

Changes in appetite, food preference, and eating habits in frontotemporal dementia and Alzheimer's disease

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J Neural Neurosurg Psychiatry 2002;**73**:371–376

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Received
18 December 2001
In revised form 29 May
2002
Accepted 14 June 2002

Frontotemporal dementia is the term currently favoured to describe progressive focal atrophy involving frontal or anterior temporal lobes or both, in association with a spectrum of non-Alzheimer pathologies.^{1,2} Patients with frontotemporal dementia may present with predominantly frontal involvement (so called frontal variant frontotemporal dementia or fv-FTD). A wide range of behavioural changes has been reported in fv-FTD, including loss of insight, disinhibition, impulsivity, apathy, poor self care, mood changes, mental rigidity, and stereotypic behaviour.^{3–6} Recent studies have highlighted the high prevalence of alterations in food preference, appetite, and eating behaviours in fv-FTD.^{7,7} Patients with the temporal variant of frontotemporal dementia, often referred to as semantic dementia in view of the predominance of anomia and impaired comprehension, also show changes in behaviour, including alterations in appetite and food preference similar to those seen in fv-FTD.⁷ In Alzheimer's disease, by contrast, changes in eating habits are said to be less common, with the exception of anorexia,^{8,9} although the results of studies have been contradictory.¹⁰

Despite numerous reports of these changes in satiety, food preference, and eating habits in patients with frontotemporal dementia, there have been very few systematic studies comparing frontotemporal dementia subgroups, or contrasting Alzheimer's disease and frontotemporal dementia. The study of such changes has both practical and theoretical relevance. From a clinical point of view, it is important to distinguish Alzheimer's disease from frontotemporal dementia, particularly with the advent of disease modifying treatments.¹¹ From a theoretical standpoint, the brain mechanisms underlying appetite control and food preference are poorly understood.

In this study we used a newly created caregiver questionnaire to examine the changing in eating behaviours in fronto-

Background: Despite numerous reports of changes in satiety, food preference, and eating habits in patients with frontotemporal dementia, there have been few systematic studies.

Objectives: To investigate the frequency of changes in eating behaviours and the sequence of development of eating behaviours in frontotemporal dementia and Alzheimer's disease, using a caregiver questionnaire.

Methods: Three groups of patients were studied: frontal variant frontotemporal dementia (fv-FTD) (n = 23), semantic dementia (n = 25), and Alzheimer's disease (n = 43). Level of education and dementia severity was similar in the three groups. The questionnaire consisted of 36 questions investigating five domains: swallowing problems, appetite change, food preference, eating habits, and other oral behaviours.

Results: The frequencies of symptoms in all five domains, except swallowing problems, were higher in fv-FTD than in Alzheimer's disease, and changes in food preference and eating habits were greater in semantic dementia than in Alzheimer's disease. In semantic dementia, the developmental pattern was very clear: a change in food preference developed initially, followed by appetite increase and altered eating habits, other oral behaviours, and finally swallowing problems. In fv-FTD, the first symptom was altered eating habits or appetite increase. In Alzheimer's disease, the pattern was not clear although swallowing problems developed in relatively early stages.

Conclusions: Change in eating behaviour was significantly more common in both of the frontotemporal dementia groups than in Alzheimer's disease. It is likely that the changing in eating behaviours reflects the involvement of a common network in both variants of frontotemporal dementia—namely, the ventral (orbitobasal) frontal lobe, temporal pole, and amygdala.

temporal dementia and Alzheimer's disease. The three main aims were: to investigate the frequency of changing in eating behaviours in frontotemporal dementia and Alzheimer's disease; to investigate the sequence of development of eating behaviours in frontotemporal dementia and Alzheimer's disease; and to establish whether the subtypes of frontotemporal dementia are characterized by different eating behavioural changes.

METHODS

This study was conducted after obtaining informed consent from all subjects or their caregiver.

Patients

Patients were identified through the memory and cognitive disorders clinic at Addenbrooke's Hospital, Cambridge, England, where they were seen by a senior neurologist (JRH), a senior psychiatrist, and clinical neuropsychologist. All patients underwent a standard psychiatric evaluation to exclude major functional psychiatric disorders such as depression, mania, and schizophrenia. Patients were assessed with a comprehensive neuropsychological test battery,¹² including the mini-mental state examination (MMSE)¹³ and clinical dementia rating (CDR).¹⁴ All patients underwent computed tomography or magnetic resonance imaging (MRI), together with the usual battery of screening blood tests to exclude treatable causes of dementia. Patients with a history of significant head trauma and alcoholism were also excluded.

Three groups of patients were involved in the study: fv-FTD (n = 23), semantic dementia (n = 25), and Alzheimer's disease (n = 43). All except six (four with frontotemporal dementia, one with semantic dementia, and one with Alzheimer's disease) were living at home. Those who were

Table 1 Demographic variables of the three patient groups

Group	fv-FTD	SD	AD
n	23	25	43
Age (years)	61.1 (6.6)	65.1 (7.0)	68.3 (7.7)
Sex (female:male)	4:19	12:13	18:25
Education (years)	11.8 (2.4)	11.4 (2.0)	12.1 (3.5)
CDR grade 0.5:1:2:3	4:10:4:5	5:4:12:4	14:14:12:3
MMSE score	22.9 (7.4) (n=22)	17.2 (8.3) (n=15)	20.6 (5.7) (n=35)

Values are mean (SD) or n.

AD, Alzheimer's disease; CDR, clinical dementia rating; fv-FTD, frontotemporal dementia, frontal variant; MMSE, mini-mental state examination; SD, semantic dementia.

institutionalised had a spouse or relative who still maintained close contact and was therefore able to complete the questionnaire. The demographic characteristics of fv-FTD, semantic dementia, and Alzheimer's disease group are summarised in table 1. All patients in the fv-FTD and semantic dementia groups fulfilled the recent consensus criteria for frontotemporal lobar degeneration, which recognises the subtypes of frontotemporal dementia (termed here fv-FTD), semantic dementia, and progressive non-fluent aphasia.¹⁵

All patients with fv-FTD presented with an informant based history of progressive change in personality and behaviour, with at least five of the following features: loss of insight, disinhibition, apathy, restlessness, emotional lability, distractibility, reduced empathy, impulsivity, social withdrawal, and poor self care. In addition of these behavioural changes, most of the patients also showed some impairment in executive functioning, as assessed by a verbal fluency task, and difficulties in rule learning and response inhibition on the Wisconsin card sorting test. Patients with significant impairment on tests of semantic memory were excluded from this group. All patients showed either frontal atrophy on MRI or frontal lobe hypoperfusion on HMPAO-SPECT.

Patients with semantic dementia presented with progressive loss of vocabulary affecting expressive and receptive language in the context of fluent speech production. All patients fulfilled the criteria for semantic dementia previously reported: anomia, impairment in single word comprehension, and impoverished semantic knowledge with relative preservation of phonology, syntax, visuospatial abilities, and day-to-day (episodic) memory.^{16, 17} In all cases, structural brain imaging by MRI showed focal atrophy involving the polar and inferolateral regions of the temporal lobe. In some cases, the atrophy was clearly bilateral, although in others it was markedly asymmetrical, if not unilateral.^{18, 19}

The diagnosis of probable Alzheimer's disease was made according to the criteria developed by the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association, which consist of inclusion and exclusion criteria.²⁰ All patients presented with a progressive cognitive impairment, predominantly affecting memory. Brain MRI was either normal, showed a mild degree of medial temporal, or showed diffuse atrophy.

Assessment of eating behaviour

A questionnaire was designed on the basis of review of published reports and our previous clinical experience of the eating and swallowing behaviours commonly reported in frontotemporal dementia groups and Alzheimer's disease. After piloting of six prototypes, the final version of the questionnaire consisted of 36 questions investigating the following five domains: swallowing problems, appetite change, food preference (including sweet food preference and food fads), eating habits (including stereotypic eating behaviours and decline in table manners), and other oral behaviours (including food cramming and indiscriminate eating) (table 2). The questionnaire is available from the authors or the Journal Web site.

Information was gathered from a caregiver familiar with the patient's eating behaviour. It was emphasised that a "symptom" should reflect a substantive change from patient's premorbid state and not a longstanding character trait. If caregivers indicated that abnormal behaviour was present, they were asked to rate the frequency (0, never; 1, occasionally, less than once per week; 2, often, about once per week; 3, frequently, several times per week but less than every day; 4, very frequently, once or more per day or continuously), severity (1, mild, easily controlled; 2, moderate, not easily controlled; 3, marked, embarrassing or otherwise disturb family), and beginning date of behaviour. For each abnormal behaviour, we derived a product of frequency times severity in keeping with the method applied in the Neuropsychiatric Inventory.²¹ Caregivers were also asked to estimate the number of pounds lost or gained to compare the weight before illness.

Data analysis and statistics

Difference in age, education, MMSE score, and CDR between three groups was analysed using Kruskal-Wallis test followed up by post hoc Scheffé's test for multiple comparison. Overall frequency of abnormal eating behaviours, frequency of each domain, frequency of each abnormal behaviour were analysed individually using χ^2 test, with post hoc Fisher's exact tests (with Bonferroni's correction). Product of frequency and severity of each domain was analysed individually using Kruskal-Wallis test followed up by post hoc Scheffé's test for multiple comparison. Weight changes were analysed using Kruskal-Wallis test.

RESULTS

The patients with Alzheimer's disease were older than the fv-FTD group ($p < 0.01$). There were also differences for MMSE between patients with fv-FTD and those with semantic dementia ($p < 0.05$). Patients in the semantic dementia group, whose test performance is characterised by profound anomia, unsurprisingly performed worse on the MMSE. There were no differences in education or in the severity of dementia according to CDR.

There was a significant difference in the overall frequency of abnormal eating behaviours between the frontotemporal dementia groups and Alzheimer's disease ($p < 0.01$ with Bonferroni's correction). Of note was the fact that 100% of fv-FTD cases, 88% of semantic dementia cases, and 58.1% of Alzheimer's disease cases showed at least one symptom. We examined the frequency of each domain in the three groups, defined as the percentage of the sample in which the behavioural change was reported to be present or to have been present. As shown in fig 1, there were no significant differences in any domains except for appetite ($p < 0.05$) between fv-FTD and semantic dementia. The frequency of changes in food preference and eating habits was very high in the fv-FTD and semantic dementia groups. Statistic analysis confirmed that the frequencies of all domains except for swallowing problems were higher in fv-FTD than in Alzheimer's disease ($p < 0.01$). Patients with semantic dementia had more

Table 2 Frequency of abnormal eating behaviours in frontotemporal dementia, frontal variant (fv-FTD), semantic dementia (SD), and Alzheimer's disease (AD)

	Frequency (%)			χ^2	p Value
	fv-FTD	SD	AD		
(A) Swallowing problems					
Difficulty in swallowing food	26	20	7	4.8	0.08
Difficulty in swallowing liquids	13	12	2	3.3	0.2
Coughs or chokes when swallowing	30	20	14	2.6	0.3
Takes a long time to swallow food or liquids	26	16	9	3.3	0.2
Places food in mouth but does not chew it	26	8	2	9.6	0.007 ^b
Chews food but does not swallow it	13	4	7	1.4	0.5
(B) Appetite change					
Loss of appetite	30	8	16	4.3	0.1
Increase in appetite	61	28	9	20.0	0.000 ^b
Seeks out food between meals	57	40	9	17.8	0.000 ^a
Overeats at meal times	48	24	5	17.1	0.000 ^b
Requests larger or second helping of food	39	20	5	12.4	0.002 ^b
Reports hunger	30	20	9	4.8	0.09
Reports being overfull	9	16	12	0.6	0.8
Other changes in appetite, such as binges	30	32	5	10.6	0.004 ^a
Needs to limit food intake	26	12	2	8.7	0.008 ^b
(C) Food preference					
Prefers sweet foods more than before	61	68	12	26.9	0.000 ^a
Drinks more soft drinks	43	24	2	17.3	0.000 ^a
Drinks more tea/coffee	35	36	7	10.7	0.005 ^a
"Taste" in food changed in another way (eg, eats more meat)	39	32	9	9.1	0.01
Adds more seasoning to their food (eg, adds more salt)	30	20	7	6.3	0.04
Developed other food fads	17	28	2	9.6	0.007 ^c
Hoards sweets or other food	13	16	2	4.4	0.1
Drinks more alcohol	30	16	2	10.6	0.006 ^b
(D) Eating habits					
Wants to cook or eat exactly the same foods each days	26	40	5	13.2	0.001 ^c
Tends to eat foods in the same order	43	12	5	12.3	0.002 ^b
Wants to eat at the same time every day	52	56	9	20.7	0.000 ^a
Decline in table manners	61	64	12	24.8	0.000 ^a
Eats with hands	17	40	9	9.5	0.007 ^c
Takes a long time to eat	35	24	23	1.1	0.6
(E) Other oral behaviours					
Tends to overfill mouth	39	28	9	8.5	0.01 ^b
Chews or sucks on things (eg, pens) without trying to eat them	26	8	0	12.7	0.001 ^b
Eats non-edible foodstuffs or things not normally eaten	9	20	0	8.9	0.009 ^c
Tends to snatch or grasp any food items within reach	30	16	2	10.6	0.006 ^b
Become a heavier smoker or taken up smoking again	26	0	5	11.9	0.002 ^d
Episodes of spontaneous vomiting	9	8	2	1.6	0.6
Episodes of self induced vomiting	4	0	0	3.0	0.3

^afv-FTD>AD and SD>AD.^bfv-FTD>AD.^cSD>AD.^dfv-FTD>SD.

frequent changes in food preference and eating habits than patients with Alzheimer's disease ($p < 0.01$).

We also examined frequency of each abnormal behaviour (table 2). Because the domain of appetite change includes an item for appetite increase and an item for loss of appetite, we analysed these items separately. The frequency of increased appetite was higher in fv-FTD than in Alzheimer's disease ($p < 0.01$). There were no significant differences in loss of appetite among three groups. To explore the features of Kluver–Bucy syndrome, we analysed the item for eating non-edible things in the "other oral behaviours" domain. Eating inedible substances was rare in all groups, although it was more common in semantic dementia (five of 25 cases) than in fv-FTD (two of 23 cases) or Alzheimer's disease (none of 43 cases) ($p < 0.05$).

Table 3 shows the total scores (frequency \times severity) for each domain in the three groups. Group differences emerged in all domains except swallowing problems. For appetite change, altered food preference, and eating habits, the scores of Alzheimer's disease group were lower than those of fv-FTD and semantic dementia ($p < 0.01$), with no difference

between the latter groups. The score for Alzheimer's disease in other oral behaviours was lower than for fv-FTD ($p < 0.01$), but was not different from semantic dementia.

Figure 2 shows the development order of each eating behaviours. In semantic dementia, the pattern of the development was very clear: a change in food preference developed initially (15 of 22 cases), followed by appetite increase and altered eating habits (mainly stereotypic behaviours), other oral behaviours, and finally swallowing. In fv-FTD, the first symptom was altered eating habits (nine of 22 cases) or appetite increase (six of 22 cases). In Alzheimer's disease, the pattern was not clear although, unlike the other two groups, swallowing problems developed at a relatively early stage.

Weight gain of more than 7.5 kg (16 pounds) was found in 30% of the fv-FTD cases, 36% of semantic dementia cases, and 7% of Alzheimer's disease cases. Weight loss of more than 7.5 kg was found in 9% of the fv-FTD cases, 8% of semantic dementia cases, and 16% of Alzheimer's disease cases. There were no significant differences in weight changes among three groups ($p = 0.063$).

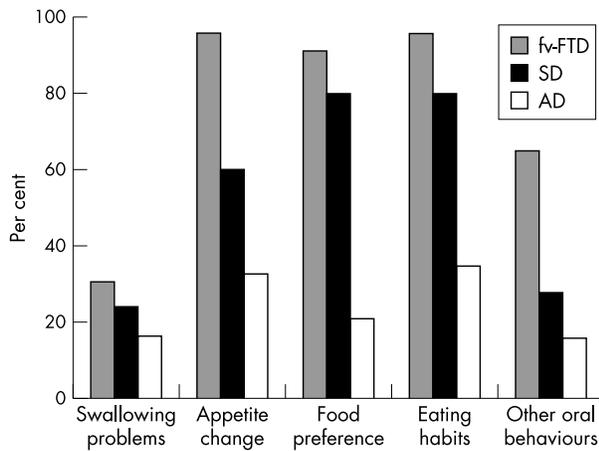


Figure 1 Frequency of each symptom domain in frontal variant frontotemporal dementia (fv-FTD), semantic dementia (SD), and Alzheimer's disease (AD) groups.

Table 3 The scores (frequency * severity) for each symptom domain in the three groups

	Frequency * severity			p Value
	fv-FTD	SD	AD	
Swallowing problems	4.3	4.1	0.9	NS
Appetite change	18.8	13.4	1.3	<0.01 ^a
Food preference	14.7	19.6	1.1	<0.01 ^a
Eating habits	12.7	17.4	2.6	<0.01 ^a
Other oral behaviours	7.7	4.3	0.6	<0.01 ^b

^afv-FTD>AD and SD>AD.

^bfv-FTD>AD.

AD, Alzheimer's disease; fv-FTD, frontotemporal dementia, frontal variant; SD, semantic dementia.

DISCUSSION

Changes in eating behaviours were significantly more common in both of the frontotemporal dementia groups compared with Alzheimer's disease. By contrast, we found no significant differences among these three groups in the frequency of swallowing problems. There were no differences between the two frontotemporal dementia subgroups in any of the abnormal eating behaviours except for heavy smoking. It is clear, therefore, that patients with fv-FTD and semantic dementia have very similar in eating behaviours, consistent with others studies^{5,6} which compared these two groups on a broad range of behavioural and psychiatric symptoms. There may, however, be a difference in the development order of eating behaviours in frontotemporal dementia groups. In semantic dementia, the first symptom was typically a change in food preference, while in fv-FTD, alterations in food preference and appetite were equally common.

There are no previous reports comparing the eating behaviours in frontotemporal dementia subgroups and Alzheimer's disease using a comprehensive instrument. Even for Alzheimer's disease, few studies have focused on the eating behaviour change and the reports of eating symptoms have been conflicting.^{8-10,22-24} This probably reflects the different instruments and groups at various stages of disease. Our current study revealed a higher percentage of abnormal eating behaviour in both Alzheimer's disease and frontotemporal dementia than previous studies.^{5,7,9} One of the reasons might be that our study was prospective and specifically designed to look for eating abnormalities in dementia. Moreover, the questionnaire evolved through six prototypes which took into account caregivers' opinions.

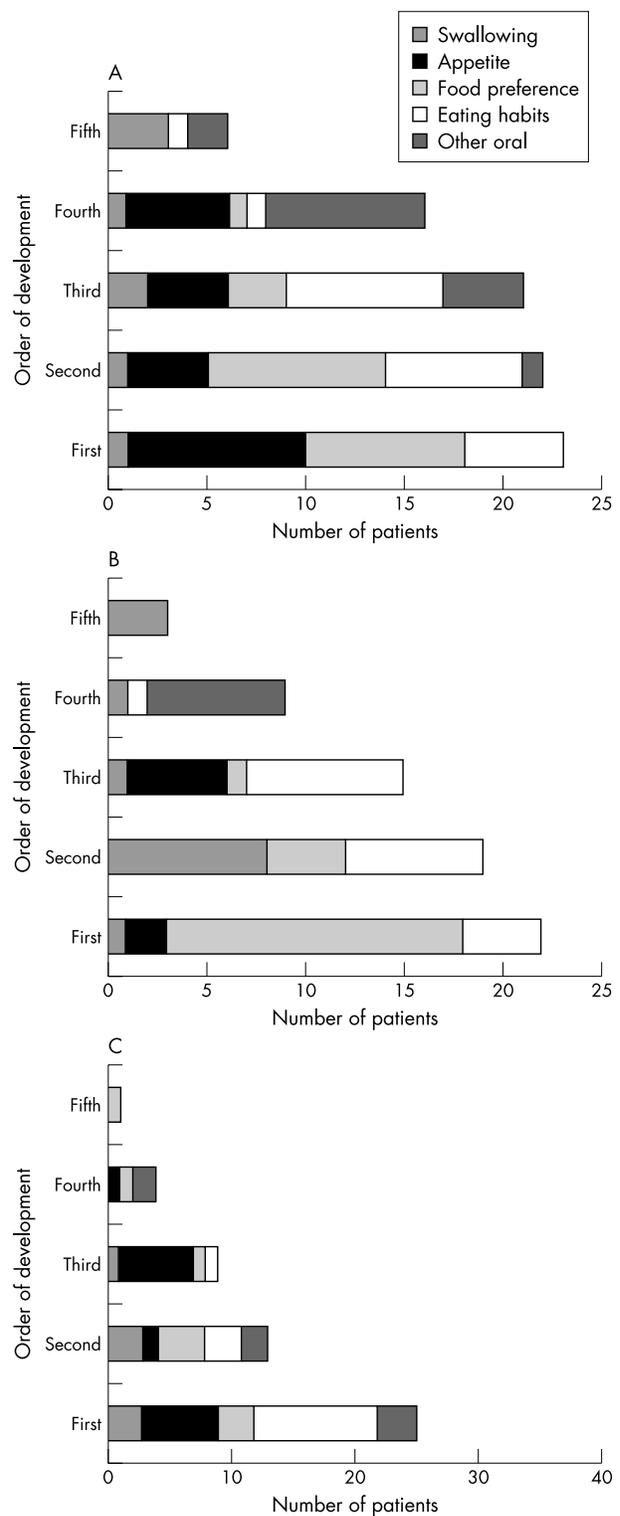


Figure 2 The development order of abnormal eating symptom in (A) frontal variant frontotemporal dementia, (B) semantic dementia, and (C) Alzheimer's disease.

Swallowing problems were rare in all groups. In both variants of frontotemporal dementia, dysphagia tended to develop at a late stage (third to fifth symptom). In Alzheimer's disease, some patients developed dysphagia at an early stage (first or second symptom). This is likely to be a considerable burden for Alzheimer's disease caregivers in their own home. A previous survey showed that one third of caregivers worry about swallowing problems.²⁵

An alteration in appetite was very commonly reported in fv-FTD. It is important to note that patients with fv-FTD and semantic dementia mainly experienced an increase in appetite, whereas those with Alzheimer's disease mainly showed loss of appetite. Significant weight gain occurred in more than 30% of frontotemporal dementia groups, but less than 10% of the Alzheimer's disease group. Appetite increase have been reported as characteristic of fv-FTD and semantic dementia.^{5,7} In Alzheimer's disease, some studies have reported that the appetite is generally decreased,^{8,9} while others have found it generally increased.¹⁰

Altered food preference toward sweet foods was a prominent and early feature in the frontotemporal dementia groups.^{5,7,26} Craving sweet foods may be distressing symptom for caregivers, especially in semantic dementia. Past studies of Alzheimer's disease have found sweet food preference in 5–39% of cases^{8–10,24}; 21% of our Alzheimer's disease patients showed food preference change, which was significantly less than the prevalence in fv-FTD (91%) and semantic dementia (80%).

Stereotypic eating behaviours were common in both the frontotemporal dementia groups. *Bozeat et al* suggested that only stereotypic behaviour, changes in eating preference, disinhibition, and features of poor social awareness reliably distinguished between the frontotemporal dementia groups and Alzheimer's disease.⁵

Other abnormal oral behaviours were also relatively common in fv-FTD patients. By contrast, in semantic dementia, the only commonly endorsed symptom was a tendency to eat non-edible things. The dissociation between appetite increase and mouthing inedible things suggests that the two may involve different underlying mechanisms.⁷

One possible confounding factor relates to the problem of differing disease severity across the various syndromes. In our study, on the basis of the MMSE, the fv-FTD group appeared less severely affected than the others, although this difference almost certainly reflects the MMSE's emphasis on memory and language, while the manifestations of this variant of frontotemporal dementia are almost entirely behavioural. The CDR was also used in an attempt to equate for severity of dementia. Although there was no statistically significant difference in the distribution of the scores, almost one third of Alzheimer's disease cases had a CDR score of 0.5, compared with 17% of fv-FTD and 20% of semantic dementia cases. On the basis of this finding, the Alzheimer's disease group appear less impaired than the other two. We also addressed this issue by examining the stage at which individual symptoms appear and found a clear difference between frontotemporal dementia syndromes and Alzheimer's disease.

Turning to the neuroanatomical implications of our findings, we hypothesise that the changes in eating behaviours reflect the involvement of a common network in both variants of frontotemporal dementia—namely, the ventral (orbitobasal) frontal lobe, the temporal pole, and the amygdala.^{4,27–29} The ventromedial frontal lobe is affected from an early stage in patients with fv-FTD and semantic dementia, either by direct pathological involvement, or indirectly through damage to the temporal pole and amygdala, which are heavily interconnected with the ventromedial frontal lobe.²⁸ Bilateral degeneration of the amygdaloid nuclear complex in monkeys, and surgical removal of the temporal lobes in man, result in the Kluver–Bucy syndrome which is characterised by hyperorality, overeating, and the eating of quasi-food items.^{30,31} Experimental studies in monkeys have shown a primary taste cortex located in the anterior insula and adjoining frontal operculum, with a secondary taste area in the orbitofrontal cortex.^{32–34} Activational neuroimaging studies in humans have also implicated the frontal operculum/insula, orbitofrontal cortex, and amygdala in processing taste.^{35,36} Future neuroimaging and behaviour studies should clarify the neural basis of eating behaviour change in patients with frontotemporal dementia.

There are also profound changes in cortical serotonin levels in frontotemporal dementia, which almost certainly contribute to the alterations in satiety and food preference.³⁷ On the basis of these findings, *Swartz et al* explored the efficacy of selective serotonin reuptake inhibitors (SSRIs) in the treatment of the behavioural symptoms of frontotemporal dementia (including disinhibition, depressive symptoms, carbohydrate craving, and compulsions).³⁸ This preliminary open study showed that half the frontotemporal dementia patients improved. The efficacy of SSRIs in other primary eating disorders^{39,40} also argues for the need for larger placebo controlled trials in frontotemporal dementia. The elucidation of the pathophysiological basis for the abnormal eating behaviour in frontotemporal dementia might throw light on the mechanisms underlying similar changes in satiety and food preference in other neuropsychiatric syndromes such as the Prader–Willi syndrome,⁴¹ the Kleine–Levin syndrome,⁴² Down's syndrome,⁴³ and bulimia nervosa.⁴⁴

Our findings also have relevance for the differentiation of frontotemporal dementia from Alzheimer's disease. Our questionnaire might be a useful tool for the evaluation of potential symptomatic treatments, especially SSRIs.

ACKNOWLEDGEMENTS

We thank Dr J S Snowden for valuable comments. We are grateful to Kate Dawson, Sharon Erzincliglu, and Marion Wilkinson for their help with data collection. This work was supported as part of an MRC programme grant to JRH.

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Competing interests: none declared.

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