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## Dietary Patterns

### Circadian Influences on Feeding Behavior

Susanne E la Fleur, Aurea S Blancas-Velazquez, Dirk Jan Stenvers, Andries Kalsbeek. *Neuropharmacology*. 2024, 9:15:256:110007. doi: 10.1016/j.neuropharm.2024.110007. [Article link](#)

Feeding, like many other biological functions, displays a daily rhythm. This daily rhythmicity is controlled by the circadian timing system of which the central master clock is located in the hypothalamic suprachiasmatic nucleus (SCN). Other brain areas and tissues throughout the body also display rhythmic functions and contain the molecular clock mechanism known as peripheral oscillators. To generate the daily feeding rhythm, the SCN signals to different hypothalamic areas with the lateral hypothalamus, paraventricular nucleus and arcuate nucleus being the most prominent. With respect to the rewarding aspects of feeding behavior, the dopaminergic system is also under circadian influence. However the SCN projects only indirectly to the different reward regions, such as the ventral tegmental area where dopamine neurons are located. In addition, high palatable, high caloric diets have the potential to disturb the normal daily rhythms of physiology and have been shown to alter for example meal patterns. Around a meal several hormones and peptides are released that are also under circadian influence. For example, the release of postprandial insulin and glucagon-like peptide following a meal depend on the time of the day. Finally, we review the effect of deletion of different clock genes on feeding behavior. The most prominent effect on feeding behavior has been observed in Clock mutants, whereas deletion of Bmal1 and Per1/2 only disrupts the day-night rhythm, but not overall intake. Data presented here focus on the rodent literature as only limited data are available on the mechanisms underlying daily rhythms in human eating behavior.

## Carbohydrates

### Nutritional and Functional Perspectives of Pseudocereals

Alisha Nandan, Pankaj Koirala, Abhishek Dutt Tripathi, Urvashi Vikranta, Kartik Shah, Abhishek J Gupta, Aparna Agarwal, et. al. *Food Chem*. 2024 Aug 1:448:139072. doi: 10.1016/j.foodchem.2024.139072. [Article link](#)


An increase in the consumption of carbohydrate-rich cereals over past few decades has led to increased metabolic disorders in population. This nutritional imbalance in diets may be corrected by substituting cereal grains with pseudocereals that are richer in high-quality proteins, dietary fibers, unsaturated fats, and bioactive compounds (e.g., polyphenols and phytosterols) as compared to cereal grains. These nutrients have been associated with numerous health benefits, such as hypolipidemic, anti-inflammatory, anti-hypertensive, anti-cancer, and hepatoprotective properties, and benefits against obesity and diabetes. In this review, the nutritional composition and health benefits of quinoa, amaranth, and buckwheat are compared against wheat, maize, and rice. Subsequently, the processing treatments applied to quinoa, amaranth, and buckwheat and their

applications into food products are discussed. This is relevant since there is substantial market potential for both pseudocereals and functional foods formulated with pseudocereals. Despite clear benefits, the current progress is slowed down by the fact that the cultivation of these pseudocereals is limited to its native regions. Therefore, to meet the global needs, it is imperative to support worldwide cultivation of these nutrient-rich pseudocereals.

## Protein

### Associations between Essential Amino Acid Intake and Functional Health Outcomes in Older Adults: Analysis of the National Health and Nutrition Examination Survey, 2001-2018

Susan N Cheung, Harris R Lieberman, Stefan M Pasiakos, Victor L Fulgoni 3rd, Claire E Berryman. *Curr Dev Nutr.* 2024 Aug;8(8):104411. doi: 10.1016/j.cdnut.2024.104411. [Article link](#)

 This research was supported by IAFNS [Protein Committee](#)

**Background:** The relationships between habitual essential amino acid (EAA) intake and body composition, muscle strength, and physical function in older US adults are not well defined. **Objectives:** This cross-sectional study evaluated associations between usual EAA intakes and body composition, muscle strength, and physical function in US adults  $\geq 65$  y. **Methods:** The Food and Nutrient Database for Dietary Studies (FNDDS) 2001-2018 was linked to the US Department of Agriculture Standard Reference database to access existing amino acid composition data for FNDDS ingredients. FNDDS ingredients without existing amino acid composition data were matched to similar ingredient codes with available data. Usual EAA, leucine, lysine, and sulfur-containing amino acid (SAA; methionine + cysteine) intakes (g/d) from National Health and Nutrition Examination Survey 2001-2018 were calculated for individuals  $\geq 65$  y ( $n = 10,843$ ). Dependent variables included muscle strength measured by isometric grip test, body mass index (BMI), waist circumference, dual-energy X-ray absorptiometry-measured appendicular lean mass and whole-body fat mass, and self-reported physical function (that is, tasks of daily living). Regression analyses were used to determine covariate-adjusted relationships between EAA, leucine, lysine, and SAA intake and functional health outcomes.  $P < 0.0013$  was considered significant. **Results:** EAA, leucine, lysine, and SAA intakes, covaried with physical activity level and usual protein intake, were not associated with muscle strength or self-reported physical function in males or females or with body composition in males. EAA intakes were positively associated with waist circumference in females ( $\beta \pm \text{SEM}$ ,  $2.1 \pm 0.6$  cm,  $P = 0.0007$ ). Lysine intakes were positively associated with BMI ( $3.0 \pm 0.7$  kg/m<sup>2</sup>,  $P < 0.0001$ ) and waist circumference ( $7.0 \pm 1.7$  cm,  $P = 0.0001$ ) in females. **Conclusions:** Habitual EAA, leucine, lysine, and SAA intakes, covaried with physical activity level and usual protein intake, were not associated with lean mass, muscle strength, or physical function in adults  $\geq 65$  y. However, EAA intakes, particularly lysine, were positively associated with measures of adiposity in older females.

### Nutritional Considerations During Major Weight Loss Therapy: Focus on Optimal Protein and a Low-Carbohydrate Dietary Pattern

Jeff S Volek, Madison L Kackley, Alex Buga. *Curr Nutr Rep.* 2024 9;13(3):422-443. doi: 10.1007/s13668-024-00548-6. [Article link](#)

**Purpose of Review:** Considering the high prevalence of obesity and related metabolic impairments in the population, the unique role nutrition has in weight loss, reversing metabolic disorders, and maintaining health cannot be overstated. Normal weight and well-being are compatible with varying dietary patterns, but for the last half century there has been a strong emphasis on low-fat, low-saturated fat, high-carbohydrate based approaches. Whereas low-fat dietary patterns can be effective for a subset of individuals, we now have a population where the vast majority of adults have excess adiposity and some degree of metabolic impairment. We are also entering a new era with greater access to bariatric surgery and approval of anti-obesity medications (glucagon-like peptide-1 analogues) that produce substantial weight loss for many people, but there are concerns about disproportionate loss of lean mass and nutritional deficiencies. **Recent Findings:** No matter the approach used to achieve major weight loss, careful attention to nutritional considerations is necessary. Here, we examine the recent findings regarding the importance of adequate protein to maintain lean mass, the rationale and evidence supporting low-carbohydrate and ketogenic dietary patterns, and the potential benefits of including exercise training in the context of major weight loss. While losing and sustaining weight loss has proven challenging, we are optimistic that appli-

cation of emerging nutrition science, particularly personalized well-formulated low-carbohydrate dietary patterns that contain adequate protein (1.2 to 2.0 g per kilogram reference weight) and achieve the beneficial metabolic state of euketonemia (circulating ketones 0.5 to 5 mM), is a promising path for many individuals with excess adiposity.

## Low- and No-Calorie Sweeteners

### An Overview of Reviews on the Association of Low-Calorie Sweetener Consumption With Body Weight and Adiposity

Higgins KA, Rawal R, Kramer M, Baer DJ, Yerke A, Klurfeld DM. *Advances in Nutrition*, Aug. 8, 2024. doi.org/10.1016/j.advnut.2024.100239 [Article link](#)



This research was supported by IAFNS [Low- and No-Calorie Sweeteners Committee](#)

**Background:** Numerous systematic reviews (SR) and meta-analyses (MA) on low calorie sweeteners (LCS) have been published in recent years, concluding that LCS have beneficial, neutral, or detrimental effects on various health outcomes, depending on the review. **Objectives:** The objective of this overview of reviews was to determine how the methodologies of SR investigating the association between LCS consumption and body weight (BW) influence their findings and whether MA results can provide a consistent estimated effect. **Methods:** Systematic searches of PubMed, Scopus, and Cochrane Library were conducted in November 2022 to identify SR of randomized controlled trials (RCT) or non-randomized studies (NRS) investigating the association between LCS consumption and BW. The methods, MA results, and conclusions were extracted from each eligible SR. **Results:** Of the 985 search results, 20 SR evaluated the association between LCS and BW, drawing from publications of 75 RCT, 42 prospective cohort studies, and 10 cross-sectional studies. There was a considerable lack of overlap of studies included within each SR attributed, in part, to the inclusion of studies based on design; thus, each SR synthesized results from distinctly different studies. Evidence synthesis methods were heterogeneous and often opaque, making it difficult to determine why results from certain studies were excluded or why disparate results were observed between SR. **Conclusions:** SR investigating the effect of LCS on BW implement different methodologies to answer allegedly the same question, drawing from a different set of heterogeneous studies, ignoring the basic assumptions required for MA, resulting in disparate results and conclusions. Previous MA show the large effects of study design, which results in inconsistent estimates of the effect of LCS on BW between MA of RCT and NRS. Given the availability of long-term RCT, these studies should be the basis of determining causal relationships (or lack thereof) between LCS and BW.

## Cognitive Health

### The Effect of Whole-Diet Interventions on Memory and Cognitive Function in Healthy Older Adults — A Systematic Review

Lina Tingo, Cecilia Bergh, Julia Rode, Maria Fernanda Roca Rubio, Jonas Persson, Linnea Brengesio Johnson, Lotte H Smit, et. al. *Adv Nutr*. 2024 Aug 16:100291. doi: 10.1016/j.advnut.2024.100291. [Article link](#)

**Background:** An increasing number of cross-sectional studies suggests that diet may impact memory and cognition in healthy older adults. However, randomized, controlled trials investigating the effects of whole-diet interventions on memory and cognition in healthy older adults are rather rare and conflicting results are often reported. **Objective:** Therefore, a systematic review was conducted to compile the current evidence regarding the potential effects of whole-diet interventions on 1) memory and, 2) other cognitive outcomes in older adults. **Methods:** Studies that reported on randomized, controlled trials with dietary interventions in healthy older adults (60 yrs. and older) were included. Studies utilizing supplements, single food items or trials in specific patient groups (ie neurodegenerative diagnoses) were excluded. **Results:** For the 23 included articles, the main outcomes examined fell into one or more of the following categories: cognitive task-based outcomes related to memory, other cognitive task-based outcomes, and additional outcomes related to cognitive function or disease risk. Three of the studies that investigated dietary interventions alone and two multi-domain study showed positive effects on memory function, whereas five multi-domain interventions and one intervention that focused on diet alone showed positive effects on other cognitive outcomes. **Conclusions:** The effect of randomized, controlled whole-diet interventions on memory and cognitive function in healthy older adults is modest and inconclusive, highlighting the need for more well-designed, sufficiently powered studies. Furthermore, the potential mechanisms by which diet impacts cognition in healthy aging need to be elucidated.

## Driving Dietary Guidance Through Innovative Approaches to Cognition and Nutrition

Marie Latulippe. *Nutrition Today*. Aug. 23, 2024. DOI: 10.1097/NT.0000000000000698. [Article link](#)



This effort was supported by IAFNS [Cognitive Health Committee](#)

In the 2020 final report, the Dietary Guidelines Advisory Committee noted it faced a literature having “considerable variation in testing methods, inconsistent validity and reliability of cognitive testing methods, and differences between dietary patterns and cognitive outcomes examined.” All of this constrained their ability to draw conclusions. Interestingly, the 2025-2030 DGAC has decided to pursue a similar topic, rephrasing the question slightly: “What is the relationship between dietary patterns and risk of cognitive decline, dementia, and Alzheimer’s disease?”

## Lipids

### Sex Differences in Energy Metabolism: A Female-Oriented Discussion

Barbara N Sanchez, Jeff S Volek, William J Kraemer, Catherine Saenz, Carl M Maresh. *Sports Med*. 2024 Aug;54(8):2033-2057. doi: 10.1007/s40279-024-02063-8. [Article link](#)

The purpose of this review is to delineate aspects of energy metabolism at rest and during exercise that may be subject to sex differences and the potential underlying mechanisms involved. It focuses on distinct aspects of female physiology with an oriented discussion following the reproductive life stages of healthy, eumenorrheic females, including premenopausal time frames, pregnancy, perimenopause, and menopause. Finally, this review aims to address methodological challenges surrounding sexual dimorphism in energy metabolism investigations and confounding factors in this field. During resting conditions, females tend to have higher rates of non-oxidative free fatty acid clearance, which could contribute to lower respiratory exchange ratio measures. At the same time, carbohydrate energy metabolism findings are mixed. In general, females favor lipid energy metabolism during moderate-intensity exercise, while men favor carbohydrate energy metabolism. Factors such as age, dietary intake, genetics, and methodological decisions confound study findings, including properly identifying and reporting the menstrual cycle phase when female subjects are eumenorrheic. Pregnancy presents a unique shift in physiological systems, including energy metabolism, which can be observed at rest and during exercise. Changes in body composition and hormonal levels during the post-menopausal period directly impact energy metabolism, specifically lipid metabolism. This change in physiological state factors into the evidence showing a reduction in our understanding of sex differences in lipid metabolism during exercise in older adults. This review reveals a need for a focused understanding of female energy metabolism that could help exercise and nutrition professionals optimize female health and performance across the lifespan.

## Sodium

### Thyroid Function and Iodine Intake: Global Recommendations and Relevant Dietary Trends

Sarah C Bath. *Nat Rev Endocrinol*. 2024 Aug;20(8):474-486. doi: 10.1038/s41574-024-00983-z. [Article link](#)

Iodine is a micronutrient that is essential for thyroid hormone production. Adequate iodine intake is especially important during pregnancy and early life, when brain development is dependent on thyroid hormones. Iodine intake recommendations vary around the world, but most recommendations generally reflect the increased requirements during pregnancy and lactation, although adequate iodine intake before pregnancy is also important. Tremendous progress has been made in improving iodine intake across the world over the past 30 years, mainly through salt-iodization programmes. However, in countries without strong iodine fortification programmes, and with shifts in dietary patterns, a need has arisen for health organizations, governments and clinicians to ensure that adequate iodine is consumed by everyone in the population. For example, in countries in which adequate iodine intake depends on individual food choice, particularly of iodine-rich milk and dairy products, intake can be highly variable and is also vulnerable to changing dietary patterns. In this Review, iodine is considered in the wider context of the increasing prevalence of overweight and obesity, the dietary trends for salt restriction for cardiovascular health and the increasing uptake of plant-based diets.



### Metformin-Induced Changes in the Gut Microbiome and Plasma Metabolome are Associated with Cognition in Men

Marisel Rosell-Díaz, Anna Petit-Gay, Clàudia Molas-Prat, Laura Gallardo-Nuell, Lluís Ramió-Torrentà, Josep Garre-Olmo, Vicente Pérez-Brocal et. al. *Metabolism*. 2024 Aug;157:155941. doi: 10.1016/j.metabol.2024.155941. [Article link](#)

**Background:** An altered gut microbiome characterized by reduced abundance of butyrate producing bacteria and reduced gene richness is associated with type 2 diabetes (T2D). An important complication of T2D is increased risk of cognitive impairment and dementia. The biguanide metformin is a commonly prescribed medication for the control of T2D and metformin treatment has been associated with a significant reduction in the risk of dementia and improved cognition, particularly in people with T2D. **Aim:** To investigate the associations of metformin use with cognition exploring potential mechanisms by analyzing the gut microbiome and plasma metabolome using shotgun metagenomics and HPLC-ESI-MS/MS, respectively. **Methods:** We explored two independent cohorts: an observational study (Aging Imageomics) and a phase IV, randomized, double-blind, parallel-group, randomized pilot study (MEIFLO). From the two studies, we analyzed four study groups: (1) individuals with no documented medical history or medical treatment (n = 172); (2) people with long-term T2D on metformin monotherapy (n = 134); (3) people with long-term T2D treated with oral hypoglycemic agents other than metformin (n = 45); (4) a newly diagnosed T2D subjects on metformin monotherapy (n = 22). Analyses were also performed stratifying by sex. **Results:** Several bacterial species belonging to the Proteobacteria (*Escherichia coli*) and Verrucomicrobia (*Akkermansia muciniphila*) phyla were positively associated with metformin treatment, while bacterial species belonging to the Firmicutes phylum (*Romboutsia timonensis*, *Romboutsia ilealis*) were negatively associated. Due to the consistent increase in *A. muciniphila* and decrease in *R.ilealis* in people with T2D subjects treated with metformin, we investigated the association between this ratio and cognition. In the entire cohort of metformin-treated T2D subjects, the *A.muciniphila/R.ilealis* ratio was not significantly associated with cognitive test scores. However, after stratifying by sex, the *A.muciniphila/R. ilealis* ratio was significantly and positively associated with higher memory scores and improved memory in men. Metformin treatment was associated with an enrichment of microbial pathways involved in the TCA cycle, and butanoate, arginine, and proline metabolism in both cohorts. The bacterial genes involved in arginine metabolism, especially in production of glutamate (*astA*, *astB*, *astC*, *astD*, *astE*, *putA*), were enriched following metformin intake. In agreement, in the metabolomics analysis, metformin treatment was strongly associated with the amino acid proline, a metabolite involved in the metabolism of glutamate. **Conclusions:** The beneficial effects of metformin may be mediated by changes in the composition of the gut microbiota and microbial-host-derived co-metabolites.

## Emerging Science

*Emerging Areas: -Omics and Aging*

### Nonlinear Dynamics of Multi-Omics Profiles During Human Aging

Xiaotao Shen, Chuchu Wang, Xin Zhou, Wenyu Zhou, Daniel Hornburg, Si Wu, Michael P Snyder. *Nat Aging*. 2024 Aug 14. doi: 10.1038/s43587-024-00692-2. [Article link](#)

Aging is a complex process associated with nearly all diseases. Understanding the molecular changes underlying aging and identifying therapeutic targets for aging-related diseases are crucial for increasing healthspan. Although many studies have explored linear changes during aging, the prevalence of aging-related diseases and mortality risk accelerates after specific time points, indicating the importance of studying nonlinear molecular changes. In this study, we performed comprehensive multi-omics profiling on a longitudinal human cohort of 108 participants, aged between 25 years and 75 years. The participants resided in California, United States, and were tracked for a median period of 1.7 years, with a maximum follow-up duration of 6.8 years. The analysis revealed consistent nonlinear patterns in molecular markers of aging, with substantial dysregulation occurring at two major periods occurring at approximately 44 years and 60 years of chronological age. Distinct molecules and functional pathways associated with these periods were also identified, such as immune regulation and carbohydrate metabolism that shifted during the 60-year transition and cardiovascular disease, lipid and alcohol metabolism changes at the 40-year transition. Overall, this research demonstrates that functions and risks of aging-related diseases change nonlinearly across the human lifespan and provides insights into the molecular and biological pathways involved in these changes.

## Engage with IAFNS

### **Low- and No-Calorie Sweeteners and Body Weight: How Systematic Reviews on Low Calorie Sweeteners Produce Disparate Results**

September 10, 2024, Virtual Event

This webinar will decipher how systematic review methodologies influence the findings produced when investigating the association between LNCS consumption and body weight.

[Register here](#)

### **IAFNS Food Microbiology Research Roundtable**

September 11, 2024, Washington, DC

The IAFNS Food Microbiology Committee will be hosting a Research Roundtable to identify research gaps in microbial food safety.

[Register here](#)

### **Menopause, Cognition and Nutrition: Understanding the Intersection**

September 11, 2024, Virtual Event

Women's health and related knowledge and research gaps have been highlighted as focus grows on incorporating population diversity into research.

[Register here](#)

### **Nutritional Considerations for Anti-Obesity Medications: Evidence-Based Guidance**

September 12, 2024, Virtual Event

Join IAFNS as Dr. Jaime Almandoz presents recent work translating the clinical experience with 'new' obesity medications into practical nutritional considerations and guidance that can support effective use.

[Register here](#)

### **Towards More Rigorous and Informative Nutrition Epidemiology**

September 25, 2024, Virtual, Event

This IAFNS meeting will discuss approaches for stronger designs, measurements, analyses, execution, and reporting to navigate the space between the differences between randomized trials and ordinary nutrition epidemiology.

[Register here](#)

### **American Association of Family Physicians – FMX 2024**

September 24-28, 2024, Phoenix, AZ

IAFNS-supported researchers will make a presentation before family physicians entitled: 'Live Dietary Microbes: Evidence That Intake Supports Health.'

[Register here](#)

### **Low- and No-Calorie Sweeteners Stakeholder Exchange**

October 15, 2024, Washington, DC

IAFNS will host its annual Low- and No-Calorie Sweeteners Stakeholder Exchange to elicit input.

[Register here](#)



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