

Comparative effects of omega-3 and creatine supplementation on cognitive function and body composition in older adults: A quasi-experimental study

Efectos comparativos de la suplementación con omega-3 y creatina sobre la función cognitiva y la composición corporal en adultos mayores: un estudio cuasiexperimental

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ABSTRACT

Introduction: cognitive decline in older adults constitutes a growing problem for public health. Evidence suggests that nutritional interventions, such as the use of omega-3 fatty acids and creatine monohydrate supplementation could produce beneficial effects in cognitive health, as well as physical and functional outcomes.

Objective: This study aimed to examine the effects of omega-3 and creatine monohydrate supplementation on cognitive function in older adults.

Materials and Methods: Quasi-experimental study with convenience sampling among 28 older adults attending a care center in Lima, Peru. Participants were allocated into two groups: omega-3 (n = 14) and creatine (n = 14), for 12 weeks. Cognitive performance was evaluated using the Adenbrooke's Cognitive Examination (ACE) and the Rowland Universal Dementia Assessment Scale (RUDAS). Anthropometric measures and functional performance were also evaluated. Within-group analyses and between-group comparisons were performed, including effect size (Cohen's d).

Results: Both groups showed statistically significant improvements in global cognitive scores on the Addenbrooke's Cognitive Examination (ACE) ($\Delta \approx +4.2$ points) and the Rowland Universal Dementia Assessment Scale (RUDAS) ($\Delta \approx +2.0$ to $+2.6$ points). Effect sizes were moderate in the omega-3 group and large in the creatine group, but these estimates should be interpreted cautiously given the small sample size and the absence of a placebo control group. In addition, creatine supplementation was associated with a modest improvement in Timed Up and Go performance, whereas omega-3 supplementation produced a small reduction in body fat percentage and a trend toward decreased abdominal circumference. No statistically significant between group differences were observed in any cognitive domain, and all findings should be interpreted as preliminary due to the small sample size and quasi-experimental design.

Conclusions: Supplementation with omega-3 fatty acids and creatine monohydrate was associated with within-group improvements in cognitive function in this exploratory sample of older adults. Both interventions represent promising strategies for the promotion of brain health, although further studies would be needed to confirm these findings.

KEYWORDS

Mild cognitive impairment; nutritional neuroscience; sarcopenia; body composition; neuroprotection; functional

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mobility; dietary intervention; cognitive aging; muscle preservation.

INTRODUCTION

Cognitive abilities and memory tend to decline in older adults, a process that is linked to significant changes in biological, biochemical, and psychological functions and body composition¹. One of the most affected aspects is cognitive performance, evidenced by memory impairments and a decreased ability to process new information², characteristics that constitute indicators of mild cognitive impairment. However, this problem can be mitigated through strategies such as timely diagnosis, physical exercise, and the adoption of a healthy diet³.

Cognitive function is influenced by both non-modifiable factors such as age and genetics, and modifiable factors, including diet and physical activity. Within this context nutrition plays a fundamental role in maintaining memory and cognitive function, so a proper diet can help prevent their decline. The consumption of omega-3 fatty acids, in particular, has demonstrated neuroprotective effects in epidemiological studies, suggesting its potential in preventing cognitive decline and reducing the risk of dementia⁴.

On the other hand, the brain requires a high energy demand for functioning, which depends on the production of adenosine triphosphate (ATP) through metabolic processes and creatine availability in the brain. There is evidence that demonstrates the significant association of these factors to brain health. In this regard, a systematic review has evidenced that supplementation with creatine exerts beneficial effects on memory in healthy individuals, probably mediated by the increase of phosphocreatine and ATP. Also, an increase has been observed in oxidative phosphorylation at the synaptic and mitochondrial level, a process essential for the maintenance of neuronal function⁴.

Additionally, several studies highlight the role of creatine in the maintenance of a healthy body composition in older adults, a stage characterized by a progressive reduction of muscle mass and an increase of fat mass⁵. Supplementation with creatine has been shown to favor the preservation and increment of muscle mass, which is particularly relevant in individuals at risk of sarcopenia or who may present this condition. On the other hand, the scientific evidence also suggests that omega-3 fatty acids contribute to improving the lipidic profile, reducing the serum levels of ApoB100⁶, in addition to favoring the reduction of fat mass and, with it, the risk of various diseases and the morbidity and mortality associated⁵⁻⁷.

Overall, the available evidence indicates that supplementation with omega-3 as well as with creatine exerts beneficial effects over cognitive function in older adults. In this context,

the present study had as its objective to evaluate the impact of both interventions in a specific population of older adults who reside in Lima, Peru, with the aim of providing contextualized evidence that contributes to the understanding of these nutritional strategies in that population.

MATERIALS AND METHODS

Study Design and Participants

A quasi-experimental study with non-probabilistic convenience sampling was conducted. The target population consisted of adults aged 60 years and older who attended a care center in Lima, Peru. The sample included 28 participants that regularly attended the center and agreed to participate by providing written informed consent.

Individuals under 60 years of age were excluded, as were those with diagnosed neurological disorders, mental illnesses, or brain pathologies. Illiterate, colorblind, or visually or hearing-impaired participants who could interfere with the proper application of the procedures were also excluded. Patients with acute or chronic kidney disease, pacemaker implants, fish allergies, and those undergoing anticoagulant treatment such as warfarin were also excluded.

Participants were consecutively and alternately assigned to two intervention groups for 12 weeks: one group receiving creatine supplementation and the other receiving omega-3 supplementation. Each group consisted of 14 participants. The creatine group included 10 women and 4 men, while the omega-3 group consisted of 12 women and 2 men.

Instruments and Procedures

Baseline and at the end of supplementation assessments were conducted. The omega-3 group received two soft gel capsules daily (830 mg total), with a composition of EPA: 205 mg, DHA: 480 mg, and other omega-3s: 145 mg (Nordic Naturals®). The creatine group received 5 g daily of creatine monohydrate (two scoops dissolved in a cup of water) (Kevin Levrone®).

Both groups were instructed to consume the supplements on an empty stomach, before breakfast, with daily follow-up via text message to verify adherence.

To assess the effects of the intervention, cognitive function, body composition, and nutritional status were evaluated. Cognitive performance was measured using the Adenbrooke's Cognitive Examination (ACE)^{8,9} and the Rowland Universal Dementia Assessment Scale (RUDAS)^{10,11}.

Anthropometric measurements took place with participants barefoot and wearing light clothing, including measurement of biceps and triceps skinfolds, Mid-Upper Arm Circumference, calf circumference, abdominal circumference, and estimates of body fat percentage, muscle mass, and visceral fat.

Height was measured using a standardized fixed wooden stadiometer (CENAN-INS, 2004), while weight and body composition were assessed with a segmented bioelectrical impedance scale (OMRON HBF-514, Tokyo, Japan), following the manufacturer's reference values. Skinfold thickness was measured using a Slim Guide caliper (Creative Health), and circumferences were obtained with a Lufkin W606PM flexible measuring tape.

Additionally, nutritional status and functional mobility were assessed using the Mini Nutritional Assessment (MNA)¹² and the Timed Up and Go (TUG) test^{13,14}, respectively.

Statistical Analysis

The information obtained was entered into Microsoft Excel and analyzed using SPSS version 29. Baseline comparisons were first performed to assess the initial comparability between groups.

The distribution of the data was verified using the Shapiro-Wilk test. For within-group analysis, the paired-samples t-test was used, while for between-group comparisons, the independent-samples t-test was used. Categorical variables were analyzed using the chi-square test.

Pre- and post-intervention changes were calculated using the delta change, along with confidence intervals and p-values to determine statistical significance. Effect size was estimated using Cohen's d, interpreted as small (0.2), moderate (0.5), and large (0.8).

Also, the deltas between the two groups were compared to assess differences in the magnitude of the effect. Values of $p < 0.05$ were considered statistically significant, with a 95% confidence level.

Given the limited sample size, all statistical analyses should be interpreted cautiously. Parametric tests were retained after verification of distributional assumptions using the Shapiro-Wilk test; however, the study was underpowered to detect small to moderate between-group differences, and effect size estimates may be unstable. Therefore, all findings should be considered exploratory and hypothesis-generating.

Ethical Considerations

The study was approved by the Ethics Committee of Universidad Le Cordon Bleu (resolution CI-ULCB-078). All procedures were conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and the current regulations related to research with human participants.

RESULTS

Baseline demographic and anthropometric characteristics were comparable between groups, suggesting an acceptable

level of baseline comparability, although the limited sample size reduced the ability to detect potentially relevant clinical differences (Table 1). Both intervention groups showed significant within-group improvements in global cognitive performance measured by ACE and RUDAS after 12 weeks of supplementation (Table 2). In the omega-3 group, ACE scores increased from 88.43 ± 5.8 to 92.64 ± 5.4 ($\Delta = +4.21$ points; $p = 0.013$; Cohen's $d = 0.77$), and RUDAS scores increased from 26.57 ± 2.90 to 28.57 ± 2.60 ($\Delta = +2.00$ points; $p = 0.043$; $d = 0.60$), corresponding to moderate within-group effect sizes. In the creatine group, ACE increased from 87.86 ± 6.20 to 92.14 ± 5.50 ($\Delta = +4.29$; $p = 0.001$; $d = 1.22$) and RUDAS from 25.64 ± 3.10 to 28.29 ± 2.70 ($\Delta = +2.64$; $p = 0.001$; $d = 1.39$), indicating large within-group effect sizes.

In ACE cognitive domains, significant within-group improvements were observed mainly in memory and visuospatial abilities in both groups, whereas language improvement reached statistical significance only in the creatine group (Table 3). However, in RUDAS cognitive domains, significant improvements were identified in memory and visuoconstruction in both groups, while praxis and language improvements were observed only in the creatine group (Table 4); both omega-3 and creatine resulted in significant changes in memory and visuospatial skills, and statistically significant within-group improvements in language and praxis were observed only in the creatine group; however, between-group differences in these domains were small and non-significant.

No statistically significant between-group differences were identified in ACE cognitive domains despite some numerically larger within-group effect sizes in the creatine group (Table 5). The mean change in ACE was similar in the omega-3 and creatine groups ($\Delta \approx +4.2$ points in both), and the between-group difference in ACE change was small and non-significant. Similarly, no significant between-group differences were observed in RUDAS domain-specific analyses (Table 6). Because both groups were evaluated twice using the same instruments and there were no placebo or usual care control group, part of the observed within group improvements in ACE and RUDAS scores may reflect practice effects inherent to repeated cognitive testing rather than specific supplementation effects. Therefore, the observed changes should be interpreted with caution and cannot be unequivocally attributed to the interventions.

In anthropometric analyses, omega-3 supplementation was associated with small reductions in body fat percentage and biceps skinfold thickness, whereas creatine supplementation was associated with increased muscle mass and reduced biceps skinfold thickness (Table 7). However, no statistically significant between-group differences were identified in anthropometric outcomes (Table 8), None-

Table 1. Baseline characteristics of participants by intervention group

Variable	Omega-3 (n = 14) (Mean ± SD)	Creatine (n = 14) (Mean ± SD)	p
Sex, n (%)			
Women	12 (85.7)	10 (71.4)	0.36
Men	2 (14.3)	4 (28.6)	
Age (years)	73.14 ± 6.33	71.78 ± 7.75	0.61
Height (cm)	157.89 ± 8.71	161.03 ± 9.39	0.38
Weight (kg)	68.51 ± 12.51	68.53 ± 10.98	0.99
BMI (kg/m ²)	27.25 ± 4.27	26.40 ± 3.96	0.58
Abdominal circumference (cm)	94.22 ± 11.46	90.52 ± 8.46	0.32
Arm circumference (cm)	27.57 ± 3.19	28.40 ± 3.08	0.46
Calf circumference (cm)	34.87 ± 3.55	35.60 ± 2.44	0.52
Biceps skinfold (mm)	14.57 ± 3.67	14.71 ± 4.82	0.93
Triceps skinfold (mm)	17.64 ± 4.58	17.50 ± 5.55	0.94
Visceral fat (BIA index)	11.15 ± 4.87	10.69 ± 3.40	0.77
Body fat (%)	38.16 ± 6.32	36.56 ± 8.28	0.55
Muscle mass (%)	25.17 ± 3.02	26.03 ± 3.32	0.47

Values are expressed as mean ± standard deviation, except for sex (absolute frequency). Visceral fat corresponds to an index estimated by bioimpedance, without physical units. BMI: body mass index. Body composition measurements were obtained using bioelectrical impedance analysis (BIA). The p-value shows no difference between the baseline characteristics of the two groups.

Table 2. Changes in Global Cognitive Performance After Omega-3 and Creatine Intervention

Group	Test	Pre (Mean ± SD)	Post (Mean ± SD)	Δ Change (Post – Pre)	p	Cohen's d	Magnitude
Omega-3	ACE	88.43 ± 5.80	92.64 ± 5.40	+4.21	0.013	0.77	Moderate
Omega-3	RUDAS	26.57 ± 2.90	28.57 ± 2.60	+2.00	0.043	0.60	Moderate
Creatine	ACE	87.86 ± 6.20	92.14 ± 5.50	+4.29	0.001	1.22	Large
Creatine	RUDAS	25.64 ± 3.10	28.29 ± 2.70	+2.64	0.001	1.39	Large

Values are expressed as mean ± standard deviation. Δ represents post-intervention minus pre-intervention values within each group.

theless, the absolute magnitude of these anthropometric changes was small, and their clinical relevance in this context remains uncertain.

In the mobility assessment using the Timed Up and Go test, the omega-3 group showed no significant changes af-

ter the intervention, with an increase in mean execution time from 8.87 ± 3.48 s to 10.05 ± 5.75 s (Δ = +1.18 s; p = 0.51; d = 0.23). In contrast, the creatine group showed a significant reduction in execution time, from 8.87 ± 3.48 s to 8.16 ± 3.49 s (Δ = -0.72 s; p = 0.028; d = -0.46).

Table 3. Within-Group Changes in ACE Cognitive Domains

Domain	Δ Omega-3	p	Δ Creatine	p
Orientation	+0.14	0.336	+0.21	0.336
Attention	+0.29	0.218	+0.43	0.212
Memory	+2.36	0.043*	+1.79	0.016*
Verbal fluency	+0.21	0.678	+0.29	0.365
Language	+0.36	0.444	+0.93	0.037*
Visuospatial	+0.79	0.015*	+0.71	0.027*

Δ indicates mean change (post – pre). * p < 0.05.

Table 4. Within-Group Changes in RUDAS Cognitive Domains

Domain	Δ Omega-3	p	Δ Creatine	p
Memory	+0.72	0.041*	+1.00	0.008*
Praxis	+0.29	0.218	+0.57	0.039*
Language	+0.29	0.264	+0.71	0.021*
Visuoconstruction	+0.65	0.032*	+0.86	0.012*
Orientation	+0.07	0.512	+0.21	0.336

Δ indicates mean change (post – pre). * p < 0.05.

DISCUSSION

Nutrition is a key determinant of brain health across the lifespan, with up to 45% of dementia cases estimated to be preventable by the modification of risk factors, with diet as a central axis¹⁵. Among the key nutrients for cognitive health, omega-3 fatty acids have received particular attention, and shown to mitigate neuroinflammation, preserve brain structure by promoting neurogenesis, and especially protect the volume of regions such as the hippocampus, which is fundamental for memory¹⁵⁻¹⁷.

Our results with omega-3 show improvement in global cognitive function and in domains such as memory, language, and visuospatial ability, consistent with what was reported by Stavrinou et al.¹⁸. However, given the absence of a placebo or usual-care control group and the repeated administration of ACE and RUDAS, part of these improvements may be driven by practice effects rather than specific supplement-related changes. Also, findings from a Korean longitudinal cohort support the positive effect of omega-3 on overall cognition and long-term memory¹⁹, which suggests that our short-term results could be amplified with longer interventions.

Table 5. Between-Group Comparison in ACE Cognitive Domains

Domain	p	Cohen's d	Magnitude
Orientation	0.590	0.15	Small
Attention	0.460	0.21	Small
Memory	0.340	0.33	Small
Verbal fluency	0.780	0.07	Small
Language	0.074	0.48	Moderate
Visuospatial	0.670	0.12	Small

No statistically significant between-group differences were observed.

Table 6. Between-Group Comparison in RUDAS Cognitive Domains

Domain	p	Cohen's d	Magnitude
Memory	0.310	0.34	Small
Praxis	0.270	0.36	Small
Language	0.140	0.48	Moderate
Visuoconstruction	0.380	0.25	Small
Orientation	0.290	0.22	Small

No statistically significant between-group differences were observed.

The improvements observed in ACE and RUDAS, including language, memory, and visuospatial and visuoconstructive functions, could be explained by the preservation of white matter integrity, maintenance of hippocampal volume, and reduction of resolving-mediated neuroinflammation. A meta-analysis of 58 randomized controlled trials reports benefits with doses between 1000 and 2500 mg/day²⁰; however, in our study, effects were observed with 850 mg/day, which could reflect a "threshold effect," in which the incorporation of omega-3 into neuronal membranes reaches an optimal level that stabilizes synaptic function without requiring higher doses²¹.

Also, omega-3 supplementation has been linked to a reduction in body fat percentage and biceps skinfold thickness, which may suggest a potentially favourable effect on subcutaneous adiposity. In addition, a downward trend in abdominal circumference was observed. These results are consistent with those reported by Salman et al., who, after 12 weeks of omega-3 supplementation, described a reduction in abdominal and visceral fat, although with neutral results on cognitive function²². For their part, Stavrinou et al. reported both cognitive improvement and a reduction in to-

Table 7. Pre- and Post-Intervention Anthropometric Changes Within Each Group

Variable	Group	Pre (Mean $\pm$ SD)	Post (Mean $\pm$ SD)	Δ Change (Post – Pre)	95% CI	p	Cohen's d
Weight (kg)	Omega-3	68.51 $\pm$ 12.51	67.94 $\pm$ 12.13	–0.57	(–2.04, 0.90)	0.150	–0.16
Weight (kg)	Creatine	68.53 $\pm$ 10.98	68.44 $\pm$ 10.77	–0.09	(–1.62, 1.44)	0.829	–0.03
BMI (kg/m ²)	Omega-3	27.25 $\pm$ 4.27	27.03 $\pm$ 4.10	–0.22	(–0.88, 0.44)	0.667	–0.05
BMI (kg/m ²)	Creatine	26.40 $\pm$ 3.96	26.36 $\pm$ 3.95	–0.04	(–0.71, 0.63)	0.300	–0.01
Abdominal circumference (cm)	Omega-3	94.22 $\pm$ 11.46	92.88 $\pm$ 10.97	–1.34	(–3.90, 1.22)	0.061	–0.55
Abdominal circumference (cm)	Creatine	90.52 $\pm$ 8.46	89.81 $\pm$ 8.02	–0.71	(–2.92, 1.50)	0.232	–0.30
Arm circumference (cm)	Omega-3	27.57 $\pm$ 3.19	27.51 $\pm$ 3.25	–0.06	(–2.12, 2.00)	0.915	–0.02
Arm circumference (cm)	Creatine	28.40 $\pm$ 3.08	28.27 $\pm$ 3.14	–0.13	(–1.50, 1.24)	0.718	–0.06
Calf circumference (cm)	Omega-3	34.88 $\pm$ 3.41	34.33 $\pm$ 3.39	–0.55	(–1.12, 0.02)	0.055	–0.56
Calf circumference (cm)	Creatine	35.61 $\pm$ 3.57	35.84 $\pm$ 3.62	+0.23	(–0.09, 0.55)	0.463	0.20
Biceps skinfold (mm)	Omega-3	14.57 $\pm$ 4.41	13.60 $\pm$ 4.18	–0.97	(–1.65, –0.29)	0.024	–0.68
Biceps skinfold (mm)	Creatine	14.71 $\pm$ 3.89	13.33 $\pm$ 3.67	–1.38	(–2.11, –0.65)	0.007	–0.85
Triceps skinfold (mm)	Omega-3	17.64 $\pm$ 5.27	16.70 $\pm$ 5.01	–0.94	(–2.15, 0.27)	0.123	–0.44
Triceps skinfold (mm)	Creatine	17.50 $\pm$ 4.91	16.89 $\pm$ 4.68	–0.61	(–1.68, 0.46)	0.252	–0.32
Visceral fat (BIA index)	Omega-3	11.2 $\pm$ 3.1	10.6 $\pm$ 3.0	–0.60	(–1.45, 0.25)	0.118	–0.38
Visceral fat (BIA index)	Creatine	10.9 $\pm$ 2.8	10.5 $\pm$ 2.7	–0.40	(–1.30, 0.50)	0.241	–0.25
Body fat (%)	Omega-3	38.16 $\pm$ 6.32	37.54 $\pm$ 6.01	–0.62	(–1.62, 0.38)	0.042	–0.35
Body fat (%)	Creatine	36.56 $\pm$ 8.28	35.74 $\pm$ 7.95	–0.82	(–2.57, 0.93)	0.112	–0.31
Muscle mass (%)	Omega-3	25.17 $\pm$ 3.02	25.18 $\pm$ 3.10	+0.01	(–1.54, 1.56)	0.986	0.00
Muscle mass (%)	Creatine	26.03 $\pm$ 3.32	27.03 $\pm$ 3.25	+1.00	(–0.30, 2.30)	0.014	0.77

Body-composition measurements were obtained using bioelectrical impedance analysis (BIA).

tal fat¹⁸. These effects could be explained by the modulation of lipoinflammation through mediators derived from DHA and EPA, such as resolvins, maresins, and protectins, which inhibit the activity of nuclear factor kappa/beta (NF- κ Beta)²³. Nonetheless, the absolute magnitude of the anthropometric changes observed in our study was small, and their clinical relevance in relatively healthy community-dwelling older adults remains uncertain.

On the other hand, creatine, widely used for its ergogenic effect, has emerged as a modulator of brain function, partic-

ularly in older adults, with evidence of benefits in memory and cognitive performance^{24,25}.

In our study, supplementation with 5 g/day during twelve weeks produced significant improvements in global cognition, with large effect sizes, as well as in memory, language, and visuospatial function domains, consistent with meta-analyses that demonstrate significant improvements in memory, especially in older populations^{4,26}. Even though some studies use higher doses²⁷ our findings are consistent with previous studies reporting cognitive benefits at moderate creatine doses, as

Table 8. Between-Group Comparison of Anthropometric Changes

Variable	Δ Omega-3	Δ Creatine	Between-Group Difference (Creatine – Omega-3)	p	Cohen's d	Magnitude
Weight (kg)	-0.57	-0.09	0.48	0.620	0.13	Small
BMI (kg/m ²)	-0.22	-0.04	0.18	0.580	0.05	Small
Abdominal circumference (cm)	-1.34	-0.71	0.63	0.470	0.26	Small
Arm circumference (cm)	-0.06	-0.13	-0.07	0.880	-0.03	Small
Calf circumference (cm)	-0.55	+0.23	0.78	0.120	0.39	Small
Biceps skinfold (mm)	-0.97	-1.38	-0.41	0.290	-0.23	Small
Triceps skinfold (mm)	-0.94	-0.61	0.33	0.410	0.18	Small
Visceral fat (BIA index)	-0.60	-0.40	0.20	0.340	0.21	Small
Body fat (%)	-0.62	-0.82	-0.20	0.790	-0.08	Small
Muscle mass (%)	+0.01	+1.00	0.99	0.099	0.74	Moderate

No statistically significant between-group differences were identified.

proposed by Ostojic et al., who describe cognitive benefits with intakes above 0.95 g/day²⁸. Also, creatine supplementation was associated with changes in body composition, with an increase in muscle mass and a reduction in biceps skinfold thickness, suggesting an anabolic effect consistent with the available evidence^{5,29}. This effect could be mediated by the activation of anabolic signaling pathways and, at the brain level, by the optimization of ATP homeostasis, which is essential for cognitive processing^{4,5,28,29}. The increase in muscle mass was accompanied by a statistically significant reduction in TUG time in the creatine group. However, the absolute change (approximately -0.7 seconds) was small, and its clinical relevance in relatively high-functioning older adults is likely modest.

Although numerically larger within-group effect sizes were observed in some cognitive domains in the creatine group, no statistically significant between-group differences emerged in either global or domain-specific outcomes. Consequently, these findings cannot be interpreted as evidence of superiority of one intervention over the other and should instead be viewed as preliminary signals that require confirmation in larger, adequately powered randomized trials. Overall, both supplements were associated with within-group cognitive improvements in this exploratory sample.

CONCLUSIONS

In this exploratory quasi-experimental study, omega-3 fatty acids and creatine monohydrate supplementation were associated with within-group improvements in cognitive outcomes among older adults. Given the absence of statistically significant

between-group differences and the small, non-randomized sample, these results should be regarded as exploratory, and larger randomized trials are required to confirm potential differential effects.

A central finding of this study is that, despite some numerically larger within-group effect sizes in certain cognitive domains in the creatine group, no statistically significant between-group differences were detected in global or domain-specific outcomes when directly comparing creatine with omega-3. The mean changes in ACE and RUDAS global scores were similar in both groups, and the between-group effect sizes for cognitive domains were generally small and non-significant. Consequently, our data do not support the conclusion that one supplement is superior to the other in this context, and any apparent numerical advantage for creatine in selected domains must be interpreted with considerable caution. Taken together, these results suggest that both omega-3 fatty acids and creatine monohydrate may be associated with within-group improvements in cognitive performance in older adults, but the quasi-experimental, non-randomized design, small sample size, and absence of a placebo or usual-care control group substantially limit causal inference and increase the risk that some of the observed changes reflect practice effects, regression to the mean, or other unmeasured factors.

Limitations and Future Perspectives

Several limitations must be considered when interpreting these findings. First, the quasi-experimental, non-randomized

design increases the risk of selection bias and residual confounding. Second, the small sample size results in limited statistical power, unstable estimates of effect size, and a high risk that some Cohen's *d* values are inflated. Third, the absence of a placebo or usual-care control group, combined with repeated cognitive assessments, introduces the possibility of practice effects, which may partially explain the within-group improvements observed in ACE and RUDAS.

Despite these limitations, the study provides preliminary evidence on the differential impact of both interventions and opens new avenues for research. In particular, the potential synergistic interaction between omega-3 and creatine, given their complementary effects on neuroinflammation and brain energy metabolism, represents an area of interest. Future studies with larger sample sizes, randomized designs, and long-term follow-up will help confirm these findings and evaluate the potential cognitive and anthropometric effects of both interventions

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