Dopaminergic Neurons and Parkinson's Disease: Current Status, Implications and Future Perspectives

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Abstract. Parkinson's disease (PD) is a common neurodegenerative disease that impairs motor functions in the affected individuals, causing increased dependence and even mortality eventually. Therefore, it has become a significant resources and financial burden to the society. Scientists and companies have carried out a myriad of studies to study potentially effective drugs to slow or cure the disease, but they barely pass the Phase III stage of clinical trials. Under these circumstances, establishing the pathogenic mechanisms is really the key to removal of obstacles in the way of mitigating PD. Degeneration of dopaminergic neurons is known as a cause of motor manifestation in PD. Instead of approaching PD from the traditional α-synuclein theory, this review emphasizes on dopaminergic neurons *per se* to discuss their unique features and how they may implicate in PD development and progression. Some latest findings and potential future directions are also summarized and discussed in this review.

Keywords: Dopaminergic Neurons, Parkinson's Disease, Calcium Ion Channels.

1. Introduction

Parkinson's disease (PD) has a morbidity that is the second most frequent in the world, affecting people with an age of 65 years and above predominantly [1]. The prevalence of PD has in According to the World Health Organization, over 8.5 million individuals were diagnosed with PD in 2019 [2]. The prevalence of PD increases at an unbelievable fast speed, such that the number of diagnoses doubled to 6 million from 1990 to 2015. This trend is expected to be maintain and the prevalence is likely to be over 12 million by 2040, as the global population ages (which is the major driving factor) [3].

As a troublesome health problem, PD has become a serious financial burden to the world. For example, the United State is estimated to spend 51.9 billion dollars in 2017 alone, including the combined direct and indirect cost, for PD, while in the United Kingdom the annual cost for PD patients is over 5 thousand pounds per person in 2018 [4,5].

PD displays a variety of motor and non-motor symptoms. Currently, PD has no effective cure or disease modifying treatments. Although numerous studies have been done, the exactly pathogenic mechanism is still unclear. However, two pathological characteristics have been identified for a long time, which are the loss or degeneration of the dopaminergic (DA) neurons and accumulation of Lewy (LB) Bodies inside the neurons. Loss of the DA neurons in the substantia nigra (SN) contributes to the cardinal motor symptoms in PD, while the LBs are abnormal intracellular protein aggregates, containing various proteins (α-synuclein ubiquitin, etc.), that impair normal neuronal functions [1].

Death of the DA neurons, a crucial part of PD pathogenesis, has not been fully understood yet. Several hypotheses and studies have indicated that a number of factors may contribute to this process, including oxidative stress, mitochondrial dysfunction, protein aggregation, etc. Interestingly, DA neurons seem to be particularly susceptible to the Lewy pathology and mitochondrial dysfunction, although the role of Lewy pathology remains controversial. The degeneration of DA neurons occurs systemically in the brain, but different areas are affected to different extent [6]. As a consequence, understanding physiology and the degenerative mechanisms of the DA neurons are critical for explaining PD pathogenesis and developing novel therapies. This review focuses on the DA neurons and which role it plays in the PD researches and treatment.

Neurophysiology Of Dopaminergic Systems Current Status And Clinical Perspectives

Louis A. Chiodo,Arthur S. Freeman

Neurophysiology Of Dopaminergic Systems Current Status And Clinical Perspectives:

Neurophysiology of Dopaminergic Systems Louis A. Chiodo,Arthur S. Freeman,1987 Dopaminergic Neurons P. Beart,1988-06-18 The proceedings of the 1987 IUPHAR symposium held in Sydney Australia are fully documented Over 100 scientists from 16 countries attended the three day conference during which time 68 multi disciplinary presentations concerning dopamine systems and their regulation were made Limbic Motor Circuits and Neuropsychiatry Peter W. Kalivas,Charles D. Barnes,2019-06-04 Published in 1993 Limbic Motor Circuits and Neuropsychiatry explores the neural circuitry employed by mammals to interpret environmental stimuli that provoke adaptive behavioral responses Internationally recognized biomedical scientists have contributed chapters that describe and evaluate the anatomy physiology pharmacology and pathophysiology of how motivationally relevant environmental or interoceptive stimuli are translated into adaptive or maladaptive behavioral responses The book also examines how classic limbic nuclei communicate with classic motor systems and the implications in neuropsychiatric disorders This reference presents exciting new information that will interest neuroscientists psychiatrists neuropsychopharmacologists and behavioral pharmacologists

The Modulation of Dopaminergic Neurotransmission by Other Neurotransmitters Charles R. Ashby, Jr.,1995-12-20 This book presents information from different scientific disciplines behavioral biochemical electrophysiological anatomical and medical to detail the interaction of the neurotransmitter dopamine DA with other neurotransmitters or neuromodulators in the brain Internationally recognized experts discuss the interaction of DA with monoaminergic transmitters such as norepinephrine GABA acetylcholine and serotonin as well as neuropeptide neurotransmitters neuromodulators such as neurotensin cholecystokinin and the opioid peptides This is also the first book to include data from positron emission tomography PET studies examining the interaction of neurotransmitters in the brain Central D1 Dopamine Receptors M. J. Goldstein,2013-11-21 The development of a selective D1 dopamine DA receptor antagonist SCH 23390 stimulated a number of studies on the functions mediated by central DA receptor subtypes It was generally assumed that the central D1 DA receptor isa molecular entity whose function awaits further discovery The papers presented in this volume clearly show that this is no longer the case and that D1 DA receptors have many behavioral fuctions which might be altered in pathological states A number of papers have recognized the interdependence of the regulatory functions of the D1 DA receptors with D2 and other receptor proteins and vice versa The biochemical pharmacological and morphological characterization of the D1 and D2 DA receptor binding proteins as well as of DARPP 32 illustrates the complex interactions between various macromolecules Procedures described for the purification of the D1 and D2 DA receptor subtypes are fundamental for future studies on the mechanisms involved in the coupling of the receptor proteins with signal transducing systems Several studies in this volume show that D1 DA receptors have behavioral functions and that they are often similar to the responses mediated by D2 DA receptors but in some instances reflect divergent neuronal activity of both systems The

knowledge of the physiology and biochemistry of the central DA receptor subtypes could lead to the development of a new generation of drugs which ameliorate some mental and neurological dysfunctions without producing severe undesirable side effects **Clinical Pharmacology in Psychiatry** Svein G. Dahl,Lars F. Gram,2012-12-06 This volume collects the invited lectures and some selected contributions presented at the 5th International Meeting on Clinical Pharmacology in Psychiatry which was held 26 30 June 1988 at the University of Troms0 Norway The 24 h of daylight at the northernmost university in the world al lowed for long pleasant and productive sessions The title of the conference as well as a number of the topics covered represent a continuation of four previous conferences the first held in Chicago in 1979 and organized by the late Earl U sdin and colleagues The earlier conferences have been documented in Clinical Pharmacology in Psychiatry edited by E Usdin Elsevier New York 1981 Clinical Pharmacology in Psychiatry Neuroleptic and Antidepressant Research edited by E Usdin S G Dahl L F Gram and o Lingjrerde Macmillan Publishers Ltd London 1981 Clinical Pharmacology in Psychiatry Bridging the Experimental Therapeutic Gap edited by LF Gram E Usdin S G Dahl P Kragh Sorensen P L Morselli and F Sjoqvist Macmillan Publishers Ltd London 1983 and Clinical Pharmacology in Psychiatry Selectivity in Psychotropic Drug Action Promises or Problems edited by S G Dahl L F Gram S M Paul and W Z Potter Psychopharmacology Series 3 Springer Heidelberg 1987 **The Biochemical Basis of Neuropharmacology** Jack R. Cooper,Floyd E. Bloom,Robert H. Roth,2003 Aside from the usual updating of material the major change in this edition is an extensive rewriting of the chapter on memory and learning to emphasize that genes that are involved in behavior are not immutable but their expression can be modified by transcription factors Thus with respect to learning that old question about which is more important nature or nuture genetics or environment should be answered with the question which leg is more important for walking the left or the right

NIDA Research Monograph ,1976 Cocaine Matthew P. Galloway,Francis J. White,1991-10-29 This book brings together for the first time state of the art research from both the basic sciences and the clinical fields to present an in depth discussion of the numerous effects of cocaine The issues discussed include metabolism and distribution of cocaine behavioral and electrophysiological actions of cocaine clinical aspects of cocaine associated with addiction and abuse on cardiovascular function and exposure of infants to cocaine during gestation The unique multidisciplinary perspective of this book regarding on going research on cocaine and drug abuse will be useful to researchers clinicians health care practitioners and graduate students who need to stay abreast of the most current information available on this drug Activation of Immediate Early Genes by Drugs of Abuse Reinhard Grzanna,Roger M. Brown,National Institute on Drug Abuse,1993 This monograph is based on the papers and discussions from a technical review on Activation of Immediate Early Genes by Drugs of Abuse held on June 3 4 1991 in Rockville MD The technical review was sponsored by the National Institute on Drug Abuse NIDA

Stimulant Drugs and ADHD Mary V. Solanto,Amy Frances Torrance Arnsten,F. Xavier Castellanos,2001 Stimulant drugs are widely used in the treatment of ADHD in children and adults Hundreds of studies over the past 60 years have

demonstrated their effectiveness in improving attention span increasing impulse control and reducing hyperactivity and restlessness Despite widespread interest in these compounds however their mechanisms of action in the central nervous system have remained poorly understood Recent advances in the basic and clinical neurosciences now afford the possibility of elucidating these mechanisms The current volume is the first to bring this expanding knowledge to bear on the central question of why and how stimulants exert their therapeutic effects The result is a careful comprehensive and insightful integration of material by well known scientists that significantly advances our understanding of stimulant effects and charts a course for future research Part I presents a comprehensive description of the clinical features of ADHD and the clinical response to stimulants Part II details the cortical and subcortical neuroanatomy and functional neurophysiology of dopamine and norepinephrine systems with respect to the regulation of attention arousal activity and impulse control and the effects of stimulants on these systems Part III is devoted to clinical research including recent studies of neuroimaging genetics pharmacodynamic and pharmacokinetic properties of stimulants effects on cognitive functions neurophysiological effects in humans with and without ADHD and in non human primates and comparison of stimulants and non stimulants in the treatment of ADHD Part IV is a masterful synthesis that presents alternative models of stimulant drug action and generates key hypotheses for continued research The volume will be of keen interest to researchers and clinicians in psychiatry psychology and neurology neuroscientists studying stimulants and those pursuing development of new drugs to treat ADHD

Molecular and Cellular MR Imaging Michel M.J. Modo,Jeff W.M. Bulte,2007-03-28 The ability of molecular and cellular imaging to track the survival migration and differentiation of cells in vivo as well as monitor particular gene expression in living subjects is rapidly moving from the research laboratory into daily clinical settings The interdisciplinary nature of the field mandates a constant dialogue among molecular and **The Basal Ganglia III** Giorgio Bernardi,Malcolm B. Carpenter,G. Di Chiara,M. Morelli,P. Stanzione,2012-12-06 This volume represents the collected papers presented at the Third Triennial Symposium of the International Basal Ganglia society IBAGS held at Capo Boi Italy June 10 13 1989 About 300 members of the society and participants attended the symposium which was held in a delightful environment conducive to the formal and informal exchange of scientific thought The interdisciplinary nature of the symposium was unique in its coverage of the neurosciences from molecular biology to clinical and behavioural studies The 80 papers collected here reflect the wide spectrum and the depth of studies on virtually all aspects of the basal ganglia Unfortunately this book does not capture the cordial and congenial atmosphere which has characterized this and all prior symposia of the Society Any cooperative endeavour of this kind requires a tremendous effort and dedication usually by a small number of individuals The Society is especially pleased to acknowledge the support and encouragement of the Italian Ministry of university and Scientific Research and the Italian National Research Council In addition the society received financial support from numerous Foundations and corporations which are listed separately under acknowledgements Finally the Editors are pleased

that Plenum Press which has published the two previous symposia has accepted this program for publication It is our hope that vast scientific efforts reflected in these pages will be widely disseminated and further encourage every kind of research related to the basal ganglia *The Basal Ganglia VI* Ann M. Graybiel,Mahlon R. Delong,Stephen T. Kitai,2012-12-06 This volume the sixth in the IBAGS series summarizes major contributions in clinical and basic research on the basal ganglia The sixth meeting of the Society was held on Cape Cod in the state of Massachusetts USA in October 1998 Altogether 16 countries were represented by 227 participants This volume contains papers contributed by participants The focus of the sixth triennial IBAGS meeting and of this volume was to bring to gether leaders in basic and clinical science to address two sets of still persisting questions in the field The first set focuses on the functions of the basal ganglia in health and disease What are the core functions of the basal ganglia and cortico basal ganglia loops How are these core functions disrupted in disorders affecting the basal ganglia How do we account for the broad range of behaviors affected by basal ganglia disorders and for the increasing evidence that the basal ganglia influence cognitive as well as motor functions These issues are addressed in the first five sections of the current volume which summarize advances in the study of basal ganglia disorders based on studies in humans Section 1 new results obtained with experimental animal models of basal ganglia disorders Section 2 results of experiments on information coding in the basal ganglia Section 3 and new information about functions of the basal ganglia related to learning and adaptive motor control Section 4 Addiction Controversies David M. Warburton,2023-04-28 In the past the prototypes for characterizing drug use were heroin and cocaine so that research has focused on possible commonalities between any substance and these drugs Addiction controversies explores the problems of the commonalities approach by looking at dissimilarities as well The first chapters of Addiction Controversies trace the development of modern medical attitudes to drug use and the current controversy over its decriminalization The second set of chapters examines the extent to which drugs have common biological and sociological mechanisms of action and contrasts these explanations The final chapters consider the extent to which the desires for different substances are the same and the biological and social explanations of relapse Clinicians researchers and students in all areas of substance use will be stimulated by these challenges to current thinking and will enjoy the comparative approach that is taken by the contributors to Addiction Controversies *Dopamine in the CNS II* Gaetano Di Chiara,2013-06-29 With contributions by numerous experts *Cocaine Treatment* Frank M. Tims,Carl G. Leukefeld,National Institute on Drug Abuse,1993 This monograph is based on the papers and discussions from a technical review on Advances in Cocaine Treatment held on August 16 17 1990 in Bethesda MD The technical review was sponsored by the National Institute on Drug Abuse NIDA **The Mesolimbic Dopamine System** P. Willner,J?rgen Scheel-Krüger,1991-05-13 The Mesolimbic Dopamine System From Motivation to Action Edited by P Willner Psychology Department City of London Polytechnic London UK and J Scheel Kr ger Psychopharmacological Research Laboratory St Hans Hospital Roskilde Denmark The mesolimbic dopamine system is a

system of neurons innervating the ventral forebrain which utilizes dopamine as its principal neurotransmitter In recent years this system has become one of the most heavily researched pathways within the brain particularly in relation to its potential involvement in major psychiatric disorders such as schizophrenia mania depression and drug dependence This volume provides a unique and timely multidisciplinary synthesis of our current knowledge of the anatomy pharmacology physiology and behavioural functions of the mesolimbic system and its operation in health and mental disorder **Antipsychotics** John G. Csernansky,2012-12-06 Antipsychotic drugs were first discovered in 1953 and not since the late 1970s has the Handbook of Experimental Pharmacology taken up this topic A new treatment of this topic would be due under any circumstances however this is now particularly true since remarkable progress has been made on several fronts in furthering our understanding of the mechanisms of antipsychotic drug action First we have learned that schizophrenia is an illness with particu lar neuroanatomical abnormalities many of which suggest that the illness is caused by errors in neurodevelopment These findings have helped to form a context for understanding neurochemical aberrations in the illness and suggest new approaches for pharmacological treatment Propelled forward by rapid advances in neurochemical anatomy current pathophysiological hypotheses of schizophrenia and antipsychotic drug action have taken on the appearance of complex electrical circuit diagrams Second molecular biology studies have now revealed that there is a multiplicity of dopamine receptors i e D DZshort j DZlong D D and D some of which may become entirely new targets for 3 4 s antipsychotic drug action Ironically the development of drugs that are selec tive for these receptors and that can be used to investigate their function lags behind yet the discovery of these new receptors offers unparalleled opportu nities for developing drugs with improved efficacy and fewer side effects **The Basal Ganglia IV** Gerard Percheron,John S. McKenzie,Jean Féger,2012-12-06 Emphasis on new issues and emerging concepts insures that the information presented is still timely A compelling source of information on recent research in the field Journal of Chemical Neuroanatomy May 1997

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