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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

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1 dietary omega-3 fatty acid intake has declined [20].
 2 Accordingly, omega-3 fatty acid concentrations in
 3 breastmilk of US women are currently among the
 4 lowest in the world [21], and only recently (2002) did
 5 DHA-fortified infant formula become commercially
 6 available in the US. Furthermore, the recent (2004) US
 7 advisory, issued jointly by the Food and Drug Admin-
 8 istration and Environmental Protection Agency warning
 9 pregnant women of the threat of mercury contamination
 10 in fish, may have inadvertently led to further deficits in
 11 maternal EPA + DHA intake [22]. Although the rami-
 12 fications of these dietary trends on future prevalence
 13 rates of psychiatric illness in the US are not known,
 14 perinatal deficits in fetal/infant brain DHA accrual may
 15 represent a modifiable risk factor for early neurocogni-
 16 tive impairment and the subsequent emergence of
 17 psychopathology [23].

18 Recently, the American Psychiatric Association
 19 (APA) convened a subcommittee tasked with the
 20 evaluation of the therapeutic use of omega-3 fatty acids
 21 in the treatment of psychiatric disorders [24]. The
 22 subcommittee concluded that omega-3 fatty acids have
 23 negligible risks and potential benefits in major depres-
 24 sion and bipolar disorder, and, in view of the high rate
 25 of comorbid cardiovascular disease in psychiatric
 26 patients, endorsed the American Heart Association's
 27 dietary guidelines of 1 g/day of EPA + DHA. Recogni-
 28 tion by the APA that omega-3 fatty acids may play a
 29 role in the pathophysiology and treatment of psychiatric
 30 illness represents an important milestone. This Special
 31 Issue was generated in an effort to provide a historical
 32 perspective on the role omega-3 fatty acids have played
 33 in cultural medicinal and religious practices [25], to
 34 provide an overview of the molecular, neurochemical,
 35 behavioral, and clinical data linking omega-3 fatty acids
 36 with psychiatric illness, and to highlight areas requiring
 37 additional experimental investigation.

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