

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

Konstance V. Almann



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 *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 *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 *Handbook of Schizophrenia Spectrum Disorders, Volume I* Michael S Ritsner, 2011-04-06 A few disorders have some of the same symptoms as schizophrenia including schizoaffective disorders schizophreniform disorder schizotypal and schizoid personality disorders delusional disorder and autism schizophrenia spectrum disorders Since the 2000 there has been significant progress in our understanding of the early presentations assessment suspected neuropathology and treatment of these disorders Recent technological breakthroughs in basic sciences hold promise for advancing our understanding of the pathophysiology of schizophrenia spectrum disorders This collective monograph reviews recent researches regarding the origins onset course and outcome of schizophrenia spectrum disorders In particular this book will be illustrate new developments in terms of conceptual models and research methodology genetics and genomics brain imaging and neurochemical studies neurophysiology and information processing in schizophrenia spectrum disorders patients Also will be highlighted new developments in our understanding of the childhood psychosis prodromal and first episode states in treatment and rehabilitation Thus the purpose of this book is to provide up to date overview of the rapid advances made in the clinical and basic science studies supporting our understanding of the relationship between cerebral processes and clinical cognitive and other presentations of the schizophrenia spectrum disorders In addition this book aims to monitor important research developments which may be relevant to treatment and rehabilitation of patients **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 **Cortical Deficits in Schizophrenia** Patricio

O'Donnell,2007-09-23 The genetics of schizophrenia have taken the driver seat in the research lated to this disorder in recent years For a long time it had been known that sharing genes with someone affected with schizophrenia conferred a 50% chance of acquiring the disease Although this is fifty times the incidence in the normal population it was evident that genes could not explain all factors involved At best one could think of a combination of gene traits conferring predisposition for the disease Now it is evident that although there are no genes that individually confer a strong liability several candidate gene alleles do confer some risk and perhaps a combination of genes could cause the emergence of symptoms in this multi faceted psychiatric condition As the research on predisposing genes soars it is becoming clear that we need to be able to identify cellular processes the genes control and to provide pat physiological scenarios that could link those cellular phenomena with sy toms In this book we have chosen to elaborate on that link The contributions to this book have been requested to reflect the current state of the connection between schizophrenia genetics and pathophysiology The book opens with a chapter by Paul Harrison highlighting the several convergence points among the diverse schizophrenia related genes Schizophrenia

Bulletin ,2009 **Neuropsychopharmacology of Psychosis: Relation of Brain Signals, Cognition and Chemistry**

André Schmidt,Stefan Borgwardt,2015-04-22 Nothing provided New Insights Into Schizophrenia-Related Neural and Behavioral Phenotypes Yuh-Man Sun, Ji Chen,2023-06-01 *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

Psychoneuroendocrinology of Psychosis Disorders Grazia

Rutigliano, Mary V. Seeman, Boris Chaumette, 2021-01-04 [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 **Drug Discovery for Schizophrenia** Tatiana V Lipina,2024-12-06 Following progress in schizophrenia since 2015 this new volume covers the advancing knowledge of scientists and clinicians in drug discovery The book enhances our understanding of pathological neural communication between the peripheral nervous system PNS and central nervous system CNS in patients with schizophrenia Although 75% of neural information passes through the PNS interactions between the PNS and CNS in schizophrenia remain understudied Consequently the current view of schizophrenia requires improvement to facilitate diagnostics and drug development In this context this second volume presents current evidence that views schizophrenia as a mild abnormal maldevelopment of the entire body This includes impaired functioning of sensory systems e g olfaction and changes in blood biochemistry and the autonomic nervous system e g vagal body to brain communication Alternative approaches to prevent and treat schizophrenia involve advanced techniques such as opto and chemo genetics as well as local administration of compounds e g intranasally targeting PNS based cellular and molecular pathways Chapters focus on the genetics of schizophrenia leveraging technological advancements in high throughput genomics and computational biology These tools help identify novel therapeutic targets and enable the safe repurposing of existing medications The book emphasizes the need to develop new strategies for creating

more suitable animal models of schizophrenia considering the crucial role of the PNS in the disorder's aetiology. While PNS based mechanisms are often overlooked, discussing them with caution is essential. Systematically accumulating knowledge about PNS/CNS pathological mechanisms will benefit psychiatric neuroscience, offering fresh perspectives for drug discovery. Overall, the book synthesizes expert opinions from academia and clinical studies covering progress in genetics, pharmacogenetics, molecular and cellular neuroscience, neurobiology, pharmacology and animal models.

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.

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

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