Update on Juice Plus+ Research

Manfred LAMPRECHT

THE JUICE PLUS+ SCIENCE INSTITUTE

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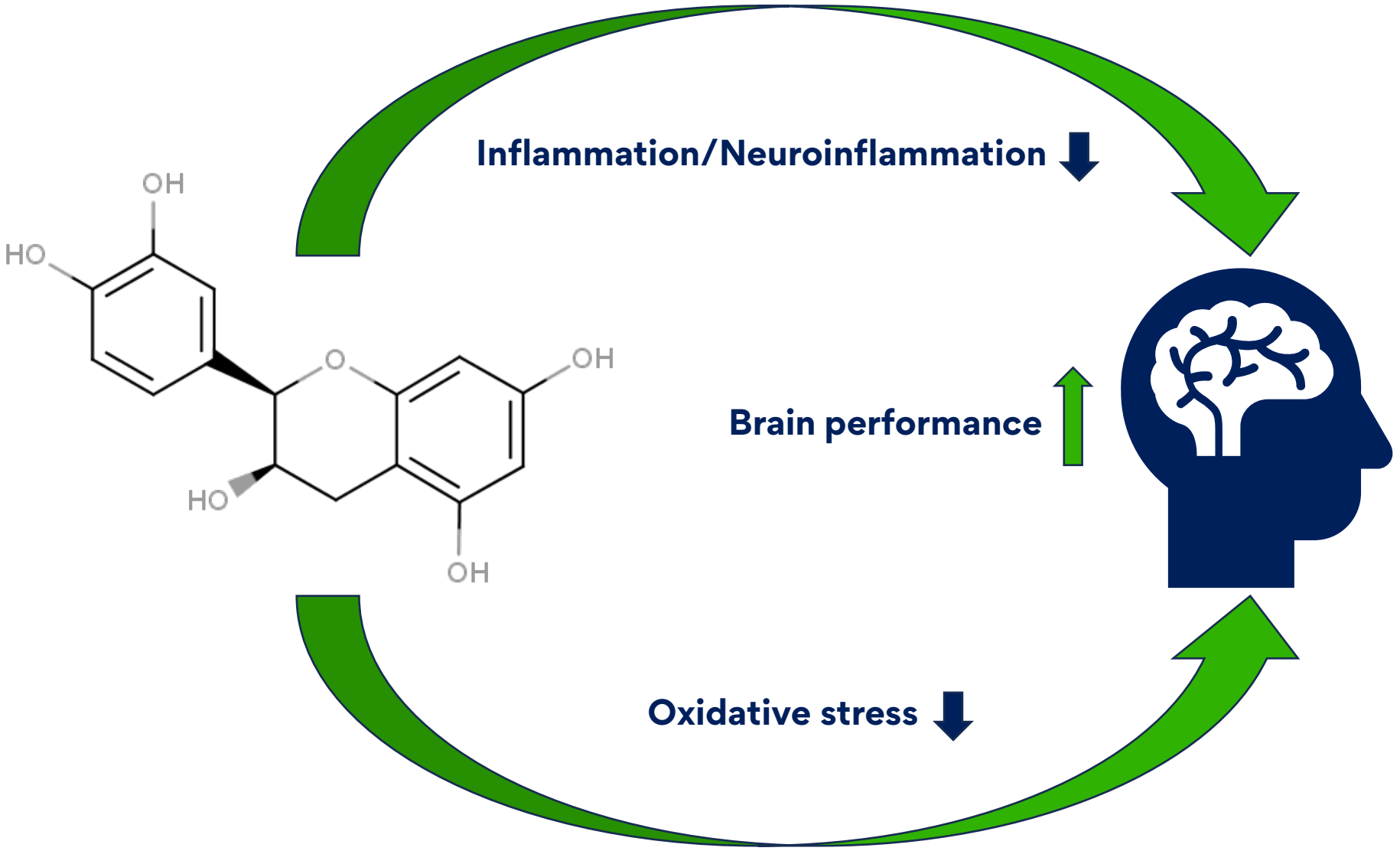
The link between polyphenols and brain performance



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JP+ and cognitive function

Aim:

The aim of this study was to evaluate the effects of an encapsulated fruit, vegetable and berry juice powder concentrate on cognitive functions in healthy adults

antioxidants

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Article

Effects of Fruit and Vegetable-Based Nutraceutical on Cognitive Function in a Healthy Population: Placebo-Controlled, Double-Blind, and Randomized Clinical Trial

Juan Ángel Carrillo, Raül Arcusa, María Pilar Zafrilla * and Javier Marhuenda

Faculty of Health Sciences, Universidad Católica de San Antonio, 30107 Murcia, Spain; jacarrillo4@alu.ucam.edu (J.Á.C.); rarcusa@ucam.edu (R.A.); jmarhuenda@ucam.edu (J.M.)
* Correspondence: mpzafrilla@ucam.edu; Tel.: +34-968-27-86-18

Abstract: There is scientific evidence of the positive effect of polyphenols from plant foods on cognition, but not enough is known about the synergistic effect when multiple polyphenols are consumed and even less in a healthy non-elderly population. The aim of the present study is to investigate the possible effects of improvements in cognitive function in healthy people as a preparation based on micronized fruit and vegetables consumed. One hundred and eight subjects were selected, stratified by sex in the control intervention group (n = 53) and placebo (n = 55). Volunteers completed the study after two 16-week periods of consumption with a 4-week wash period between each phase. At the beginning and the end of each phase, volunteers performed the Stroop, TESEN, and RIST tests for the measurement of different cognitive function patterns. The results revealed statistically significant differences in all the variables of the tests carried out, especially compared with the placebo. Specially, the results obtained in the Stroop and TESEN test, in addition to the processing speed even with semantic interferences, were markedly better after the treatment with the product under study. Moreover, the consumption of the product under study clearly improves short-term memory, verbal and non-verbal, according to the results obtained in the RIST test. The results showed an improvement in executive function in terms of short-term memory, working memory, selective and sustained attention, and speed of processing.

Keywords: cognition; polyphenols; executive function; memory; attention; Stroop; TESEN; RIST

check for updates

Citation: Carrillo, J.Á.; Arcusa, R.; Zafrilla, M.P.; Marhuenda, J. Effects of Fruit and Vegetable-Based Nutraceutical on Cognitive Function in a Healthy Population: Placebo-Controlled, Double-Blind, and Randomized Clinical Trial. *Antioxidants* **2021**, *10*, 116. https://doi.org/10.3390/antiox10010116

Received: 10 December 2020
Accepted: 12 January 2021
Published: 15 January 2021

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1. Introduction

Polyphenols, including phenolic acids, flavonoids, such as anthocyanins or flavonols and tannins, vary depending on the fruits or vegetables where they are present: berries, onions, apples, parsley, celery, broccoli... [1,2]. They have a considerable capacity to neutralize free radicals and exert anti-inflammatory and neuroprotective effects [3,4] and are considered important in cognitive function. Although the mechanisms of action have not yet been clarified, these compounds are known to modulate cerebral blood flow, inducing changes in memory processing [5,6], improving neuronal connectivity and neuronal growth in the hippocampus [7], and synaptic plasticity [8] related to variations in nitric oxide (NO) levels [9].

The effect of bioactive compounds also depends on consumption and frequency levels [10,11] since there is evidence of the effects in acute consumption [12], but not so much in prolonged consumption over time. The brain is especially sensitive and prone to oxidative damage and the accumulation of reactive oxygen species (ROS) due to increases in oxygen consumption [13]. Polyphenol supplementation decreases the vulnerability of elderly people who present higher risk factors to oxidative stress, improving neuronal communicability [14,15].

There are authors who have investigated the synergistic effects of various plant compounds [16,17], but their effects have not been clearly demonstrated and more randomized

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Study design:

- Randomized, double-blinded, placebo-controlled clinical trial with a crossover design
- 4 study visits: start of study, 16 weeks (after 16th week: 4 weeks wash-out), 20 weeks and 36 weeks

Intervention:

- 6 capsules/day of an encapsulated fruit, vegetable and berry juice powder concentrate (Juice Plus+®) or placebo

Participants

- 94 generally healthy subjects finished the study → 18 – 65 years of age
- BMI ≥ 18.5 ≤ 35 kg/m2
- Consumption of ≤ 3 servings of fruits or vegetables/day

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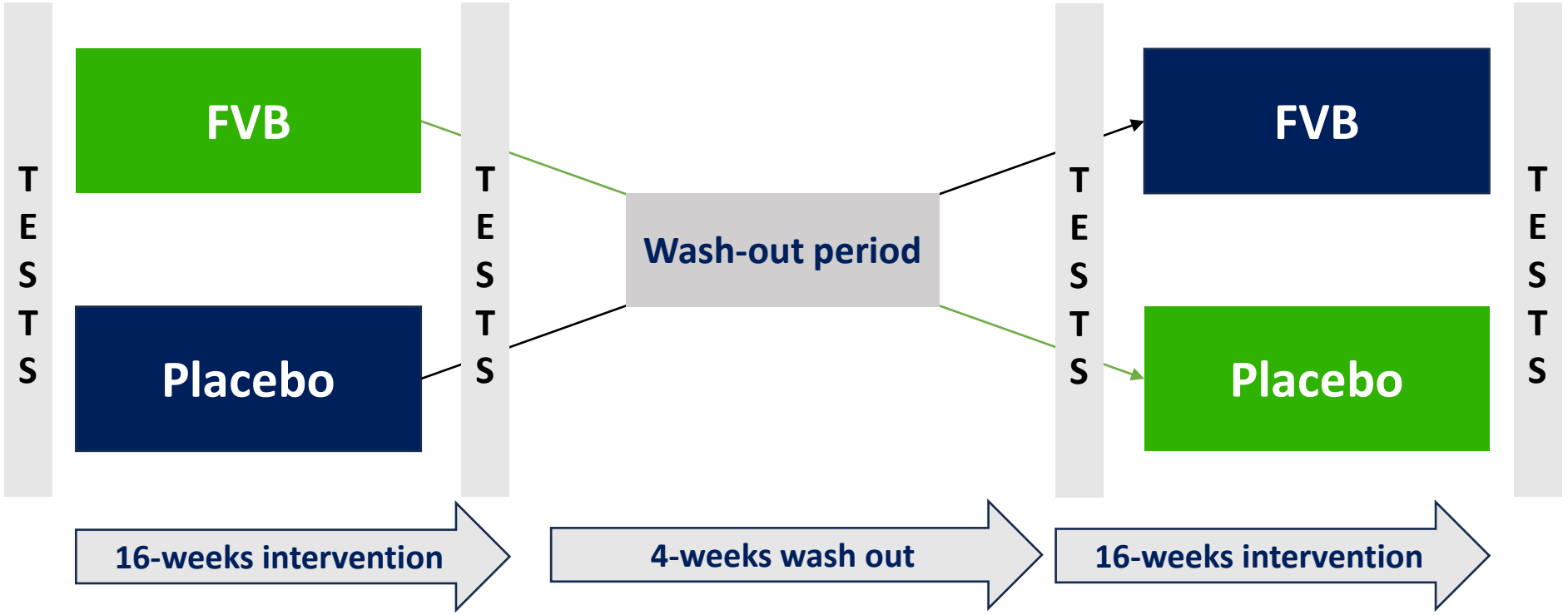

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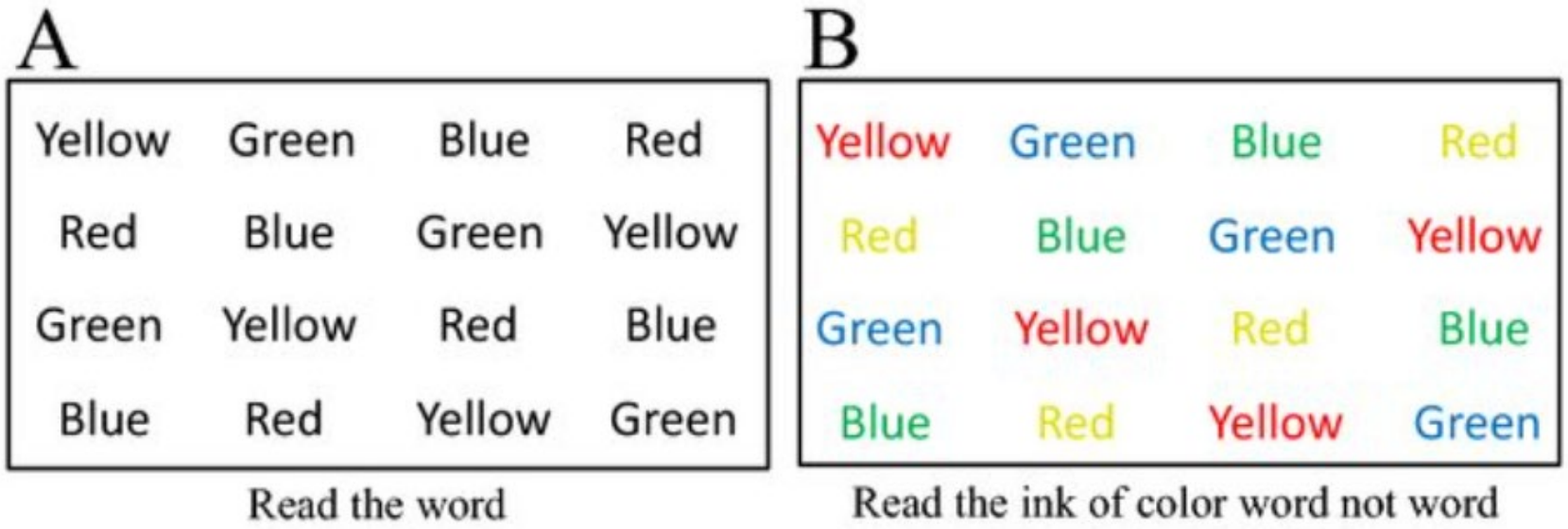
- **Cognitive tests applied (o.a.):**
  - Stroop Test → evaluates selective attention
  - TESEN Test (based on Trail making test) → evaluates executive functions and working memory

Stroop Test



Sato et al. 2023

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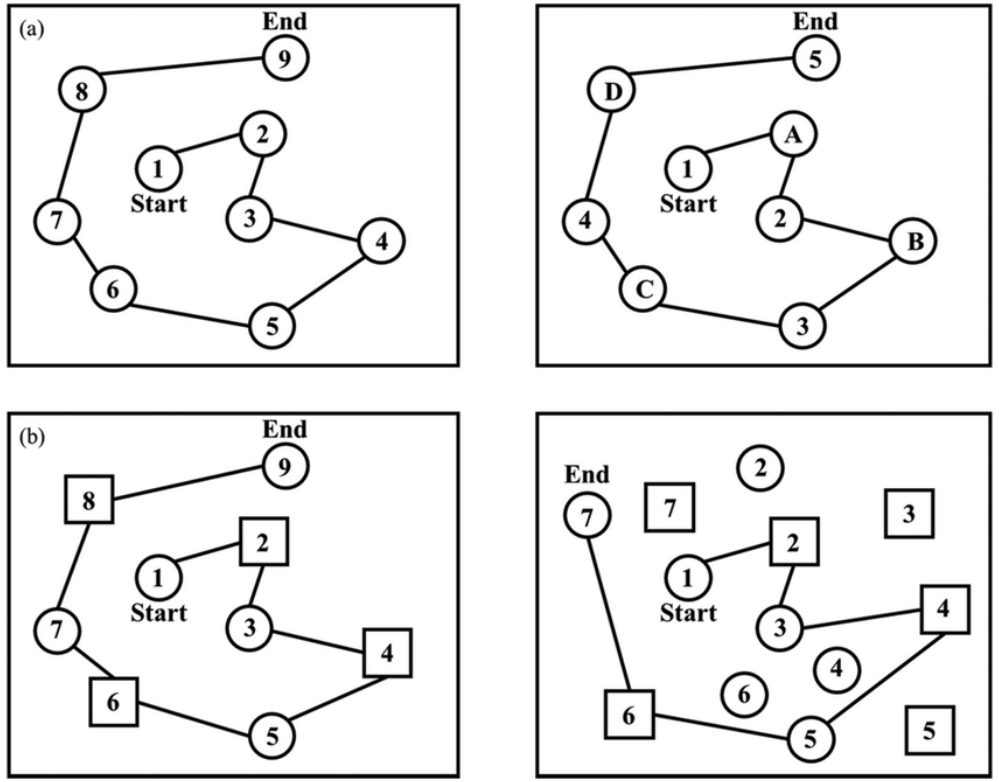
TESEN Test (Trail Making Test)



Simfukwe et al. 2021

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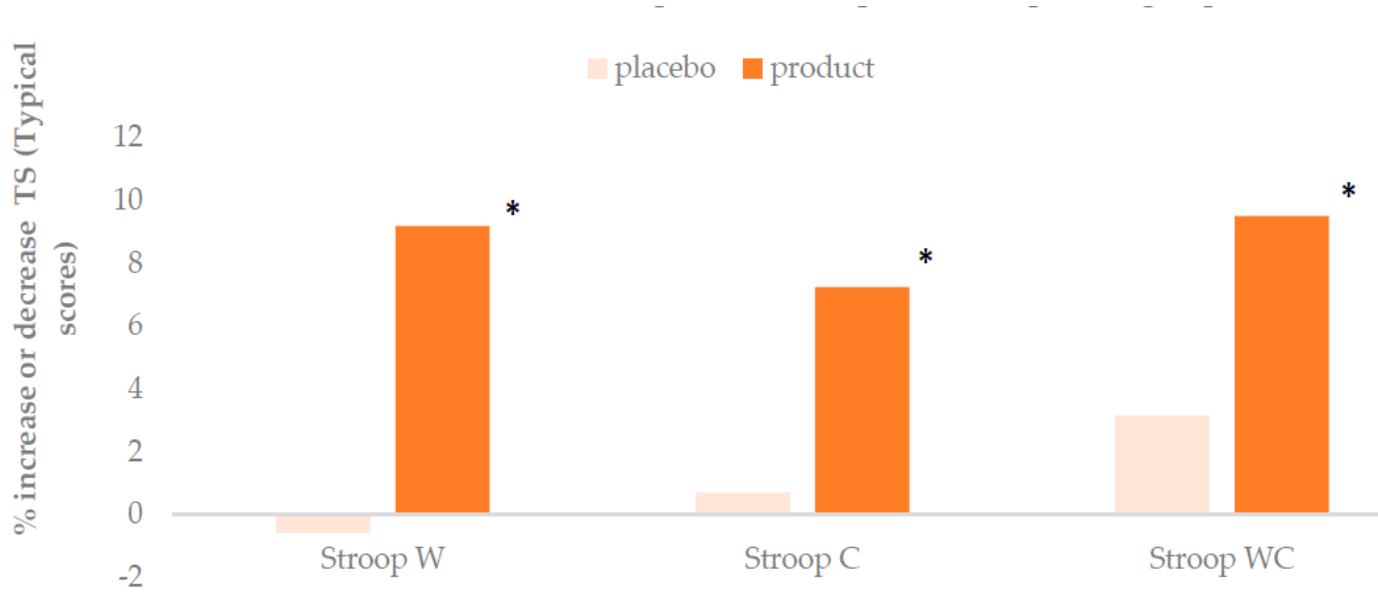
- **Results of the Stroop Test:**
  - Compared to placebo, supplementation resulted in significant improvements in all 3 variables of the Stroop test (W, C, WC)
  - Placebo intake showed no statistical improvement in either variable of the test



Evolution of results in the different variables of Stroop test in percentage increase or decrease. *indicate significant differences ($p < 0.05$)

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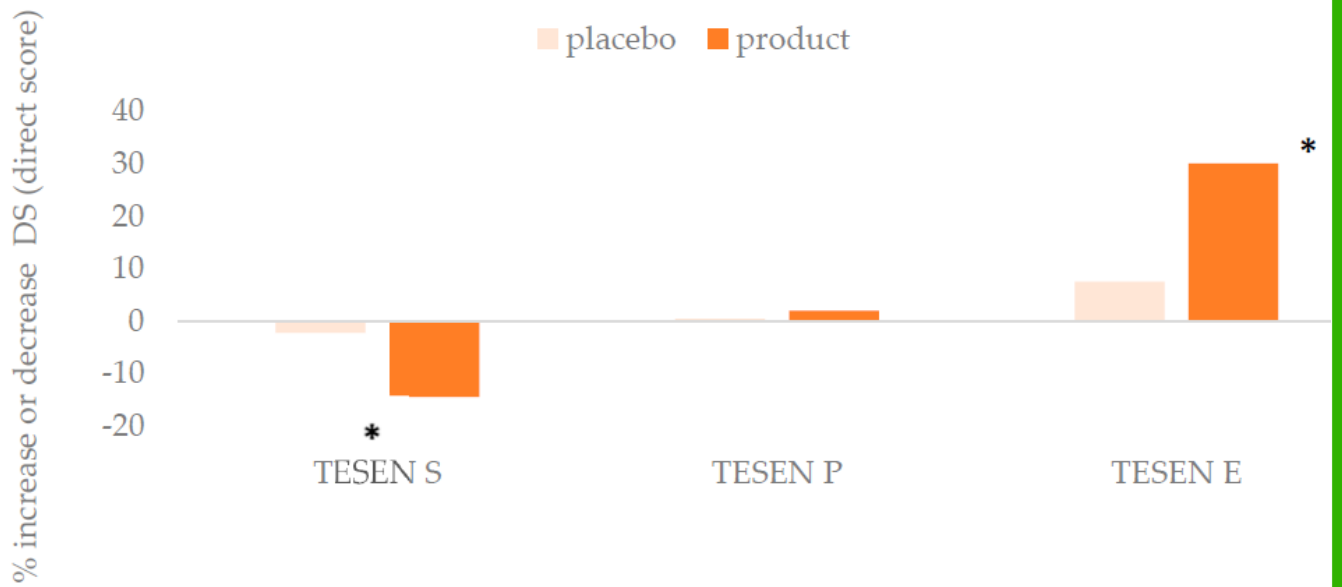
- **Results of the TESEN Test:**
  - Compared to baseline, supplementation resulted in significant improvements in speed of execution (S), precision in terms of number of hits and misses (P), and execution in relation to speed and precision in execution (E)
  - Compared to placebo, supplementation showed a significant increase in speed (S) and a significant improvement in execution (E)
  - Placebo intake showed no significant improvement in either variable of the test



Evolution of results in the different variables of TESEN test in percentage increase or decrease. *indicate significant differences ($p < 0.05$)

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+ Conclusion

Supplementation with an encapsulated fruit, vegetable and berry juice powder concentrate, rich in polyphenols, resulted in improved executive function, working memory, selective and sustained attention, and speed of processing

antioxidants

MDPI

Article

Effects of Fruit and Vegetable-Based Nutraceutical on Cognitive Function in a Healthy Population: Placebo-Controlled, Double-Blind, and Randomized Clinical Trial

Juan Ángel Carrillo, Raül Arcusa, María Pilar Zafrilla * and Javier Marhuenda

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+ 2 more peer-reviewed publications from the Murcia-Study !!!

molecules

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Article

Effects of a Fruit and Vegetable-Based Nutraceutical on Biomarkers of Inflammation and Oxidative Status in the Plasma of a Healthy Population: A Placebo-Controlled, Double-Blind, and Randomized Clinical Trial

Raúl Arcusa, Juan Ángel Carrillo, Raquel Xandri-Martínez, Begoña Cerdá, Débora Villaño, Javier Marhuenda * and María Pilar Zafrilla

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antioxidants

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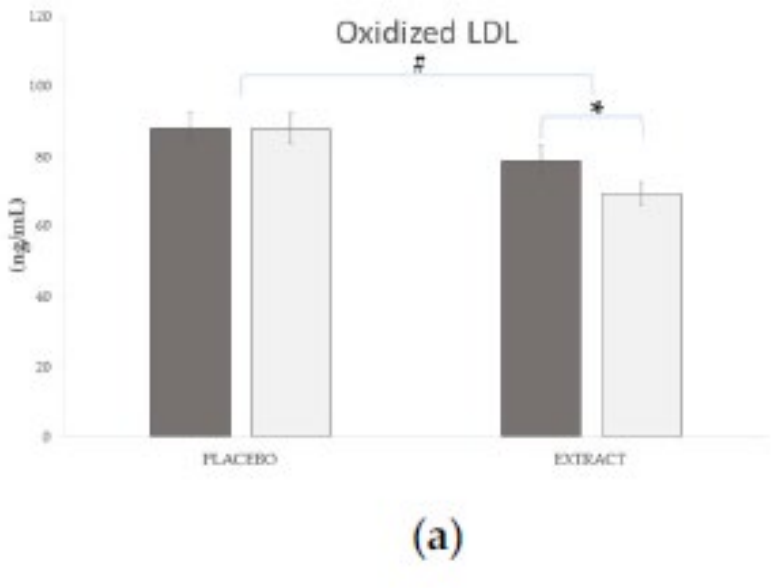
JP+: cognitive function, oxidative stress and inflammation



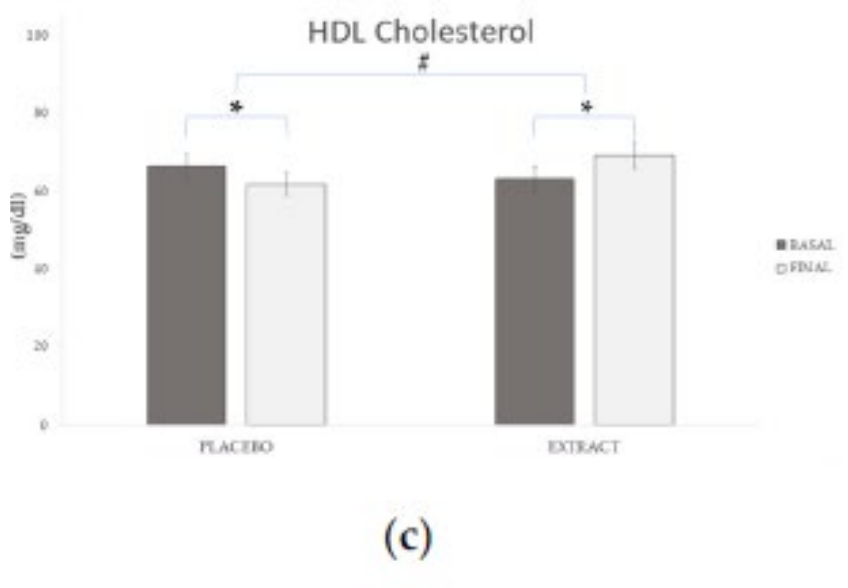


Figure 2. Evolution of (a) oxidized low-density lipoprotein (OxLDL), (c) high-density lipoprotein (HDL) during the study. *Means significant statistical differences when comparing the evolution between the baseline and final ($p<0.05$). # Means significant statistical differences when comparing the evolution between groups ($p<0.001$)

Arcusa et al, Molecules 2021

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JP+: cognitive function and neurotransmitter

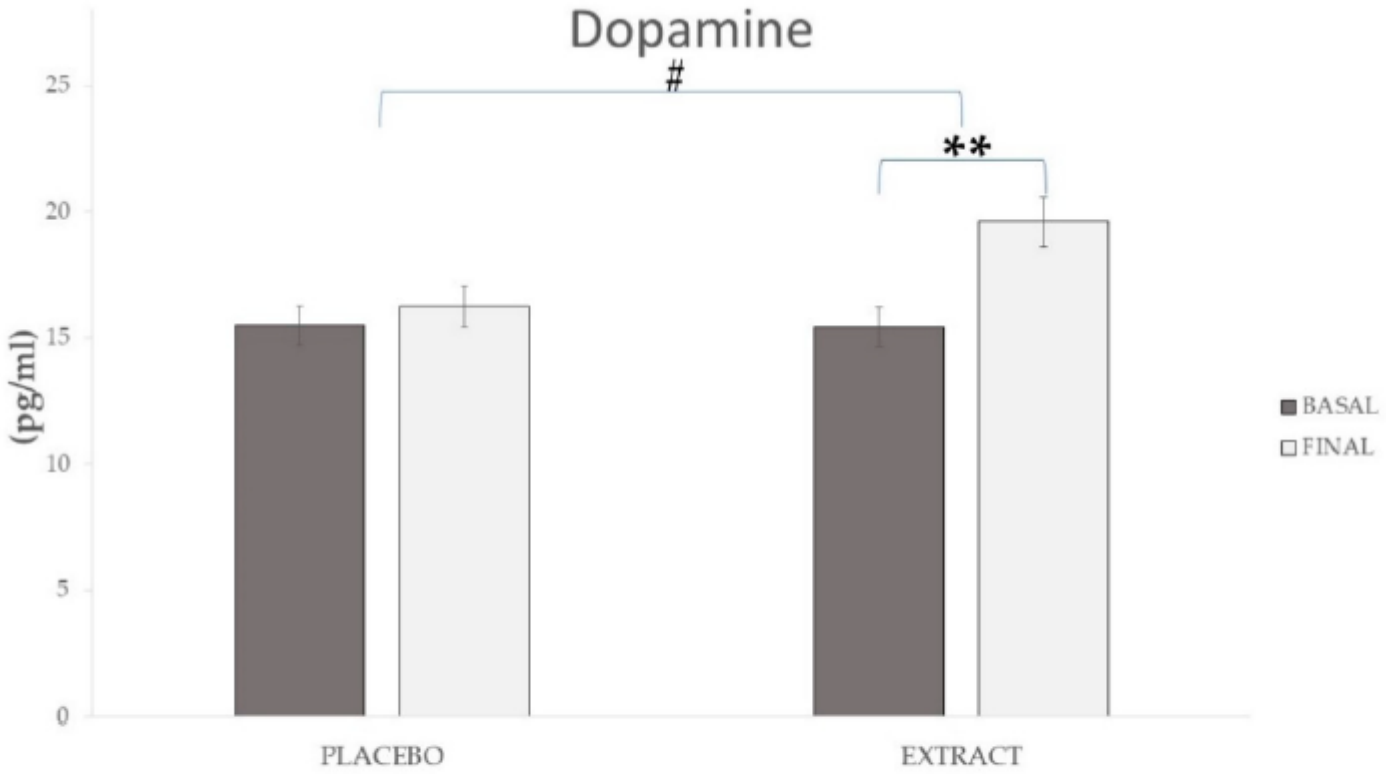

Figure 3. Evolution of dopamine during the study. ** Means significant statistical differences comparing the evolution between baseline and final ($p < 0.001$). # Means significant statistical differences comparing the evolution between groups ($p < 0.001$).

Arcusa et al, Molecules 2021

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+ 2 more peer-reviewed publications from the Murcia-Study

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antioxidants

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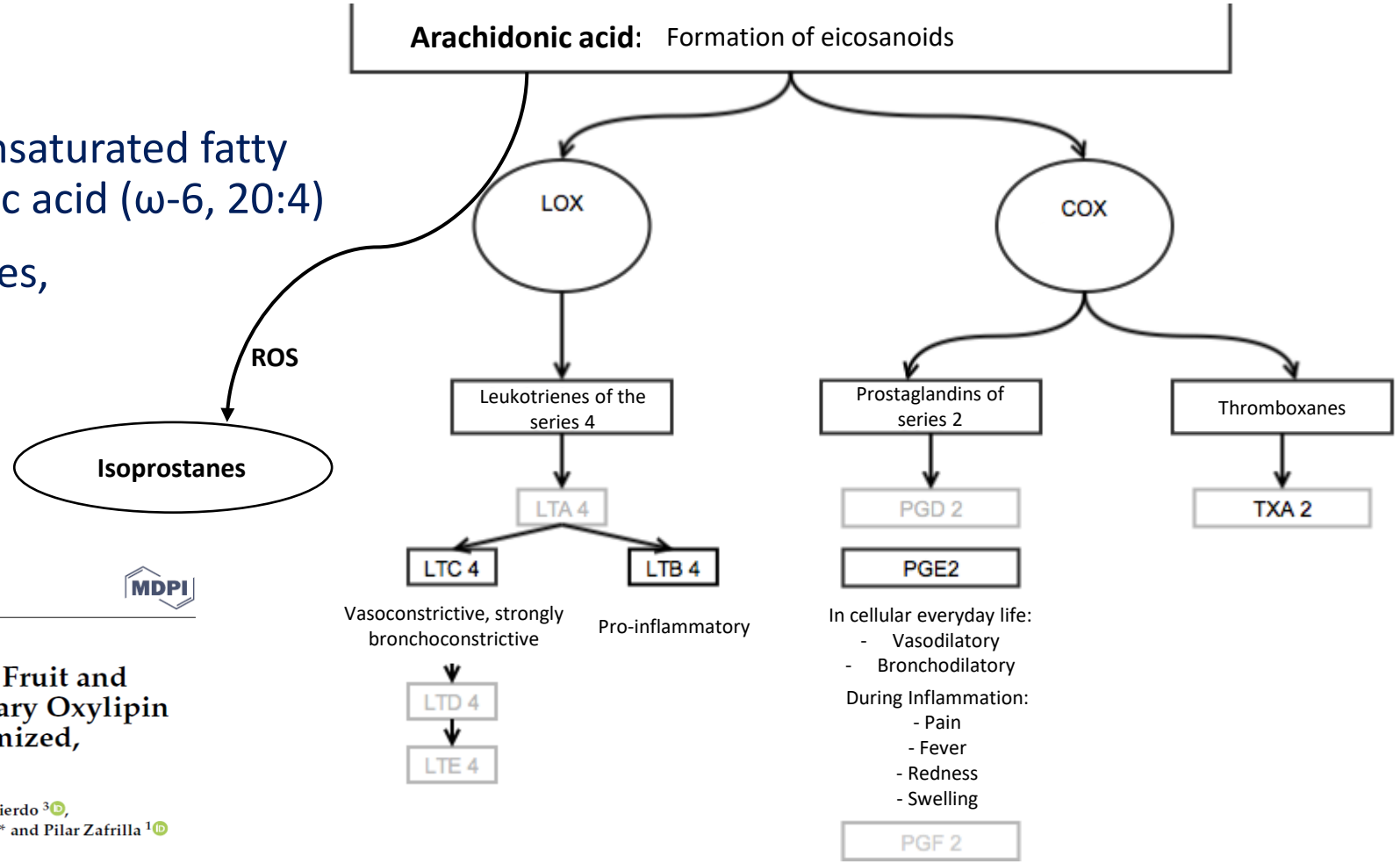
Oxylipins

- Oxidation products of polyunsaturated fatty acids, particularly arachidonic acid (ω-6, 20:4)
- Prostaglandins, Thromboxanes, Leukotrienes, Isoprostanes



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JP+: cognitive function, oxidative stress and inflammation

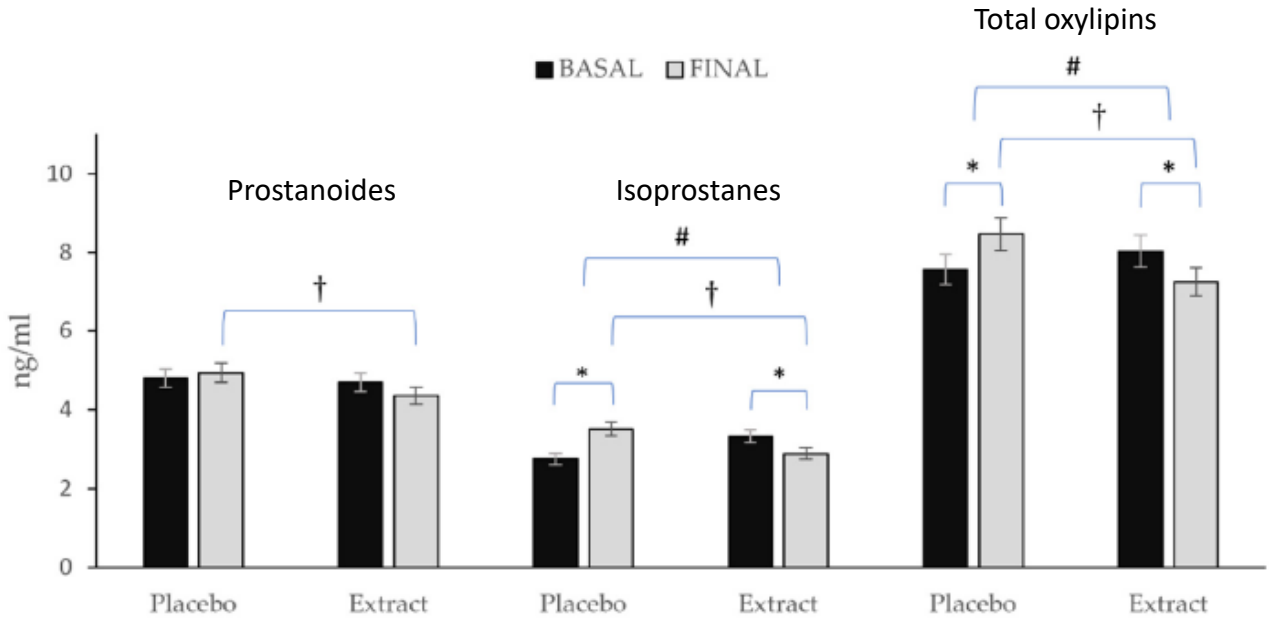

Figure 4. Variation in total prostanoids, total IsoPs, and total oxylipins in each group during the intervention. * Means significant statistical differences comparing the evolution between baseline and final intragroup ($p < 0.05$). † Means significant statistical differences comparing final moment between groups at the end of the intervention ($p < 0.001$). # Means significant statistical differences comparing evolution between groups during the intervention ($p < 0.05$).

Arcusa et al, Antioxidants 2022

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Update on Juice Plus+ Research

Current Research Projects

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Current studies / projects

- University of Newcastle: "Muscle function / Mobility in an older population" (RCT with Juice Plus+ COMPLETE)
- Texas A&M University and Texas Extension Education Foundation: "Mechanisms of action of Juice Plus+ on various factors of the Metabolic Syndrome" (In-vitro study with FVB, OMEGA)
- University of Reading: "Improvement of learning ability and memory after supplementation with Juice Plus+ Omega in adolescents" (RCT with Omega Blend)
- Medical University of Graz: "Effects of long-term consumption of two plant-based supplements on cardiovascular health and low-grade inflammation in older adults" (RCT with Juice Plus+ FVB, OMEGA)
- University of California Los Angeles und University of Ulster, NIH-Study: "Polyphenols, microbiome, cognitive functions, and Alzheimer's prevention" (RCT with Juice Plus+ Berry Blend)

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Current studies / projects

Topic: **Muscle function and mobility in an older population**

Study site:
Hunter Medical Research Institute,
University of Newcastle, Australia

Design: randomized, controlled study, 2 parallel groups, men and women 65+ years

Intervention: Juice Plus+ Complete, 2x/day, for 12 weeks compared to control group, same exercise program in both groups

Outcomes: muscle strength & function, body composition, bone density, low-grade inflammation, gene expression of inflammatory proteins

Status: Experiments completed, awaiting publication

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Current studies / projects

Topic: Metabolic Syndrome

Study site:
Department of Horticultural Science,
Texas A&M University, USA

Design: In-vitro study in various cell lines associated with obesity, inflammation, and insulin resistance

Intervention: FVB + Omega

Outcomes: Prebiotic effects of Juice Plus+ on microbiome cells of normal-weight and overweight individuals, characterization of the mechanisms of action on metabolic syndrome

Status: Experiments completed, awaiting publication

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Current studies / projects

Topic: **Learning ability and memory**

Study site:
School of Psychology and Clinical Language Sciences,
University of Reading, Reading, UK

Design: Randomized, placebo-controlled, double-blind, parallel-group study in adolescents (male and female, 13-14 years)

Intervention: Juice Plus+ Omega Blend for 16 weeks compared to placebo

Outcomes: Cognitive performance, Omega-3 index, EEG spectral activity, and event-related potentials

Status: Experiments completed, awaiting publication

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Current studies / projects

Topic: Cardiovascular health, low-grade inflammation, biological age

Cardiovascular & InflammAging Study, “CIA Study”

Study site:
Institute of Medical Chemistry / Center for Medical Research (ZMF) Medical University, Graz, Austria

Design: Randomized, controlled, parallel-group study, men and women, 55–80 years

Intervention: FVB + Omega for 1 year compared to control (no intervention)

Outcomes: Cardiovascular health, oxidative stress, low-grade inflammation, biological age, cognitive function, bioavailability, bone health

Status: Recruitment, experiments ongoing (publications expected in 2026)

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Current studies / projects

Topics: Polyphenols, microbiome, cognitive functions, Alzheimer‘s

“MAEVE-Study: Microbial-mediated flAvonoid mEtabolites for cogniti Ve hEalth”

Study sites:
University of California Los Angeles, USA, und University of Ulster, Northern-Ireland

NIH funded study!!!

NIH National Institutes of Health
Turning Discovery Into Health

Project funding amount: 10 000 000 USD, J+ - part: 250 000 USD (2,5 %)

(Surrogate-)Marker/Outcomes (among others):
Cognitive functions, cardiovascular parameters, microbiome…..

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The National Institutes of Health (NIH)

- The National Institutes of Health (NIH) is the largest public funder of biomedical research in the world (approximately 50 billion USD per year);
- The NIH is part of the U.S. Department of Health and Human Services and represents the national medical research institution;
- NIH-funded research has led to significant discoveries in medical sciences to provide people with healthier and longer lives or to offer better treatments/therapies.

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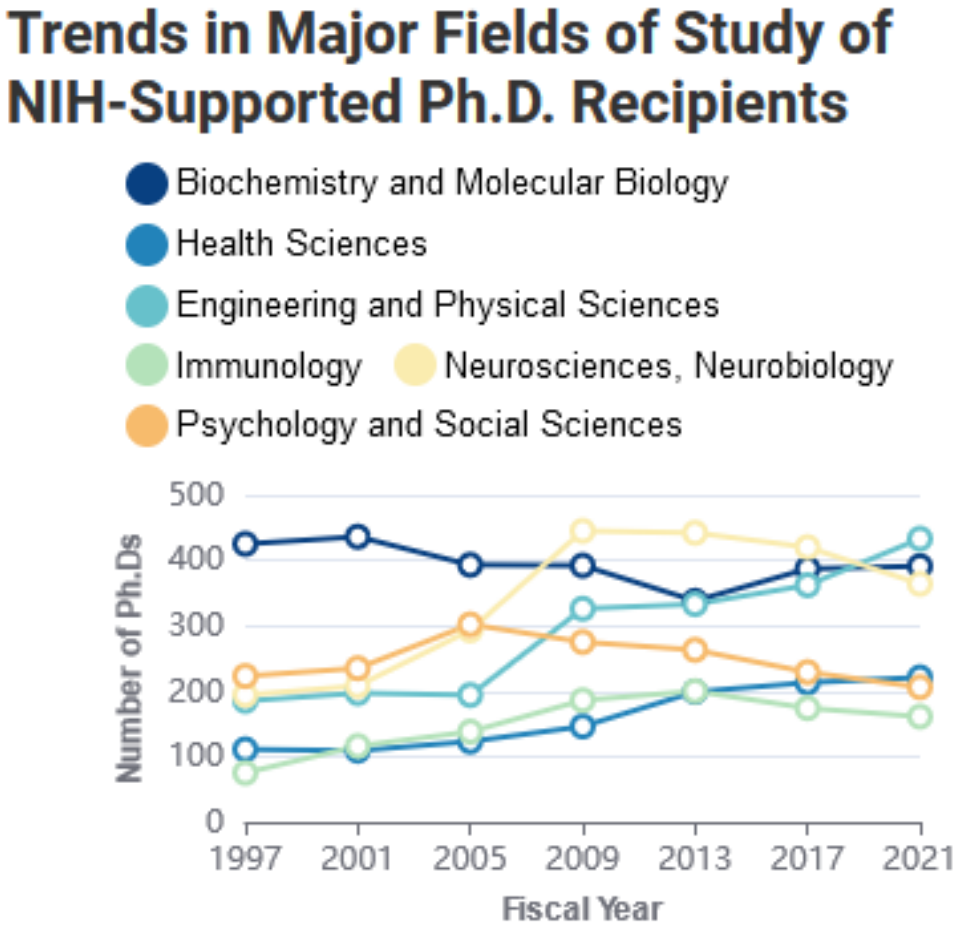
The National Institutes of Health (NIH)

Categories of biomedical research:



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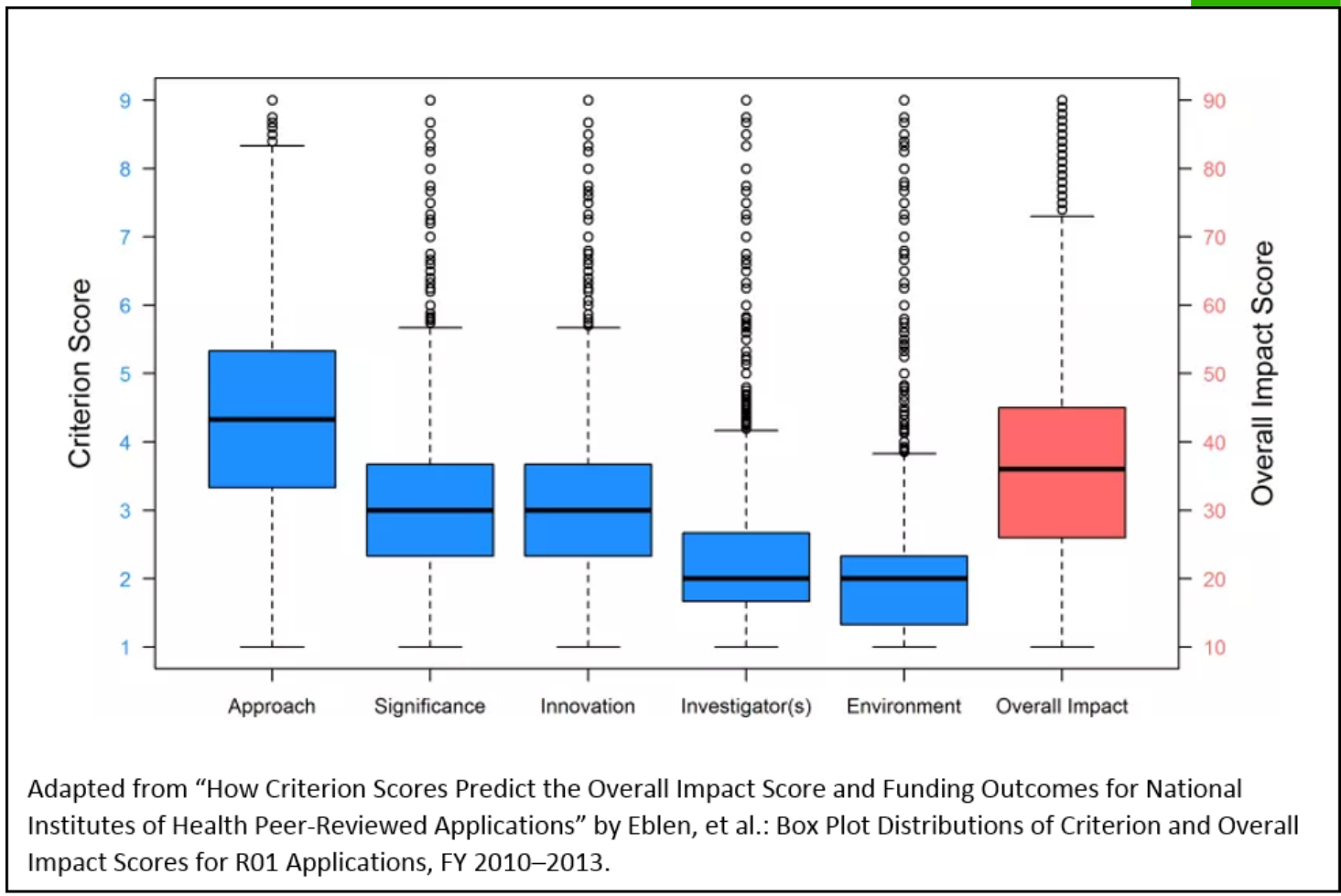
The National Institutes of Health (NIH)

5 main criteria/funding conditions:

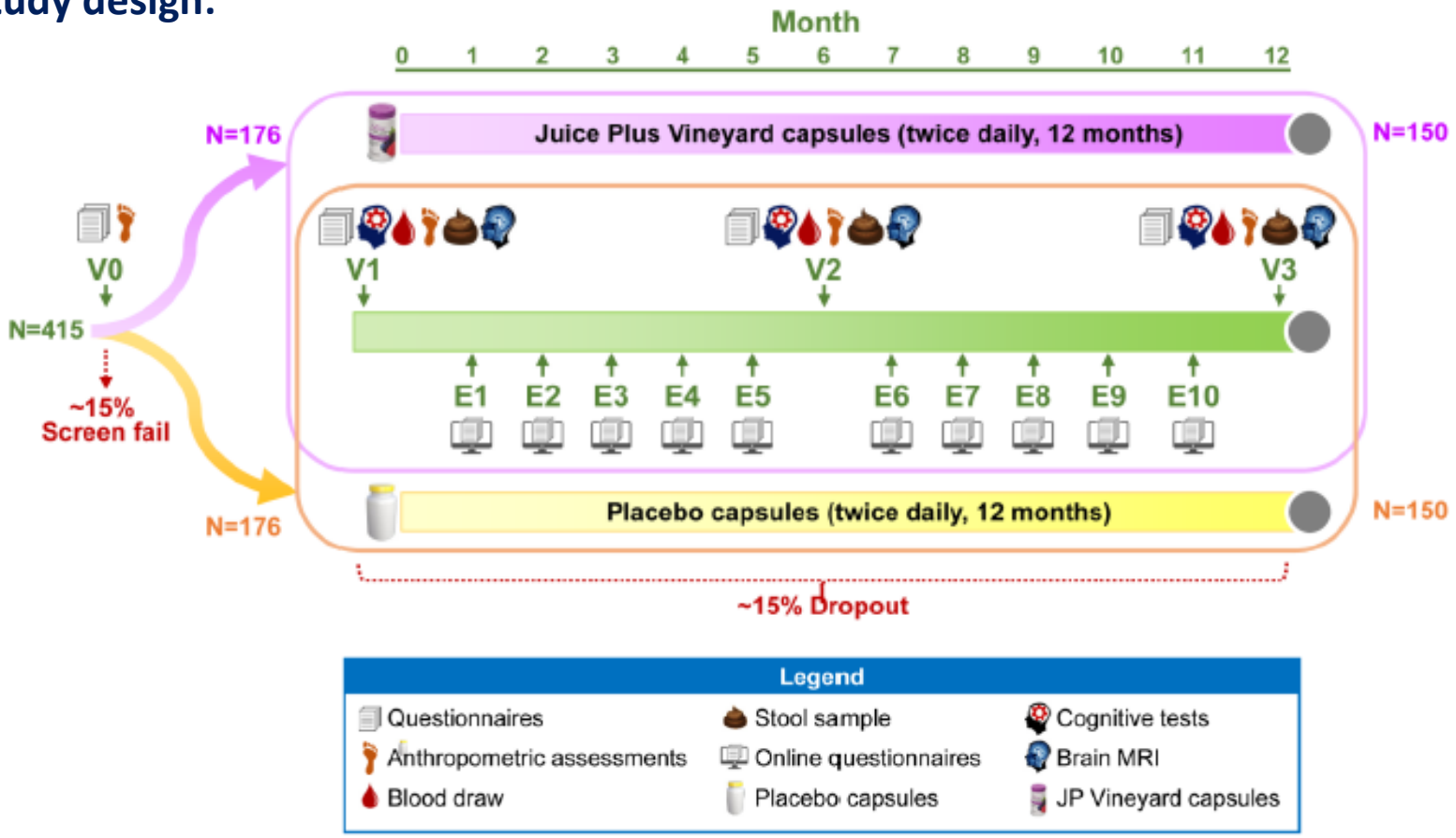
- Scientific approach
- Significance of outcomes
- Innovation/Novelty
- Reputation of researchers
- Research institution and environment



Adapted from "How Criterion Scores Predict the Overall Impact Score and Funding Outcomes for National Institutes of Health Peer-Reviewed Applications" by Eblen, et al.: Box Plot Distributions of Criterion and Overall Impact Scores for R01 Applications, FY 2010–2013.

NIH Study with J+ Berry Blend

Study design:



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NIH Study with J+ Berry Blend

Topics: Polyphenols, microbiome, cognitive functions, Alzheimer´s

“MAEVE-Study: Microbial-mediated flAvonoid mEtabolites for cognitiVe hEalth”

Outcomes:
Cardiovascular health, oxidative stress, low-grade inflammation, aging process, cognitive functions, brain MRI, PSS, HADS, metabolomics (LC-MS), microbiome composition, bioavailability, safety (liver, kidney), QoL, BIA, food diary, exercise profiles...

Status:
Project preparations, product and placebo production, etc. (publications expected in 2027)

Juice Plus+
Science Institute
Advancing plant-based nutrition

Summary of the entire J+ research (1995 – 2024): Unique research background in fruit, vegetable, and berry capsules:

- 48 scientific articles ("peer-reviewed")
- Published in over 30 different scientific journals
- 33 clinical studies across 4 continents
- 23 "Gold Standard" clinical studies
- More than 2,500 participants studied
- Nearly 50 universities and clinics
- Total impact score: >225!

Topics: Bioavailability, cardiovascular health, phytonutrients and polyphenols, nutrigenomics, brain health, immune system, skin health, dental health, oxidative stress, inflammation, etc.

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Update on Juice Plus+ Research

Manfred LAMPRECHT

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