

# Down Syndrome: From Understanding the Neurobiology to Therapy

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Down syndrome (DS) is the most common example of a neurogenetic aneuploid disorder leading to mental retardation. In most cases, DS results from an extra copy of human chromosome 21 producing deregulated gene expression in brain that gives rise to subnormal intellectual functioning. Understanding the consequences of dosage imbalance attributable to trisomy 21 (T21) has accelerated because of recent advances in genome sequencing, comparative genome analysis, functional genome exploration, and the use of model organisms. This has led to new evidence-based therapeutic approaches to prevention or amelioration of T21 effects on brain structure and function (cognition) and has important implications for other areas of research on the neurogenetics of cognition and behavior.

## Introduction

Trisomy for human chromosome 21 (Hsa21) is the most frequent live-born aneuploidy and results in Down syndrome (DS). This is a well recognized syndrome with variable phenotypic expression. DS results in cognitive impairment, dysmorphic features, and a number of mostly nonspecific manifestations for which severity and frequency are highly variable among different individuals.

In DS, deficits in learning, memory, and language lead to a general cognitive impairment, which is typically in the mild-to-moderate range. Morpho-syntax, verbal short-term memory, and explicit long-term memory are usually more impaired, whereas visual-spatial short-term memory, associative learning, and implicit long-term memory are better preserved (for review, see Lott and Dierssen, 2010). However, there is broad phenotypic variability among individuals with DS, and this is likely the result

in part of genetic and epigenetic variation, environmental factors, and stochastic events. Individuals with DS have reduced brain volume with disproportionately smaller volumes in frontal and temporal areas and cerebellum. Lenticular nuclei as well as posterior parietal and occipital cortical gray matter are relatively preserved. For unknown reasons, the parahippocampal gyrus appears larger in DS than in the typical population. Recent evidence also points to a nonmotor contribution from the cerebellum. Seizures occur in a bimodal distribution with ~50% occurring before 1 year of age and 50% occurring in mid-adult life, and are considered to reflect structural brain abnormalities including a paucity of inhibitory neurons and defects in cortical lamination. The latter often herald the development of dementia, and our data suggest that the presence of seizures during the early phase of dementia is associated with poor cognitive performance and rapid decline (I. Lott et al., unpublished observations). These features may be dependent on morphogenetic alterations, but also on a reduced remodeling potential and impaired neural plasticity (Dierssen et al., 2009).

DS presents a unique platform for studying changes of brain aging across the lifespan. By age 40 years, there is a ubiquitous occurrence of plaques and tangles suggestive of Alzheimer disease (AD), but dementia is variable. The earliest manifestations of dementia in DS appear to reflect frontal lobe dysfunction with changes in sociability, emotional-based language, and depressive symptoms. However, physical-chemical dating of amyloid has suggested that it is first deposited in the frontal and entorhinal cortices. The amyloid burden in DS is, in part, related to increases in the expression of the amyloid precursor protein gene, but other factors are likely involved. Oxidative stress secondary to

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# Down Syndrome From Understanding The Neurobiology To Therapy Progress In Brain Research

**Michael R. Kreutz, Carlo Sala**



## **Down Syndrome From Understanding The Neurobiology To Therapy Progress In Brain Research:**

*Down Syndrome: From Understanding the Neurobiology to Therapy* Mara Dierssen, Rafa de la Torre, 2012-06-19 Down syndrome DS is the most common example of neurogenetic aneuploid disorder leading to mental retardation In most cases DS results from an extra copy of chromosome 21 HSA21 producing deregulated gene expression in brain that gives raise to subnormal intellectual functioning The topic of this volume is of broad interest for the neuroscience community because it tackles the concept of neurogenomics that is how the genome as a whole contributes to a neurodevelopmental cognitive disorders such as DS and thus to the development structure and function of the nervous system This volume of Progress in Brain Research discusses comparative genomics gene expression atlases of the brain network genetics engineered mouse models and applications to human and mouse behavioral and cognitive phenotypes It brings together scientists of diverse backgrounds by facilitating the integration of research directed at different levels of biological organization and by highlighting translational research and the application of the existing scientific knowledge to develop improved DS treatments and cures Leading authors review the state of the art in their field of investigation and provide their views and perspectives for future research Chapters are extensively referenced to provide readers with a comprehensive list of resources on the topics covered All chapters include comprehensive background information and are written in a clear form that is also accessible to the non specialist *Changing Brains*, 2013-12-03 This volume of Progress in Brain Research focuses on the applying brain plasticity to advance and recover human ability The volume starts off discussing brain plasticity in the young adults and old brains with follow on discussions regarding the type of neuroscience based training that is on offer in impaired child populations as well as discussing the therapeutics involved in adults Applying brain Plasticity and advances and recover human ability **Synaptic Plasticity** Michael R. Kreutz, Carlo Sala, 2012-02-17 This book introduces the current concepts of molecular mechanisms in synaptic plasticity and provides a comprehensive overview of cutting edge research technology used to investigate the molecular dynamics of the synapses It explores current concepts on activity dependent remodeling of the synaptic cytoskeleton and presents the latest ideas on the different forms of plasticity in synapses and dendrites Synaptic Plasticity in Health and Disease not only supplies readers with extensive knowledge on the latest developments in research but also with important information on clinical and applied aspects Changes in spine synapses in different brain disease states so called synaptopathies are explained and described by experts in the field By outlining basic research findings as well as physiological and pathophysiological impacts on synaptic plasticity the book represents an essential state of the art work for scientists in the fields of biochemistry molecular biology and the neurosciences as well as for doctors in neurology and psychiatry alike *Literature, Neurology, and Neuroscience: Neurological and Psychiatric Disorders*, 2013-12-11 This well established international series examines major areas of basic and clinical research within neuroscience as well as emerging and promising subfields This volume on the neurosciences

neurology and literature vividly shows how science and the humanities can come together and have come together in the past Its sections provide a new broad look at these interactions which have received surprisingly little attention in the past Experts in the field cover literature as a window to neurological and scientific zeitgeists theories of brain and mind in literature famous authors and their suspected neurological disorders and how neurological disorders and treatments have been described in literature In addition a myriad of other topics are covered including some on famous authors whose important connections to the neurosciences have been overlooked e g Roget of Thesaurus fame famous neuroscientists who should also be associated with literature and some overlooked scientific and medical men who helped others produce great literary works e g Bram Stoker s Dracula There has not been a volume with this coverage in the past and the connections it provides should prove fascinating to individuals in science medicine history literature and various other disciplines This book looks at literature medicine and the brain sciences both historically and in the light of the newest scholarly discoveries and insights

**International Review Research in Developmental Disabilities** ,2022-11-08 International Review of Research in Developmental Disabilities Volume 63 highlights new advances in the field with this new volume presenting interesting chapters written by an international board of authors including updates on Theoretical Issues in Adult Siblings Effects of Challenging Behavior on Others Transition among Latino Families Career and Technical Education for adults with IDD and Emotion Regulation and Social Anxiety in Autism Spectrum Disorders Provides the authority and expertise of leading contributors from an international board of authors Presents the latest release in the International Review of Research in Developmental Disabilities series Literature, Neurology, and Neuroscience: Historical and Literary Connections ,2013-11-25 This well established international series examines major areas of basic and clinical research within neuroscience as well as emerging and promising subfields This volume on the neurosciences neurology and literature vividly shows how science and the humanities can come together and have come together in the past Its sections provide a new broad look at these interactions which have received surprisingly little attention in the past Experts in the field cover literature as a window to neurological and scientific zeitgeists theories of brain and mind in literature famous authors and their suspected neurological disorders and how neurological disorders and treatments have been described in literature In addition a myriad of other topics are covered including some on famous authors whose important connections to the neurosciences have been overlooked e g Roget of Thesaurus fame famous neuroscientists who should also be associated with literature and some overlooked scientific and medical men who helped others produce great literary works e g Bram Stoker s Dracula There has not been a volume with this coverage in the past and the connections it provides should prove fascinating to individuals in science medicine history literature and various other disciplines This book looks at literature medicine and the brain sciences both historically and in the light of the newest scholarly discoveries and insights *Cerebellar Learning* ,2014-06-07 Progress in Brain Research is the most acclaimed and accomplished series in neuroscience firmly established as

an extensive documentation of the advances in contemporary brain research The volumes some of which are derived from important international symposia contain authoritative reviews and original articles by invited specialists The rigorous editing of the volumes assures that they will appeal to all laboratory and clinical brain research workers in the various disciplines neuroanatomy neurophysiology neuropharmacology neuroendocrinology neuropathology basic neurology biological psychiatry and the behavioral sciences This volume *The Cerebellum and Memory Formation Structure Computation and Function* covers topics including feedback control of cerebellar learning cortico cerebellar organization and skill acquisition cerebellar plasticity and learning in the oculomotor system and more Leading authors review the state of the art in their field of investigation and provide their views and perspectives for future research The volume reflects current thinking about the ways in which the cerebellum can engage in learning and the contributors come from a variety of research fields The chapters express perspectives from different levels of analysis that range from molecular and cellular mechanisms through to long range systems that allow the cerebellum to communicate with other brain areas

*The Oxford Handbook of Down Syndrome and Development* Jacob A. Burack, Jamie Edgin, Leonard Abbeduto, 2023 The chapter traces some key historical developments in the field of Down syndrome After describing general issues of classification in intellectual disabilities we describe Langdon Down's identification of the syndrome in the 1860s the movement to name the syndrome after Down the identification of trisomy 21 as the syndrome's cause and the beginnings of sustained research attention to the syndrome We end with a glimpse into the future discussing issues of longer life spans more integrated lives and the roles of families organizations and self advocates Working together researchers practitioners and individuals and their families can all continue to advance the lives of persons with Down syndrome

**The Mathematical Brain Across the Lifespan**

, 2016-06-20 The Mathematical Brain Across the Lifespan is the latest volume in the Progress in Brain Research series that focuses on new trends and developments This established international series examines major areas of basic and clinical research within the neurosciences as well as popular and emerging subfields Provides a comprehensive review of the most recent progress in the mathematical brain across the lifespan Explores new trends and developments in the field Enhances the literature of neuroscience by further expanding the established ongoing international series Progress in Brain Research

**Orexin/Hypocretin System** Anantha Shekhar, 2012-09-05 In *The Orexin Hypocretin System Physiology and Pathophysiology* leading researchers and clinicians set the stage for further research on the loss of orexin hypocretin neurons in humans regulation of sleep and wakefulness by the orexin hypocretin system and the role of the orexin hypocretin system in many other physiological processes including feeding autonomic regulation and neuroendocrine regulation Topics of interest include an assessment of the functions and the physiology of orexin hypocretin its pathophysiology in human narcolepsy cataplexy and possible pharmacological treatments The authors also introduce several experimental methods for orexin hypocretin research and using multidisciplinary approaches explain their uses and limitations Authoritative and state

of the art The Orexin Hypocretin System Physiology and Pathophysiology will aid scientists in the search for novel bioactive peptides and their receptors as well as novel physiological insights and opportunities for the clinical treatment of not only narcolepsy but also a broad range of diseases associated with endocrine feeding and body weight regulation R sum de l

diteur **Breathing, Emotion and Evolution** ,2014-09-04 Respiration is one of the most basic motor activities crucial for survival of the individual It is under total control of the central nervous system which adjusts respiratory depth and frequency depending on the circumstances the individual finds itself For this reason this volume not only reviews the basic control systems of respiration located in the caudal brainstem but also the higher brain regions that change depth and frequency of respiration Scientific knowledge of these systems is crucial for understanding the problems in the many patients suffering from respiratory failure This well established international series examines major areas of basic and clinical research within neuroscience as well as emerging subfields **Dopamine** ,2014-06-23 Progress in Brain Research is a well

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**During Neocortical Development** Yuki Hirota,Victor Borrell,Chiaki Ohtaka-Maruyama,2021-06-30 **The Fine Arts, Neurology, and Neuroscience** ,2013-09-12 This volume on neuroscience neurology and the fine arts brings several disciplines together It presents current thoughts and modern examples about how science medicine and the arts have interacted in the past and are still converging This volume specifically explores the history and modern perspective on neurology and neuroscience This volume explores the history and modern perspective on neurology and neuroscience

*Odor Memory and Perception* ,2014-04-23 This well established international series examines major areas of basic and clinical research within neuroscience as well as emerging and promising subfields This volume explores interdisciplinary research on invertebrate and vertebrate models of odor memory and perception as well as human odor memory and perception This book brings together a collection of authors that cut across model systems techniques levels of analysis and

questions to highlight important and exciting advances in the area of olfactory memory and perception The chapters highlight the unique aspects of olfactory system anatomy local circuit function odor coding and plasticity The authors are leading authorities in the field Written by the leading researchers in the field of olfactory perception and memory Includes diverse models systems from invertebrates to humans Includes diverse technical approaches to the study of olfactory memory and perception Includes overview of the most recent research advances in this field **Children with Autism** Colwyn

Trevarthen,1998 This completely revised and substantially expanded new edition embraces new developments in this rapidly developing field Every chapter has been rewritten with the addition of new material and a new final chapter on Putting the Pieces Together reflects the authors conviction that the complexity of autism means that many kinds of information are valuable and need to be taken into account in providing therapy or teaching for children with autism Other chapters updated from the first edition include a description of the latest information on the findings of brain research put into the context of the development of the human brain and its effect on communication in early childhood and the contributions of music therapy and psychoanalysis A very much enlarged chapter on educational provision for children with autism and Asperger s Syndrome provides information on the latest methods for improving the learning of these children to give them the best possible preparation for a life of greater autonomy and maximum self satisfaction in the pleasure of human company New appendices summarise medical diagnostic systems checklists and questionnaires for identifying autism and the glossary has been considerably expanded The wealth of up to date information provided will be invaluable not only for researchers and students but also for psychologists teachers and other professionals and parents carers and family members in search of comprehensive and helpful information **Biomedical Index to PHS-supported Research: pt. A. Subject access A-H**

,1992 Research Awards Index ,1989 **The Central Nervous System Control of Respiration** ,2014-04-17 Respiration is one of the most basic motor activities crucial for survival of the individual It is under total control of the central nervous system which adjusts respiratory depth and frequency depending on the circumstances the individual finds itself For this reason this volume not only reviews the basic control systems of respiration located in the caudal brainstem but also the higher brain regions that change depth and frequency of respiration Scientific knowledge of these systems is crucial for understanding the problems in the many patients suffering from respiratory failure This well established international series examines major areas of basic and clinical research within neuroscience as well as emerging subfields Das Alter der Gefühle Tanja Sappok,Sabine Zepperitz,2019-08-12 Geistige Behinderung ist kein rein kognitives Problem auch die sozio emotionale Entwicklung kann beeinträchtigt sein und verzerrt oder unvollständig ablaufen Dadurch entstehen unter Umständen schwere Verhaltensauffälligkeiten und in der Folge psychische Störungen Dies kann zu weitreichenden Konsequenzen wie vermeidbaren Krankenhausaufenthalten hohen psychopharmakologischen Behandlungen Arbeits und Wohnplatzverlust bis hin zur Exklusion aus der Gesellschaft führen Unter Einbezug des emotionalen Entwicklungsaspekts ermöglichen Tanja

Sappok und Sabine Zepperitz einen neuen ganzheitlichen Blick auf Menschen mit geistiger Behinderung Verhaltensauffälligkeiten können vor diesem Hintergrund besser verstanden und zielgerichtete pädagogisch therapeutische Maßnahmen eingeleitet werden Die Autorinnen tragen mit Das Alter der Gefühle dazu bei die psychische Gesundheit und Lebensqualität von Menschen mit geistiger Behinderung substantiell zu verbessern indem sie allen im Gesundheitswesen und in der Eingliederungshilfe Tätigen ein wirksames Hilfsmittel zur Hand geben um die damit verbundenen Herausforderungen zu meistern Das Buch wurde für die zweite Auflage grundlegend bearbeitet es wurde unter anderem an das neue Diagnostikinstrument SEED angepasst das Zusammenspiel von emotionaler Entwicklung und psychischer Erkrankung wird neu thematisiert und das Entwicklungsmodell um die Phase der 2. Individuation bzw der Adoleszenz erweitert



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