

Nutrition Briefs

Dietary Patterns

Consumption of a Variety of Vegetables to Meet Dietary Guidelines for Americans' Recommendations Does Not Induce Sensitization of Vegetable Reinforcement Among Adults with Overweight and Obesity: A Randomized Controlled Trial

Casperson SL, Jahns L, Temple JL, Appleton KM, Duke SE, Roemmich JN. *J Nutr.* 2021 Mar 23:nxabo49. doi: 10.1093/jn/nxabo49. [Article link](#)

Significance: Provision of vegetables to adults with overweight and obesity for 8 weeks to induce consumption in line with federal recommendations does not appear to stimulate a long-term increase in vegetable consumption.



Background: Food reinforcement, or the motivation to obtain food, can predict choice and consumption. Vegetable consumption is well below recommended amounts for adults, so understanding how to increase vegetable reinforcement could provide valuable insight into how to increase consumption. **Objectives:** We sought to determine whether daily consumption of the Dietary Guidelines for Americans (DGA) recommendations for vegetable intake induces sensitization of vegetable reinforcement in adults with overweight and obesity. **Methods:** Healthy adults with a BMI ≥ 25 kg/m² who consumed ≤ 1 cup-equivalent of vegetables/day were randomly assigned to a vegetable intervention (VI; n = 55) or an attention control (AC; n = 55) group. The VI consisted of the daily provision of vegetables in the amounts and types recommended by the DGA (~ 270 g/day) for 8 weeks. Participants were followed for an additional 8 weeks to assess sustained consumption. Compliance was measured weekly by resonance Raman light-scattering spectroscopy (RRS). Vegetable reinforcement was tested at weeks 0, 8, 12, and 16 using a computer choice paradigm. **Results:** In the VI group, RRS intensity increased from week 0 to 8 (from 22,990 to 37,220), returning to baseline by week 16 (27,300). No change was observed in the AC group. There was no main effect of treatment (P = 0.974) or time (P = 0.14) and no treatment x time interaction (P = 0.44) on vegetable reinforcement. There was no moderating effect of sex (P = 0.07), age (P = 0.60), BMI (P = 0.46), delay discounting (P = 0.24), 6-n-propylthiouracil taster status (P = 0.15), or dietary disinhibition (P = 0.82) on the change in vegetable reinforcement. **Conclusions:** These findings suggest no effects of the provision of a variety of vegetables to meet DGA recommendations for 8 weeks on vegetable reinforcement and highlight the difficulty in increasing vegetable consumption in adults.

Protein

The Impact of Protein Supplementation on Appetite and Energy Intake in Healthy Older Adults: A Systematic Review with Meta-Analysis

Ben-Harchache S, Roche HM, Corish CA, Horner KM. *Adv Nutr.* 2021 Mar 31;12(2):490-502. doi: 10.1093/advances/nmaa115. [Article link](#)

Significance: Protein supplementation may represent a viable solution to increase protein intakes in healthy older adults without compromising energy intake by suppressing the appetite.

Protein supplementation is an attractive strategy to prevent loss of muscle mass in older adults. However, it could be counterproductive due to adverse effects on appetite. This systematic review and meta-analysis aimed to determine the effects of protein supplementation on appetite and/or energy intake (EI) in healthy older adults. MEDLINE, The Cochrane Library, CINAHL, and Web of Science were searched up to June 2020. Acute and longitudinal studies in healthy adults ≥ 60 y of age that reported effects of protein supplementation (through supplements or whole foods) compared with control and/or preintervention (for longitudinal studies) on appetite ratings, appetite-related peptides, and/or EI were included.

Random-effects model meta-analysis was performed on EI, with other outcomes qualitatively reviewed. Twenty-two studies (9 acute, 13 longitudinal) were included, involving 857 participants (331 males, 526 females). In acute studies (n = 8), appetite ratings were suppressed in 7 out of 24 protein arms. For acute studies reporting EI (n = 7, n = 22 protein arms), test meal EI was reduced following protein preload compared with control [mean difference (MD): -164 kJ; 95% CI: -299, -29 kJ; P = 0.02]. However, when energy content of the supplement was accounted for, total EI was greater with protein compared with control (MD: 649 kJ; 95% CI: 438, 861 kJ; P < 0.00001). Longitudinal studies (n = 12 protein arms) showed a higher protein intake (MD: 0.29 g · kg⁻¹ · d⁻¹; 95% CI: 0.14, 0.45 g · kg⁻¹ · d⁻¹; P < 0.001) and no difference in daily EI between protein and control groups at the end of trials (MD: -54 kJ/d; 95% CI: -300, 193 kJ/d; P = 0.67). While appetite ratings may be suppressed with acute protein supplementation, there is either a positive effect or no effect on total EI in acute and longitudinal studies, respectively. Therefore, protein supplementation may represent an effective solution to increase protein intakes in healthy older adults without compromising EI through appetite suppression.

Lipids

Perspective: The Saturated Fat-Unsaturated Oil Dilemma: Relations of Dietary Fatty Acids and Serum Cholesterol, Atherosclerosis, Inflammation, Cancer, and All-Cause Mortality

Lawrence GD. *Adv Nutr.* 2021 Mar 9;nmab013. doi: 10.1093/advances/nmab013. [Article link](#)

Significance: Misconceptions regarding how dietary lipids regulate serum cholesterol are explored. After careful review of evidence, this review concludes that dietary saturated fats seem to be less harmful than the proposed alternatives.

PUFAs are known to regulate cholesterol synthesis and cellular uptake by multiple mechanisms that do not involve SFAs. Polymorphisms in any of the numerous proteins involved in cholesterol homeostasis, as a result of genetic variation, could lead to higher or lower serum cholesterol. PUFAs are susceptible to lipid peroxidation, which can lead to oxidative stress, inflammation, atherosclerosis, cancer, and disorders associated with inflammation, such as insulin resistance, arthritis, and numerous inflammatory syndromes. Eicosanoids from arachidonic acid are among the most powerful mediators that initiate an immune response, and a wide range of PUFA metabolites regulate numerous physiological processes. There is a misconception that dietary SFAs can cause inflammation, although endogenous palmitic acid is converted to ceramides and other cell constituents involved in an inflammatory response after it is initiated by lipid mediators derived from PUFAs. This article will discuss the many misconceptions regarding how dietary lipids regulate serum cholesterol, the fact that all-cause death rate is higher in humans with low compared with normal or moderately elevated serum total cholesterol, the numerous adverse effects of increasing dietary PUFAs or carbohydrate relative to SFAs, as well as metabolic conversion of PUFAs to SFAs and MUFAs as a protective mechanism. Consequently, dietary saturated fats seem to be less harmful than the proposed alternatives.

Carbohydrates

Do Lower-Carbohydrate Diets Increase Total Energy Expenditure? An Updated and Reanalyzed Meta-Analysis of 29 Controlled-Feeding Studies

Ludwig DS, Dickinson SL, Henschel B, Ebbeling CB, Allison DB. *J Nutr.* 2021 Mar 11;151(3):482-490. doi: 10.1093/jn/nxaa350. [Article link](#)

Significance: Lower-carbohydrate diets transiently reduce total energy expenditure, with a larger increase after about 2.5 weeks. These findings underscore the importance of longer trials to understand chronic macronutrient effects and facilitate weight loss strategies.

Background: The effect of macronutrient composition on total energy expenditure (TEE) remains controversial, with divergent findings among studies. One source of heterogeneity may be study duration, as physiological adaptation to lower carbohydrate intake may require 2 to 3 wk. **Objective:** We tested the hypothesis that the effects of carbohydrate [expressed as % of energy intake (EI)] on TEE vary with time. **Methods:** The sample included trials from a previous meta-analysis and new trials identified in a PubMed search through 9 March 2020 comparing lower- and higher-carbohydrate diets, controlled for EI or body weight. Three reviewers independently extracted data and reconciled discrepancies. Effects on TEE were pooled using inverse-variance-weighted meta-analysis, with between-study heterogeneity assessed using the I² statistic. Meta-regression was used to quantify the influence of study duration, dichotomized at 2.5 wk. **Results:** The 29 trials ranged in duration from 1 to 140 d (median: 4 d) and included 617 participants. Difference in carbohydrate between intervention arms ranged from 8% to 77% EI (median: 30%). Compared with reported findings in the prior analysis (I² = 32.2%), we found greater heterogeneity (I² = 90.9% in the reanalysis, 81.6% in the updated analysis). Study duration modified the diet effect on TEE (P < 0.001). Among 23 shorter trials, TEE was reduced on lower-carbohydrate diets (-50.0 kcal/d;

95% CI: -77.4, -22.6 kcal/d) with substantial heterogeneity ($I^2 = 69.8$). Among 6 longer trials, TEE was increased on low-carbohydrate diets (135.4 kcal/d; 95% CI: 72.0, 198.7 kcal/d) with low heterogeneity ($I^2 = 26.4$). Expressed per 10% decrease in carbohydrate as %EI, the TEE effects in shorter and longer trials were -14.5 kcal/d and 50.4 kcal/d, respectively. Findings were materially unchanged in sensitivity analyses. **Conclusions:** Lower-carbohydrate diets transiently reduce TEE, with a larger increase after ~2.5 wk. These findings highlight the importance of longer trials to understand chronic macronutrient effects and suggest a mechanism whereby lower-carbohydrate diets may facilitate weight loss.

Low-Calorie Sweeteners

The Effects of Low-Calorie Sweeteners on Energy Intake and Body Weight: A Systematic Review and Meta-Analyses of Sustained Intervention Studies

Rogers PJ, Appleton KM. *Int J Obes (Lond)*. 2021 Mar;45(3):464-478. doi: 10.1038/s41366-020-00704-2. [Article link](#)

Significance: The evidence from human intervention studies supports the use of LCS in weight management, with an upper limit of constraint imposed by the amount of added sugar that LCS can displace in the diet.



Previous meta-analyses of intervention studies have come to different conclusions about effects of consumption of low-calorie sweeteners (LCS) on body weight. The present review included 60 articles reporting 88 parallel-groups and cross-over studies ≥ 1 week in duration that reported either body weight (BW), BMI and/or energy intake (EI) outcomes. Studies were analysed according to whether they compared (1) LCS with sugar, (2) LCS with water or nothing, or (3) LCS capsules with placebo capsules. Results showed an effect in favour of LCS vs sugar for BW (29 parallel-groups studies, 2267 participants: BW change, -1.06 kg, 95% CI -1.50 to -0.62, $I^2 = 51\%$), BMI and EI. Effect on BW change increased with 'dose' of sugar replaced by LCS, whereas there were no differences in study outcome as a function of duration of the intervention or participant blinding. Overall, results showed no difference in effects of LCS vs water/nothing for BW (11 parallel-groups studies,

1068 participants: BW change, 0.10 kg, 95% CI -0.87 to 1.07, $I^2 = 82\%$), BMI and EI; and inconsistent effects for LCS consumed in capsules (BW change: -0.28 kg, 95% CI -0.80 to 0.25, $I^2 = 0\%$; BMI change: 0.20 kg/m², 95% CI 0.04 to 0.36, $I^2 = 0\%$). Occurrence of adverse events was not affected by the consumption of LCS. The studies available did not permit robust analysis of effects by LCS type. In summary, outcomes were not clearly affected when the treatments differed in sweetness, nor when LCS were consumed in capsules without tasting; however, when treatments differed in energy value (LCS vs sugar), there were consistent effects in favour of LCS. The evidence from human intervention studies supports the use of LCS in weight management, constrained primarily by the amount of added sugar that LCS can displace in the diet.

Bioactives

Polyphenol Exposure, Metabolism, and Analysis: A Global Exposomics Perspective

Oesterle I, Braun D, Berry D, Wisgrill L, Rompel A, Warth B. *Annu Rev Food Sci Technol*. 2021 Mar 25;12:461-484. doi: 10.1146/annurev-food-062220-090807. [Article link](#)

Significance: The application of newly available exposomic and metabolomic technology including high-resolution mass spectrometry in the context of polyphenols is reviewed. This new era of nontargeted analysis and omic-scale exposure assessment offers a unique chance for better assessing exposure to, as well as metabolism of, polyphenols.

Polyphenols are generally known for their health benefits and estimating actual exposure levels in health-related studies can be improved by human biomonitoring. Here, the application of newly available exposomic and metabolomic technology, notably high-resolution mass spectrometry, in the context of polyphenols and their biotransformation products, is reviewed. Comprehensive workflows for investigating these important bioactives in biological fluids or microbiome-related experiments are scarce. Consequently, this new era of nontargeted analysis and omic-scale exposure assessment offers a unique chance for better assessing exposure to, as well as metabolism of, polyphenols. In clinical and nutritional trials, polyphenols can be investigated simultaneously with the plethora of other chemicals to which we are exposed, i.e., the exposome, which may interact abundantly and modulate bioactivity. This research direction aims at ultimately eluting into a true systems biology/toxicology evaluation of health effects associated with polyphenol exposure, especially during early life, to unravel their potential for preventing chronic diseases.

Sodium

Potassium Chloride-Based Replacers: Modeling Effects on Sodium and Potassium Intakes of the US Population with Cross-Sectional Data from NHANES 2015-2016 and 2009-2010

Murphy MM, Scrafford CG, Barraji LM, Bi X, Higgins KA, Jaykus LA, et al. *Am J Clin Nutr*. 2021 Mar 23; nqabo20. doi: 10.1093/ajcn/nqabo20. [Article link](#)

Significance: Replacement of 294 mg/d sodium with 390 mg/d potassium in the 18 top-ranking sources of dietary sodium in this study predicts a sodium intake reduction to a level consistent with the short-term intake goal targeted by the FDA of 3000 mg/d, with the mean potassium intake remaining in the range recommended for the apparently healthy population.



This research was supported by the IAFNS [Sodium Committee](#).

Background: Sodium intake in the USA exceeds recommendations. The replacement of added sodium chloride (NaCl) with potassium chloride (KCl) provides a potential strategy to reduce sodium intake. **Objective:** The purpose of this study was to quantitatively estimate changes in intakes of sodium and potassium by the US population assuming use of potassium-based NaCl replacers in top dietary sodium sources. **Methods:** Data collected in the What We Eat in America (WWEIA) component of the 2015-2016 and 2009-2010 NHANES were used to identify top-ranking sources of dietary sodium among the population aged 2 y and older based on contributions from food categories aligning with the FDA draft guidance for voluntary sodium reduction. Predicted nutrient intakes were estimated in models assuming total and feasible and practical (F&P) replacement of added NaCl with KCl in foods and ingredients within the top food sources of sodium. An expert elicitation was conducted to collect information on the F&P KCl replacement of added NaCl. **Results:** Using 2015-2016 consumption data, the total replacement of added NaCl with KCl in the 18 top-ranking sources of dietary sodium results in a predicted sodium intake of 2004 mg/d from the replacement of 1406 mg/d sodium with 1870 mg/d potassium as KCl. Modeled F&P replacement predicted sodium intakes of 3117 mg/d (range of 2953 to 3255 mg/d) from the replacement of 294 mg/d sodium (155 to 457 mg/d) with 390 mg/d potassium (206 to 608 mg/d). Similar results are seen with 2009-2010 data. **Conclusions:** The F&P replacement of NaCl with KCl in top-ranking sources of dietary sodium modeled in this study can result in decreased sodium to a level consistent with the short-term intake goal targeted by the FDA of 3000 mg/d, with the mean potassium intake remaining in the range recommended for the apparently healthy population.

Gut Microbiome

Diet and the Microbiota-Gut-Brain Axis: Sowing the Seeds of Good Mental Health

Berding K, Vlckova K, Marx W, Schellekens H, Stanton C, Clarke G, et al. *Adv Nutr*. 2021 Mar 9:nmaa181. doi: 10.1093/advances/nmaa181. [Article link](#)

Significance: Several mechanisms for gut-to-brain communication have been identified, including microbial metabolites, immune, neuronal and metabolic pathways—some of which could be prone to dietary modulation. Focusing on these could improve brain and mental health.

Over the past decade, the gut microbiota has emerged as a key component in regulating brain processes and behavior. Diet is one of the major factors involved in shaping the gut microbiota composition across the lifespan. However, whether and how diet can affect the brain via its effects on the microbiota is only now beginning to receive attention. Several mechanisms for gut-to-brain communication have been identified, including microbial metabolites, immune, neuronal, and metabolic pathways, some of which could be prone to dietary modulation. Animal studies investigating the potential of nutritional interventions on the microbiota-gut-brain axis have led to advancements in our understanding of the role of diet in this bidirectional communication. In this review, we summarize the current state of the literature triangulating diet, microbiota, and host behavior/brain processes and discuss potential underlying mechanisms. Additionally, determinants of the responsiveness to a dietary intervention and evidence for the microbiota as an underlying modulator of the effect of diet on brain health are outlined. In particular, we emphasize the understudied use of whole-dietary approaches in this endeavor and the need for greater evidence from clinical populations. While promising results are reported, additional data, specifically from clinical cohorts, are required to provide evidence-based recommendations for the development of microbiota-targeted, whole-dietary strategies to improve brain and mental health.