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DEPRESSION, DIABETES AND METABOLIC-NUTRITIONAL FACTORS IN ELDERLY HISPANICS

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Abstract: *Objective:* To examine the relationship of depression to metabolic and nutritional risk factors in older Hispanics. *Design:* Crossectional study. *Setting:* Subjects were part of a community-based, cognitive evaluation project that examined 301 subjects in the Eastern San Fernando Valley of Southern California. *Participants:* Two elderly Hispanic groups: 53 clinically depressed, with memory complaints but not demented subjects, and 33 generally healthy, cognitively asymptomatic subjects. *Measurements:* The results of functional and nutritional questionnaires, a medical and neurological examination, 12-hour fasting clinical laboratory tests, MRI or CT scans, and neuropsychological testing. *Results:* Both groups were nearly identical along socio-demographic variables. However, the depressed group differed significantly from the general healthy group not only in percent of diabetics (38% vs.18%), but in the amount of poorly controlled diabetes, and the depressed group consumed about half the amount of fish that the generally healthy group did. *Conclusions:* This study suggests that factors such as poorly controlled diabetes combined with low consumption of foods high in omega-3 fatty acid content such as sea fish may be associated with an increased risk of developing depression in late life. These factors may be socio-economically and culturally influenced and are therefore amenable to modification.

Key words: Depression, metabolic-nutritional factors, elderly hispanics, sea fish.

Introduction

The number of elderly Hispanics in the United States, is expected to grow exponentially in the next three decades nearly tripling from the current 5% of the total U.S. Hispanic population of more than 40 million (1). Hispanics suffer more frequently than non-Hispanics from diabetes, obesity, depression and cognitive impairment (2-5). Depression has been found to be a risk factor for developing cognitive impairment (6), cardiovascular disease (7), and type 2 diabetes (8). Depression is more common among those with diabetes, and depressive symptoms increase a pattern of physiological risk that contributes to the metabolic syndrome (9, 10). Furthermore, high levels of depressive symptoms concomitant with major chronic medical conditions elevate the risk for death among older Mexican Americans (11, 12).

Diabetes is also independently associated with a greater incidence of cognitive impairment (13, 14) with a worse prognosis following these conditions. The co-existence of depressive symptoms and diabetes further extends risk for cognitive decline and functional disability (15). Alzheimer disease is up to four times more common in diabetics (16).

Studies suggest that nutritional factors may play an important role in the development or prevention of diabetes, depression and cognitive impairment or even dementia (17, 18). For example, diets rich in seafood with high taurine content are thought to help prevent obesity and diabetes (19). Studies also link depression to nutritional changes. Sweet, fatty foods long have been suggested to alleviate stress in vulnerable people through actions that enhance serotonergic activity (20, 21).

We identified a subgroup of subjects with previously undiagnosed depression from an ongoing community based study of cognitive and health status of aged Hispanics. This paper examines the relationship of depression to metabolic and nutritional risk factors, and functional capacity in depressed but non-demented, elderly Hispanic subjects with a cognitive complaint, and compares them to healthier, no complaint, elder Hispanics from the same community. Based on the cited literature, we expected depression to be associated with a higher incidence of type 2 diabetes, more functional impairment, and lower dietary fish consumption.

Methods

Subjects

Subjects were recruited from a large community of elderly Hispanics by lectures on cognitive problems of aging given by research team members at diverse community venues such as local senior centers, churches, primary health care professionals, adult community schools and social services

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agencies (i.e. Meals on Wheels, Adult Day Care Centers, etc.). Other community outreach (recruitment) methods included Spanish radio and television talk shows, bilingual community flyer distributions, and articles published in local Spanish-language newspapers. Subjects were identified and recruited through community outreach efforts conducted by a fully bilingual, bicultural research staff.

Subjects were drawn exclusively from the greater Eastern San Fernando Valley which has an estimated population of approximately one million, with a racial/ethnic composition of 56% Hispanic, 33% White non-Hispanic, 5% African American, 5.4 Asian-Pacific Islander and 0.4% other (22). Two-way transportation service, with door-to-door pick-up was provided for those who did not have the transportation means to come to the medical center for an evaluation.

A total of 301 participants received complete neuropsychiatric evaluations including medical and psychiatric histories, neuropsychological testing, neurological exam, clinical laboratory tests and either CT or MRI scans. Fifty three clinically depressed subjects and a comparison group of 33 generally healthy, asymptomatic elders were identified from the larger group and form the basis of the present study.

The depressed population was defined as outreached, community dwelling Hispanic elders, age 55 or older, with no previous diagnosis of a clearly stated cognitive complaint, but who met DSM IV criteria for clinical depression after neuropsychiatric evaluation. The over 55 years limit was chosen because of similar levels of dysfunction to 65 year old non-Hispanic White populations, as evidenced by published and preliminary studies (23, 24). Table 1 describes the study inclusion and exclusion criteria. The healthy comparison group consisted of 33 identically outreached, community-dwelling Hispanic volunteers aged 55 years or older with no cognitive complaints or mood symptoms and no serious, concurrent, acute or unstable medical conditions, no concurrent non-dementing, central neurologic disease or previous major psychiatric illness but who showed an interest in participating in this memory related research. Relatives of subjects were excluded. Diabetes, hypertension and other features of metabolic syndrome did not form part of the exclusionary criteria for either group. The comparison group was used in this study to evaluate the impact of diabetes and dietary fish intake on mood.

Assessments and diagnoses

This study was approved by the Internal Review Board at Olive View-UCLA Medical Center. Informed consent in verbal and written Spanish or English was obtained from all participants. Consented symptomatic subjects were required to have a designated informant that had daily contact with the subject. All subjects initially received the Mini-Mental Status Examination (25) and the validated Spanish version of the Mini-Mental Status Examination adjusted for age and education (MMSAdj) (26) and questionnaires eliciting demographic, social, family, medical and medication information. The MMSAdj version (0-30 points) is a screening test for cognitive and memory impairment that has shown better sensitivity and specificity than the traditional MMSE, for detecting cognitive impairment across education levels.

Table 1

Inclusion criteria
1. Hispanic, or of Hispanic origin, background or descendent
2. Aged 55 or over
3. Meets DSM IV criteria for recent minor or major depression
4. Recent history of at least one memory or cognitive complaint
5. English or Spanish speaking
6. Stable health status
Exclusion Criteria
1. Younger than 55 years of age
2. Presence of acute systemic or severe medical illness
3. History or presence of any previous diagnosed major psychiatric illness (e.g. schizophrenia, schizoaffective, bipolar disorder, Obsessive Compulsive Disorder, Major Depression Disorder, etc.)
4. History of psychiatric hospitalization
5. Presence of any central nervous system disease (e.g. dementia, stroke, neurodegenerative disease)
6. Ethnic background other than Hispanic

Hispanics in our sample were identified by self-identification, place of birth, ancestry and language. The examining investigators, all of whom are native Hispanics, conducted the identification procedures. Hispanic subjects' self-reported Spanish and English language proficiency was assessed, as was their level of acculturation to the United States by using the Marin acculturation scale (27). The presence of depression was established by experienced clinicians according to criteria for Major or Minor Depression of the DSM–IV-TR (28). All cases of depression were deemed clinically significant and warranted treatment. The exclusion of subjects with dementia was based on application of criteria for dementia of the DSM–IV-TR. The metric Body Mass Index (BMI) formula was used to calculate BMI index score (29). Metabolic syndrome was established when at least 3 out 5 of the following conditions were met: 1) Fasting glucose (FBS) $\geq$110 mg/dL; those on anti-diabetic medications with <110 mg/dL ; 2) Fasting triglycerides $\geq$150 mg/dL and those with triglycerides <150 mg/dL on medication for high cholesterol; 3) High density lipoprotein (HDL; female $\leq$50 mg/dL and male $\leq$40 mg/dL); 4) High blood pressure (HBP) (resting systolic $\geq$140 mm Hg and / or diastolic $\geq$90 mm Hg, and those with BP <140/90 mm Hg on anti-hypertensive medications); 5) BMI $\geq$28 kg/m^2.

All study subjects and comparison subjects received an extensive neuropsychiatric diagnostic assessment before they were stratified into diagnostic groups. The neuropsychiatric evaluation included neuropsychological testing, a neurological examination, twelve-hour fasting laboratory tests (subjects were reminded by phone the night before and asked about fasting in the morning) including, thyroid function tests (TFTs) (TSH, Tri-iodothyronine (T^3) and Free thyroxine), vitamin B^{12} and folate, fasting blood sugar (FBS), hemogram, kidney panel, lipid panel, liver panel, vitamins A C and E , homocysteine and apolipoprotein (APOE) status, and either brain magnetic resonance imaging (MRI) or computed tomography (CT)

depending on the presence or absence of MRI contra-indications. Additional clinical values obtained included blood pressure (mm/hg), weight (kg) and height (cm). The Geriatric Depression Scale-15 items (GDS) (30) was used to estimate the severity of subjects' depressive symptoms in subjects diagnosed with clinical depression and to confirm the absence of significant depressive symptoms in the comparison group. The normed and standardized neuropsychological tests for Hispanics (31) used in the study included the assessment of attention-concentration, memory, language, visual-spatial, motor coordination, and executive functions. The Spanish version of UCLA Alzheimer Disease Center's Activity of Daily Living Inventory (ADLI) was also administered. A self-reported Seafood Consumption Questionnaire in Spanish was developed for this study by the study's native speakers. The self-reported questionnaire was designed to assess the type of seafood consumed, its origin, amount and frequency of consumption. The amount consumed on a weekly and monthly basis by weight was estimated through the use of three dimensional models of known portion sizes of fish shown directly to subjects. In view of the low fish consumption of many subjects, all data was converted to grams of fish consumed per month. The questionnaire was pilot tested with a focus group of elderly Hispanic subjects and adjusted according to the group feedback on terminology and other facets of the questionnaire and its presentation. Then, the revised questionnaire was retested for validity and accuracy in a small number of elderly Hispanics from the original population (unpublished data). The same native Spanish-speaking investigator presented the Seafood Consumption Questionnaire to all subjects. All diagnoses made in this study were established after diagnostic consensus conferences involving clinicians from the other UCLA ADRC sites.

Data analysis

Differences between depressed and comparison subjects on the demographic and outcome measures described above were tested using two-tailed t-tests for independent groups for continuous variables and the chi square test of independence for categorical variables, with alpha = 0.05. Effects of confounding or correlated variables were controlled by including them as covariates in a univariate analysis of variance with group as a between subject factor.

Results

Subject Characteristics

As shown in table 2 the depressed and comparison groups were very similar along demographic and psychosocial variables, except for differences in age, GDS score and MMSAdj score. The healthier, non-depressed comparison group was significantly older (72.3, ±6.3) than the depressed group (63.7, ±7.0), ($p < .000$). As expected, the depressed group had significantly higher GDS (10.2, ±3.3), and lower MMSAdj scores (28.2 ±2.5) than the comparison group, GDS (.50, ±1.0) $p < .000$, and MMSAdj (29.7, ±0.7) $p < .002$. No significant differences in education, annual income (estimated average), Marin Acculturation Scale score, weight, height and BMI were found between the groups. The percentage of females was high in both depressed (81.1%) and comparison (84.8%) groups, but no difference between them was found.

Table 2
Psychosocial and Demographic Variables

Demographic and Psychosocial Variables	Groups (n=53) Depression x (SD)	(n=33) Controls x (SD)	Test value	P value
Age	63.7 (7.0)	72.3 (6.9)	F= .018	.000
Gender (% Female)	81.1%	84.8%	-	ns
GDS score [a]	10.2 (3.3)	.50 (1.0)	F= 4.726	.000
MMSAdj score [b]	28.2 (2.5)	29.7 (0.76)	F=22.219	.002
Education (yrs)	6.6 (3.6)	7.9 (3.7)	-	ns
Approximated Annual Mean Income (US$)	11,084 (7,867)	11,287 (8,752)	-	ns
Marin Acculturation Scale score	1.51 (0.93)	1.58 (1.03)	-	ns
Weight (kg)	68.3 (12.3)	68.8 (12.6)	-	ns
Height (cm)	155.7 (9.7)	154.2 (11.2)	-	ns
BMI (kg/m^2) [c]	28.9 (5.3)	29.0 (4.4)	-	ns

a. Geriatric Depression Scale; b. Mini-Mental Status Examination adjusted for education and Age; c. Body Mass Index

Depression, Type 2 Diabetes and Metabolic Syndrome

The rate of diabetes in the depressed group (38%) was more than twice that of the comparison group (18%), even though mean BMI for both groups was nearly identical. No difference between groups was found in pharmacologic treatment for diabetes. Two thirds of diabetics in each group received treatment. Non-treated diabetics either did not know they had diabetes or chose not to take treatment. Figure 1 shows that despite reported treatment, a significant difference in mean fasting glucose level was found between the depressed (124.3, ±71.3), and the comparison (94.2, ±21.2), $p < .000$) groups. A univariate analysis of variance, using BMI as a covariate, found that the effect of depression on fasting glucose levels was independent of BMI ($F=4.899$, $p < .030$) in these groups.

Table 3 shows the list of outcome variables. As shown, statistically significant differences were found between the depressed and the control groups on mean fasting glucose (elevated in the depressed group, 124.3, ±71.3 vs. 94.2 ±21.2; $p < .021$), ADLI mean scores (higher in the depressed group, 11.5 ±4.8 vs. 8.1 ±0.5; $p < .000$), and mean grams of fish consumption per month (lower in the depressed group, 134.7, ±19.0 vs. 162.5, ±58.4; $p < .000$). However, a significantly lower systolic blood pressure was found for the depressed subjects (134.7, ±19.0 vs. 148.7, ±26.0; $p < .006$). Vitamin levels were normal in both groups and no other statistically significant differences were found in measured diabetic and vascular disease risk factors.

Table 3
Groups Outcome Variables

Psychosocial, Nutritional and Metabolic Variables	Normal ranges	Groups (n=53) Depression mean (SD)	(n=33) Controls Mean (SD)	Test Value (F)	P value*
Fasting glucose (mg/dL)	60-109	124.3 (71.3)	94.2 (21.2)	5.516	.021
ADLI score†	-	11.5 (4.8)	8.1 (.5)	14.540	.000
Fish consumption (gm/month)	-	89.2 (80.7)	162.5 (58.4)	19.169	.000
Systolic blood pressure (mm/Hg)	90-120	134.7 (19.0)	148.7 (26.0)	7.958	.006
Diastolic blood pressure (mm/Hg)	60-80	76.1 (11.0)	73.9 (13.5)	-	ns
Total cholesterol (mg/dL)	< 199	210.3 (35.4)	209.6 (39.0)	-	ns
Triglycerides (mg/dL)	< 149	176.8 (76.2)	210.6 (162.4)	-	ns
Low density (mg/dL) lipoprotein	< 100	118.4 (37.3)	117.9 (33.0)	-	ns
High density (mg/dL) lipoprotein	> 40	56.5 (16.1)	52.9 (16.3)	-	ns
Homocysteine (mmol/l)	< 10.3	9.5 (3.7)	10.7 (2.0)	-	ns
Metabolic syndrome (%)		56%	55%	-	ns

* Analysis of Variance; † Activity of Daily Living Inventory

No statistically significant difference was found between groups on the rate of diabetes plus pre-diabetic metabolic syndrome (54.7% in the depressed group vs. 54.5% in the control group). The comparison group had a higher rate of pre-diabetic metabolic syndrome (44.4%) than the depressed group (27.3%) after controlling for diabetes, but the difference was not statistically significant. Certain subjects in both groups who had metabolic syndrome were treated: Thirty percent (10/33) of comparison subjects were on cholesterol lowering agents and 45% (15/33) on anti-hypertensive medications, while in the depressed group, 26% (14/53) reported being on cholesterol-lowering drugs and 42% (22/53) on anti-hypertensive medication. No specific triglyceride therapy was reported by either group. Cholesterol levels did not correlate with level of depression and no group differences were found in possible depressogenic medications (e.g. propranolol, corticosteroids, etc.) or drugs known to increase insulin resistance.

Depression and Daily Functioning

Measures in Activity of Daily Living Inventory (ADLI) between the depressed (11.5, ±4.8) and comparison group (8.1, ±0.5) differed significantly ($p < .000$), with the depressed group scores showing more functional impairment than the comparison group (See Table 2). This difference held after including MMSAdj as a covariate in the analysis, ($F=6.625$, p. 012), indicating that the group difference was related to depression and not to the small difference between groups in cognitive status (28.2 vs. 29.7).

Depression and Diet

Whereas several depressed subjects reported diminished enjoyment of food, substantial alterations of eating patterns and major weight loss were not reported. Analysis of weight, BMI and vitamin values between depressed and comparison subjects revealed no significant differences (Table 2). However, analysis of estimated fish consumption through the Seafood Consumption Questionnaire (SFQ) yielded notable results. There was an overwhelming preference and consumption in both groups for salt water over lake or stream fish. Figure 1 illustrates monthly mean fish consumption for the comparison group (162.5, ±58.4) versus the depressed group (89.2, ±80.7, $p. < .000$). A univariate analysis of variance, using fasting glucose level as a covariate, found that the difference between depressed subjects and controls in fish consumption was independent of fasting glucose level ($F=17.128$, $p < 000$) in these groups. This indicates that the effect of fish consumption on depression was not due to dietary effects on diabetes.

Figure 1
All subjects

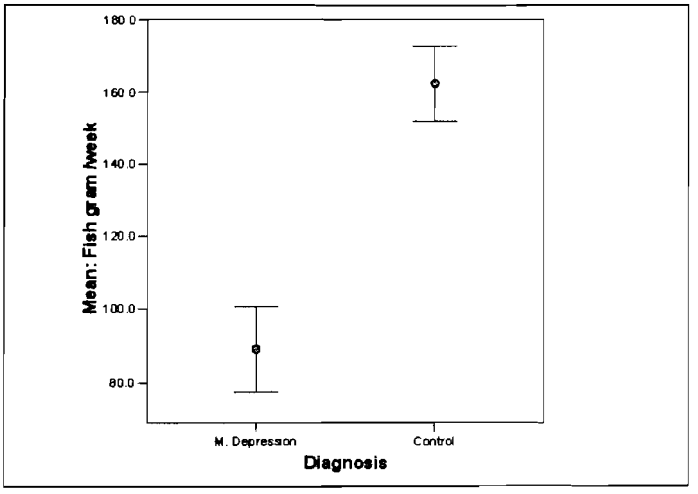
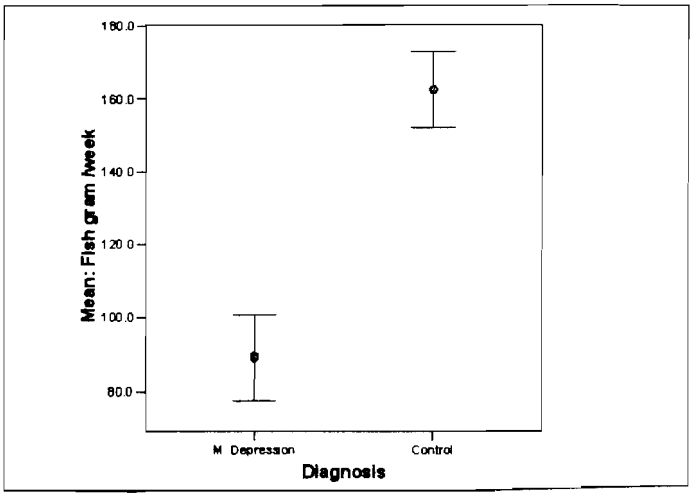


Figure 2
Mean of fasting glucose level compared between groups



Discussion

This study compared a group of community outreached Hispanic elders who initially voiced a cognitive complaint, but who were found to be depressed and not demented, to a similarly community-recruited group of generally healthy Hispanic elders with no complaint. Originating in the same community, both groups were nearly identical along the psychosocial-demographic continuum. As would be expected the depressed group had higher GDS and ADLI scores, and slightly lower, but still normal, MMSAdj scores than the comparison group. Somewhat unexpected was the older age of the comparison group.

When the groups were compared along multiple metabolic/nutritional variables they were indistinguishable, with the exception of fasting blood glucose level and reported monthly fish consumption where the differences between the depressed and comparison groups were highly significant. The comparison group consumed nearly twice the amount of sea fish as the depressed group and had a group mean fasting blood glucose well within normal limits, whereas the depressed group's mean was almost in the diabetic range. The depressed group had many more diabetic subjects and higher representation of diabetics with fasting blood sugars in the diabetic range than did the comparison group. Furthermore, the comparison group consumed nearly twice the amount of fish per month than did the depressed subjects, and this was an independent effect from diabetic status since the strong difference between groups persisted after diabetics were removed from both groups.

Our results are consistent with previous reports in the literature on the high prevalence of diabetes in Hispanic-American populations, though less is known about diabetes in older Hispanics. Some studies on Hispanics have suggested that the vulnerability to diabetes is related to the amount of American-native admixture present. Both, comparison and depressed groups in this study show a considerably higher prevalence of diabetes than seen in older Americans of European descent even when recent increases in diabetes in the American population at large are taken into consideration. Both study groups' high adiposity is also noteworthy. Striking, however, is the particularly high proportion of diabetics in the somewhat younger depressed group. In all of the depressed subjects the initial complaint was a cognitive one, even though no significant cognitive deficit was found after extensive neuropsychological testing. The literature also reports a relationship between diabetes and subsequent development of depression or eventual development of diseases associated with cognitive decline (8, 32-36). This study is consistent with these reports and in addition shows a strong association between depression and poorer fasting glycemic control.

While the present study design does not permit the determination of causality, it does suggest that tighter glycemic control might help in reducing the risk of developing symptomatic depression if diabetes is present, although other factors may also be involved. For example, there is a linkage between insulin resistance, the generation of reactive oxygen species and chronic inflammation (37). Lower socio-economic status has been related to greater chronic inflammation including higher tumor necrosis factor (TNF)-alpha in Hispanics (38). Future studies should target the role of good glycemic control on the manifestation of depressive symptoms in older persons with type II Diabetes and on the emergence of treatment resistant depression.

Another finding was the diabetes-independent relationship of amount of sea-fish consumption to depression. While both comparison and depressed groups were very low consumers of fish when compared to consumption amounts advocated by the Food and Drug Administration (12 oz varied sea fish per week), sea-fish consumption in the depressed group was dramatically low (3 oz per month). Sea-fish such as salmon, mackerel, tuna, sardines, etc., are major sources of omega-3 fatty acids (eicosapentanoic acid-EPA, and docosahexanoeic acid-DHA) in the diet. Epidemiological, experimental and new clinical studies have shown a strong connection between low consumption of foods rich in omega-3 fatty acids and increased depression (39), though not every study has shown a clear association (40). Animal studies have shown that deficiencies in the omega-3 fatty acids (EPA and DHA) can produce deficits in dendritic arborization and synaptic function, involving neurotransmitters (acetylcholine, serotonin, dopamine) implicated in mood disorders (40, 41) and deficits in BDNF, a major neurotrophic factor with depression associated deficits (42). Supplementation with omega-3 fatty acids typically mitigates the synaptic and neurotransmitter deficits and may also improve arborization, while fish oil supplementation can mitigate depression-related behavior in animal models (43).

NIH studies have shown that higher national fish consumption for a country correlates with lower depression rates when compared to countries consuming the least amount of fish (44, 45). Researchers are now observing increasing rates of depression in regions of the world that are moving away from traditional omega-3 rich diets to typical Western foods with high omega-6 fatty acids intake (39). In a recent clinico-pathologic study, McNamara et al. (2006) demonstrated selective deficits in omega-3 fatty acid, DHA, content in the postmortem cortex of patients with Major Depressive Disorder (55). Clinical studies have demonstrated that those with depression do have lower levels of omega-3 fatty acids in the blood (17, 46, 47). Results of clinical trials have shown improvement of depressive symptoms in depressive illness or treatment resistant depression over placebo when subjects were given omega 3 fatty acid treatment in modest doses (48, 49). The mechanisms by which omega-3 fatty acids may influence mood have not been elucidated, but it is clear that these substances are important to brain micro-structure and neurotransmitter metabolism and may have the capacity to lower levels of immune agents such as tumor necrosis factor

alpha (TNFa), interleukin 1 beta (IL-1B), and prostaglandin E2, substances which have been reported to be elevated in depression (17).

Factors which limit the generalizability of the study results include the modest sample size and non-random selection of subjects and the high proportion of women, although the community sample used in this study has advantages over the more traditional samples taken from hospital or outpatient populations. The study is also crossectional and correlational in design not allowing for the identification of exclusive causal factors in the development of depression. Finally, the depressed subjects who responded initially to recruitment with a cognitive concern may not be characteristic of all depressed older Hispanics. Furthermore, California Hispanics are overwhelmingly of Mexican and Central American origin and represent about two-third of the Hispanics in the U.S., but are not representation of all U.S. Hispanics many of whom come from other cultural and racially distinct areas.

In conclusion, depressed older Hispanics initially presented with a cognitive complaint but were not demented. The depressed group differed significantly from the healthier, asymptomatic comparison group particularly in the amount of poorly controlled diabetes found. In addition, the depressed group consumed very small quantities of fish, half the amount the comparison group did. This study suggests that factors such as poorly controlled diabetes combined with very low consumption of omega-3 fatty acids may greatly increase the risk of developing depression in late life. These factors may be socio-economically and culturally influenced and are therefore amenable to modification.

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Author Contributions: Indicate authors' role in study (1) concept and design, (2) acquisition of subjects and/or (3) data, analysis and interpretation of data, and (4) preparation of manuscript. (List all author(s) name). Author Name: L. Jaime Fitten, M.D., 1,3,4; Author Name: Freddy Ortiz, M.A., 2,3,4; Author Name: Lynn Fairbanks, Ph.D., 3,4; Author Name: Mark Rosenthal, M.D., 3,4; Author Name: Greg Cole, Ph.D., 4; Author Name: Fatemeh Nourhashemi, M.D., 2; Author Name: Mary Anne Sanchez, 2

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