

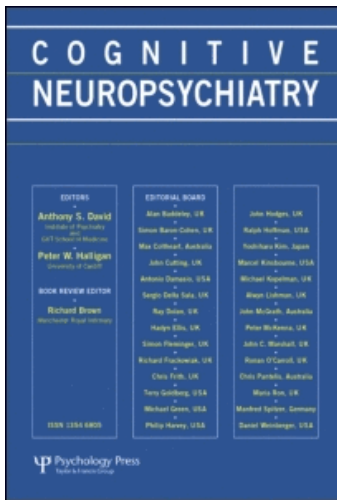
This article was downloaded by: [CDL Journals Account]

On: 16 June 2009

Access details: Access Details: [subscription number 912375045]

Publisher Psychology Press

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



## Cognitive Neuropsychiatry

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title-content=t713659088>

### Altered emotional morality in frontotemporal dementia

Mario F. Mendez<sup>ab</sup>; Jill S. Shapira<sup>ab</sup>

<sup>a</sup> Departments of Neurology and Psychiatry & Biobehavioral Sciences, University of California at Los Angeles,  
<sup>b</sup> V. A. Greater Los Angeles Healthcare Center, Los Angeles, USA

Online Publication Date: 01 May 2009

**To cite this Article** Mendez, Mario F. and Shapira, Jill S.(2009)'Altered emotional morality in frontotemporal dementia',Cognitive Neuropsychiatry,14:3,165 — 179

**To link to this Article:** DOI: 10.1080/13546800902924122

**URL:** <http://dx.doi.org/10.1080/13546800902924122>

## PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

## Altered emotional morality in frontotemporal dementia

Mario F. Mendez and Jill S. Shapira

*Departments of Neurology and Psychiatry & Biobehavioral Sciences,  
University of California at Los Angeles, and V. A. Greater Los Angeles  
Healthcare Center, Los Angeles, USA*

*Introduction.* Frontotemporal dementia (FTD), a disorder characterised by abnormal social behaviour and potential sociopathy, provides a window to the neurobiology of moral behaviour. This study investigated the basis of altered moral judgements in patients with FTD.

*Methods.* We administered an inventory of moral knowledge, five “reasoned” moral dilemmas, and five “emotional” moral dilemmas where subjects may cause direct harm to another through their own actions, to 21 patients with FTD compared to 21 comparably mildly impaired patients with Alzheimer’s disease (AD) and 21 normal controls. Among the FTD patients, the results were compared to findings on functional neuroimaging.

*Results.* All groups showed retention of knowledge for moral behaviour and the ability to make reasoned moral judgements. In contrast to the other groups, the FTD patients were altered in their ability to make emotional moral judgements. Among the FTD patients, the altered moral judgements corresponded to right hemisphere frontotemporal involvement.

*Conclusions.* In FTD patients, these findings suggest a decreased emotional responsiveness to others and a tendency to respond to moral dilemmas in a calculated fashion. Such a disturbance may result from ventromedial frontal dysfunction in FTD and supports the presence of a “morality” network in the brain, predominantly in the right hemisphere.

**Keywords:** Brain; Ethics; Frontotemporal dementia; Morality

### INTRODUCTION

Frontotemporal dementia (FTD) is a neurodegenerative disorder that produces alterations in social and emotional behaviour. FTD results in progressive deterioration of the frontal and anterior temporal lobes,

---

Correspondence should be addressed to Mario F. Mendez, Departments of Neurology and Psychiatry & Biobehavioral Sciences, University of California at Los Angeles, and V.A. Greater Los Angeles Healthcare Center, 11301 Wilshire Blvd., Los Angeles, CA 90073, USA. E-mail [mmendez@UCLA.edu](mailto:mmendez@UCLA.edu)

---

© 2009 Psychology Press, an imprint of the Taylor & Francis Group, an Informa business  
<http://www.psypress.com/cogneuropsychiatry> DOI: 10.1080/13546800902924122

particularly the ventromedial prefrontal cortex (VMPFC), but also the orbitofrontal and anterior temporal cortex. In contrast to the memory and cognitive deficits of Alzheimer's disease (AD) and other dementias, the core features of FTD are transgression of social norms including sociopathic behaviour, a loss of empathy or appreciation of the feelings of others, and a loss of insight for their behaviour and its consequences (Mendez, Lauterbach, Sampson, & Committee on Research, 2008).

These core features of FTD may be a window into the neurobiological basis of moral behaviour (Mendez, Anderson, & Shapira, 2005). Morality is about ideals of human conduct based on values shared with other members of society. Disturbed social behaviour in FTD suggests an underlying disturbance in moral behaviour. Investigations show that lesions in the orbitofrontal and ventromedial prefrontal cortex impair moral judgement, and early lesions of these areas impair the development of moral knowledge and judgement (Anderson, Barrash, Bechara, & Tranel, 2006). Moreover, functional magnetic resonance imaging (fMRI) in normals show activation of these areas during tasks of moral reasoning (Moll, de Oliveira-Souza, & Eslinger, 2003; Moll et al., 2002).

Recent investigations point to an automatic and emotion-based process for moral judgement involving the VMPFC (Greene, Sommerville, Nystrom, Darley, & Cohen, 2001), a core area of pathology in FTD. Greene and colleagues (2001) have proposed that medial prefrontal areas mediate strong emotional reactions to moral dilemmas, which prevent individuals from implementing morally impermissible acts. Moral dilemmas are situations in which persons face a conflict between opposing moral demands. In "reasoned" moral dilemmas, the conflicts do not result in direct harm to others unless it is due to a logical, nonpersonal deflection of any existing threat onto fewer people. In contrast, "emotional" moral dilemmas involve directly harming others through one's own actions, and this possibility of harming others causing distress in most people (Greene, Nystrom, Engell, Darley, & Cohen, 2004; Haidt, 2007).

In FTD, altered "emotional" morality could account for defective moral judgement and many of the clinical manifestations of this disorder. Our preliminary work suggested a lack of moral emotional reactions in patients with FTD (Mendez, Anderson, & Shapira, 2005). This study investigated the response to moral knowledge questions, reasoned moral dilemmas, and emotional moral dilemmas among patients with FTD compared to those with AD and normal controls.

## METHODS

### Subjects

All FTD and AD participants in this study presented for evaluation to university-affiliated specialty clinics in dementing disorders. The patients were community-based, mildly impaired patients who underwent a comprehensive neurobehavioural evaluation, laboratory assessment, and magnetic resonance imaging. The study excluded patients on medications, particularly antipsychotic drugs, or with medical, neurological, or psychiatric disorders that could otherwise account for stereotypical movements. Study participation included written informed consent according to institutional review board guidelines.

All 21 FTD patients presented with progressive behavioural changes consistent with a decline in social interpersonal conduct, impairment in regulation of personal conduct, emotional blunting, and loss of insight for their disease. The clinical diagnosis of FTD was based on Consensus Criteria for FTD (Neary et al., 1998) plus frontotemporal-predominant changes on positron emission tomography (PET) or single photon emission computer tomography (SPECT).

The FTD patients were compared to 21 AD patients who met NINCDS-ADRDA criteria for clinically probable AD (McKhann et al., 1984). These patients were derived from the same clinic as those with FTD. The AD patients were relatively early onset patients chosen to match the FTD patients, as close as possible, in age, gender, education, and dementia severity. In order to ensure that the FTD and AD patients could complete this study, they had to be mildly impaired, defined as a Mini-Mental State Examination (MMSE) score of  $\geq 23$  and a Clinical Dementia Rating (CDR) score of  $\leq 1.0$  (Folstein, Folstein, & McHugh, 1975; Morris, 1993). Neuropsychological measures included verbal fluency, the Boston Naming Test (15-item version), constructions (copy of a circle, rhombus, overlapping rectangles, cube), a verbal list learning test, auditory comprehension, and the Frontal Assessment Battery (Dubois, Slachevsky, Litvan, & Pillon, 2000; Kiernan, Mueller, Langston, & van Dyke, 1987; Welsh et al., 1994). Additional normal controls (NC) were recruited primarily from spouses of patients. They were chosen so as to correspond with the overall age, gender, and education of the FTD and AD patients. None of the controls had a history of neurological or psychiatric disease.

### Procedures

*Part 1.* Participants were administered the Moral Behaviour Inventory, a questionnaire consisting of 24 items originally based on the Moral Behaviour Scale (see Table 1; Rettig & Pasamanick, 1959). This instrument minimises

TABLE 1  
Moral behaviour inventory

This questionnaire presents acts for you to evaluate in terms of right or wrong. Please answer to the best of your ability. Choose 1 if the item seems Not Wrong. Choose 4 if the item seems Severely Wrong. Use 2 for Mildly Wrong and 3 for Moderately Wrong.

*How wrong is it if you:*

- \_\_\_ Fail to keep minor promises
- \_\_\_ Take the last seat on a crowded bus
- \_\_\_ Sell someone a defective car
- \_\_\_ Drive after having one drink
- \_\_\_ Cut in line when in a hurry
- \_\_\_ Don't give blood during blood drives
- \_\_\_ Are mean to someone you don't like
- \_\_\_ Say a white lie to get a reduced fare
- \_\_\_ Drive out the homeless from your community
- \_\_\_ Always let others pay at a restaurant
- \_\_\_ Not help someone pick up their dropped papers
- \_\_\_ Keep over-change at a store
- \_\_\_ Not offer to help after an accident
- \_\_\_ Ignore a hungry stranger
- \_\_\_ Fail to vote in minor elections
- \_\_\_ Keep money found on the ground
- \_\_\_ Temporarily park in a handicap spot
- \_\_\_ Cut off drivers on the freeway
- \_\_\_ Take the largest piece of a pie
- \_\_\_ Falsely get out of jury duty
- \_\_\_ Ask others do some of your homework
- \_\_\_ Take credit for others' work
- \_\_\_ Refuse to help people who don't deserve it
- \_\_\_ Get more time off than your co-workers

From Mendez, Anderson, and Shapira (2005).

cultural and religious influences and maximises the content validity of empathy and the sense of fairness. The individual items are simple and have been previously administered to a series of normal adults and dementia patients (Mendez, Anderson, & Shapira, 2005). In order to facilitate administration and comprehension in dementia patients, the items were read aloud to the participants. The items were repeated as many times as necessary to assure comprehension. The participants were then asked if the item was "not wrong," "mildly wrong," "moderately wrong", or "severely wrong", a 4-point Likert scale. In our preliminary study, the split-half reliability (Cronbach's coefficient alpha) for 78 participants was  $r_{kk} = .73$  (.72-.76 for individual groups) (Mendez, Anderson, & Shapira, 2005).

*Part 2.* Participants were administered ten moral dilemmas (five reasoned and five emotional) modified from Greene and colleagues (2001);

available in original form at [www.sciencemag.org/cgi/content/full/293/5537/2105/DC1](http://www.sciencemag.org/cgi/content/full/293/5537/2105/DC1)). For this study, the dilemmas were simplified for administration to dementia patients. Our preliminary study was limited to the first reasoned (“Standard Trolley”) and the first emotional (“Footbridge”) dilemmas administered to an overlapping but not identical group of subjects (Mendez, Anderson, & Shapira, 2005).

Participants were read the dilemmas in the form of vignettes. In order to facilitate administration to dementia patients, these dilemmas were read aloud while simultaneously presented on a laptop screen. Because the patients had a dementia with variable baseline rates of comprehension and response speed, their responses were not timed, and the dilemmas could be reread, as necessary. In order to reduce fatigue, patients received the dilemmas in five blocks of two with breaks in-between. The dilemmas were administered in a counterbalanced fashion, both in terms of reasoned versus emotional and in the direction of response (“yes” vs. “no”).

The five reasoned moral dilemmas included the following:

1. “Standard Trolley”: Imagine that you are at the wheel of a runaway trolley quickly approaching a fork in the tracks. On the tracks going to the left is a group of five railway workmen. On the tracks going to the right is a single railway workman. If you do nothing, the trolley will proceed to the left, causing the deaths of the five workmen. The only way to avoid the deaths of these workmen is to hit a switch on your dashboard that will cause the trolley to proceed to the right, causing the death of the single workman. Would you hit the switch in order to avoid the deaths of the five workmen?
2. “Résumé”: You have a friend who has been trying to find a job for a long time but without success. He has a family to support, and he is desperate. It occurs to him that he would be more likely to get a job if he just had a more impressive résumé. He decided to put some false information on his résumé in order to make it more impressive. By doing this he ultimately got a job, beating out several other more qualified candidates. Was it OK for your friend to put false information on his résumé in order to help him get the job?
3. “Taxes”: You are the owner of a small business worried about surviving, making ends meet, and paying your taxes. It occurs to you that you can lower your taxes by pretending that some of your personal expenses are business expenses. For example, you could pretend that the stereo in your home is being used in your business office, or that your dinners out with your wife are dinners with clients. Is it OK for you to report personal expenses as business expenses in order to survive and make ends meet?

4. “Standard Fumes”: You are the night watchman in a hospital. There is an accident and deadly fumes in the ventilation system are travelling to the hospital rooms. In one room there are three patients. In another room there is a single man. If you do nothing the fumes will go into the room with the three patients and kill them. The only way to avoid this is to hit a switch that will reroute the fumes into the other room with the single man, killing him instead. Is it appropriate for you to hit the switch in order to avoid the deaths of the three patients?
5. “Lost Wallet”: You are walking down the street when you come across a wallet lying on the ground. You open the wallet and find that it contains several hundred dollars in cash. From the credit cards and other items in the wallet, it’s clear that it belongs to a very wealthy man. You, on the other hand, are very poor and need money. You consider sending the wallet back to the owner without the money, keeping the money for yourself. Would you keep the money you found in the rich man’s wallet?

The five emotional moral dilemmas included the following:

1. “Footbridge”: Imagine that a runaway trolley is heading down the tracks toward five workmen who will be killed if the trolley keeps going. You are on a footbridge over the tracks, in between the approaching trolley and the five workmen. Next to you on this footbridge is a stranger who happens to be very large. The only way to save the lives of the five workmen is to push this stranger off the bridge and onto the tracks below where his large body will stop the trolley. The stranger will die if you do this, but the five workmen will be saved. Would you to push the stranger onto the tracks in order to save the five workmen?
2. “Transplant”: You are a doctor. You have five patients, each of whom is about to die due to a failing organ of some kind. You have another patient, a young man who is healthy. The only way that you can save the lives of the first five patients is to transplant five of this young man’s organs (against his will) into the bodies of the other five patients. If you do this, the young man will die, but the other five patients will live. The families and staff beg you to do this. Would you refuse their requests to do the transplants that would save five of your patients?
3. “Smother for dollars”: You are in the hospital visiting a sick friend. A young man sitting next to you is visiting his very sick father who has only a week to live. He tells you that his father has a large life insurance policy that runs out at midnight. If his father dies before midnight, this young man gets millions of dollars. The money would mean a great deal to him, and he sees no value in his father’s suffering for a few more

- days. He offers you a million dollars to go up to his father's room and smother his father with a pillow. Would you smother this man's father in order to get money for yourself and this young man?
4. "Crying Baby": Enemy soldiers have taken over your village. They have orders to kill everyone. You have hidden in the basement of a large house along with other people. Outside you hear the voices of soldiers who have come to search the house. Your baby begins to cry loudly. You cover his mouth to block the sound. If you remove your hand from his mouth the soldiers will hear his crying and will kill you, your baby, and the other people hiding in the basement. To save yourself and the others you must smother your child to death. Would you smother your child in order to save yourself and the other people?
  5. "Modified Lifeboat": You are on a cruise ship when there is a fire on board, and the ship has to be abandoned. Unfortunately, the lifeboat that you get in has too many people and may sink. Your lifeboat is beginning to fill with water. If nothing is done your lifeboat will sink before the rescue boat arrives and everyone may die. However, there is a seriously injured person in the lifeboat. The other passengers ask you to help them throw that person overboard so that the lifeboat will not sink. Would you refuse to help the others throw this person overboard in order to save as many passengers as possible?

After reading the dilemmas, the participants were asked several questions. First, they were asked to repeat back the dilemma in their own words. If they could not describe the dilemma, the vignette was reread, clarified, and simplified. The patients were asked again to explain the dilemma. This process was repeated as much as necessary until they could sufficiently remember and understand the nature of the dilemma. Second, they were required to commit to a "yes" or "no" answer, whichever they were most comfortable with. They were given as much time as they needed to think about the dilemma before committing to their response. During this process, the examiner was not allowed to prompt a response in any way. Reading all the dilemmas took about 1 hour. Finally, after completion, the participants were asked their impressions of the study. The participants did not express any discomfort or emotional conflict with their decisions on the dilemmas.

The clinical PET and SPECT scans on the FTD patients, which were obtained from different scanners and medical centres, were reread by two independent and experienced raters, blind to the clinical diagnosis. This technique has been previously reported (Mendez et al., 2006). The raters initially graded the scans for hypometabolism or hypoperfusion as absent, mild, moderate, or severely present (0–3 point scale) for each of left frontal, right frontal, left anterior temporal, and right anterior temporal regions. The combination of the two raters led to determinations of whether the scans



had significant or nonsignificant involvement of each of the four regions of interest. Our prior interrater reliability for this method of regional PET/SPECT ratings was high ( $r_s = .714$  for 296 ratings;  $p < .001$ ) (Mendez et al., 2006).

## Data analysis

The comparison of the three groups on basic characteristics, dementia measures, and the Moral Behaviours Inventory used analysis of variance (ANOVA). Because of the nonparametric nature of the dilemma responses, the analysis of group differences on the dilemmas used chi-square and the Kruskal-Wallis ( $H$ ) test. Finally, among the FTD patients, the relationship of the dilemma responses to the functional neuroimaging changes used the Wilcoxon ( $W$ ) test and Spearman ( $r_s$ ) correlations. For the functional neuroimaging variables, the study evaluated left hemisphere, right hemisphere, frontal region, and temporal region scores.

## RESULTS

There were no statistically significant differences between the FTD patients and normal control groups on age, sex, or education. The two dementia groups did not differ statistically on the MMSE and the global CDR; both were mildly impaired on these measures. There were no differences on the reasoned and emotional dilemmas based on age, gender, education, or MMSE and CDR score; however, consistent with their diagnoses, the AD patients were significantly worse than the FTD patients on memory tests and constructions and better on the FAB (Table 2). On the Moral Behaviour Inventory, the three groups did not show significant differences, consistent with intact knowledge of right or wrong among all three groups.

The FTD patients diverged from the other groups on the emotional moral dilemmas but not on the reasoned moral dilemmas. When analysed individually, there were no group differences on the reasoned moral dilemmas between the FTD, AD, and normal control groups (Table 3). When analysed as total "reasoned" or "emotional" dilemma scores, both dementia groups were more likely to endorse an opposite moral response compared to the normal controls. This was true for both reasoned dilemmas,  $H = 14.17$  overall;  $H = 17.85$  FTD vs. NC;  $H = 14.44$  AD vs. NC (all  $ps < .001$ ) and emotional dilemmas,  $H = 51.45$  overall;  $H = 32.43$  FTD vs. NC;  $H = 18.74$  AD vs. NC (all  $ps < .001$ ). Further analysis did not show differences between the FTD and AD groups on the reasoned dilemmas,  $H = 1.02$ , *ns*; however, the FTD and AD groups differed significantly on the emotional dilemmas,  $H = 32.96$ ,  $p < .001$ . Many FTD patients responded in a "logical" way to

TABLE 2  
Participant characteristics: Means (standard deviations)

	<i>FTD, n=21, 10M, 11F</i>	<i>AD, n=21, 10M, 11F</i>	<i>NC, n=21, 10M, 11F</i>	<i>Significance</i>
Age	59.9 (8.1)	63.2 (8.9)	61.4 (8.4)	ns
Education (years)	14.2 (4.4)	14.4 (4.2)	14.6 (3.8)	ns
MMSE <sup>A</sup>	25.19 (1.25)	24.62 (1.36)	29.7 (0.90)	ns
CDR <sup>B</sup>	0.62 (0.35)	0.86 (0.23)	—	ns
Moral Behavior Inventory <sup>C</sup>	62.54 (10.41)	65.11 (9.09)	64.22 (9.10)	ns
Verbal Digit Span	6.62 (1.02)	6.29 (0.96)	—	ns
Verbal Fluency—"animals"	11.71 (2.61)	10.33 (2.82)	—	ns
Mini-Boston Naming Test	13.29 (1.62)	13.43 (1.63)	—	ns
NCSE <sup>D</sup> Aud. Comprehension	5.33 (0.80)	5.29 (0.78)	—	ns
CERAD <sup>E</sup> Savings score	7.24 (1.26)	5.43 (1.66)	—	$t = 3.98, p < .001$
CERAD <sup>E</sup> Recognition score	8.81 (1.08)	7.57 (1.80)	—	$t = 2.70, p < .01$
Constructions score	9.67 (0.66)	7.52 (1.44)	—	$t = 6.22, p < .001$
FAB <sup>F</sup> Total score	15.38 (1.50)	16.33 (1.39)	—	$t = -2.13, p < .05$

FTD = frontotemporal dementia; AD = Alzheimer's disease; NC = normal controls.

<sup>A</sup>MMSE = Mini-Mental State Examination. No difference between the two dementia groups.

<sup>B</sup>CDR = Global Clinical Dementia Rating scores based on Washington University scoring rules.

<sup>C</sup>Total scores may vary between 24 and 72.

<sup>D</sup>Neurobehavioral Cognitive State Exam (Kiernan et al., 1987).

<sup>E</sup>CERAD: Consortium to Establish a Registry in Alzheimer's Disease memory tests: Savings Score (Delayed Recall/Trial III proportion of 10 words) and Recognition (Welsh et al., 1994).

<sup>F</sup>Frontal Assessment Battery (Dubois et al., 2000).

emotional moral dilemmas even at the cost of inflicting direct harm on another. All of these alternative emotional moral response came from 17 (81%) of the FTD patients, and the majority (59%) came from just 12 (57%) of the FTD patients.

### PET/SPECT findings

Among the FTD patients, the total imaging ratings for the two raters included means of 2.57 (1.08) for left hemisphere, 3.71 (1.68) for right hemisphere, 3.33 (1.24) for frontal regions, and 3.00 (1.00) for temporal regions. The FTD patients had greater right hemisphere involvement than the other groups,  $W = 109.0$ ,  $p \leq .05$ , but there were no frontal versus temporal regional differences,  $W = 47.0$ , *ns*.

Responses on the reasoned and emotional dilemmas correlated with each other,  $r_s = .99$ ,  $p < .001$ , and with right hemisphere changes on PET/SPECT,  $r_s = .47$  for reasoned and  $r_s = .49$  for emotional dilemmas (both  $ps < .05$ ). Neither significantly correlated with left hemisphere involvement,  $r_s = .31$  and  $r_s = .28$ , respectively. Finally, greater alternative moral responses on both reasoned and emotional dilemmas were associated with both greater frontal,  $r_s = .66$  and  $.65$ ,  $p < .01$ , and temporal,  $r_s = .70$  and  $.71$ ,  $p < .001$ , involvement.

## DISCUSSION

This study evaluated emotionally-based moral behaviour in FTD using a moral behaviour inventory and moral dilemmas to distinguish between reasoned and emotionally based moral judgements (Greene et al., 2001; Thomson, 1986). The patients with FTD were more likely to approve emotional moral violations compared to the patients with AD and the normal controls. Yet, they retained knowledge about moral values and conventional rules. The results of this study support an impairment in emotional moral judgement in FTD in the face of relatively preserved moral knowledge and the ability to tell right from wrong.

FTD is a model to understand morality and the brain. FTD patients have a loss of social tact and propriety early in their course and may commit sociopathic acts (Mendez, Chen, Shapira, & Miller, 2005; Miller, Darby, Benson, Cummings, & Miller, 1997). Among FTD patients, investigators have reported shoplifting (Gustafson, 1993; Lynch et al., 1994), inappropriate or unsolicited sexual behaviour (Gustafson, 1987; Miller et al., 1997), traffic violations (Mendez, Chen, et al., 2005; Miller, et al., 1997), acts of violence (Gustafson, 1993), and even paedophilia (Mendez, Chow, Ringman, Twitchell, & Hinkin, 2000). Moreover, FTD patients often appear

TABLE 3  
Proportion of subjects who gave "yes/no" responses to moral dilemmas

	FTD	AD	NC	$\chi^2$ 3-Grps <sup>A</sup> $\chi^2$ FTDvAD <sup>B</sup>	$p$ 3-Grps <sup>A</sup> $p$ FTDvAD <sup>B</sup>
Reasoned dilemmas					
Standard Trolley Car <sup>C</sup>	18/3	19/2	21/0	ns	
Resume	4/17	3/18	0/21	ns	
Taxes	4/17	3/18	0/21	ns	
Standard Fumes <sup>C</sup>	18/3	19/2	21/0	ns	
Lost Wallet	3/18	2/19	0/21	ns	
Emotional dilemmas					
Footbridge	12/9	4/17	2/19	13.07 <sup>A</sup> 4.95 <sup>B</sup>	=.001 <sup>A</sup> =.026 <sup>B</sup>
Transplant <sup>C</sup>	7/14	16/5	19/2	16.71 <sup>A</sup> 6.15 <sup>B</sup>	<.001 <sup>A</sup> =.013 <sup>B</sup>
Smother for Dollars	15/6	5/16	1/20	22.29 <sup>A</sup> 7.73 <sup>B</sup>	<.001 <sup>A</sup> =.005 <sup>B</sup>
Crying Baby	12/9	4/17	1/20	15.63 <sup>A</sup> 4.95 <sup>B</sup>	<.001 <sup>A</sup> =.026 <sup>B</sup>
Modified Lifeboat <sup>C</sup>	6/15	16/5	19/2	19.42 <sup>A</sup> 7.73 <sup>B</sup>	<.001 <sup>A</sup> =.005 <sup>B</sup>

FTD = frontotemporal dementia; AD = Alzheimer's disease; NC = normal controls,  $\chi^2$  = chi-squared.

<sup>C</sup>The direction of the "yes/no" responses are counterbalanced, so that expected normal responses would be "yes" on the these dilemmas and "no" on the others.

unconcerned for the emotional consequences of their transgressions and appear impaired in the ability to infer others' mental states and feelings (Gregory et al., 2002).

FTD and other brain disorders that damage the medial frontal region and its connections can impair an emotionally based moral system (Greene et al., 2004; Haidt, 2001; McNamara, Durso, & Harris, 2007). Haidt (2001) proposed a "social intuitionist model" where moral judgements result from fast and automatic emotional intuitions of the actions of themselves or others. Functional MRI studies indicate that discomfort at the prospect of causing direct harm to another drive automatic, emotionally based moral responses which are associated with increased activity in the medial VMPFC (Greene & Haidt, 2002; Greene et al., 2004). Although there are other systems for moral emotions, especially an orbitofrontostriatopallidal brain system with a reward role (Braun, Léveillé, & Guimond, 2008; Takahashi et al., 2008), this VMPFC system appears to have primacy for immediate moral decision making. The VMPFC mediates a rapid, emotional response that signals potential moral violations of social norms and that attributes feelings of blame and wrongdoing (Amodio & Frith, 2006; Kliemann, Young, Scholz, & Saxe, 2008).

Studies of patients with focal lesions of the VMPFC indicate insensitivity to emotional moral decision making (Bechara, Damasio, Damasio, & Anderson, 1994; Bechara, Tranel, & Damasio, 2000; Koenigs et al., 2007; Saver &

Damasio, 1991). A major example of this are the behavioural changes described in Phineas Gage, one of neurology's most famous patients, who sustained bilateral VMPF injury from the explosion of a railroad spike (Damasio, 1994). Patients with VMPF lesions have diminished emotional experience with loss of concern for others, decreased autonomic responsiveness, and possible "acquired sociopathy" (Barrash, Tranel, & Anderson, 2000; Brower & Price, 2001; Damasio, Tranel, & Damasio, 1990; Eslinger, 1998; Tranel, 1994). Despite this, they are aware of their actions, have preserved logical reasoning and knowledge of social and moral norms, and can anticipate future outcomes (Anderson, Bechara, Damasio, Tranel, & Damasio, 1999; Koenigs & Tranel, 2007; Saver & Damasio, 1991). In a study using moral dilemmas, Ciaramelli, Muccioli, Ladavas, and di Pellegrino (2007) showed VMPFC activation during contemplation of emotional moral dilemmas (vs. reasoned and nonmoral) in seven patients with VMPFC lesions compared to twelve healthy individuals in emotional moral dilemmas. Compared to normal controls, their patients were more willing to judge emotional moral violations as acceptable behaviours in emotional moral dilemmas. Many other studies of patients with focal VMPF lesions, especially on the right, show attenuated feelings of emotional discomfort for sociomoral violations, impaired empathy, and reduced responsiveness to victims (Amodio & Frith, 2006; Bechara et al., 1994, 2000; Berthoz, Grezes, Armony, Passingham, & Dolan, 2006; Blair & Cipolotti, 2000; Cushman, Young, & Hauser, 2006; Damasio et al., 1990; Greene et al., 2004; Harenski & Hamann, 2006; Hauser, Cushman, Young, Jin, & Mikhail, 2006; Koenigs et al., 2007; Shamay-Tsoory, Tomer, Berger, Goldsher, & Aharon-Peretz, 2005; Tranel, 1994; Tranel, Bechara, & Denburg, 2002).

Early FTD disproportionately affects the VMPFC (Rosen, et al., 2002), and this study shows corresponding impairments in emotionally based personal moral judgements. FTD patients who lack strong moral emotions may not be able to override drives, compulsions, disinhibitions, or tendencies, such as for paedophilia (Mendez et al., 2000). Finally, there appears to be a greater role for the right hemisphere, compared to the left hemisphere, in mediating these sociomoral responses (Tranel et al., 2002).

There are potential limitations of this study. A possible confound is whether the dementia patients could sufficiently understand the moral dilemmas. In order to assure understanding, this study included only mildly impaired patients and administered the moral vignettes in a way that maximised comprehension. Second, there may be a tendency to give the socially acceptable answers to moral vignettes. This was controlled by the reasoned versus emotional differences and the variation in yes/no valence of responses. Third, as previously noted in the literature (Braun et al., 2008), the moral vignettes are artificial situations. Nevertheless, as outlined earlier, many investigators have successfully used these moral dilemmas in fMRI

and in brain lesion studies. Finally, the moral dilemmas could not be administered in a blind fashion. The investigators, however, were extremely cognisant of the need not to prime or bias the patients' responses.

In conclusion, this study strongly suggests impairments in emotionally based moral behaviour in FTD. In patients with FTD or focal VMPFC lesions, especially on the right, abnormalities in moral behaviour appear to result from decreased emotional moral judgements. FTD patients, however, can reason normally and make reasoned moral judgements as long as an immediate moral emotion is not required. Future investigations can further clarify the intriguing relationship between the brain and our "moral sense" (Pinker, 2008; Wilson, 1993).

Manuscript received 24 November 2008

Revised manuscript received 17 March 2009

## REFERENCES

- Amodio, D. M., & Frith, C. D. (2006). Meeting of minds: The medial frontal cortex and social cognition. *Nature Reviews Neuroscience*, 7(4), 268–277.
- Anderson, S. W., Barrash, J., Bechara, A., & Tranel, D. (2006). Impairments of emotion and real-world complex behavior following childhood- or adult-onset damage to ventromedial prefrontal cortex. *Journal of the International Neuropsychological Society*, 12(2), 224–235.
- Anderson, S. W., Bechara, A., Damasio, H., Tranel, D., & Damasio, A. R. (1999). Impairment of social and moral behavior related to early damage in human prefrontal cortex. *Nature Neuroscience*, 2(11), 1032–1037.
- Barrash, J., Tranel, D., & Anderson, S. W. (2000). Acquired personality disturbances associated with bilateral damage to the ventromedial prefrontal region. *Developmental Neuropsychology*, 18(3), 355–381.
- Bechara, A., Damasio, A. R., Damasio, H., & Anderson, S. W. (1994). Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition*, 50(1–3), 7–15.
- Bechara, A., Tranel, D., & Damasio, H. (2000). Characterization of the decision-making deficit of patients with ventromedial prefrontal cortex lesions. *Brain*, 123(11), 2189–2202.
- Berthoz, S., Grezes, J., Armony, J. L., Passingham, R. E., & Dolan, R. J. (2006). Affective response to one's own moral violations. *Neuroimage*, 31(2), 945–950.
- Blair, R. J., & Cipolotti, L. (2000). Impaired social response reversal. A case of "acquired sociopathy". *Brain*, 123(6), 1122–1141.
- Braun, C. M. J., Léveillé, C., & Guimond, A. (2008). An orbitofrontostriatopallidal pathway for morality: Evidence from postlesion antisocial and obsessive-compulsive disorder. *Cognitive Neuropsychiatry*, 13(4), 296–337.
- Brower, M. C., & Price, B. H. (2001). Neuropsychiatry of frontal lobe dysfunction in violent and criminal behaviour: A critical review. *Journal of Neurology, Neurosurgery and Psychiatry*, 71(6), 720–726.
- Ciaramelli, E., Muccioli, M., Ladavas, E., & di Pellegrino, G. (2007). Selective deficit in personal moral judgment following damage to ventromedial prefrontal cortex. *Social Cognitive and Affective Neuroscience*, 2(2), 84–92.
- Cushman, F., Young, L., & Hauser, M. (2006). The role of conscious reasoning and intuition in moral judgment: Testing three principles of harm. *Psychological Science*, 17(12), 1082–1089.
- Damasio, A. R. (1994). *Descartes' error*. New York: Putnam.

- Damasio, A. R., Tranel, D., & Damasio, H. (1990). Individuals with sociopathic behavior caused by frontal damage fail to respond autonomically to social stimuli. *Behavioural Brain Research*, 41(2), 81–94.
- Dubois, B., Slachevsky, A., Litvan, I., & Pillon, B. (2000). The FAB: A Frontal Assessment Battery at bedside. *Neurology*, 55(11), 1621–1626.
- Eslinger, P. J. (1998). Neurological and neuropsychological bases of empathy. *European Neurology*, 39(4), 193–199.
- Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). “Mini-Mental State”: A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, 12(3), 189–198.
- Greene, J., & Haidt, J. (2002). How (and where) does moral judgment work? *Trends in Cognitive Science*, 6(12), 517–523.
- Greene, J. D., Nystrom, L. E., Engell, A. D., Darley, J. M., & Cohen, J. D. (2004). The neural bases of cognitive conflict and control in moral judgment. *Neuron*, 44(2), 389–400.
- Greene, J. D., Sommerville, R. B., Nystrom, L. E., Darley, J. M., & Cohen, J. D. (2001). An fMRI investigation of emotional engagement in moral judgment. *Science*, 293(5537), 2105–2108.
- Gregory, C., Lough, S., Stone, V., Erzincinoglu, S., Martin, L., Baron-Cohen, S., et al. (2002). Theory of mind in patients with frontal variant frontotemporal dementia and Alzheimer’s disease: Theoretical and practical implications. *Brain*, 125, 752–764.
- Gustafson, L. (1987). Frontal lobe degeneration of non-Alzheimer type. II. Clinical picture and differential diagnosis. *Archives of Gerontology and Geriatrics*, 6(3), 209–223.
- Gustafson, L. (1993). Clinical picture of frontal lobe degeneration of non-Alzheimer type. *Dementia*, 4(3–4), 143–148.
- Haidt, J. (2001). The emotional dog and its rational tail: A social intuitionist approach to moral judgment. *Psychological Review*, 108(4), 814–834.
- Haidt, J. (2007). The new synthesis in moral psychology. *Science*, 316(5827), 998–1002.
- Harenski, C. L., & Hamann, S. (2006). Neural correlates of regulating negative emotions related to moral violations. *Neuroimage*, 30(1), 313–324.
- Hauser, M. D., Cushman, F. A., Young, L. L., Jin, K.-X., & Mikhail, J. (2006). A dissociation between moral judgments and justifications. *Mind Language*, 22, 1–21.
- Kiernan, R. J., Mueller, J., Langston, J. W., & van Dyke, C. (1987). The Neurobehavioral Cognitive Status Examination: A brief but quantitative approach to cognitive assessment. *Annals of Internal Medicine*, 107(4), 481–485.
- Kliemann, D., Young, L., Scholz, J., & Saxe, R. (2008). The influence of prior record on moral judgment. *Neuropsychologia*, 46(12), 2949–2957.
- Koenigs, M., & Tranel, D. (2007). Irrational economic decision-making after ventromedial prefrontal damage: Evidence from the ultimatum game. *Journal of Neuroscience*, 27(4), 951–956.
- Koenigs, M., Young, L., Adolphs, R., Tranel, D., Cushman, F., Hauser, M., et al. (2007). Damage to the prefrontal cortex increases utilitarian moral judgements. *Nature*, 446(7138), 908–911.
- Lynch, T., Sano, M., Marder, K. S., Bell, K. L., Foster, N. L., Defendini, R. F., et al. (1994). Clinical characteristics of a family with chromosome 17-linked disinhibition-dementia-Parkinsonism-amyotrophy complex. *Neurology*, 44(10), 1878–1884.
- McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., & Stadlan, E. M. (1984). Clinical diagnosis of Alzheimer’s disease: Report of the NINCDS-ADRDA work group under the auspices of department of health and human services task force on Alzheimer’s disease. *Neurology*, 34(7), 939–944.
- McNamara, P., Durso, R., & Harris, E. (2007). Machiavellianism’ and frontal dysfunction: Evidence from Parkinson’s disease. *Cognitive Neuropsychiatry*, 12(4), 285–300.
- Mendez, M. F., Anderson, E., & Shapira, J. S. (2005). An investigation of moral judgement in frontotemporal dementia. *Cognitive Behavioral Neurology*, 18(4), 193–197.

- Mendez, M. F., Chen, A. K., Shapira, J. S., & Miller, B. L. (2005). Acquired sociopathy and frontotemporal dementia. *Dementia and Geriatric Cognitive Disorders*, 20(2-3), 99-104.
- Mendez, M. F., Chow, T., Ringman, J., Twitchell, G., & Hinkin, C. H. (2000). Pedophilia and temporal lobe disturbances. *Journal of Neuropsychiatry and Clinical Neuroscience*, 12(1), 71-76.
- Mendez, M. F., Lauterbach, E., Sampson, S., & Committee on Research. (2008). An evidence-based review of the psychopathology of frontotemporal dementia: A report of the ANPA Committee on Research. *Journal of Neuropsychiatry and Clinical Neuroscience*, 20, 130-149.
- Mendez, M. F., McMurtray, A., Chen, A. K., Shapira, J. S., Mishkin, F., & Miller, B. L. (2006). Functional neuroimaging and presenting psychiatric features in frontotemporal dementia. *Journal of Neurology: Neurosurgery and Psychiatry*, 77(1), 4-7.
- Miller, B. L., Darby, A., Benson, D. F., Cummings, J. L., & Miller, M. H. (1997). Aggressive, socially disruptive and antisocial behaviour associated with fronto-temporal dementia. *British Journal of Psychiatry*, 170, 150-154.
- Moll, J., de Oliveira-Souza, R., & Eslinger, P. J. (2003). Morals and the human brain: A working model. *Neuroreport*, 14(3), 299-305.
- Moll, J., de Oliveira-Souza, R., Eslinger, P. J., Bramati, I. E., Mourao-Miranda, J., Andreiuolo, P. A., et al. (2002). The neural correlates of moral sensitivity: A functional magnetic resonance imaging investigation of basic and moral emotions. *Journal of Neuroscience*, 22(7), 2730-2736.
- Morris, J. C. (1993). The clinical dementia rating (CDR): Current version and scoring rules. *Neurology*, 43(11), 2412-2414.
- Neary, D., Snowden, J. S., Gustafson, L., Passant, U., Stuss, D., Black, S., et al. (1998). Frontotemporal lobar degeneration: A consensus on clinical diagnostic criteria. *Neurology*, 51(6), 1546-1554.
- Pinker, S. (2008, 13 January 2008). The moral instinct. *The New York Times Magazine*, p. 33.
- Rettig, S., & Pasamanick, B. (1959). Changes in moral values among college students: A factorial study. *American Sociological Review*, 24, 856-863.
- Rosen, H. J., Perry, R. J., Murphy, J., Kramer, J. H., Mychack, P., Schuff, N., et al. (2002). Emotion comprehension in the temporal variant of frontotemporal dementia. *Brain*, 125(10), 2286-2295.
- Saver, J. L., & Damasio, A. R. (1991). Preserved access and processing of social knowledge in a patient with acquired sociopathy due to ventromedial frontal damage. *Neuropsychologia*, 29(12), 1241-1249.
- Shamay-Tsoory, S. G., Tomer, R., Berger, B. D., Goldsher, D., & Aharon-Peretz, J. (2005). Impaired "affective theory of mind" is associated with right ventromedial prefrontal damage. *Cognitive Behavioural Neurology*, 18(1), 55-67.
- Takahashi, H., Kato, M., Matsuura, M., Koeda, M., Yahata, N., Suhara, T., et al. (2008). Neural correlates of human virtue judgment. *Cerebral Cortex*, 18(8), 1886-1891.
- Thomson, J. J. (1986). *Rights, restitution and risk*. Cambridge, MA: Harvard University Press.
- Tranel, D. (1994). "Acquired sociopathy": The development of sociopathic behavior following focal brain damage. *Progress in Experimental and Personal Psychopathological Research*, 285-311.
- Tranel, D., Bechara, A., & Denburg, N. L. (2002). Asymmetric functional roles of right and left ventromedial prefrontal cortices in social conduct, decision-making, and emotional processing. *Cortex*, 38(4), 589-612.
- Welsh, K. A., Butters, N., Mohs, R. C., Beekly, D., Edland, S., Fillenbaum, G., et al. (1994). The consortium to establish a registry for Alzheimer's disease (CERAD). Part V. A normative study of the neuropsychological battery. *Neurology*, 44(4), 609-614.
- Wilson, J. Q. (1993). *The moral sense*. New York: Simon & Schuster.