

**THE ADVISORY COMMITTEE ON HEALTH RESEARCH**

# **STRESS AND THE NERVOUS SYSTEM**

This document arises from a WHO meeting held in Athens, Greece, 5-7 May 1998. It considers the definition of stress and the nervous system.

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**World Health Organization  
Geneva**

This document results from a WHO meeting on "Stress and the nervous system", held in Athens, Greece, 5-7 May 1998. The following experts participated:

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# Preface

The nervous system regulates homeostasis and the response to stress, and is in turn regulated by homeostatic mechanisms and by stress mediators. Thus, homeostatic processes - the stress response - modulate the onset, course, outcome, and treatment response in neurological disorders. A World Health Organization meeting was held in Athens on 5-7 May 1998 to assess recent progress on the role of homeostatic mechanisms and the mediators of the stress response in neurological disorders, to review the state of research in this field and to identify new directions for investigation, to propose future work that better characterizes the nature of stress during the course of clinical illness, and to discuss novel therapeutic applications of this line of investigation.

The concept of a stable internal environment that responds to environmental demands has existed since antiquity. In modern times this concept was refined by Claude Bernard, who introduced the concept of the "internal milieu", by Cannon, who coined the term "homeostasis", and by Selye, who described the general adaptation syndrome and introduced the concept of "stress", borrowed from physics, into physiology and medicine. Recent advances in molecular medicine and clinical investigation have led to the identification at the molecular, cellular and integrative levels of the molecules and pathways that transduce the response to stress and maintain homeostasis in the context of an ever-changing environment.

By bringing together basic scientists and clinical investigators the WHO Meeting on Stress and the Nervous System bridged the gap between fundamental and applied research. The neurobiology of stress and its role in the regulation of dopaminergic and neuroimmune pathways, and in sleep, served as a background for a series of presentations on the role of stress in various disorders of the nervous system, including infectious, vascular, motor, psychiatric and neurodegenerative diseases.

The general consensus of the meeting was that the stress response is the key to the maintenance of homeostasis and normal nervous system function. The response to stress is affected by disorders of the nervous

system, and at the same time stressors contribute to modulate the onset, course, outcome, and response to treatment of those diseases. The interface between stress and brain pathology is therefore complex. We all agreed that our mission is not only to identify the areas of interface between stressors, stress response, brain functioning, and disorders of the nervous system, but also to use the tools of contemporary biology to conduct studies that elucidate the mechanisms and pathways subserving the nervous system response to and regulation of stress in health and disease. The contributions to this volume cover recent progress in basic science and the clinical implications of the interface between the stress response and normal and abnormal nervous system function.

C.L. Bolis

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# Preamble

## INTRODUCTION

A WHO meeting on stress in neurological disorders was held in Athens, Greece, on 5-7 May 1998. The meeting was opened by Professor C. Liana Bolis, Consultant, Office of Research Policy and Strategy Coordination, who described the historical development of the concept of stress and the role of stress in disorders of the nervous systems. Because neurological disorders directly affect the nervous system, a better understanding of the role of stress in those disorders can enhance the understanding of the central regulators of the response to stress, and that knowledge basis can be later applied to diseases of other organ systems. There is a wide range of clinical course and outcome for the various neurological disorders, which include conditions of known or unknown causes and abrupt or insidious onset. All neurological disorders are marked by biological alterations in the functioning of the nervous system. The nervous system regulates homeostasis and the response to stress, and it is in turn regulated by homeostatic mechanisms and by stress mediators. Thus, homeostatic processes and the stress response interact with various neurological substrates to modulate the onset, course, outcome, and response to treatment in neurological disorders.

## SCOPE OF THE MEETING

Professor Bolis outlined the scope of the meeting as follows:

1. To assess recent progress on the role of homeostatic mechanisms and mediators of the stress response in neurological disorders.
2. To review the state of research in this field.
3. To identify new directions for investigation in this rapidly developing area of biomedical science.
4. To propose future work that better characterizes the nature of stress during the course of clinical illness.
5. To discuss new clinical and therapeutic applications of this line of investigation.

## **2 Stress and the nervous system**