Stress in Health and Disease

Edited by Bengt B. Arnetz and Rolf Ekman



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# Biology of Depression

From Novel Insights to Therapeutic Strategies

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Edited by Bengt B. Arnetz and Rolf Ekman



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#### Foreword

The discovery of the stress syndrome by Hans Selye 70 years ago has had a great impact on many areas of biomedicine. The present volume presents a multicolored picture of this complex phenomenon in a series of chapters authored by a large number of eminent experts in a variety of stress-related fields. It will no doubt prove useful as a source of information on various aspects of stress and stimulate further research to deepen our knowledge of this field, which is so important for our society.

Living organisms are constructed to increase the chances for survival of the individual and the species. They should thus be able to cope with various unfavorable environmental and internal conditions. If the resulting stress on the system exceeds a certain level, damage will ensue. On the other hand, if the coping machinery is understimulated, damage may likewise ensue. A fundamental problem in stress research is thus trying to define the limit where stress starts to have a negative impact. Unfortunately this is not easy. What kind of endpoints can be used to settle the switch point? An obvious area in the search for endpoints deals with health and perhaps the most robust endpoint would be the length of life.

The length of human life has undergone a dramatic change during the past centuries. This phenomenon is probably observed worldwide but has been most precisely recorded in developed countries. It is best described as the "squaring off" of the survival curve. The data available from the past 500 years demonstrate a continuous increase in life expectancy. In a shorter perspective, looking at the second half of the previous century, this increase in the human lifespan has continued. Moreover, there is a clear correlation between survival and health. In Gothenburg, Sweden, for example, the general health, activity and well-being of 70-year-old people have continuously improved from one decade to the next.

How can one reconcile these observations with the statement that stress forms an increasing threat to our health? I have not been able to find a good answer to this question. However, it seems clear that the impact of stress has undergone a profound change in the sense of being more and more of psychosocial character than before. The role of infection, malnutrition and poor housing has decreased dramatically. Psychosocial influences during different periods are hard to measure objectively. Possibly their negative impact has also been reduced, but certainly not at all to the same extent as the more material factors. In fact, according to some authorities, psychosocial stress brings an increasing threat to our modern society.

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In any event this threat is severe enough to call for careful attention. Not least, the evolutionary perspective seems to be relevant. Various mechanisms that long ago were essential for survival now have the potential to create serious problems.

The enormous knowledge accumulated in the present volume should provide a useful basis for reaching an integrated view based on further analysis. A careful study of this impressive treatise can thus be strongly recommended.

Nobel Laureate in Medicine 2000

Arvid Carlsson

## Preface

Groundbreaking research during the first part of the 20th century by researchers such as Pavlov, Cannon, Hess, and Selye has provided us with a better understanding of the physiological consequences of fear and mental stress. In the second part of last century, Mason, McEwan, and Salpolsky, just to mention a few, were able to demonstrate the specificity of the stress response. Researchers also identified structures and mechanisms in the brain coordinating stress response and enhanced our understanding of short- and long-term consequences on health and well-being.

Today, we recognize that stress is of paramount importance both in health and disease. Without a healthy, timely and temporarily defined stress response, we are unlikely to survive, neither on the Savanna thousands of year ago, nor today challenged by microbes, nor in the globalized and increasingly competitive society. However, sustained activation of the stress response will attenuate our ability to stay healthy and increase our likelihood to succumb to environmental challenges and disease.

Some of today's most challenging public health threats, including cardiovascular and Alzheimer's diseases, premature aging, metabolic syndrome, obesity, and diabetes are all linked to stress. Stress might not be the root cause, but a contributing factor in the initiation and progress of diseases. These major public health threats, in addition to malignant conditions, appear to have immunological malfunction in common. Moreover, it is not sufficient to be genetically at risk; environmental factors appear to play an important triggering role. This is apparent in understanding the socioeconomic gradient of many public health disorders, that is, the better off we are as compared to others, the healthier we are.

In order to understand the mechanisms behind stress, our body's response to stress, its relationship to health and disease, and, ultimately, the treatment and prevention of stress, we need to cross scientific silos. No one discipline will have the ultimate answers. Not even one scientific paradigm is likely to come with the ultimate answers. We need to think trans-disciplinarily. We need to consider how we can move knowledge, not only from the lab bench to the clinic and society at large, but also how to reverse this information flow. We truly need a new roadmap, just as has been proposed by the NIH Director Dr. Zerhouni.

Actually, stress might be one of the most fruitful areas in which to apply innovative new thinking and paradigms in order to not only improve mechanistic understanding, but to enhance our ability to implement new knowledge into society and improve overall public health. In the current book, *Stress in Health and Disease*, we decided not to take the easy route. It would have been simpler to only invite some of the world's most renowned biological and molecular stress researchers, or some of the most recognized organizational stress researchers. But we did not think such a format would have added sufficiently to the vast amount of stress literature already published. Rather we decided to take the challenge and invite globally outstanding researchers representing a wide array of scientific disciplines, all relevant to stress, but which rarely meet in today's busy research environment.

We asked experts on history, molecular medicine, endocrinology, brain imaging, sleep, recovery, organizational stress, global health and a range of other disciplines to tell us their view and perspective on stress. We requested a lot from these authorities. We asked them to be very specific and focused on their area of expertise. We asked them to challenge the current paradigm. We also asked them to accept sometimes rather harsh editing in order to make sure the book met the mission – understanding stress in health and disease from a multitude of perspectives. Thus, when you read the book, be aware of the active role the editors played. We take full responsibility for this, with the ultimate vision to offer a book that not only presents the state of the art when it comes to stress in health and disease, but also contributes to new and challenging questions that will encourage the coming generation of stress researchers to stretch their experimental design and hypotheses. We also hope the book will encourage meetings and collaborations of researchers and practitioners from a wide array of fields.

This is the first attempt to create a truly trans-disciplinary book on stress – both with regard to the disciplines included as well as its application to real-life settings. The book represents a work in progress. We would be very happy to hear from you how we can improve the book in coming editions and if there are areas you, the reader, think we should have included. Or, are there perhaps superfluous areas that do not belong in a book on stress?

We hope you enjoy this book, that you find some things familiar and universally "true" and other things challenging. We also hope the book generates new approaches in the study and application of stress research.

Finally, we would like to thank all contributing authors. It has been a true joy to work with you all. Without your open minds and timely collaboration, we would not have succeeded. We also would like to thank our publisher, Wiley-VCH, which met the challenge to release a trans-disciplinary book on stress in health and disease. We owe a tremendous amount of thanks to our project editor, Dr. Rainer Muenz, as well as the copy editor, Mrs. Cathy Beesley, and the production manager, Mrs. Dagmar Kleemann, who provided endless professional and social support, ensuring that the editors were optimally challenged and stressed (with sufficient recovery time).

"Boundaries between disciplines are not barriers, challenges us to find new words and approaches"

Bengt B. Arnetz, MD, PhD Detroit April 2006 Rolf Ekman, MD, PhD Göteborg April 2006

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A Multifaceted View of Stress

# 1 Modern Fatigue: A Historical Perspective

Karin Johannisson

"There exists, both within and without the ranks of the medical profession, a widespread belief that the exigencies of modern life are producing an ever-increasing amount of nervous diseases." - H. C. Wood, *Brain-Work and Overwork* (1896)

#### 1.1 Introduction

At the general meeting of the British Society of Medical Psychology held on 21 November 1900, a dramatic increase in mental disorder cases was discussed. Three major causes were indicated: heredity, internal and external toxins, and *stress*. Laboratory experiments had demonstrated that stress was a triggering factor; rats had been placed in treadmill-cages and subjected to extreme stress. Physiologically, the process of illness could be described as a loss of energy. "If, then, it is a disease in which the danger lies in stress," one doctor pointed out, "we must see many people whose nervous systems will go to pieces unless they can be taken away from the stress in which they are living, whether that be on the stock exchange, or in any other professional occupation where the nineteenth century pressure is very great" [1].

The similarity between the situation at the turn of the 19th century and that of today is striking in regard to an increasing decline in mental health. Both eras define their times as being characterized by major changes, increased information flows, and heavy demands on the urban individual – and all of it happening in a whirling market economy. At both points in time, new diagnoses appear that identify and legitimize the symptoms of stress and internal discomfort in a culture strongly marked by competition, achievement, and a high tempo.

The unifying component in this case, seems to be the perception of an accelerated rate of change, an ever-growing flow of innovations which, on a subjective level, is in danger of creating spontaneous feelings of inadequacy, of not being

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able to keep up mentally, physically, and emotionally. This is what makes up modernity's identity – the expectation that the individual be limitlessly adaptable, flexible and progress-oriented. Modernity means being involved in a world where, "all that is solid melts into air," says modernity researcher Marshall Berman, citing Karl Marx. "To be modern is to find ourselves in an environment that promises us adventure, power, joy, growth, transformation of ourselves and the world – and, at the same time, that threatens to destroy everything we have, everything we know, everything we are" [2].

One concrete way to relate the perception of mental stress at the he last turn of the century to that at the recent one is to compare two medically and culturally legitimized diagnoses that – within their respective contexts – are considered to reflect abnormal fatigue. These diagnoses are neurasthenia and chronic fatigue syndrome.

However, the purpose here is not primarily to find absolute similarities, something that would be based on the concept that illness can be reduced to historically neutral phenomena, but rather to study how the clinical pictures are constructed and which scientific and cultural explanatory models work well together. Ultimately it also involves a new way of approaching the complicated process by which diagnoses are created.

### 1.2 Overstrain and Modern Society in 1900

During the last half of the 19th century, the Western world underwent a dramatic social change. Industrialization, an expanding capital market, and massive urbanization created new patterns of human contact. New technology represented an altered living environment. Special risk scenarios and pathology myths surrounded electrification and the telegraph. New kinds of transportation – trains, streetcars, and later the automobile – represented new relationships between the individual and time and space. The railway, particularly, was considered to carry special risks. The mental and physical stress was symbolized in the speed itself, in the train's shaking, vibrations, and sudden stops, as well as in the hustle and bustle of the railroad stations. Timetables, crowding, loudspeaker announcements, warning bells; all of this, together with the city's disorder, created an uncontrolled stream of sensory stimulation.

A number of scientific theories on modern society's effects on the vulnerable individual were developed. These included the theory of evolution that, in its social Darwinist formulation, emphasized the battle for survival; the theory of thermodynamics maintaining that the individual's energy was limited; and various civilization theories that saw alienation and fragmentation as the inevitable price of progress.

All of the prominent contemporary sociologists – Georg Simmel, Émile Durkheim, Ferdinand Tönnies, and Max Weber – pointed out the inner conflicts that appeared when old ways of life were replaced by new ones, and the individual,