8.07f/W(Jul162004) XML:ver:5.0.1 YPLEF : 900 Prod.Type:FTP pp.1–3(col.fig.:NIL) ED:AjithG.P. PAGN:VG SCAN:

ARTICLE IN PRESS

Available online at www.sciencedirect.com

ScienceDirect

ELSEVIER

Prostaglandins, Leukotrienes and Essential Fatty Acids ▮ (▮▮▮▮) ▮▮▮–▮▮▮

Prostaglandins Leukotrienes and Essential Fatty Acids

www.elsevier.com/locate/plefa

Editorial

The emerging role of omega-3 fatty acids in psychiatry

Major advances in the treatment and prevention of psychiatric illness will be facilitated by the identification of modifiable risk factors conferring liability. To this end, aggressive efforts have been made to identify genes that confer susceptibility, though a consistent pattern has yet to emerge [1]. Moreover, subtotal heritability estimates, monozygotic twin concordance rates, and adoption studies suggest that pre- and postnatal 'environmental' risk factors confer equal if not greater liability for psychiatric illness. Therefore, equally aggressive efforts need to be made to identify environmental risk factors, particularly in view of their greater amenability to modification, and multiple putative environmental risk factors have been identified [2]. For example, several epidemiological surveys have identified perinatal nutritional deprivation as an environmental risk factor for schizophrenia [3–5], though the specific nutrient(s) remain to be identified. While the role of dietary/nutritional factors in risk liability are receiving increasing experimental or theoretical attention, diet and nutrition remain largely neglected aspects of psychiatric clinical practice.

In the field of cardiology diet is recognized as a critical factor in the pathaetiology of cardiovascular disease. For example, it is now well documented that diets low in omega-3 fatty acids, including docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), increase risk of cardiovascular morbidity and mortality [6–8]. Because mammals cannot synthesize omega-3 fatty acids de novo, they are entirely dependent on dietary sources in order to obtain and maintain adequate tissue levels. Accordingly, the American Heart Association has established dietary guidelines which recommend that patients with coronary heart disease consume ~1 g/day of EPA + DHA in their diet [9]. This recommendation stems from evidence from four primary areas of research: (1) cross-national and cross-sectional epidemiological surveys finding a reduced incidence of cardiovascular disease and mortality in populations whose diets contain high levels of fish/seafood (a surrogate for EPA + DHA intake), (2) antemortem (plasma, red blood cells) fatty acid composition studies demonstrating an inverse correlation between tissue EPA + DHA concentrations and cardiovascular disease morbidity and mortality, (3) randomized, double-blind, placebo-controlled clinical trials and prospective studies demonstrating that elevating dietary EPA + DHA intake reduces risk of sudden cardiac death, and (4) preclinical and clinical data demonstrating the beneficial effects of EPA + DHA on myocardial physiology and function.

The brain, like the heart, is composed of specialized cells whose membranes are composed of phospholipids that play a central role in the regulation of their physiology and function [10]. Analogous to the cardiology model, evidence in support of dietary omega-3 fatty acid deficiency as a risk factor for neuropsychiatric illness is provided by four primary areas of research: (1) cross-national and cross-sectional epidemiological surveys demonstrating reduced incidence and/or symptom severity of psychiatric illness in populations whose diets contain high levels of omega-3 fatty acid-rich fish/seafood, (2) antemortem (plasma, red blood cells, adipose tissue) and postmortem brain fatty acid composition studies demonstrating significant deficits in omega-3 fatty acid concentrations in psychiatric patients, (3) randomized, double-blind, placebo-controlled clinical trials, open-label trials, and case studies demonstrating that elevating dietary intake of EPA + DHA or the ethyl ester of EPA reduces symptom severity, and (4) preclinical data demonstrating the negative effects of perinatal EPA + DHA deficiency on multiple clinically relevant neurochemical processes, including dopamine and serotonin neurotransmission [11], and behavioral processes, including indices of mood and cognition [12]. Indeed, there is now evidence suggesting that omega-3 fatty acid deficiency may contribute to the pathophysiology of attention-deficit/hyperactivity disorder [13], depression [14,15], bipolar disorder [16], and schizophrenia [17].

The slow emergence of omega-3 fatty acids in psychiatric practice in the US likely reflects the relatively recent appreciation that omega-3 fatty acids are important for multiple aspects of human health [18,19]. Unlike other countries including the UK and Canada, a Recommended Daily Allowance for omega-3 fatty acids has yet to be established in the US, and

0952-3278/$ - see front matter © 2006 Published by Elsevier Ltd.
doi:10.1016/j.plefa.2006.07.003

Please cite this article as: Robert K. McNamara, The emerging role of omega-3 fatty acids in psychiatry, Prostaglandins, Leukotrienes and Essential Fatty Acids (2006), doi:10.1016/j.plefa.2006.07.003.

dietary omega-3 fatty acid intake has declined [20]. Accordingly, omega-3 fatty acid concentrations in breastmilk of US women are currently among the lowest in the world [21], and only recently (2002) did DHA-fortified infant formula become commercially available in the US Furthermore, the recent (2004) US advisory, issued jointly by the Food and Drug Administration and Environmental Protection Agency warning pregnant women of the threat of mercury contamination in fish, may have inadvertently led to further deficits in maternal EPA + DHA intake [22]. Although the ramifications of these dietary trends on future prevalence rates of psychiatric illness in the US are not known, perinatal deficits in fetal/infant brain DHA accrual may represent a modifiable risk factor for early neurocognitive impairment and the subsequent emergence of psychopathology [23].

Recently, the American Psychiatric Association (APA) convened a subcommittee tasked with the evaluation of the therapeutic use of omega-3 fatty acids in the treatment of psychiatric disorders [24]. The subcommittee concluded that omega-3 fatty acids have negligible risks and potential benefits in major depression and bipolar disorder, and, in view of the high rate of comorbid cardiovascular disease in psychiatric patients, endorsed the American Heart Association's dietary guidelines of 1 g/day of EPA + DHA. Recognition by the APA that omega-3 fatty acids may play a role in the pathophysiology and treatment of psychiatric illness represents an important milestone. This Special Issue was generated in an effort to provide a historical perspective on the role omega-3 fatty acids have played in cultural medicinal and religious practiced [25], to provide an overview of the molecular, neurochemical, behavioral, and clinical data linking omega-3 fatty acids with psychiatric illness, and to highlight areas requiring additional experimental investigation.

The authors gratefully acknowledge Mehar Manku for initiating and assisting in the creation of this Special Issue. This work was supported in part by NIH/NIMH Grants MH073704 and MH074858.

References

[1] K.R. Merikangas, A. Chakravarti, S.O. Moldin, H. Araj, J.C. Blangero, M. Burmeister, J. Crabbe Jr., J.R. Depaulo, E. Foulks, N.B. Freimer, D.S. Koretz, W. Lichtenstein, E. Mignot, A.L. Reiss, N.J. Risch, J.S. Takahashi, Future of genetics of mood disorders research, Biol. Psychiatry 52 (2002) 457–477.

[2] W. Eaton, S. Buka, A.M. Addington, J. Bass, S. Brown, et al., Risk factors for major mental disorders: a review of the epidemiological literature, Workgroup on risk factors in the human environment for major mental disorders, 2004. 〈http://apps1.jhsph.edu/weaton/MDRF/main.pdf〉.

[3] E.S. Susser, S.P. Lin, Schizophrenia after prenatal exposure to the Dutch Hunger Winter of 1944–1945, Arch. Gen. Psychiatry 49 (1992) 938–983.

[4] E. Susser, R. Neugebauer, H.W. Hoek, A.S. Brown, S. Lin, D. Labovitz, J.M. Gorman, Schizophrenia after prenatal famine. Further evidence, Arch. Gen. Psychiatry 53 (1996) 25–31.

[5] D. St Clair, M. Xu, P. Wang, Y. Yu, Y. Fang, F. Zhang, X. Zheng, N. Gu, G. Feng, P. Sham, L. He, Rates of adult schizophrenia following prenatal exposure to the Chinese famine of 1959–1961, J. Am. Med. Assoc. 294 (2005) 557–562.

[6] H.C. Bucher, P. Hengstler, C. Schindler, G. Meier, *N*-3 polyunsaturated fatty acids in coronary heart disease: a meta-analysis of randomized controlled trials, Am. J. Med. 112 (2002) 298–304.

[7] S.P. Whelton, J. He, P.K. Whelton, P. Muntner, Meta-analysis of observational studies on fish intake and coronary heart disease, Am. J. Cardiol. 93 (2004) 1119–1123.

[8] K. He, Y. Song, M.L. Daviglus, K. Liu, L. Van Horn, A.R. Dyer, P. Greenland, Accumulated evidence on fish consumption and coronary heart disease mortality: a meta-analysis of cohort studies, Circulation 109 (2004) 2705–2711.

[9] R.M. Krauss, R.H. Eckel, B. Howard, L.J. Appel, S.R. Daniels, R.J. Deckelbaum, J.W. Erdman, P. Kris-Etherton, I.J. Goldberg, T.A. Kotchen, A.H. Lichtenstein, W.E. Mitch, R. Mullis, K. Robinson, J. Wylie-Rosett, S. St Jeor, J. Suttie, D.L. Tribble, T.L. Bazzarre, AHA Dietary Guidelines: revision 2000: a statement for healthcare professionals from the Nutrition Committee of the American Heart Association, Circulation 102 (2000) 2284–2299.

[10] R.K. McNamara, M. Ostrander, W. Abplanalp, N.M. Richtand, S. Benoit, D Clegg, Modulation of phosphoinositide-protein kinase C signal transduction by omega-3 fatty acids: implications for the pathophysiology and treatment of recurrent neuropsychiatric illness, Prostoglandinis Leukot. Essent. Fatty Acids, in press.

[11] S. Chalon, Omega-3 fatty acids and monoamine neurotransmission, Prostaglandins Leukot. Essent. Fatty Acids, in press.

[12] I. Fedorova, N. Salem, Omega-3 fatty acids and rodent behavior, Prostaglandins Leukot. Essent. Fatty Acids, in press.

[13] C.J. Antalis, L.J. Stevens, M. Campbell, R. Pazdro, K. Ericson, J.R. Burgess, Omega-3 fatty acid status in attention-deficit/hyperactivity disorder, Prostaglandins Leukot. Essent. Fatty Acids, in press.

[14] M.P. Freeman, Omega-3 fatty acids and perinatal depression: a review of the literature and recommendations for future research, Prostaglandins Leukot. Essent. Fatty Acids, in press.

[15] L.R.G. Nieminen, K.K. Makino, N. Mehta, M. Virkkunen, H.Y. Kim, J.R. Hibbeln, Relationship between omega-3 fatty acids and plasma neuroactive steroids in alcoholism, depression and controls, Prostaglandins Leukot. Essent. Fatty Acids, in press.

[16] L.B. Marangell, T. Suppes, T.A. Ketter, E.B. Dennehy, H. Zboyan, B. Kertz, A. Nierenberg, J. Calabrese, S.R. Wisniewski, G. Sachs, Omega-3 fatty acids in bipolar disorder: clinical and research considerations, Prostaglandins Leukot. Essent. Fatty Acids, in press.

[17] M. Peet, The metabolic syndrome, omega-3 fatty acids and inflammatory processes in relation to schizophrenia, Prostaglandins Leukot. Essent. Fatty Acids, in press.

[18] R.T. Holman, The slow discovery of the importance of omega 3 essential fatty acids in human health, J. Nutr. 128 (1998) 427S–433S.

[19] A.P. Simopoulos, Essential fatty acids in health and chronic disease, Am. J. Clin. Nutr. 70 (1999) S560–S569.

[20] A.P. Simopoulos, The importance of the ratio of omega-6/omega-3 essential fatty acids, Biomed. Pharmacother. 56 (2002) 365–379.

[21] 〈www.DHAdoc.com/articles.html〉.

Please cite this article as: Robert K. McNamara, The emerging role of omega-3 fatty acids in psychiatry, Prostaglandins, Leukotrienes and Essential Fatty Acids (2006), doi:10.1016/j.plefa.2006.07.003.

[22] E. Oken, K.P. Kleinman, W.E. Berland, S.R. Simon, J.W. Rich-Edwards, M.W. Gillman, Decline in fish consumption among pregnant women after a national mercury advisory, Obstet. Gynecol. 102 (2003) 346–351.

[23] R.K. McNamara, S.E. Carlson, Role of omega-3 fatty acids in brain development and function: potential implications for the pathogenesis of psychopathology, Prostaglandins Leukot. Essent. Fatty Acids, in press.

[24] M.P. Freeman, J.R. Hibbeln, K.L. Wisner, J.M. Davis, D. Mischoulon, M. Peet, P.E. Keck, L.B. Marangell, A.J. Richardson, J. Lake, A.L. Stoll, Omega-3 fatty acids: Evidence basis for treatment and future research in psychiatry, J. Clin. Psychiatry, in press.

[25] L.C. Reis, J.R. Hibbeln, Cultural symbolism of fish and the psychotropic properties of omega-3 fatty acids, Prostaglandins Leukot. Essent. Fatty Acids, in press.

Robert K. McNamara
Department of Psychiatry, University of Cincinnati, College of Medicine, 231 Albert Sabin Way, Cincinnati, OH 45267-0559, USA
E-mail address: robert.mcnamara@psychiatry.uc.edu.

Please cite this article as: Robert K. McNamara, The emerging role of omega-3 fatty acids in psychiatry, Prostaglandins, Leukotrienes and Essential Fatty Acids (2006), doi:10.1016/j.plefa.2006.07.003.