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Dietary protein and protein-rich food in relation to severely depressed mood: A 10 year follow-up of a national cohort

Allen R. Wolfe [a,b], Cassandra Arroyo [a], Stuart H. Tedders [a], Yanfeng Li [c], Qi Dai [d], Jian Zhang [a,*]

[a] Jiann-Ping Hsu College of Public Health, Georgia Southern University, Statesboro, GA, USA
[b] Ross University School of Medicine, Miami, Florida, FL, USA
[c] Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, Columbia, SC, USA
[d] Department of Medicine and Vanderbilt-Ingram Cancer Center, Vanderbilt University, Nashville, TN, USA

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ABSTRACT

High-protein diets are advocated to facilitate weight loss, and improve cardiovascular risk factors, but data on psychiatric effects are lacking. We analyzed data from 1947 men and 2909 women aged 25–74 years when examined in 1971–1975 as the baseline of the National Health and Nutrition Examination Follow-Up Study. The amounts of macronutrients were obtained from a 24-hour recall, and frequencies of eating protein-rich foods were estimated using a 3-month food frequency questionnaire. Severely depressed mood (SDM) was defined as Center for Epidemiologic Studies Depression Scale score ≥ 22 or taking anti-depression medication after an average of 10.6 years of follow-up. A significant gender difference was observed in the prevalence of SDM and its association with protein intake. The weighted prevalence of SDM was 11.45 (SE = 0.96) % and 17.45(1.05) % respectively among men and women. Among men, the relative risk (RRs) of SDM were 1.00, 0.46 (95% CI = 0.22–0.99) and 0.38 (0.16–0.92) respectively for the lowest, middle and highest third protein intake (p for trend = 0.0347). Among women, the RRs were 1.00, 1.93 (1.23–3.08) and 2.47 (1.24–4.90) respectively with lowest, middle and the highest third intakes (p for trend = 0.0023). These estimates were adjusted for cigarette smoking, alcohol consumption, BMI, socioeconomic status at baseline, and the history of cancer, stroke, heart attack and diabetes assessed at follow-up interview. The authors concluded that increased intake of protein demonstrated a protective effect among men but a deleterious effect among women.

1. Introduction

Recently, there has been a resurgence in the popularity of low-carbohydrate (high-protein) diets largely due to the emerging pandemic of obesity (Blanck et al., 2006; US News and World Report 2009). Proponents of these high-protein popular diets have long claimed that higher amounts of dietary protein not only facilitate weight loss but also improve cardiovascular risk factors (Hu, 2005). However, little information is available on their effects on long-term mental-well being (Brinkworth et al., 2009). Therefore, an advisory by the American College of Preventive Medicine stated that there was currently little evidence to support the safety and effectiveness of popular diets that promote excess consumption of protein or fat (Katz, 2003). Although there was no compelling evidence indicating that high-protein diets negatively impact the mentality and induce or exacerbate mental disorders, these diets have been linked to worsening of mood, increasing fatigue, dizziness, irritability, headaches, confusion, and sleep problems from small-scaled clinical observations (Lloyd et al., 1994; Wells and Read, 1996; Butki et al., 2003). The investigation into the effects of protein intakes on behavior and mood has centered on the level of serotonin (5-HT), particularly, the brain concentration of tryptophan (Trp), 5-HTs essential amino acid precursor (Wurtman et al., 2003). Since the enzyme that catalyzes the initial and rate-limiting step of brain 5-HT synthesis has a very low affinity for Trp and is highly unsaturated at brain (Lovenberg et al., 1968), the brain Trp concentration is largely a function of the ratio of circulating plasma Trp to large neutral amino acids (Trp/LNAA) (Wurtman et al., 2003). An experimental study showed that high-glycemic-index carbohydrates had the ability to increase Trp/LNAA via a direct action of insulin, which promoted a selective muscle uptake of LNAAs (Berry et al., 1991). Dietary proteins, in contrast to carbohydrates, lower Trp/LNAA because they contribute less Trp than do other LNAAs to the circulation. An experimental study demonstrated that high-protein foods similar to those Americans regularly eat can cause substantial differences in the Trp/ LNAA (Wurtman et al., 2003). However, it is worth noting that many of the

Abbreviations: 5-HT, serotonin (5-HT); CES-D, Center for Epidemiologic Studies Depression Scale; FFQ, food frequency questionnaire; LNAA, large neutral amino acids; NHANES, National Health and Nutrition Examination Survey; NHEFS, National Health and Nutrition Evaluation Survey Epidemiologic Follow-up Study; SES, socioeconomic status; SDM, Severely depressed mood (SDM); Trp, tryptophan.

* Corresponding author. PO Box 8015, Statesboro, GA 30460-8015, USA. Tel.: +1 912 681 5653; fax: +1 912 681 581.
E-mail address: Jianzhang@georgiasouthern.edu (J. Zhang).

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earlier studies on human protein and amino acid needs were conditioned by the levels of food energy that had been fed experimentally, and were laboratory artifact with limited relevance to human being. Epidemiological investigation on the association between human nitrogen metabolism, dietary protein, and mood disorder is warranted.

The dearth of epidemiological studies and the crucial public importance of identifying a weight control strategy with high safety and efficacy motivated the current research. We took advantage of the prolonged follow-up experience of a nationally representative sample of the US men and women who participated in the first National Health and Nutrition Examination Survey (NHANES I) with dietary intake assessed at baseline and mood assessed after more than 10 years follow-up.

2. Methods

2.1. Study population

This study used data from the National Health and Nutrition Evaluation Survey Epidemiologic Follow-up Study (NHEFS). Detailed descriptions of NHEFS have been published elsewhere (Madans et al., 1986a,1986b; Ingram and Makuc, 1994). In brief, the NHEFS cohort was a study of adults who originally participated in the NHANES I from 1971 to 1975 (n = 14,407) as the baseline survey when they were aged between 25 and 74 year old. In the 1982–1984 study, of the original NHEFS cohort, 15.1% were deceased, 7.1% were lost to follow-up, and 73% (n = 10,523) of the participants were successfully traced and interviewed. The current study included the subgroup of NHEFS participants who remained alive and had completed information on depressive symptoms assessed in 1982–1984 (n = 9517). We excluded participants with 24-hour dietary recall recorded as unsatisfactory (n = 70), those with protein intake calculated from a 24 h dietary recall missed (n = 2262), those with an incomplete information on alcohol drinking, cigarette smoking (n = 1778), and these with uncompleted data on socioeconomic status (SES), i.e. income level, education attainment, marital status, and type of residential area (n = 199). Additional 351 participants were excluded due to an unavailability of data on body mass index, serum total cholesterol, self-evaluated health status from baseline survey, and short of information on diagnoses of cancer, stroke, heart attack and diabetes from follow-up survey, leaving 4873 available for final analysis.

2.2. Severely depressed mood (SDM)

Depressed mood was assessed in the 1982–1984 follow-up using the Center for Epidemiologic Studies Depression Scale (CES-D) questionnaire developed for epidemiologic surveys of the general population to measure depressive feelings and behaviors during the past week (Weissman et al., 1977). The CES-D questionnaire consists of 20 descriptive statements of depressed mood, feelings of worthlessness, hopelessness, and loneliness; loss of appetite; sleep disturbances; concentration problems; and psychomotor retardation. Participants were asked to rate each item according to the frequency experienced in the past week and scored on a standard four-point scale from 0 to 3. The 20 items had a potential range of 0–60, with the higher scores representing responses in the depressed range. Only persons who answered all 20 items on the questionnaire were included in the current analysis. Those with a total score on the CES-D ≥ 16, which corresponds approximately to the 80th percentile score among general population, were considered to have moderately or severely depressed mood. In the preliminary analyses, we observed that having CES-D ≥ 16 (among men, n = 584 and % = 27.74; among women, n = 1184 and % = 38.41) as the cut-off was not able to identify distinct levels of severity of the symptoms and provide adequate statistical power to detect the association. We finally categorized participants as having severely depressed mood (CES-D ≥ 22, n = 200 and % = 9.65 among men; n = 462 and% = 14.92 among women) and non-severe symptoms. The individuals who were taking anti-depression medication when the follow-up interview were conducted (n = 143, and 72 with CES-D score ≥ 22) were also included as having severely depressed mood.

2.3. Qualified dietary intake of protein

A 24-h dietary recall, administered by the same trained staff prior to beginning the food frequency questionnaire (FFQ), provided such information as specific food items and their quantities ingested for all regular meals, between meal foods and snacks consumed on the day, midnight to midnight, preceding the interview for each sample person interviewed. Food portion models were used to aid in estimation of portions. Nutrient intakes were obtained by a computerized process. Each food item was assigned a unique food code and the approximate portion was coded. The food codes matched those on the nutrient composition of over 3000 food items obtained from the U.S. Department of Agriculture, food manufacturers, and other sources. From the above information, all food consumed during the 24-h period was then reduced by a computer program to standard units of measurement for actual dietary intake during 24-h recall period, including protein, saturated, linoleic and oleic fatty acids, total cholesterol and total dietary calories ingested in 24 h.

2.4. Frequency of consuming high-protein food

A 3-month FFQ was administered at the baseline survey (1971–75) by trained interviewers, usually registered dieticians. The questionnaire covered the 3 months prior to the interview and referred to usual consumption excluding periods of illness or dieting. Information was collected on 18 groups ingested daily and/or weekly in the usual pattern accounting for all regular meals eaten as well as for between meal foods or snacks, Monday through Sunday, weekends and holidays (National Center for Health Statistics, 1996). The interviews were conducted in specially designed mobile examination units. On-site evaluations, review of questionnaires, and taped interviews were conducted as part of the data quality control. Only dietary records coded as satisfactorily completed by interviewers were used in this analysis. The protein-high foods were further grouped as meat/poultry, milk, cheese/buttermilk, fish/seafood, egg and legumes, in the order of caloric contribution estimated by the previous study (Block et al., 1985). Categories of consumption frequency used in the analysis for each group of food rich in protein were selected to identify distinct levels of consumption and to provide adequate numbers at risk in each level.

2.5. Covariates

Potential confounders were selected from the literature, including gender, socioeconomic status (SES) or social deprivation indicators, behavioral and dietary characteristics, self-evaluated health status and the history of medical illness. Since more than 90% of the samples were whites, ethnicities were recorded as “whites” and “others”. Mexicans were included with “White” unless definitely known to be American Indian or of other nonwhite race. Educational attainment at baseline was measured as the highest completed grade of school and categorized as 4 levels. Marital status was collapsed into two categories: married and others. Poverty status was defined by the ratio of family income to the federal poverty line threshold established annually by the US Bureau of the Census. Other SES variables included employment status, occupation (farm/non-farm), and type of residence area (urban, suburban and rural).

The category for alcohol consumption separated heavy drinkers (every/just about every day) and moderate drinkers (2 to 3 times a week or 1–4 a month) from less regular drinkers or non-drinkers. They were defined on the basis of answers to questions about frequency and amount of alcohol consumed. Information on smoking status was