

Cytogenetic and Neurobiological Advances in Down syndrome

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Título: Avances Citogenéticos y Neurobiológicos en el Síndrome de Down.

Resumen: El síndrome de Down es una alteración autosómica que, tradicionalmente, ha sido estudiada de forma independiente, desde ámbitos como la medicina, la biología o la psicología. En este artículo pretendemos ir más allá e incorporar una perspectiva multidisciplinar que contemple, por una parte, los principales hallazgos de estas disciplinas y por otra, las teorías que intentan explicar las complejas relaciones que se producen entre dichos hallazgos. Con este objetivo, revisamos los avances que se han realizado en el campo de la genética, la neuroanatomía y la neuroquímica en relación a este síndrome, así como las explicaciones que se han desarrollado para intentar entender el perfil neuropsicológico asociado con esta alteración. Creemos que la incorporación de esta perspectiva ayudará a abordar una visión general sobre los correlatos psicobiológicos del síndrome de Down.

Palabras Clave: Síndrome de Down; genética; neuroanatomía; neuroquímica; neuropsicología; psicobiología.

Abstract: Down syndrome is an autosomal trisomy that traditionally has been studied independently from fields such as medicine, biology or psychology. In this article, we intend to go further and incorporate a multidisciplinary approach that includes, on the one hand, the main findings of these disciplines and, the theories that attempt to explain the complex relationships that occur between such findings. With this aim, we review the progress that has been made in the field of genetics, neuroanatomy and neurochemistry in relation to this syndrome, as well as the explanations that have been developed to try to understand the neuropsychological profile associated with this condition. We believe that the incorporation of this perspective will help achieve an overview of the psychological correlates of Down syndrome.

Key words: Down syndrome; genetics; neuroanatomy; neurochemistry; neuropsychology; psychobiology.

Introduction

Down syndrome (DS) is the most common genetic cause of intellectual disability (Nadel, 2003; Patterson, 2007). It was first described by Langdon Down in 1866, in an article published in the London Hospital Reports (Parajuli-Pozo & Casis-Arquero, 2000; Sherman, Freeman, Allen & Lamb, 2005). In this publication was already highlighted the presence of intellectual disability and a range of distinctive facial features, which to the author were similar to those of some eastern populations. The presence of these characteristic facial features allowed Langdon Down to define DS as a specific clinical entity (Carvajal, Iglesias & Loeches, 1994; Mégarbane et al., 2009).

Initially many hypotheses about the origin of DS were raised that alluded that DS was a throwback to more primitive races, or it was due, either diseases or additions of parents, problems during pregnancy, endocrine disorders, age of the mother or even gynecological irregularities (Mardomingo, 1995).

Afterwards, Waardenburg raised its genetic origin in 1932 (Capone, 2001). But it was not until 1959 when Lejeune and his colleagues confirmed the presence of an extra chromosome in pair 21 in nine children with DS (Lejeune, Gautier & Turpin, 1959). Moreover, the advancement of cytogenetic techniques also revealed the existence of three underlying chromosomal abnormalities on the onset of the syndrome: regular trisomy, translocation trisomy and mosaicism (Patterson, 2007; Seres, Cuatrecasas & Catalá, 2005). In the first and second case, the error occurs in the formation of gametes or the first mitotic division so it affects all somat-

ic cells of the organism, the main difference being that in the case of regular trisomy has 47 whole chromosomes whereas in the translocation case has 46 chromosomes and an extra portion of chromosome 21 (HSA21). In contrast, in mosaicism the error occurs from the second mitotic division, which gives rise to two different cell lines, one with 47 chromosomes and one with a normal genetic endowment.

Currently, it is widely known that between 90-95% of cases are due to regular trisomy of HSA21, while the rest are due to HSA21 trisomy by translocation or mosaicism (Bornstein et al., 2010; Patterson, 2007).

When it was compared the phenotype of people with regular trisomy against the phenotype of people with DS due to translocation no significant differences were found. In any case, the varying extension of certain phenotypic traits seems to be related to the amount of additional genetic material, but this does not seem to exert influence on the intellectual level (Bornstein et al., 2010; Devlin & Morrison, 2004a; Loeches, Iglesias & Carvajal, 1991). However, when this comparison has been carried out with cases caused by mosaicism it was observed that the latter present less accurate phenotypic characteristics in relation to the number of cells affected (Devlin & Morrison, 2004b; Drews et al., 2008; Seres et al., 2005). However, as in the previous case, the existence of this relationship has not been demonstrated in the case of intellectual level (Carvajal et al., 1994).

In addition to its relationship with intellectual disability, regular trisomy appears to lead to a specific neuropsychological profile (Kistler, Krinsky-McHale & Devenny, 2006; Menghini, Costanzo & Vicari, 2011; Ruggieri & Arberas, 2003), mainly characterized by : a) deteriorated language skills, affecting this impairment more to the production than to the comprehension, as well as to the phonological and morphological domain than the semantic and pragmatic (Fidler, Philofsky & Hepburn, 2007; Galeote, Soto, Sebastián, Rey & Checa, 2012; Vicari, Caselli, Gagliardi, Tomucci

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Molecular Genetics of Neurological and Neuromuscular Disease Stefano DiDonato, Salvatore DiMauro, Angelo Mamoli, Lewis P. Rowland, 1988 Rosenberg's Molecular and Genetic Basis of Neurological and Psychiatric Disease, Seventh Edition Roger N. Rosenberg, Juan M. Pascual, 2024-10-04 Rosenberg's Molecular and Genetic Basis of Neurologic and Psychiatric Disease Seventh Edition provides a comprehensive introduction and reference to the foundations and key practical aspects relevant to neurologic and psychiatric disease This volume has been thoroughly revised and includes newly commissioned chapters on ethics genetic counselling and genet therapy for the central nervous system disorders A favorite of over four generations of students clinicians and scholars this new edition retains and expands the informative concise and critical tone of the previous edition This is an essential reference for general medical practitioners neurologists psychiatrists geneticists and related professionals and for the neuroscience and neurology research community at large Both volumes combined provide a comprehensive coverage on the neurogenetic foundation of neurological and psychiatric disease This volume provides a detailed introduction on both the clinical and basic research implications of molecular and genetics surrounding the brain Includes new chapters on genomics of human neurological disorders CRISPR and genome engineering Genomics, Proteomics, and the Nervous System James D Clelland, 2010-12-03 This newest volume of Advances in Neurobiology discusses the utilization of genomic and proteomic technologies to address facets of neurobiology including development and epigenetic regulation functions in learning and memory and changes associated with neurological and psychiatric disorders

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Advances in Gene Technology Richard L. Rotundo, 1989 This volume provides coverage of many diverse areas of molecular neurobiology and pharmacology It includes information on recent advances in the understanding of memory formation sensory perception neurological diseases and the controversial area of neural transplantation this unique volume is of use to specialists in this field as well as researchers in a wide variety of other areas who need a convenient source of recent developments

Elements of Molecular Neurobiology C. U. M. Smith, 2002-11-01 This edition of the popular text incorporates recent advances in neurobiology enabled by modern molecular biology techniques Understanding how the brain works from a molecular level allows research to better understand behaviours cognition and neuropathologies Since the appearance six years ago of the

second edition much more has been learned about the molecular biology of development and its relations with early evolution This evodevo as it has come to be known framework also has a great deal of bearing on our understanding of neuropathologies as dysfunction of early onset genes can cause neurodegeneration in later life Advances in our understanding of the genomes and proteomes of a number of organisms also greatly influence our understanding of neurobiology Well known and widely used as a text throughout the UK good reviews from students and lecturers Good complement to Fundamentals of Psychopharmacology by Brian Leonard This book will be of particular interest to biomedical undergraduates undertaking a neuroscience unit neuroscience postgraduates physiologists pharmacologists It is also a useful basic reference for university libraries Maurice Elphick Queen Mary University of London I do like this book and it is the recommended textbook for my course in Molecular Neuroscience The major strength of the book is the overall simplicity of the format both in terms of layout and diagrams

Methods in Genomic Neuroscience Hemin R. Chin, Steven O. Moldin, 2001-09-26

The past few years have witnessed extraordinary advances in molecular genetic techniques and the accumulation of structural genomics information and resources in both human and model organisms With the development of new technologies and the availability of resources like the sequence of eukaryotic genomes problems of a previously unthinkable scope

Molecular Genetics in Developmental Neurobiology 1986

Genetics and Genomics of Neurobehavioral Disorders Gene S. Fisch, 2003-01-07

A clear and comprehensive account of how genetic abnormalities neurobiology and neuropsychology work together to manifest cognitive behavioral dysfunction The authors review the current status of research in autosomal disorders that produce cognitive behavioral dysfunction and syndromal and nonsyndromal disorders that produce mental retardation Comprehensive and up to date Genetics and Genomics of Neurobehavioral Disorders integrates the molecular genomic neuropsychological and neurobehavioral factors that produce learning disabilities and mental retardation into a coherent framework for the understanding and assessment of neurobehavioral disorders

Molecular Genetics in Developmental Neurobiology Yasuzō Tsukada, 1986-01-01

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Advances in Gene Technology Richard L. Rotundo, 1989

Molecular Neurobiology Steve Heinemann, James Patrick, 2012-12-06 This book is a collection of papers describing some of the first attempts to apply the techniques of recombinant DNA and molecular biology to studies of the nervous system We believe this is an important new direction for brain research that will eventually lead to insights not possible with

more traditional approaches At first glance the marriage of molecular biology to brain research seems an unlikely one because of the tremendous disparity in the histories of these two disciplines and the problems they face Molecular biology is by nature a reductionist approach to biology Molecular biologists have always tried to attack central questions in the most direct approach possible usually in the most simple system available a bacterium or a bacterial virus Important experiments can usually be repeated quickly and cheaply in many cases by the latest group of graduate students entering the field The success of molecular biology has been so profound because the result of each important experiment has made the next critical question obvious and usually answerable in short order Studies of the nervous system have a very different history First the human brain is what really interests us and it is the most complex structure that we know in biology The central question is clear How do we carry out higher functions such as learning and thinking How ever at present there is no widely accepted and testable theory of learning and no clear path to such a theory

Gene Therapy of the Central Nervous System: From Bench to Bedside Michael G. Kaplitt, Matthew During, 2006 Few areas of biomedical research provide greater opportunities to capitalize upon the revolution in genomics and molecular biology than gene therapy This is particularly true for the brain and nervous system where gene transfer has become a key technology for basic research and has recently been translated to human therapy in several landmark clinical trials Gene Therapy in the Brain From Bench to Bedside represents the definitive volume on this subject Edited by two pioneers of neurological gene therapy this volume contains contributions by leaders who helped to create the field as well as those who are expanding the promise of gene therapy for the future of basic and clinical neuroscience Drawing upon this extensive collective experience this book provides clear and informative reviews on a variety of subjects which would be of interest to anyone who is currently using or contemplating exploring gene therapy for neurobiological applications Basic gene transfer technologies are discussed with particular emphases upon novel vehicles immunological issues and the role of gene therapy in stem cells Numerous research applications are reviewed particularly in complex fields such as behavioral neurobiology Several preclinical areas are also covered which are likely to translate into clinical studies in the near future including epilepsy pain and amyotrophic lateral sclerosis Among the most exciting advances in recent years has been the use of neurological gene therapy in human clinical trials including Parkinson's disease Canavan disease and Batten disease Finally readers will find insider information on technological and regulatory issues which can often limit effective translation of even the most promising idea into clinical use This work provides up to date information and key insights into those gene therapy issues which are important to both scientists and clinicians focusing upon the brain and central nervous system

Advances in Molecular Neurobiology Markus Rothmel, 2020-07

Behavioral Neurogenetics John F. Cryan, Andreas Reif, 2012-05-09 This book covers a wide array of topics relevant to behavioral genetics from both a preclinical and clinical standpoint Indeed in juxtaposing both areas of research the reader will appreciate the true translational nature of the field Topics covered range from technical advances in genetic analysis in

humans and animals to specific descriptions of advances in schizophrenia attention disorders depression and anxiety disorders autism aggression neurodegeneration and neurodevelopmental disorders The importance of gene environment interactions is emphasised and the role of neuroimaging in unravelling the functional consequences of genetic variability described This volume will be valued by both the basic scientist and clinician alike who may use it as a detailed reference book It will also be of use to the novice to the field to whom it will serve as an in depth introduction to this exciting area of research

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