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Depression and Glycemic Intake in the Homebound Elderly

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Abstract

Background—Depression is associated with an increase in the incidence of type 2 diabetes, but the mechanism is unclear. We aimed to study the relationship between depression and glycemic intake in the elderly, and examine whether antidepressant use modified this relationship.

Design, Setting and Participants—We evaluated 976 homebound elders in a cross-sectional study. Depressed was defined by having a Center for Epidemiological Studies Depression (CES-D) score ≥ 16. Antidepressant use was documented. Glycemic index (GI), Glycemic load (GL), and fasting blood insulin levels were measured.

Results—Depressed elders had slightly higher GI (Mean ± SD: 55.8 ± 3.8 vs. 55.1 ± 3.7, P = 0.003) and higher insulin levels (Median: 84.0 vs. 74.4 pmole/ml, P = 0.05) than non-depressed elders. Depressed elders receiving antidepressants, primarily selective serotonin reuptake inhibitors (SSRI), had lower GI (Mean ± SD: 55.1 ± 4.7 vs. 56.2 ± 3.4, P = 0.002) and GL (Median: 170.3 vs. 6826.3, P = 0.03) than those not taking antidepressants. After adjusting for potential confounding variables, GI remained positively associated with depression (β = + 0.65, SE = 0.28, P = 0.02); logarithm of GL was positively associated with depression (β = + 0.33, SE = 0.17, P = 0.05) and negatively associated with antidepressant use (β = − 0.54, SE = 0.18, P = 0.003).

Conclusions—Prospective studies are needed to examine whether high glycemic intake is a mediating factor between late life depression and the risk of type 2 diabetes.

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1. Introduction

Human studies have shown that depression or depressive symptoms at middle to late life increase the risk of type 2 diabetes (Carnethon et al., 2007; Demakakos et al.; Engum, 2007; Everson-Rose et al., 2004; Golden et al., 2008; Knol et al., 2006; Pouwer et al.). The mediating factor(s) of this relationship has not yet been elucidated. Craving for and the overeating of high glycemic carbohydrates is a common phenomenon in humans in the face of perceived stress and depressive symptoms (Rosenthal et al., 1989; Wurtman, 1988; Wurtman and Wurtman, 1989). In severely depressed patients, especially young ones, however, appetite is often poor with decreased overall food consumption rather than excessive carbohydrate intake (Fernstrom, 1989). Thus, the relationship between depression and carbohydrate intake may be different between young and elderly depressed patients. In addition, antidepressants are widely prescribed, especially for young patients. In animal studies, it has been found that while selective serotonin reuptake inhibitors (SSRI) antidepressants suppress carbohydrate intake (Wurtman and Wurtman, 1979), tricyclic antidepressants (TCA) increase carbohydrate intakes (Leibowitz et al., 1985). Most studies examining the relationship between depression and carbohydrate intake employed young subjects, and antidepressant use might confound interpretation of results from the various studies.

Homebound elderly have high rates of depression, obesity and type 2 diabetes, and depressed elderly are less likely to take antidepressants than the young patients (Qiu et al., in press; Sun et al., 2007). Using a homebound elderly sample from a community, we aimed to study glycemic index (GI), glycemic load (GL), and insulin levels in those with and without depression in the context of antidepressant uses.

2. Methods

Study Population and Recruitment

We studied a group of 976 subjects from the *Nutrition, Aging and Memory in the Elderly (NAME)* study, a cross-sectional, population-based study, who had been characterized for depression status and glycemic intake. We excluded subjects with the insulin treatment in the analysis because exogenous insulin can artificially manipulate the insulin level in blood. The protocol of the study was described in our previously published paper (Scott et al., 2006). Of all eligible subjects, 66% enrolled, and gave informed consent approved by Tufts Medical Center IRB to participate in the study. The population was screened for significant cognitive impairment using the Mini Mental State Examination (MMSE) (Folstein et al., 1975). Those with MMSE ≤ 10 were not eligible to continue in the study, and eligible subjects were subsequently examined.

Definition of Depression

Depression—Depressive symptoms were evaluated by using the Center for Epidemiological Studies Depression scale (CES-D) (Radloff, 1977). A CES-D score of ≥ 16 was used as the cut-off point for clinical depression (Fuhrer and Rouillon, 1989). In the 106 subjects in our study, this CES-D cut-off point had a sensitivity of 0.90 and a specificity of 0.83 for the DSM-IV diagnosis of major depression as made by a board-certified psychiatrist.

Antidepressants—The research assistants documented the names of the medications as indicated on the bottle labels. All medications were coded, and antidepressants were classified into 1) SSRI; 2)TCA; 3) trazodone; and 4) all others including venlafaxine,

bupropion and mitazapine. Antidepressants in this latter group were lumped together because only a small number of subjects were taking each of them.

Glycemic Index

Using a semi-quantitative food frequency questionnaire a dietary history of the previous year was taken (Rimm et al., 1992). If more than 12 food items were left blank on the questionnaire the results were considered invalid and excluded from further analysis. GI is carbohydrate quality and GL is carbohydrate quantity (Murakami et al., 2007; Murakami et al., 2006) and are described for the other studies (Foster-Powell and Miller, 1995; Salmeron et al., 1997; Wolever et al., 1991). The reference food for GI is either glucose or white bread. GL is calculated by multiplying the carbohydrate content of each food by its glycemic index, then multiplying this value by the frequency of consumption and summing the values from all foods. Some food with high GI, for example watermelon, has a low GL because the portion consumed is low.

Other measurements

Subjects were classified as having cardiovascular disease (CVD) if they had been informed by a doctor that they had congestive heart failure, coronary heart disease, angina pectoris or a heart attack. Subjects were classified to have diabetes if they were prescribed anti-diabetic medication or had fasting glucose values greater than 126 mg/dl (available for 96% of subjects). Stroke history was recorded. Subjects were considered to have hypertension if the average of two systolic blood pressure readings was > 140 mm Hg or diastolic blood pressure > 90 mm Hg or if the subject was taking antihypertensive medications. Apolipoprotein E alleles were characterized (Sun).

Statistical Analysis

Statistical analysis was performed using SAS (version 9.1). Mean ± SD and T-test or ANOVA were used for the variables with a normal distribution, and median (Q1, Q3) and Wilcoxon rank sum test or Kurskal-Wallis test were used for the variables with a skewed distribution. The Chi-Square test was used to compare proportions for binary endpoints. GL was transformed to $\log_{10}$ (LogGL) due to its skewedness prior to inclusion in multivariate regression analysis. Linear regression was used to examine associations between GI or LogGL as outcomes and depression, antidepressant usage or ApoE4 allele while adjusting for potential confounders including age, race, gender, education, BMI and diabetes. The two-sided significance levels of 0.05. In the case of multiple comparisons the significance levels used was 0.0167.

3. Results

Study Population

Nine hundreds seventy six subjects with evaluations on depression and dietary history in the NAME study were used in this data analysis. The average age for the sample was 75.3 (SD = 8.4) years old, and 76% were female. The sample was multi-ethnic with 61% Caucasian, 35% African American and 4% other ethnicities. Sixty-three percent of the subjects completed high school or higher education. Depression, defined as a CES-D score ≥ 16, was observed in 34% (332/976) of the subjects. GI had normal distribution with median =55.6, minimum = 29.3 and maximum = 69.3. Distributions of GL and insulin levels were skewed: GL (median: 186.0; minimum: 40.5 and maximum: 39038.2) and insulin (median: 76.3 pmole/ml, minimum: 1.9 pmole/ml and maximum: 1922.8 pmole/ml).

Depression and Glycemic Status

Subjects with depression were younger (age mean ± SD: 74.0 ± 8.5 vs. 76.1 ± 8.5, P = 0.0003), and tended to have lower education than those without depression (Table 1). Those with depression had a higher rate of CVD (48% vs. 37%, P = 0.0004) than those without depression. No differences were found in gender, ethnicity, rates of hypertension and stroke between those with and without depression. Subjects with depression had a slightly higher average GI using glucose as the reference food (Mean ± SD: 55.8 ± 3.8 vs. 55.1 ± 3.7, P = 0.003) or using white bread as the reference food (Mean ± SD: 79.8 ± 5.5 vs. 77.7 ± 5.4, P = 0.0002) and a tendency to higher GL than those without depression (Table 1). Subjects with depression had higher levels of insulin (Median: 84.0 vs. 74.4, P = 0.05) compared to those without depression (Table 1). No differences in total carbohydrate intake, BMI, glucose and rate of diabetes were found between those with and without depression.

Depression, Antidepressants and Glycemic Status

A greater number of subjects with depression were taking antidepressants than those without depression (44% vs. 24%, P < 0.0001) (Table 1). The majority of subjects with depression, however, were not on antidepressants (56%), and a large number of elderly who were on antidepressants were depressed (49%). Among the 323 subjects on antidepressants, 61% (197/323) were prescribed SSRIs, 16% (53/323 TCAs, 23% (73/323) trazodone and 20% (66/323) other antidepressants. It is appreciated that TCAs may often have been prescribed for pain management, and trazodone for insomnia.

Subjects were divided into four subgroups (Table 2). Among the depressed subjects, those receiving antidepressant treatment had lower levels of GI (Mean ± SD: 55.1 ± 4.7 vs. 56.2 ± 3.4, P = 0.002) and GL (Median: 170.3 vs. 6826.3, P = 0.03) than those not receiving antidepressants. Similarly, in the elders who were not depressed, those on antidepressants had lower GL (Median: 162.7 vs. 197.6l, P = 0.03) than those not receiving antidepressants. After excluding subjects with diabetes, these findings persisted (data not shown). Using multivariate linear regression analysis, GI was positively associated with depression (β Estimate = + 0.65, SE = 0.28, P = 0.02), but not with antidepressant usage, after adjusting for age, gender, race, BMI and diabetes (Table 3). GL was transformed to $\log_{10}$ (LogGL) due to its skewedness. LogGL was positively associated with depression (β Estimate = + 0.33, SE = 0.17, P = 0.05) and negatively with antidepressant usage (β Estimate = − 0.54, SE = 0.18, P = 0.003) after adjusting for the confounders. Being Caucasian was negatively associated with GI or GL. These relationships persisted after controlling for MMSE score or protein intake (data not shown). When the subset of subjects with MMSE > 20 was examined, GI and GL were still associated with depression and antidepressant use (data not shown).

4. Discussion

When humans feel low or depressed, they have a tendency to overeat carbohydrates (Benton and Donohoe, 1999). One study showed a trend for an association between postpartum depression and high glycemic intake (Murakami et al., 2008). Our results showed that in a homebound elderly population depressed subjects had significantly higher GI intake and a higher level of fasting insulin than those without depression (Tables 1 and 2). High GI and GL intake in late-life depression could lead to elevated insulin levels resulting in the release of tryptophan from protein, that in the brain is metabolized to serotonin (Fernstrom and Wurtman, 1971), and thus represents a self-treatment of depression. Though possibly alleviating depression, this dietary pattern could result in an increase in the incidence of type 2 diabetes observed in several studies (Carnethon et al., 2007; Demakakos et al.; Engum, 2007; Everson-Rose et al., 2004; Golden et al., 2008; Knol et al., 2006; Pouwer et al.).

Over half of our depressed subjects were not taking antidepressants (Table 2), and the homebound elderly population had high rates of obesity and type 2 diabetes (Qiu et al. in press). The depressed subjects not on antidepressants may have chosen carbohydrates with high GI to sooth their moods (Tables 2 and 3). Of the subjects who were taking antidepressants, most were on SSRIs, which have been shown to suppress carbohydrate intake in an animal study (Wurtman and Wurtman, 1979). Indeed, in our study those depressed subjects on antidepressants had lower glycemic intake than depressed subjects not on antidepressants (Table 2). Our finding also suggests that antidepressants may suppress GI intake independent of their effect on mood.

Limitations of this study include: 1) Although the cross-sectional design does not allow us to determine whether high glycemic intake is the mediating factor leading to type 2 diabetes in late life depression, the high rates of obesity and diabetes in this population may imply the causal relationship. 2) The diagnosis of depression was based on the CES-D score rather than DSM-IV criteria. Thus our study sample from an elderly community probably included a large number of subjects who suffered from subclinical depression and did not want to take antidepressants. This is in contrast to depressed patients in a psychiatry clinic; the clinic population is younger, more depressed, and appetite is often decreased. 3) The lack of data on indication of dosage and duration for medications was another limitation.

5. Conclusion

These data from a late life sample link late life depression with high glycemic intake and are in line with the clinical literature on the bidirectional relationship between diabetes and depression. Prospective studies and clinical trials are needed to determine whether modifying diet and treatment with SSRI antidepressants will reduce the incidence of type 2 diabetes in late life depression.

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Table 1

Glycemic status of homebound elderly with and without depression

	Depression (N = 332)	No depression (N =644)	P value
Age, year, mean ± SD	74.0 ± 8.5(n = 332)	76.1 ± 8.5(n = 644)	0.0003
Female, n/total (%)	253/332 (76%)	486/644 (75%)	0.80
High School and above, n/total (%)	214/331 (65%)	442/641 (69%)	0.13
Caucasians, n/total (%)	209/332 (63%)	411/644 (64%)	0.79
ApoE4, n/total (%)	62/315 (20%)	150/606 (25%)	0.08
Antidepressant usage, n/total (%)	145/322 (44%)	152/644 (24%)	<0.0001
Status on Carbohydrate Metabolism			
BMI, kg/m^2, mean ± SD	31.3 ± 8.2 (n = 319)	30.8 ± 8.2 (n = 590)	0.34
Diabetes, n/total (%)	102/309 (33%)	180/619 (28%)	0.24
Total carbohydrates, gm	247.9 ± 102.1 (n = 332)	244.1 ± 87.2 (n = 642)	0.66
Glycemic index	55.8 ± 3.8 (n = 332)	55.1 ± 3.7 (n = 644)	0.003
Glycemic index/bread	79.8 ± 5.5 (n = 152)	77.7 ± 5.4 (n =257)	0.0002
Glycemic load	227.9 (120.5, 12339.9) (n = 332)	180.3 (121.3, 11176.5) (n = 644)	0.16
Glucose, mg/dL, mean ± SD	114.4 ± 41.9 (n = 303)	108.1 ± 28.7 (n =611)	0.15
Insulin, pmole/L	84.0 (48.0, 134.3) (n = 289)	74.4 (44.7, 120.6) (n =590)	0.05

Mean ± SD and T-test or Median (Q1, Q3) and Wilcoxon Sum Ranks or n/total (%) and the Chi-Square test are presented. P values for statistical significance are shown. Depression is defined by Center for Epidemiological Studies Depression scale (CES-D) ≥ 16

Table 2

Comparisons of glycemic status in those without depression stratified by antidepressant usage

Whole sample	Depression		No depression	
	Antidepressants N = 145	No antidepressants N = 187	Antidepressants N = 152	No antidepressants N = 492
CES-D Score, mean ± SD	26.0 ± 8.4***	23.4 ± 6.7	7.2 ± 4.5	6.8 ± 4.5
Diabetes, n/total (%)	46/137 (34%)	60/179 (34%)	42/150 (28%)	143/483 (30%)
Glycemic index, Mean ± SD	55.1 ± 4.7***	56.2 ± 3.4	55.0 ± 3.6	55.1 ± 3.8
Glycemic load, Median (Q1, Q3)	170.3	6826.3	162.7	197.6
	(111.4, 10257.4)**	(132.0, 12641.3)	(113.7, 9190.3)**	(122.5, 11756.8)

Subgroups with and without antidepressants were compared in those with and without current depression. Median (Q1, Q3) and Wilcoxon Sum Ranks, or mean ± SD and t-Test analyses , or Chi Square were applied and presented.

*P < 0.10

P < 0.05

*** P < 0.01

Table 3

Multivariate linear regression analysis on the relationship between glycemic status and depression

	Glycemic Index N = 843		Log Glycemic Load N = 839	
	β Estimate (SE)	**P value**	**β Estimate (SE)**	**P value**
Age	− 0.002 (0.02	0.91	+ 0.03 (0.01)	0.006
Female	− 0.35 (0.31)	0.25	+ 0.23 (0.19)	0.24
Caucasian	− 0.60 (0.28)	0.03	− 0.17 (0.06)	0.002
School	− 0.09 (0.04)	0.04	− 0.03 (0.03)	0.28
BMI	− 0.03 (0.02)	0.14	− 0.002 (0.01)	0.83
Diabetes	− 0.34 (0.29)	0.24	− 0.06 (0.18)	0.73
ApoE4	− 0.01 (0.30)	0.97	− 0.33 (0.19)	0.08
Antidepressant usage	− 0.31 (0.30)	0.29	− 0.54 (0.18)	0.003
Depression	+ 0.65 (0.28)	0.02	+ 0.33 (0.17)	0.05

GL was transformed to $\log_{10}$ (LogGL) due to its skewedness.