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NONMOTOR PARKINSON'S: THE HIDDEN FACE
THE MANY HIDDEN FACES
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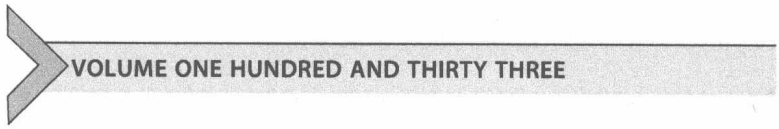
EDITED BY
K. RAY CHAUDHURI
NATALIYA TITOVA



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Nonmotor Parkinson's: The Hidden Face

The Many Hidden Faces

Edited by

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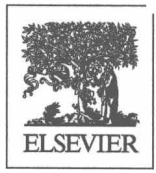

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PREFACES

MESSAGE FROM PROFESSOR GÜNTHER DEUSCHL, EUROPOEAN ACADEMY OF NEUROLOGY

Parkinson's disease is one of several important degenerative diseases, but it has become the model for research and clinical progress for neurodegenerative conditions in general. Many aspects of neurodegeneration have been studied and successfully understood for the first time in this disease. It was the first disease for which a clearly identified pathology was discovered, the first with a known transmitter deficit which could be replaced, the first in which cell transplantation for the brain was used, and the first for which deep brain stimulation was discovered as a knowledge-based therapy.

While most of this significant progress has been made during the past 5 decades, the study of the clinical symptoms lagged somewhat behind, and nowadays it is hard to understand why the clinicians' views were so much focused on the motor symptoms alone. This is nicely documented by looking at the Webster Scale of 1968 which contained Seborrhea as the only nonmotor symptom. The Hoehn and Yahr Scale of 1967 which we still currently use is only focused on the motor symptoms and does not even mention dementia in stage 5 of the condition. Certainly psychiatric issues were also dealt with in these days, but it was considered a concomitant disease—mostly Alzheimer's—rather than an integral part of Parkinson's disease. Urinary problems were certainly also recognized and treated, but it was not considered an important feature of the disease process. Only a handful papers were discussing such nonmotor features as a manifestation of the disease itself in the past century, and the systematic study of nonmotor symptoms started not before the early 21st century.

Beyond a number of review articles the current book is for the first time summarizing the current knowledge on nonmotor conditions, their pathologic, biochemical, and neurophysiological basis on the one hand and the many clinical manifestations on the other hand. Particular care has been taken to cover the therapeutic options for nonmotor symptoms which we are just starting to understand. K Ray Chaudhuri, and the Non-Motor Study Group of the Movement Disorder Society (particularly the trainee section represented by Nataliya Titova) which he leads have done an excellent job in systematically discover the many ramifications of clinical symptoms. Together with the new concepts of progression of disease pathology

and the subsequent involvement of many different neuronal circuits we now understand these symptoms as part and parcel of the "whole-brain" disease—Parkinson's disease. This book is a wonderful and concise summary of the progress which has been made so far. The authors and the editors owe our thanks for undertaking this huge task.

I wish this book a broad readership and hope that it will further help to disseminate the new concept of Parkinson's disease, and that it will help to better understand the disease, our patients, and their needs.

GÜNTHER DEUSCHL
President of the European Association of Neurology (EAN)

MESSAGE FROM PROFESSOR CHRISTOPHER G. GOETZ, INTERNATIONAL PARKINSON'S AND MOVEMENT DISORDERS SOCIETY

Coinciding with the 200th anniversary of the celebrated *Essay on the Shaking Palsy* by James Parkinson, this remarkably complete work focuses on a burgeoning area of research and clinical challenge: the nonmotor elements of Parkinson's disease. The importance of nonmotor problems in a disease that is diagnosed by criteria strictly related to the motor system may seem counterintuitive, but the gamut of autonomic, cognitive, and behavior elements of Parkinson's disease justifies this pointed focus. The editors have recruited a wide array of international authors, some the most senior in the field and some more junior colleagues with high credentials, to compose a large, two-volume reference source with chapters covering historical, clinical, genetic, neurochemical, and physiological underpinnings of nonmotor elements of Parkinson's disease and related disorders. Such topics have been summarized briefly in prior texts, but basic scientists and the neurological, psychiatric, and medical professionals who confront Parkinson's disease on a daily basis have not heretofore had a comprehensive reference source of this dimension. An excellent introductory chapter by B. Hurwitz on Parkinson himself and his appreciation of nonmotor symptoms in *paralysis agitans* documents the few words Parkinson devoted to these problems and places his seminal study in historical context. Genetics issues, so important to 21st century science, are covered in two particularly well-developed chapters by E.-K. Tan and C. Klein. More elusive topics of pivotal concern to clinicians are discussed with sophistication, two examples being the excellent chapter on Apathy by J. Pagonabarraga and J. Kulisevsky, and a highly up-to-date discussion of Fatigue by B. Kluger. In an era of increasing focus on ancillary interventions and resources, Nutrition, Exercise, and the concept of Personalized Care are included into the Management section. Thanks to the editors' particular attention, each chapter is a separate and autonomous discussion, but works well with the entire volume, ensuring a natural flow from one topic to another.

Setting this large and impressive new work next to James Parkinson's tiny 1817 pamphlet is a fitting visual image of the progress made over 200 years. This current contribution elegantly expands on the observations by Parkinson, but the editors and authors are duly cognizant that the *Essay* remains the inspirational source for this modern work. *Nonmotor Symptoms:*

The Hidden Face of Parkinson's beautifully and humbly complements the original work by Parkinson, honoring 200 years of scientific progress and bearing no intent to replace Parkinson's original work. In my view, the tenor taken by the author team and the editors echoes the clarity and integrity for which James Parkinson himself was known. In this light, I cite the words of Jean-Martin Charcot, the most celebrated clinical neurologist of the 19th century whose 1888 comments on Parkinson's essay resonate with regard to the quality of this new scientific contribution:

> Read the entire book and it will provide you with the satisfaction and knowledge that one always gleans from a direct clinical description made by an honest and careful observer.

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THE EDITORS WORDS

James Parkinson the famous London physician who described Parkinson's disease (PD) 200 years back was an astute clinician and observer. He was said to have given several Ale-House (currently known as a pub) sermons where he spoke on medicine and geology. His medical foresight is reflected in the fact that he described not just the core motor features but also several nonmotor features we now regard as integral to the phenotype of PD. These include dribbling of saliva, dysphagia, constipation, sleep dysfunction, delirium, and pain. In addition, he also mentioned presymptomatic "brachial" pain. This was the first suggestion that nonmotor symptoms (NMS) may appear in the prodromal stage of PD.

Yet the scientific community was distracted by the dramatic response of motor symptoms of PD to levodopa, a seminal discovery in the 1960s. Unfortunately this meant that the critical role of NMS in PD was somewhat ignored. While individual NMS were recognized, no measures addressed the holistic concept of NMS till the early 2000. Relevant holistic tools were developed and validated in early 2000 around the time when Bill Langston described the NMS of PD as the submerged part of the iceberg that is PD.

This book is therefore dedicated to celebrate the 200 years since James Parkinson described the eponymous condition. The book is meant to celebrate the advances we have made in the nonmotor aspects of PD in the last 100 years. The concept of NMS in PD ranges from neuropathological heterogeneity highlighted by work from Braak as well as Jellinger to a multitude of neurotransmitter deficiency and clinical phenotypes supported by varying biomarkers. We have tried to highlight these issues in the chapters included in two volumes of this book, possibly the most extensive book on the topic ever written.

The book reflects a global reach and we are indeed grateful to key opinion leaders around the world who have agreed to contribute to the book in spite of working through a holiday period in December–January 2016–2017. The range of topics also reflects the diversity of NMS in PD, but we have also for the first time attempted to address NMS in parkinsonism as well as related movement disorders. These include essential tremor, cerebrovascular disease, chorea, Wilson's disease, Huntington's disease, amyotrophic lateral sclerosis, tics, and dystonia. An unique feature is a carer-focused chapter contributed to by a real-time caregiver for PD as well

as contributions from allied health specialists. There are also chapters focused on palliative care, exercise, and complimentary therapies and their impact on NMS.

There are several other points related to this book that is worth mentioning. The concept and the idea for this book was developed between Nataliya Titova (N.T.) and K Ray Chaudhuri (K.R.C.) based on the fact that many general neurologists did not appear to have a grasp of nonmotor issues in PD. This unmet need brought together a relatively established clinical scientist (K.R.C.) coediting this book with an emerging neurologist and scientist (N.T.) representing the trainee as well as the junior subsection of the movement disorders community. The trainee and junior involvement is also evident in several chapters where the trainees have either taken the lead or coauthored chapters. The engagement of trainees as well as juniors is indeed a key strategy for the MDS as well as the EAN, and we are privileged that the presidents of both societies have written forewords for this book.

It is sad that in spite of the foresight of Parkinson, nonmotor aspects of PD remain a key unmet need in PD. Although awareness has grown and learned societies such as the MDS have now dedicated nonmotor study groups, yet for much of the world PD remains a pure motor disorder. The overwhelming evidence that NMS burden drives quality of life of the patient and carers thus has remained unexplored and is the hidden face of PD. The book cover we chose reflects this fact and comes from the Ukrainian artist Oleg Shupliak. Oleg Shupliak is known for illusory or camouflage painting which are presented as if not one, but two, or even three pictures. The viewers can discover for themselves the different images that are apparent or hidden. We felt this style of art is analogous to our message of NMS of PD being the hidden but a real face of PD. The cover hides the face of the famous Dutch painter Van Gogh. A museum celebrating the life and works of Van Gogh is located in Amsterdam, and it so happens that the EAN 2017 congress was held in Amsterdam. This was the reason we aimed for the book launch in this city.

From a personal angle both K.R.C. and N.T. acknowledge the enormous effort and work that went into the planning of this book over the Christmas period in 2016 and the gratitude we feel toward all authors, most of whom we approached over this period. Their contributions, within a strict deadline we enforced, have ensured that the book is not just destined for the shelf but is credible, relevant, and hopefully will be widely cited.

Finally the book will not be complete without the support of Elsevier Press and in particular Andrea Gallego Oritz who has worked ceaselessly

to support us and other authors. N.T. would also like to acknowledge the support from the Department of Neurology, Neurosurgery and Medical Genetics of N.I. Pirogov Russian National Research Medical University. In particular, she would like to acknowledge the help, support, and advice from Professor Elena Katunina. In addition, she would also acknowledge Professor G.N. Avakyan for entry to the world of neurology and movement disorders and Professor E.I. Gusev, the head of the department, for the opportunity to develop her career in movement disorders. We also acknowledge the media interest in the book in countries such as India and hope that general neurologists, physicians, as well as trainees from all walks of neuroscience and related specialities will benefit from the chapters. We also hope allied health specialists as well as expert PD patients and carers will find the book of interest. If this is achieved, we will feel we have gone someway toward unraveling the hidden face of PD.