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High-Concentration rTG EPA+DHA Fish Oil in Brain Lipid Nutrition and Cognitive Aging: A Translational Evidence Framework

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Abstract: Neuronal membranes contain substantial DHA, whereas EPA contributes more strongly to circulating lipid mediators and systemic inflammatory regulation. We used the BCLC® high-concentration rTG fish oil as a defined exposure platform and examined human evidence on brain lipid nutrition and cognitive ageing. The ingredient contained 68.9–71.4% EPA+DHA and 81.7–84.0% triglyceride-type lipids; residual ethyl esters were low and oxidation indices were controlled. The larger trials in cognitively healthy older adults were mainly neutral. OPAL enrolled 867 participants, an 18-month DHA-rich trial randomized 403 participants, and the VITAL cognitive ancillary studies included more than 4,000 participants. Smaller trials and a recent dose-response analysis produced a less uniform pattern. In a 2024 meta-analysis of 24 randomized studies (n=9,660), executive function showed a potential upward trend under selected exposure conditions. Baseline omega-3 status, daily dose, treatment duration, cognitive domain, and mild cognitive impairment may therefore separate responsive from nonresponsive settings. Future studies of the BCLC® rTG formulation can test that question by pairing Omega-3 Index measurements with domain-specific cognition and baseline nutritional status.

Keywords: DHA; EPA; brain lipids; cognition; healthy aging; omega-3 index; rTG fish oil

Introduction

Cognitive aging is accompanied by gradual changes in neuronal membrane organization, synaptic signaling, vascular support, and inflammatory regulation. Long-chain n-3 polyunsaturated fatty acids have therefore remained a major nutritional focus in research on later-life brain health. DHA is highly represented in neural phospholipids, including synaptic and photoreceptor membranes, where it contributes to membrane fluidity, receptor organization, vesicle activity, and lipid-mediator signaling. Brain EPA concentrations are lower, but EPA contributes to circulating lipid-mediator pools and systemic inflammatory regulation. Systematic reviews of randomized trials

have consistently recognized this biological rationale while also emphasizing the heterogeneity of cognitive outcomes [1], [2], [3].

That heterogeneity is particularly clear in cognitively healthy older adults. In the OPAL trial, 867 adults aged 70-79 years received 200 mg EPA plus 500 mg DHA daily for 24 months, with no significant between-group difference in cognitive outcomes [4]. A 26-week study of 302 adults aged 65 years or older likewise found no overall cognitive-domain advantage with either 400 or 1,800 mg/day EPA+DHA [5]. In a separate 18-month trial involving 403 cognitively normal adults aged 65-90 years, a DHA-rich intervention did not preserve overall cognitive performance [6]. The VITAL cognitive ancillary studies, which included more than 4,000 older adults, similarly found no significant effect of 1 g/day marine omega-3 on annual cognitive change over approximately 2-3 years [7]. These large trials indicate that increasing omega-3 intake does not automatically translate into measurable improvement in broad cognitive composites when baseline cognition is relatively stable.

Signals have nevertheless emerged under more selective exposure and population conditions. A 2024 dose-response meta-analysis of 24 randomized studies (n=9,660) reported a potential upward trend in executive function under selected dose and status conditions [8]. In older adults with mild cognitive impairment, EPA- and DHA-focused interventions have produced variable findings in memory, executive function, and related outcomes [9]. DHA supplementation has also been associated with cognitive benefits in age-related cognitive decline [10], whereas a randomized trial in Alzheimer disease did not show a generalized slowing of cognitive decline [11]. More recent mild-cognitive-impairment trials and pooled analyses continue to show that the direction and magnitude of response differ according to intervention design, cognitive domain, and participant characteristics [12], [13], [14], [15].

Several factors may help explain why these studies do not converge on a single effect estimate. Baseline omega-3 status determines the exposure contrast created by supplementation; daily dose and DHA:EPA ratio alter the composition of that exposure; treatment duration influences the time available for incorporation into circulating and cellular lipids; and cognitive phenotype determines whether a study is testing prevention, slowing of decline, or domain-specific improvement. Age, APOE genotype, baseline nutritional status, and the sensitivity of the selected cognitive tests can further modify the ability of a trial to detect change. For this reason, nominal capsule dose alone is not sufficient to describe the biological exposure achieved in a cognition study.

Formulation characteristics add another translational layer. The BCLC® platform is derived from mackerel and was developed as a high-concentration EPA+DHA preparation in which triglyceride-type lipids predominate and oxidation is controlled. In the optimized preparations evaluated here, EPA+DHA accounted for 68.9-71.4% of total material, triglyceride-type lipids for 81.7-84.0%, and residual ethyl esters remained low. Defining these attributes before clinical interpretation makes it possible to connect assigned dose with a reproducible ingredient profile and, in future studies, with achieved Omega-3 Index.

Accordingly, the present study used the BCLC® high-concentration rTG fish oil as a defined exposure platform and integrated its analytical profile with randomized human evidence on brain lipid nutrition and cognitive aging. The objective was not to infer cognitive efficacy from ingredient chemistry alone, but to identify the exposure conditions, study populations, and cognitive domains that best explain the coexistence of large neutral trials and more selective signals of benefit. This framework is intended to guide a future formulation-specific study in which baseline nutritional status and achieved omega-3 exposure are measured alongside domain-specific cognitive outcomes.

Materials and Methods

1. Ingredient characterization. Mackerel lipids were recovered and refined under low-oxygen conditions. Ethyl esters were concentrated by two-stage molecular distillation, converted by enzymatic re-esterification, and polished by short-path distillation. We measured EPA+DHA,

triglyceride-type lipids, residual ethyl esters, and oxidation indices in the final optimized preparations.

2. Evidence search. PubMed, PMC, and primary journal sources were searched through August 2026. Search terms included EPA, DHA, fish oil, omega-3, cognition, executive function, memory, mild cognitive impairment, older adults, randomized, placebo, and Omega-3 Index. Randomized controlled trials and meta-analyses in adults aged 40 years or older received priority.
3. Evidence framework. Each trial was classified by baseline cognitive status, daily EPA+DHA exposure, duration, cognitive domain, and biochemical evidence of incorporation. Neutral trials were retained. They are necessary for identifying the settings in which a cognitive response was absent as well as those in which a domain-specific signal appeared.

Results

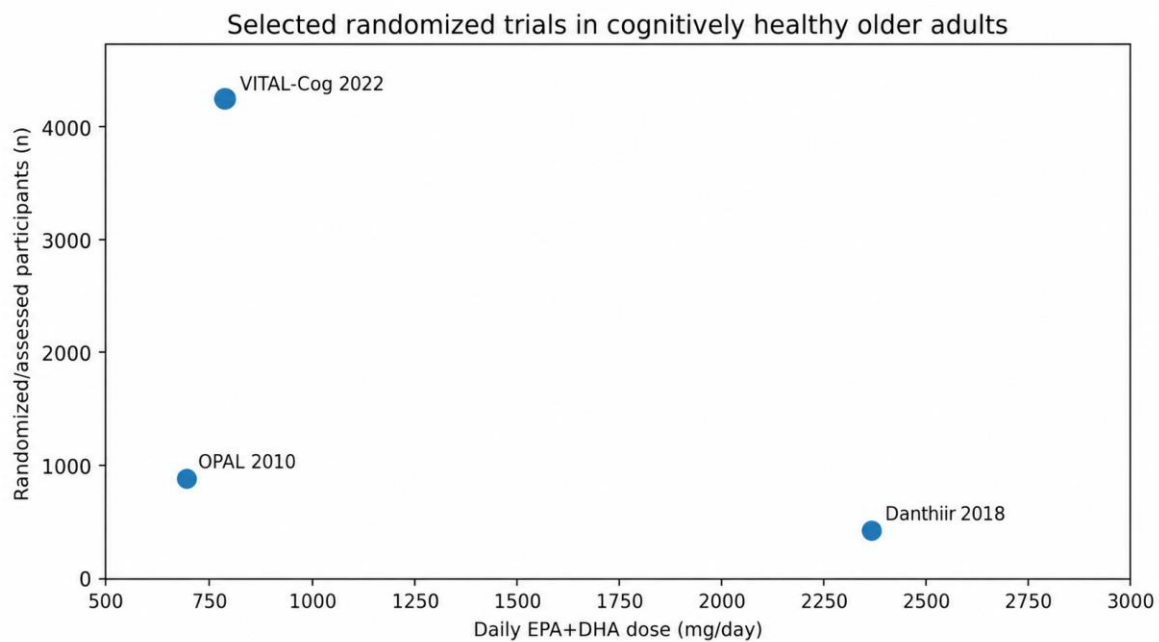
1. 3.1 Formulation profile. EPA+DHA ranged from 68.9% to 71.4% across the three optimized preparations. Triglyceride-type lipids accounted for 81.7–84.0%, residual ethyl esters for 7.9–10.6%, and TOTOX was 15.0–17.0. The resulting matrix had a defined composition for controlled dosing in cognition studies.
2. 3.2 Trials in cognitively healthy older adults. OPAL assigned 867 adults aged 70-79 years to 200 mg EPA plus 500 mg DHA or olive oil for 24 months. Serum EPA and DHA increased, but cognitive performance did not differ between groups [4]. In another trial, 302 participants received 400 or 1,800 mg/day EPA+DHA for 26 weeks; no overall advantage was detected across the cognitive domains [5]. A separate 18-month study randomized 403 cognitively normal adults aged 65-90 years to 1,720 mg DHA plus 600 mg EPA or control. Overall cognitive performance was not preserved by the intervention [6].
3. Large-scale pragmatic evidence. The VITAL cognitive ancillary studies tested 1 g/day marine omega-3, containing 460 mg EPA and 380 mg DHA, in more than 4,000 older adults for approximately 2-3 years. Annual cognitive change was similar to placebo [7]. In this relatively healthy population, increasing omega-3 intake did not produce a detectable short-to-medium-term change in broad cognitive composites.
4. Evidence for context-dependent response. Mild-cognitive-impairment trials have reported variable findings, including memory or executive-function changes in some EPA- or DHA-focused interventions [9], [12], [13]. The 2024 dose-response meta-analysis included 24 studies and 9,660 participants. Executive function showed an upward trend during the first 12 months, particularly when daily n-3 PUFA intake exceeded 500 mg and EPA intake reached approximately 420 mg/day. Signals were stronger where blood DHA+EPA levels were not very low [8].

Table 1. Selected formulation attributes relevant to long-term cognitive trials

Preparation	EPA+DHA (%)	TG-type lipids (%)	Residual (%)	EE	TOTOX
F1	70.6	83.2	8.8		15.0
F2	68.9	81.7	10.6		16.4
F3	71.4	84.0	7.9		17.0

Table 2. Representative randomized evidence on omega-3 supplementation and cognition

Study	Participants duration	/ EPA+DHA exposure	Overall cognitive context
Dangour et al. OPAL [4]	867 healthy adults 70-79 y; 24 months	200 mg EPA + 500 mg DHA/day	No significant between-group difference in cognitive outcomes
van de Rest et al. [5]	302 adults ≥65 y; 26 weeks	400 or 1,800 mg/day EPA+DHA	No overall cognitive-domain advantage
Danthiir et al. [6]	403 randomized adults 65-90 y; 18 months	1,720 mg DHA + 600 mg EPA/day	No overall preservation of cognitive performance; subgroup heterogeneity
Kang et al. VITAL-Cog [7]	>4,000 older adults; ~2-3 years	460 mg EPA + 380 mg DHA/day	No significant effect on annual cognitive change
Suh et al. meta-analysis [8]	24 RCTs; n=9,660	Variable doses / 3-36 months	Potential executive-function signal under selected dose/status conditions

**Figure 1.** Daily EPA+DHA dose and trial scale for three representative randomized studies in cognitively healthy older adults. The figure describes study design scale only, not effect magnitude [4], [6], [7].

Discussion

The trial record does not support a simple linear relation between omega-3 intake and global cognition in healthy older adults. In populations with stable cognition and slow decline, large increases in circulating omega-3 may still produce changes too small for broad composite scores to detect over short or medium follow-up [4]-[7]. Cochrane and later systematic reviews reached similarly cautious conclusions for universal supplementation [1]-[3].

Executive function may behave differently from global cognition. The 2024 dose-response analysis reported its clearest signal under selected dose and exposure conditions [8]. Cognitive domains need not respond equally to membrane composition, vascular support, or inflammatory

tone. Baseline omega-3 status also changes the exposure contrast created by supplementation; nominal dose alone does not show how much EPA+DHA entered circulating and cellular lipids.

The triglyceride-rich structure of the BCLC® oil is relevant at this step because it defines the administered lipid matrix and can be measured alongside achieved omega-3 status. For a cognition trial, a well-characterized lipid form removes part of the uncertainty between capsule dose and achieved Omega-3 Index.

A useful study population would have measurable risk of decline, low-to-moderate omega-3 status, or mild cognitive impairment. Domain-specific tests should accompany any global score. Repeated Omega-3 Index measurements can confirm target exposure and permit cognitive change to be analyzed against achieved biological status rather than assigned capsule dose.

Conclusion

BCLC® high-concentration rTG fish oil supplied a stable EPA+DHA-rich matrix in which triglyceride-type lipids predominated. Large randomized trials in cognitively healthy older adults were generally neutral. Domain-specific trials and pooled analyses, however, indicate that daily dose, baseline omega-3 status, cognitive vulnerability, and exposure time may influence the result. A targeted study using verified Omega-3 Index change and defined cognitive phenotypes is the appropriate next test of this formulation in healthy cognitive ageing.

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