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There are many success stories in the history of Parkinson's disease. Our understanding of the condition has greatly evolved since it was first identified as the shaking palsy 193 years ago. We have made progress in defining the underlying pathology and tracking disease progression, and better treatments improve patient quality of life. Yet, a cure remains elusive.

Unlike other neurodegenerative conditions, Parkinson's disease has had a successful symptomatic drug available for more than 40 years. Levodopa is the mainstay of Parkinson's disease treatment, but although its pharmacology and delivery have been altered and improved over the years, it is still far from ideal. And herein lies perhaps the ultimate frustration: despite several decades of searching, levodopa is still the best there is.

That is not the only challenge. Can we detect the disease before major, perhaps irreversible degeneration has occurred? What will it take to replicate this disease in animal models to enhance our understanding of it and aid development of novel treatments? And how can new, potentially disease-modifying therapies be appropriately tested in patients?

As this *Nature Outlook* reveals, we might be on the brink of a revolution in the diagnosis and treatment of Parkinson's disease. The frustration of failing to find a simple or single cause is giving way to the hope that the complex web of gene and protein interactions might be starting to untangle. Candidate biomarkers for earlier diagnosis are emerging, and many new and exciting treatments are working their way into the clinic.

We are pleased to acknowledge financial support from Abbott in producing this Outlook. As always, *Nature* carries sole responsibility for all editorial content.

Michelle Grayson,
Associate Editor, *Nature Outlooks*

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CITING THE OUTLOOK

Cite as a supplement to *Nature*, for example, *Nature* Vol XXX, No. XXXX suppl., Sxx-Sxx (2010).

VISIT THE OUTLOOK ONLINE

The *Nature Outlook Parkinson's Disease* supplement can be found at www.nature.com/nature/outlook/parkinsons/. It features all newly commissioned content as well as a selection of relevant previously published material. All featured articles will be freely available for 3 months.

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