

Introduction

The Times They Are a-Changin': Parkinson's Disease 20 Years from Now

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Last year, we were all reminded about the 200th anniversary of James Parkinson's "Essay on the Shaking Palsy" (one can hardly label this as a celebration, as it would have been much better if this anniversary had never taken place). At the *Journal of Parkinson's Disease*, we chose to publish a special issue last year that highlighted eight of the most important advances in Parkinson's research over the past 60 years, and we were fortunate to have several scientists who made those original findings contribute review articles [1–8]. It was fascinating to read personal accounts of how major strides had been made, and to get a look behind the scenes of some remarkable discoveries.

As we were working on that special issue, we frequently commented on how the pace of research into Parkinson's disease has accelerated to a sometimes remarkable extent in recent years. Several of the discoveries made during the past two decades have been driven by the availability of advanced and automated laboratory apparatus, molecular technologies, computer science and bioinformatics. On the clinical side, the development of advanced brain imaging techniques and the realization of the importance of large clinical cohorts and collection of biosamples have speeded up further discoveries. We started to discuss what the future might hold, and we speculated that we might see more advances in the treatment and

care of Parkinson's during the coming 20 years than were evident during the preceding 200 years. Thus, the idea of a collection of short, forward-looking and visionary articles was born.

After some brainstorming sessions, we identified 19 areas where we anticipated that a very significant progress might be realized during the coming 20 years. We had lively discussions about who might be suited to author the articles describing these topics and who would broadly present some of the best ideas from an assigned topic. Eventually, we decided to bring together two or more authors from centers that typically do not work together. In that way, we felt that many viewpoints would be represented for each topic and we hoped to spark even more creative visions for the future. The authors were given strict instructions to focus their article on the future, spending only a short section on describing the state of the art. We encouraged the use of graphical display items and tables.

We are very excited about the outcome. "The times they are a-changin'", sang Bob Dylan in 1964, and this special issue clearly shows that the field of Parkinson's is no exception. Indeed, the special issue comprises 19 compelling articles that propose several innovative concepts for the future. They discuss a very wide range of topics, including how Parkinson's disease, and its prodrome, should be defined, and a challenging series of observations that the disease seems to be on an unprecedented rise in incidence. Some of them address the root causes of

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Parkinson's and discuss what parts we are missing in the puzzle of genetic and environmental influences, and whether changes outside the brain (e.g., the gut) are the primary sites for the triggering of Parkinson's disease. Some of the articles discuss how current pharmacological therapies (both dopamine-based and non-dopaminergic) can be optimized, and whether there will be pharmacological treatments that might eventually slow or even halt the progression of Parkinson's.

With the advent of these new therapies, the provocative question arises whether humankind will be fortunate and not need to witness a 300th anniversary of Parkinson's. At the same time, it is a reality that there are millions of persons worldwide living with Parkinson's today, and that this will be the case for at least several decades to come. This is why we also considered it important to highlight new possibilities for innovative symptomatic therapies to support those large numbers of patients, including ones that embrace existing concepts (e.g. exercise and rehabilitation) but launching them more effectively at a community-based level to provide improved quality of life. With the emergence of new technologies, one article predicts that in the near future, monitoring of patients will increasingly be done in the home and not in the clinic. Some of these developments may well take much less than 20 years to reach us. Another paper addresses innovative ways of using digital pathways to deliver treatments to Parkinson patients in a much more personalized manner, which is a top priority for our patients.

We were equally excited to consider topics that encompass the rapid development of new advanced technologies such as brain imaging, therapies based on genetically engineered stem cells, gene therapy and closed-loop deep brain stimulation. All of these will help to create a better life for the many patients with Parkinson's in the coming 20 years.

Did we miss any areas where there will be advances? Most certainly, it is likely we did. That

is the nature of the beast. Predicting the future is difficult and in medical research it should be! We are obviously hoping for unexpected advances that will significantly improve the lives of people living with Parkinson's disease. A dream scenario would be that our understanding of the origins of Parkinson's disease reaches a level where it will be possible to launch preventative measures that, if not eradicate the disease, will dramatically reduce its prevalence. Moreover, we all hope that disease-modifying interventions will reach the stage of clinical application, so that the course of the disease may be slowed – and who knows even halted – among those already affected by the disease. Even in the absence of such advances, we hope this special issue will trigger several fruitful discussions in the fields of both Parkinson's research and care, providing some guidance as to where they could move during the next 20 years. Finally, in doing so, we hope that the articles in this special issue will also help, in a small way, to shape the unpredictable future of Parkinson's disease.

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