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The impact of an omega-3 fatty acid-rich diet on brain and heart health

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Agnieszka Kowalska^{1*}

ABSTRACT

Fatty acids build cell membranes, and the polyunsaturated group includes the essential omega-3s: alpha-linolenic acid, eicosapentaenoic acid, and docosahexaenoic acid. Looking at the literature, it is clear that eating fish and marine omega-3s is linked to a lower risk of cardiovascular disease, largely because these fats help lower triglycerides and blood pressure while helping fight inflammation. High doses of pure EPA (4 g/day) have been shown to effectively cut the risk of cardiac events, whereas the standard doses of mixed EPA and DHA often fail to yield the same results in the general population. In the brain, DHA is the dominant fatty acid, playing a vital function in preserving cell membrane fluidity and helping neurotransmitters function properly. Animal research shows that omega-3s safeguard the brain during ischemic events by preventing cell death and reducing inflammation, and they also show promise in relieving depression symptoms, with EPA being especially effective. These benefits come with risk, however, as using high doses has been linked to a dose-dependent chance of developing atrial fibrillation. Ultimately, this analysis points out the need to personalize supplementation, accounting for the distinct effects of different fatty acids rather than treating them all the same.

Keywords: Fatty acids, EPA and DHA, omega-3 fatty acid, heart health

1. INTRODUCTION

Fatty acids build our cell membranes, and among them, the polyunsaturated types - omega-3 and omega-6 - are especially important (Saini et al., 2021). As humans cannot create omega-3s internally, dietary sources remain the only way to obtain them (Wierenga & Pestka, 2021). The main forms include alpha-linolenic acid, found in plant foods such as flaxseeds and walnuts, and the marine-derived EPA and DHA, which primarily come from fatty fish and algae (Saini et al., 2021; Dighriri et al., 2022).

There is evidence that these fats are advantageous for cardiovascular health. Higher omega-3 intake is linked to a lower risk of cardiovascular disease (Innes & Calder, 2020). Maintaining a healthy omega-3 index may be one of the most effective ways to counter chronic inflammation, which drives many modern lifestyle diseases (Wierenga & Pestka, 2021).

For the brain, DHA plays a particularly key role - it makes up more than 40% of the polyunsaturated fats in our neurons. It helps keep cell membranes flexible, supports neurotransmitter function, provides defense, and may even lower the risk of neurodegenerative disorders (Dighriri et al., 2022).

The challenge is that many modern diets are heavily skewed toward omega-6 fats, which promote inflammation when consumed in excess (Wierenga & Pestka, 2021). On top of that, our bodies are not very efficient at converting plant-based alpha-linolenic acid (ALA) into the more biologically active EPA and DHA. Because these fatty acids each play unique functions in promoting cardiac and brain health (Saini et al., 2021), this review pulls together the current evidence on how they work and the best ways to obtain them.

2. REVIEW METHODS

We searched the literature using several related terms, including omega-3 fatty acids, EPA, and DHA. Articles in English or Polish published over the past ten years were considered if the full text was available. Only studies reporting clinical data were included. Other types of publications were not used. Three authors reviewed the papers separately. The selection process is shown in Figure 1.

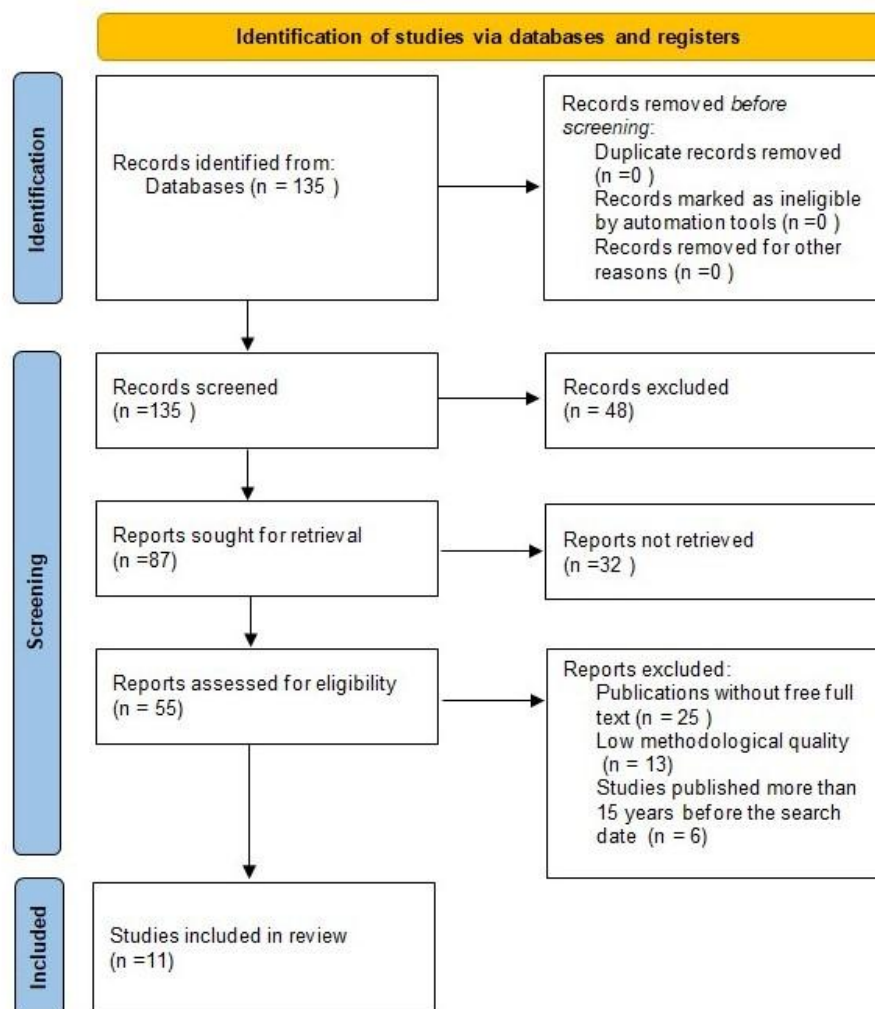


Figure 1: PRISMA chart

3. RESULTS & DISCUSSION

Impact on Heart Health

One of the most well-established benefits of omega-3 fatty acids is their ability to lower triglyceride (TG) levels. Taking 3–4 g of EPA per day, or a combination of EPA and DHA, can reduce triglycerides by 20–50% in people with elevated triglyceride levels (Elagizi et

al., 2021). Research suggests that DHA may be even more effective than EPA in this regard - increasing DHA intake by just 1 g per day has been linked to a 23% drop in TG, while EPA has a milder effect (Ghasemi Fard et al., 2019).

However, DHA has a downside: it can raise LDL cholesterol by about 8%, whereas pure EPA does not appear to do so (Ghasemi Fard et al., 2019). High-dose DHA supplementation - unlike EPA - has also been shown to improve arterial stiffness and enhance endothelial function, as measured through flow-mediated dilation (FMD) (Elagizi et al., 2021). DHA additionally helps lower inflammatory markers such as C-reactive protein, interleukin-6, and tumor necrosis factor (Ghasemi Fard et al., 2019). These anti-inflammatory effects are important for preventing atherosclerosis and may help explain the positive outcomes seen in studies using high doses of omega-3s in patients with heart failure (Elagizi et al., 2021).

DHA also seems more effective than EPA at lowering basal heart rate and improving heart rate variability (HRV) (Ghasemi Fard et al., 2019). On the other hand, EPA - especially when taken at high doses and in its pure form - has been shown to reduce the risk of heart attack and stroke, as demonstrated in the REDUCE-IT trial. This level of benefit has not been observed to the same extent in EPA+DHA mixtures (Elagizi et al., 2021).

Impact on Mental Abilities and Brain Health

The impact of omega-3 fatty acids on the brain encompasses both psychiatric (e.g., depression) and neurological (e.g., neuroprotection, cognitive function) aspects. A meta-analysis showed that omega-3 fatty acids have an overall beneficial effect on depression symptoms (Liao et al., 2019). Investigations stress that success in treating depression depends heavily on the ratio of fatty acids used. Specifically, formulations with a high EPA concentration (> 60%) delivered at a dose of ≤1 g/day proved clinically effective. On the other hand, DHA-rich or pure DHA supplements appeared to offer no significant benefit in the management of depression (Liao et al., 2019). Studies on animal models provide evidence for the neuroprotective action in conditions of brain ischemia. Supplementation following global cerebral ischemia in rats prevented hippocampal neuronal degeneration and reversed spatial memory deficits (Nobre et al., 2016). What is more, dietary supplementation with omega-3 fatty acids reduced the volume of microinfarcts in the cerebral cortex and inhibited neuronal apoptosis in a mouse model (Luo et al., 2018).

The main neuroprotective mechanisms identified in the literature are:

- Anti-inflammatory action: Reduction of the expression of proinflammatory cytokines (TNF-alpha, IL-1beta) and enzymes iNOS and COX-2 in the hippocampus (Nobre et al., 2016).
- Inhibition of apoptosis: Omega-3s inhibit the cell death pathway dependent on RIPK1 kinase and the activation of caspases 3 and 8 (Luo et al., 2018).
- Modulation of neurotransmitters: Omega-3s restore the balance of dopamine and noradrenaline levels in the striatum, which are disturbed by ischemia (Nobre et al., 2016).

Memory and Mental Abilities

In humans, results regarding mental abilities are mixed. DHA supplementation improved memory and reaction speed in young adults with low baseline intake of this acid, and slowed the decline in cognitive function in elderly people with mild cognitive impairment (MCI). However, other large studies did not show a significant effect of supplementation on mental abilities in healthy elderly individuals (Ghasemi Fard et al., 2019). Key studies and meta-analyses discussed in the analyzed papers are summarized in Table 1.

Table 1. Overview of selected clinical trials and meta-analyses regarding the impact of omega-3 on heart and brain health

| | | | |
|---------------------------------|---|-------------------------------------|---|
| REDUCE-IT(Elagizi et al., 2021) | Patients with CVD/diabetes and high TG (n=8179) | 4 g/day icosapent ethyl (pure EPA) | 25% reduction in the risk of the composite CVD endpoint; 26% reduction in MACE (Elagizi et al., 2021). |
| STRENGTH (Huh & Jo, 2023) | High CVD risk, high TG (n=13078) | 4 g/day EPA + DHA (carboxylic acid) | No reduction in CVD risk; significant increase in the risk of atrial fibrillation (HR 1.69) (Huh & Jo, 2023). |
| VITAL (Elagizi et al., 2021) | Primary prevention (n=25871) | 1 g/day EPA + DHA | No reduction in overall CVD risk; 28% reduction in myocardial infarctions; 40% reduction in myocardial infarctions in people with low fish intake (Elagizi et |

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| | | | al., 2021). |
| Meta-analysis Liao et al., (2019) | Patients with depression (n=2160) | Various (EPA/DHA) | Reduction of depression symptoms at a dose ≤ 1 g/day EPA (formulation $\geq 60\%$ EPA) (Liao et al., 2019). |
| Cochrane Review (Abdelhamid et al., 2018) | Review of 79 RCTs (n=112059) | EPA+DHA or ALA | Little or no effect on total mortality and cardiovascular events; reduction of triglycerides (Abdelhamid et al., 2018). |

Factors Influencing Effectiveness

- **Dose:** Differences between study results are largely related to dose selection. In cardiology, higher doses seem to matter. Benefits are mainly seen at doses around 4 g per day, while the commonly used 1 g dose often does not differ from placebo in patients receiving standard therapy (Elagizi et al., 2021). The situation is different in mental health. In studies on depression, lower doses of EPA (≤ 1 g) appear to be more effective, possibly because higher doses may overwhelm cerebral metabolic processes (Liao et al., 2019).
- **Source and Composition:** Differences between EPA and DHA are fundamental. EPA appears to be responsible for reducing the risk of coronary events and for antidepressant effects, while DHA plays a key role in membrane structure and cognitive function (Ghasemi Fard et al., 2019).
- **Interactions with Diet (Baseline Level):** Populations with high fish consumption (e.g., in Japan) may require lower supplemental doses than Western populations to achieve a therapeutic omega-3 index (Elagizi et al., 2021).

Study Limitations

The most important new safety limitation is the risk of atrial fibrillation (AF). Omega-3 supplementation is associated with an increased risk of AF, with a dose-dependent effect. In studies using doses >1 g/day, this risk increased by nearly 50% (HR 1.49). This is a major constraint, especially at high doses used to reduce triglycerides (Huh & Jo, 2023).

4. CONCLUSION

Research clearly shows that omega-3 fatty acids have an important role in both heart and brain health. Cardiovascular benefits, such as reduced inflammation and lower triglycerides, are dictated largely by the specific dosage and fatty acid profile. High-dose pure EPA offers the most consistent reduction in cardiac risk; DHA presents a trade-off: it modulates lipids but may unintentionally elevate LDL cholesterol. On the neurological front, omega-3s act as a shield for nerve tissue and stabilize neurotransmitters, with low-dose EPA showing notable potential for treating depression. Yet, there is a clear safety ceiling. Daily intake exceeding 1 gram drives up the risk of atrial fibrillation. Given these variables, supplementation demands a customized plan rather than a generic, one-size-fits-all regimen.

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List of Abbreviations

AF: Atrial fibrillation
 ALA: Alpha-linolenic acid
 CVD: Cardiovascular disease
 DHA: Docosahexaenoic acid
 EPA: Eicosapentaenoic acid
 FMD: Flow-mediated dilation
 HR: Hazard ratio
 HRV: Heart rate variability
 MACE: Major adverse cardiovascular events
 MCI: Mild cognitive impairment
 TG: Triglycerides

Authors' Contributions

Conceptualization: Agnieszka Kowalska, Michał Wójcicki.

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Visualization: Agnieszka Kowalska, Milena Kędzierska.

All authors have read and agreed with the published version of the manuscript.

Informed consent

Not applicable.

Ethical approval

Not applicable. This article does not contain any studies with human participants or animals performed by any of the authors.

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Conflict of interest

The authors declare that they have no conflicts of interest, competing financial interests or personal relationships that could have influenced the work reported in this paper.

Data and materials availability

All data associated with this study will be available based on reasonable request to the corresponding author.

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