Original Investigation

Quantifying the Eating Abnormalities in Frontotemporal Dementia

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IMPORTANCE Presence of eating abnormalities is one of the core criteria for the diagnosis of behavioral variant frontotemporal dementia (bvFTD), yet their occurrence in other subtypes of frontotemporal dementia (FTD) and effect on metabolic health is not known.

OBJECTIVE To define and quantify patterns of eating behavior and energy, sugar, carbohydrate, protein, and fat intake, as well as indices of metabolic health in patients with bvFTD and semantic dementia (SD) compared with patients with Alzheimer disease (AD) and healthy control participants.

DESIGN, SETTING, AND PARTICIPANTS Prospective case-controlled study involving patient and caregiver completion of surveys. Seventy-five participants with dementia (21 with bvFTD, 26 with SD, and 28 with AD) and 18 age- and education-matched healthy controls were recruited from FRONTIER, the FTD research clinic at Neuroscience Research Australia in Sydney.

MAIN OUTCOMES AND MEASURES Caregivers of patients with FTD and AD completed validated questionnaires on appetite, eating behaviors, energy consumption, and dietary macronutrient composition. All participants completed surveys on hunger and satiety. Body mass index and weight measurements were prospectively collected.

RESULTS The bvFTD group had significant abnormalities in the domains of appetite ($U = 111.0$, $z = 2.7$, $P = .007$), eating habits ($U = 69.5$, $z = 3.8$, $P = .001$), food preferences ($U = 57.0$, $z = 4.1$, $P = .001$), swallowing ($U = 109.0$, $z = 3.0$, $P = .003$), and other oral behaviors ($U = 141.0$, $z = 2.6$, $P = .009$) compared with the AD group. The bvFTD and SD groups tended to have increased energy consumption. Compared with controls, the bvFTD group had significantly increased carbohydrate intake (251 vs 170 g/d; $P = .05$) and the SD group had significantly increased sugar intake (114 vs 76 g/d; $P = .049$). No significant differences in total fat or protein intake between the groups were found. Despite similar energy intake, the SD group had lower hunger and satiety scores compared with the bvFTD group. In contrast, hunger and satiety scores did not differ between the bvFTD group and controls. The abnormal eating behavior was found in the 2 groups (bvFTD and SD) with the highest body mass index ($F = 4.2$, $P = .008$) and waist circumference ($F = 6.4$, $P = .001$).

CONCLUSIONS AND RELEVANCE Abnormal eating behaviors are prominent in patients with bvFTD and those with SD and are not limited to increased appetite. The observed higher intake of sugar and carbohydrates was found in patients with the FTD subtypes and those with higher body mass index and waist circumference and was not explained simply by increased hunger or lower satiety.

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Eating abnormalities are present in up to 60% of patients with frontotemporal dementia (FTD) and are one of the 6 core symptoms required for the diagnosis of behavioral variant FTD (bvFTD).[1] Typically, patients are described as having appetite changes, increased carbohydrate craving, and changes in food preference, including increased sweet preference.[2] Eating changes are also reported in patients with semantic dementia (SD), another FTD syndrome, in which patients typically exhibit stereotypical eating and food fads.[3,4] Systematic comparisons of eating changes in patients with bvFTD and SD are lacking, with one exception.[5]

Eating behavior is modulated by a number of variables including metabolic processes, environmental cues, cognition, and sensory processing, including liking and wanting certain foods. These factors contribute to appetite (food preference, selection motivation, and intake), hunger (conscious sensation reflecting a mental urge and drive to eat), and satiety (process that leads to inhibition of further eating, decline in hunger, and increased fullness after a meal is finished).[6]

Damage to the hypothalamus and brainstem can result in decreased or increased eating. Complex eating abnormalities are also observed following lesions to the frontal and temporal lobe regions.[7] Several studies have implicated the right ventral, insula striatum, orbitofrontal cortices,[8,9] and posterior hypothalamus[10] as being responsible for abnormal eating habits in FTD. To our knowledge, no studies to date, however, have quantified food type and caloric intake and examined hunger and satiety in these patients to determine whether these variables may be responsible for abnormal eating in FTD.

Furthermore, the consequences of abnormal eating behavior on the health of patients with FTD are unknown. While weight gain has been reported,[2,3] the effects of abnormal eating behaviors on the metabolic health of patients with FTD have not been systematically documented to date.

This study aimed to contrast eating habits, as well as measures of hunger and satiety, in 2 FTD syndromes (bvFTD and SD). We compared these behaviors, along with general indices of health, with those found in patients with Alzheimer disease (AD) and with healthy control participants using caregiver- and patient-based questionnaires. We hypothesized that the bvFTD and SD groups would exhibit different profiles of abnormal eating behavior and that these behaviors would be more common in the 2 FTD groups compared with the AD group.

Methods

Patients

Seventy-five participants with dementia (21 with bvFTD, 26 with SD, and 28 with AD) were recruited from FRONTIER, the FTD clinic at Neuroscience Research Australia in Sydney. All participants underwent a comprehensive assessment, which included a clinical interview, neurologic examination, cognitive assessment, and structural brain magnetic resonance imaging. All patients met the current clinical diagnostic criteria for probable bvFTD, SD, or AD,[1,11,12] and diagnosis was established by consensus between the neurologist, the neuropsychologist, and the occupational therapist. In addition, 18 age- and education-matched healthy controls were included into the study. These individuals were either spouses of patients or were recruited from a panel of healthy study volunteers. All healthy controls scored above 88 (of 100) on the Addenbrooke's Cognitive Examination Revised screening test[13] and 0 on the Clinical Dementia Rating scale.[14] Exclusion criteria included significant extrapyramidal features; history of stroke, epilepsy, alcoholism, or significant traumatic brain injury; or presence of ferrous metal implants in the body. Patients with an uncertain diagnosis or for whom a caregiver was not available were also excluded from the project. This study was approved by the South Eastern Sydney and Illawarra Area Health Service and the University of New South Wales Human Ethics Committees. Written informed consent was obtained from the participants and/or primary caregivers.

Assessment of Eating Behavior

Caregivers completed the Appetite and Eating Habits Questionnaire (APEHQ) (eAppendix in the Supplement) and the Cambridge Behavioral Inventory (CBI).[15] The APEHQ comprises 34 questions that examine changes in eating behaviors in the following domains: swallowing, appetite, eating habits (stereotypic eating behavior and table manners), food preference (including sweet preference and other food fads), and other oral behaviors (eg, food cramming, increased smoking). Caregivers were asked to rate the frequency (0 = never, 1 = less than weekly, 2 = about once a week, 3 = several times a week, 4 = daily or continuously) and severity (0 = N/A [not applicable], 1 = mild, 2 = moderate, and 3 = marked) for each behavior. A composite score of frequency × severity was calculated for each question, and an overall score was derived for each domain. The 4 questions from the CBI that are specifically related to eating behavior (sweet preference, same foods, change in appetite, and table manners) were also analyzed. Each CBI item is rated using a 5-point scale (0 = never, 1 = a few times per month, 2 = a few times per week, 3 = daily, and 4 = constantly).

Assessment of Hunger and Satiety

Participants' levels of hunger and satiety before and after breakfast, lunch, and dinner during a 24-hour period were also measured. In an interview-style manner on a visual analog scale ranging from 1 to 10, caregivers asked the patients to rate their hunger, how satisfied they felt, how full they felt, how much they thought they could eat, and how much they desired something sweet, salty, savory, or fatty to eat. Caregivers were provided with prompting questions to aid the patients in answering the questions. Control participants were also asked to rate these items themselves independently. A hunger-satiety index was calculated using the following formula:

Hunger-Satiety Index = How Hungry the Person Feels + (100 − How Empty the Person Feels) + (100 − How Full the Person Feels) + How Much the Person Thinks They Can Eat.

In other words, the higher the score, the more hungry the person is reporting to be.

Assessment of Daily Food Intake

Information on general food habits, such as overall caloric intake, macronutrient composition, and food preferences, was

Table 1. Demographics and Cognitive Scores for the Dementia and Control Groups[a]

Demographics and Cognitive Score	bvFTD	SD	AD	Controls	*F* Value	Post Hoc Test
Sex, No. (male:female)	16:5	17:9	21:7	9:9	NS	NA
Age, y	63 (8.3)	66 (6.1)	67 (7.2)	70 (5.1)	3.3[b]	Controls>bvFTD
Disease duration, y	6.2 (2.9)	5.4 (2.0)	4.4 (2.4)	NA	3.6[b]	bvFTD>AD
ACE-R total score (out of 100)	76 (15.9)	56 (18.4)	61 (21.1)	94 (4.7)	21.0[c]	Controls>patient groups; bvFTD>AD, SD
ACE-R language score	21.0 (4.9)	10.8 (5.1)	19.5 (5.9)	24.7 (1.0)	33.8[c]	SD<AD, bvFTD, controls; controls>AD
CBI abnormal behaviors score	11.7 (6.5)	6.6 (6.1)	3.7 (3.5)	NA	12.8[c]	bvFTD>AD, SD
Global CDR score	1.4 (0.8)	0.8 (0.5)	0.9 (0.4)	0	5.8[b]	bvFTD>AD, SD

Abbreviations: ACE-R, Addenbrooke's Cognitive Examination Revised; AD, Alzheimer disease; bvFTD, behavioral variant frontotemporal dementia; CBI, Cambridge Behavioral Inventory; CDR, Clinical Dementia Rating; NA, not applicable; NS, not significant; SD, semantic dementia.

[a] Values are given as mean (SD) unless otherwise noted.

[b] $P < .05$.

[c] $P < .001$.

obtained using the Dietary Questionnaire for Epidemiological Studies (http://www.cancervic.org.au/research/cancer-statistics/nutritional_assessment_services) and was completed either by caregivers (for the dementia participants) or by the control participants. Output provides comprehensive information on food and drink intake (eg, water, kilojoules, total fat, total protein, carbohydrates, sugars, cholesterol, and vitamins, as well as fatty acids and glycemic index).

Assessment of Physical Measurements

Height, waist circumference, and weight were measured (shoes removed). Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Waist circumference was measured to the nearest centimeter midway between the ribs and anterior superior iliac spine.

Data Analysis

Data were analyzed using SPSS statistics (version 21.0; IBM). Kolmogorov-Smirnov tests were run to determine suitability of variables for parametric analyses. Analyses of variance, followed by Tukey post hoc tests, were used to explore the main effects of group (controls, bvFTD, SD, and AD) for the following variables: hunger-satiety index, BMI, weight, and sugar and carbohydrate intake ($P < .05$ considered significant). Analyses of covariance were used to investigate the effect of specific variables (eg, age) on waist circumference and BMI. Cambridge Behavioral Inventory scores and product of frequency and severity of the APEHQ for all domains were analyzed individually using Kruskal-Wallis tests followed by post hoc Mann-Whitney tests corrected for multiple comparisons ($P < .01$ regarded as significant). Differences in frequency patterns of categorical variables (eg, sex) were examined with χ^2 tests.

Results

Demographics

The 2 FTD groups were well matched for all demographic characteristics (sex distribution, age, and disease duration) (**Table 1**). Other group comparisons showed that the AD group had a shorter disease duration than the bvFTD group ($P = .03$) and that the control group was slightly older than the bvFTD group ($P = .02$). On measures of global cognition and dementia severity, the control group scored higher than the patient groups on the Addenbrooke's Cognitive Examination Revised screening test ($P < .001$), with the bvFTD group also performing better than the SD ($P = .02$) and AD ($P = .001$) groups. On the language scale of the Addenbrooke's Cognitive Examination Revised screening test, the SD group scored significantly lower than the other groups ($P < .001$), but the other dementia groups did not differ significantly. In contrast, the bvFTD group scored significantly higher than the SD group on the CBI abnormal behavioral subscale. These findings confirmed that the SD group had predominant language difficulties. On the global Clinical Dementia Rating scale, patient groups obtained scores that were significantly higher than the control group. In addition, the global Clinical Dementia Rating score was higher in the bvFTD group than in the AD ($P = .02$) and SD ($P = .005$) groups.

Assessment of Eating Behavior

Significant group differences were found in all domains of the APEHQ (**Table 2**). The bvFTD group had significantly higher scores than the AD group for all 5 domains: swallowing ($U = 109.0$, $z = 3.0$, $P = .003$), appetite ($U = 111.0$, $z = 2.7$, $P = .007$), eating habits ($U = 69.5$, $z = 3.8$, $P = .001$), food preferences ($U = 57.0$, $z = 4.1$, $P = .001$), and other oral behaviors ($U = 141.0$, $z = 2.6$, $P = .009$). In addition, the bvFTD group also scored significantly higher than the SD group for the swallowing domain ($U = 95.0$, $z = 3.1$, $P = .002$). No other significant differences were present between the SD and bvFTD groups or between the SD and AD groups.

On the CBI (**Figure 1**A), significant group differences were found on 3 of the 4 questions related to eating behavior, with significantly higher changes related to sweet preference ($U = 105.0$, $z = 3.8$, $P < .001$), eating the same foods ($U = 72.5$, $z = 4.7$, $P = .001$), and table manners ($U = 173.0$, $z = 2.7$, $P = .007$) in the bvFTD group compared with the AD group. No significant differences were observed on these items between the 2 FTD syndromes.

Hunger and Satiety Measures

No significant mean (SD) differences in hunger-satiety index scores were observed across groups at any time during the day: before breakfast: bvFTD, 226 (85); SD, 172 (80); AD, 186 (75); and controls, 224 (49); lunch: bvFTD, 131 (67); SD, 97 (76); AD, 99 (57); and controls, 91 (63); and dinner: bvFTD, 131 (86); SD,

Table 2. Appetite and Eating Habits Questionnaire Results[a]

Domain	bvFTD	SD	AD	Kruskal-Wallis *H*	Post Hoc Test
Swallowing	10.4 (17.0)	0.7 (1.8)	1.1 (2.6)	13.1[b]	bvFTD>AD, SD
Appetite	18.4 (15.9)	8.4 (9.6)	7.5 (13.6)	9.1[c]	bvFTD>AD
Eating habits	12.9 (12.5)	8.6 (10.4)	2.7 (4.9)	13.4[b]	bvFTD>AD
Food preferences	25.4 (18.6)	12.5 (16.1)	3.9 (6.5)	17.6[b]	bvFTD>AD
Other oral behaviors	4.5 (8.2)	2.0 (3.9)	1.0 (3.3)	6.9[d]	bvFTD>AD

Abbreviations: AD, Alzheimer disease; bvFTD, behavioral variant frontotemporal dementia; SD, semantic dementia.

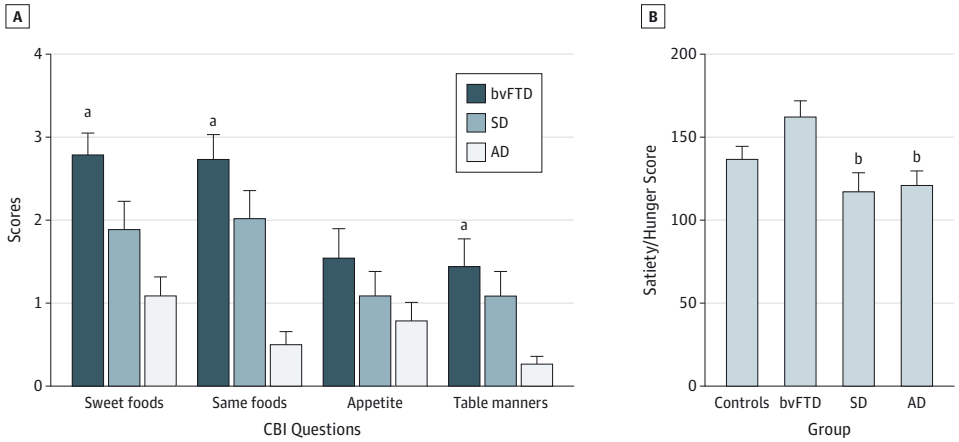
[a] Values are given as mean (SD) unless otherwise noted. High scores denote increased abnormal features. For each section, the overall score reflects the combination of frequency and severity of each relevant feature investigated by the questionnaire.

[b] $P < .001$.

[c] $P < .01$.

[d] $P < .05$.

Figure 1. Assessment of Eating Behavior



A, Cambridge Behavioral Inventory (CBI) eating scores. B, Average hunger-satiety scores over 24 hours. Scores are mean (SEM); composite hunger-satiety score combines prebreakfast, lunch, and dinner index scores. AD indicates Alzheimer disease; bvFTD, behavioral variant frontotemporal dementia; and SD, semantic dementia.

[a] bvFTD>AD, $P < .01$.

[b] bvFTD>SD and AD, $P < .05$.

78 (81); AD, 86 (59); and controls, 95 (69). Combining these measures into an overall score for the day, however, revealed a significant group difference (F = 3.6, $P = .02$), with the bvFTD group showing a significantly higher hunger-satiety index score than the SD ($P = .02$) and AD groups ($P = .03$) but not the control group ($P = .38$) (Figure 1B).

Energy and Food Intake

The bvFTD and SD groups tended to have higher daily energy intake compared with the AD and control groups; however, this difference did not reach statistical significance (**Figure 2**A). In contrast, daily carbohydrate intake was significantly different across the groups ($F = 2.7$, $P = .05$), with the bvFTD group (Figure 2B) having significantly higher intake compared with controls (251 vs 170 g/d, $P = .05$). Total daily sugar intake (Figure 2C) was also significantly different across groups ($F = 2.9$, $P = .04$), with the SD group showing a significantly higher sugar intake compared with controls (114 vs 76 g/d, $P = .049$). No significant between-group differences were found for total fat intake ($F = 1.9$, $P = .13$) or protein intake ($F = 1.0$, $P = .41$).

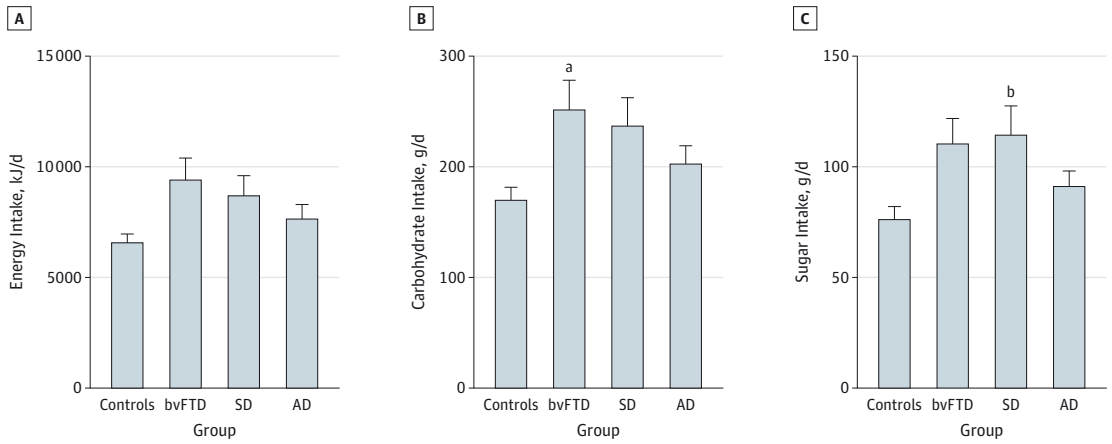
BMI and Waist Circumference

Significant group differences were observed for BMI ($F = 4.2$, $P = .008$) and waist circumference ($F = 6.4$, $P = .001$). Post hoc tests showed that the bvFTD (106.2 cm) and SD (101.3 cm) groups had significantly higher waist circumference compared with the control group (91.2 cm) ($P < .01$ for both) (**Figure 3**). In addition, the bvFTD group also had significantly higher waist circumference compared with the AD group (95.5 cm) ($P = .01$). Compared with the control group (24.05), both the bvFTD (29.65) and SD (28.71) groups had significantly higher BMIs ($P = .009$ and .04, respectively). Group differences in BMI and waist circumference remained significant even after age was added as a covariate.

Discussion

To our knowledge, this study is the first to formally quantify eating behavior abnormalities in FTD subtypes. It demonstrates that patients with bvFTD and those with SD consume significantly more carbohydrates and sugar in grams per day

Figure 2. Energy and Food Intake

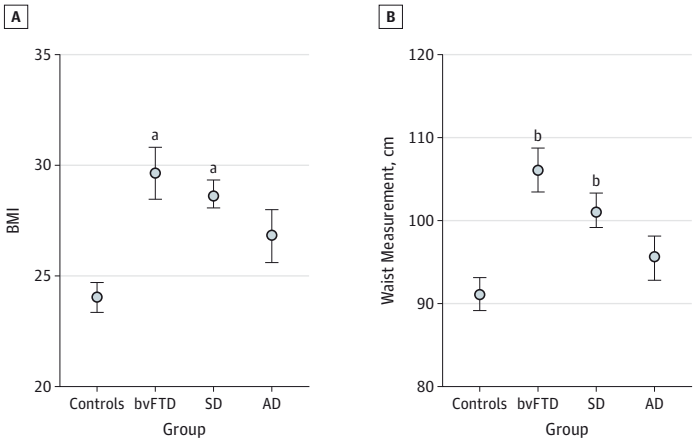


A, Energy (in kilojoules), B, carbohydrate (in grams), and C, sugar (in grams) intake over 24 hours. Scores are mean (SEM). AD indicates Alzheimer disease; bvFTD, behavioral variant frontotemporal dementia; and SD, semantic dementia.

[a] bvFTD>controls, $P < .05$.

[b] SD>controls, $P < .05$.

Figure 3. Body Mass Index (BMI) and Waist Circumference



A, BMI (calculated as weight in kilograms divided by height in meters squared). B, Waist circumference. Scores are mean (SEM). AD indicates Alzheimer disease; bvFTD, behavioral variant frontotemporal dementia; and SD, semantic dementia.

[a] bvFTD and SD>controls, $P < .01$; bvFTD>AD, $P < .01$.

[b] bvFTD and SD>controls, $P < .01$.

than do healthy controls and patients with AD. This abnormal eating behavior does not appear to be explained by increased hunger or decreased satiety. The 2 FTD groups, who showed the highest carbohydrate and sugar intake, also had increased weight, BMI, and waist circumference.

On the APEHQ,[5] the bvFTD group had significantly higher scores in all 5 domains of swallowing, appetite change, eating habits, food preference, and other oral behaviors compared with the AD group. The bvFTD group showed the greatest changes in the domain of food preference (including sweet craving), followed by appetite and eating habits (including stereotypic eating behavior). With the exception of swallowing, the SD group obtained scores on this questionnaire that were similar to those of the bvFTD group. Furthermore, the scores in the domains of appetite, eating habits, and food preferences were higher in the SD group than in the AD group, although these differences did not reach statistical significance. Eating abnormalities between the bvFTD and AD groups were also detected on the CBI in the domains of sweet preference, eating the same foods, and table manners. This finding suggests that the CBI is a suitable short screening questionnaire to detect eating abnormalities in which further investigation may be required with detailed instruments, such as the APEHQ.

Changes in eating habits in patients with bvFTD have generally been characterized by gluttony, binge or indiscriminate eating, and increased sweet preference.[2,3,8,16] In the present study, the most marked change in this group was an alteration in food preferences, which included sweet craving. Patients with bvFTD also demonstrated changes in eating habits and stereotypic eating as well as prominent swallowing difficulties. We can only speculate about the etiology of these changes. Given the overlap between FTD and amyotrophic lateral sclerosis,[16,17] it is possible that the swallowing

difficulties represent incipient bulbar dysfunction, at least in a proportion of cases. Swallowing abnormalities have also been thought to reflect deficits in cortical and subcortical pathways connecting to the brainstem swallowing center.[18,19]

The literature on the eating behavior changes in patients with SD is limited. Patients with SD have been described as having increased selectivity and food fads in their eating behavior, as well as changes in flavor identification.[3,4] Changes in food preferences and eating habits have been previously reported in patients with SD on the same instrument.[5] While the patients with SD in our study showed changes in food preference and abnormal eating habits, the difference from the patients with AD was not significant. Changes in the AD group were low except for alterations in appetite, in keeping with prior literature.[5,20]

Changes in sweet preference and carbohydrate intake in patients with bvFTD have been previously reported,[2,8] but quantification of these abnormal behaviors has been lacking until now. This study demonstrates that patients with bvFTD and those with SD tend to have an increased overall daily food intake (in kilojoules), as well as elevated levels of sugar and carbohydrate intake compared with the AD and control groups. Of the 2 FTD syndromes, the SD group had the higher sugar intake (114.16 g/d) compared with the bvFTD group (109.92 g/d). These results confirm the anecdotal reports of increased sweet preference and carbohydrate craving in patients with bvFTD; notably, these findings extend to patients with SD. Together, these findings suggest that increased carbohydrate and sugar intake, but not total fat and protein intake, may be helpful markers to differentiate FTD from other forms of dementia. Increased sugar intake has not been reported previously in patients with SD. This finding suggests that the mechanisms and structures of abnormal eating behavior in patients with SD may be similar to those in patients with bvFTD.

In this study, participants used visual analog scales to rate their sensation of hunger, appetite, and satiety, a reliable method to predict food intake.[6,21] No significant differences in hunger and satiety scores were present between patients with bvFTD and controls, suggesting that changes in hunger and satiety do not fully explain the occurrence of abnormal eating behavior observed in patients with bvFTD. This finding is confirmed by the observation that patients with SD reported a significantly lower satiety hunger index for the day compared with the bvFTD group. This difference occurred despite a higher sugar consumption and similar carbohydrate and energy consumption between the SD and bvFTD groups. Similar findings have been reported in bvFTD,[8] with patients continuing to binge eat despite reporting satiety.

Feelings of satiety or hunger in obese individuals are typically similar to those of healthy individuals and do not correlate with food intake.[22] Overeating appears related to disinhibition (ie, a tendency to overeat and eating opportunistically) in many instances.[23] Disinhibition is associated with novelty seeking, impulsiveness, and inability to resist external cues[24] and may reflect abnormal involvement of the insula cortex.[25] In keeping with this hypothesis, binge eating behavior in FTD has also been related to atrophy in the right orbitofrontal insula cortex.[8] The relationship between disinhibition, a common feature in bvFTD,[26] alterations in eating, and orbitofrontal cortex integrity is clearly worthy of further investigation.

The possible role of the hypothalamus and regulatory peptides in the abnormal eating behavior found in FTD is of particular interest given the association between disinhibition and the eating peptides leptin, ghrelin, and peptide YY.[23,27] These peptides act peripherally and centrally on the arcuate and ventromedial nucleus of the hypothalamus.[28] This association raises an interesting possibility that these peptides, or their sites of action, may be affected, especially as hypothalamic atrophy has been demonstrated in patients with FTD and high feeding disturbance.[10]

The metabolic profile of patients with FTD is likely to be abnormal,[29] as suggested by the increased BMI and waist circumference in both FTD syndromes compared with control participants. High BMI and increased waist circumference have been associated with reduced metabolic health and the metabolic syndrome (hypertension, dyslipidemia, type 2 diabetes mellitus, and hyperinsulinemia) in population studies.[30,31] Recent work has shown that patients with amyotrophic lateral sclerosis, many of whom share a common pathology (TDP-43 protein inclusions) with patients with bvFTD,[32,33] have a distinct metabolic profile with a low BMI.[34,35] It has been suggested that cholesterol and metabolic changes in patients with amyotrophic lateral sclerosis, including insulin resistance, may affect disease progression and prognosis.[36,37] Further research is required into the metabolic profile in FTD and how this profile compares with amyotrophic lateral sclerosis.

Conclusions

In this study, data regarding abnormal eating behavior and food intake were drawn from caregiver questionnaires. It will be important to confirm the eating changes in FTD cohorts using ecologically valid approaches over multiple time points. One potential avenue is a test meal approach in which patients are observed eating an ad-lib meal and their intake and behavior directly measured. Satiety and hunger could also be measured by visual analog scales before and after the test meal. Future research could also incorporate actinography to understand caloric intake vs expenditure.

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Study concept and design: Hodges, Piguet.
Acquisition, analysis, or interpretation of data: Ahmed, Irish, Kam, van Keizerswaard, Bartley, Samaras, Piguet.
Drafting of the manuscript: Ahmed, Irish, Kam, van Keizerswaard, Bartley, Samaras, Piguet.
Critical revision of the manuscript for important intellectual content: Ahmed, Hodges, Piguet.
Statistical analysis: Ahmed, Irish, Kam, van Keizerswaard, Bartley, Samaras.
Obtained funding: Piguet.
Study supervision: Hodges, Piguet.

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REFERENCES

1. Rascovsky K, Hodges JR, Knopman D, et al. Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. *Brain*. 2011;134(pt 9):2456-2477.

2. Miller BL, Darby AL, Swartz JR, Yener GG, Mena I. Dietary changes, compulsions and sexual behavior in frontotemporal degeneration. *Dementia*. 1995;6(4):195-199.

3. Snowden JS, Bathgate D, Varma A, Blackshaw A, Gibbons ZC, Neary D. Distinct behavioural profiles in frontotemporal dementia and semantic dementia. *J Neurol Neurosurg Psychiatry*. 2001;70 (3):323-332.

4. Omar R, Mahoney CJ, Buckley AH, Warren JD. Flavour identification in frontotemporal lobar degeneration. *J Neurol Neurosurg Psychiatry*. 2013; 84(1):88-93.

5. Ikeda M, Brown J, Holland AJ, Fukuhara R, Hodges JR. Changes in appetite, food preference, and eating habits in frontotemporal dementia and Alzheimer's disease. *J Neurol Neurosurg Psychiatry*. 2002;73(4):371-376.

6. Blundell J, de Graaf C, Hulshof T, et al. Appetite control: methodological aspects of the evaluation of foods. *Obes Rev*. 2010;11(3):251-270.

7. Uher R, Treasure J. Brain lesions and eating disorders. *J Neurol Neurosurg Psychiatry*. 2005;76 (6):852-857.

8. Woolley JD, Gorno-Tempini ML, Seeley WW, et al. Binge eating is associated with right orbitofrontal-insular-striatal atrophy in frontotemporal dementia. *Neurology*. 2007;69(14): 1424-1433.

9. Whitwell JL, Sampson EL, Loy CT, et al. VBM signatures of abnormal eating behaviours in frontotemporal lobar degeneration. *Neuroimage*. 2007;35(1):207-213.

10. Piguet O, Petersén A, Yin Ka Lam B, et al. Eating and hypothalamus changes in behavioral-variant frontotemporal dementia. *Ann Neurol*. 2011;69(2): 312-319.

11. Gorno-Tempini ML, Hillis AE, Weintraub S, et al. Classification of primary progressive aphasia and its variants. *Neurology*. 2011;76(11):1006-1014.

12. McKhann GM, Albert MS, Grossman M, Miller B, Dickson D, Trojanowski JQ; Work Group on Frontotemporal Dementia and Pick's Disease. Clinical and pathological diagnosis of frontotemporal dementia: report of the Work Group on Frontotemporal Dementia and Pick's Disease. *Arch Neurol*. 2001;58(11):1803-1809.

13. Mioshi E, Dawson K, Mitchell J, Arnold R, Hodges JR. The Addenbrooke's Cognitive Examination Revised (ACE-R): a brief cognitive test battery for dementia screening. *Int J Geriatr Psychiatry*. 2006;21(11):1078-1085.

14. Morris JC. The Clinical Dementia Rating (CDR): current version and scoring rules. *Neurology*. 1993; 43(11):2412-2414.

15. Bozeat S, Gregory CA, Ralph MA, Hodges JR. Which neuropsychiatric and behavioural features distinguish frontal and temporal variants of frontotemporal dementia from Alzheimer's disease? *J Neurol Neurosurg Psychiatry*. 2000;69 (2):178-186.

16. Lillo P, Mioshi E, Zoing MC, Kiernan MC, Hodges JR. How common are behavioural changes in amyotrophic lateral sclerosis? *Amyotroph Lateral Scler*. 2011;12(1):45-51.

17. Burrell JR, Kiernan MC, Vucic S, Hodges JR. Motor neuron dysfunction in frontotemporal dementia. *Brain*. 2011;134(pt 9):2582-2594.

18. Liu W, Miller BL, Kramer JH, et al. Behavioral disorders in the frontal and temporal variants of frontotemporal dementia. *Neurology*. 2004;62(5): 742-748.

19. Langmore SE, Olney RK, Lomen-Hoerth C, Miller BL. Dysphagia in patients with frontotemporal lobar dementia. *Arch Neurol*. 2007; 64(1):58-62.

20. Mendez MF, Licht EA, Shapira JS. Changes in dietary or eating behavior in frontotemporal dementia versus Alzheimer's disease. *Am J Alzheimers Dis Other Demen*. 2008;23(3):280-285.

21. Stubbs RJ, Hughes DA, Johnstone AM, et al. The use of visual analogue scales to assess motivation to eat in human subjects: a review of their reliability and validity with an evaluation of new hand-held computerized systems for temporal tracking of appetite ratings. *Br J Nutr*. 2000;84(4): 405-415.

22. Barkeling B, King NA, Näslund E, Blundell JE. Characterization of obese individuals who claim to detect no relationship between their eating pattern and sensations of hunger or fullness. *Int J Obes (Lond)*. 2007;31(3):435-439.

23. Bryant EJ, King NA, Blundell JE. Disinhibition: its effects on appetite and weight regulation. *Obes Rev*. 2008;9(5):409-419.

24. Gendall KA, Joyce PR, Sullivan PF, Bulik CM. Personality and dimensions of dietary restraint. *Int J Eat Disord*. 1998;24(4):371-379.

25. DelParigi A, Chen K, Salbe AD, Reiman EM, Tataranni PA. Sensory experience of food and obesity: a positron emission tomography study of the brain regions affected by tasting a liquid meal after a prolonged fast. *Neuroimage*. 2005;24(2): 436-443.

26. Hornberger M, Geng J, Hodges JR. Convergent grey and white matter evidence of orbitofrontal cortex changes related to disinhibition in behavioural variant frontotemporal dementia. *Brain*. 2011;134(pt 9):2502-2512.

27. Martins C, Robertson MD, Morgan LM. Impact of restraint and disinhibition on PYY plasma levels and subjective feelings of appetite. *Appetite*. 2010; 55(2):208-213.

28. Coll AP, Farooqi IS, O'Rahilly S. The hormonal control of food intake. *Cell*. 2007;129(2):251-262.

29. Dupuis L, Petersen A, Weydt P. Progranulin bridges energy homeostasis and fronto-temporal dementia. *Cell Metab*. 2012;15(3):269-270.

30. Janssen I, Katzmarzyk PT, Ross R. Body mass index, waist circumference, and health risk: evidence in support of current National Institutes of Health guidelines. *Arch Intern Med*. 2002;162(18): 2074-2079.

31. Katzmarzyk PT, Janssen I, Ross R, Church TS, Blair SN. The importance of waist circumference in the definition of metabolic syndrome: prospective analyses of mortality in men. *Diabetes Care*. 2006; 29(2):404-409.

32. Clark CM, Forman MS. Frontotemporal lobar degeneration with motor neuron disease: a clinical and pathological spectrum. *Arch Neurol*. 2006;63 (4):489-490.

33. Hodges J. Familial frontotemporal dementia and amyotrophic lateral sclerosis associated with the C9ORF72 hexanucleotide repeat. *Brain*. 2012; 135(pt 3):652-655.

34. Desport JC, Preux PM, Truong CT, Courat L, Vallat JM, Couratier P. Nutritional assessment and survival in ALS patients. *Amyotroph Lateral Scler Other Motor Neuron Disord*. 2000;1(2):91-96.

35. Stambler N, Charatan M, Cedarbaum JM; ALS CNTF Treatment Study Group. Prognostic indicators of survival in ALS. *Neurology*. 1998;50(1): 66-72.

36. Jawaid A, Salamone AR, Strutt AM, et al. ALS disease onset may occur later in patients with pre-morbid diabetes mellitus. *Eur J Neurol*. 2010;17 (5):733-739.

37. Dupuis L, Corcia P, Fergani A, et al. Dyslipidemia is a protective factor in amyotrophic lateral sclerosis. *Neurology*. 2008;70(13):1004-1009.