

Guest Editorial

Food, Micronutrients, and Psychiatry

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Nutritional biochemistry is not a subject with which most psychiatrists, psychologists, and psychopharmacologists are familiar. A stream of recent epidemiological studies and clinical trials, however, indicates that understanding of nutritional biochemistry is soon going to be essential for anyone working with mentally ill patients. Those who are tempted to dismiss this statement as airy-fairy holistic nonsense will benefit from reading some recent issues of the *American Journal of Psychiatry*, *British Journal of Psychiatry*, *Archives of General Psychiatry*, *Schizophrenia Research*, *Journal of Affective Disorders*, and *New England Journal of Medicine*.

Nutrition is important in psychiatry at two levels. First, all essential nutrients are required if the brain is to function normally. Second, certain specific nutrients, particularly folic acid and essential fatty acids, are emerging as specific treatments for particular psychiatric disorders.

At the first level, the brain is the most metabolically active organ of the body, utilizing around 20% of total energy while being only 2% of body weight. Metabolic activity requires the essential nutrients, vitamins, minerals, and essential fatty

acids as cofactors. Without an adequate intake of *all* the required essential nutrients, the brain simply cannot function normally. Trying to apply any treatment modality, whether psychological, pharmacological, or social, to a brain that cannot function normally because of lack of an essential nutrient is like trying to run a 220-volt electrical appliance on a 120-volt system. Yet anyone who works with mentally ill patients, particularly the severely depressed, those with schizophrenia, or the elderly, knows that diets are often appalling and micronutrient deficits are common and serious. However, rarely is anything done about it. Occasionally there might be a half-hearted referral to a dietician, as though patients are going to be any better than the rest of us in changing our diet. But much more usually, nothing at all is done.

This is bizarre, when the remedy is simple and cheap. Prescribe any of the excellent one-a-day multivitamin/multimineral supplements that are readily available. Most patients are happy to take these. Moreover, these supplements will correct all the micronutrient deficits quickly and much more effectively than any attempt at dietary change. Many professionals may then

be surprised at how much more effective their own favored intervention may become, once their patients have a brain that is no longer stuttering biochemically because of micronutrient deficits.

Those who require stronger evidence than biochemical good sense and clinical experience should read an extraordinary report in the July 2002 issue of the *British Journal of Psychiatry* (Gesch et al., 2002). Violence among young offenders is a problem that has defied an extraordinarily diverse set of proposed solutions. Gesch and his colleagues realized that most violent young people eat an appalling diet and are therefore likely to be deficient in multiple micronutrients. They hypothesized that such deficits might actually be contributing to the violent behavior and they set up a very simple but compelling study to test this. Prisoners in a young offenders institution were randomized to receive each day a multivitamin and an essential fatty acid capsule or identical-appearing placebos. There was no other intervention. The outcome was the number of violent acts as recorded in the usual way by the prison officers. All prisoners were given the opportunity to participate for as long as they were detained. Over 170 young offenders took the active or placebo supplements for a minimum of 2 weeks and a maximum of 9 months. In the period prior to supplementation, the two groups committed near-identical numbers of serious violent acts, around 16/1,000 person days. During the intervention, the active group committed 10.4 offenses/1,000 patient days whereas the placebo group committed 15/1,000 patient days ($p < .001$). So in this very unlikely setting, a simple multinutrient had a dramatic effect on behavior, reducing violence by 35%.

With regard to specific nutrients being important, the strongest evidence points to folic acid on the one hand and one of the essential fatty acids, eicosapentaenoic acid, on the other. Folic acid is required for a large number of biochemical reactions in the brain, including the synthesis of serotonin and other neurotransmitters (Abou Saleh & Coppen, 1986; Botez et al., 1979, 1982), and in phospholipid-related signal transduction (Bottiglieri et al., 1994), a process that follows activation of almost all neurotransmitter receptors. Deficits of folic acid are common in the general population. Also common are enzyme variants, particularly an enzyme called methylenetetrahydrofolate reductase (MTHFR), which increase the requirement for folic acid. A consequence of folic acid deficiency is elevation of homocysteine, a neurotoxic and vasculotoxic amino acid.

Deficits of folic acid, and of three other vitamins (B_{12} , riboflavin, and pyridoxine) with which it interacts synergistically in methylation processes and homocysteine control, seem to play major roles in depression and dementia. Folic acid deficits are common in depressed patients (Abou Saleh & Coppen, 1986; Bottiglieri et al., 1994; Fava et al., 1997) and recent studies from both Japan and Europe have shown that the MTHFR variant, which leads to an increased folate requirement, is overrepresented in depressed populations (Arimami et al., 1997; Kelly et al., 2002). Most compelling, however, is a randomized trial that compared 0.5 mg/day folic acid and placebo as adjuncts to fluoxetine in the treatment of depression (Coppen & Bailey, 2000). Among women given fluoxetine plus placebo, the response as expected was about 55%, whereas in

women given fluoxetine plus folic acid, the response was 92%. Men did not show the differential, possibly because males require more folic acid than females and the dose was too low for males.

The epidemiological evidence for an association between high homocysteine, low folic acid, and dementia is becoming just as compelling. Both the Framingham study in the US and the Optima study in the UK have shown that elevated homocysteine predicts by many years the risk of dementia (Clarke et al., 1998; Seshadri et al., 2002). As yet there are no completed intervention studies but several are in progress.

The relationship between depression and eicosapentaenoic acid deficits is emerging as a strong one. Studies in Europe, North America, Australia, and Japan have shown that depressed patients have lower blood eicosapentaenoic acid levels than normal individuals (Adams et al., 1996; Edwards et al., 1998; Maes et al., 1999; Peet et al., 1998; Seko, 1997). Between-country prevalence studies have shown a strong inverse correlation between depression and the consumption of fish, the main dietary source of eicosapentaenoic acid (Hibbeln, 1998). Individual patient studies in Finland have obtained a similar result (Tanskanen et al., 2001). Most compellingly, a detailed case study and three randomized, placebo-controlled trials have shown that ethyl-eicosapentaenoate, a prodrug for eicosapentaenoic acid, is effective in treating treatment-unresponsive depression and bipolar depression (Frangou & Lewis, 2002; Nemets et al., 2002; Peet et al., 2002; Puri et al., 2002).

No psychiatric patients have fluoxetine or paroxetine deficiencies. In contrast, there is increasingly compelling evidence

that patients with depression have folic and eicosapentaenoic acid deficits, and that most psychiatrically disturbed individuals have several micronutrient deficiencies. Randomized, placebo-controlled interventions suggest that in many patients these deficiencies may indeed be causal. Mental health professionals should be well advised to learn some nutritional biochemistry to keep abreast of this area of scientific development.

Declaration of Interest

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