Research Proposal: Peanut consumption and human weight management

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Focus

Domain - Nutrition Region - Global

Background

Obesity is a global epidemic. Despite substantive efforts, the problem is growing. In the United States, 65% of adults are now either overweight or obese (1). Only 8% of states have prevalence less than 20% and the rate is greater than 25% in 44% of the states (1). Internationally, the World Health Organization (WHO) estimates that currently there are 1.6 billion adults (aged 15+) who are overweight and at least 400 million adults who are clinically obese. This represents a doubling of the prevalence of 200 million in 1995 and the WHO projects that by 2015, approximately 2.3 billion adults will be overweight and more than 700 million will be obese (2). Over 115 million people suffer from obesity-related problems in developing countries. While under nutrition remains a terrible crisis warranting vigorous intervention, as of 2000, the number of people in the world who were obese exceeded the number of people suffering from malnutrition (3). Currently some 824 million people suffer from chronic hunger (4) while 1.6 billion are overweight (2). Excess bodyweight is one of the most important risk factors contributing to the overall burden of disease worldwide (5). Obesity is a cause or contributing factor in a number of diseases including type 2 diabetes, heart disease, high blood pressure, and stroke. Eighty percent of type 2 diabetics are overweight. Type 2 diabetes is no longer an adult disease. As obesity increases in children, there is a parallel rise of type 2 diabetes in this group. It has recently been proposed that obesity also increases the probability that those children at risk for type 1 diabetes will develop the disease (6). When diabetes is developed at

a younger age, there is an increased probability of developing the long-term complications of the disease, such
as kidney failure, heart disease, blindness and neuropathy, and these complications will occur at an earlier age (7). Death from diabetes is predicted to increase by over 50 per cent in the next 10 years (9), rising from the 171 million recorded in 2000 to an estimated 366 million in 2030 (10). Indeed, several studies have found that increasing obesity could actually lead to decreases in life- expectancy in the worst affected countries (11).

Obesity is the result of positive energy balance. Some argue that the primary problem lies in a low level of energy expenditure. Others emphasize energy intake noting that, within limits, shifts of expenditure are not inherently problematic for energy balance unless there is a failure of intake to adjust appropriately. Thus, the primary problem is viewed as dietary. In particular, the act of ingestion is key for energy regulation. Assuming food availability, weight stability is only achieved when the signals controlling eating prompt behaviors that result in energy balance. Sustained dysregulation of these cues results in under or overweight. In the present environment, inhibitory ingestive controls have not matched those that promote consumption, leading to positive energy balance, weight gain and overweight/obesity.

Peanuts are a high fat, energy dense food. It has been proposed that foods with these characteristics are especially problematic for weight gain because they lead to incomplete dietary compensation. Although evidence is accumulating that other characteristics of peanuts offset these properties and that peanuts may be incorporated into diets without posing a threat to weight gain (12, 13), concern remains among policy makers, health care providers and consumers. This is one of the most substantial obstacles to increased consumption. Although additional evidence is needed that moderate levels of peanut consumption do not promote weight gain, efforts must now be directed to establishing the mechanisms by which this occurs. Documentation of mechanisms will add credibility to the behavioral weight balance evidence and further recommendations to increase peanut consumption for the other health benefits they offer (e.g., reduction of cardiovascular disease risk and possibly diabetes risk). In particular, expanded knowledge is needed on the effects of peanuts on appetitive sensations, physiological energy regulatory systems and optimal approaches for their inclusion in the diet. These will be addressed in this proposal.

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Technical Review

Trial 1 General Methods A randomized, four-arm, cross-over design is proposed. The four arms will entail having participants ingest: A) roasted, unsalted peanuts; B) roasted, salted peanuts; C) honey roasted peanuts or D) hot (spicy - capsaicin) roasted peanuts. Thus, responses to an unflavored, salty, sweet and spicy form of peanuts will be contrasted.

Participant Characteristics Participants will be recruited through public advertisements. Eligibility criteria for will be as follows: age range 18-50 years of age, body mass index (BMI)18-25kg/m2, male or female, weight stable (< 3 kg within last 3 months), no eating disorder (score <20 of the Eating Attitude Test (EAT-26), constant habitual activity patterns (no deviation > 1x/wk @ 30 min/session within last 3 months), not taking medications known to influence appetite, not diabetic, no history of GI pathology, no peanut allergy and self-reported consumer of breakfast and lunch.

Screening Individuals responding to recruitment advertisements will be scheduled for a screening visit. They will be presented a consent form, all study-related questions will be answered and those interested in participating will sign the consent document. They will then be characterized along dimensions related to ingestive behavior and risk for obesity. Both state and trait measures will be included.

Cognitive Restraint "Individuals are classified according to the Three Factor Eating Questionnaire (1). This is a measure of cognitive control over eating. Disinhibition "Individuals are classified according to the Three Factor Eating Questionnaire (1). This is a measure of loss of control over eating following disruption of an individual's normal ingestive practices. Hedonic Hunger - Individuals are classified on the Power of Food Scale (2). This is a sale that quantifies an individual's appetitive responsiveness to the rewarding/hedonic

properties of foods. Food Craving - Individuals are classified on the Food Craving Questionnaire "State Version (3). Stress "Individuals are classified on the Perceived Stress Scale (4). This scale measures the degree to which an individual perceives life as stressful. Depression "Individuals are classified on the Zung Self-Rating Scale (5). Eating Attitudes Test "Individuals are classified on the Eating Attitudes Test (6). This is a measure of disordered attitude towards food.

Test Sessions to reduce novelty effects, participants will be required to consume 56 grams of one of the flavored peanuts for 6 consecutive days as a midafternoon snack. On the 7th day, they will eat a standard breakfast and nothing more until they report to the laboratory for their midday meal. After having a catheter placed in an antecubital vein and collection of a 10ml blood sample, they will consume a standard lunch of macaroni and cheese with a fixed volume of water until they reach a level of fullness self-rated as a 7 on a 9-point category scale. Additional blood samples will be collected 15, 60 and 105 minutes after the meal. Participants will record their appetitive sensations (hunger, fullness, desire to eat, prospective consumption desire for something sweet, desire for something salty, desire for something fatty, desire for something spicy, thirst) at 30 minute intervals after the meal for 2 hours. They will then consume 56 grams of the same flavored peanuts that they consumed the prior 6 days with 250 ml of water within 15 minutes. Appetitive sensations will continue to be recorded at 30 minute intervals for 3 hours. Additional blood samples will be obtained at 30 minute intervals during this time, but starting 15 minutes after peanut consumption. Thus, the appetite ratings and blood draws will be offset by 15 minutes over the 3 hour post load period. They will then be presented with a standardized dinner and asked to eat to a comfortable level of fullness. The amount consumed will be covertly recorded as an index of satiety. They will provide appetitive ratings immediately, 15 and 30 minutes after completing the meal and then be free to leave. They will continue to record all foods and beverages consumed for the balance of the test day. This will be repeated with each flavored peanut in a random order.

Measurements Anthropometric Measures: Height will be measured with participants in bare feet with a Holtain stadiometer. Fasting-state body weight (gown only) will be measured to the nearest 0.1 kg after the participant has voided on a digital clinical scale. Body composition will be determined by tetra polar bioelectrical impedance analysis (RJL Systems, Detroit, MI).

Hormone and Glucose Assays: We are aware that there are a large number of gut peptides that contribute to the appetitive responses to foods that could be measured here. We are proposing to measure those with documented responses to orosensory stimulation. They will also provide indices of activity in different facets of nutrient processing. We believe these are part of a complex signaling system to optimally digest foods and absorb and utilize their nutrients. The hormones include: Insulin (potential modulator of responsiveness of the gut peptides); Pancreatic polypeptide (PP: index of non-specific vagus activation); CCK (proximally released GI satiety factor); GLP-1

(distally released GI satiety factor) Ghrelin (orexigenic hormone-active form containing the octanoyl group on serine 3) and glucose.

These hormones will be quantified using the Luminex ® bead-based multiplex detection system and the Human Gut Hormone Panel 5-Plex (Millipore Corp). This technology will allow the simultaneous measurement of all hormones except CCK in 25 ul of serum. The Luminex detection system is available to our collaborator Robert Considine, an expert in measurement of gut and adipocyte hormones. The current sensitivity of the assay for each analyte is as follows: insulin (44.5 pg/ml), PP (2.4 pg/ml), GLP-1 (5.2 pg/ml), and ghrelin (1.8 pg/ml). CCK will be quantified using the Euria CCK assay (Alpco Diagnostics).

Glucose will be measured using a Roche COBAS MIRA clinical analyzer.

Appetite: Appetite sensations will be collected using a handheld electronic appetite system that is based on palm pilot technology. This will pose questions relating to hunger, fullness, and desire to eat, thirst and desire to eat in general and for foods with selected characteristics (salty, fat, sweet, spicy). The programmed software presents the relevant questions to participants and stores the responses. This poses limited burden to participants and, because each measurement has a time and date stamp, it assures recordings are made at the stipulated times. It also improves data accuracy by eliminating transcription errors and facilitates data manipulation and analyses. This approach has been validated (7,8) and used by our group for years.

Food Intake: Where feeding will be monitored in the laboratory, foods will be surreptitiously weighed before and after presentation to participants. For foods consumed outside the laboratory, food records will be analyzed using country-specific databases.

Sample size justification and statistical analyses: To assess the effects of peanut flavor, the appetitive ratings and hormone/glucose concentrations will be compared between the treatments by repeated measures analysis of variance. The criterion for statistical significance will be $p<0.05$, two-tailed. Assuming flavor accounts for 40% of the within-subject variance in ratings or concentrations, power calculations indicate a sample of 24 individuals will allow detection of a treatment effect with 80% power at the 5% level of probability.

Trial 2 General Methods A parallel group, two-arm design is proposed. The two arms will entail having participants ingest: A) a single form of roasted peanuts that are unsalted, salted, honey roasted or spicy (each participant can select their preferred form) versus B) freedom to select any of these flavored forms on a daily basis. Thus, acceptability and chronic intake of a single flavor versus varied flavors of peanuts will be contrasted along with their impact on appetite, total diet quality (energy and nutrient content), resting glucose and insulin concentrations and blood pressure. Responses will also be compared

between individuals rated as high or low on hedonic hunger.

Participant Characteristics Participants will be recruited through public advertisements. Eligibility criteria will be as follows: age range 18-50 years, male or female, weight stable (< 3 kg within last 3 months), constant habitual activity patterns (no deviation > 1x/wk @ 30 min/session within last 3 months), not taking medications known to influence appetite, not diabetic or hypertensive, no history of GI pathology, not a daily peanut or tree nut consumer, and no peanut allergy. Eligibility will also be based on scores on hedonic hunger - Individuals categorized as high and low on this scale will be sought. Additional personality traits will be determined during a screening session via validated questionnaires, but will only be descriptive, not eligibility criteria.

Screening Individuals responding to recruitment advertisements will be scheduled for a screening visit. They will report in a fasting state and be presented a consent form. All study- related questions will be answered and those interested in participating will sign the consent document. They will then be measured for height, weight, body composition and blood pressure. A single blood sample will be drawn to assess their resting blood glucose and insulin concentrations and erythrocyte fatty acid composition. They will also complete a series of questionnaires and be characterized along dimensions related to ingestive behavior and risk for obesity. Both state and trait measures will be included.

Cognitive Restraint "Individuals are classified according to the Three Factor Eating Questionnaire (1). This is a measure of cognitive control over eating. Disinhibition "Individuals are classified according to the Three Factor Eating Questionnaire (1). This is a measure of loss of control over eating following disruption of an individual's normal ingestive practices. Hedonic Hunger - Individuals are classified on the Power of Food Scale (2). This is a sale that quantifies an individual's appetitive responsiveness to the rewarding/hedonic properties of foods. Food Craving - Individuals are classified on the Food Craving Questionnaire "State Version (3). Stress "Individuals are classified on the Perceived Stress Scale (4). This scale measures the degree to which an individual perceives life as stressful. Depression "Individuals are classified on the Zung Self-Rating Scale (5). Eating Attitudes Test "Individuals are classified on the Eating Attitudes Test (6). This is a measure of disordered attitude towards food.

Procedures For the next 12 weeks, participants will be required to consume 56 grams of peanuts, as per their assigned group, daily. No restrictions will be placed on when or how the peanuts are to be consumed. Indeed, this will be one of the dependent variables. During weeks 1, 4, 8 and 12, they will record their appetitive sensations on a personal digital assistant with specialized software as well as all of their food/beverage intake on 3 random days. They will also keep a log of their daily intake of the peanuts and any deviations from the prescribed daily load. Actual compliance will be assessed during these weeks via assessment of erythrocyte membrane fatty acid composition

via a blood sample. Body weight and blood pressure will be measured at weeks
2, 4, 6, 8, 10 and 12 when participants return to the laboratory for their supply of peanuts or study termination.

Measurements Anthropometric Measures: Height will be measured with participants in bare feet with a Holtain stadiometer. Fasting-state body weight (gown only) will be measured to the nearest 0.1 kg after the participant has voided on a digital clinical scale. Body composition will be determined by tetra polar bioelectrical impedance analysis (RJL Systems, Detroit, MI).

Insulin and Glucose Assays: Insulin will be measured on an Elecsys 2010. The %CV is approximately 2.6%. Glucose will be measured using a Roche COBAS MIRA clinical analyzer. The %CV is approximately 1%.

Appetite: Appetitive sensations will be collected using a handheld electronic appetite system that is based on palm pilot technology. This will pose questions relating to hunger, fullness, thirst and desire to eat in general and for foods with selected characteristics (salty, fat, sweet, spicy). The programmed software presents the relevant questions to participants and stores the responses. This poses limited burden to participants and, because each measurement has a time and date stamp, it assures recordings are made at the stipulated times. It also improves data accuracy by eliminating transcription errors and facilitates data manipulation and analyses. This approach has been validated (7,8) and used by our group for years.

Food Intake: Food records will be analyzed using country-specific databases.

Sample size justification and statistical analyses: Analyses will be based on a mixed model, repeated measures analysis of variance. The between subject's factors will be peanut load (single form versus varied) and hedonic hunger (high or low). Within subjects factors will be appetite ratings, glucose and insulin concentrations, erythrocyte fatty acid composition and blood pressure. The criterion for statistical significance will be $p<0.05$, two-tailed. The sample size calculation is based on the between subjects factors as this will also assure adequate power for the within subjects tests. If the critical effect size is equal to a standardized difference of 1, groups of 25 individuals will permit detection of treatment effects with 90% power. This a total sample of 100 participants (i.e., 25 with low and 25 with high hedonic hunger receiving a single peanut flavor and 25 with low and 25 with high hedonic hunger receiving a variety of peanut flavors) will be recruited.

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Problem Statement

Obesity is a global public health problem. It contributes to the onset and manifestations of numerous chronic diseases, compromises the quality of life and poses an economic burden to individuals and every nation's health care system. High fat foods have historically been viewed as problematic for weight gain so, have been avoided by consumers. This has limited peanut consumption. Additional evidence documenting that peanuts do not promote weight gain and the mechanisms by which this occurs should allay concerns about their increased consumption thereby promoting sales and health.

Vision and Approach

Goals

The goals of this project are to extend the work conducted during previous cycles of support through the Peanut CRSP. We have demonstrated that peanuts pose little challenge to energy balance. The goals for the upcoming three years are to: A) Evaluate a likely mechanism for this effect; B) Explore the factors that may aid or discourage chronic peanut consumption; and C) Train researchers in our host country and the US in methods for clinical research. More specifically, we will:

A. Conduct a clinical trial where we will quantify the effects of peanut consumption of the release of satiety factors that may curb appetite and decrease energy intake. The high fat and protein content of peanuts should stimulate the release of cholecystokinin (CCK) and glucose- like peptide-1 (GLP-1) while decreasing ghrelin and post-prandial glycaemia.
B. Conduct a feeding trial where participants characterized on an array of traits consume either the same peanut product of peanuts with varied flavors to determine their compliance with the dietary manipulation. It is hoped that this knowledge will facilitate more targeted recommendations

to successfully increase peanut consumption on a chronic basis in selected population sub-groups.

C. Train host country and US scientists in the methods of clinical research so they can pursue further study of the health effects of peanut consumption.

Objectives

1. Document the effects of peanuts on gut satiety peptide release, reward system activity (hedonics) and GI transit.
2. Determine compliance with a recommendation for chronic inclusion of single versus varied forms (i.e., sensory properties) of peanuts in the diet among individuals with different characteristics (e.g., flavor preferences, cognitive restrained, variety seeking).
3. Train investigators in human clinical research methods.
4. A new clinical trial is planned for this year in Brazil. The goal is to assess the effect of daily peanut (commercial unpeeled and peeled peanuts) consumption (8 weeks) on: intestinal permeability, gut micro biota, inflammatory and oxidative biomarkers.

Research Approach

The model we used over the prior 10 years has been to conduct the research as multi-center trials. That is, the investigators from each site (U.S. and Brazil) develop and agree to a research protocol and each site conducts a component of the work. This same approach is proposed here where each partner will conduct identical trials and contribute half of the total data. These data will be pooled, collectively analyzed, and the findings incorporated into manuscripts of joint authorship.

Training & Capacity Development Approach

We are proposing the conduct two clinical trials. It is expected that one or more students will be on the research team for each trial from each country. Through this exposure, they will gain knowledge and experience in human clinical research. Our prior experience is that this work serves to satisfy the research component of requirements for advanced degrees (masters and PhD). Over the past 5 year funding period alone, our studies funded by the Peanut CRSP provided training for 7 graduate students in host countries and 8 additional undergraduate students. An additional 3 graduate students were supported in the US along with numerous undergraduates.

Intended Benefits & Impact Responsiveness

Development Benefits

Benefits will be realized at various levels. First, some research participants may experience improved health through study activities. Second, the proposed clinical trials will serve as a training exercise for students, helping to build host country research infrastructure. Third, the proposed work should generate knowledge that can provide a scientific basis for public health policy

and improved health of the nation. This should also help the nation's economic conditions. Fourth, the work should aid peanut growers, processors, food companies and others related to the business of peanut production. Documentation of health benefits should drive demand and sales.

US Benefits

Benefits will be realized at various levels. First, some research participants may experience improved health through study activities. Second, the proposed clinical trials will serve as a training exercise for students, helping to launch their research careers. Third, the proposed work should generate knowledge that can provide a scientific basis for public health policy and improved health of the nation. This should also help the nation's economic conditions. Fourth, the work should aid peanut growers, processors, food companies and others related to the business of peanut production. Documentation of health benefits should drive demand and sales.

Potential Impacts

The full impacts of research are difficult to measure. It is our understanding that the work on health benefits of peanuts helped to reverse a downward trend in sales. Thus, there is a tremendous opportunity for economic gain. The opportunity to train young scientists in clinical research provides a continuum of expertise in each nation to evaluate problems and solutions to health issues. The work supported through the proposed study will not only apply to the specific objectives of this work, but these trained young scientists are expected to amplify understanding of the health benefits of peanut consumption through continued work in the field. To the degree that the proposed work modifies health policy and consumer concerns about peanut consumption, intake may increase resulting in positive health outcomes and economic gains for workings in the peanut industry.

Equipment

It is not possible to definitively answer this now. All necessary equipment is currently available in the U.S. When we know who our host country partner(s) will be, we will assess their equipment needs.

Project Timeline

Objective 1 - Months 1-15 Objective 2 - " Months 16-30 Objective 3 - " Months 31-45 Objective 4 - " Months 46-60 Objective 5 - " Months 1-60

USAID Mandate Responsiveness

MDGs

Poverty/Hunger: Improved Health: Raised Rural Incomes: Sustainable Development

Foreign Assistance Framework

Governance: Human Capacity: Economic Structure: Persistent Dire Poverty:

Global Issues (HIV and Infectious Diseases, climate change, biodiversity)

IEHA

Science and Tech Applications: Increased demand for peanuts: Market Access: Increased Trade

USAID Focal Areas

Greater incomes: Greater value and market demand: Public Health: Food Security: Sustainable Value Chain: Improved Human Capacity