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HEART HEALTH

Do EPA and DHA Protect the Heart in the Same Way?

The heart-protecting benefits of the omega-3 fatty acids in seafoods—known as EPA and DHA—have been well established, especially in people who already have heart disease. But does each of these fatty acids have the same effect? Because EPA and DHA occur together in fish and fish oils, it takes individual purified fatty acids to answer this question. Most fish oils have about one and a half times as much EPA as DHA, with some notable exceptions. For example, tuna oil may have as much as 5 times more DHA than EPA. If one fatty acid were more effective than the other, this might have implications for certain patients.

Researchers at the University of Western Australia looked at what was known about the individual effects of EPA and DHA. Their review concluded that both fatty acids are similar in lowering blood triglyceride (fat) levels. Both had little effect on total cholesterol and were associated with small or no increases on LDL ("bad") cholesterol. However, when it came to HDL ("good") cholesterol, DHA was linked to increases of about 20% in patients with abnormal blood lipids, such as type 2 diabetics, whereas EPA had little apparent effect in such patients.

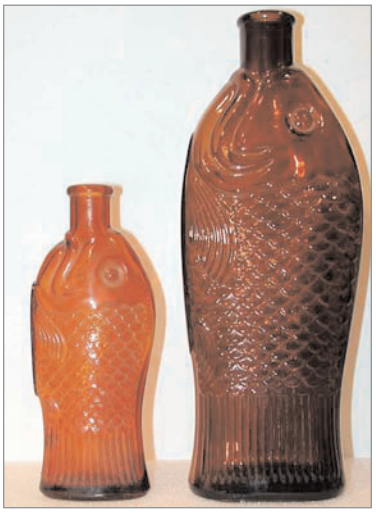
Both EPA and DHA lower blood triglyceride (fat) levels . . . but for several risk factors, DHA was likely to be more effective than EPA. However, these observations were found with high doses of these fatty acids.

DHA had other effects not observed with EPA. These included greater reductions in blood pressure, lower heart rate, improved blood flow and reduced blood clotting. However, these findings were observed in overweight people with high blood pressure, using high doses (4 grams/day) of these fatty acids. This is about 4 times what you would find in a serving of salmon.

The authors also noted similarities in the two fatty acids. Both reduce "oxidative stress" (the production of damaging fatty acid breakdown products) and weaken the production of inflammatory substances. They concluded, however, that for several risk factors, DHA was likely to be more effective than EPA. What their review could not determine was whether the differences between DHA and EPA would be observed at lower, more practical intakes and whether they would apply more broadly to the diverse populations at risk of heart disease.

Cod Liver Oil Improves Blood Flow in Patients with Chronic Heart Failure

Patients with chronic heart failure experience the consequences of ischemic heart disease in fatigue, breathlessness and impaired blood circulation. These conditions reduce the activities a person can undertake and increase the likelihood of tissue damage. One way to improve the condition is to increase blood circulation. Fish oils, with their high content of long-chain omega-3 fatty acids, might be helpful. Several studies have reported that these omega-3 fatty acids improve the function of blood vessels, increase blood circulation, and enhance the dynamic properties of blood as it moves. Whether they do so in most patients across the spectrum of heart disease is not clear.



Researchers at Queen's University in Belfast, U.K., decided to see whether consuming 10 ml (about 2 teaspoons) of cod liver oil would affect blood flow in the forearm of patients with chronic heart failure. For comparison, they used olive oil. The 20 participants consumed each oil for 6 weeks, with a 6-week period of no treatment in between. Blood flow in the forearm in response to different stimulants was measured at the beginning and end of each dietary period.

After they consumed cod liver oil for 6 weeks, patients experienced a 42% increase in forearm blood flow. After the olive oil period there was no significant

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change in blood flow. As other patients at high-risk of cardiovascular events—those with type 2 diabetes, hyperlipidemia, or a heart transplant—have also experienced increased blood flow with the omega-3s in fish oil, it appears that these fatty acids may improve blood flow in patients whose circulation is impaired by heart disease. Improved circulation may be another cardioprotective benefit of increased fish or fish oil consumption.

Fish Consumption Unrelated to Certain Dangerous Heart Rhythms in Older People

We would all like a clear answer to the question: do fish oils or the omega-3 fatty acids they contain make dangerous heart rhythms less likely? So far, the data do not provide a simple answer. First, there are distinctions between abnormal rhythms in the heart's upper (atria) and lower (ventricles) chambers. Atrial fibrillation is the medical term for irregular rapid beats in the upper chambers of the heart. When present, they can interfere with the lower chambers' ability to pump blood. In turn, this increases the chance of fatal arrhythmias.

Figure. Illustration of the disorganized blood flow in the atria in atrial fibrillation. *Courtesy of the Heart Rhythm Society, www.hrsonline.org.*

One report described a reduction of 50% in the risk of developing atrial fibrillation in coronary by-pass patients taking omega-3s from fish oil. Another study reported that fish oil did not did not change the risk. Now, findings from the long-running Rotterdam Study suggest that fish consumption is unrelated to the chance of developing atrial fibrillation. The Rotterdam Study monitors more than 5,000 people over the age of 55 in The Netherlands to see which lifestyle factors affect cardiovascular, neurological, motor, and visual diseases—the most common afflictions in aging.

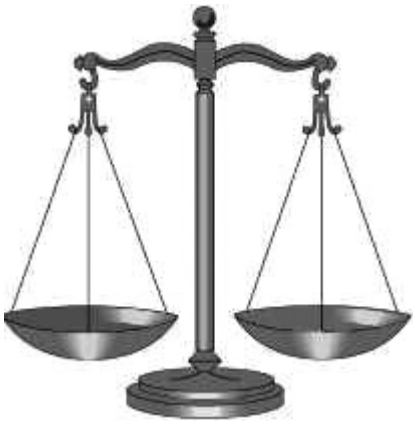
The investigators collected data on the participants' food intake and medical events for more than 6 years. When they examined the number of cases of atrial fibrillation according to how often the participants ate fish, they could find no differences among those who ate no fish, those who ate up to 20 grams of fish/day or those who consumed more than 21 grams/day.

In the Rotterdam Study, there were no differences in cases of atrial fibrillation according to how often participants ate fish.

Possible explanations could be that fish or their omega-3s really have no effect on atrial fibrillation, the amounts consumed were too low to be effective, or fish consumption affects the ventricles more than the atria. Evidence from animal and cell studies shows clearly that the omega-3s in fish have pronounced effects on the heart's rhythms. In people, however, the situation is more complex. There is no reason to think these participants differed from their other European or American counterparts. One hopes that the randomized controlled clinical trials currently underway will deepen our understanding of the inconsistent observations on fish oils, omega-3s, and heart arrhythmias.

Controversial Analysis of Omega-3s Sparks Media Storm

In April 2006, the *British Medical Journal* published a combined analysis of studies linking the omega-3 fatty acids found in fish or plants with three main outcomes—mortality from all causes, cardiovascular disease events, and cancer incidence. When the study hit the press, it was the proverbial shot heard round the world. The report, in an esteemed medical journal, concluded that neither fish or plant-based omega-3 fatty acids have a clear effect on total mortality, combined cardiovascular events, or cancer. How did the authors reach that conclusion when so much evidence seems to point the other way?



A careful look provides some explanation. For one, the authors chose outcomes where the data are well known to be inconsistent—total mortality and cancer. Although some studies have shown significant reduction in the

The report, in an esteemed medical journal, concluded that fish or plant-based omega-3 fatty acids have a clear effect on total mortality, combined cardiovascular events, or cancer . . . but inclusion of a single study . . . swayed the overall analysis.

risk of all causes of death, many more have not. Reductions in total mortality with omega-3s are always smaller than the decreases specifically linked to heart disease. When it comes to fatal cardiovascular disease, the data remain highly favorable for significantly lower risk in people who eat fish or omega-3s regularly. Although the data are stronger for fish or the omega-3s they contain than for plant-based omega-3s, many studies have reported lower risk of cardiovascular mortality with plant-based omega-3s. They should not be discounted.

The study found no evidence that omega-3 fatty acids reduced the chance of developing cancer. It did not look at prolonging life or reducing disease progression. This finding, too, is consistent with most of the literature, so it was unsurprising.

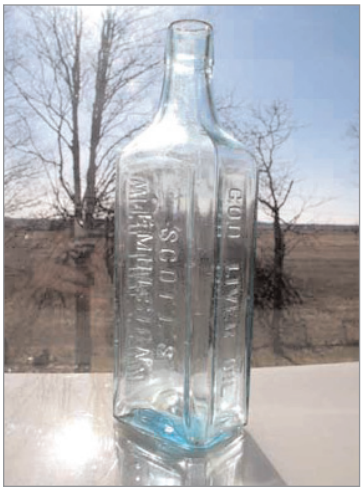
What provoked howls from many critics was the paper's inclusion of a single study that reported increased mortality risk with long-term consumption of fish oil in men with angina, a painful chest condition associated with coronary artery disease. This single study had a disproportionately strong effect on the overall outcome because of the direction and strength of its findings. But, it had weaknesses of great concern, and as an "outlier," it swayed the overall analysis. When this study was excluded, the analysis showed benefits on cardiovascular mortality from omega-3s. Further, this one exceptional study led the authors to conclude that risk increased the longer one consumed omega-3 fatty acids. There are no data to support this conclusion, save this one unexplained study.

To be sure, there have been negative findings with the use of fish oil or omega-3 fatty acid supplements, but these have been observed most frequently in severely ill patients. The quality of studies varies considerably and the statistical assumptions applied to these combined analyses are challenging. All systematic analyses face hurdles and can be criticized. But this particular report brought the critics out in force. Too bad the news media bought it hook, line and sinker.

MOTHERS & INFANTS

High Blood Pressure in Pregnancy Linked to High Intake of Cod Liver Oil and Multi-Vitamins

In about 5 to 10% of pregnancies, the mother develops high blood pressure, a condition that may put the health of the mother and infant at risk. High blood pressure alone is called gestational hypertension. A riskier form known as pre-eclampsia includes protein excretion as well as high blood pressure.



Vintage cod liver oil bottle. ***Courtesy, www.sentex.net.***

In Iceland, women commonly consume cod liver oil during pregnancy, either as liquid oil or capsules. What is remarkable is that the liquid oil has 10 times more omega-3s than 3 cod liver oil capsules and many times more vitamins D and E. Researchers at the University of Iceland were curious whether these supplements might be linked to either of these high blood pressure conditions.

They recruited 488 pregnant women at their first prenatal visit and assessed their diet, use of supplements, pregnancy outcomes and development of high blood pressure. Ninety percent of the women did not develop the condition, but of the 49 who did, 30 developed gestational hypertension and 19 developed pre-eclampsia.

The investigators found that women who developed gestational hypertension were significantly more likely to have consumed liquid, rather than encapsulated, cod liver oil compared with healthy women. They were also twice as likely to take multi-vitamins late in pregnancy

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as healthy women. These differences amounted to an 8-fold greater intake of omega-3s and more than twice the amount of vitamins A and D as women who did not consume any supplements. When the researchers did the math, consumption of liquid cod liver oil increased the chance of developing gestational hypertension by 5 times. Risk of pre-eclampsia was not associated with consuming either cod liver oil or multi-vitamin supplements, perhaps because the number of women with pre-eclampsia was small.

Additional analysis of the data revealed that the risk associated with cod liver oil was increased only in women who took the greatest amount early in pregnancy. For vitamins A and D, risk was only greater for women who consumed the largest amounts—above what 90% of all women took. In other words, only at the highest levels of intake early in pregnancy were these nutrients of significant risk. Further, which nutrients might have contributed the most to gestational hypertension could not be determined from this study.

For most women, consumption of multi-vitamins in recommended amounts and cod liver oil in small amounts poses no risk. A range of 100 to 200 mg/day of the omega-3s in fish and cod liver oil has been recommended by authorities in Australia and New Zealand and the European Commission. The dictum of Paracelsus, the 15th Century alchemist and physician, applies: "Only the dose makes a thing a poison."

IMMUNITY & INFLAMMATION

Lipoxins: Triggers to End Inflammatory Responses

What triggers inflammation and how it protects us from dangerous invaders is reasonably well understood. How the immune system turns itself off when the job is done is only now becoming clear. Findings from Dr. Charles Serhan's research group in Boston, USA, have provided new insights into this process. Additionally, the team's work further explains how aspirin fights inflammation.

How the immune system turns itself off when the job is done is only now becoming clear.

Polyunsaturated fatty acids (PUFAs) from vegetable oils are the starting materials for the production of substances that trigger and enhance inflammation. These products or mediators are produced in several types of cells—white blood cells, platelets and epithelial cells lining the blood vessels and airways. They relay signals from one place to another. This spreads the protection around, halting damage from dangerous substances. But when these responses are too exuberant, as in asthma and rheumatoid arthritis, additional remedies are required to restrain the inflammation.

The PUFAs derived from vegetable oils generate a variety of substances that stimulate inflammatory responses. In contrast, the omega-3 PUFAs in fish reduce production of these substances and generally ease inflammation. Serhan's group uncovered a different family of substances derived from both fish and vegetable oil PUFAs called lipoxins. These appear to call a halt to inflammation. They are made only when certain types of cells interact with each other. For example when leukocytes (a type of white blood cell) interact with platelets, epithelial cells or endothelial cells they cause the cells to make lipoxins instead of inflammatory products. These cell-to-cell interactions have two results: reduced production of inflammatory agents and synthesis of anti-inflammatory lipoxins.

Aspirin enters the picture because it modifies a key enzyme responsible for making certain inflammatory mediators. Once affected by aspirin, the enzyme shifts to making a slightly modified lipoxin with potent ability to stop cells from spreading. It also makes less of the inflammatory mediators. These changes reduce the inflammation process.

Serhan's team looked at the immune responses of healthy volunteers who took different amounts of aspirin for 8 weeks. People who consumed the lowest dose, 81 mg/day, responded to aspirin with a 10%

At low doses, aspirin increased lipoxin production, but at higher doses, lipoxin production did not change.

increase in lipoxin production, but those on the higher doses showed no changes in lipoxin production. The researchers also noted that women tended to produce more lipoxins as they grew older, while men tended to produce less.

It is interesting to note that in women, aspirin reduces the risk of stroke, whereas in men it reduces the chance of myocardial infarction. These differences may relate in part to differences in lipoxin production and corresponding changes in inflammatory mediators. We can expect to hear more about these substances as the details of their activities unfold. These observations suggest that lipoxins may have potential as therapeutic agents to limit inflammation.

Sorting Out the Effects of Fatty Acids in the Immune System

The immune system responds to dietary fat, with its various fatty acids, in different ways. This means that diet provides an opportunity to influence and weaken immune responses, particularly when they are excessive. An example is the effect of fairly large amounts of fish oil in reducing the symptoms of asthma and rheumatoid arthritis. The omega-3 fatty acids found in fish are known to dampen the strong inflammatory activity of these conditions.

Some polyunsaturated fatty acids, particularly those of the omega-6 family, tend to trigger or enhance inflammatory responses, while those of the omega-3 family, weaken them. However, the situation is not so clear-cut.

As a way to assess immune function, scientists measure specific biomarkers—substances that regulate immune responses—to determine how the immune system responds to change and what controls it. Low-level inflammation, one of the body's defense systems, accompanies many chronic diseases and contributes to the damage they cause. Some polyunsaturated fatty acids (PUFAs), particularly those of the omega-6 family, tend to trigger or enhance inflammatory responses, while those of the omega-3 family, weaken them. This helps explain why people who eat fish regularly tend to have lower levels of inflammatory biomarkers compared with those who seldom eat fish. However, the situation is not so clear-cut. A study from Italy shows why.

Italian investigators examined several markers of immune function in a cross-section of people aged 20 to over 85 years to see if they were related to the PUFAs in their blood. Generally speaking, PUFA levels reflect dietary intake. In this population, some substances that promote inflammatory responses were higher when concentrations of both omega-6 and omega-3 fatty acids were low. Those that weaken inflammatory signals tended to increase as PUFA levels increased. These observations suggest that both fatty acid families had pro and anti-inflammatory properties. Figuring out what these observations mean may not be straightforward and they may relate to other conditions not reflected in these measurements. But these observations indicate that thinking of one type of fatty acid as promoting inflammation and the other counteracting it, is too simplistic. Conditions have to be right for one set of responses to prevail and we do not quite understand enough about that.

CLINICAL CONDITIONS

Alzheimer's Disease

DHA Protects Brain Cells from Harmful Alzheimer's Protein

If you have an aging parent or relative whose memory has deteriorated and who functions with limited ability, he or she may be a victim of Alzheimer's disease. With this condition, brain cells lose their ability to communicate with each other as proteins build up in deposits outside the cell. Much research into the causes and treatment for this debilitating disease has focused on the abnormal proteins that form these destructive deposits.

The proteins that form the plaques characteristic of Alzheimer's disease originate in the membranes of certain brain cells or neurons. Normally, enzymes chop off pieces of these proteins, forming fragments that are shuttled to the cell's internal processing facilities. As

long as these fragments remain unclustered inside the cell, they do no harm. However, when conditions inside the cell or at the cell membrane change, so does the behavior of these protein fragments. It is thought that fatty acids released from the cell membrane may turn these harmless proteins into toxic ones.

Growing the neuronal cells with DHA or EPA protected them nearly completely from Abeta-linked destruction.

A team of researchers at the National Polytechnic Institute in Nancy, France, explored the effects of two different polyunsaturated fatty acids (PUFAs) on these protein fragments in neurons. They focused mainly on arachidonic acid (AA), a PUFA derived from vegetable oils, and DHA an omega-3 PUFA from fish. Both PUFAs are concentrated in neuronal membranes. They studied neurons cultured in the laboratory so they could alter the growing environment of the cells. Knowing that a particular form of the protein fragment, known as Abeta, was toxic to the cells, they examined whether exposure to the omega-3s from fish would have any effect on Abeta's harmful effects. They discovered that growing the cells with DHA or EPA protected them nearly completely from Abeta-linked destruction.

To learn more about what was happening when DHA was present, the researchers examined the internal structure of the cells. They saw that Abeta in the absence of DHA severely damaged the internal network of fibers that holds the cell together. But when DHA was available, the internal structure of the cell was unharmed. Like a highway system, this internal network provides a transport system for proteins to get around the cell and reach the outside membrane. The network also facilitates enzyme activity essential to cell survival. Once the cell's internal framework is deranged it cannot survive.

The investigators also showed that DHA was involved in regulating the activity of certain enzymes that communicate signals from events happening at the membrane to internal proteins. When DHA was absent or insufficient, harmful agents like the Abeta fragments were free to facilitate the destructive reactions that ultimately cost the cell its life. There is much more to learn about what these Alzheimer's proteins and their fragments are doing in brain and how they are affected by different PUFAs. However, when it comes to Abeta proteins, DHA may be a question of a brain cell's life or death.

Prostate Cancer

Arachidonic Acid Enhances Spread of Prostate Cancer

Prostate cancer, the second most common cancer in men, may take a long time to advance, but when it does, it heads for the bones. Why? Is there some chemical magnet luring cancer cells there? Once they arrive, they make themselves at home.

When prostate cancer cells spread, they head straight for bone. Why? Is there some chemical magnet luring them there?

Dr. Michael Brown and his colleagues at the Paterson Institute for Cancer Research, University of Manchester, U.K., sought answers to these questions, wondering if fat, or specifically, the polyunsaturated fatty acids (PUFAs) abundant in bone might have something to do with it. They knew at the outset that blocking the PUFA pathways leading to the synthesis of potent cell regulators stopped the prostate cancer cells in their tracks.

To explore these questions, the investigators cultivated human prostate cancer cells in the supporting tissue from bone called stroma. For comparison, they grew the cells in the corresponding stroma from prostate. Once the cells were stained, it became clear that the cancer cells clustered in lipid-rich (fatty) areas in the bone stroma (Figure). In contrast, the cancer cells grown in prostate tissue, which lack such fatty areas, were isolated. The researchers were able to see that not only did

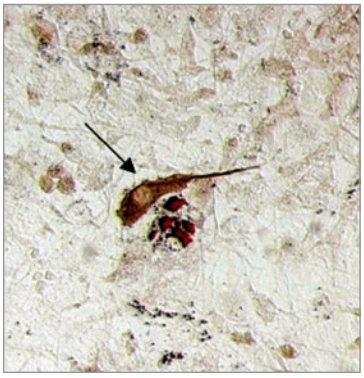

Figure. The arrow points to a prostate cancer cell (brown) clustered around a lipid-rich area (red) in bone stroma. *Photomicrograph courtesy of Michael Brown, Paterson Institute for Cancer Research, University of Manchester, U.K.*

the cells grow around lipid-rich areas in the bone stroma, they incorporated the lipids into the cell. These appeared as lipid droplets. The scientists showed further that in bone stroma, the cancer cells concentrated the fatty acid arachidonic acid (AA). The body makes AA from the main PUFA in vegetable oils, linoleic acid.

In additional studies, the investigators showed that AA was a powerful stimulant to cancer cell invasion. However, when the cells were exposed to the omega-3s from fish, EPA or DHA, invasion was no greater than background levels. Both omega-3s inhibited invasion. The scientists showed further that some of the derivatives of AA were able to overcome the block on invasion induced by EPA, but not the block achieved by DHA. The effect of these omega-3s differed in some way that wasn't obvious. Additional studies showed that PGE2, a derivative of AA, was also a powerful stimulant of cancer cell invasion. It, too, freed the cells from the inhibition produced by either EPA or DHA. PGE2 was almost as powerful a stimulant to invasion as the bone stroma itself.

Taken together, these studies provide a good explanation for why prostate cancer cells are attracted to bone and for the involvement of PUFAs and related substances. In this case, AA, which is abundantly made from the large quantities of vegetable oil PUFAs in Western diets, appears to be a potent stimulant for the spread of prostate cancer. Some of its derivatives are also potent stimulants. In contrast, the omega-3 PUFAs from fish block the migration of malignant prostate cells to bone. One can speculate that the balance between these two families of PUFAs is probably important. A word of caution is needed. These findings need to be confirmed in animal studies and clinical trials. AA is an essential PUFA for many cell functions. In prostate cancer, however, a little may be good, but more is clearly not better.

Breast Cancer

Risk of Breast Cancer Unrelated to Fish Consumption in 6-Year Study

Many studies have looked at whether fish consumption is related to the likelihood of developing breast cancer. Even after some 25 investigations, the results are inconclusive. When the findings are so unclear, it often means that too many other factors that may overlap are influencing the risk. However, it is challenging to combine and analyze studies because of the many differences among them. Competing or confounding factors need to be sorted out so that you don't miss something important.

The conclusion from a recent analysis of food intake and breast cancer information from 10 European countries is that fish consumption is not associated with the risk of breast cancer in either pre- or post-menopausal women. Whether people ate fatty fish or just any fish made no difference to the risks. What at first looked like a small increase in risk from the crude data disappeared when the data considered important confounding factors such as fat, energy and alcohol consumption and others. If an association between one factor and a particular outcome remains statistically significant after accounting for other related influences, it is more likely that the relationship is real and not something concealed in the pockets of another condition.

One of the strengths of this study is the large number and diversity of participants—over 310,000 people from 35 to 70 years. Fish consumption covered a wide range, varying from as little as 11 grams (less than half an ounce) to 92 grams (just over 3 ounces) daily. On the other hand, the use of different food frequency questionnaires in different countries made the collective assessment less precise. As a result, it was more difficult to assess dietary intake consistently. Further, it may be that that the 6-year follow-up period was simply too short to detect differences in cancer incidence, as breast cancer takes years to develop.

Glaucoma

Low Omega-3 Status Reported in Glaucoma Patients

Glaucoma is a frequent cause of impaired vision, especially in older people. It is particularly common in African-Americans and Hispanics. The condition is a

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Figure. Impaired visual field resulting from glaucoma. ***Photo courtesy of the National Eye Institute.***

result of pressure building up in the eye and results in a loss of the visual field. Objects in the center may be clear, but everything in the surrounding area appears blurred (Figure).

It is well known that omega-3 fatty acids found in fish have important function in the retina. In fact, retina has the highest concentration of DHA, one of the main marine omega-3s, anywhere in the body. DHA has been linked to various visual functions such as infant visual acuity and age-related macular degeneration. Now, a report from Nigeria suggests that low omega-3 status may be linked to the development of glaucoma.

Omega-3 PUFAs in the red blood cells of glaucoma patients were significantly lower than in their healthy siblings. PUFAs derived from vegetable oils were significantly higher.

To find out if there was a link with omega-3s, researchers at the Institute of Brain Chemistry and Human Nutrition in London, U.K. working with colleagues in Enugu, Nigeria, measured the fatty acids in the red blood cells of patients with glaucoma and their siblings who were free of the condition. They used red blood cells because you can't sample the eye directly and because red cells are a primary delivery vehicle for fatty acids to the eye. The fatty acids in red blood cells usually reflect the fatty acids in eye and brain tissue.

The investigators reported that glaucoma patients, but not their healthy siblings, had significantly greater amounts of the kinds of polyunsaturated fatty acids (PUFAs) derived from vegetable oils, including some PUFAs that do not usually accumulate. The omega-3 PUFAs in the patients were significantly lower than in the siblings. EPA was reduced by half and DHA by about a fifth. This pattern of fatty acids is similar to what is observed in omega-3 fatty acid deficiency and suggests that these fatty acids were below healthy levels. The study could not tell, however, whether these alterations in fatty acid status affected the development of glaucoma or whether the changes resulted from the condition. But they do suggest that further inquiry might be worthwhile.

FRONTIERS IN RESEARCH

Growing Neurons Need Long-Chain PUFAs

Neurons are brain cells responsible for the communication of messages in and out of the brain. Receipt and dissemination of messages depends on a process known as cell signaling, which translates electrical or chemical signals into meaningful responses, such as vision. Neurons are built for heavy trafficking. They have many projections from the main cell body that form an elaborate network for receiving inputs. Growing and repairing these nerve branches (dendrites) involves producing plenty of new membrane material to extend their tips, where growth occurs. Researchers are studying the growth process to see if they can encourage new growth after tissue damage or disease.

Figure. Neuronal cell with axon and nerve growth cone. ***Courtesy of Dr. Guo-li Ming, Johns Hopkins University School of Medicine.***

Investigators Frédéric Darios and Bazbek Davletov of the Laboratory of Molecular Biology in Cambridge, U.K., recently reported how the long-chain polyunsaturated fatty acids (LC-PUFAs) made from vegetable oils or those found in fish oils are involved in neuron growth. Quite simply, without these fatty acids, growth does not occur.

The main LC-PUFAs involved are arachidonic acid (AA), a fatty acid made from the major PUFA in vegetable oils, and docosahexaenoic acid (DHA), one of the main omega-3 LC-PUFAs in fish oils. Both fatty acids reside in the cell's membrane and can be released from it by enzyme activity.

Dendrites grow by extension of the nerve growth cones at the tips (Figure). To grow, the cones require the participation of several proteins located in their membranes. These proteins receive and add new membrane material brought to them from inside the cell. Darios and Davletov discovered that both AA and DHA, which are concentrated in the growth cones, are necessary for this process to be successful. Their job is to "turn on" a specific membrane protein so that more new membrane can be formed.

In their studies, Darios and Davletov discovered that adding AA or DHA to growing neurons stimulated nerve cell growth. They identified the particular membrane protein—syntaxin 3— that is activated by these fatty acids and showed that without AA, the dendrites could not grow.

In additional experiments, they observed that omega-3 PUFAs also activated syntaxin 3 and permitted neurons to grow. These studies are a good example of different PUFAs, omega-6 and omega-3, working similarly for cell growth and survival.

The investigators showed that AA activates a particular membrane protein—syntaxin 3—necessary for dendrites to grow. Omega-3 PUFAs also activated syntaxin 3 and permitted neurons to grow.

Fascinating in their own right, these detailed studies have implications for human health. They provide additional evidence of the importance of LC-PUFAs for proper brain cell growth and development, which begins long before birth. They also suggest the importance of having adequate supplies of these fatty acids available for nerve growth regeneration as needed in brain cell injury or degenerative disease. The situation is likely to be more complicated than simply having adequate dietary intake, but that seems a wise place to start for omega-3 PUFAs, which are relatively scarce in many Western diets. In contrast, AA is abundantly available from the ready conversion of the predominant PUFA in vegetable oils.

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