Preface

Brain function depends on the complex architecture of neuronal networks and this complexity arises from the morphological intricacy that neurons acquire during the course of differentiation, a process, which is regulated by growth factors, cytokines, transcription factors and soluble as well as membrane-bound receptors. The metabolic syndrome is a highly prevalent condition that affects a considerable number of adult Americans and has become increasingly relevant to many disciplines in clinical medicine. At the molecular level, metabolic syndrome is accompanied not only by dysregulation in the expression of adipocytokines, cytokines, and chemokines, but also by alterations in levels of lipid mediators. These changes modulate immune response and inflammation that lead to alterations in the hypothalamic "bodyweight/appetite/satiety set point" resulting in the initiation and development of the metabolic syndrome. Metabolic syndrome is a risk factor for neurological disorders such as stroke, depression, and Alzheimer disease (AD). Having the metabolic syndrome approximately doubles the risk of having a stroke, AD, and depression compared with age-matched healthy humans.

Recent studies have also indicated that patients with metabolic syndrome and AD show insulin resistance. Insulin not only modulates levels of β-amyloid protein aggregation, the primary constituent of senile plaques and neuropathological hallmarks of AD, but also inhibits the activity of glycogen synthase kinase-3, preventing the phosphorylation of tau protein and thereby inhibiting the formation of neurofibrillary tangles, the other neuropathological hallmark of AD. Psychosocial factors activate the HPA axis, producing hypersecretion of corticotrophin-releasing hormone, adrenocorticotropic hormone, and cortisol. This dysregulation of the HPA axis promotes deposition of visceral adipose tissue which secretes adipocytokines and inflammatory cytokines. These adipokines and cytokines have been implicated in insulin resistance, an important component of the metabolic syndrome. The molecular mechanism underlying the mirror relationship between metabolic syndrome and neurological disorders is not fully understood. However, all cellular and biochemical alterations observed in metabolic syndrome such as impairment of endothelial cell function, abnormality in essential fatty acid

metabolism, and alterations in lipid mediators along with abnormal insulin/leptin signaling, and insulin resistance may represent a pathological bridge between metabolic syndrome and neurological disorders such as stroke, AD, and depression.

Information on the link among metabolic syndrome, stroke, AD, and depression is scattered throughout the literature mainly in the form of original papers and some reviews. Many books are available on the biochemical aspects of metabolic syndrome, but at present there are no books on the relationship between metabolic syndrome and neurological disorders. As baby boomers grow older, the enormous impact of metabolic syndrome and the above mentioned neurological disorders will be felt by the American society. At present more than 800,000 people suffer from stroke every year (approximately 1 person every 45 s), approximately 5.1 million people over the age of 65 in the USA suffer from AD, and about 38 million US adults have experienced depression at some point during their lifetime. The projected cost to Medicare for treating these neurological diseases is estimated to be about 5 trillion dollars by 2050. This number does not include other visceral and neurological diseases. Such an amount will not only burst National Institute of Health budget but will seriously affect the US economy. Available drugs may not reverse the stroke, AD, and depression. However, healthy diet, regular exercise, and retardation of metabolic syndrome may produce beneficial effects not only on motor and cognitive functions but also on memory deficits that occur to some extent during normal aging and to a large extent in stroke, AD, and depression. This monograph provides readers with a comprehensive and cutting-edge description of links among metabolic syndrome, stroke, AD, and depression in a manner that is useful not only to students and teachers but also to researchers, dietitians, nutritionists, and physicians.

This monograph has ten chapters. The first chapter describes the effects of lifestyle on metabolic syndrome and neurological disorders. Chapter 2 describes glucose and fructose-induced toxicity in the liver and brain. Chapter 3 deals with the effects of essential fatty acid metabolism on metabolic syndrome and neurological disorders. Chapters 4 and 5 focus on cutting edge information on the contribution of lipid mediators in the pathogenesis of metabolic syndrome and neurological disorders and molecular aspects of obesity and insulin resistance in metabolic syndrome and neurological disorders. Chapter 6 describes the effect of dietary phytochemicals on metabolic syndrome and neurological disorders. Chapters 7 and 8 are devoted to molecular mechanisms associated with the metabolic link among metabolic syndrome, stroke, and AD. Chapter 9 describes the cutting-edge information on signal transduction processes and the metabolic link between metabolic syndrome and depression. Chapter 10 provides readers with a perspective that will be important for future research work on the relationship between metabolic syndrome and neurological disorders. My presentation and demonstrated ability to present complicated information on signal transduction processes in metabolic syndrome and neurological disorders will make this book particularly accessible to neuroscience graduate students, teachers, and fellow researchers. It can be used as a supplemental text for a range of neuroscience and biochemistry courses. Clinicians, neuroscientists, neurologists, and pharmacologists will find this book useful for understanding

the molecular aspects of metabolic syndrome and its impact on the brain and its vulnerability to neurological disorders. To the best of my knowledge, this monograph will be the first to provide a comprehensive description of signal transduction processes associated with the relationship between metabolic syndrome and neurological disorders.

The choices of topics presented in this monograph are personal. They are based not only on my interest in the biochemistry of metabolic syndrome, stroke, AD, and depression but also on areas where major progress has been made. I have tried to ensure uniformity and mode of presentation as well as a logical progression of subjects from one topic to another and have provided the extensive bibliography. For the sake of simplicity and uniformity a large number of figures with chemical structures of drugs used for the treatment of metabolic syndrome and neurological disorders along with line diagrams of colored signal transduction pathways are also included. I hope that my attempt to integrate and consolidate the knowledge on metabolic links among metabolic syndrome, stroke, AD, and depression will initiate more studies on molecular mechanisms that link metabolic syndrome with neurological disorders. This knowledge may be useful in developing novel therapeutic interventions for metabolic syndrome, stroke, Alzheimer's disease, and depression.

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http://www.springer.com/978-1-4614-7317-6

Metabolic Syndrome
An Important Risk Factor for Stroke, Alzheimer Disease, and Depression
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2013, XX, 412 p., Hardcover
ISBN: 978-1-4614-7317-6