test as a covariate, with identical results (group effect: $F(1, 28) = 13.13$, $p < 0.005$; cartoon effect: $F(1, 28) = 12.93$, $p < 0.005$; group × cartoon type interaction: $F(1, 28) = 16.9$, $p < 0.001$; covariate effect: $F(1, 28) = 11.59$, $p < 0.005$).

3.3.2. Advanced Theory of Mind stories

A two-way 2 (group: fvFTD and controls) × 2 (story type: ToM and physical) ANCOVA with score on the Hayling as the covariate was performed on the data. This showed a main effect of story type ($F(1, 28) = 6.65$, $p < 0.05$); the ToM stories were more difficult than the physical stories. However, there was no main effect of group ($F(1, 28) < 1$, ns) and the group by story type interaction indicated only a very weak trend ($F(1, 28) = 2.64$, $p < 0.12$) (see Table 2). Performance on the comprehension ques-

Table 2
Performance on ToM tasks, moral/conventional distinction task and social situations task by frontal variant FTD (fvFTD) and control subjects showing mean (±standard deviation and maximum possible scores)

	FvFTD	Controls	Maximum score
ToM cartoons			
Mental state	2.4 (2.1)	6.4 (1.5)	8.0
Physical state	8.1 (1.9)	9.2 (0.9)	8.0
ToM stories			
Mental state	3.3 (2.4)	4.8 (2.0)	8.0
Physical state	4.5 (2.4)	7.0 (0.8)	8.0
Comprehension	16.3 (9.0)	25.6 (4.8)	32.0
MvC moral			
Permissibility	7.6 (1.0)	8.0 (0.0)	8.0
Seriousness	60.0 (21.1)	66.2 (15.7)	80.0
Absent rules	12.7 (4.1)	4.2 (2.0)	16.0
MvC conventional			
Transgression	7.5 (1.0)	6.6 (1.2)	8.0
Seriousness	49.7 (20.5)	40.2 (17.3)	80.0
No rules	7.8 (4.9)	5.5 (3.5)	16.0
Social situations			
Identified normative	7.4 (1.9)	8.3 (0.9)	9.0
Identified violation	7.4 (2.9)	9.0 (2.5)	9.0
Appropriateness score	10.5 (5.1)	12.9 (5.0)	36.0

tion in the task was impaired in the fvFTD patients relative to controls ($t_{28} = 3.8$, $p < 0.005$). The covariate, score on the Hayling task, had a highly significant relationship with performance on the story task ($F(1, 28) = 17.48$, $p < 0.001$), although there was no significant interaction with story type. The analysis was then performed using the results of the Brixton test as a covariate. This showed very similar results with a strong effect of the covariate ($F(1, 28) = 27.99$, $p < 0.001$) and a trend towards an effect of group ($F(1, 28) = 3.20$, $p = 0.09$). These two executive function measures correlated strongly with the performance of fvFTD patients on the comprehension questions in the task (Pearson r: Hayling 0.67, $p < 0.005$; Brixton 0.81, $p < 0.001$). In short, participants with lower scores on the Hayling and Brixton tests had poorer performance on the story task. Again, the relationship of executive function measures used in this task, was with the general ability to successfully process the stories rather than with the specific processes involved in the representation of the mental states of others.

3.4. Social norms tests

3.4.1. Moral/conventional distinction task (Table 2, MvC; Fig. 2)

Preliminary ANCOVAs indicated that score on the Hayling and Brixton tasks had no significant relationship or interactions with the participant's responses to either the permissibility or seriousness questions, so these were re-analyzed as 2 (group: fvFTD and controls) × 2 (transgression type: moral and conventional) ANOVAs. For the permissibility judgement, there was no significant group difference ($F(1, 29) < 1$, ns). However, there was a significant main effect of transgression type ($F(1, 29) = 18.90$, $p < 0.01$); moral transgressions were judged as less permissible than conventional transgressions. Importantly, there was also a significant group by transgression type interaction ($F(1, 29) = 16.10$, $p < 0.01$). Only controls, but not fvFTD patients, were significantly more likely to judge the conventional transgressions as more permissible than the moral transgressions ($F(1, 12) = 12.5$, $p < 0.001$); i.e., only controls made a moral/conventional distinction for the permissibility question.

For the seriousness judgement, there was also no significant group difference ($F(1, 29) < 1$, ns). There was, however, a significant main effect of transgression type ($F(1, 29) = 32.73$, $p < 0.001$); moral transgressions were judged as more serious than conventional transgressions. Importantly, there was also a significant group by transgression type interaction ($F(1, 29) = 6.63$, $p < 0.05$). Only controls, but not fvFTD patients, judged the moral transgressions as significantly more serious than the conventional transgressions ($F(1, 12) = 60.86$, $p < 0.001$); i.e., similar to above, fvFTD patients made no moral/conventional distinction for the seriousness question.

For the absent rules judgement, the 2 (group: fvFTD and controls) × 2 (transgression type: moral and conventional) ANCOVAs found only a significant interaction of the covariate scores on both the Hayling and Brixton tasks, with transgression type; i.e., within this sample as a whole, the ability to allow conventional transgressions in the absence of rules was highly related to the ability to inhibit responses in a sentence generation task

Table 3
Performance on facial emotion processing task by frontal variant FTD (fvFTD) and control subjects showing mean (±standard deviation) score

	FvFTD	Controls
Anger	3.0 (2.0)[***]	1.1 (1.0)
Disgust	2.4 (2.0)[**]	0.7 (1.0)
Sadness	2.7 (1.8)[*]	1.4 (0.9)
Fear	3.1 (1.8)[*]	1.8 (1.2)
Surprise	1.6 (1.5)	0.9 (1.2)
Happiness	0.3 (1.0)	0.0 (0.0)

[*] $p < 0.05$.
[**] $p < 0.01$.
[***] $p < 0.005$.

and to the ability to detect and adapt to spatial rule changes, both measures of executive function.

3.4.2. Social situations (Dewey) task (Table 2, social situations)

A 2 (group: fvFTD and controls) × 2 (social situation: norm and norm violation) ANCOVA with score on the Hayling as the covariate was performed on the data from this task. While there was also no significant group difference ($F(1, 27) = 1.36$, ns), there was a significant group by social situation interaction ($F(1, 27) = 3.80$, $p < 0.05$ one-tailed). Planned follow-up univariate ANCOVAs, showed that fvFTD patients were significantly less likely to identify the norm *violations* than controls ($F(1, 27) = 2.95$, $p < 0.05$ one-tailed). However, there was no significant group difference for norms identified ($F(1, 28) = 2.45$, ns). The covariate, score on the Hayling task, had a significant interaction with social situation ($F(1, 27) = 5.44$, $p < 0.05$). With the Brixton score used as a covariate in the analysis, there was a trend towards an effect on processing of social situations ($F(1, 28) = 3.22$, $p < 0.1$). In short, the ability to identify socially inappropriate behaviour was related to executive function.

3.4.3. Recognition of facial emotion expression (Table 3)

As a preliminary ANCOVA found that score on the Hayling task had no significant relationship or interaction with the participant's ability to recognise emotional expressions, this ability was re-analyzed as a 2 (group: fvFTD and controls) × 6 (expression type: anger, disgust, sadness, fear, surprise and happiness) ANOVA. This revealed a main effect of group ($F(1, 29) = 12.71$, $p < 0.001$) but no significant group by condition interaction ($F(5, 145) = 1.83$, $p = 0.11$). Overall, the patients showed impairment in expression recognition. As can be seen in Table 3, follow-up ANOVAs indicated that the patient's impairment was most pronounced for the expressions of anger and disgust. There was a effect of group ($F(1, 28) = 5.3$, $p < 0.05$) and of the Brixton score when used as a covariate in the ANCOVA ($F(1, 28) = 18.00$, $p < 0.001$), but there was no interaction with emotion expression type.

3.4.4. Interpersonal Reactivity Index (Table 4; Fig. 3)

Wilcoxon signed rank tests were conducted to compare relatives' ratings of current and past empathy status on the four subscales. The results indicate a significant drop in rat-

Table 4
Carers' ratings on the IRI showing mean (±standard deviation) before and current scores with discrepancy and significance from Wilcoxon signed ranks test

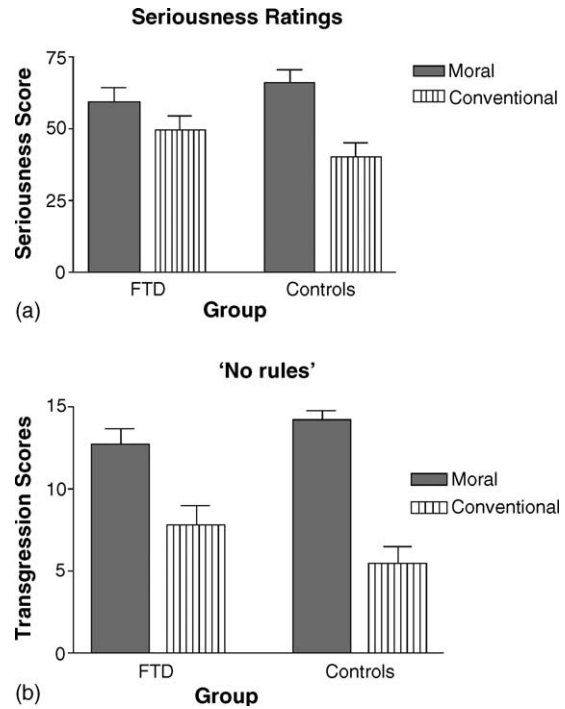|	Before	Current	Discrepancy
Empathic concern	13.4 (6.6)	7.1 (4.9)	−6.3[**]
Perspective taking	9.1 (4.8)	2.1 (2.4)	−7.0[**]
Fantasy	11.1 (6.2)	11.9 (6.7)	+0.8 ns
Personal distress	8.1 (5.3)	11.3 (8.4)	+3.2 ns

[**] $p < 0.01$.

Fig. 2. (a) Seriousness scores for moral and conventional transgressions (mean ± S.E.M.) and (b) transgression scores in the absence of rules (mean ± S.E.M.).

ings of empathic concern and perspective taking over time ($p < 0.01$), but no change in ratings of fantasy and personal distress (see Table 4). The difference scores shown in Fig. 2 illustrate the changes. Follow-up correlations indicated no
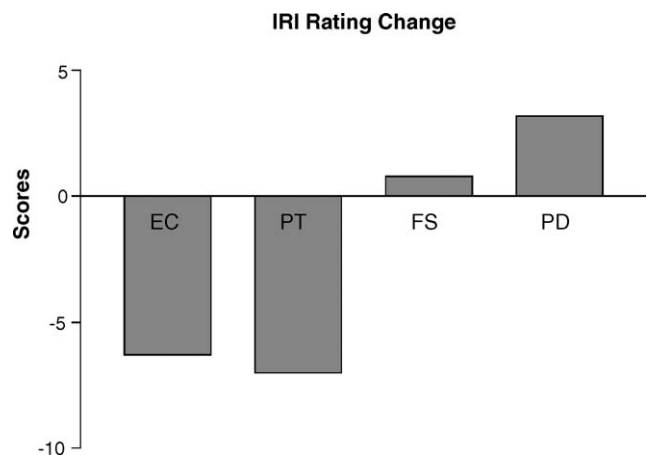

Fig. 3. Changes pre- and post-illness in carers' IRI ratings.

relationship of score on the Hayling task with changes in the IRI measures.

4. Discussion

We have confirmed previous work showing that ToM is defective in patients with fvFTD, and in addition, demonstrated impairments in other aspects of social cognition such as moral reasoning, emotion processing and empathy. The results of the moral–conventional reasoning test were particularly revealing in that patients showed an inability to integrate social knowledge with its affective connotations. Empathy was especially impaired as demonstrated by changes on the IRI. The findings are of theoretical and clinical importance with respect to our understanding and management of fvFTD.

Both the ToM cartoons and strange stories have been shown in earlier functional imaging studies to activate structures implicated in the Theory of Mind, notably the superior temporal sulcus (STS), temporal pole and regions of the medial prefrontal cortex (Gallagher et al., 2000; Vogeley et al., 2001). Performance by fvFTD patients on the cartoon task was markedly impaired for cartoons requiring a mental state inference, compared with those purely dependent on a physical explanation. A similar effect was noted for the story task, but the interaction was much weaker. The difference between these two tasks is likely to reflect their psychometric properties; cartoons are more sensitive, and less influenced by extraneous processing factors than the stories. The working memory demands of the story task are considerable, and no doubt compromised performance of fvFTD patients. This is supported by their impaired performance on the comprehension aspect of the stories task, as well as the strong relationship between the executive function measures used in this study, and the results of the ToM stories. Presentation by means of cartoons presumably reduces such demands, and may also add further clues such as facial expressions and implied movements that are not immediately apparent with the stories. In keeping with this hypothesis it has been shown that ToM-based cartoons activate brain regions such as the fusiform face region and the precuneus (Gallagher et al., 2000); this medial parietal region is also active when observing social interaction (Iacoboni et al., 2004).

Turning to the controversial issue of the relationship between ToM and executive function, while some authors argue for a dependence of ToM on executive function (Channon & Crawford, 2000), others emphasise its modularity by demonstrating double dissociations, or by controlling for executive function in their results (Fine, Lumsden, & Blair, 2001; Gregory et al., 2002; Lough et al., 2001; Perner & Lang, 1999; Rowe, Bullock, Polkey, & Morris, 2001). Patients with fvFTD show heterogeneity in their performance on traditional executive tasks, and it has been argued, that patients with more executive function disturbance show greater impairment on ToM tasks (Snowden et al., 2003). We found impairment on both the Hayling (response inhibition) and the Brixton (set-shifting) tests in fvFTD patients. Moreover, the executive measures correlated strongly with the comprehension scores derived from the control questions in the story task. Score on the Hayling task was used as an initial covariate in our

subsequent analyses for two reasons. First, it showed the greatest group difference with respect to controls, and second, this form of executive function is thought to mediate performance on Theory of Mind tasks (Carlson & Moses, 2001). Since performance on the Hayling test may be influenced by a number of factors, we also used score on the Brixton test as an alternative measure of executive function with virtually identical results. Our findings suggest that the relationship of score on executive function measures is with the general ability to process cartoons or stories, irrespective of their mental state content. This is consistent with a supporting role for executive function in mental state attribution, but also clearly indicates that ToM dissociates from it.

The prior finding of impaired judgement of social faux pas raised questions as to whether fvFTD patients show appropriate responsiveness to social rules, and to what extent such responsiveness might be related to ToM ability. In this study, we have demonstrated subtle, but potentially important, impairments on the moral–conventional and social situations task. Although knowledge of social rules about normal behaviour was intact in the fvFTD patients, they were worse than controls in their ability to detect violations of these rules (social situations task). Scrutinising violations more closely using the moral/conventional distinction task, patients with fvFTD differed significantly from controls on transgression and seriousness scores. Interestingly, this was due to the fact that *controls* maintained a distinction between moral and conventional transgressions and rated them accordingly. There was a 'flattening' in the ability of fvFTD patients to qualify their responses in this task. This may be akin to the inability to estimate appropriate magnitudes by patients with frontal lobe lesions. The results of these two tasks provide evidence that their moral reasoning is abnormal, but that their basic knowledge of social rules is not. Furthermore, the ability to process rule violations, and consider the appropriateness of transgressions in the absence of prohibiting rules is significantly influenced by the degree of executive dysfunction, as was indicated by the interaction effect between these tasks with the executive function measures used in this study.

The social situations task is thought to have similar functional requirements as the faux pas task; i.e., it involves both the representation of the mental states of others and emotional responsiveness, particularly to expectations of others' anger (Berthoz et al., 2002; Blair & Cipolotti, 2000). Patients with autism, as well as those with acquired lesions of the orbitofrontal cortex who are poor at responding to the emotional signals of others, have impairment on both of these tasks (Blair & Cipolotti, 2000; Stone, Baron-Cohen, & Knight, 1998). Detection of rule violations on the social situations task might therefore relate to their ToM deficit, or their impairment in emotion processing (see below). In contrast, performance on the moral/conventional distinction is not thought to be dependent on the ability to represent the mental states of others. Patients with autism who show ToM impairment are still able to distinguish moral from conventional social norm violations (Blair, 1996; Joseph & Tager-Flusberg, 2004). Recent work does indicate, however, that moral reasoning is reliant on appropriate emotional responses to "victims". These, in turn depend on the integrity of the amygdala and medial

orbitofrontal cortex (Blair & Cipolotti, 2000; Greene & Haidt, 2002; Moll et al., 2002); regions which degenerate in fvFTD (Broe et al., 2003; Kril & Halliday, 2004).

The ability to recognise emotion from facial expressions was significantly compromised in fvFTD patients, particularly for anger and disgust. A number of studies have linked the orbitofrontal cortex (OFC) to a generalised impairment in expression recognition (Hornak et al., 2003; Hornak, Rolls, & Wade, 1996). The right OFC appears to be particularly involved in the neural response to angry expressions (Blair, Morris, Frith, Perrett, & Dolan, 1999), and together with the insula, which may modulate disgusted expression recognition (Murphy, Nimmo-Smith, & Lawrence, 2003), is markedly affected in fvFTD (Broe et al., 2003; Kril & Halliday, 2004). It has been suggested that in order to perform successfully on these tasks, a subject needs to activate an association with an earlier situation where others have shown anger (Blair & Cipolotti, 2000). It is also known that fvFTD patients are impaired in their ability to reverse previously rewarded contingencies (Rahman, Sahakian, Hodges, Rogers, & Robbins, 1999), a function ascribed to the OFC (Rolls, 2000). It is likely that fvFTD disrupts the ability patients to interact socially by disturbing their ability to represent the mental state of others, and also by disrupting the appropriate modulation of their social interactions by non-verbal and emotional cues.

Abnormal emotion processing extends to other aspects of social functioning in fvFTD. Empathy impairment in the emotional aspects of social interaction, and in particular, reduced empathy is frequently reported by caregivers of this group. We have confirmed these anecdotal reports: on the Interpersonal Reactivity Index, dramatic reductions in empathic concern and 'perspective taking' were observed. The other two factors, 'fantasy' and ratings of 'personal distress', did not change appreciably. The ability to empathise is a complex and uniquely human ability, which depends upon the ability to appreciate the emotional and mental state of others (Baron-Cohen & Wheelwright, 2004; Eslinger, 1998), and relates strongly to dimensions of social functioning (Cliffordson, 2002). As measured by caregivers on the IRI, it is demonstrative, involving an outward response, and may be considered along the lines of a social executor as described by Eslinger et al. We would suggest that empathy is not simply the sum of ToM, executive function and emotional responsiveness, but might well involve a social executive function modulated by these other processes.

Since imaging was not performed in this study, it was not possible to directly infer an anatomical locus for the abnormal social cognition demonstrated in these patients. Despite this limitation, there is a remarkable co-incidence between regional atrophy demonstrated on pathological and imaging studies (Broe et al., 2003; Kril & Halliday, 2004; Rosen et al., 2002) in fvFTD, and brain regions involved in social cognition. A number of studies have reported ToM localization to the medial prefrontal cortex, in particular the anterior paracingulate cortex (BA 9/32), in both individuals with frontal lobe lesions and healthy volunteers (Gallagher & Frith, 2003; Gallagher et al., 2000; Rowe et al., 2001; Vogeley et al., 2001). Activation of the lateral orbitofrontal and medial prefrontal cortex has been reported when considering violations of social norms (Berthoz et al., 2002), and Moll et al. (2002) identified medial orbitofrontal activation in moral judgements. Both the amygdala and the insula cortex have a role in emotion processing, particularly for emotions such as fear and possibly disgust. Early in the course of fvFTD there is degeneration of the orbitofrontal, anterior cingulate and amygdala, but over time temporal lobe and insula cortex involvement is seen, culminating in generalised brain atrophy and death (Broe et al., 2003; Kril & Halliday, 2004). Such converging evidence not only provides insight into the probable neural correlates of disturbed social functioning in fvFTD, but highlights a potential role for this group of patients in dissecting these brain–behaviour relationships.

In conclusion, we have produced clear evidence of impaired ToM and emotion processing in fvFTD. We have also demonstrated that patients with fvFTD show impairment in the processing of social transgressions. Not only do they fail to adequately recognise social norm violations, but they are also unable to distinguish moral and conventional transgressions in their judgements. Executive dysfunction underlies some of these deficits, but in itself does not adequately explain them all. They show reduced empathy, which may compound their impaired social functioning, and be particularly difficult for their carers. Tests of ToM, emotion regulation, social rule judgements and empathy may give objective evidence of disturbance of social conduct, and may also be more sensitive to impairment than other means of testing such as standard neuropsychological batteries. This is of particular importance where typically there is a lack of insight by the patient, and complex decisions regarding care must be made. Future studies should attempt to more accurately replicate the real-time dynamic that is implicit in social interactions by attempting more 'ecological' methods of testing, and should aim to parametrically vary aspects of ToM in an attempt to better understand this ability. Such studies should also attempt to include a wide range of executive function measures in order to better characterise the nature of this deficit in impaired social functioning. Correlations with regional brain atrophy would further help validate the neural basis of social cognition.

Appendix A. Task details

A.1. Moral/conventional distinction instructions and examples of scenes

Instructions: I am going to be describing to you some short scenes. All these scenes are set in a school. The scenes concern things children frequently do at school. I am going to be asking you your opinion about what is occurring in these scenes. There are no right or wrong answers. I am just interested in your opinion.

A.1.1. Example moral transgression scene

One child runs up to another child and hits them in the face.

A.1.2. Example conventional transgression scene

One child stands up and walks straight out of the classroom without asking permission in the middle of a lesson.

The participant is asked:

(1) "Was it right or wrong for X to do Y?" (examining the participant's judgement of the permissibility of the scene).
(2) "On a scale of 1 to 10 how right (or wrong depending on the answer to 1) was it for X to do Y?" (examining the participant's judgement of the seriousness of the act).
(3) "Why was it right (or wrong depending on the answer to 1) for X to do Y?" (examining the participant's theories about the act) If the participant had said the act was wrong in response to question 1, the participant was told: "Now what if the teacher had said before the lesson", before X did the transgression, that "At this school anybody can Y if they want to".
(4) And then asked a final question: "Would it be ok for X to do Y if the teacher says X can?" (examining the rule's authority jurisdiction).

A.2. Social situations task instructions and example story

Instructions: In the following stories some parts are in italics. Immediately following there is a pair of brackets ( ). Rate the behaviour which is illustrated by the portion in italics according to how most people would judge the behaviour if they witnessed it. Use this scale.

Fairly normal in that situation	1
Rather strange behaviour in that situation	2
Very eccentric behaviour in that situation	3
Shocking behaviour in that situation	4

Keith, age 25 years, is a file clerk who worked in an office in the city. At noon he took his lunch to a small park and sat on a bench to eat. *Often he tore part of a sandwich into bits, scattering it on the ground for the pigeons* ( ). One day when he came to his favourite bench a baby carriage was parked beside it. Keith noticed that a young woman was swinging an older child nearby. The baby in the carriage began to cry but the mother did not hear this because the swing was squeaking. Now, Keith had learned that when his baby nephew screamed, sometime this meant that a pin in his nappy had opened. *Rather than bother the mother in the park, Keith quickly checked the baby's clothing to see if he could feel an open pin* ( ).

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