Fish oil and mood

Multiple studies have identified and confirmed that Omega-3 fatty acids can enhance the quality of life in persons with certain types of depression. There is also modest benefit when fish oil is added to traditional medical therapy for schizophrenia.

Below, in bibliographical form, are abstracts from scientific research papers that have shown the relationship between Omega-3 Fatty Acids and mood. Links to full text articles are provided when available.

Marangell LB, Martinez JM, Zboyan HA, Kertz B, Kim HF, Puryear LJ. **A double-blind, placebo-controlled study of the omega-3 fatty acid docosahexaenoic acid in the treatment of major depression.** Am J Psychiatry. 2003 May;160(5):996-8.

http://ajp.psychiatryonline.org/cgi/reprint/160/5/996

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OBJECTIVE: This study was an evaluation of the omega-3 fatty acid docosahexaenoic acid (DHA) for the treatment of major depression. METHOD: Thirty-six depressed patients were randomly assigned to receive DHA, 2 g/day, or placebo for 6 weeks. Response was defined a priori as a > or =50% reduction in the score on the Montgomery-Asberg Depression Rating Scale. Thirty-five participants were evaluable; 18 received DHA, and 17 received placebo. RESULTS: Response rates were 27.8% in the DHA group and 23.5% in the placebo group. The difference in response rates between groups did not reach statistical significance. CONCLUSIONS: This trial failed to show a significant effect of DHA monotherapy in subjects with major depression.

Su KP, Huang SY, Chiu CC, Shen WW. **Omega-3 fatty acids in major depressive disorder. A preliminary double-blind, placebo-controlled trial.** Eur Neuropsychopharmacol. 2003 Aug;13(4):267-71.

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Patients with depression have been extensively reported to be associated with the abnormality of omega-3 polyunsaturated fatty acids (PUFAs), including significantly low eicosapentaenoic acid and docosahexaenoic acid in cell tissue contents (red blood cell membrane, plasma, etc.) and dietary intake. However, more evidence is needed to support its relation. In this study, we conducted an 8-week, double-blind, placebo-controlled trial, comparing omega-3 PUFAs (6.6 g/day) [corrected] with placebo, on the top of the usual treatment, in 28 patients with major depressive disorder. Patients in the omega-3 PUFA group had a significantly decreased score on the 21-item Hamilton Rating Scale for Depression than those in the placebo group ($P < 0.001$). From the preliminary findings in this study, omega-3 PUFAs could improve the short-term course of illness and were well tolerated in patients with major depressive disorder.

Frangou S, Lewis M, McCrone P. **Efficacy of ethyl-eicosapentaenoic acid in bipolar depression: randomised double-blind placebo-controlled study.** Br J Psychiatry. 2006 Jan;188:46-50.

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BACKGROUND: Epidemiological and clinical studies suggest that increased intake of eicosapentaenoic acid (EPA) alleviates unipolar depression. AIMS: To examine the efficacy of EPA in treating depression in bipolar disorder. METHOD: In a12-week, double-blind study individuals with bipolar depression were randomly assigned to adjunctive treatment with placebo (n=26) or with 1 g/day (n=24) or 2 g/day (n=25) of ethyl-EPA. Primary efficacy was assessed by the Hamilton Rating Scale for Depression (HRSD), with changes in the Young Mania Rating Scale and Clinical Global Impression Scale (CGI) as secondary outcome measures. RESULTS: There was no apparent benefit of 2 g over 1 g ethyl-EPA daily. Significant improvement was noted with ethyl-EPA treatment compared with placebo in the HRSD (P=0.04) and the CGI (P=0.004) scores. Both doses were well tolerated. CONCLUSIONS: Adjunctive ethyl-EPA is an effective and well-tolerated intervention in bipolar depression.

Osher Y, Bersudsky Y, Belmaker RH. **Omega-3 eicosapentaenoic acid in bipolar depression: report of a small open-label study.** J Clin Psychiatry. 2005 Jun;66(6):726-9.

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INTRODUCTION: Epidemiologic studies have suggested that consumption of cold water fish oils may have some protective function against depression. This proposition is supported by a series of biochemical and pharmacologic studies that have suggested that fatty acids may modulate neurotransmitter metabolism and cell signal trans-duction in humans and that abnormalities in fatty acid and eicosanoid metabolism may play a causal role in depression. Aware of the critical need for antidepression treatments that might not carry the risk of precipitating a manic episode in bipolar patients, we decided to conduct an open-label add-on trial of eicosapentaenoic acid (EPA) in bipolar depression. METHOD: Twelve bipolar I outpatients with depressive symptoms diagnosed by DSM-IV were treated with 1.5 to 2 g/day of the omega-3 fatty acid EPA for up to 6 months. The study was conducted between September 2001 and January 2003. RESULTS: Eight of the 10 patients who completed at least 1 month of follow-up achieved a 50% or greater reduction in Hamilton Rating Scale for Depression scores within 1 month. No patients developed hypomania or manic symptoms. No significant side effects were reported. LIMITATIONS: This study is limited both by the open-label design and by the small sample size. As in all previous reported studies, patients in this study were treated in an outpatient setting, so that the most severely depressed bipolar patients (requiring hospitalization) are not represented. CONCLUSIONS: Although the ultimate utility of omega-3 fatty acids in bipolar depression is still an open question, we believe that these initial results are encouraging, especially for mild to moderate bipolar depression, and justify the continuing exploration of its use.

Young G, Conquer J. **Omega-3 fatty acids and neuropsychiatric disorders.** Reprod Nutr Dev. 2005 Jan-Feb;45(1):1-28.

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Epidemiological evidence suggests that dietary consumption of the long chain omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), commonly found in fish or fish oil, may modify the risk for certain neuropsychiatric disorders. As evidence, decreased blood levels of omega-3 fatty acids have been associated with several neuropsychiatric conditions, including Attention Deficit (Hyperactivity) Disorder, Alzheimer's Disease, Schizophrenia and Depression. Supplementation studies, using individual or combination omega-3 fatty acids, suggest the possibility for decreased symptoms associated with some of these conditions. Thus far, however, the benefits of supplementation, in terms of decreasing disease risk and/or aiding in symptom management, are not clear and more research is needed. The reasons for blood fatty acid alterations in these disorders are not known, nor are the potential mechanisms by which omega-3 fatty acids may function in normal neuronal activity and neuropsychiatric disease prevention and/or treatment. It is clear, however, that DHA is the predominant n-3 fatty acid found in the brain and that EPA plays an important role as an anti-inflammatory precursor. Both DHA and EPA can be linked with many aspects of neural function, including neurotransmission, membrane fluidity, ion channel and enzyme regulation and gene expression. This review summarizes the knowledge in terms of dietary omega-3 fatty acid intake and metabolism, as well as evidence pointing to potential mechanisms of omega-3 fatty acids in normal brain functioning, development of neuropsychiatric disorders and efficacy of omega-3 fatty acid supplementation in terms of symptom management.

Ohara K. **[Omega-3 fatty acids in mood disorders]** Seishin Shinkeigaku Zasshi. 2005;107(2):118-26. [Article in Japanese]

Department of Psychiatry, Shinshiro Municipal Hospital.

The etiology and treatment of mood disorders has not yet been elucidated. Omega (omega)-3 fatty acids are essential fatty acids, which cannot be synthesized in the human body. Eicosapentanoic acid (EPA) and docosahexaenoic acid (DHA) are representative omega-3 fatty acids which are found in fish (eg., mackerel, herring, Chinook salmon) and vegetables (eg., flax, walnut, canola). The peripheral level of EPA and DHA decrease in patients with major depression, and EPA is useful for its treatment. Further research is required on omega-3 fatty acids in patients with mood disorders.

Silvers KM, Woolley CC, Hamilton FC, Watts PM, Watson RA. **Randomised double-blind placebo-controlled trial of fish oil in the treatment of depression.** Prostaglandins Leukot Essent Fatty Acids. 2005 Mar;72(3):211-8.

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Converging evidence suggests that omega-3 polyunsaturated fatty acids have aetiological importance in depression. To determine the effect of adding fish oil to existing therapy in participants who were being treated for depression in a community setting, 77 participants were randomly assigned to receive 8 g of either fish or olive oil per day in addition to their existing therapy. Fifty-nine (77%) participants completed 12 weeks of treatment. Dietary, biochemical and lifestyle factors were measured throughout the study. Mood was assessed using the Short Form Hamilton Depression Rating Scale (HDRS-SF) and the Beck Depression Inventory II. Sample size calculations were based on the HDRS-SF. Intention-to-treat and per protocol analyses were carried out using residual maximum likelihood. There was no evidence that fish oil improved mood when compared to the placebo oil, despite an increase in circulating omega-3 polyunsaturated fatty acids. However, mood improved significantly in both groups within the first 2 weeks of the study ($P<0.001$) and this improvement was sustained throughout. In conclusion, fish oil was no more effective than the control as an add-on therapy for depression in this setting.

Hakkarainen R, Partonen T, Haukka J, Virtamo J, Albanes D, Lonnqvist J. **Is low dietary intake of omega-3 fatty acids associated with depression?** Am J Psychiatry. 2004 Mar;161(3):567-9.

http://ajp.psychiatryonline.org/cgi/reprint/161/3/567

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OBJECTIVE: This study examined the association between the dietary intake of omega-3 fatty acids and low mood, major depression, and suicide. METHOD: A total of 29,133 men ages 50 to 69 years participated in a population-based trial in Finland. The intake of fatty acids and fish consumption were calculated from a diet history questionnaire. Self-reported depressed mood was recorded three times annually, data on hospital treatments due to a major depressive disorder were derived from the National Hospital Discharge Register, and suicides were identified from death certificates. RESULTS: There were no associations between the dietary intake of omega-3 fatty acids or fish consumption and depressed mood, major depressive episodes, or suicide. CONCLUSIONS: Dietary intake of omega-3 fatty acids showed no association with low mood level.

Peet M. **Eicosapentaenoic acid in the treatment of schizophrenia and depression: rationale and preliminary double-blind clinical trial results.** Prostaglandins Leukot Essent Fatty Acids. 2003 Dec;69(6):477-85.

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It has been hypothesised that polyunsaturated fatty acids (PUFA) play an important role in the aetiology of schizophrenia and depression. Evidence supporting this hypothesis for schizophrenia includes abnormal brain phospholipid turnover shown by 31P Magnetic Resonance Spectroscopy, increased levels of phospholipase A2, reduced niacin skin flush response, abnormal electroretinogram, and reduced cell membrane levels of n-3 and n-6 PUFA. In depression, there is strong epidemiological evidence that fish consumption reduces risk of becoming depressed and evidence that cell membrane levels of n-3 PUFA are reduced. Four out of five placebo-controlled double- blind trials of eicosapentaenoic acid (EPA) in the treatment of schizophrenia have given positive findings. In depression, two placebo-controlled trials have shown a strong therapeutic effect of ethyl-EPA added to existing medication. The mode of action of EPA is currently not known, but recent evidence suggests that arachidonic acid (AA) if of particular importance in schizophrenia and that clinical improvement in schizophrenic patients using EPA treatment correlates with changes in AA.

Young C, Martin A. **Omega-3 fatty acids in mood disorders: an overview.** Rev Bras Psiquiart. 3003 Sep;25(3):184-7.

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This review addresses the potential role of omega-3 fatty acids in mood disorders, from the biochemical rationale for their use to the growing body of data supporting their clinical efficacy.

Zanarini MC, Frankenburg FR. **omega-3 Fatty acid treatment of women with borderline personality disorder: a double-blind, placebo-controlled pilot study.** Am J Psychiatry. 2003 Jan;160(1):167-9.

http://ajp.psychiatryonline.org/cgi/reprint/160/1/167

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OBJECTIVE: The purpose of this study was to compare the efficacy of ethyl-eicosapentaenoic acid (E-EPA) and placebo in the treatment of female subjects with borderline personality disorder. METHOD: The authors conducted an 8-week, placebo-controlled, double-blind study of E-EPA in 30 female subjects meeting Revised Diagnostic Interview for Borderlines and DSM-IV criteria for borderline personality disorder. RESULTS: Twenty subjects were randomly assigned to 1 g of E-EPA; 10 subjects were given placebo. Ninety percent of those in both groups completed all 8 weeks of the trial. Analyses that used random-effects regression modeling and controlled for baseline severity showed E-EPA to be superior to placebo in diminishing aggression as well as the severity of depressive symptoms. CONCLUSIONS: The results of this study suggest that E-EPA may be a safe and effective form of monotherapy for women with moderately severe borderline personality disorder.

Cott J, Hibbeln JR. **Lack of seasonal mood change in Icelanders.** Am J Psychiatry. 2001 Feb;158(2):328.

http://ajp.psychiatryonline.org/cgi/reprint/158/2/328

Mischoulon D, Fava M. **Docosahexanoic acid and omega-3 fatty acids in depression.** Psychiatr Clin North Am. 2000 Dec;23(4):785-94.

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Geographic areas where consumption of DHA is high are associated with decreased rates of depression. DHA deficiency states, such as alcoholism and the postpartum period, also are linked with depression. Individuals with major depression have marked depletions in omega-3 FAs (especially DHA) in erythrocyte phospholipids compared with controls. These data suggest that DHA may be associated with depression, and the limited data available on supplementation with DHA or other omega-3 FAs seem to support the hypothesis that DHA may have psychotropic effects. Overall, the use of EFAs is promising, particularly in view of the many illnesses potentially treatable with these substances; however, larger, carefully designed studies are needed to establish whether DHA is an effective and safe antidepressant, mood stabilizer, or antipsychotic. A few preliminary trials of DHA are in progress, but no studies comparing DHA against placebo or against an established antidepressant have been carried out. Studies to address this issue are being developed at the Massachusetts General Hospital. Studies likely will require escalating doses of DHA, eventually reaching high levels so as to ensure that patients will avoid a potentially ineffective subclinical dose. Careful monitoring of dietary intake among subjects also will necessary because a high intake of omega-3-rich foods may confound results. Finally, large-scale, placebo-controlled, double-blind trials comparing the efficacy and safety of DHA against standard antidepressants are required before psychiatrists can recommend DHA therapy as effective and safe for the treatment of depression and other mood disorders. Given the popularity of self-medication by patients who already are taking marketed antidepressants, studies examining the use of DHA as an augmentor to standard antidepressants may answer whether DHA can occupy a niche as an augmenting agent for patients who have made a partial response or have not responded to conventional antidepressants. Considering that natural medications generally seem best for treating mild to moderate illness, the role of DHA as a therapy for minor and subsyndromal depression also should be considered. It is hoped that studies of these types will help to clarify some of the knowledge gaps outlined in this article.

Freeman MP. **Omega-3 fatty acids in psychiatry: a review.** Psychiatr Clin North Am. 2000 Dec;23(4):785-94.

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Omega-3 fatty acids are long-chain, polyunsaturated fatty acids found in plant and marine sources. Unlike saturated fats, which have been shown to have negative health consequences, omega-3 fatty acids are polyunsaturated fatty acids that have been associated with many health benefits. Omega-3 fatty acids may prove to be efficacious in a number of psychiatric disorders. Mood disorders have been associated with abnormalities in fatty acid composition. Several lines of evidence suggest that diminished omega-3 fatty acid concentrations are associated with mood disorders. Clinical data are not yet available regarding omega-3 fatty acids in the treatment of major depression. However, one double-blind treatment trial has been conducted in bipolar disorder. Also, substantial evidence does exist supporting a potential role of omega-3 fatty acids in schizophrenia, although treatment data are needed. A case has been reported in which a patient with schizophrenia was successfully treated with omega-3 fatty acids. Controlled studies are necessary to explore the potential treatment of schizophrenia with omega-3 fatty acids. Omega-3 fatty acids may also be helpful in the treatment of dementia. Furthermore, omega-3 fatty acids may prove to be a safe and efficacious treatment for psychiatric disorders in pregnancy and in breastfeeding.

Maidment ID. **Are fish oils an effective therapy in mental illness--an analysis of the data.** Acta Psychitr Scand. 2000 Jul;102(1):3-11.

Hellesdon Hospital, Norwich, Norfolk, UK.

OBJECTIVE: To review the literature regarding the use of fish oils in the treatment of psychiatric illness. METHOD: A Medline search was conducted in September 1999. RESULTS: Five papers have investigated omega-3 fatty acids levels in depression. One study used omega-3 fatty acids as an adjunctive therapy in bipolar disorder. Four studies used fatty acids as an adjunctive therapy in schizophrenia. CONCLUSION: There is a great deal of current research in this field. While omega-3 fatty acids levels may be lowered in depression, there are no data suggesting that omega-3 fatty acids are effective. One paper indicates that omega-3 fatty acids are effective in bipolar disorders. The data on schizophrenia are conflicting. Omega-3 and omega-6 fatty acids have proved effective. Most of the evidence suggests that the main effect is an improvement in negative symptoms. One recent study showed that omega-3 fatty acids had no effect on negative symptoms.

Frangou S, Lewis M, McCrone P. **Efficacy of ethyl-eicosapentaenoic acid in bipolar depression: randomised double-blind placebo-controlled study.** Br J Psychiatry. 2006 Jan;188:46-50.

Section of Neurobiology of Psychosis, PO66, Institute of Psychiatry, De Crespigny Park, London SE5 8AF, UK. s.frangou@iop.kcl.ac.uk

BACKGROUND: Epidemiological and clinical studies suggest that increased intake of eicosapentaenoic acid (EPA) alleviates unipolar depression. AIMS: To examine the efficacy of EPA in treating depression in bipolar disorder. METHOD: In a12-week, double-blind study individuals with bipolar depression were randomly assigned to adjunctive treatment with placebo (n=26) or with 1 g/day (n=24) or 2 g/day (n=25) of ethyl-EPA. Primary efficacy was assessed by the Hamilton Rating Scale for Depression (HRSD), with changes in the Young Mania Rating Scale and Clinical Global Impression Scale (CGI) as secondary outcome measures. RESULTS: There was no apparent benefit of 2 g over 1 g ethyl-EPA daily. Significant improvement was noted with ethyl-EPA treatment compared with placebo in the HRSD (P=0.04) and the CGI (P=0.004) scores. Both doses were well tolerated. CONCLUSIONS: Adjunctive ethyl-EPA is an effective and well-tolerated intervention in bipolar depression.

Peet M, Stokes C. **Omega-3 fatty acids in the treatment of psychiatric disorders.** Drugs. 2005;65(8):1051-9.

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The importance of omega-3 fatty acids for physical health is now well recognised and there is increasing evidence that omega-3 fatty acids may also be important to mental health. The two main omega-3 fatty acids in fish oil, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have important biological functions in the CNS. DHA is a major structural component of neuronal membranes, and changing the fatty acid composition of neuronal membranes leads to functional changes in the activity of receptors and other proteins embedded in the membrane phospholipid. EPA has important physiological functions that can affect neuronal activity. Epidemiological studies indicate an association between depression and low dietary intake of omega-3 fatty acids, and biochemical studies have shown reduced levels of omega-3 fatty acids in red blood cell membranes in both depressive and schizophrenic patients.Five of six double-blind, placebo-controlled trials in schizophrenia, and four of six such trials in depression, have reported therapeutic benefit from omega-3 fatty acids in either the primary or secondary statistical analysis, particularly when EPA is added on to existing psychotropic medication. Individual clinical trials have suggested benefits of EPA treatment in borderline personality disorder and of combined omega-3 and omega-6 fatty acid treatment for attention-deficit hyperactivity disorder. The evidence to date supports the adjunctive use of omega-3 fatty acids in the management of treatment unresponsive depression and schizophrenia. As these conditions are associated with increased risk of coronary heart disease and diabetes mellitus, omega-3 fatty acids should also benefit the physical state of these patients. However, as the clinical research evidence is preliminary, large, and definitive randomised controlled trials similar to those required for the licensing of any new pharmacological treatment are needed.

Bourre JM. **[Omega-3 fatty acids in psychiatry]** [Article in French] Med Sci (Paris). 2005 Feb;21(2):216-21.

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The brain is one of the organs with the highest level of lipids (fats). Brain lipids, formed of fatty acids, participate in the structure of membranes, for instance 50 % fatty acids are polyunsaturated in the gray matter, 1/3 are of the omega-3 family, and are thus of dietary origin. The omega-3 fatty acids (mainly alpha-linolenic acid, ALA) participated in one of the first experimental demonstration of the effect of dietary substances (nutrients) on the structure and function of the brain. Experiments were first of all carried out on ex vivo cultured brain cells, then on in vivo brain cells (neurons, astrocytes and oligodendrocytes) from animals fed ALA deficient diet, finally on physicochemical (membrane fluidity), biochemical, physiological, neurosensory (vision an auditory responses), and behavioural or learning parameters. These findings indicated that the nature of polyunsaturated fatty acids (in particular omega-3) present in formula milks for human infants determines to a certain extend the visual, neurological, and intellectual abilities. Thus, in view of these results and of the high polyunsaturated fatty acid content of the brain, it is normal to consider that they could be involved in psychiatric diseases and in the cognitive decline of ageing. Omega-3 fatty acids appear effective in the prevention of stress, however their role as regulator of mood is a matter for discussion. Indeed, they play a role in the prevention of some disorders including depression (especially post partum), as well as in dementia, particularly Alzheimer's disease. Their role in major depression and bipolar disorder (manic-depressive disease), only poorly documented, is not clearly demonstrated. The intervention of omega-3 in dyslexia, autism, and schizophrenia has been suggested, but it does not necessarily infer a nutritional problems. The respective importance of the vascular system (where the omega-3 are actually active) and the cerebral parenchyma itself, remain to be resolved. However, the insufficient supply of omega-3 fatty acids in today diet in occidental (less than 50 % of the recommended dietary intakes values for ALA) raises the problem of how to correct inadequate dietary habits, by prescribing mainly rapeseed (canola) and walnut oils on the one hand, fatty fish (wild, or farmed, but the nature of fatty acids present in fish flesh is the direct consequence of the nature of fats with which they have been fed), and eggs from laying hens fed omega-3 fatty acids.

Murck H, Song C, Horrobin DF, Uhr M. **Ethyl-eicosapentaenoate and dexamethasone resistance in therapy-refractory depression.** Int J Neuropsychopharmacol. 2004 Sep;7 (3):341-9. Epub 2004 Mar 5.

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Preliminary evidence shows that ethyl-eicosapentaenoate (E-EPA) has a marked clinical effect when used as an adjunct in therapy-refractory depression. EPA belongs to the class of polyunsaturated omega-3 fatty acids. The mechanism of its action in depression is not fully understood. There are two related fields where the pathophysiology of refractory depression meets the effect of EPA. First, a general immunosuppressive effect of EPA meets a general immunoactivation in severe depression, especially an increase in CD4/CD8 ratio, neutrophilia, and an increase in interleukins (IL)-6 and IL-12 and of prostaglandin E2 (PGE2). Secondly, a resistance to dexamethasone (Dex) suppression of the HPA axis meets the effects of EPA on multidrug resistance reversing and HPA axis suppression. The effects of EPA on the immune system, the HPA axis, and multidrug resistance are connected through the action of a transport protein called p-glycoprotein (p-gp). Physiological and synthetic steroids such as cortisol and Dex are substrates of p-gp, and so Dex resistance in depression may be related to dysfunction of this protein. In addition, expression of p-gp is induced by PGE2, and EPA inhibits the synthesis of PGE2. The reversal of drug resistance by EPA may be mediated via this immunological mechanism and lead to its antidepressive efficacy. In addition, antidepressants such as amitriptyline, which have special efficacy in severe depression, decrease p-gp function. EPA may, furthermore, enhance the action of antidepressants, like many SSRIs that are p-gp substrates, which are actively transported out of the intracerebral space at the level of the blood-brain barrier.

Tiemeier H, van Tuijl HR, Hofman A, Kiliaan AJ, Breteler MM. **Plasma fatty acid composition and depression are associated in the elderly: the Rotterdam Study.** Am J Clin Nutr. 2003 Jul;78(1):40-6.

http://www.ajcn.org/cgi/reprint/78/1/40

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BACKGROUND: It has been hypothesized that n-3 polyunsaturated fatty acids (PUFAs) are involved in mood regulation, but epidemiologic evidence for such a link in the general population is lacking. OBJECTIVE: This study examined whether community-dwelling elderly persons with depression have a fatty acid composition that is different from that of nondepressed persons. DESIGN: We screened 3884 adults aged > or = 60 y for depressive symptoms as part of the Rotterdam Study. Subjects who screened positive had a psychiatric interview to diagnose depressive disorders. All eligible subjects had their blood drawn for measurement of plasma phospholipid concentrations. We compared percentages of n-3 and n-6 PUFAs and their ratios between 264 subjects with depressive symptoms, including 106 subjects with depressive disorders, and 461 randomly selected reference subjects. We also investigated whether atherosclerosis or the inflammatory response as measured by C-reactive protein underlies the relation between fatty acid composition and depression. RESULTS: Subjects with depressive disorders had a higher ratio of n-6 to n-3 PUFAs, but differences in individual PUFAs were mostly small. However, depressed subjects with normal CRP concentrations (< 1.5 mg/L) had a substantially altered fatty acid composition; percentages of n-3 PUFAs and ratios of n-6 to n-3 PUFAs were significantly lower and higher, respectively, in subjects with depressive disorders than in control subjects [5.2% compared with 5.9% (P = 0.02) and 7.2 compared with 6.6 (P = 0.01), respectively]. This relation was not due to atherosclerosis. CONCLUSIONS: In community-dwelling persons, fatty acid composition is related to depression. Because this relation was not secondary to inflammation, atherosclerosis, or possible confounders, it suggests a direct effect of fatty acid composition on mood.

Fenton WS, Dickerson F, Boronow J, Hibbeln JR, Knable M. **A placebo-controlled trial of omega-3 fatty acid (ethyl eicosapentaenoic acid) supplementation for residual symptoms and cognitive impairment in schizophrenia.** Am J Psychiatry. 2001 Dec;158(12):2071-4.

http://ajp.psychiatryonline.org/cgi/reprint/158/12/2071

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OBJECTIVE: This study determined if augmentation of neuroleptics with 3 g/day of ethyl eicosapentaenoic acid (EPA) improves symptoms and cognition in patients with schizophrenia or schizoaffective disorder. METHOD: Eighty-seven patients meeting criteria for schizophrenia or schizoaffective disorder who had residual symptoms despite neuroleptic treatment were randomly assigned to receive either 3 g/day of ethyl EPA (N=43) or placebo (N=44) in a 16-week, double-blind supplementation trial. Assessments were performed at baseline and at weeks 1, 2, 4, 8, 12, and 16; a cognitive battery was administered at baseline and at week 16. RESULTS: No differences were found between groups in positive or negative symptoms, mood, cognition, or global impression ratings. Results were similar for the intention-to-treat (N=87) and completer (N=75) groups. CONCLUSIONS: For schizophrenia patients treated with 3 g/day of ethyl EPA, improvement in residual symptoms and cognitive impairment was no greater than for schizophrenia patients treated with placebo.