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Declines in dietary macronutrient intake in persons with HIV infection who develop depression

Rita Isaac[1], Denise Jacobson[1], Christine Wanke[1], Kristy Hendricks[1], Tamsin A Knox[1,2] and Ira B Wilson[3,*]

[1]Nutrition/Infection Unit, Department of Public Health and Family Medicine, Tufts University School of Medicine, Boston, MA, USA: [2]Division of Gastroenterology, Tufts–New England Medical Center, Boston, MA, USA: [3]Institute for Clinical Research and Health Policy Studies, Tufts–New England Medical Center, 750 Washington Street #345, Boston, MA 02111, USA

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Abstract

Background: The effect of depression on dietary intake has not, to our knowledge, been examined in persons with HIV infection.

Methods: We conducted a longitudinal analysis of participants in the Nutrition for Healthy Living Study (NFHL). We measured changes in dietary macronutrient intake in participants who developed depression and, using multiple regression analysis, compared the changes with a control group of patients who did not become depressed.

Results: Ninety patients developed depression during the observation period, and we compared these with 152 non-depressed controls. The two groups had similar age and body mass index (BMI) at baseline, but those who developed depression were more likely to be female, less educated and had lower incomes. After adjustment, compared with non-depressed participants, those who developed depression had significantly greater decreases in the following daily intakes: total energy (−341 kcal, $P = 0.006$), protein (−12.3 g, $P = 0.02$), total fat (−18.5 g, $P = 0.008$), carbohydrate (−36.8 g, $P = 0.02$), total fibre (−4.3 g, $P = 0.001$) and saturated fat (−6.7 g, $P = 0.01$). There were no significant differences in the daily intakes of simple sugars and long-chain $n-3$ fatty acids, or BMI.

Conclusion: Depression is associated with decreases in total daily energy intake and in six of the eight dietary components we measured. Clinicians should be aware that depression-associated nutritional deficiencies may complicate the care of persons with HIV.

Keywords
HIV
Depression
Nutrition
Dietary intake

Malnutrition and weight loss continue to coexist with HIV disease in resource-adequate countries, despite the wide use of highly active antiretroviral therapy (HAART). The severity of weight loss has diminished compared with the pre-HAART era, but the incidence of weight loss has not[1–3]. The causes of persisting weight loss and malnutrition in HIV-infected individuals are multifactorial, with decreased energy intake due to anorexia and nausea related to HIV-associated illness or medications, increased energy demands related to chronic infection, HAART use, trouble swallowing/other oral problems and malabsorption/other gastrointestinal disorders all playing a role[4–9].

Another potential contributor to HIV-related nutritional problems is depression. Estimates of the prevalence of depression in HIV-infected persons vary widely from 5 to 20%, depending on the population studied, stage of HIV infection, the prevalence of other complicating conditions such as substance abuse and the assessment method[10]. Poor appetite and weight loss are listed as the major diagnostic features of depression in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM), 4th edition. Although depression may interfere with the quantity and quality of dietary intake, to our knowledge there is no published research that examines the relationship between depression and dietary macronutrient intake in persons with HIV. Furthermore, only a few studies in the broader literature have examined associations between depression and dietary intake. A cross-sectional study of 29 depressed subjects and a matched group of non-depressed subjects found that depressed subjects consumed a diet of poorer quality, with more carbohydrates and less protein, than subjects who were not depressed. The increase in carbohydrate consumption primarily came from an increase in sucrose (simple carbohydrate) intake[11]. With regard to micronutrients, two studies found an association between depression and low intake or serum levels of $n-3$ fatty acids[12,13] and several studies

*Corresponding author: Email iwilson@tufts-nemc.org © The Authors 2007

have found an association between depression and folate and vitamin B_{12} deficiency[14–17].

We therefore conducted a longitudinal analysis using data from a cohort study of persons with HIV, the Nutrition for Healthy Living Study (NFHL), to examine the relationship between depression and changes in dietary macronutrient intake. To strengthen our ability to draw causal inferences, we studied the diets of patients who screened negative for depression at two consecutive 6-month study visits, and then screened positive for depression at the next two study visits. We compared these patients with a control group of study patients who screened negative for depression at all four visits. We had one main study question: how does dietary macronutrient intake change in those who develop depression compared with those without depression? To our knowledge this is one of the first studies to focus on the impact of depression on dietary intake in an HIV-infected population.

Methods

Participants

The sample for this analysis of depression and diet was drawn from the NFHL cohort. NFHL is an observational cohort study of nutritional problems in HIV-infected adults, with sites in Boston, Massachusetts and Providence, Rhode Island, followed for 10 years from 1995 to May 2005. Patients aged 18 years or older at all stages of HIV disease, irrespective of their antiretroviral use, were eligible for NFHL, and special efforts were made to enrol women and minorities. Participants were recruited through advertisements in local newspapers, radio, health clinics and physician networks in Boston and Providence. Those with pregnancy, severe diarrhoea, thyroid disease, malignancies other than Kaposi's sarcoma or poor English language fluency at the time of recruitment were excluded. The following data were collected at a baseline clinic visit and at semi-annual follow-up visits: socio-demographics, weight, height, anthropometric measurements, dietary intake, clinical status, symptoms of depression, CD4 cell count, HIV viral load, and use of HIV-related medications and other medications. The NFHL study enrolled a total of 881 participants during the 10-year study period. All protocols and procedures of the study were reviewed and approved by the Institutional Review Board at each institution.

Variables

Depression

Depression was measured in NFHL by an interviewer-administered eight-item screening questionnaire developed by Burnam *et al.*[18]. This screener was developed for use in the Medical Outcomes Study[19], and includes six items from the Center for Epidemiological Studies Depression Scale (CES-D)[20–23] and two from the Diagnostic Interview Schedule[24,25] (see Appendix for items). It has been used in a wide variety of studies[26–32]. Burnam *et al.* developed a weighted scoring strategy to maximise the prediction of depressive disorder, as defined in the 3rd edition of the DSM (DSM-III), from these eight items. To classify participants as depressed, we used the cut-off recommended in the original paper of 0.06[18]. This cut-off is interpreted as the probability, estimated from the prediction equation, that an individual has a DSM-III-defined depressive disorder. The cut-off was chosen by Burnam *et al.* after multiple empirical analyses suggested that it represented a clinically sensible balance between sensitivity and specificity.

Daily dietary intake

Dietary intake in this study was assessed by 3-day food record or 24-hour recall, and the intake of eight macronutrients (total energy, carbohydrate, total fat, protein, total fibre, saturated fat, simple sugars and long-chain $n-3$ polyunsaturated fatty acids) in the diet was calculated. Every effort was taken to collect reliable dietary data, which included provision of written material instructing participants in keeping a food record, a sample demonstration day of recorded food intake, and a review of the study-specific food record booklet. The trained study staff instructed the participants on how to keep accurate diet records. Participants were given a food scale (Sunbeam Corporation) and a ruler to accurately measure portion sizes. The NFHL study dietitian checked the diet records with the participants for completion and accuracy. If the participant failed to complete the 3-day food record, a 24-hour recall was obtained. Ninety per cent of the whole cohort provided a 3-day record. The food records were analysed by using the Nutrition Data System for Research software, version 4 (Nutrition Coordinating Center, University of Minnesota). A specially trained coder entered the data from the diet records into the database. The complete dietary analysis contains 92 nutrients, but this study used data on eight macronutrients as detailed above.

Symptom score

The components of symptom score included the following 13 items: headaches that are new, severe or persistent; fevers or night sweats or chills; pain in mouth gums or lips; white patches in mouth; painful rashes or sores on skin, around anus or vagina/penis; nausea or loss of appetite; trouble with eyes; a sinus infection pain or discharge; pain numbness or tingling in hands or feet; persistent coughing or difficulty in breathing for more than one week; vomiting; pain discomfort in the stomach or abdomen; diarrhoea or loose watery stools. Those who

had experienced any of the above symptoms were asked to assess the severity of each symptom, expressed as 'How much did the symptom interfere with your normal activities?' Response options had five levels ranging from 'not at all' to 'extremely'. Not at all was coded as zero. An aggregate symptom score was the sum of the severity of all symptoms, on a scale from 0 (no symptoms) to 100 (maximum symptom severity). This approach to symptom assessment closely parallels that taken in the HIV Costs and Services Utilization Study (HCSUS)[33].

Laboratory tests

CD4 count was determined by flow cytometry. HIV RNA was determined using the Roche Amplicor Monitor (Roche Molecular Systems). The lower detection limit was 400 copies per ml. Results are reported as $\log_{10}$ HIV viral load.

Sociodemographics

The following variables were included in this analysis: education (low, ≤high school; middle, some college or technical education; high, college and graduate programme), race (African American, White, Hispanic/Latino and others) and personal annual income (<$10 000, $10 000–$50 000, >$50 000).

Analyses

Creation of depressed and non-depressed analytic groups

NFHL participants who had at least four study visits were considered for this analysis. The 'depressed group' were those participants who had two consecutive visits on which the screening questionnaire indicated no depression followed by two consecutive visits for which the screening questionnaire indicated depression. We required two consecutive visits because the depression measurement instrument is a screener, not a diagnostic instrument. Requiring two consecutive visits increases the chance that those who screened positive had major depression. The total time between the first and the fourth visit ranged from 18 to 24 months. Thus, these were participants who developed depression while being followed in NFHL. The 'non-depressed group' had four consecutive visits on which they were not depressed. For the non-depressed group, these were their first four visits in the NFHL study. During the entire study period patients continued to join the cohort, so these first four visits occurred at a variety of different calendar times, ranging from 1995 to 2003. Using this approach, there were 90 participants in the depressed group and 152 in the non-depressed group.

Descriptive statistics by depression status

To evaluate baseline differences between those who became depressed and those who did not become depressed, we compared baseline sociodemographic, clinical and nutritional characteristics of the two groups using the χ^2 statistic for categorical variables, the *t*-test for normally distributed continuous variables and the Mann–Whitney *U*-test for non-normally distributed continuous variables. The difference in macronutrient intake across groups at baseline was compared separately for men and women. The median (interquartile range) values of macronutrients intake are reported since the macronutrient intakes were not normally distributed. We also examined changes (the difference between values at visit 4 and visit 1) in viral load, CD4 count, body mass index (BMI) and symptom score for depressed and non-depressed participants using the Wilcoxon signed rank test for related samples.

Univariate and multivariate analyses

In univariate analyses, for each macronutrient, we calculated the change in intake between visit 4 and visit 1 (a negative value meaning a decrease over time). We did not evaluate the visit just prior to (second visit) and just after (third visit) becoming depressed because we thought that dietary habits might still be in transition. In a separate model for each macronutrient, we calculated the association between developing depression or not (independent variable) and change in macronutrient intake using linear regression analysis. We first performed these models unadjusted for potential confounders. Next, in multivariate models, we tested the association between depression and change in each macronutrient intake (dependent variable) adjusted for confounding using multiple regression analysis.

The potential confounders were baseline values of age, gender, education, race, personal income, BMI, aggregate symptom score, $\log_{10}$ viral load and CD4 count. To determine which variables to include as confounders in each model, we evaluated the association between each potential confounder with the change in each macronutrient intake using Spearman's correlation test for continuous variables, the Mann–Whitney *U*-test for dichotomous variables and the Kruskal–Wallis test for variables with more than two levels. We used methods described by Rothman and Greenland to test for confounding[34,35]. Variables that were associated with a change in macronutrient intake at $P < 0.2$ on the univariate analysis were entered into the multivariate models. They remained in the final model if they changed the β coefficient for depression by more than 10% when they were removed. Each model was also adjusted for the baseline value of each macronutrient intake. For multivariate comparisons, we included only participants with complete data on all covariates. We examined for influential observations using Cook's distance and centred leverage values. All statistical analyses were performed using SPSS for Windows 11.5 (SPSS Inc.). Significance was defined as a two-tailed *P*-value equal to or less than 0.05.

Results

Participant characteristics

Of the 242 participants who screened negative for depression on their first two study visits, 37% (90/242) screened positive for depression at visits 3 and 4 (Table 1). Those in the depressed and non-depressed groups were similar in age and BMI at baseline. Compared with non-depressed participants, those who developed depression were significantly more likely to be women (37.9 vs. 20.1%, $P = 0.003$), less educated (23.3 vs. 45.5% college graduates, $P = 0.008$), poorer (54.4 vs. 36.4% with annual income <$10 000, $P = 0.008$) and had a higher symptom score (15 vs. 9, $P = 0.007$). Those who developed depression had higher median CD4 cell counts than the non-depressed group at baseline (470 vs. 340 per mm^3, $P = 0.03$).

Baseline dietary quality

At baseline, there were no differences between depressed and non-depressed participants in total daily energy intake or in any component of intake (Table 2).

Changes in key clinical variables between visit 1 and visit 4

The median levels of $\log_{10}$ viral load (3.0 vs. 3.0 copies per ml, $P = 1.0$, Table 3) and CD4 count (470 vs. 440 per mm^3, $P = 0.9$) were similar at the first and fourth visit in those who became depressed, whereas there was a significant decrease in viral load (2.3 vs. 2.5 copies per ml, $P = 0.002$) and a significant increase in CD4 count (330 vs. 437 per mm^3, $P < 0.001$) in non-depressed participants. There was a significant increase in the symptom score (15 vs. 18, $P = 0.008$) among those who became depressed, but no change (9 vs. 10, $P = 0.1$) in non-depressed participants. The data also showed a trend towards a decrease in BMI (25 vs. 24 $kg\,m^{-2}$, $P = 0.06$) among those who developed depression during the study period.

Multivariate analysis of changes in macronutrient intake

For each macronutrient, the difference in the change in that nutrient intake in the depressed vs. the non-depressed group, adjusted for confounding and baseline intake of that macronutrient, is shown in Table 4. Compared

Table 1 Baseline characteristics

Variable	Developed depression: Yes ($n = 90$)	Developed depression: No ($n = 152$)	*P*-value
Sociodemographic characteristics			
Age (years), mean (SD)	42.1 (7.0)	41.9 (8.6)	0.9
Female, *n* (%)	34 (37.9)	31 (20.1)	0.003
Race, *n* (%)			
African American	28 (31.1)	37 (24.3)	0.36
Hispanic/Latino	7 (7.8)	7 (4.6)	
White	52 (57.8)	99 (65.1)	
Others	3 (3.3)	9 (5.9)	
Education, *n* (%)			
High school	43 (47.8)	48 (31.6)	0.002
Trade/technical/some college	26 (28.9)	35 (23.5)	
College/graduate	21 (23.3)	69 (45.4)	
Personal annual income ($), *n* (%)			
<10 000	49 (54.4)	55 (36.4)	0.008
10 000–50 000	38 (42.2)	79 (52.3)	
>50 000	3 (3.4)	18 (11.3)	
Clinical characteristics			
$CD4^+$ cell count (per mm^3), median (IQR)	470 (234, 643)	340 (189, 550)	0.03
HIV load ($\log_{10}$ copies per ml), median (IQR)	3.1 (2.3, 4.1)	3.3 (2.3, 4.5)	0.1
Symptom score, median (IQR)	15 (7.7, 26.3)	9 (5, 20)	0.007
BMI ($kg\,m^{-2}$), *n* (%)			
Men			
<19	3 (5.4)	6 (5)	1.0
19–24	26 (46.4)	57 (47.9)	
25–30	22 (39.3)	46 (38.7)	
>30	5 (8.9)	10 (8.4)	
Women			
<19	1 (2.9)	0 (0)	0.7
19–24	11 (32.4)	13 (41.9)	
25–30	12 (35.3)	10 (32.3)	
>30	10 (29.4)	8 (25.8)	

SD – standard deviation; IQR – interquartile range; BMI – body mass index.

Table 2 Baseline daily dietary intake comparisons in depressed and non-depressed group

Macronutrient	Median baseline intake (IQR)		*P*-value
	Depression	Controls	
Total energy (kcal)			
Men	2777 (2303, 3641)	2933 (2424, 3420)	0.6
Women	2027 (1551, 2499)	2190 (1420, 2836)	0.8
Protein (g)			
Men	113 (90, 126)	114 (88, 136)	0.6
Women	67 (55, 92)	85 (62, 110)	0.2
Total fat (g)			
Men	113 (86, 138)	111 (87, 140)	0.9
Women	76 (60, 101)	78 (55, 119)	0.8
Carbohydrate (g)			
Men	348 (271, 467)	354 (264, 444)	1.0
Women	250 (193, 376)	306 (189, 365)	0.9
Total fibre (g)			
Men	18.5 (14.0, 24.0)	19.4 (13.6, 25.6)	0.9
Women	13 (9.0, 15.3)	15.9 (9.4, 22.7)	0.08
Saturated fat (g)			
Men	43 (31, 49)	39 (30, 49)	0.7
Women	28 (24, 35)	29 (19, 42)	0.9
Simple sugars (g)			
Men	169 (137, 229)	159 (118, 227)	0.6
Women	126 (85, 213)	138 (90, 198)	0.7
$n-3$ fatty acids (g)			
Men	0.17 (0.07, 0.44)	0.11 (0.05, 0.34)	0.3
Women	0.08 (0.04, 0.21)	0.12 (0.05, 0.37)	0.2

IQR – interquartile range.

Table 3 Visit 1 to visit 4 changes in clinical characteristics, median (IQR)

Variable	Depression			Controls		
	Visit 1	Visit 4	*P*-value	Visit 1	Visit 4	*P*-value
Viral load ($\log_{10}$ copies per ml^3)	3.0 (2.3, 4.1)	3.0 (2.3, 4.1)	1.0	3.3 (2.3, 4.5)	2.3 (2.3, 3.8)	0.002
CD4 cell count (per mm^3)	470 (242, 643)	440 (259, 605)	0.9	330 (179, 530)	437 (246, 625)	<0.001
Symptom score	15 (8, 28)	18 (9, 31)	0.008	9 (5, 20)	10 (5, 17)	0.1
BMI (kg m^{-2})	25 (23, 28)	24 (22, 28)	0.06	24 (22, 27)	25 (22, 28)	0.3

IQR – interquartile range; BMI – body mass index.

Table 4 Individual multivariate models of changes (visit 1 to visit 4) in daily nutrient intake

Variable	Change in intake (95% CI)	*P*-value	Covariates
Total energy (kcal)	−341 (−585, −96)	0.006	Education, viral load, symptom score, baseline energy intake
Protein (g)	−12.3 (−22.6, −2.0)	0.02	Income, symptom score, baseline protein intake
Total fat (g)	−18.5 (−32.1, −4.9)	0.008	Education, viral load, baseline total fat
Carbohydrate (g)	−36.8 (−66.5, −6.9)	0.02	Symptom score, baseline carbohydrate intake
Total fibre (g)	−4.3 (−6.7, −1.8)	0.001	Baseline fibre
Saturated fat (g)	−6.7 (−11.9, −1.4)	0.01	Education, baseline saturated fat
Simple sugars (g)	−16.5 (−37.0, 4.0)	0.15	CD4 count, baseline sugar intake
$n-3$ fatty acids (g)	0.03 (−0.16, 0.09)	0.45	Race, baseline $n-3$ fatty acids intake
BMI (kg m^{-2})	0.29 (−0.35, 0.93)	0.37	Sex, race, viral load, education

CI – confidence interval; BMI – body mass index.

with non-depressed participants, depressed participants had significantly greater decreases in the following daily intakes: total energy (−341 kcal, $P=0.006$), protein (−12.3 g, $P=0.02$), total fat (−18.5 g, $P=0.008$), carbohydrate (−36.8 g, $P=0.02$), total fibre (−4.3 g, $P=0.001$) and saturated fat (−6.7 g, $P=0.01$). There were no differences in simple sugars or long-chain $n-3$ fatty acids. There was a non-significant trend toward reduced BMI among depressed patients (−0.29 kg m^{-2}, $P=0.37$).

Discussion

We found that total energy intake, and intake of six of eight dietary components, fell in patients who developed depression. The patients we studied who developed depression did not appear to change the composition of their diet, but they did take in significantly fewer total calories. That is, they seemed to eat less of everything. Of particular note, our findings did not suggest any increase

in carbohydrate intake or sugar intake associated with depression, as reported by Christensen and Somers in their study[11]. While decreased intake of total and saturated fat may be beneficial, these changes were not accompanied by increases in protein or fibre, and so overall dietary composition did not appear to change. Interestingly, energy intake did not decrease so much that there was a significant reduction in BMI. It is unclear from our analysis why BMI did not fall more than it did. One possibility is that these depressed patients exercised less and in general expended less energy, which would reduce the impact of reduced energy intake on BMI. However, we did not have quantitative data on exercise or physical activity that we could use in this analysis. HIV clinicians should be aware that their patients who develop depression may have decreased total energy intake, and watch for weight loss.

There are several study limitations. First, determining a clear cause-and-effect relationship between depression and dietary intake for patients with a complex disease such as HIV is difficult. The particular longitudinal design we used has important strengths, but also some weaknesses. Because we examined changes in an individual's dietary intake before and after the development of depression, many potentially confounding factors were effectively held constant by the study design, such as race, attitudes towards food and eating, and beliefs about mental health diagnoses and treatments. This important feature of the longitudinal design notwithstanding, some important factors can change for individuals over time, such as the manifestations of co-morbid diseases. Participants who developed depression had more symptoms of associated medical conditions and, in contrast to the control group, there was no improvement in their disease status as measured by CD4 count and viral load during the study period, which in theory might contribute to the development of depression. However, we controlled for this and other potential confounders in our multivariate analyses. A minor weakness is that because we collected data every 6 months, we do not have an exact date for either the onset of depression or the changes in intake that we observed. Thus, it is theoretically possible that these dietary changes caused participants to develop depression, and not the reverse, although we think that this is unlikely.

Second, the validity of self-reported dietary data, particularly data from less-educated and obese individuals, has been controversial[36,37]. Nevertheless, diet records are the most accurate method of dietary analysis for studies that include many subjects of ethnic minorities. A study has been published showing good correlation between dietary intake inadequacy and the presence of hunger in this cohort that supports the general validity of the dietary record data for this cohort[38]. Third, we used a short screening instrument to detect depression (the only short depression screener that had been carefully validated in 1995 when our study began). Screening instruments, designed to be sensitive, almost invariably overestimate disease rates. However, the scale used in this study has a reasonable sensitivity for recent (6 months) and current depression (74–89%) and quite a high specificity (95%) at the cut-off we used. Furthermore, because we required that participants had two consecutive visits without depression, and then two consecutive visits with depression, we believe that we have reduced the false positive rate significantly. Fourth, our findings might not be generalisable to other populations with HIV with different characteristics, or to those who do not have HIV. Finally, while we were interested in macronutrient intake, further studies that focus on the relationship between micronutrient intake and depression in persons with HIV would be valuable.

In conclusion, we found that patients who developed depression also reported reduced total energy intake and reductions in intake of six of eight dietary components. To our knowledge, this is the first time that changes in dietary intake have been associated with depression in persons with HIV. Depression has been associated with increased mortality in a number of studies[39–42], but the mechanisms that might explain the association are not known. Our findings suggest that poor nutrition should be explored as a potential contributing factor.

These finding have two main implications for physicians. First, even though the reductions in energy intake that we show were not significantly associated with decreases in BMI, our findings should be a reminder to clinicians to include depression in the differential diagnosis for persons with HIV-related weight loss. Second, while it is not practical for HIV clinicians to monitor energy intake of patients with depression, they should carefully monitor depressed patients' weight, and provide adequate education and treatment when weight loss is discovered.

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Appendix – Depression Screener Items

1. In the past year, have you had 2 weeks or more during which you felt sad, blue, or depressed; or when you lost all interest or pleasure in things that you usually cared about or enjoyed? (Yes/No)

2. Have you had 2 years or more in your life when you felt depressed or sad most days, even if you felt okay sometimes? (Yes/No) *If no, go to question 3.*

2a. Have you felt depressed or sad much of the time in the past year? (Yes/No)

3. For each statement below, mark one circle that best describes how much of the time you felt or behaved this way during the past week. Response options are:

0: Rarely or none of the time (less than one day)
1: Some or a little of the time (1–2 days)
2: Occasionally or moderate amount of the time (3–4 days)
3: Most or all of the time (5–7 days)

During the past week:

a. I felt depressed
b. I had crying spells
c. I felt sad
d. I enjoyed life
e. My sleep was restless
f. I felt that people disliked me