

Preface

Parkinson's disease is the second most common neurodegenerative disorder after Alzheimer's disease, and affects more than 5 million people worldwide. Today, the clinical management of Parkinson's disease chiefly relies on the use of the so called "dopamine replacement therapy" in order to re-establish the function of the dopaminergic system, which is affected by the neurodegeneration underlying the disease. While this approach effectively counteracts the motor deficits featuring Parkinson's disease, the chronic use of dopamine replacement therapy eventually leads to the emergence of motor complications (e.g., dyskinesia and motor fluctuations) that greatly limit its therapeutic potential. Moreover, dopamine replacement therapy has no apparent beneficial effects on the progression of dopaminergic degeneration featuring Parkinson's disease. Based on these considerations, there is a need for the development of alternative therapies that could help to overcome these limitations.

In these years, drugs acting as antagonists of the adenosine A_{2A} receptors have emerged as new promising candidates for the therapy of Parkinson's disease. When evaluated in experimental animal models of the disease, these drugs counteract motor deficits and amplify the beneficial effects of dopaminergic drugs without worsening their dyskinetic effect. Moreover, experimental evidence also indicates that adenosine A_{2A} receptor antagonists might slow down or arrest the dopaminergic degeneration that underlies Parkinson's disease. Building on this evidence, the research in this field has recently made significant progress, leading to the approval of the first A_{2A} receptor antagonist for clinical use as adjunct to L-DOPA (istradefylline, marketed under the name of NOURIAST®), and the ongoing clinical evaluation of other promising drugs (e.g., tozadenant).

This book covers basic biological aspects of the adenosine system relevant to Parkinson's disease, and also discusses recent experimental findings at both the preclinical and clinical level. Attention is dedicated to the localization and function of adenosine A_{2A} receptors, to their interaction with dopaminergic and non-dopaminergic receptors in the brain, and to the development of novel molecules that may target A_{2A} receptors. The critical role of the adenosine system in the regulation of neurotrophic factors, neuroinflammation, and neurotoxicity is also covered, and the relevance of these phenomena to the etiology of Parkinson's disease discussed. Moreover, the book thoroughly describes the effects of adenosine A_{2A} receptor

antagonists observed in experimental models of Parkinson's disease on both motor (akinesia, dyskinesia, tremor) and non-motor (cognition, peripheral functions, sleep) symptoms. Finally, attention is dedicated to the clinical relevance of the adenosinergic system, by describing the development of the first ever approved adenosine A_{2A} receptor antagonist (istradefylline), the most advanced clinical trials with these drugs, the use of A_{2A} receptor antagonist in neuroimaging, and the epidemiological evidence that links the adenosine system with the onset and progression of Parkinson's disease.

By gathering updated and high-quality chapters written by world-leading experts in the field, this book provides essential information to preclinical and clinical researchers interested in the development of new therapies against Parkinson's disease and related neurodegenerative disorders.

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The Adenosinergic System

A Non-Dopaminergic Target in Parkinson's Disease

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