

Preface

In neural membrane glycerophospholipids, essential polyunsaturated fatty acids, namely arachidonic acid (ARA) and docosahexaenoic acid (DHA), are exclusively located at the *sn*-2 position of glycerol moiety. Because humans do not possess desaturases that insert either the *n*-3 or the *n*-6 double bonds, these fatty acids are derived from diet. DHA can be obtained from fish or from the precursor α -linolenic acid (ALA), which is found in nuts. The common precursor for ARA is dietary linoleic acid (LA) from plant sources. The high intake of food enriched in vegetable oils elevates levels of ARA-derived eicosanoids and upregulates the expression of proinflammatory cytokines. ARA-derived eicosanoids have prothrombotic, proaggregatory, and proinflammatory properties. In contrast, diet enriched in eicosapentaenoic acid (EPA) and DHA (fish and fish oil) generates docosanoids, which not only downregulates proinflammatory cytokines but also have antiinflammatory, antithrombotic, antiarrhythmic, hypolipidemic, and vasodilatory effects. Thus, levels of eicosanoids and docosanoids in neural and non-neural tissues are partly regulated by diet. The present Western diet is deficient in DHA, but has high amounts of ARA. The deficiency of *n*-3 fatty acids in diet results in a number of abnormalities in animals and human infants such as impaired vision, abnormal electroretinogram, and several behavioral abnormalities. In addition, inclusion of *n*-3 fatty acids in diet not only prevents cardiovascular disease but also protects from stroke, epilepsy, and other neurological and neurodegenerative diseases such as Alzheimer disease, Parkinson disease, and peroxisomal diseases.

There have been remarkable developments on DHA and ARA metabolism in brain in the past 20 years. The main objective of this book is to present readers with cutting-edge and comprehensive information on metabolism and roles of neural membrane DHA in a manner that is useful not only to students and teachers but also to researchers, dietitians, nutritionists, and physicians. This monograph has 11 chapters. Chapters 1 and 2 describe the importance of fish oil in human diet along with transport and importance of DHA in brain. Chapters 3 and 4 describe cutting-edge information on the release and catabolism of DHA in brain along with neurochemical effects of its lipid mediators. Chapter 5 describes roles of DHA in brain. Chapter 6 is devoted to alterations in DHA with aging and consequences of DHA deficiency in brain. Chapters 7

and 8 describe the status and therapeutic importance of DHA and EPA in acute metabolic trauma (stroke), neurotraumatic disorders (spinal cord and head injuries), and neurodegenerative diseases (Alzheimer disease, Parkinson disease, Huntington disease). Chapter 9 describes the status and therapeutic importance of DHA and EPA in neuropsychiatric disorders (schizophrenia, depression, bipolar disorders, and attention-deficit/hyperactivity disorder). Chapter 10 provides information on the importance of DHA and EPA in other neural (peroxisomal) and some non-neural (rheumatoid arthritis, cystic fibrosis, chronic obstructive pulmonary disease, dermatological conditions, and gastrointestinal disorders) diseases. Finally, Chapter 11 provides readers and researchers with perspective that will be important for future research work on DHA and EPA in brain tissue.

This monograph can be used as supplemental text for a range of neuroscience and nutrition courses. Neurologists and nutritionists will find this book useful for understanding molecular aspects of DHA and EPA metabolism in neurological disorders. To the best of my knowledge, no one has written a monograph on the role of DHA and EPA and their lipid mediators (docosanoids) in brain tissue, and this monograph is the first to provide a comprehensive description of docosanoids and their interactions with ARA-derived eicosanoids in normal brain and in brain tissue from patients with neurological disorders. This monograph not only provides background and refresher information on DHA metabolism in brain for readers not working in the field of fatty acid metabolism but also presents new knowledge on DHA-derived lipid mediators and therefore broadens our understanding of DHA function in health and neurological disorders. The monograph offers a thorough and unique overview of the neurobiology of $n-3$ and $n-6$ fatty acids and their association with neurological disorders. It is anticipated that nutritionists and clinicians may gain insight into problems associated with nutrition in the 21st century and resolve difficulties experienced in their research on fatty acid metabolism and DHA- and ARA-derived lipid mediators in their laboratories.

The choices of topics presented in this monograph are personal. They are based not only on my interest in DHA and ARA metabolism in neurological disorders but also in area where major progress has been made. I have tried to ensure uniformity in mode of presentation as well as a logical progression of subject from one topic to another and have provided extensive bibliography. For the sake of simplicity and uniformity, a large number of figures and line diagrams of signal transduction pathways are also included. I hope that my attempt to integrate and consolidate the knowledge of DHA metabolism and signal transduction processes in normal and diseased brain will provide the basis of more dramatic advances and developments on the determination, characterization, and roles of DHA- and ARA-derived lipid mediators in neurological disorders.

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