Rainer H. Straub

Understanding Aging, Fatigue, and Inflammation

When the Immune System and Brain Compete for Energy in the Body

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Rainer H. Straub
Department of Internal Medicine
University Hospital Regensburg
Regensburg, Germany

ISBN 978-3-662-68903-5 ISBN 978-3-662-68904-2 (eBook)
https://doi.org/10.1007/978-3-662-68904-2

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The registered company address is: Heidelberger Platz 3, 14197 Berlin, Germany

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The misfortune of the creature is the unwanted energy expenditure that prevents desired energy expenditures for physical and mental efforts.

For Jürgen Schölmerich,
a friend and supporter of lateral thinking

Foreword

The digitized world brings with it the fact that via Facebook, WhatsApp, blog pages, and many other variants, writing activity on even the most irrational topics is constantly increasing and is omnipresent. A significant disadvantage of this is that while an unmanageable amount of short communication messages and comments flow through the air or the earth cables, a meaningful context to overarching topics is rarely discernible. Sustainability is also usually not recognizable in this, although there might possibly be some clever ideas behind it if one were to think them through to the end and also put them into words.

Exactly this path has been taken by one of the most innovative minds of our time, my long-time colleague and friend, Rainer H. Straub—once again—by summarizing and channeling ubiquitous questions and unsolved mysteries, thus opening a new perspective for the inclined readers.

In this book, the brain and immune system compete, allowing us to sense how much contradiction operates within our body and how much these two "egoists" depend on each other. This problem can be understood especially in conversations with patients with systemic-inflammatory immunological diseases every day, as hardly any of these patients report that they are fully mentally and physically capable despite their disease being inactive under therapy, even though "all" (laboratory) parameters show no activity of their inflammatory disease. This reflects the "concept of the two realms" also contemplated and newly formulated by the author, guided by egotists (brain and immune system) who assist each other in energetic emergencies, but still compete for the limited resources in the body in the long term.

The imbalance of the energy balance and the resulting problems are therefore also the central intersection of this book, and it is very interesting to trace how the author transforms this wealth of information into sometimes deliberately humorous, but easily understandable streams of thought and reading.

For those who are not only interested in the basic culture of conflict between the two egoists (brain and immune system), but also in practical examples and many explanations of individual symptoms and disease states, the third part of the book is intended, in which the individual problems of this energetic imbalance are explained in detail. A special feature is that the author, although he is not yet to be classified in this age group, provides an outlook on the egoistic-energetic processes with increasing age and explains comprehensibly why due to these processes physical youthfulness cannot always be maintained. However, since this only applies to a limited extent to the brain, every interested person is advised to read this work. The mental performance of the reader, even in old age, will certainly be sustainably supported by reading this book.

With special thanks to Rainer H. Straub and his not insignificant efforts to write this work.

Ulf Müller-Ladner
Bad Nauheim/Gießen
im Herbst 2017

Preface

With the description of the genetic material (DNA) in the 1950s, we experienced an unprecedented **molecular revolution**. True to the motto "Everything is molecule and molecule is everything", many scientists lose themselves in details. Since then, biomedical science has increasingly focused on tiny individual parts of the cell machinery, and the view of the whole is often lost. The patient laments this.

Clinically active, researching physicians, who actually always consider the entire human being and not just a single cell, adhere to this **detail-oriented thinking**. Therefore, research projects often have a single molecule at their center. Even epidemiologically oriented physicians (human geneticists) focus on a tiny genetic detail in order to relate it to diseases in population-based studies using mathematical methods. This focus on detail leads to the problem of a clear description of the transition from cellular events to the problem for the entire human being, the symptom. The patient experiences or feels a symptom, and from there it is a long way to the interior of a cell and to the molecule.

Thus, there are **symptoms** such as depressive mood, fatigue, sleep disorders, loss of appetite and the associated malnutrition and undernutrition, muscle atrophy, bone loss, weight gain and weight loss, dwindling libido and reduced fertility, high blood pressure, increased blood clotting, back pain and much more. Of course, cellular and molecular processes are behind this, but describing the transitions from the intracellular to the whole is extremely difficult. This is probably because we have so far hardly developed a scientific method for assessing and describing the whole. However, in the last two decades, physicians, psychologists, and natural scientists have made important progress by relating various research areas to each other (this began in Germany in the early 1990s).

On the one hand, this is the field of **Psycho-Neuro-Endocrino-Immunology**, where the linking factors between the brain and body—namely nerve fibers (Neuro), hormonal glands (Endocrino) and immune cells (Immuno)—are considered. In doing so, these researchers draw on molecular insights from the individual sub-disciplines, focus on the linking paths between the organ systems, and thus consider the whole. In the USA, this field is often referred to as Mind-Body Medicine today.

Furthermore, in the last two decades, the field of **Evolutionary Medicine** has emerged, adopting the concepts of evolutionary biology for medicine. Evolutionary medicine provides an extraordinarily valuable perspective on the whole. It explains relationships by asserting that they must have a benefit in the context of reproduction (English: "fitness"). If a benefit arises for the individual, genes and the pathways dependent on them are conserved in the gene pool of the offspring. Over many generations, this phylogenetic development leads to traits that exist today (including genes and molecules in us humans), which have a measurable benefit in the context of reproduction. The individual molecule, the gene, or entire signaling pathways, which we usually consider in the context of a disease, probably have entirely different roles in the context of reproduction, for which they were positively selected. Evolutionary medicine sharpens this view, thus creating a new approach to the whole.

Then there is the field of **energy regulation**, which deals more closely with the body's energy supply. Hardly any process in our body takes place without energy, which is why energy-rich substrates must be constantly supplied. However, energy is also constantly lost for heat production and many other functions. Energy-rich substrates are glucose, fatty acids, and proteins, from which cellular energy is obtained. Thus, energy intake and energy expenditure take place at the level of a single cell, but also at the level of the entire body. The energy consumption and energy intake of the human body can be determined exactly using scientifically flawless methods, so that we get a wonderful view of the whole with these procedures.

Within psycho-neuro-endocrino-immunology, many pathways can be explained by the fact that they serve the **energy regulation of the entire body** and reproduction. Starting from the physical role of energy, the first part of the book deals with energy regulation of the entire body. Furthermore, evolutionary medicine is presented, which provides valuable insights throughout the book. The second part of the book presents energy expenditures for various aspects such as immune defense, pain, psychological stress, sleep disorders, anxiety, and others in more detail. With this information, a connection between energy regulation, evolutionary medicine, and the above-mentioned symptoms is made in the third part of the book. The fourth part summarizes everything. Following the text, there is an appendix with a glossary that explains important terms in detail. In addition, there is an extensive keyword index attached.

The author worked for many years in the field of Psycho-Neuro-Endocrino-Immunology (specifically in relation to chronic inflammatory diseases), to then integrate the two elements of evolutionary medicine and energy regulation. This book was created with the desire to represent a transition between molecular and holistic medicine. The content should remain as simple as possible. This may not always have been successful, although a lot of help flowed in from outside.

Such a book is never created entirely on its own, and therefore here too a few very helpful people have given good advice for the German version of the book. The book was critically read and significantly improved, making it more generally understandable. We scientists live in an ivory tower, and we are so blinkered that we urgently need this help. In this sense, the book was read by Dr. Anne Asmacher, Dr. Hubert Stangl, Verena Straub and Gabriele Konanz. Valuable help also came from the Springer publishing house from Dr. Christine Lerche and Claudia Bauer. If inclined readers provide further tips, the author is grateful, because improvements are collected and then added in a further edition.

Rainer H.Straub
Regensburg
im Herbst 2017

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The book aims to provide a comprehensible explanation of typical problems associated with aging and chronic inflammation. These problems were mentioned in the preface, and fatigue is such a critical and central symptom that it made it into the title of the book. However, before we can reach the level of understanding these elements in Parts II and III of the book, we need to acquire the necessary tools in Part I.

▶ Chapter 1 begins with the physical consideration of energy. It describes the energy-rich substrates important to us humans (glucose, fatty acids, and proteins), the energy expenditure of the human body, and the body's own regulation of energy storage and energy release. It becomes clear that the brain and the immune system are the main consumers of energy. The 1st chapter of Part I is challenging, and perhaps one might need to read it twice, but it is the important platform for the rest of the book.

▶ Chapter 2 summarizes—starting from the two discoverers Darwin and Wallace—the contents of the modern theory of evolution and the significance of evolutionary biology for medicine. Evolutionary biological examples are presented that are relevant to today's human medicine. From the special roles of the brain and immune system, the energy egoism of these two organ systems is derived. And it becomes clear that the brain and the immune system dominate the energy regulation.

▶ Chapter 3 demonstrates the special roles of the brain and immune system and explains the memory function of both in the context of the energy question. It presents the competition between the two organ systems, but also the mutual immediate assistance in energy regulation.

Part I summarizes the mechanisms of energy regulation dominated by the brain and immune system.

Energy and Body

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R. H. Straub, *Understanding Aging, Fatigue, and Inflammation*,
https://doi.org/10.1007/978-3-662-68904-2_1

1.1 The Pfühlbach and the Dispute

The ten-year-old son of a pharmacist, Robert, played at the Pfühlbach, a small river near Heilbronn that flows into the river Neckar. He passionately built simple water mills, dreaming of inventing a *perpetual motion machine*. A perpetual motion machine is a utopian machine that performs work indefinitely without an energy supply. It would have been something if Robert had invented such a machine. He conducted many experiments, only to have to admit with a heavy heart that a *perpetual motion machine* could not be built. These experiments never left Robert. Many mill wheels ran hot and left a lasting memory in him: "Mechanical work and the associated heat cannot be created out of nothing."

The interest of Julius Robert Mayer (1814–1877) did not come out of nowhere, as his father instilled in him a love for science. Mayer Senior filled the house to the brim with various chemical and physical instruments, botanical and mineralogical collections, medicinal plants, and many books. Robert often accompanied his father on excursions, and gradually began to conduct chemical and physical experiments on his own.

Nevertheless, Robert Mayer did not choose a natural science subject, but instead studied medicine, which he completed in March 1839. After a one-year adventure as a ship's doctor aboard the *Java* in the East Indian Ocean, Mayer began to ponder important questions of physics from 1840 onwards. Analogous to the indestructibility of matter, he was fascinated by the topic of the indestructibility of physical forces, and he summarized these considerations in a first publication in June 1841 at the age of 27. Indestructibility meant for him that a force (cause) produces an effect (result), so that this effect generates a new force that produces a next effect, and so on. Everything should be traceable back to a primal force. Energy or work in the modern physical sense was not yet spoken of at that time.

This first attempt at publication in the *Annalen der Physik und Chemie*, the most important German publication organ in the natural sciences of his time, was unsuccessful, as the editor Johann Christian Poggendorf never responded despite receiving three letters from Mayer. The following year, Mayer published the slightly modified text in the *Annalen der Chemie* under the editorship of Justus Liebig. In principle, this early work already discusses energy conservation and energy transfer—for example, from mechanical processes to heat.

Through elegant analogies and thought experiments, Mayer succeeded in establishing a correct relationship between the mechanical work of lifting a weight and the work of heating a quantity of gas. He calculated that a 1 gram body would have to be lifted and dropped 367 meters (mechanical work) to heat one cubic centimeter of air from an initial temperature of 0 degrees Celsius to 1 degree. Work and heat were thus closely related, and he had correctly recognized this. He himself always referred to this relationship as "the mechanical equivalent of heat." One can easily imagine how complicated wooden constructions of mill wheels in the Pfühlbach slowly heated up or even smoked. This must have deeply imprinted itself on him.

Mayer himself never used the terms work or energy, which were only later introduced by other physicists such as Rudolf Clausius, James Joule, William Thomson (Lord Kelvin), William Rankine, and others. Nevertheless, he succeeded in describing the principle of energy conservation and "the mechanical equivalent of heat" for the first time. From 1848, he argued with James Joule for several years over the