

Neurobiology of Lipids

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opening note commentary

NEUROBIOLOGY OF LIPIDS

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The number of studies and scientific papers, which can be classified as related to the general area of neurobiology of lipids, has constantly grown during years. The "popularity" of the field is based not only on new technology and research tools, but also on the emergence of new theoretical avenues.

INTRODUCTION

Three major systems in the body mediate "information" traffic, namely the nervous system, the endocrine system, and the immune system. Chemical or electrical signals to or from other cells are generated and received, signals are modified, and tissues, organs, and muscles are activated as a result of their activities. Conventional wisdom considered each system as independent from the others, and able to interact only with component members of its own domain. More recently, this notion has been challenged, and studies have shown that each system is able to interact with external signals and stimuli, and moreover that each system could interact with the other two systems. Representative reviews of the bidirectionalities within these systems have been provided elsewhere. The biochemical modulation and mediation of the various activities of these systems and, by extension, the behavioral consequences, has received less attention than deserved among behavioral neuroscientists. In this note I will attempt to focus attention on the role of lipids as they impact the multifactorial world of body function. In addition, while the bidirectionality that

exists globally between behavior and physiology is largely beyond the scope of this note, the considerations of stress effects on the dynamics of PUFA regulation and associated behaviors are particularly relevant.

EXPERIMENTAL APPROACHES TO THE GENERAL FIELD OF NEUROBIOLOGY OF LIPIDS

There are several experimental approaches to the general field of neurobiology of lipids. These approaches include the analysis of lipids according to:

- A** The chemical structure of lipids (e.g. fatty acids, essential fatty acids, triglycerides, phospholipids, and cholesterol).
- B** The tissue (e.g. brain, heart, blood cells) where various lipids exert their activity (site of action).
- C** The level (normal level, or deficiency states) of various lipids.
- D** The involvement of lipids in various disorders (e.g., cardiovascular disorder (CVD), neurological disorders (e.g., Alzheimer's, Parkinson's and epilepsy) and psychiatric disorders (schizophrenia, and depression).
- E** The possible interaction between lipids and the immune system (e.g., pro- and anti-inflammatory prostaglandins).
- F** The possible interaction between lipids and the endocrine system (effect of lipids on ACTH and cortisol levels, stress mediation).
- G** The possible interaction between lipids and neurotransmitters and releasing factors in the brain (mainly the dopaminergic system).
- H** Lipids that interact with brain receptors, such as amide fatty acids, which control sleep.

AN EXAMPLE OF THE INTEGRATED APPROACH

The following is an example of the integrated approach to the study of the neurobiology of lipids. Such an analysis can easily be carried out on other types of lipids as well.

One group of molecules in particular, the polyunsaturated fatty acids (PUFA), seems to play an important role in each of these three systems (neurological, immunological, and endocrinological systems). Previous studies have shown that PUFA has a profound effect in all three systems, such as altering neuronal membrane fluidity and in the production and function of neurotransmitters. PUFA has also been shown to modify the production and activity of releasing factors and certain hormones, as well as the activity of certain cytokines

The central hypothesis of this note is that PUFA occupies a major role in being able to modify the activity of each system and the interaction between them. Psychological functions, such as cognition, learning, mood, stress, pain and brain related states or clinical neurological disorders, could be best understood by appreciating the unifying elements of these systems.

Few topics in nutrition cause as much controversy and concern, and are as widely misunderstood, as fat. The dominant message from the medical profession has been to drastically reduce the amount of fat we eat, in the interest of combating risks associated with cardiovascular disorders, diabetes, and other chronic disorders. At the same time, deficiencies in fat intake are equally likely to contribute to health hazards, including increased risk of infection, dysregulation of chronobiological activity, and impaired cognitive and sensory functions (especially in infants). A consensus has emerged from recent research suggesting that it is not so much the amount of fat we eat, as the balance of the different types of fats. The type of dietary fat affects the behavior of each cell, that is, how well it can perform its vital functions and the ability to resist disease.

The two polyunsaturated fatty acids (PUFA), linoleic and α -linolenic acid, are necessary for good health. Referred to as "essential fatty acids" (EFA) because the body cannot manufacture them, but is dependent on their being provided through nutritional intake, EFAs have beneficial effects when available in moderation. Excesses of the otherwise beneficial fatty acids may, however, exert harmful effects, with high intakes of saturated and hydrogenated fats being linked to an increase in a number of health risks, including degenerative

diseases, cardiovascular disease, cancer and diabetes.

Linoleic acid is a member of the omega-6 (n-6) fatty acids family, while α -linolenic acid belongs to the omega-3 (n-3) fatty acids. These terms refer to characteristics in the chemical structure of the fatty acids. Other omega-6 fatty acids can be manufactured in the body using linoleic acid as a starting point. These include gamma-linoleic acid (GLA), dihomo-gamma-linoleic acid (DHGLA) and arachidonic acid (AA). Similarly, other omega-3 fatty acids that are manufactured in the body using alpha linolenic acid as a starting point, include eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).

Essential fatty acids are involved in energy production, the transfer of oxygen from the air to the bloodstream, and the manufacture of hemoglobin. They are also involved in growth, cell division and nerve function. Essential fatty acids are found in high concentrations in the brain and are essential for normal nerve impulse transmission and brain function.

Among the significant components of cell membranes are the phospholipids, which contain fatty acids. The type of fatty acids in the diet determines the type of fatty acids present in cell membranes. A phospholipid made from a saturated fat has a different structure and is less fluid than one that incorporates an essential fatty acid. In addition, linoleic and α -linolenic acids per se have an effect on the neuronal membrane fluidity index. They are able to decrease the cholesterol level in the membrane yielding the decrease of membrane fluidity. This would make it difficult for the cell to carry out its normal functions, and increase the cell's susceptibility to injury and death. These consequences for cell function are not restricted to absolute levels of FAs, rather the relative amounts of omega-3 fatty acids and omega-6 fatty acids in cell membranes have also been shown to affect cellular function.

At least five categories of PUFA effects on brain functions have been noted and discussed previously, namely:

- A** modifications of membrane fluidity;
- B** modifications of the activity of membrane bound enzymes;
- C** modifications of the number and affinity of receptors;
- D** modifications of the function of ion channels; and
- E** modifications of the production and activity of neurotransmitters.

Symptoms of essential fatty acid deficiency may include fatigue, skin problems, immune weakness, gastrointestinal disorders, heart and circulatory problems, growth retardation, and sterility. In addition to these symptom conditions, a lack of dietary essential fatty acids has been implicated in the development or aggravation of breast cancer, prostate cancer, rheumatoid arthritis, asthma, pre-eclampsia, depression, schizophrenia and ADHD (attention deficit/hyperactivity disorder). This list is neither exhaustive nor conclusive.

PROSPECT

The study of the neurobiology of lipids includes many important theoretical issues, but no less important are the pressing practical issues, such as the supplementation of baby formulas with essential fatty acids, and the role of various fatty acids and lipids as nutraceuticals for various indications (e.g., memory, pain, sleep, depression, cardiovascular disorder, and obesity).

The multidisciplinary approach to the neurobiology of lipids is a necessity to better understand the pivotal role of the various types of lipids in physiological and pathological processes in the brain and in the body.

The establishment of a journal, which is devoted to the neurobiology of lipids, will certainly enhance the awareness of the scientific community to this important issue, and will serve as a focal point for information and ideas being exchanged between scientists from different scientific disciplines.

Neurobiology of Lipids

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