

Interactive report

Schizophrenia: pathophysiological mechanisms — a synthesis¹

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Abstract

A Nobel Symposium, 'Schizophrenia: Pathophysiological Mechanisms' was held in Stockholm, October 1–3, 1998. The topics ranged from etiology, genetics, neuropathology, neurotransmitter, brain imaging, to integrative aspects including cognition and language. The collective amount of information is already enormous and will rapidly increase with advances in molecular pathology, gene transcript profiling and non-invasive imaging techniques. Probably reflecting the complexity is the absence of a disease model that can accommodate the data and explain its roots. In the process of moving from simplistic mechanisms involving single or a few interacting neurotransmitters or circuits and turning to more complex interactive models, there is a need for improved data storage and retrieval. Stochastic search in chemical libraries for potential new drug candidates coupled with rational approaches in their final design may improve therapeutic efficacy. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Schizophrenia; Etiology; Neurodevelopment; Neuropathology; Neuropharmacology

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1. Introduction

The purpose of the Nobel Symposium, Schizophrenia: Pathophysiological Mechanisms, October 1–3, 1998, was to address fundamental aspects on the pathophysiology of schizophrenia. Despite the substantial research efforts that have been made to date, there is still no single theoretical framework that fits the data. Particularly frustrating is that the fundamental questions of today are more or less the same as originally posed by Kraepelin and Bleuler (see

Andreasen this volume). Principally important is the question whether the variable symptoms registered from and experienced by schizophrenics can be characteristic of one disease and not several. Presentations at the symposium highlighted schizophrenia as a disease with very variable clinical manifestations. Terms used by the different contributors to this symposium to characterize schizophrenia varied from an emotional disease to a cognitive disease, congruent with Kraepelin's term 'dementia praecox'. The variable terminology is probably more a reflection of the focus or methodology that a particular author is familiar with, rather than a real difference. My percept perpetuated at the symposium was that schizophrenia is a disease and

¹ Published on the World Wide Web on 3 November 1999.

Schizophrenia Pathophysiological Mechanisms

**György Németh, Peter Falkai, Agata
Szulc**



Schizophrenia Pathophysiological Mechanisms:

Trajectories of Brain Abnormalities in Early Schizophrenia Antonio Vita, Luca De Peri, Stefan Borgwardt, 2021-10-20

Visual Dysfunction in Schizophrenia: A View into the Mechanisms of Madness? Randolph Blake, Steven Silverstein, Brian P. Keane, Michael Green, Szabolcs Kéri, 2015-05-11 Research on visual perception in schizophrenia has a long history. However, it is only recently that it has been included in mainstream efforts to understand the cognitive neuroscience of the disorder and to assist with biomarker and treatment development e.g. the NIMH CNTRICS and RDoC initiatives. Advances in our understanding of visual disturbances in schizophrenia can tell us about both specific computational and neurobiological abnormalities and about the widespread computational and neurobiological abnormalities in the illness of which visual disturbances constitute well studied replicable low level examples. Importantly, far from being a passive sensory registration process, visual perception is active, inferential and hypothesis generating and therefore can provide excellent examples of breakdowns in general brain functions in schizophrenia. Despite progress made in understanding visual processing disturbances in schizophrenia, many challenges exist and many unexplored areas are in need of examination. For example, the directional relationships between perceptual and cognitive disturbances e.g. in attention, memory, executive function, predictive coding remain unclear in many cases, as do links with symptoms including visual hallucinations. The effect of specific visual disturbances on multisensory integration in schizophrenia has also not been explored. In addition, few studies of vision in schizophrenia have used naturalistic stimuli including real world objects and almost no studies have examined processing during interaction with objects or visual exploration which can provide important data on functioning of the perception for action pathway. Relatedly, studies of visual processing in schizophrenia have also not been conducted within contexts that include emotional stimulation and the presence of reinforcers characteristic of many real world situations and the consequences of this are likely to be an incomplete view of how and when perception is abnormal in the condition. An additional important area involves treatment of visual disturbances in schizophrenia. Two major questions regarding this are 1) can visual processing be improved in cases where it is impaired and by what types of interventions affecting which cognitive and neurobiological mechanisms and 2) what are the clinical and functional benefits of improving specific visual functions in people with schizophrenia. Other important and understudied questions concern 1) the extent to which indices of visual functioning can serve as biomarkers such as predictors of relapse, treatment response and/or recovery, 2) the potential role of visual functioning in diagnosing and predicting illness, 3) the extent to which some visual perception disturbances are diagnostically specific to schizophrenia and 4) the extent to which visual disturbances are truly manifestations of disease as opposed to aspects of normal variation that in combination with disease serves to modify the clinical presentation. This Frontiers Research Topic explores some of these and other issues facing this exciting interface between vision science and schizophrenia research. We include papers that span the entire range of

different Frontiers paper types including those that are data driven using psychophysics electroencephalography neuroimaging computational and animal models and other methods reviews hypotheses theories opinion methods areas of impact and historical perspectives **Schizophrenia Bulletin** ,2011 Neurobiology of Mental Illness Dennis S. Charney, Eric J. Nestler, 2005-07-21 The new edition of this definitive textbook reflects the continuing reintegration of psychiatry into the mainstream of biomedical science The research tools that are transforming other branches of medicine epidemiology genetics molecular biology imaging and medicinal chemistry are also transforming psychiatry The field stands poised to make dramatic advances in defining disease pathogenesis developing diagnostic methods capable of identifying specific and valid disease entities discovering novel and more effective treatments and ultimately preventing psychiatric disorders The Neurobiology of Mental Illness is written by world renowned experts in basic neuroscience and the pathophysiology and treatment of psychiatric disorders It begins with a succinct overview of the basic neurosciences followed by and evaluation of the tools that are available for the study of mental disorders in humans The core of the book is a series of consistently organized sections on the major psychiatric disorders that cover their diagnostic classification molecular genetics functional neuroanatomy neurochemistry and pharmacology neuroimaging and principles of pharmacotherapy Chapters are written in a clear style that is easily accessible to practicing psychiatrists and yet they are detailed enough to interest researchers and academics For this second edition every section has been thoroughly updated and 13 new chapters have been added in areas where significant advances have been made including functional genomics and animal models of illness epidemiology cognitive neuroscience postmortem investigation of human brain drug discovery methods for psychiatric disorders the neurobiology of schizophrenia animal models of anxiety disorders neuroimaging studies of anxiety disorders developmental neurobiology and childhood onset of psychiatric disorders the neurobiology of mental retardation the interface between neurological and psychiatric disorders the neurobiology of circadian rhythms and the neurobiology of sleep disorders Both as a textbook and a reference work Neurobiology of Mental Illness represents a uniquely valuable resource for psychiatrists neuroscientists and their students or trainees **Dopaminergic Alterations in Schizophrenia** Silvia Gatti McArthur, Pierre Michel Llorca, Carol A. Tamminga, Andrew J. Grottick, Mark David Tricklebank, Jean-Claude Martel, 2021-05-03 **Neuroimaging Genetics** Kristin L. Bigos, Ahmad R. Hariri, Daniel R. Weinberger, 2016-02-03 The field of neuroimaging genetics has grown exponentially over the past decade To date there are more than 10 000 published papers involving MRI PET MEG and genetics Neuroimaging Genetics Principles and Practices is the comprehensive volume edited by Drs Bigos Hariri and Weinberger and co authored by the preeminent scholars in the field This text reviews the basic principles of neuroimaging techniques and their application to neuroimaging genetics The work presented in this volume elaborates on the explosive interest from diverse research areas in psychiatry and neurology in the use of imaging genetics as a unique tool to establish and identify mechanisms of risk establish biological significance and extend statistical evidence

of genetic associations Examples throughout highlight the application of imaging genetics to understand neurochemical systems and pathways explore relationships between genetics and the structural and functional connectivity in human brain and provide insight into mechanisms of risk for psychiatric and neurologic illness

Schizophrenia Bernard Fried, Bernard Sherma, 2009-09-30 Edited by the president of the World Federation of Societies of Biological Psychiatry and featuring an international list of world renown contributors Schizophrenia Second Edition provides psychiatrists neurologists and psychologists with a comprehensive handbook on the latest schizophrenia research and management from diagnosis through treatment

Charney & Nestler's Neurobiology of Mental Illness Dennis S. Charney, Pamela B. Sklar, Eric J. Nestler, Joseph D. Buxbaum, 2018 In the years following publication of the DSM 5 R the field of psychiatry has seen vigorous debate between the DSM's more traditional diagnosis oriented approach and the NIMH's more biological dimension based RDoC research domain criteria approach Charney Nestler's Neurobiology of Mental Illness is an authoritative foundation for translating information from the laboratory to clinical treatment and its fifth edition extends beyond this reference function to acknowledge and examine the controversies different camps and thoughts on the future of psychiatric diagnosis In this wider context this book provides information from numerous levels of analysis including molecular biology and genetics cellular physiology neuroanatomy neuropharmacology epidemiology and behavior Sections and chapters are edited and authored by experts at the top of their fields No other book distills the basic science and underpinnings of mental disorders and highlights practical clinical significance to the scope and breadth of this classic text In this edition Section 1 which reviews the methods used to examine the biological basis of mental illness in animal and cell models and in humans has been expanded to reflect critically important technical advances in complex genetics including powerful sequencing technologies and related bioinformatics epigenetics stem cell biology optogenetics neural circuit functioning cognitive neuroscience and brain imaging This range of established and emerging methodologies offer groundbreaking advances in our ability to study the brain as well as unique opportunities for the translation of preclinical and clinical research into badly needed breakthroughs in our therapeutic toolkit Sections 2 through 7 cover the neurobiology and genetics of major psychiatric disorders psychoses including bipolar disorder mood disorders anxiety disorders substance use disorders dementias and disorders of childhood onset Also covered within these sections is a summary of current therapeutic approaches for these illnesses as well as the ways in which research advances are now guiding the search for new treatments Each of these parts has been augmented in several different areas as a reflection of research progress The last section Section 8 reconfigured in this new edition now focuses on diagnostic schemes for mental illness This includes an overview of the unique challenges that remain in diagnosing these disorders given our still limited knowledge of disease etiology and pathophysiology The section then provides reviews of DSM 5 R which forms the basis of psychiatric diagnosis in the United States for all clinical work and of RDoC which provides an alternative perspective on diagnosis in heavy use in the research community Also included are

chapters on future efforts toward precision and computational psychiatry which promise to someday align diagnosis with underlying biological abnormalities

Schizophrenia Research Trends Konstance V. Almann, 2007 Schizophrenia is a chronic severe and disabling psychosis which is an impairment of thinking in which the interpretation of reality is abnormal Psychosis is a symptom of a disordered brain Approximately One percent of the population worldwide develops schizophrenia during their lifetime Although schizophrenia affects men and women with equal frequency the disorder often appears earlier in men usually in the late teens or early twenties than in women who are generally affected in the twenties to early thirties People with schizophrenia often suffer symptoms such as hearing internal voices not heard by others or believing that other people are reading their minds controlling their thoughts or plotting to harm them The current evidence concerning the causes of schizophrenia are many It is quite clear that multiple factors are involved These include changes in the chemistry of the brain changes in the structure of the brain and genetic factors Viral infections and head injuries may also play a role New molecular tools and modern statistical analyses allow focusing in on particular genes that might make people more susceptible to schizophrenia by affecting for example brain development or neurotransmitter systems governing brain functioning State of the art imaging techniques are being used to study the living brain They have recently revealed specific subtle abnormalities in the structure and function of the brains of patients with schizophrenia In other imaging studies early biochemical changes that may precede the onset of disease symptoms have been noted prompting examination of the neural circuits that are most likely to be involved in producing those symptoms This book presents new and important research in the field

The Bereitschaftspotential Marjan Jahanshahi, Mark Hallett, 2012-12-06 Kornhuber and Deecke first recorded and reported the Bereitschaftspotential in 1964 The aim of this book is to bring together in a single volume some of the important research on the Bereitschaftspotential and other movement related cortical potentials and to highlight and address some of the pertinent questions relating to the Bereitschaftspotential and to identify the key issues for future investigation in this field This book represents a unique compilation of information about the Bereitschaftspotential and related cortical potentials and techniques for measuring preparatory processes in the brain The book will be of interest to motor physiologists psychologists and neurologists working in clinical or research laboratories

Neuroinflammation and Schizophrenia Golam M. Khandaker, Urs Meyer, Peter B. Jones, 2020-01-22 This book provides a comprehensive summary of the cutting edge scientific evidence regarding the role of immune system in the pathogenesis and treatment of schizophrenia and related psychotic disorders It illustrates the role of inflammation and immunity in schizophrenia drawing on both basic science and clinical research The chapters provide up to date summaries of immunological risk factors for schizophrenia and related psychotic disorders and underlying mechanisms as informed by neuroimaging genetic clinical and animal experimental studies In addition the book will illuminate the scope for immunological treatment for schizophrenia

Novel Antipsychotics Within and Beyond Clinical Trials: The Treatment of Overlapping Psychiatric Disorders with

D3-D2 Partial Agonists György Németh, Peter Falkai, Agata Szulc, 2022-11-10 **Handbook of Laboratory Animal Science** Jann Hau, Steven J. Schapiro, Gerald L. Van Hoosier Jr., 2002-12-26 The conservative nature of animal evolution makes animal models the ideal tool for learning about human biology The Handbook of Laboratory Animal Science Second Edition Animal Models Volume II addresses the development and application of models in different areas of biomedical research and details the criteria used to choose animal species and *Deep Brain Stimulation (DBS) Applications* Tipu Aziz, Alex Green, 2018-03-23 This book is a printed edition of the Special Issue Deep Brain Stimulation DBS Applications that was published in Brain Sciences **Functional Aspects of Mesoscopic Brain Oscillations: Insights From in Vivo and in Vitro Studies** Gürsel Caliskan, Sanja Mikulovic, Gabrielle Girardeau, 2022-08-01 *Advances in Schizophrenia Research 2009* Wagner F. Gattaz, Geraldo Busatto Filho, 2009-11-12 Schizophrenia remains an important challenge to psychiatry with its causes and underlying brain mechanisms yet to be fully revealed Currently available treatments are neither universally effective nor without unwanted effects These aspects together with the high prevalence of schizophrenia its often debilitating nature and the associated family and social burden make this mental disorder one of the most complex public health issues of our times The purpose of the Advances in Schizophrenia Research series is to provide comprehensive periodic reviews of the wide range of research studies carried out around the world with the dual purpose of solving the schizophrenia puzzle and providing clues to new forms of treatment and prevention for this disorder A special feature of the series is its broad scope virtually encompassing all fields of schizophrenia research epidemiology and risk factors psychopathology diagnostic boundaries cognition outcome and prognosis pathophysiology genetics pharmacological and psychological forms of treatment and rehabilitation community care and stigmatization **Serotonin** Bernard Haber, 2012-12-06 The vast growth of knowledge in recent years concerning the functional role of serotonergic systems in central nervous system function prompted the organization of the symposium The organizing committees felt at the onset that the field of serotonin research had grown so rapidly that it would be impossible to cover every aspect of it in individual symposia Thus it was felt that certain areas of research had to be omitted due to time constraints and we extend an apology to the researchers in areas not included in these proceedings Rather it was hoped to provide a balance overview of the field starting with the anatomy of serotonergic systems and proceeding to the level of the serotonergic receptors at the cell membrane and then inside the neuron to discuss the regulation of serotonin biosynthesis and integration within indoleamine systems The functional aspects of serotonergic transmission focused on the emerging role of this amine in the processing of nociceptive information singly or in tandem with other neurotransmitters or neuromodulators A separate symposium dealt with a variety of animal models suitable for the analysis of the role of serotonin in behavior and finally led to the evaluation of serotonin metabolism in the study of abnormal human behavior The editors would like to dedicate these proceedings on Serotonin Current Aspects of Neurochemistry and Function to two pioneers in this field Dr Irving Page and Dr Maurice Rapport **Novel**

Antischizophrenia Treatments Mark A. Geyer, Gerhard Gross, 2012-08-31 This volume will try to put current therapy achievements shortcomings remaining medical needs and emerging new targets into the context of increasing knowledge regarding the genetic and neurodevelopmental contributions to the pathophysiology of schizophrenia Some of the chapters will also deal with respective experimental and clinical methodology biomarkers and translational aspects of drug development The volume will concentrate on reviewing the ongoing research attempting to identify novel treatments for the cognitive deficits and negative symptoms of schizophrenia which are not treated adequately by current antipsychotic medications

Personalized Nutrition Artemis P. Simopoulos, John A. Milner, 2010 Awareness of the influence of our genetic variation to dietary response nutrigenetics and how nutrients may affect gene expression nutrigenomics is prompting a revolution in the field of nutrition Nutrigenetics Nutrigenomics provide powerful approaches to unravel the complex relationships among nutritional molecules genetic variants and the biological system This publication contains selected papers from the 3rd Congress of the International Society of Nutrigenetics Nutrigenomics held in Bethesda Md in October 2009 The contributions address frontiers in nutrigenetics nutrigenomics epigenetics transcriptomics as well as non coding RNAs and posttranslational gene regulations in various diseases and conditions In addition to scientific studies the challenges and opportunities facing governments academia and the industry are included Everyone interested in the future of personalized medicine and nutrition or agriculture as well as researchers in academia government and industry will find this publication of the utmost interest for their work

Psychosis Kenjiro Fukao, 2022-02-02 Psychosis has been the central subject of psychiatric research for more than a century and yet it remains an intriguing enigma This volume reviews the current status of research on psychosis in three different aspects namely phenomenology which is the philosophical conceptual basis of psychosis psychopathology which is the clinical manifestations of psychosis and pathophysiology which is the scientific pursuit for the mechanism of psychosis Chapters focus on schizophrenia covering such topics as clinical staging negative symptoms epigenetics DNA methyltransferases and more

Reviewing **Schizophrenia Pathophysiological Mechanisms**: Unlocking the Spellbinding Force of Linguistics

In a fast-paced world fueled by information and interconnectivity, the spellbinding force of linguistics has acquired newfound prominence. Its capacity to evoke emotions, stimulate contemplation, and stimulate metamorphosis is truly astonishing. Within the pages of "**Schizophrenia Pathophysiological Mechanisms**," an enthralling opus penned by a very acclaimed wordsmith, readers set about an immersive expedition to unravel the intricate significance of language and its indelible imprint on our lives. Throughout this assessment, we shall delve into the book's central motifs, appraise its distinctive narrative style, and gauge its overarching influence on the minds of its readers.

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