

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

**Daniel C. Javitt, Abel Lajtha, Joshua
Kantrowitz**



Schizophrenia Pathophysiological Mechanisms:

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

Schizophrenia Bulletin, 2011 **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, characteristics 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

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 an 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 *The Spectrum of Psychotic Disorders* Daryl Fujii,Iqbal Ahmed,2007-03-08 The spectrum of psychotic disorders encompasses as many as 25 different etiologies ranging from the primary psychoses through those secondary to medical conditions drugs and medications and sensory impairments This book provides a one stop comprehensive review of these disorders and gives quick comparisons for diagnostic decision making to help with difficult differential diagnoses Every chapter is uniformly structured to show comparisons between each disorder of presentation course and underlying neuropathology Evidence for each etiology is also rated indicating the confidence level the reader can place in the current findings The international team of authors also examines data supporting a unitary neurobiological model of psychosis and the hypothesis that psychosis is a neurobiological syndrome similar to aphasia or apraxia This book represents a paradigm shift in understanding classifying and diagnosing these disorders providing directions for future research and treatment It will be of great interest to psychiatrists and neuroscientists alike

Schizophrenia Daniel R. Weinberger,Paul Harrison,2011-07-13 Schizophrenia is one of the most complex and disabling diseases to affect mankind Relatively little is known about its nature and its origins and available treatments are inadequate for most patients As a result there are inevitable controversies about what causes it how to diagnose it and how best to treat it However in the past decade there has been an explosion of new research with dramatic discoveries involving genetic etiology and epidemiological risk factors There has also been a catalog of new drugs coming to market and controversy about the relative advantages and disadvantages of newer compared with older therapies In addition developing technologies in genomics molecular biology and neuroimaging provide streams of new information This book represents a definitive essential and up to date reference text on schizophrenia It extensively and critically digests and clarifies recent advances and places them within a clinical context The Editors one American and one British highly respected clinical psychiatrists and researchers and acknowledged experts on schizophrenia have again assembled an outstanding group of contributors from the USA UK Europe and Australia It will be of value to practising psychiatrists and to trainees as well as to clinical and neuroscience researchers interested in keeping up with this field or coming into it The book consists of four sections descriptive aspects biological aspects physical treatments and psychological and social aspects It reviews the theoretical controversies over symptomatology classification and aetiology particularly pertinent as DSM V is being developed the relationship of schizophrenia to the other psychoses the significance of positive and negative symptoms and pre morbid personality It describes a variety of approaches to integrating the vast research data about schizophrenia including neurodevelopmental genetic pharmacological brain imaging and psychological findings The biological treatment section reviews the comparative efficacy of various drugs the management of drug resistant patients and both neurological and

metabolic complications The final section looks at psychological therapies social outcomes and the economics of schizophrenia Highly Commended in the Psychiatry section of the 2012 BMA Book Awards **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

Inflammation in Neuropsychiatric Disorders Rossen Donev, 2012-08-02 Published continuously since 1944 the Advances in Protein Chemistry and Structural Biology serial has been a continuous essential resource for protein chemists Covering reviews of methodology and research in all aspects of protein chemistry including purification expression proteomics modeling and structural determination and design each volume brings forth new information about protocols and analysis of proteins while presenting the most recent findings from leading experts in a broad range of protein related topics Covers reviews of methodology and research in all aspects of protein chemistry Brings forth new information about protocols and analysis of proteins while presenting the most recent findings from leading experts in a broad range of protein related topics

Foundations and Practical Applications of Cognitive Systems and Information Processing Fuchun Sun, Dewen Hu, Huaping Liu, 2013-09-21 Foundations and Practical Applications of Cognitive Systems and Information Processing presents selected papers from the First International Conference on Cognitive Systems and Information Processing held in Beijing China on December 15 17 2012 CSIP2012 The aim of this conference is to bring together experts from different fields of expertise to discuss the state of the art in artificial cognitive systems and advanced information processing and to present new findings and perspectives on future development This book introduces multidisciplinary perspectives on the subject areas of Cognitive Systems and Information Processing including cognitive sciences and technology autonomous vehicles cognitive psychology cognitive metrics information fusion image video understanding brain computer interfaces visual cognitive processing neural computation bioinformatics etc The book will be beneficial for both researchers and practitioners in the fields of Cognitive Science Computer Science and Cognitive Engineering Fuchun Sun and Huaping Liu are both professors at the Department of Computer Science Technology Tsinghua University China Dr Dewen Hu is a professor at the College of Mechatronics and Automation National University of Defense Technology Changsha China

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 *The Prefrontal Cortex: Its Structure, Function and Pathology* J.P.C. de Bruin, M.A. Corner, M.G.P. Feenstra, C.G. Van Eden, H.B.M. Uylings, 1991-03-05

Thanks to a resurgence of interest and a recent proliferation of research techniques much new and illuminating data has emerged during the last decade relating to the prefrontal cortex particularly in primates and rodents In view of this progress the 16th International Summer School of Brain Research was held in Amsterdam The Netherlands from 28 August to 1 September 1989 devoted to the topic of The Prefrontal Cortex Its Structure Function and Pathology The edited proceedings embodied in this 85th volume of Progress in Brain Research fall into three sections the first of which following two introductory chapters discusses the present knowledge of the organization of prefrontal cortical systems In the second section developmental and plasticity aspects in rodent and human cortex are considered whilst the third section deals extensively with the functional aspects characteristic for the prefrontal cortex in primates rats and rabbits The last section reviews several topics on dysfunction of prefrontal cortex in rat and man including a historical review on psychosurgery

Handbook of Neurochemistry and Molecular Neurobiology Daniel C. Javitt, Abel Lajtha, Joshua Kantrowitz, 2009-09-22 This volume of the Handbook of Neurochemistry and Molecular Neurobiology focuses on neurochemical aspects of schizophrenia Chapters cover the full range of schizophrenia symptoms and anatomical pathologies from neurochemical and molecular biology perspectives Topics include changes in neurotransmitter systems alteration in receptors neurotransmitter release genetic factors protein alterations and redox dysregulation *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 *Personalized Nutrition* A.P. Simopoulos, J.A.

Milner, 2010-04-30 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

Electrophysiology and Psychophysiology in Psychiatry and Psychopharmacology Veena Kumari, Petr Bob, Nash N.

Boutros, 2014-11-08 Psychophysiology is an ever expanding field The application of psychophysiological investigations to psychiatric disorders is likewise expanding and has in fact shed much light on some of the neural processes contributing to the development of psychiatric symptoms and or their amelioration following treatment In the first part of this volume we have selected a number of conditions where psychophysiological investigations have recently provided some insight into the pathophysiology of a particular manifestation e g dissociation or a disorder Although this volume has a main focus on electrophysiological investigative modalities where neuroimaging was complimentary this added insight was included The second part of the volume focuses on novel uses of psychophysiological measures combining it with neuropsychology and imaging where possible in the context of neuropsychiatric research and describes advanced analytical tools Both basic and clinical investigators in this field should find the reviews and interpretations provided clear and informative Clinicians will find this volume easy to assimilate While direct clinical applications may be down the road the insights provided should help the practicing clinicians to have firmer understanding of the complexity of the disorder they manage in everyday practice

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 **New Insights Into Schizophrenia-Related Neural and Behavioral Phenotypes** Yuh-Man Sun, Ji Chen, 2023-06-01 *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

The Enigmatic Realm of **Schizophrenia Pathophysiological Mechanisms**: Unleashing the Language is Inner Magic

In a fast-paced digital era where connections and knowledge intertwine, the enigmatic realm of language reveals its inherent magic. Its capacity to stir emotions, ignite contemplation, and catalyze profound transformations is nothing short of extraordinary. Within the captivating pages of **Schizophrenia Pathophysiological Mechanisms** a literary masterpiece penned with a renowned author, readers set about a transformative journey, unlocking the secrets and untapped potential embedded within each word. In this evaluation, we shall explore the book's core themes, assess its distinct writing style, and delve into its lasting affect the hearts and minds of those who partake in its reading experience.

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