

## **New Findings About Omega-3 Fatty Acids and Depression**

By Alan C. Logan, ND, FRSH

Omega-3 fatty acids are polyunsaturated fatty acids that are considered essential because they cannot be synthesized by the human body. Dietary sources of omega-3 fatty acids include plants (particularly flax, canola, walnuts and hemp) and fish (particularly ocean fish such as sardines, anchovies, salmon and mackerel). Plants contain the parent omega-3, alpha-linolenic acid (ALA), which can be converted into eicosapentanoic acid (EPA) and docosahexanoic acid (DHA).<sup>1</sup>

Dietary fish and fish oil supplements are a direct source of EPA and DHA. The influence of ALA, EPA and DHA in human health has been the subject of intense research over the last three decades. Although best known for cardiovascular benefits, new findings indicate that the influence of omega-3 fatty acids in mental health, particularly EPA, may currently be underestimated. Epidemiological, experimental and new clinical studies have all shown a strong connection between omega-3 fatty acids, or a lack thereof, and major depression.

These exciting new findings are not entirely surprising when one considers that the brain itself is 60 percent fat and that one-third of all fatty acids are of the polyunsaturated variety.<sup>2,3</sup> As discussed below, the current research highlights the critical role of these fatty acids in the central nervous system (CNS).

### **Omega-3 Intake Declines, Depression Rates Climb**

There has been a significant drop-off in omega-3 fatty acid intake within Western countries over the last century. The opposite can be said of omega-6 intake. Although essential, omega-6-rich oils are found in abundance in the North American food supply. Currently these omega-6 oils (corn, safflower, sunflower, cottonseed, sesame) are outnumbering omega-3 fatty acids by a ratio of up to 20:1.<sup>4,5</sup>

This ratio is a long way off the close to 1:1 omega-6 to omega-3 ratio as recommended by the international panel of essential fatty acid experts in the Journal of the American College of Nutrition.<sup>6</sup> The average daily intake of EPA/DHA combined is 130mg in North America, 520mg short of published recommendations and 870mg short of the 1000mg recommended by the American Heart Association in cases of heart disease.<sup>1</sup>

In direct contrast to the depletion of omega-3 fatty acids from the Western food supply, the rates of depression have dramatically increased in Western countries. In addition, depression is now occurring more commonly in younger persons. The average age of onset of depression has continued to dip over the last 100 years. Scientists investigating the change in rates of depression have made it clear that these findings cannot be explained away by changes in attitudes of health professionals or society, diagnostic criteria, reporting bias, institutional or other artifacts.<sup>7,8</sup> Perhaps the inadequate omega-3 intake, the major deviations in fatty acids ratios and the quarter-century-old message that all fat is unhealthy has had an untold influence on rates of depression.

### **Fish Consumption and Depression**

There have been a number of studies that have examined national and international fish consumption data and compared them to rates of depression. Dr. Joseph Hibbeln of the National Institutes of Health is a pioneer in this area. He, and his group, have shown that higher national consumption of fish for a nation equals lower rates of depression versus countries consuming the

least amount of fish.<sup>9</sup> He has also shown that higher fish consumption is correlated with lower risk of postpartum depression<sup>10</sup> and seasonal affective disorder.<sup>11</sup>

Other researchers have shown that even within a nation, fish consumption is associated with lower risk of depression and higher mental health status.<sup>12,13</sup> Finally, researches are now observing increasing rates of depression in regions of the world that are moving away from traditional omega-3-rich diets to typical Western foods.<sup>14</sup>

### Laboratory Tests in Depression

The epidemiological studies clearly suggest that adequate omega-3 fatty acids may be an important protective factor in depression. Correlation, however, does not prove causation. To add to the strength of the epidemiological studies, scientists have examined the levels of omega-3 fatty acids in the blood cells and fat storage cells of those with major depression.

Four studies have shown that those with depression do indeed have lower levels of omega-3 fatty acids in the blood.<sup>15-18</sup> One of the studies showed that the lower the level of EPA, the more severe the clinical depression.<sup>15</sup> In addition, a recent study showed that the patients with depression have 35 percent less DHA in fat storage cells versus healthy controls.<sup>19</sup>

### Experimental Studies

Over the last decade, neuroscientists have been examining the consequences of omega-3 deficiencies in the central nervous system. Alterations in serotonin and dopamine levels, as well as the functioning of these two important neurotransmitters is evident in an omega-3 deficiency. The changes observed in omega-3 deficiency in animals is strikingly similar to that found in autopsy studies of human depression.<sup>20</sup>

In addition to changing serotonin and dopamine levels and functioning, omega-3 deficiencies are known to compromise the blood-brain barrier, which normally protects the brain from unwanted matter gaining access.<sup>21</sup> Omega-3 deficiency can also decrease normal blood flow to the brain,<sup>22,23</sup> an interesting finding given the studies which show that patients with depression have compromised blood flow to a number of brain regions.<sup>24,25</sup> Finally, omega-3 deficiency also causes a 35 percent reduction in brain phosphatidylserine (PS) levels.<sup>26</sup> This is also of relevance when considering that PS has documented antidepressant activity in humans.<sup>27,28</sup>

### Mechanisms of EPA/DHA Regulation of Mood

DHA is found in high levels in the cells of the central nervous system (neurons); here it acts as a form of scaffolding for structural support.<sup>29</sup> When omega-3 intake is inadequate, the nerve cell becomes stiff as cholesterol and omega-6 fatty acids are substituted for omega-3.<sup>30</sup> When a nerve cell becomes rigid, proper neurotransmission from cell to cell and within cells will be compromised.<sup>31</sup>

While DHA provides structure and helps to ensure normal neurotransmission, EPA may be more important in the signaling within nerve cells.<sup>32</sup> Normalizing communications within nerve cells has been suggested to be an important factor in alleviating depressive symptoms.<sup>33</sup> In addition, EPA can lower the levels of two important immune chemicals, tumour necrosis factor alpha (TNF $\alpha$ ) and interleukin 1 beta (IL-1 $\beta$ ), as well as prostaglandin E2.<sup>34</sup>

All three of these chemicals are elevated in depression.<sup>35-38</sup> In fact, higher levels of TNF $\alpha$  and IL-1 $\beta$  are associated with severity of depression.<sup>39</sup> Finally, EPA has been hypothesized to increase brain-derived neurotrophic factor (BDNF), which is known to be lower in depressed patients.<sup>20</sup> BDNF is neuroprotective, enhances neurotransmission, has antidepressant activity and supports normal brain structure. BDNF may prevent the death of nerve cells in depression.

### Clinical Studies

There have been some published case reports indicating that flaxseed oil may be helpful in cases of bipolar depression and the anxiety disorder agoraphobia.<sup>40</sup> The first controlled clinical trial indicating that omega-3 fatty acids may be of benefit in depression was published in 1999. In this case, 9:6 g of EPA/DHA versus placebo led to longer periods of remission and improvement in depressive symptoms in those with bipolar depression.<sup>41</sup>

Some researchers theorize that such high doses of EPA/DHA may not be necessary and that low levels of pure EPA may be of benefit.<sup>32</sup> In a study published in the American Journal of Psychiatry, researchers showed that just 2g of pure EPA could improve the symptoms of treatment-resistant depression. The researchers found that the EPA (versus placebo), when added to an ineffective antidepressant for one month, significantly improved depressive symptoms.<sup>42</sup>

A larger study published in Archives of General Psychiatry replicated these findings, however, this time various doses of EPA were examined. Those on ineffective antidepressants were given 1g, 2g or 4g of pure EPA or a placebo in addition to the medication. Interestingly, the 1g daily dose of EPA led to the most significant improvements over the three-month study; it appeared that less was more. There were significant improvements in depressive symptoms, sleep, anxiety, lassitude, libido and thoughts of suicide.<sup>43</sup>

Researchers from Taiwan Medical University published a recent study in which they found that a 4.4g EPA and 2.2g DHA mix could alleviate depression versus placebo in those with treatment-resistant depression. This was a two-month study involving patients who were on antidepressants that were not working. As with the other omega-3 studies discussed, the fish oil was well tolerated and no adverse events were reported.<sup>44</sup>

There is also evidence that omega-3 oils may be of benefit in treating depressive symptoms outside of major depressive disorder. Canadian researchers showed that Antarctic krill oil (400mg EPA, 240mg DHA) could improve depressive symptoms associated with premenstrual syndrome.<sup>45</sup> Harvard researchers have also shown that just 1g of pure EPA is beneficial in the treatment of borderline personality disorder. This personality disorder, which is particularly difficult to treat, is characterized by both depressive and aggressive symptoms. This was a two-month placebo-controlled study and the results showed that EPA has a mood-regulating effect, improving both depression and aggression versus placebo.<sup>46</sup>

To date, with one exception, all studies conducted on omega-3 fatty acids and mood have had a positive outcome. The singular negative study examined pure DHA in patients with depression. The results in the case showed that DHA alone was no better than placebo in alleviating depressive symptoms.<sup>47</sup>

### Conclusion

Although an influence of EPA and DHA on brain physiology and structure is apparent, the precise mechanisms whereby omega-3 fatty acids may alleviate depression remain unknown. The

results of the clinical trials reinforce the epidemiological and experimental studies, underscoring the importance of adequate omega-3 intake in those with depression.

The long-term studies of fish oil supplements in the area of cardiovascular health, some spanning three-plus years, have shown that they are safe and well tolerated.<sup>48,49</sup> Patients with depression or depressive symptoms should discuss omega-3 fatty acids with their health care providers. While scientists continue to unravel the neuropsychological influences of omega-3 fatty acids, it should be recognized that they are not a substitute for appropriate mental health evaluation and care.

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