

Dietary Influences on the Synthesis
of Neurotransmitters in the Brain

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An interesting paper with the above title, by John H. Growdon and Richard J. Wurtman, was recently published in this journal.¹

The authors point out that traditional concerns with the effects of nutrition on the brain have centered on the consequences of protein or protein-calorie restriction for the immature nervous system. They then say that they and their associates have been interested in another aspect of nutritional effects on the brain, that is, the changes in its biochemical composition that occur normally, after consumption of a single meal. They say that eight years ago (1972) they observed² that the composition of each meal can influence the synthesis of the neurotransmitter serotonin, and that subsequent studies have shown that this kind of control is fairly general. They noted that the availability of tryptophan and tyrosine to the brain causes major changes in the rates at which neurons synthesize serotonin and the catecholamines, respectively. They also say that the rate-limiting step in the formation of serotonin is the hydroxylation of tryptophan to 5-hydroxytryptophan, catalyzed by the enzyme tryptophan hydroxylase, and, since tryptophan hydroxylase is not fully saturated with its amino-acid substrate at normal values of the brain tryptophan concentration, variations in this concentration can control the rate of serotonin synthesis. A similar effect of increasing the intake of choline (usually as lecithin, phosphatidylcholine) to increase the saturation of the enzyme choline acetyltransferase and thus cause increased synthesis of acetylcholine was reported by them³ in 1975. It has been found, moreover, that a high intake of lecithin has clinical value in the treatment of tardive dyskinesia,⁴ and the authors suggest that an

increased intake of choline or lecithin might have value also in treating Huntington's disease, Friedreich's ataxia, Alzheimer's dementia, mania, loss of memory, and aberrant social behavior.

Growdon and Wurtman say that "Taken together, these findings illustrate a novel and previously unsuspected aspect of nutrition's effects on the brain and provide the basis for new modes of therapy for patients with some neurologic and psychiatric brain diseases. . . . Certainly it is startling to discover that dietary constituents normally influence such an important process as neurotransmitter synthesis. . . . This general principle provides a new strategy for designing treatments for non-nutritional neurologic and psychiatric diseases in which physicians may wish specifically to increase cholinergic, serotonergic, or catecholaminergic tone. "

Some of these statements are seriously misleading. Their findings do not "illustrate a novel and previously unsuspected aspect of nutrition's effects on the brain;" they do not "provide the basis for new modes of therapy;" it was not "startling to discover that dietary constituents normally influence such an important process as neurotransmitter synthesis;" and their "new strategy" is not new.

Growdon and Wurtman give no references to the literature before 1972, except for one 1961 paper on the origin of blood choline. There is, however, an extensive body of early publications in this field. In 1968 I summarized the earlier literature and formulated the general principles in my paper⁵ "Orthomolecular Psychiatry," which had the subtitle

"Varying the concentrations of substances normally present in the human body may control mental disease." After mentioning the methods then principally used for treating patients with mental disease, I wrote that "I have reached the conclusion, through arguments summarized in the following paragraphs, that another general method of treatment, which may be called orthomolecular therapy, may be found to be of great value, and may turn out to be the best method of treatment for many patients. Orthomolecular psychiatric therapy is the treatment of mental disease by the provision of the optimum molecular environment for the mind, especially the optimum concentrations of substances normally present in the human body." In this paper there is emphasis on the vitamins and amino acids. Tryptophan is mentioned, but not choline. Choline is, of course, an orthomolecular substance, normally present in the human body (both by synthesis by methylation of ethanolamine and from ingested foods), and the "novel and previously unsuspected aspects of nutrition" and "new methods of therapy" mentioned by Growdon and Wurtman are just those of orthomolecular psychiatry, formulated and clearly expressed in 1968 and then discussed at length in the 1973 book "Orthomolecular Psychiatry: Treatment of Schizophrenia."⁶

The close similarity of the discussion by Growdon and Wurtman and my earlier discussion can be seen by comparing their paper with mine. In my 1968 paper there are the following sentences: "The functioning of the brain and nervous tissues is more sensitively dependent on the rate of chemical reactions than the functioning of other organs and tissues.

I believe that mental disease is for the most part caused by abnormal reaction rates, as determined by genetic constitution and diet, and by abnormal molecular concentrations of essential substances. . . . The rate of an enzyme-catalyzed reaction is approximately proportional to the concentration of the reactant, until concentrations that largely saturate the enzyme are reached. The saturating concentration is larger for a defective enzyme with decreased combining power for the substrate than for the normal enzyme. For such a defective enzyme the catalyzed reaction could be made to take place at or near its normal rate by an increase in its substrate concentration. . . . This mechanism of action of gene mutation is only one of several that lead to disadvantageous manifestations that could be overcome by an increase, perhaps a great increase, in the concentration of a vital substance in the body. These considerations obviously suggest a rationale for megavitamin therapy."

The discoveries about the effect of an increased intake of choline or lecithin in increasing the rate of synthesis of acetylcholine and in controlling some neurological diseases, discussed by Growdon and Wurtman, are important contributions to the field of orthomolecular medicine, illustrating the general principles that had been formulated more than a decade ago, but neither changing them or expanding them. □

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