Man's Molecules
The Contribution of Molecular Biology To Orthomolecular Psychiatry

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Introduction

In this paper, some reflections are presented on the biological significance of the molecular composition of man. Enzymes fulfill a crucial role in the expression of the genetic endowment; environmental influences can modify this process, but in order to do so, they have to be translated to the molecular level; there they can alter the functioning of enzymes.

Enzymes build the molecules that are essential to the structure and function of an organism, and which find their ultimate expression in human form and behavior. If in this process something goes wrong, any dimension of the final form and behavior may be disturbed. For the brain, this means that there are neurophysiological, neurological, and psychopathological correlates of any molecular dysfunctioning of the brain.

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Enzymes are however very much alike in the different cells of an organism and be tween species. Besides their protein component they contain a co-factor which may be a vitamin or trace metal; for their activity they need activators, notably trace metals. Their structure is under genetic control, but the synthesis of enzymes and their functioning can be modified by manipulating the supply of vitamins and trace metals (Pauling, 1968).

Orthomolecular psychiatry takes advantage of this possibility, correcting the chemical milieu of the brain by supplementation of trace elements and vitamins (Osmond, 1973; Pfeiffer et al., 1973). Thus, the psychopathology is corrected at its molecular basis, as it has been reconstructed by molecular biology.

History

In the last century, there was a growing awareness that living organisms were organized on a chemical basis. The specific approach to this problem began in 1847, when in Berlin "Die Gesellschaft Fur Physik

und Chemie" was founded. Its members first sought for the organic-chemical and later physico-chemical laws according to which life was organized (Hess, 1970). By the end of the last century, research had revealed that colloids were essential elements of all living organisms. The function of some of them was discovered in 1893 by Ostwald, who demonstrated that ferments were catalysts in the classical physico-chemical sense. The clarification of the primary, secondary, and tertiary structure of proteins was possible in the twenties and thirties of this century, thanks to technical developments. In 1929 Warburg discovered in his research on oxidative phosphorylation that a metal is a necessary part of an enzyme; iron was the metal involved. In 1935-1936 von Euler, Theorell, and Warburg discovered that coenzymes were similar to vitamins (Karlson, 1964).

In 1945, nearly a century after this story starts, research was focused on biologically interesting macromolecules; for this area, Astbury coined the name "Molecular Biology" (Knippers, 1972). Then two lines of research became important. First, the transmission of information; Delbruck and his colleagues in Pasadena were able to show that virus injected into bacteria multiplied itself and thus passed over its genetic information by using the material of the bacteria. And second, the structure of molecules; in Cambridge, Kendrew and the Braggs had developed crystallography into a powerful tool for the structural analysis of molecules. Moulding of these two lines of evidence resulted in the masterpiece of molecular biology, when Watson and Crick created in 1953 their double helix model as the bearer of the genetic information. The genetic code was pinned down in its molecular components (Watson, 1970; Knippers, 1972)!

In 1946, Butenandt and Kuhn had already described that enzymes are necessary for the expression of genetic factors (Karlson, 1964).

Watson and Crick formulated succinctly the expression mode of the genetic code by saying, "one gene, one enzyme"; later research on these marcromolecules enlarged the concept to, "one gen family, one enzyme."

The research since 1847 had proved true the assumptions from which it started. Watson summarizes the state of the art (1970) by saying that the functioning of living cells is based upon the same laws that control the chemical behavior of molecules outside the living cell. Cells contain no atoms unique to the living state; they can synthesize no molecules which the chemist, with inspired hard work, cannot some day make. There is no special chemistry of the living cells. So, one can say that biological systems, man included, are organized on a molecular basis. The principle of Orthomolecular psychiatry, that the mental processes are critically dependent on the molecular environment of the brain, (Pauling, 1968; 1974), finds its justification precisely here.

Atomic Composition of Man

What are the atoms out of which man's unique structure is built? When their occurrence is computed as a percentage of the total of atoms, they can be divided into three classes (Frieden, 1972). The most abundant are hydrogen (63 percent), oxygen (25 percent), carbon (9.5 percent) and nitrogen (1.4 percent); together they make up 98.9 percent of the total, and they are among the lightest eight elements of the periodic system. Next comes a class that contributes almost the whole remaining 1.1 percent; in order of frequency it is calcium (0.31 percent), chloride (0.3 percent), phosphorus (0.22 percent), potassium (0.06 percent), sulfur (0.05 percent), sodium (0.03 percent) and magnesium (0.01 percent). They are among the light elements of the periodic system.

The last class consists of metals that are found only in trace amounts. Among these are copper (100 mg) and zinc (250 mg), and others like cobalt, iron, etc. (Davies, 1972; Bogert, 1973). They are the heaviest elements that are found in the human body.

This chemical composition is not very much different from that of seawater. The genetic code has wrought, however, another structure. Economies of weight are surprising, since the lightest elements too, serve structural purposes, and the trace elements functional ones.

The trace elements are co-factors or activators of enzymes. In psychopathology, the functioning of brain enzymes will have been altered. So, it is reasonable that trace elements are used in Orthomolecular psychiatry, to normalize disturbed brain enzyme activity (Pfeiffer, et al, 1973; Hoes, 1976).

Phylogenetic Differences in Molecular Composition

On the chemical level, nitrogen-containing organic molecules are the cornerstone of proteins and thus of living organisms. Those molecules can be produced by reaction of simpler molecules as was shown by Miller for the combination of water, methane, hydrogen and ammonia (Knippers, 1972). Molecular biologists consider that evolution might have progressed from such molecules, be it by hazard, by necessity, or otherwise (Monod, 1970).

In evolution, organisms display a progressive grade of complexity in their behavior; this presupposes a growing complexity of the organic structures and notably of the brain (Eccles, 1970; 1973). So, the genetic code must contain information regarding the more complicated structure of the molecules in the species, ascending the evolutionary tree.

The unraveling of metabolic disorders has revealed that even one molecular defect in the genetic code can have dramatic consequences to the survival, form, and behavior of man (Hoes et al., 1978; Stanbury etal., 1972).

The genetic contribution to psychiatric disorders must have a molecular counterpart in the genetic code. Here the consequences relate not to survival but mainly to behavior. So, what has been altered is the functional capacity. Up to now no structural anomalies have been discovered at the molecular level, but in schizophrenia or affective disorders, numerous disorders of enzyme function have been found.

The protein composition of enzymes cannot be altered; but by supplying cofactor, one can induce the synthesis of enzyme and by supplying activators one can speed up their activity.

In Orthomolecular psychiatry the niacin-dependency has proved a valuable treatment model for schizophrenia, or at least a class of it (Hoffer, 1973; Osmond, 1973); the treatment was developed on an empirical basis, and although the precise biochemical processes which are dependent on niacin remain to be elucidated, one is now able to see the pathophysiological structure in which it can be fitted. Certainly, niacin may trap labile methylmolecules, but one wonders whether it doesn't speed up the biosynthesis of enzymes that contain niacin as cofactor and are pathophysiologically involved in schizophrenia; thus the quantity of such enzyme(s) can be augmented.

Individual Differences In Molecular Composition

The molecular basis for difference in form and behavior between individuals of the same species may be twofold. First, molecular variations in the composition of the nucleic acids may result in changes in the genetic code, which do not affect the survival of the individual. So, at the same gene locus, different alleles may be found. The second factor concerns the modulation of the activity of the tools that mediate the final expression of the code. Enzyme functioning can be altered by a lot of chemical and physical influences; and psychosocial influences, too, can by mobilizing corticosteroids profoundly affect enzyme quantity and reaction speed (Schepartz, 1973; Selye, 1976). This may be done by altering the transcription or translation of the genetic material, or by alterations in the supply of cofactors or activators. The dramatic effect of this transformation of psychosocial influences to the molecular level, may be illustrated by emotional dwarfism.

On these individual disorders, the coenzymes and activators can exert a therapeutic influence. Coenzymes of functionally diminished enzymes can speed up their synthesis. Activators as trace metals have a special function; at many levels, from the earth where they are found, up to a complex biochemical reaction, a biological antagonism has been demonstrated between

couples of these metals. So, for example, between copper and zinc (Davies, 1972).

In Orthomolecular psychiatry these principles are used. Pauling has shown that vitamins as coenzymes, can optimalize enzyme functions, not overstimulate them (1968); and the use of trace elements has its place in the treatment of schizophrenia (Pfeifferetal., 1973).

The Molecular Basis of Orthomolecular Psychiatry

The study of the molecular basis of life has made it possible to understand how nature conserves the characteristics of its organisms. The expression of these possibilities is critically dependent on a physiologically sound chemical milieu within the cells. Enzymes fulfill a pivot function as they are the tools that effectuate the genetic code and are critically submitted to the changes in the chemical cell milieu.

Study has revealed that there is no real difference between the chemistry inside or outside the body; biochemistry is the chemistry operative inside the living cell. In any organ, brain included, the chemical building blocks, the chemical laws, and the chemical tools are alike. There is no quantitatively major difference in atomic composition between man and seawater. The structure, as dictated by the genetic code, which is made of these molecules, is however different, and finds its expression in different form and behavior, ascending the evolutionary tree.

This process is modulated in the individual by external influences, that must be transformed to molecular messages to exert their effect.

One can influence this process by activating the biosynthesis of enzymes in supplying vitamins as cofactor, or by speeding up their activity by supplying trace metals as activators or cofactor.

The molecular structures are the fundament of every dimension of living organisms, man's psychopathology included. Mental processes are dependent on the chemical milieu inside the brain. On this basis, treatment by vitamins and trace metals was developed in Orthomolecular psychiatry. Molecular biology has provided the model of the processes where these agents can be placed, as a physiological treatment of psychiatric patients.

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