Pantothenate’s Possible Role in Schizophrenia Pathogenesis

To the Editor:

Pantothenic acid, also called pantothenate or vitamin B₅, is a water-soluble vitamin that is an essential nutrient for many animals playing an important role in the synthesis of coenzyme A (CoA), as well as in the synthesis and metabolism of proteins, carbohydrates, and fats. Pantothenic acid is the amide between pantoyl and β-alanine, which has its name derived from the Greek pantothēn meaning “from everywhere” because of the presence of small quantities of this vitamin in nearly every food. Because of its important role in the production of CoA, a possible role of pantothenic acid in the pathogenesis of schizophrenia may exist, and a subsequent role of this vitamin could be considered for the treatment of some patients with schizophrenia.

Many genome-wide expression studies have demonstrated that several genes involved in myelination are down-regulated in postmortem brain tissue from patients with schizophrenia. These findings are supported by the demonstration that the levels of major myelin membrane components, such as sphingomyelin and galactocerebroside, were reduced in postmortem brains of patients with schizophrenia. Central nervous system myelin is synthesized by oligodendrocytes. The myelin coating of axons is a prerequisite for rapid impulse conduction and maintenance of axonal function. Glial cells serve an important role in the supply of adequate amounts of cholesterol. Chromosome 5q22–33 is one of the regions likely to contain risk genes for schizophrenia. This fragment encodes, among others, the acyl-CoA synthetase long-chain member 6 (ACSL6) gene. Long-chain acyl-CoA synthetases are necessary for fatty acid degradation, phospholipid remodeling, and the production of long acyl-CoA esters that regulate many physiological processes. These Long-chain acyl-CoA synthetases are membrane-bound enzymes that act on nonpolar hydrophobic substrates, fatty acids, generating acyl-CoAs which are important activated intermediates in lipid synthesis pathways. ACSL6 is one of the major forms expressed in neuronal cells playing an important role in the plasticity of their plasma membrane. ACSL6 preferred substrates include arachidonic acid (AA), eicosapentaenoic acid, and docosahexaenoic acid (DHA). It has been hypothesized that membrane phospholipid defects may be involved in the pathophysiology of schizophrenia, of which AA plays a central role. Indeed, in many studies, the amount of AA, eicosapentaenoic acid, and DHA in cell membranes has been found to be reduced in schizophrenia patients. Treatments with these polyunsaturated fatty acids may improve symptoms. Overexpression in cultured cells increases DHA and AA internalization primarily during neuronal differentiation, stimulating phospholipid synthesis and enhancing neurite outgrowth.

As mentioned previously, pantothenic acid or pantothenate or vitamin B₅ is essential for the synthesis of CoA. Pantothenate kinase 2 mutation is responsible for the appearance of psychotic symptoms in patients carrying it. Accordingly, pantothenate may play an important role in the pathogenesis of at least some presentations of schizophrenia, and its subsequent therapeutic role in patients with schizophrenia should be further evaluated.

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Conflicts of Interest and Source of Funding: The author has no conflicts of interest to declare.

REFERENCES