



# Study design for a randomized controlled trial to increase the relative reinforcing value of vegetable consumption using incentive sensitization among obese and overweight people



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## ARTICLE INFO

### Article history:

Received 18 May 2016

Received in revised form 15 August 2016

Accepted 22 August 2016

Available online 24 August 2016

### Keywords:

Relative reinforcing value  
Randomized controlled trial  
Food reinforcement  
Vegetables  
Substitution  
Self-efficacy

## ABSTRACT

In this manuscript, we present the protocol for a study that applies incentive sensitization theory to improve vegetable intake in overweight and obese adults. This 8-week, randomized, controlled, community-based feeding study with an 8-week follow-up seeks to use repeated exposure to amounts of vegetables recommended by federal guidance to increase the primary outcome of the relative reinforcing value of vegetables compared to a snack food. A community-based design is used to give participants autonomy in choosing their method of exposure. Secondary outcomes include: 1) Determine potential moderators of incentive sensitization of vegetables, including genetic polymorphisms associated with food reinforcement and obesity, 6-n-propylthiouracil tasting status, and delay discounting. 2) Determine whether adding vegetables to the diet results in participants substituting low-energy-dense vegetables for energy-dense foods or whether energy-dense food consumption is independent of vegetable consumption. 3) Determine whether reductions in adiposity are associated with substitution of vegetables in the diet. 4) Determine if markers of bone turnover change. 5) Assess changes in self-reported secondary outcomes measured by questionnaire such as self-efficacy to eat vegetables. The results of this study will provide information about the drivers of individual choice to consume recommended amounts of vegetables. The understanding gained will help increase the effectiveness and sustainability of behavior-based interventions focused on improving vegetable intake. This information may also be used to assist in setting dietary guidance targets for the amounts and types of vegetables Americans can, and should, consume.

Published by Elsevier Inc.

## 1. Introduction

The 2015 Dietary Guidelines for Americans (DGA) recommends increased consumption of vegetables [1]. However, adherence is low; only 11% of the population report meeting recommendations [2].

One potential ingress into behavior change of vegetable consumption is behavioral economics theory, which draws from economic and psychology literatures to provide a framework for understanding individual and environmental factors that influence the choice between alternative behaviors. All people have limited resources of time and most also have limited money. According to behavioral economics theory,

individuals must make choices of how to allocate these limited resources to acquire various reinforcers based on the constraints placed on their access. Such constraints can vary in magnitude and take the form of price, behavioral work necessary to gain access, or physical access within the environment [3]. One factor that affects behavioral choice is the *reinforcing value* (RV) of the alternative reinforcers. Food is highly reinforcing because it is necessary to sustain life. Food reinforcement motivates people to eat. Some foods are more reinforcing than others. Among healthy-weight individuals, highly palatable snack foods are more reinforcing than vegetables or fruits [5]. If access to two foods is equal, people usually choose the more reinforcing food. If the reinforcing value of foods is equal, then people would usually choose to engage in the more accessible food. In many situations both access to, and the reinforcing value of, foods are different, and both factors are considered when making the decision of which food to eat [4].

There are individual differences in the RV of food, as food is more reinforcing for obese individuals [6]. The RV of a food is measured by the amount of work a person will perform to gain access to the food. To determine the *relative reinforcing value* (RRV) of one alternative over another, such as a highly reinforcing food over one with lesser reinforcing value, reinforcement can be quantified by providing access to two

*Abbreviations:* DGA, Dietary Guidelines for Americans; RV, reinforcing value; RRV, relative reinforcing value; PROP, 6-n-propylthiouracil; FTO, fat mass and obesity associated gene; SNP, single nucleotide polymorphism; BMI, body mass index; RMR, resting metabolic rate; LMS, Labeled Magnitude Scale; TFEQ, Three-Factor Eating Questionnaire; FAB, Food Attitudes and Behavior Survey; RRS, resonance Raman spectroscopy; ASA24®, Automated Self-Administered 24-h dietary recall system; DEXA, dual energy X-ray absorptiometry.

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foods under independent and concurrent progressive ratio schedules of reinforcement. In such a system the individual must choose which type of food to earn [7]. The RV of addictive substances, such as drugs, can be increased through repeated exposures, this increase in RV is known as *incentive sensitization* [8]. Among non-obese individuals, repeated exposure (daily consumption) of a snack food *decreases* its RV when subjects are told to consume it every day [9]. Among obese individuals who are directed to eat a single snack food daily, the RV *increases*, directly opposite of the effect found in non-obese people [10].

In adults, repeated exposure to both whole grain foods [12], and to fruits [13], increases self-reported consumption. The brain systems responsible for producing motivation are different than those for hedonic responses or “liking” [14]. As predicted by incentive sensitization theory, repeated exposures to the same food in adults is associated with decreased liking in obese women while RV increases, showing that RV is more predictive than liking for eating specific foods [10]. What is unknown is whether the RRV of vegetables among overweight and obese adults can be increased by repeated exposure. The primary aim of this randomized controlled trial is to determine whether the RRV of vegetables compared to a snack food can be increased in overweight and obese individuals through repeated exposure to amounts of vegetables recommended by the DGA. Our primary hypothesis is that repeated exposure to recommended amounts of vegetables will increase vegetable RRV more than exposure to the amount currently consumed. In addition, there are five secondary aims to the study: 1) Determine potential moderators of incentive sensitization of vegetables, including genetic polymorphisms, PROP tasting status, and delay discounting. 2) Determine whether participants *substitute* vegetables for other food groups or whether they are independent reinforcers as determined by a consumption log and by diet record. 3) Determine whether reductions in adiposity are associated with greater substitution of vegetables in the diet. 4) Determine whether consumption of vegetables favorably impacts markers of bone turnover. 5) Assess changes in self-reported secondary outcomes measured by questionnaire such as self-efficacy to eat vegetables. The rationale for secondary aims is found below.

## 2. Specific and secondary aims

### 2.1. Secondary aim 1: potential moderators

PROP tasting status, delay discounting, FTO SNPs and other potential moderators of sensitization of food reinforcement (dietary restraint, disinhibition of eating, hunger, and binge eating) will be examined. Each potential moderator will be tested separately in the primary model.

#### 2.1.1. PROP tasting

Genetic variants in the ability to taste bitter flavors impact liking and consumption of vegetables and may influence the ability to increase vegetable consumption. Bitter taste as measured by 6-n-propylthiouracil (PROP) is associated with polymorphisms in the TAS2R38 taste receptor gene [15]. Individuals who perceive PROP as extremely bitter consume fewer vegetables than those who do not perceive PROP bitterness [15,16].

#### 2.1.2. Delay-discounting

Delay-discounting, or impulsivity, refers to a person's ability to delay gratification. For instance, a person with high impulsivity (low ability to delay-discount), when faced with an opportunity to receive a small reward immediately or a larger reward in a week, would choose the immediate reward. An individual who believes that eating vegetables rather than eating high energy-dense snack foods will lead to better health in the future and has low impulsivity may be more likely to choose the vegetables than someone with the same beliefs who highly discounts future reward. Likewise, when faced with palatable foods, a person may choose to overeat despite having a longer-term goal to

lose weight, and women who find food highly reinforcing and discount the future are more likely to be obese [17]. Adults with a combination of a low ability to delay gratification and high relative reinforcing value of snack foods consume greater energy in ad libitum eating testing [18] and have greater BMI [19]. A low ability to delay gratification for snack foods may moderate the duration that individuals will engage in the RRV task or to work for the snack or vegetable alternatives.

### 2.1.3. Genetic polymorphisms

Genetic differences may also be associated with the relationship between incentive sensitization and RRV of vegetables. The fat mass and obesity associated (FTO) single nucleotide polymorphism (SNP) rs9939609 is associated with increased BMI in both children and adults [20]. Recently, Scheid et al., found that a series of FTO SNPs (rs12921970, rs9936768, rs12446047, rs7199716, rs8049933 and rs11076022) moderate the association of food reinforcement with energy intake [21], indicating that genotype may moderate the effects of incentive sensitization on vegetable reinforcement.

## 2.2. Secondary aims 2 and 3: substitution and adiposity

The public often believes that eating vegetables per se is sufficient for health and weight loss, but in the absence of caloric deficit there is no evidence that vegetables promote weight loss. In addition, it is not known whether the observed associations of greater vegetable and fruit consumption with better health [22–26] are due to nutrients found in them, such as folate, magnesium, potassium, dietary fiber, vitamins A, C, and K, carotenoids, flavonoids and other compounds or due to displacement of less healthy foods [27]. Increasing intake of vegetables leads to a decrease in intake of less-healthy foods in children [28], but little is known about how adults incorporate vegetables into a daily diet. When attempting to eat healthier, vegetables may be independent in that individuals may simply add vegetables to their usual diet without reducing consumption of other foods. Alternatively, as vegetables are low-energy-dense, individuals consuming them may decrease consumption of other foods (substitution). Although unknown, it is unlikely that simply adding vegetables to the diet would result in weight loss or maintenance of a healthy body weight without a decrease in energy intake. Some experimental and longitudinal studies have shown an inverse relationship between vegetable consumption and adiposity, but the mechanisms are unclear and the evidence is weak [29]. One potential reason for the lack of observed evidence is lack of sensitive enough measures of adiposity. Body mass index is not a measure of change in body composition; therefore we will use dual energy X-ray absorptiometry (DEXA) to assess change in adiposity. The current DGA recommends that vegetables should be substituted for higher calorie foods. Distinguishing between the two means of incorporation of vegetables into the diet has implications for behavior change interventions. For instance, if vegetables are found to be added to the diet in an independent fashion in most individuals resulting in overall greater energy consumption, specific emphasis and education would be placed on using vegetables as a substitute for higher energy-dense foods, such as refined grains [30]. A secondary aim of this study is to determine whether vegetables provided to participants as part of the study are added in an independent fashion to the diet or whether they act as substitutes for other foods such as refined grains or snack foods. We hypothesize that due to the low energy density and large volume of vegetables, participants will substitute vegetables for more energy-dense foods, resulting in lower energy intake. We will assess substitution by 2 means; a) self-report of substitution and b) changes in dietary intake based on days of diet recalls. How vegetables are incorporated into the diet may also determine whether increasing vegetable intake affects adiposity. Thus, a third secondary aim is to determine whether greater use of vegetables as substitutes for energy-dense foods is associated with reductions in adiposity. We hypothesize that those participants with greater

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