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Randomized, Double-Blind, Controlled Trial of Memory and Attention Enhancement in Adolescents via DHA-Enriched Fish Oil Combined with Galangal Extract

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Abstract: This randomized, double-blind, controlled trial aimed to explore the effects of DHA-enriched fish oil alone or combined with galangal extract on memory and attention in adolescents. A total of 68 adolescents aged 12-18 years were recruited, with 66 completing the 90-day intervention. They were divided into four groups: high-dose combo group (HCG, 600 mg fish oil plus galangal extract daily), high-dose group (HG, 600 mg fish oil daily), low-dose group (LG, 300 mg fish oil daily), and control group (CG, placebo). Participants took the test product for 90 consecutive days, and their attention and memory levels were assessed using the sub-item memory scales and MQ task and the IQ test at baseline (D0), day 30 (D30), and day 90 (D90). Repeated-measures analysis of variance revealed that the combined intervention group exhibited significant improvements in all core memory subscale scores and MQ values. Specifically, at D30, the HCG showed marked increases in all memory subscale scores ($P<0.01$ or $P<0.001$), with further prominent enhancements at D90 (all $P<0.001$). The single-intervention groups (HG and LG) showed moderate improvements in partial memory subscale scores at D30 ($P<0.05$) and D90 ($P<0.05$ or $P<0.01$), but these improvements were significantly weaker than those in the combined intervention group (all $P<0.05$ at D90).The control group showed no significant changes in any memory or cognitive outcomes (all $P>0.05$). No significant changes in IQ-related indicators were observed in the CG, LG, and HG (all $P>0.05$), while the HCG showed significant improvements in key IQ dimensions at D30 ($P<0.05$ or $P<0.01$) and D90 (all $P<0.01$). These findings support that DHA combined with galangal extract improves attention, memory, and decision-execution accuracy in adolescents, and further enhances key IQ-related cognitive functions contributing to cognitive health management. Over the 90-day period, the effects of DHA combined with galangal extract were significantly superior to those of the other three groups.

1. Introduction

Adolescence is a critical period for brain development, during which the hippocampus, prefrontal cortex, and other brain regions closely related to memory and attention[1]. However, contemporary adolescents face high levels of stress and academic pressure, which may lead to memory impairment and attention deficits[2]. Studies have shown that 25-30% of students engage in regular binge drinking and exhibit mild to severe depressive symptoms[3,6], which are associated with deficits in high-interference memory tasks. Additionally, cognitive impairments during adolescence may have long-term impacts on learning ability and mental health[4].

Nutritional interventions have emerged as a promising approach to support adolescent cognitive development[5]. Omega-3 polyunsaturated fatty acids, particularly docosahexaenoic acid (DHA), are key components of neuronal cell membranes and play a vital role in maintaining hippocampal function, synaptic plasticity, and neurotransmitter regulation[6]. Clinical trials have demonstrated that DHA supplementation can improve attention, memory, and cognitive flexibility in both children and adults[7]. Galangin, a flavonoid compound derived from Alpinia galanga (L.) Willd, inhibits acetylcholinesterase, enhances cholinergic transmission, and improves spatial memory while mitigating neurotoxicity-induced memory impairment[8,9]. Previous studies have shown that galangin can increase hippocampal acetylcholine concentrations and exert neuroprotective effects through antioxidant and anti-inflammatory mechanisms[10].

This study tested the synergistic effect of DHA combined with galangal extract on improving adolescents' memory and attention (superior to DHA alone) via the sub-item memory scales (MQ calculation) and IQ test in a 90-day randomized, double-blind, controlled trial, providing evidence for combined nutritional supplements in adolescent cognitive health management.

2. Methods

2.1. Participant

2.1.1. Selection criteria

This study adopted a voluntary recruitment method[12]. A total of 68 teenagers aged 12-18 years (mean 15.30±1.53 years) were recruited as potential participants. The inclusion criteria were: (1) healthy adolescents aged 12-18 years, with a roughly balanced ratio of males to females; (2) no history of neurodevelopmental disorders (e.g., ADHD, ASD) confirmed by participants or guardians; (3) no use of medications or supplements affecting cognitive function; (4) normal or corrected-to-normal vision (due to the visual nature of the tasks); (5) willingness to comply with the study protocol and complete all assessments.

2.1.2. Ethical statement

All participants and their guardians provided signed informed consent. The study was conducted in full compliance with the ethical standards stipulated by the Declaration of Helsinki[13].

2.2. Memory assessment procedure

2.2.1. Five-core sub-item memory scales and MQ calculation

Standardized tools assessed five core memory sub-scales (Directed Memory, Paired-Associate Learning, Free Picture Recall, Meaningless Figure Recognition, Portrait-Characteristic Connection Recall). Memory Quotient (MQ) was calculated via the weight ratio of each dimension's contribution to overall memory function[11].Assessments were conducted at baseline (D0, pre-intervention) and repeated after 30 (D30) and 90 consecutive days (D90) of administration. A consistent test environment (e.g., quietness, lighting) and sequence were maintained to minimize external interference[14].

2.2.2. Stanford-binet intelligence scale testing method

Based on the "Two-Factor Theory of Intelligence", this scale covers core cognitive dimensions (e.g., language comprehension, logical reasoning) and is used here to eliminate intelligence-difference interference on memory assessment[15]. Qualified assessors conducted tests (40-60 minutes per session, to avoid fatigue) in quiet, distraction-free environments with prepared materials; consistent, unified procedures were applied at D0, D30, and D90[16].

2.3. Statistics analysis

Statistical software handled descriptive statistics (mean, standard deviation [SD]) for each measurement variable. For MQ: raw scores of the 5 memory sub-scales are converted to standard scores. MQ is then calculated via weighted ratios (memory orientation:20%, associative learning:25%, free image recall:20%, meaningless graphic recognition:15%, facial feature association:20%), with weights determined by each dimension's contribution to overall memory. For IQ: IQ is derived from standard scores, and inter-group IQ differences are compared across experimental groups. These results support subsequent test evaluations.

3. Results

3.1. Sub-item memory scales and MQ calculation

In this 90-day intervention study, five-dimensional datasets associated with memory were documented for different groups at discrete time points throughout the experimental period(Table 1).

In detail, the control group (CG, n=16) showed no significant changes in all memory subscales during the intervention (all $P>0.05$), confirming the placebo's ineffectiveness(Figure 1A). In the low-dose fish oil group (LG, n=16)(Figure 1B), memory indices showed no difference from the baseline (71.0-72.8) at D30. By D90, scores rose to 78.5-79.8, 3 subscales (e.g. Paired-Associate Learning) improved significantly ($P<0.01$), with an overall increase of 7.3%-14.5%.The high-dose fish oil group (HG, n=17)(Figure 1C) followed a similar improvement trend to LG but with a slightly greater magnitude. At D30, except for Recognition of Meaningless Figures (77.2±4.2, $P<0.01$), the other 4 subscales improved significantly ($P<0.05$), with scores 78.5-79.8. By D90, all subscale scores reached 82.2-85.2; 3 subscales improved significantly ($P<0.01$), with an 12.3%–14.9% increase from baseline, and intra-group ANOVA F-values ranging from 32.8 to 42.7 (all $P<0.01$).

The high-dose fish oil combined with galangal extract group (HCG, n=17)(Figure 1D) demonstrated the most prominent memory improvement, with an earlier onset and longer duration. At D30, all 5 subscales showed extremely significant improvements; 3 (e.g., Paired-Associate Learning: 85.5±4.1) were extremely significant ($P<0.001$), with a 17.8%-22.9% increase from the baseline (71.1-72.4). By D90, all subscale scores peaked at 92.5-96.3, with a 27.5%-36.4% increase from baseline (all $P<0.001$), and were significantly higher than those of LG and HG at the same time point (all inter-group $P<0.05$).

Five-dimensional values were converted to MQ scores per the weighting coefficients of the standard assay(Figure 2). Intergroup MQ discrepancies increased markedly over the experimental duration, demonstrating that fish oil supplementation exerts a beneficial effect on memory enhancement. Furthermore, this effect was significantly potentiated by co-administration of a compound extract of galangal, consistent with the aforementioned findings.

Table 1: Memory subscale scores and baseline characteristics of participants (66 people).

Variable		CG(n=16)		LG(n=16)		HG(n=17)		HCG(n=17)		ANOVA F
		M	SD	M	SD	M	SD	M	SD	
Female		8		8		9		8		
Male		8		8		8		9		
Age		15.2	2.3	14.9	2.2	15.1	2.4	14.8	2.3	0.78 n.s.
D0	Directed Memory	72.5	3.8	72.2	3.9	72.8	3.2	72.4	3.6	0.62 n.s.
	Paired-Associate Learning	72.0	4.0	71.8	4.1	72.3	3.9	71.9	3.9	0.57 n.s.
	Free Recall of Pictures	71.2	4.1	71.0	4.2	71.5	4.0	71.1	3.9	0.60 n.s.
	Recognition of Meaningless Figures	73.5	3.7	73.3	3.8	73.8	3.6	73.4	3.7	0.59 n.s.
	Recall of the Connection between Portraits and Their Characteristics	70.8	3.2	70.5	4.3	71.0	4.1	70.6	4.0	0.63 n.s.
D30	Directed Memory	73.1	3.7	72.6	3.8	77.9*	3.7	85.3**	5.0	8.85*
	Paired-Associate Learning	72.5	3.9	72.2	4.0	78.2*	4.3	85.5***	4.1	12.36**
	Free Recall of Pictures	71.7	4.0	71.3	4.1	78.8*	5.4	86.3***	6.2	13.62**
D30	Recognition of Meaningless Figures	74.0	4.9	73.5	4.7	77.2*	3.3	83.4**	3.1	9.42*
	Recall of the Connection between Portraits and Their Characteristics	71.3	3.3	70.9	4.2	79.0**	4.5	86.8***	5.3	14.18**
D90	Directed Memory	73.6	3.8	78.5*	4.0	83.7*	3.2	94.2***	3.9	35.42***
	Paired-Associate Learning	73.0	4.0	78.7*	4.2	84.0**	4.3	95.0***	4.0	37.9***
	Free Recall of Pictures	74.4	4.7	77.5	5.3	82.2*	5.4	92.5***	3.1	40.3***
	Recognition of Meaningless Figures	72.7	4.0	77.8**	4.2	82.9**	4.1	93.6***	4.0	32.8***
	Recall of the Connection between Portraits and Their Characteristics	71.8	4.2	79.8*	5.3	85.2**	5.5	96.3***	6.2	42.7***

Note: 1. Interpretation of significance markers: $p \geq 0.05$,"n.s."means no statistical difference; $p<0.05$, indicating significant difference; where"*"means $0.01 \leq p<0.05$; "**"means $0.001 \leq p<0.01$; "***" means $p<0.001$.

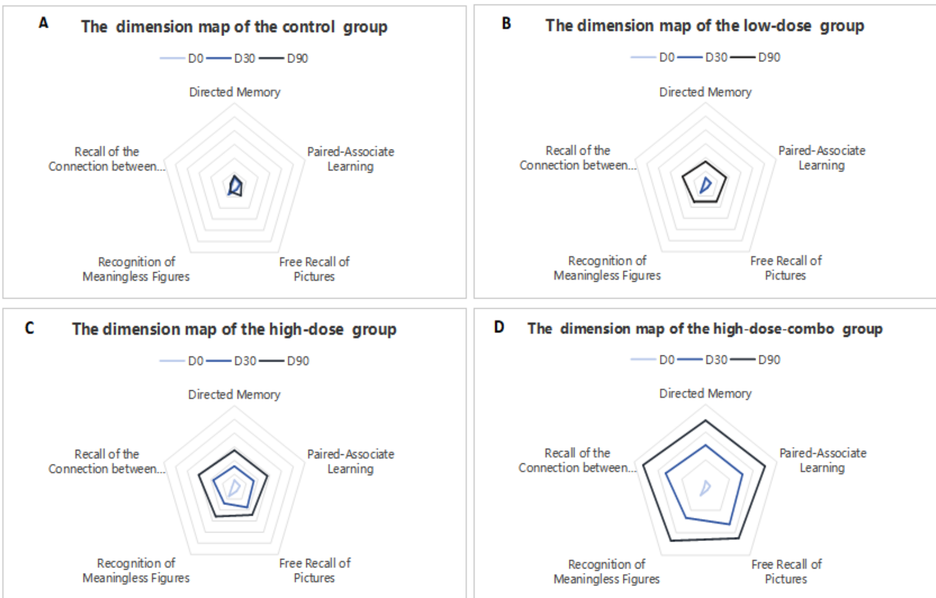

Figure 1: Analysis of the core itemized memory Scale before and after use.

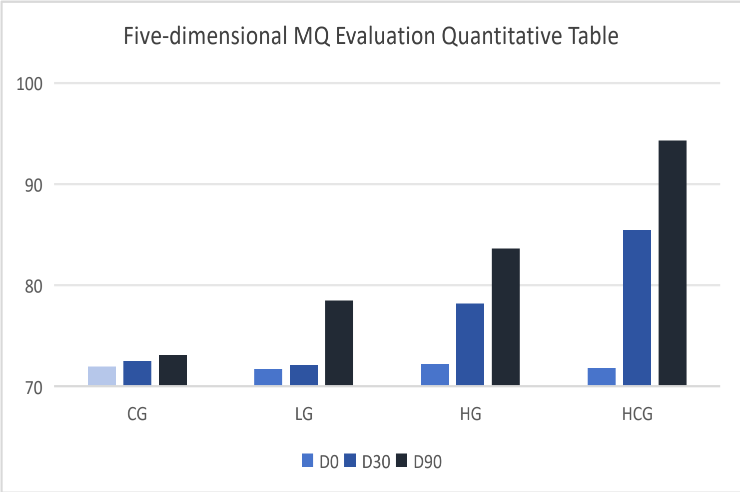

Figure 2: Analysis of MQ calculations at different time periods.

3.2. Stanford-Binet Intelligence Scale Testing Method (IQ test)

CG, LG, and HG showed no significant changes in IQ-related indicators over 90 days (all P>0.05, Table 2). In contrast, HCG exhibited marked improvements; by D30, Fluid Reasoning and Crystallized Knowledge were extremely significant (P<0.01), while Quantitative Reasoning and Working Memory were significant (P<0.05); by D90, all four dimensions reached extremely significant levels (P<0.01). Visual-Spatial Processing remained unchanged across all groups (P>0.05).

The IQ scores of CG, LG, and HG maintained a stable trend with minimal fluctuations (<1.5 points per dimension) from D0 to D90 (Figure 3), which ruled out the confounding effect of intelligence differences on memory assessment. For the HCG group, the significant IQ improvements were consistent with the memory enhancement trend, further supporting the synergistic effect of DHA and galangal extract on cognitive function. This verifies that the significant cognitive improvements (both memory and IQ observed in HCG) were specifically attributed to the nutritional intervention rather than external factors.

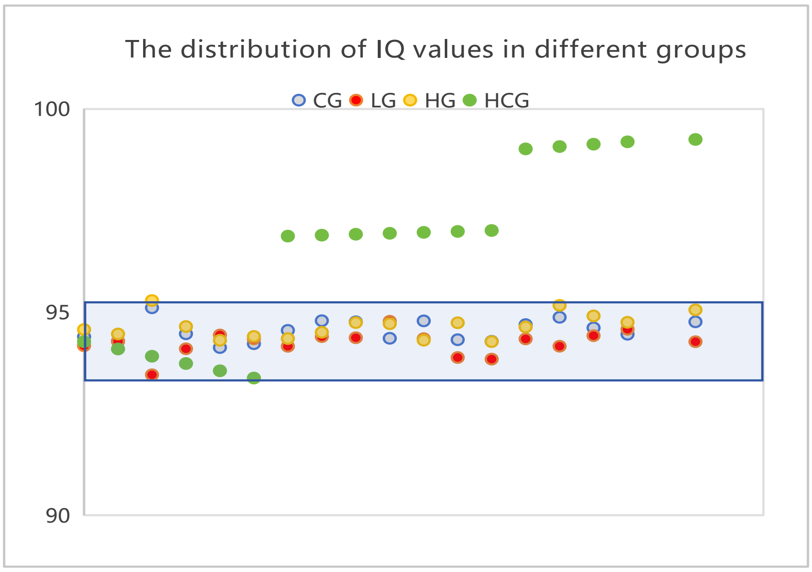

Figure 3: Analysis of IQ for each group of test subjects.

Table 2: Stanford-Binet Intelligence Scale results (66 people).

Variable		CG(n=16)		LG(n=16)		HG(n=17)		HCG(n=17)		ANOVA F
		M	**SD**	**M**	**SD**	**M**	**SD**	**M**	**SD**	
D0	Fluid Reasoning	94.3	3.4	94.1	3.5	94.5	3.6	94.2	3.2	0.48(n.s.)
	Crystallized Knowledge	101.3	3.2	101	3.3	101.4	3.0	101.1	3.1	0.43(n.s.)
	Quantitative Reasoning	89.6	3.7	89.4	3.8	89.8	3.6	89.5	3.7	0.22(n.s.)
	Visual-Spatial Processing	92.5	3.8	92.3	3.9	92.7	3.7	92.4	3.8	0.79(n.s.)
	Working Memory	93.8	3.4	93.6	3.5	94.0	3.3	93.7	3.3	0.51(n.s.)
D30	Fluid Reasoning	94.5	3.2	94.3	3.6	94.4	4.6	97.7**	3.8	6.66*
	Crystallized Knowledge	101.3	4.2	101.1	3.9	101.2	3.0	103.5**	3.7	9.4^{5**}
	Quantitative Reasoning	89.8	4.7	89.4	2.8	89.1	3.7	92.6*	3.9	6.68*
	Visual-Spatial Processing	92.7	2.8	92.3	4.9	92.6	3.7	93.3	3.8	0.83(n.s.)
	Working Memory	94.0	3.4	93.2	3.1	94.0	3.2	96.7*	3.3	7.71*
D90	Fluid Reasoning	94.7	3.4	94.5	3.6	94.2	3.6	99.1**	4.7	12.50**
	Crystallized Knowledge	101.7	3.2	100.6	2.3	101.9	4.0	105.1**	3.1	14.30**
	Quantitative Reasoning	89.5	3.7	89.2	3.8	90.0	3.3	94.2**	3.9	13.83**
	Visual-Spatial Processing	92.9	3.9	92.4	3.3	92.6	3.6	96.5	4.0	0.86(n.s.)
	Working Memory	94.2	3.2	94.6	3.5	94.0	4.3	99.8**	5.2	10.74**

Note: 2. Interpretation of significance markers: p≥0.05,"n.s."means no statistical difference; p<0.05, indicating significant difference; where"*"means 0.01≤p<0.05; "**"means 0.001≤p<0.01; "***" means p<0.001.

3.3. Cross-factor analysis

3.3.1. Baseline consistency analysis

At baseline (D0), there were no significant differences among the four groups (HCG, HG, LG, CG) in terms of all core memory subscale scores and Memory Quotient (MQ) (Table 1). Specifically, the mean scores of each memory subscale across groups ranged from 70.5-73.8, with ANOVAF values between 0.57-0.63 (all P>0.05). Additionally, no significant intergroup differences were observed in all IQ-related dimensions at baseline (Table 2), with ANOVA F values ranging from 0.22-0.79 (all P>0.05). The consistent baseline performance in memory and IQ indicators among groups ensured the reliability and comparability of subsequent intervention effect analyses, eliminating the interference of initial individual differences on the study results.

3.3.2. Temporal effect analysis

Intergroup comparisons of temporal effects revealed that the combined-intervention group (HCG) exhibited significantly higher improvement rates in all core memory subscale scores, MQ values and key IQ dimensions across all intervention time points compared to the single-intervention groups (HG, LG) and control group (CG) (Figure 1-3).

Notably, the gap in cognitive enhancement between the HCG and the other three groups widened over time. At D90, the overall memory improvement of the HCG (27.5%-36.4%) was 2.3-3.5 times that of the single-intervention groups (7.3%-14.5%) and significantly higher than the control group (<2%). The temporal effect analysis revealed that the cognitive benefits of the combined intervention continued to increase over the 90-day period, while the effects of DHA alone plateaued after 30 days. This suggests that the synergistic effect of DHA and galangal extract may require a longer intervention period to be fully manifest， and the synergistic improvements in both memory and IQ further confirms the comprehensive cognitive benefit of the combined nutritional intervention.

4. Conclusions

This study demonstrated that 90-day supplementation with DHA-enriched fish oil combined with galangal extract significantly improved attention and memory in adolescents, with superior effects compared to DHA alone (either high or low dose). The combined intervention group showed the greatest improvements in tests, indicating enhanced executive function, information processing speed, and episodic memory.

The synergistic effect of DHA and galangal extract may be attributed to their complementary mechanisms of action. DHA, as a key component of neuronal membranes, enhances synaptic plasticity and hippocampal function by regulating neurotransmitter release and reducing oxidative stress[16]. Previous studies have shown that DHA supplementation increases brain-derived neurotrophic factor (BDNF) levels and improves NMDA receptor function, which are critical for learning and memory[17]. Galangin, a flavonoid in galangal extract, inhibits acetylcholinesterase activity, thereby increasing hippocampal acetylcholine concentrations and enhancing cholinergic transmission[8]. Additionally, galangin exerts antioxidant and anti-inflammatory effects, mitigating neurotoxicity induced by reactive oxygen species and pro-inflammatory cytokines[18]. These mechanisms collectively promote cognitive function by protecting neuronal integrity and improving synaptic communication. In conclusion, this study provides evidence that DHA-enriched fish oil combined with galangal extract is a safe and effective nutritional intervention for improving attention and memory in adolescents.

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