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and science
of the integrated care

THE MANUAL

Francesco Bottaccioli
Anna Giulia Bottaccioli

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edra

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We dedicate this book to young people
who are preparing for care professions,
with the hope that its reading will help to develop
critical spirit and independence of judgement,
for the advance of knowledge and the care
of the human being in its entirety.

Francesco e Anna Giulia Bottaccioli

Preface

We dedicate the English version of our book to the memory of Bruce S. McEwen, Ph.D. Alfred E. Mirsky Professor Head, Harold and Margaret Milliken Hatch, Laboratory of Neuroendocrinology The Rockefeller University. A few days before his sudden passing, which happened on January 2nd 2020, prof. McEwen had agreed to record on video his final report at the IV National Congress of the Italian Society of Psychoneuroendocrine Immunology in Florence 20-22 March 2020, which unfortunately his sudden death did not allow to achieve.

McEwen was a great scientist, with 700 published papers which received 130,000 citations. He was the world leader in research in the field of Psychoneuroendocrine Immunology and, at the same time, was a deep and courageous intellectual engaged in researching both the molecular aspects and the social conditions that determine health and disease.

Indeed, the range of McEwen's research was wide, it held together molecular biology, epigenetics, the person as a whole and his socio-environmental context. A few years ago, in a long essay that appeared in a special issue of the *Journal of Endocrinoloy*, dedicated to "sixty years of neuroendocrinology", McEwen wrote:

"This article describes research in our, and other laboratories, that redefined neuroendocrinology as a field that also studies two-way brain body communication via the neuroendocrine, autonomic, immune and metabolic systems. This research has uncovered the remodeling of brain architecture mediated by hormones working together with other cellular mediators. These actions occur via epigenetic mechanisms involving both genomic and non-genomic processes over the life course, and there is ongoing translation of the findings in animal models to the human condition, including the effects of adverse early life experiences and the relationship of socioeconomic status and health through the development of the concept of allostatic load"[1].

In these words lies the path that led science from neuroendocrinology to neuroendocrinoimmunology and then to Psychoneuroendocrinoimmunology.

Our Manual is indebt to the scientific work of this giant of the 20th century, to whom goes our passionate admiration and gratitude.

Finally, please note that the English edition has been updated and, where needed, expanded

Francesco and Anna Giulia Bottaccioli
Rome, 19.01.2020

[1] McEwen B.S., Gray J.D., Nasca C. (2015) 60 years of neuroendocrinology: Redefining neuroendocrinology: stress, sex and cognitive and emotional regulation, J Endocrinol 226(2): T67-T83.

Preface to the Italian edition

I started working on PNEI 30 years ago. At the time there were no summaries, because the first edition of *Psychoneuroimmunology* was actually a small collection of articles curated by Robert Ader. Concerning the relationship between the nervous system and the immune system, the most relevant scientific text was a review by Edwin Blalock from 1989 which documented for the first time that lymphocytes had receptors for hormones and neurotransmitters produced by the brain and which at the same time produced hormones and neurotransmitters entirely similar to those of the brain. It was a strong evidence that the two systems communicated between them, but many obstacles still needed to be overcome in order to scientifically describe the bidirectional communication between brain and immunity. I mentioned these obstacles in my book *Psiconeuroimmunologia* from 1995, the only text in Italian and among the few on an international scale; the latter shared the characteristic of being a collection of articles by various authors on individual aspects.

But in that book I tried to gather the existing scientific documentation on the communication between biological systems and the psyche while at the same time trying to extract from those data (presented in a clear way) their general meaning, which was really revolutionary: the human organism functions like a network of structured and interconnected systems, that influence and are influenced by the psychic dimension.

I therefore presented an emerging scientific paradigm, with a high power of integration of knowledge and theories from both the biological field and the psychological and philosophical field.

With the present volume, through the 23 chapters that compose it, the psychoneuroendocrinoimmunology paradigm presents itself in its full extension: from the first part, which describes the historical and philosophical bases of the paradigm; to the second, that shows the biological revolution underway, which through the bursting of epigenetics radically changes the traditional view of genetics and of the evolution of the human species; the third, which describes in detail the nervous, neuroendocrine, immune, psychic systems and their reciprocal influences; the fourth that, based on a rigorous examination of the facts, shows the modulation tools of the human network for preventive and therapeutic uses, such as nutrition, physical activity, psychotherapy, meditation and other behavioural and natural medicine techniques; up to the fifth part that, chapter by chapter, disease after disease, in critical dialogue with reductionist physiopathology and clinical hyperspecialisation, presents integrated care schemes, proposed on the basis of the available scientific evidence, for acute cardiovascular diseases, disturbances of the psyche-brain system (from depression to anxiety disturbances, schizophrenia, autism, neurodegeneration), immune disorders, eating and metabolism disorders, reproductive and sexual dysfunctions and cancer.

The illustration (*Figure 1*) shows the need of studying the "very small" in the framework of a vision of the entirety. The examination of the microscopic details provides us with a level of knowledge of reality that is essential for scientific progress but does not constitute its last and real level. If I only see the picture on the right, I lose the vision of the flower; similarly, if I only see the cholesterol level, I lose the vision of the patient. We certainly need to know the molecular organisation of the flower and of the patient, but we need

Figura 1 L'immagine *a sinistra* ritrae un fiore di alcea, quella *a destra* l'interno del fiore, dove si notano le antere schiuse presenti sugli stami con la fuoriuscita del polline, il cui diametro medio è di circa 60 μm. La fotografia *a destra*, che è stata acquisita con una fotocamera professionale corredata da un'ottica customizzata con diaframma f/45 e luce flash, è opera di Massimiliano Benvenuti, che ringraziamo per la cortese autorizzazione alla pubblicazione.

to evaluate those data not as simple and unique determinants that explain the complexity of the plant or animal organism. We must instead read them in the context of the entirety.

This is moreover the criticism of reductionism that George Engel presented 40 years ago: no objection to the increasingly precise study of the molecular and particulate organisation of life, which is the engine of scientific research, but radical criticism to the presumption of reducing to simple determinants the explanation of complex phenomena such as health and disease.

The resulting scientific reductionism and clinical hyperspecialisation have their pillar in the industrialisation of medicine, which is the main obstacle to the change of paradigm. The growing technological power that is currently available, which will take a spectacular leap with the pervasive application of the new form of artificial intelligence (machine learning), should be separated from the private interest of industry, if we want to release the enormous potential of knowledge and care already imprisoned in the meshes of the search for maximum profit.

The PNEI paradigm therefore also requires the decisive contribution of philosophers, sociologists, computer scientists, technicians (I feel like saying: of politicians, but this is just a utopia!), because there can be no change in treatment without any changes in the cognitive and operating apparatuses that determine it.

This is why we have availed ourselves, as we were writing this book, of the contribution not only of medical experts, psychologists, physiologists, neuroscientists and other professionals from the care world, but also of philosophers and scholars of contemporary culture. However, as the reader can see, the book is not a collection of texts by various authors, but has its unitary narration, which avails itself of specialised insights into the themes illustrated in the text.

I have been systematically helped during my writing by my daughter Anna Giulia, who has written whole parts, has carried out punctual bibliographic researches, has discussed with me the chapters and the relevant passages of the text with the curiosity and the competence of a young woman, doctor, PNEI scholar, who is completing her training in internal medicine, the most systemic specialisation of conventional medicine.

Fatherly pride, in this case, is accompanied by the duty to recognise her work as an author and also to pay tribute to the young scientists and healthcare professionals to whom this book is dedicated, who are often obscured and sometimes exploited by their teachers and directors.

A last warning: this book, while being voluminous, is not and cannot be exhaustive of human physiopathology. Its ambition is to constitute a platform, a paradigm, in the dual role of "disciplinary matrix" and "operating models" (Kuhn), to be implemented over the next few years with the research and clinical experiences that it will manage to encourage.

Francesco Bottaccioli

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