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The effect of a brain-targeted beverage on cognition in an older population

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ABSTRACT

Dementia is untreatable, so dietary modification may be the best strategy for prevention. Paradoxically, the typical American diet increases dementia risk and worsens cognition. The purpose of this prospective, single-arm, six-week, study was to explore the effects of a nutrient-dense, brain-targeted beverage on cognitive function. Seven individuals (86% females; 59 ± 6 years) consumed two of the beverages daily. All summary measures of the Cognitive Failure Questionnaire improved after 3 weeks, and again more at week 6. Most (67%) of the quality of life questions improved. An easy-to-prepare beverage containing nutrients shown to support the brain helps improve cognition.

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Introduction

Dementia is the greatest global challenge for health and social care in the 21st century [1]. It occurs mainly in people older than 65 years, so the increases seen in numbers and costs are driven by increased longevity. No treatments are available, so prevention is the best way to slow the incidence of dementia [2].

Besides age, modifiable risk factors of dementia are mostly related to the lifestyle factors of diet and exercise [1]. Diet-related chronic conditions like cardiovascular disease and type 2 diabetes mellitus also increase risk. Adopting a healthy lifestyle can reduce risk of dementia even in those with a high genetic risk [3]. Genetically-predisposed individuals who adopt a healthy lifestyle are reported to have only a 1.13% risk compared to 1.78% for those at risk who did not adopt a healthy lifestyle.

Up until 2010, scientists at the National Institutes of Health and other prominent institutes all but dismissed diet as having any role in preventing Alzheimer's disease [4]. However, eight years later, 109 scientists from 36 countries wrote a letter to the G8 Dementia Summit in London, stating that enough evidence exists to support a role for consuming a healthy, nutrient-dense diet because it reduces the risk of Alzheimer's disease. Other risk factors identified in this correspondence included maintaining a healthy body weight, not smoking, and avoiding hypertension. Adoption of these factors can reduce the risk of dementia by 35%, which has more of an impact than genetic risk factors.

Dietary modifications to the reduce risk of dementia have been studied extensively and the results are remarkably consistent. Adopting healthy diets such as the Mediterranean diet and the MIND diet have been shown to improve cognitive function and reduce dementia risk in an aging population [5,6]. The MIND diet reduced cognitive decline by the equivalent of 7.5 years. Others have shown that both diets are likely to be effective because they are rich in fruits and vegetables [7]; low in saturated fats [8]; and high in polyunsaturated fats and are nutrient-dense [8-10]. Despite these positive findings on what dietary patterns to adopt to slow cognitive decline, most Americans do not consume foods that are found in the Mediterranean diet or MIND diet [5-6,11]. Specifically related to cognition, Americans eat too few fruits and vegetables, too many foods rich in saturated fats, and do not get enough of the essential nutrients.

Besides food components, bioactive compounds have shown promise in enhancing cognitive function. Phosphatidylserine (PS) supports many aspects of human cognitive function including: short-term memory, long-term memory, creating new memories, retrieving old memories, learning and recalling information, focusing, concentrating, reasoning and problem solving, and communicating skills [12-14]. Two naturally occurring compounds not ordinarily consumed in the diet, acetyl-L carnitine (ALC) and alpha-lipoic acid (ALA), are highly effective anti-oxidants [15]. Both ingredients protect brain cells from oxidation, allowing for maintenance of healthy energy production at a cellular level. N-acetyl cysteine (NAC) is a potent antioxidant offering protection to the brain cell mitochondria, thereby supporting memory [16]. Epidemiological studies indicate that moderate consumption of red wine, rich in quercetin, may lower the relative risk for Alzheimer's dementia [17]. Coenzyme Q-10, another antioxidant, may protect against mitochondrial brain cell damage [18]. Brain mitochondria have antioxidant defenses inferior to the greater cell, making mitochondrial DNA 10-100 times more likely to

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become damaged than nuclear DNA. The exact mechanism of how antioxidants protect against mitochondrial damage is unknown, but oxidation is a universal contributor to all neuro-degenerative disorders.

The purpose of this prospective study is to evaluate the effect of a nutrient-rich beverage with bioactive compounds on cognitive function in an older population.

Methods

This is a single-armed, prospective study. Baseline data were obtained for cognition using two surveys, dietary habits, quality of life, exercise routines, and anthropometry. Subjects then began consuming two brain-targeted shakes daily for 6 weeks. Weekly data were monitored for compliance with the dietary intervention and quality of life. At weeks 3 and 6, additional cognitive testing using the same surveys occurred. Data were stored in a HIPAA-compliant area and no participant was identified by name.

Participants

Subjects were recruited through social media (e.g., Facebook, Instagram) and asked if they were worried about cognitive decline. Entry criteria included: being age 50-70 years, having a Body Mass Index (BMI) 25-40 kg/m^2, having not been diagnosed with Alzheimer's disease or mild cognitive impairment (MCI), and may have a chronic condition like diabetes or high blood pressure, but it is well controlled. All participants signed a consent that abided by the *Helsinki Declaration*, seventh revision and willingly participated in the study. All participants were assigned a coach to help with dietary compliance and completing the electronically-submitted data collection forms that included information about anthropometry (body weight and waist circumference), and questions related to cognition and quality of life.

Dietary intervention and anthropometry

Participants were provided two servings of a brain-targeted beverage daily for 6 weeks at no charge. The product was provided as a powder, which could be reconstituted with water, milk, or a milk substitute (e.g., nut, soy). Each serving contained one-third of the Daily Value for every vitamin and mineral, except sodium and chloride (http://nutrientfoods.com). At least 25% Adequate Intakes (AI) for omega-3s and 33% of the AI for choline (370 mg; based on the need of males) were included in each serving. Free nutrition coaching was provided to assist with questions about the dietary intervention and aid compliance. Each week, the participants reported how many of the two brain-targeted beverages they consumed and how much of each they drank.

Dietary information potentially related to cognitive function was obtained at baseline, including the frequency of intake of: red meat/cold cuts, alcohol, seed/nut intake, fruit and vegetables, fast food, sugar, and fish.

Participants provided body weight measurements weekly, and waist circumference readings at baseline, week 3, and week 6 [19].

Cognitive testing

*Cognitive Failures Questionnaire (CFQ) [*20]

The CFQ probes minor mistakes that most people make occasionally but sometimes they happen more frequently. The survey was developed to assess the frequency that individuals experience these mistakes in cognitive function, such as absent-mindedness, in everyday life -- slips and errors of perception, memory, and motor functioning. The CFQ scoring system used for each question was: 0=Never; 1=Very rarely; 2=Occasionally; 3=Quite often; 4=Very often. Summed sub-scale scores with similar attributes were also determined for a Total CFQ score; Forgetfulness (a tendency to forget something that is known or planned, for example, names, intentions, appointments, and words); Distractibility (mainly in social situations such as being absentminded or easily disturbed with one person or in a group); and False triggering (interrupted ability to pay attention leading to making errors in thinking and acting logically).

Subjective Memory Questionnaire (SMQ)

The Subjective Memory Questionnaire (SMQ) that includes 43 questions has been validated [21,22]. However, we used a sub-set of these questions (i.e., 33) that specifically examine difficulty with memory [23]. A sliding-scale scoring system 1 (Poor), 3 (Good), and 7 (Excellent) was used, with higher scores relating to fewer subjective memory difficulties. The summed scores relates to: ≥200 = minimal subjective memory difficulties; 100-200 = noticing a moderate degree of memory challenge; and below 100 = a greater self-awareness of memory difficulties.

Quality of life questions

At baseline and weekly, subjects answered eight questions about their quality of life. Each was rated on a scale of 1 to 5, with 5 being the best and 1 being the worst. The questions asked were: general feeling, fullness, mood, energy level, any gastrointestinal symptoms (GI), sleep quality, appearance, and diet quality. Data were compared at baseline, week 3, and week 6, and the percentage change between the mean scores at baseline and week 6 was calculated.

Statistics

Data are presented as means ± standard deviations. Both unpaired t-test and paired t-test were used to determine significance of the cognitive function tests.

Results

Eight subjects started the study and seven completed it (88% retention). One male and six females participated with an average age of 59 ± 6 years. The mean body mass index of the group was 30 ± 5 kg/m^2. The male had a normal waist circumference (91 cm), but the mean waist circumference of the females exceeded the healthy limit of ≤ 88 cm (97 ± 14 cm). Patients remained weight stable and no change occurred in waist circumference (data not shown). This was an objective of the study so weight change would not be a confounding variable to changes in cognitive function.

One participant had no co-morbidities, three had hypertension, and one each had these conditions: arthritis, small cerebral vessel ischemic disease, and prediabetes. Five required medications to treat these conditions.

Baseline dietary and exercise information

All participants claimed that they were not provided dietary counseling by a healthcare professional about preserving

memory with aging. At baseline, participants provided information about typical dietary intakes related to cognitive function. About one-third claimed they rarely consumed sugar (29%), many (86%) consumed fish once weekly, about half (42%) rarely ate at fast food restaurants, nearly half (43%) consumed less than one serving of red meat and cold cuts weekly, about three-quarters of the group (71%) consumed one or fewer servings of fruits and vegetables daily, most (81%) ate seeds or nuts once or less each week, and about three-quarters (71%) had at least one alcoholic beverage per week.

Four of seven subjects regularly used dietary supplements: four took fish or krill oil, multivitamins, vitamin D, glucosamine, turmeric, probiotics, and prebiotics. Five participants exercised weekly for a total of 30-60 minutes total with walking being the most common form.

Dietary intervention

During the first three weeks, four subjects consumed the two prescribed brain-targeted beverages daily, two others consumed about one and one-half of the two, and one participant consumed one of the two beverages. Those who consumed less than the recommended amount reported to the assigned coach that they found the two beverages over-satiating. Subsequently, compliance with the dietary regimen improved and by week 6, all were consuming the two assigned brain-targeted beverages. Four participants prepared the beverage with water and three used milk (e.g., cow, coconut), and the majority added other foods like peanut butter, berries, syrups, and ice.

Cognitive test

Cognitive Failures questionnaire (CFQ)

Each of the summed sub-scale scores improved over time (i.e., scores went down) (Table 1). At week 3, compared to baseline, Total CFQ score was 20% lower; Forgetfulness was 14% lower, Distractibility was 26% lower, and False triggering was 19% lower. At week 6, compared to baseline, each sub-scale score improved more. The Total CFQ score was 36% lower, Forgetfulness was 33 % lower, Distractibility was 35% lower, and False triggering was 44% lower. All but one participant experienced improvement in the Total CFQ score.

All 25 individual responses improved over 6 weeks and mimicked the summed sub-scale scores (Table 2). Most (60%) of the responses improved compared to baseline at week 3, and further improvement was observed at week 6 compared to both baseline and week 3. The questions that exhibited the most improvement were for no longer forgetting where to turn off a road (75% lower score); no longer losing track of paying bills and now noticing sign posts (both with 67% lower scores); and less forgetfulness of whether a light was turned off or a door locked (50% lower score).

Subjective Memory questionnaire responses (SMQ)

The mean baseline total score for the 33 SMQ questions represented a group that had a modest appreciation of losing memory (175.71 ± 34.44) (Table 3). Three subjects had normal memory (a score of 200 points or more) and four had modest impairment (scores of 100-200) at baseline. Compared to baseline, at week 3, the improvement of the total score was 7% and at week 6, improvement doubled (14%). Those with higher total scores at the beginning of the study (worse cognition) improved most (Figure 1).

Some individual SMQ questions yielded significant improvements (data not shown). Participants were better able to remember what someone recently told them (P = 0.04, week 3 compared to baseline; P = 0.005, week 6 compared to baseline); and were able to remember the opening paragraph after completing an article (P = 0.02, baseline compared to

Table 1. Changes in summed sub-scale scores for the Cognitive Failures Questionnaire (CFQ)

	Total CFQ score	Forgetfulness	Distractibility	False triggering
Baseline	28.43 ± 18.20	11.57 ± 5.86	9.29 ± 6.21	8.14 ± 6.59
Week 3	22.86 ± 10.76	10.00 ± 2.89	6.86 ± 4.14	6.57 ± 4.28
vs. Baseline	20% lower	14% lower	26% lower	19% lower
Week 6	18.43 ± 11.89	7.71 ± 4.92	6.00 ± 3.51	4.57 ± 4.35
vs. Baseline	36% lower	33% lower	35% lower	44% lower

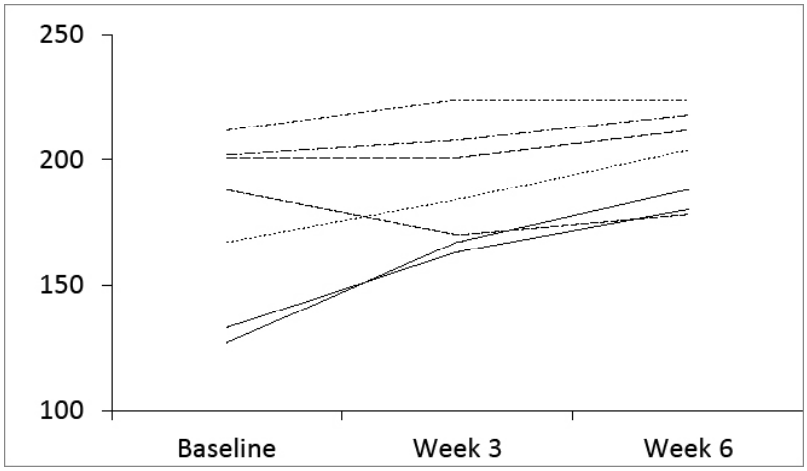

Figure 1. The baseline Subjective Memory questionnaire total scores of the participants are all above 100, indicating that no one had a great self-awareness of memory difficulties. Moreover, this figure shows that the total scores increased over time, and that those having lower scores at baseline experienced the most beneficial change.

Table 2. Cognitive Failures Questionnaire responses to individual questions

Question	Baseline	Week 3*	Week 6*
Do you read something and find you haven't been thinking about it and must read it again ?	1.71 1.1	1.43 ± 0.79 17% lower	1.14 ± 0.69 33% lower
Do you find you forget why you went from one place of the house to the other?	1.57 1.13	1.43 ± 0.78 9% lower	1.0 1.00 36% lower
Do you fail to notice signposts on the road?	0.86 ± 1.07	0.57 ± 0.70 33% lower	0.29 ± 0.49 67% lower
Do you find you confuse right and left when giving people directions?	0.86 ± 1.21	0.71 ± 1.25 17% lower	0.57 ± 0.79 33% lower
Do you bump into people?	1.00 ± 0.79	1.14 ± 1.25 14% higher	0.71 ± 0.76 29% lower
Do you find you forget whether you've turned off a light or locked the door?	1.43 0.79	1.43 ± 0.97 No change	0.71 ± 0.76 50% lower
Do you fail to listen to people's names when you are meeting with them?	1.29 1.25	1.14 ± 1.07 11% lower	0.86 ± 0.90 33% lower
Do you say something and realize afterwards that it might be taken as insulting?	1.43 ± 1.13	1.00 ± 0.82 30% lower	0.86 ± 0.90 40% lower
Do you fail to hear people speaking to you when you are doing something else?	1.00 ± 1.00	0.71 ± 0.76 29% lower	0.57 ± 0.79 43% lower
Do you lose your temper and regret it?	1.00 ± 0.82	0.43 ± 0.79 57% lower	0.57 ± 0.79 43% lower
Do you lose track of paying bills?	0.43 ± 0.79	0.29 ± 0.76 33% lower	0.14 ± 0.38 67% lower
Do you find you forget which way to turn on a road you know well but rarely use?	0.57 ± 0.98	0.14 ± 0.38 75% lower	0.14 ± 0.38 75% lower
Do you fail to see what you want in a supermarket (although it's there)?	0.57 0.79	0.43 ± 0.53 25% lower	0.71 ± 0.76 25% higher
Do you find yourself suddenly wondering whether you've used a word correctly?	1.29 ± 1.11	1.00 ± 1.15 22% lower	0.71 ± 0.76 44% lower
Do you have trouble making up your mind?	1.14 ± 0.90	1.00 ± 0.58 12% lower	0.86 ± 0.9 25% lower
Do you find you forget an appointment?	0.43 ± 0.79	0.43 ± 0.79 No change	0.29 ± 0.49 33% lower
Do you forget where you put something like a newspaper or a book?	1.43 ± 0.98	1.26 ± 0.49 10% lower	1.14 ± 0.69 20% lower
Do you find you accidentally misplace things like placing the fruit in the cupboard and the bowel in the refrigerator?	0.71 ± 1.11	0.43 ± 0.79 40% lower	0.57 ± 0.79 20% lower
Do you daydream when you ought to be listening to something?	1.71 ± 1.38	1.14 ± 0.69 33% lower	1.14 ± 0.90 33% lower
Do you find you forget people's names?	1.86 ± 0.69	1.43 ± 0.96 23% lower	1.00 1.00 46% lower
Do you start doing one thing at home and get distracted and do something else (unintentionally)?	2.00 ± 1.29	1.86 ± 1.35 7% lower	1.57 ± 0.98 21% lower
Do you find you can't quite remember something although it's "on the tip of your tongue"?	1.71 ± 0.76	1.57 ± 0.53 8% lower	1.29 ± 0.76 25% lower
Do you find you forget what you came to the store to buy?	1.00 ± 1.00	0.57 ± 0.79 43% lower	0.57 ± 0.79 43% lower
Do you drop things?	1.00 ± 1.00	0.86 ± 0.69 14% lower	0.57 ± 0.53 43% lower
Do you find you can't think of anything to say?	0.43 ± 0.53	0.43 ± 0.79 No change	0.43 ± 0.79 No change

*Compared to Baseline. Scoring goes from 0 (never) to 4 (very often); lower number is better.

Table 3. Changes in Subjective Memory questionnaire responses

	Total score	Mean individual score
Baseline	175.71 ± 34.44	5.32 ± 1.04
Week 3 vs. Baseline	188.14 ± 23.35 7 % increased	5.70 ± 0.71 7 % increased
Week 6 vs. Baseline	200.57 ± 18.64 14 % increased	6.08 ± 0.56 14 % increased

Table 4. Changes in quality of life

Quality of life questions	Baseline	Week 3	Week 6
How did you generally feel?	3.57 ± 0.98	3.43 ± 0.98	4.00 ± 0.82 12%*
Did you feel full?	2.86 ± 0.90	3.86 ± 1.07 ^	4.29 ± 0.76 # 50%
How was your mood?	4.14 ± 1.07	4.43 ± 0.54	4.14 ± 0.69 0%
How was your energy?	3.57 ± 0.53	3.71 ± 0.49	3.86 ± 0.38 8%
Did you experience any GI issues?+	4.57 ± 0.53	4.14 ± 0.69	4.00 ± 0.82 -12%
How did you sleep?	3.14 ± 1.21	3.57 ± 0.98	3.71 ± 0.95 18%
How was your appearance?	3.43 ± 0.53	3.57 ± 0.53	3.86 ± 0.69 13%
How was your diet quality?	3.29 ± 0.95	3.57 ± 0.79	3.71 ± 0.76 13%

*Represents the percentage change from baseline to week 6
^P = 0.08 vs. Baseline by paired t-test
#P = 0.007 vs. Baseline by paired t-test
+2 subjects had no symptoms; 1 with fewer bowel movements; and 4 had more gas and bloating, and more bowel movements

week 6). Other questions approached near-significance (P > 0.05 and < 0.1): better able to remember names (baseline to week 3); remembering phone numbers that were just looked up and those used frequently (compared to baseline for both weeks 3 and 6); recalling words (compared to baseline for both weeks 3 and 6); and remembering things that were done last month (compared to baseline for week 6).

Quality of life questions

At the end of the study, six of the eight quality of life questions improved (general feeling of wellbeing, fullness, energy, sleep, appearance, and diet quality) (Table 4). The largest improvements between week 6 and baseline were for fullness (50% increase), sleep (18% increase), and appearance and diet quality (both with a 13% increase). Compared to baseline, feeling full increased significantly (P = 0.007) at week 6. Mood did not change over time and gastrointestinal symptoms worsened due to one subject having fewer bowel movements and four experiencing more gas, bloating, and bowel movements. Compliance with the dietary regimens were not affected by these gastrointestinal issues.

Discussion

No treatments exist for dementia including Alzheimer's disease, and prevention is the only option to avoid cognitive decline with aging. Diet is the most important prevention therapy and there is much scientific agreement as to what to eat [5-10]. Paradoxically, most Americans consume a diet that is rich in things that worsen cognition and avoid nutrient-dense foods that arrest decline [11]. We demonstrated that a dietary intervention with two nutrient-rich beverages containing brain-targeted ingredients improved cognitive function and quality of life over six weeks. Participants remained weight stable, which was an objective of the study. It is possible that weight change could have affected cognitive function.

The Cognitive Failures Questionnaire (CFQ) [23] for all sub-scale scores improved: Total CFQ, False triggering, Forgetfulness, and Distractibility. Individual responses improved for 60% of the 25 questions. Responses for the Subjective Memory Questionnaire (SMQ) were less impressive likely because the baseline scores represented a population that had only a modest appreciation memory loss. It is possible that this test would have been more robust in seeing changes related to diet if the baseline cohort was more cognitively impaired.

The benefits in cognitive function observed in the study may be explained in three ways. First, diet quality improved from the nutrient-rich, brain-targeted beverages. Consumption of the two brain-targeted shakes daily, as per the protocol, provided two-thirds of the daily requirement for every vitamin and mineral, while being low in ingredients that worsen cognition (i.e., sugar, sodium, and saturated fat). Second, the beverages contained brain-targeted ingredients that have been shown to improve cognitive function [12-18]. These compounds serve as antioxidants to protect the brain and one, phosphatidylserine, has been shown to improve cognitive function [12-14]. Phosphatidylserine even has a Qualified Health Claim from the Food and Drug Administration because of its reported efficacy [24]. Third, the two beverages provided two-thirds of daily AI for choline. Choline is under-consumed unless the diet regularly includes egg yolks, red meats, and seafood [25]. Higher dietary choline intakes, especially as phosphatidylcholine from food or supplements, is associated with better cognitive performance and a lower risk of dementia [26].

The finding that the dietary intervention improved the quality of life was not surprising, given that similar improvements were observed in prospective studies with different conditions (e.g., hypertension, type 2 diabetes, and males with reduced libidos) [27-29]. In these studies, participants consumed similar nutrient-dense foods but without the brain-targeted ingredients.

The diet quality of most Americans is poor, mainly due to lacking essential nutrients and having too many components that increase the risk of chronic disease including dementia

(e.g., salt, sugar, and saturated fats) [11]. From baseline dietary questionnaires, the participants had dietary habits that mimicked the American public. The subjects over consumed sugar, frequented fast food restaurants that offer foods rich in salt and saturated fats, and had sub-optimal intakes of fruits, vegetables, seeds, and nuts. This nutrient-poor dietary pattern contains too many calories from sugar and fats, especially saturated fats, and has been shown to increase mortality and the risk of chronic conditions [30,31].

Brain-targeted dietary interventions have been shown to improve cognitive function in those with mild cognitive impairment as a result of Alzheimer's disease or pre-Alzheimer's [32,33]. The dietary program, metabolic enhancement of neurodegeneration, includes a healthy eating program, which emphasizes whole foods (i.e., fruits, vegetables, whole grains), seafood rather than red meats, and limiting processed foods, especially refined carbohydrates. In addition to dietary recommendations, a more personalized approach is provided that includes recommending dietary supplements like vitamins D, and E; minerals like zinc; fish oil to provide omega-3 fatty acids; and others like coenzyme Q10, and alpha lipoic acid. Reversal of cognitive decline was observed in 100 patients, who have undergone this targeted dietary approach [33]. Improvement was demonstrated in cognitive function tests, reports from family members, and in some cases, electrophysiology (imaging).

Conclusion

Prevention is the only viable option to arrest cognitive decline with aging, and necessary as no treatments exist for dementia. Most of the evidence supports a role for a heathy, nutrient-rich diet that is low in sugar, sodium, and saturated fats. The participants in this study consumed two brain-targeted shakes that satisfied these criteria and included other bioactive compounds known to enhance cognitive function. After six weeks, improvements were observed in sub-categories of the Cognitive Failures Questionnaire and total scores for Subjective Memory questions. In addition, subjects experienced improvement in quality of life related to general feeling of wellbeing, fullness, energy levels, sleep, and eating better. These promising findings present an easy way to enhance diet and improve cognition.

Conflicts of Interest and Source of Funding

Dr. Bell, Ms. Bauer, and Mr. Marsland have received a full-time salary from Nutrient, Reno, Nevada, which is the company that manufactures and sells the beverages used in this study. Dr. Gomez-Pinilla is on the Scientific Advisory Board of Nutrient. Dr. Ling was paid as a statistical consultant.

Nutrient, a company in Reno, Nevada, supplied the nutrient-dense beverages at no charge to the participants.

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