

Nutritional Neurosciences

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This book series aims to publish volumes focusing on both basic and clinical research in the field of nutritional neuroscience with a focus on delineating the effect of nutrition on brain function and behavior. The books will examine the role of different nutrients, food agents and supplements (both macro and micro) on brain health, neurodevelopment, neurochemistry, and behaviour. The books will examine the influence of diet, including phytochemicals, antioxidants, dietary supplements, food additives, and other nutrients on the physiology and metabolism of neurons, neurotransmitters and their receptors, cognition, behavior, and hormonal regulations.

The books will also cover the influence of nutrients and dietary supplements on the management of neurological disorders. It details the mechanism of action of phytonutrients on signaling pathways linked with protein folding, aggregation, and neuroinflammation. The books published in the series will be useful for neuroscientists, nutritionists, neurologists, psychiatrists, and those interested in preventive medicine.

Wael Mohamed • Nicola Luigi Bragazzi •
Richard M. Kostrzewa
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Brain-Iron Cross Talk

 Springer

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It is with genuine gratitude and warm regard that I dedicate this work to Menoufia Medical School: Thank you so much for unending financial and logistical support during my Ph.D. Journey and afterward during my sabbatical leave. I could not do any of this without your love and glory.

Wael Mohamed
Pahang
Malaysia

Foreword

Iron is an essential micronutrient for humans and plays a vital role in most brain physiological processes, including neurotransmitter synthesis, myelination of neurons, as well as mitochondrial function. There is a precise and well-ordered mechanism to regulate iron in the brain. Disruption of iron homeostasis in the brain, both conditions of iron overload and iron deficiencies are detrimental to the brain, as they can affect brain plasticity, cognitive function, and social behavior, which eventually contributes to the development of a diverse set of neuro-pathologies. These include mood, neurodevelopmental and neurodegenerative disorders.

The book *Brain-Iron Cross Talk* edited by Dr. Wael Mohamed, Dr. Nicola Luigi Bragazzi, and Dr. Richard M. Kostrzewa provides an excellent compilation of advanced works delineating the multilevel impacts of iron neurochemistry in the brain, starting from cellular levels to clinical manifestations. The contribution by authors includes discussion on the potential nutritional therapeutic opportunities targeting brain degenerative diseases induced by iron overload, the relation between Mediterranean Diet and Alzheimer's disease, the iron neurochemistry in the progression of Parkinson's disease, the homeostasis of iron and calcium and related ferroptosis, the dysregulation of iron homeostasis and its implication in multiple sclerosis and epilepsy, the role of iron after subarachnoid hemorrhage, and the complex relationship between iron deficiency and psychiatric disorders.

This book forms a valuable addition to the existing body of knowledge and is especially intended for students, scholars, neuroscientists, and clinicians who wish to deepen their understanding about the intricate cross talk between the iron and the brain.

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August 2022

Chester Chong Seng Choi

Preface

To study the phenomenon of disease without books is to sail an uncharted sea, while to study books without patients is not to go to sea at all.

William Osler (1849–1919)

Recently, the impact of nutrition and food intake has been highly investigated to study its impact on our brain function and its development as it was shown that the diet we take will determine the outcome of certain brain disorders such as in brain injury and stroke. Along with its effects on cardiovascular diseases and cancer development, nutrition and diet have been shown to be involved in preserving our mental cognitive function and behavior. Recent studies have implicated the development or exacerbation of certain neurological disorders to imbalance in our nutritional intake and our diet especially iron. The current *Brain-Iron Cross Talk* book will be published by Springer Nature under the Nutritional Neurosciences series (<https://www.springer.com/series/16639>). The aim of this project is to assemble global perspectives concerning the relationship between iron and the brain. This book will be part of the Nutritional Neurosciences series that covers multiple domains within nutritional neuroscience. The inclusion of iron in this prestigious series will help introduce new readers to the sub-discipline and increase the number of global conversation partners.

In the human body, iron is the most plentiful trace element. It is well known that iron is an essential component of the oxygen conveying hemoglobin. Iron also participates in the tricarboxylic acid cycle and in oxidative phosphorylation as a component of various enzymes. Iron in the nervous system is often involved in the catecholamine neurotransmitter synthesis and is involved in myelin assembly. Previous studies have shown that iron deficiency in the brain triggers mental impairment for infants and young children, for example, verbal and body coordination delays and psychomotor disorders. However, if iron is accumulated excessively in the aged brain, the resulting disorders, including Alzheimer's, Parkinson's, or Friedreich's ataxia, are closely related. Therefore, the mechanism and control of brain iron

metabolism should be researched and understood thoroughly. On this basis, it is important to explore the relationship between brain iron control and the incidence of nervous system diseases and discover new iron metabolism-related therapeutic targets in order to break down the limitation of nervous system diseases prevention and treatment.

Brain-Iron Cross Talk addresses cutting-edge areas of research of high significance for public health and translational medicine. The book discusses the comprehensive research history of iron and its significant role in the pathogenesis of the central nervous system (CNS) diseases. The book also identifies how iron supports function as well as the molecular mechanisms underlying their neuroprotectant activity. This topic is among the most interesting and challenging areas of contemporary translational biological and medical research, with implications for preventive and therapeutic approaches in age-related neurodegenerative disorders. This book explores the molecular mechanisms of brain iron including age-related metabolic pathways, mitochondrial nutrients, neurodegeneration and CNS disorders, cell signalling, and neuronal functions.

Coming from the background in the areas of neuropsychiatric health research, the editors (Drs. Mohammed, Bragazzi, and Kostrzewa) have decided to collaborate with other colleagues with expertise in areas of nutritional neuroscience to have a comprehensive book entitled *Brain-Iron Cross Talk* which included 13 chapters divided into two sections.

In the first section, entitled *Iron, Brain function, and Behavior* we have four chapters that describe various outcomes and effects of iron on brain functions (Sara Omer), neurodegenerative diseases (Haitham et al.), and Mediterranean diet (Abu Saleh et al.).

The second section of the book focuses on *brain disorders related to iron*. We are excited to have number of chapters that dissect how iron imbalance would modulate several known neurological disorders. In the first chapter, we discuss the iron relation to Parkinson's disease (Monika Kadian). In the next chapter, iron-calcium cross talk (Monika Kadian) is evaluated in terms of mechanisms and interaction; this is followed by an elegant chapter by Dr. Shi Hui et al., where they elaborate on iron and its relation to Alzheimer's disease. Other areas of discussion are introduced involving iron and multiple sclerosis where Arora et al. discussed the role of iron imbalance in multiple sclerosis. Interestingly, the following chapter discusses iron and epilepsy (Rajesh Thangarajan) followed by another overview chapter discussing iron and subarachnoid hemorrhage (Anika Zainab). This section is concluded with three chapters discussing nutrition in relation to psychiatric disorders (Haitham et al.), neurodevelopmental disorders (Rajesh Thangarajan), and finally iron and neuropathies (Asia Afzal).

Overall, this new book provides updated and novel concepts in the field of neurological disorders and its relation to the iron. The new compilation will be of high interest among researchers and clinical scientists involved in neuropsychiatry, nutrition, and biochemistry.

Finally, we thank all the authors for their significant effort in writing such excellent chapters for this new edition. We are also sincerely grateful to each author for their patience during the compilation and final editing of this book.

Kuantan, Malaysia
Toronto, ON, Canada
Johnson City, TN, USA

Wael Mohamed
Nicola Luigi Bragazzi
Richard M. Kostrzewa

Acknowledgments

First, we would like to send a great appreciation for all the authors who contributed to this timely project. The high level of devotion and dedication between the authors and editors made writing this book an enjoyable journey. In addition, we also extend our gratefulness to the authors who are in the fields of medical psychiatry and neuropsychiatric research for delivering years of their experience and work in different areas psychiatric disorders to deliver such an elegant piece of work. The herein discussed topics and applications are of a great value in the areas of nutrition, psychiatry, neurological disorders, and neurodegeneration. Finally, we would like to thank the encouragement of many of our friends and colleagues for their unconditional love, encouragement, and inspiration throughout the endeavor of the project. Thank you.

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Nicola Luigi Bragazzi received his MD in general medicine and surgery from Genoa University (Genoa, Italy) in 2011, his Ph.D. in biophysics from Marburg University (Marburg, Germany) in 2014, and his specialization in Public Health from Genoa University (Genoa, Italy) in 2017. He is a member of the Cochrane Association (Cochrane Reviewer) for the Cochrane Epilepsy Group. President Carlo Azeglio Ciampi awarded him Young Knight of the Italian Republic in 2005. Recently, in 2019, he has been nominated as one of the top five biomedical researchers worldwide aged less than 40 years in terms of several publications, articles in Q1 biomedical journals. He is currently working on infectious disease and vaccination modeling and extensive data mining in biomedicine at York University.

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