LYSOVETA®

Research Summary

LPC'S UNIQUE BRAIN BENEFITS THROUGH PRECISION OMEGA-3 DELIVERY

INTRODUCTION

LYSOVETA®: Next-Generation Targeted Brain Nutrition

LYSOVETA®: A NOVEL LPC-BOUND OMEGA-3 SUPPLEMENT FOR COGNITIVE VITALITY

Cognitive health sits at the intersection of scientific research and consumer wellness. This paper distills cutting-edge research on lysophosphatidylcholine-bound omega-3 polyunsaturated fatty acids (LPC bound omega-3) and explores how Aker BioMarine's Lysoveta® is a genuine breakthrough innovative product in the growing brain health supplement market. By translating complex neuroscience into clear language, we aim to inform scientists, product developers and marketers about the science, efficacy and opportunities around this unique ingredient.

WHY NOW? THE GROWING IMPORTANCE OF COGNITIVE HEALTH

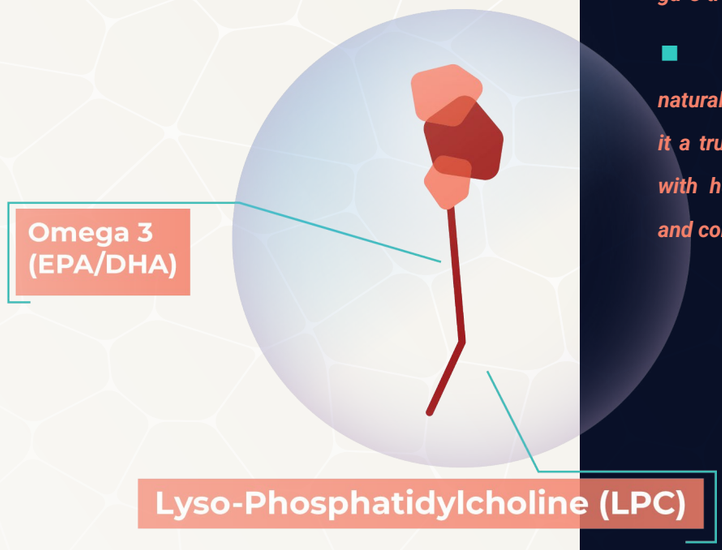
The brain health supplement market is experiencing strong growth as consumers increasingly recognize the role of nutrition in supporting mental performance and protecting cognitive function across the lifespan. Rising life expectancy, the increasing prevalence of age-related cognitive decline, and growing awareness of mental wellness are key drivers behind this trend.

- ***Rising global consumer concern***. Modern lifestyles, longer lifespans and digital overload mean people are increasingly aware of memory, attention and mood. The global brain-health supplement industry reflects this interest. According to Grand View Research's 2023 report, the brain health supplements market was valued at ***US $8.63 billion in 2022*** and is projected to reach ***US $23.41 billion by 2030***, representing a compound annual growth rate (CAGR) of around 13%[1]. North America currently holds about 40% of the market, while Asia–Pacific is expected to grow fastest. The largest segment is memory enhancement (>25 % share), highlighting that consumers are largely motivated by everyday cognitive needs such as focus and recall rather than clinical disease management[1].

- ***Generational differences.*** Different generations are approaching cognitive health from distinct perspectives. Younger consumers seek products that enhance daily brain performance, helping them manage stress, focus, and productivity in fast-paced, demanding environments. Older generations, in contrast, prioritize maintaining long-term brain health and preventing decline, focusing on memory, resilience, and sustained cognitive capacity with age.

- ***Specialized demand.*** Importantly, consumers today are also looking beyond broad "general wellness" products. There is a clear demand for ingredients that are tailored specifically for brain health, designed to deliver measurable effects on memory, learning, focus, and neuroprotection, rather than supplements that only support cognition as a secondary benefit[1].

Together, these dynamics create an opportunity for innovative formulations that genuinely improve brain nutrient delivery setting the stage for science-backed, brain-targeted solutions.



1 Transparency Market Research. (2024, January). Brain health supplements market - Global industry analysis, size, share, growth, trends, and forecast, 2023–2031. Transparency Market Research. www.transparencymarketresearch.com/brain-health-supplements-market.html

WHAT IS LYSOVETA®?

- ***Lysoveta® is a proprietary lysophosphatidylcholine (LPC)-based ingredient delivering EPA/DHA nutrients to the brain. Lysoveta® consists of the omega-3 fatty acids docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), esterified to lysophosphatidylcholine (LPC).***

- ***Lysoveta® is derived from Antarctic krill that has been specialized to up-concentrate the LPC form of omega-3 fatty acids.***

- ***Unlike conventional fish oil, algae oil or krill oil supplements that deliver DHA/EPA in triacylglycerol (TG) or phospholipid (PC) form, Lysoveta's LPC-bound fatty acids are structurally similar to the endogenous molecules used by the brain for omega-3 transport.***

- ***Lysoveta® is the only commercially available, natural source of LPC-bound EPA and DHA, making it a truly ground breaking and innovative ingredient, with huge interest spanning scientific, commercial and consumer landscapes.***

WHY DOES OMEGA-3 FORM MATTER FOR BRAIN HEALTH?

1. *DHA is essential for brain function.*

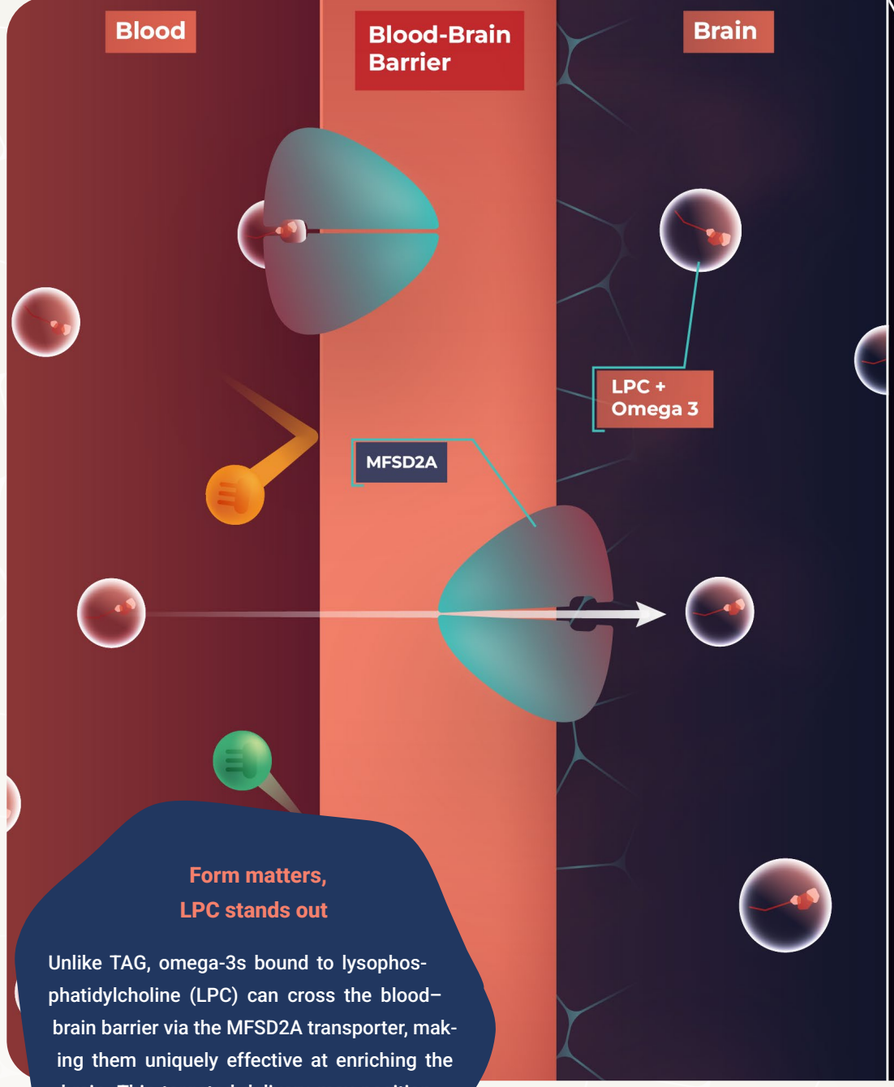
DHA makes up about 40% of the polyunsaturated fatty acids in the brain. It contributes to membrane fluidity, synaptic plasticity and anti-inflammatory signalling. Depending on the bound form of the EPA or DHA molecule, this will have different implications for where the omega-3 fatty acids are delivered throughout the body[2].

2. *Shortcomings of conventional supplements.*

Most omega-3 supplements supply DHA and EPA as TAGs (fish and algae oils). During digestion, these are hydrolysed to free fatty acids and then repackaged into TAGs for transport in chylomicrons, which limits direct uptake into the brain[3]. As a result, DHA and EPA from fish or algal oil enriches peripheral tissues but fails to substantially increase brain DHA[2]. This inefficiency partly explains why typical omega-3 supplements have had limited impact on cognitive outcomes, or often result in failed outcomes in clinical trials[4].

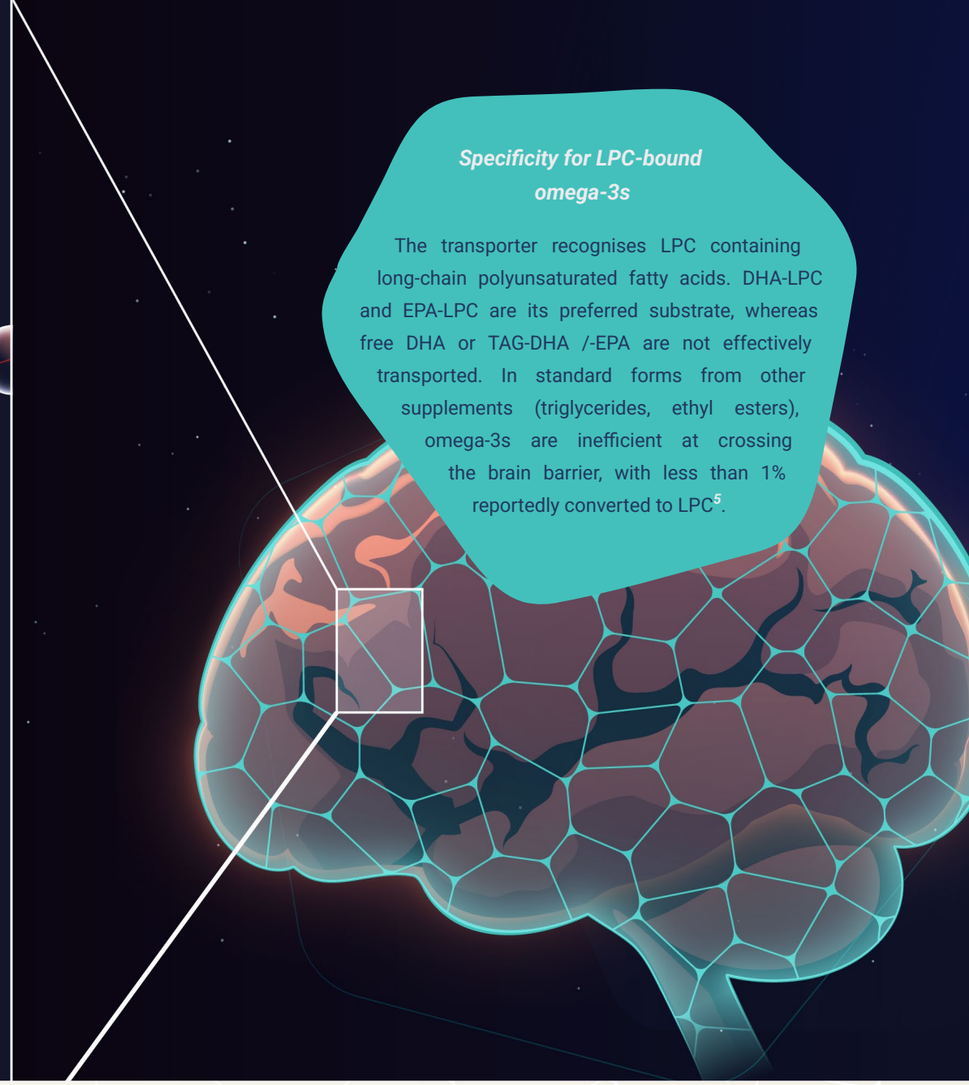
3. *Association with neurodegeneration.*

Low brain DHA is linked with neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, schizophrenia and depression[2]. Thus, improving brain DHA delivery could have broad implications for brain resilience.



Form matters, LPC stands out

Unlike TAG, omega-3s bound to lysophosphatidylcholine (LPC) can cross the blood–brain barrier via the MFSD2A transporter, making them uniquely effective at enriching the brain. This targeted delivery may position LPC as the most efficient form for supporting cognitive health, resilience, and long-term brain function.



Specificity for LPC-bound omega-3s

The transporter recognises LPC containing long-chain polyunsaturated fatty acids. DHA-LPC and EPA-LPC are its preferred substrate, whereas free DHA or TAG-DHA /-EPA are not effectively transported. In standard forms from other supplements (triglycerides, ethyl esters), omega-3s are inefficient at crossing the brain barrier, with less than 1% reportedly converted to LPC[5].

WHY LYSOVETA® WORKS: THE SCIENCE OF LPC AND OMEGA-3 BRAIN UPTAKE

Crossing the blood–brain barrier. The brain is protected by the blood–brain barrier (BBB), a layer of endothelial cells with tight junctions that restrict the entry of most circulating molecules, only allowing certain ones through. For essential lipids like DHA and EPA, the brain uses a specific transporter called Mfsd2a (major facilitator superfamily domain 2a). Mfsd2a is abundantly expressed on BBB endothelial cells and selectively transports LPC-bound polyunsaturated fatty acids into the brain[5].

2 **Sugasini D, et al.** Enrichment of brain docosahexaenoic acid (DHA) is highly dependent upon the molecular carrier of dietary DHA: lysophosphatidylcholine is more efficient than either phosphatidylcholine or triacylglycerol. J Nutr Biochem. 2019 Dec;74:108231. doi: 10.1016/j.jnutbio.2019.108231

3 **Scheinman SB, et al.** LPC-DHA/EPA-Enriched Diets Increase Brain DHA and Modulate Behavior in Mice That Express Human APOE4. Front Neurosci. 2021;15:690410. doi: 10.3389/fnins.2021.690410

4 **Chew EY, et al.** Effect of omega-3 fatty acids, lutein/zeaxanthin, or other nutrient supplementation on cognitive function: the AREDS2 randomized clinical trial. JAMA. 2015;314(8):791-801. doi: 10.1001/jama.2015.9677

5 **Nguyen LN, et al.** Mfsd2a Is a Transporter for the Essential omega-3 Fatty Acid Docosahexaenoic Acid. Nature. 2014 May 22;509(7501):503-6. doi: 10.1038/nature13241

LYSOVETA®'S ADVANTAGE: DELIVERING OMEGA-3 EPA AND DHA IN THE FORM THE BRAIN USES

Because Lysoveta delivers DHA and EPA already esterified to LPC, it can directly utilize the MfsD2a transporter to gain access to the brain. The molecules are resistant to hydrolysis and can cross both the intestinal barrier and BBB intact. Once inside the brain, LPC-DHA and LPC-EPA are re-acylated into phosphatidylcholine pools or incorporated into neuronal membranes. By bypassing the rate-limiting steps faced by conventional omega-3 supplements, Lysoveta achieves superior brain nutrient enrichment. Several pre-clinical studies have shown better brain uptake, enhanced memory performance and neuroprotective effects along with increases in BDNF (brain derived neurotrophic factor), with wide applications for several aspects of brain and cognitive health [2,6,7].

2 **Sugasini D, et al.** Enrichment of brain docosahexaenoic acid (DHA) is highly dependent upon the molecular carrier of dietary DHA: lysophosphatidylcholine is more efficient than either phosphatidylcholine or triacylglycerol. J Nutr Biochem. 2019 Dec;74:108231. doi: 10.1016/j.jnutbio.2019.108231

6 **Yalagala PCR, et al.** Dietary Lysophosphatidylcholine-EPA Enriches Both EPA and DHA in the Brain: Potential Treatment for Depression. J Lipid Res. 2019;60(3):566-78. doi: 10.1194/jlr.M090464

7 **Yalagala PCR, et al.** Lipase treatment of dietary krill oil, but not fish oil, enables enrichment of brain eicosapentaenoic acid and docosahexaenoic acid. Mol Nutr Food Res. 2020;64(12):2000059. doi: 10.1002/mnfr.202000059

Key benefits

SUMMARY OF BRAIN HEALTH CLAIMS SUPPORTED BY PRE-CLINICAL STUDIES

1. LPC boosts brain omega-3 levels

Evidence shows that omega-3 uptake and absorption is more complex than we think. Tissue distribution and where the omega-3 fatty acids go in the body is highly dependent on the form that the omega-3 comes in, which can have huge implications for the received health benefit of the omega-3 fatty acid. When it comes to brain health, the message is clear: *LPC-omega-3s significantly increase brain levels of DHA and EPA compared to other omega-3s.*

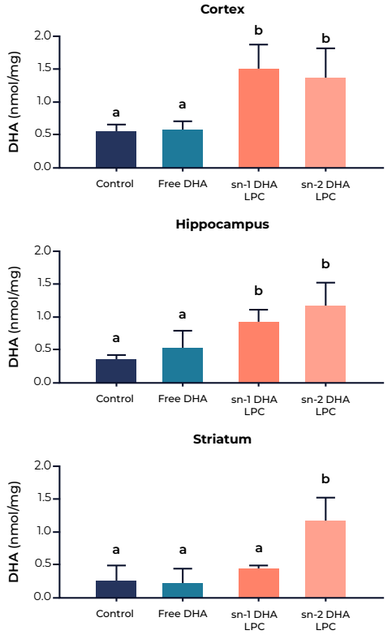


Figure 1. | Different forms of dietary DHA were tested for their ability to reach the brain. Compared to free DHA, both forms of LPC-DHA significantly boosted DHA levels across multiple brain regions, including the cortex, hippocampus, and striatum.
Bars with non-identical letters on top are significantly different from each other in each panel.

1. LPC-DHA supplementation accumulates more DHA in the brain.

In a 30-day feeding study, rats consuming sn-1 or sn-2 LPC-DHA nearly doubled uptake of brain DHA levels compared with controls (Figure 1), whereas TAG-DHA increased DHA mainly in adipose tissue and heart[8]. The groups with elevated brain DHA also showed higher brain-derived neurotrophic factor (BDNF) levels (Figure 4) and improved spatial memory in the Morris water maze[8].

2. LPC-EPA raises both brain EPA and DHA.

Mice given LPC-EPA for 15 days showed a 100-fold increase in brain EPA and a two-fold increase in brain DHA, even at human-equivalent doses of less than 0.25 g/day[6]. This demonstrates that EPA can cross the BBB when delivered as an LPC species and suggests synergy in raising both EPA and DHA pools.

3. Lysoveta oil containing both EPA and DHA enhances brain DHA/EPA.

A lipase treated krill oil yields an oil rich in LPC-DHA/EPA (Lysoveta). LPC-DHA/EPA produced five-fold higher brain DHA enrichment in wild-type mice versus non LPC form and significantly raised brain EPA (Figure 2)[3]. These findings together showcase the high affinity the brain has for omega-3 fatty acids in LPC form, opening up ample possibilities for new products targeting brain absorption.

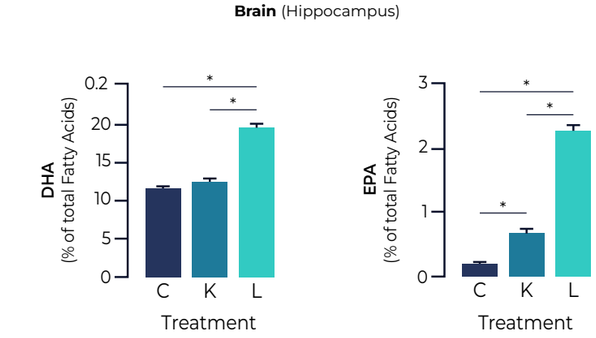


Figure 2. | LPC-DHA/EPA (L) led to higher brain levels of both DHA and EPA compared to untreated krill oil (K) and control diet (C). This demonstrates that the LPC-DHA/EPA form significantly improves delivery of omega-3s to the brain.

4. Evidence in APOE4 mice.

Human APOE4 carriers (increased risk for Alzheimer's) may have reduced DHA delivery to the brain. In APOE4 targeted replacement mice, LPC-DHA/EPA increased plasma and hippocampal DHA levels (Figure 3) and elevated the synaptic vesicle protein SV2A[3]. APOE4 mice treated with LPC-DHA/EPA performed better in the novel object recognition test, suggesting improved memory[3].

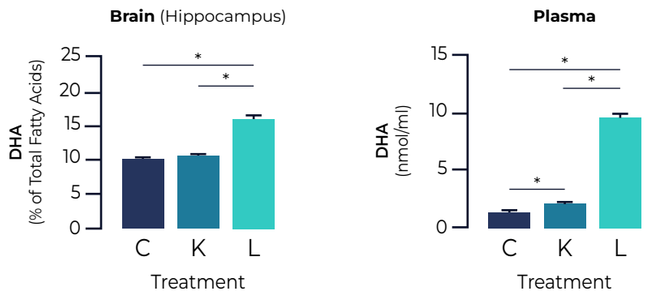


Figure 3. | In APOE4 mice, LPC-DHA/EPA (L) increased DHA levels in both brain and plasma compared to untreated krill oil (K) and control diet (C). Notably, APOE4 mice—who typically show reduced DHA delivery—also benefited, highlighting improved brain uptake of DHA with LPC-DHA/EPA.

6 **Yalagala PCR, et al.** Dietary Lysophosphatidylcholine-EPA Enriches Both EPA and DHA in the Brain: Potential Treatment for Depression. J Lipid Res. 2019;60(3):566-78. doi: 10.1194/jlr.M090464

8 **Sugasini D, et al.** Dietary docosahexaenoic acid (DHA) as lysophosphatidylcholine, but not as free acid, enriches brain DHA and improves memory in adult mice. Sci Rep. 2017;7:11263. doi: 10.1038/s41598-017-11766-0

3 **Scheinman SB, et al.** LPC-DHA/EPA-Enriched Diets Increase Brain DHA and Modulate Behavior in Mice That Express Human APOE4. Front Neurosci. 2021;15:690410. doi: 10.3389/fnins.2021.690410

Key benefits

SUMMARY OF BRAIN HEALTH CLAIMS SUPPORTED BY PRE-CLINICAL STUDIES

2. LPC preserves neurons and supports brain development

LPC-DHA and LPC-EPA have been shown to increase brain-derived neurotrophic factor (BDNF), a central regulator of brain development, neuroplasticity, and cognitive resilience. Elevated BDNF supports the growth of new neurons and dendrites, strengthens synaptic connections, and enhances learning and memory. Beyond this, LPC-omega-3s also help defend neurons from oxidative stress, contributing to maintaining resilience in the face of both aging and environmental challenges.

1. UNLOCKING BRAIN GROWTH SIGNALS - BDNF.

Preclinical studies confirm these effects: Sugasini et al. (2019) showed that LPC-EPA enriched both EPA and DHA in the brain and significantly increased BDNF expression (Figure 4)[2]. These findings highlight that LPC forms of omega-3s do more than deliver structural lipids to the brain, they also activate molecular pathways critical for neurogenesis and long-term brain function.

2. IMPACT OF IMPAIRED LPC TRANSPORT.

Genetic evidence underscores the importance of this pathway: loss-of-function mutations in the MFSD2A transporter - responsible for carrying LPC-DHA across the blood–brain barrier - cause severe neurodevelopmental outcomes such as microcephaly[5]. A lack of LPC omega-3 delivery to the brain results in impaired neuronal growth, including underdeveloped dendrites (Figure 5), which compromises the ability of brain cells to form the connections needed for proper signaling and cognitive development[9].

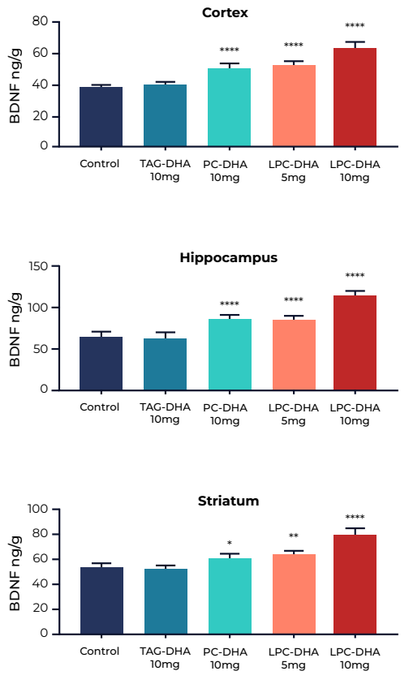


Figure 4. | Supplementation with LPC-DHA increased levels of brain-derived neurotrophic factor (BDNF) in the cortex, hippocampus, and striatum compared to control and other DHA forms. Higher BDNF indicates enhanced support for neuronal growth and brain function.

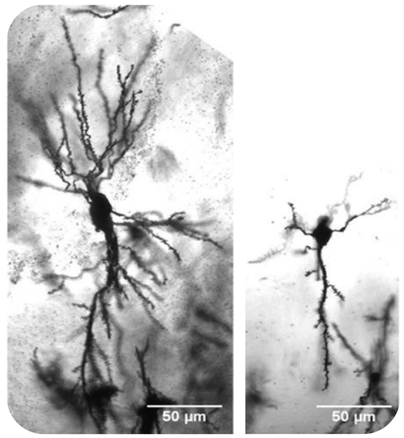


Figure 5. | Stained hippocampal neurons from normal mice with the Mfsd2a transporter (left) and mice lacking this transporter due to a genetic deletion (right). Without Mfsd2a, neurons show reduced dendritic growth, reflecting impaired brain connectivity when LPC-omega-3 delivery is disrupted.

3. PROTECTION AFTER BRAIN INJURY.

Protective effects have also been demonstrated in models of oxidative stress and brain injury. Hermans et al. (2024) found that dietary LPC-DHA/EPA reduced brain lesion size in newborn mice after hypoxic–ischemic injury, while *in vitro* studies showed neuronal protection against oxidative stress (Figure 6)[10]. These results highlight that LPC-omega-3s can both nourish and defend the brain under vulnerable conditions.

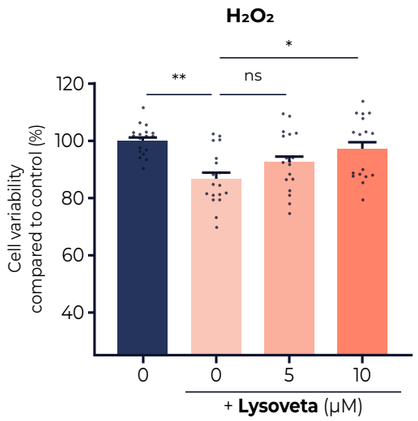


Figure 6. | In a cell model of oxidative stress, treatment with Lysoveta (LPC-DHA/EPA) improved cell survival compared to untreated cells. Increasing doses of Lysoveta helped protect neurons from damage caused by hydrogen peroxide, highlighting its neuroprotective potential.

Together, the evidence shows that LPC-bound omega-3s not only deliver essential fatty acids to the brain but also activate key molecular pathways and protective mechanisms. By stimulating BDNF, supporting dendritic growth, and safeguarding neurons from injury, they play a dual role in driving brain development and preserving cognitive function across the lifespan.

2 **Sugasini D, et al.** Enrichment of brain docosahexaenoic acid (DHA) is highly dependent upon the molecular carrier of dietary DHA: lysophosphatidylcholine is more efficient than either phosphatidylcholine or triacylglycerol. J Nutr Biochem. 2019 Dec;74:108231. doi: 10.1016/j.jnutbio.2019.108231

5 **Nguyen LN, et al.** Mfsd2a Is a Transporter for the Essential omega-3 Fatty Acid Docosahexaenoic Acid. Nature. 2014 May 22;509(7501):503-6. doi: 10.1038/nature13241

9 **Chan JP, et al.** The lysolipid transporter Mfsd2a regulates lipogenesis in the developing brain. PLoS Biol. 2018 Aug 3;16(8):e2006443. doi: 10.1371/journal.pbio.2006443

10 **Hermans EC, et al.** Dietary LPC-Bound n-3 LCPUFA Protects against Neonatal Brain Injury in Mice but Does Not Enhance Stem Cell Therapy. Nutrients. 2024 Jul 12;16(14):2252. doi: 10.3390/nu16142252

3. LPC improves memory and learning

LPC-omega-3s have been shown to enhance memory, learning, and behavioral outcomes in animal models, highlighting their potential to directly support cognitive performance.

1. SUPERIOR MEMORY GAINS WITH LPC-DHA.

In a landmark study, Sugasini et al. (2017) demonstrated that mice supplemented with LPC-DHA showed seven times greater improvement in memory performance compared with mice given free DHA[8]. Using a maze-based learning and memory test, the researchers found that LPC-DHA administration more than doubled brain DHA levels and significantly improved spatial learning and memory. By contrast, free DHA did not increase brain DHA and had no effect on memory performance. This study provided the first clear evidence that LPC-bound omega-3s can deliver functional cognitive benefits far beyond what conventional omega-3 forms achieve.

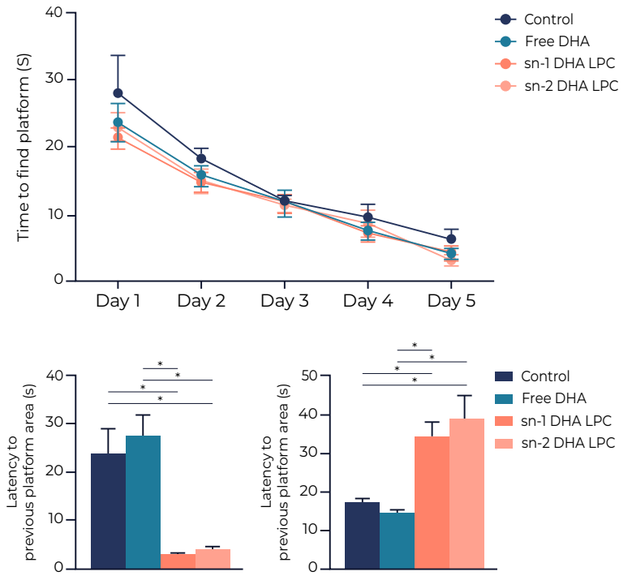


Figure 7. | In a memory test, mice treated with LPC-DHA performed better than those given free DHA or control diets.
During the learning phase (above), all groups improved similarly in finding the hidden platform.
In the probe trial (below), LPC-DHA–treated mice reached the previous platform area faster and spent more time in the correct location, showing enhanced memory performance.

8 **Sugasini D, et al.** Dietary docosahexaenoic acid (DHA) as lysophosphatidylcholine, but not as free acid, enriches brain DHA and improves memory in adult mice Sci Rep. 2017;7:11263. doi: 10.1038/s41598-017-11766-0

2. COGNITIVE RESCUE IN GENETIC RISK MODELS.

Similarly, Scheinman et al. (2021) investigated diets enriched with LPC-DHA/EPA in mice carrying the human APOE4 gene, a known genetic risk factor for Alzheimer's disease. LPC-supplemented diets increased plasma and hippocampal DHA, restored BDNF expression, and improved memory and behavioral outcomes in these at-risk animals[3]. These findings suggest that LPC-omega-3s may help overcome genetic vulnerabilities that impair brain lipid uptake and cognition.

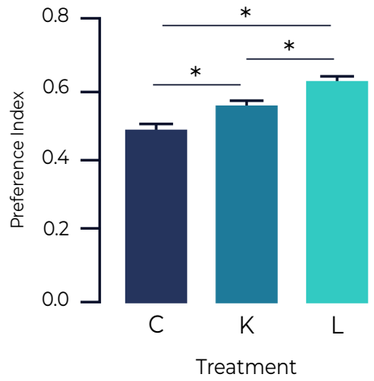
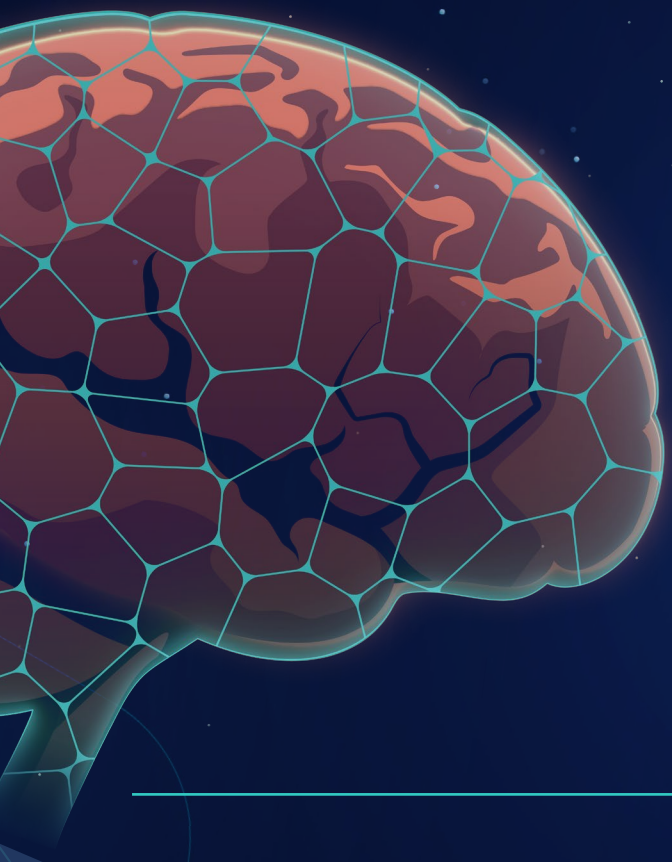


Figure 8. | In the novel object recognition test, APOE4 mice treated with LPC-DHA/EPA (L) performed better than those given regular krill oil (K) or control diet (C). This suggests that LPC-omega-3s can help overcome genetic risk for impaired memory.

Together, these studies highlight the powerful effect of LPC-bound omega-3s in improving memory and learning, not just increasing brain omega-3 levels, but translating that enrichment into measurable functional outcomes.

3 **Scheinman SB, et al.** LPC-DHA/EPA-Enriched Diets Increase Brain DHA and Modulate Behavior in Mice That Express Human APOE4. Front Neurosci. 2021;15:690410. doi: 10.3389/fnins.2021.690410



SUMMARY OF BENEFITS

- LPC FOR BRAIN TARGETED OMEGA-3
- EFFICIENTLY INCREASES BRAIN EPA/DHA LEVELS
- SUPPORTS NEURON PROTECTION
- COGNITIVE PERFORMANCE AND DEVELOPMENT

HOW IT WORKS

Lysoveta® uses LPC to transport omega-3s across the Blood-Brain-Barrier via the Mfsd2a transporter.

This leads to targeted delivery, making it more effective than standard omega-3 supplements.

WHY CHOOSE LYSOVETA®

- *First and only LPC-bound omega-3 in the market*
- *40+ global patent rights*
- *Backed by 14+ pre-clinical trials*

Clinical trials are now underway to validate these promising findings in humans, paving the way for Lysoveta® to establish a new gold standard in cognitive nutrition.

Visit www.lysoveta.com for more information.

LYSOVETA®