available at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/brainres

BRAIN RESEARCH

Review

The promise and the pitfalls of autism research: An introductory note for new autism researchers

*David G. Amaral**

Department of Psychiatry and Behavioral Sciences, The M.I.N.D. Institute, University of California, Davis, 2825 50th St., Sacramento, CA 95817, USA

ARTICLE INFO

Article history:
Accepted 21 November 2010
Available online 1 December 2010

Keywords:
History
Autism
Research
Funding

ABSTRACT

The last decade has seen an enormous growth in the quantity of research directed at understanding the biological underpinnings of autism spectrum disorders. This increase has been spurred on, in part, by research funding provided through private, parent advocacy groups. While increased funding and entry into autism research by scientists from many disciplines has facilitated the speed of discoveries germane to establishing the etiologies of autism, there remain a number of roadblocks to understanding autism sufficiently well to foster new treatments. This short article provides a brief overview of some of the achievements and some of the difficulties in conducting autism research.

Contents

1. Introduction

1.1. *The promise*

The last two decades have seen an explosive growth of research into the biological bases of autism spectrum disorders. A survey of PubMed citations using the search terms autism and autistic shows that, for the single year 1990, there were 213 papers published. In 2000, this grew to 441, and in 2009, this has more than tripled with 1522 papers published on this topic. The disorder that we now know as autism was first formally described in 1943 by the Austrian born child

* Fax: +1 916 703 0237.
E-mail address: dgamaral@ucdavis.edu.

0006-8993/$ – see front matter © 2010 Elsevier B.V. All rights reserved.
doi:10.1016/j.brainres.2010.11.077

psychiatrist Leo Kanner in his seminal paper *Autistic disturbances of affective contact* (Kanner, 1943). For many years after the publication of his paper, "infantile autism" was considered to be a very rare disorder affecting fewer than 5 in 10,000 individuals (Lotter, 1966). There was so little interest in this disorder, in fact, that Kanner's paper was only referenced 34 times between 1943 and 1954. By contrast, it was referenced nearly 140 times in 2009 alone.

Clearly, recent estimates that 1:110 children in the United States are affected by some form of autism spectrum disorder (Rice, 2009) have galvanized both advocates and scientists alike to keep up the pressure for additional support and more intensive research. In addition to the emotional toll on family life, Ganz (2007) has estimated that the lifetime societal cost of a child with autism is on the order of $3.2 million or $35 billion for all individuals diagnosed each year over their lifetimes. These modern statistics of the autism world have motivated political action culminating in the Combating Autism Act signed by President Bush in December of 2006. Under the new law, NIH funding for autism research is mandated to increase to $210 million by 2011 (Stokstad, 2007) and an additional $21 million will be provided to the Centers for Disease Control. In addition, the Defense Appropriations Bill set aside $7.5 million for autism research in fiscal year 2007 and similar appropriations have continued more recently.

This increased impetus for autism research comes in the midst of an ongoing process that has brought autism out of the darkness of psychiatric institutions onto the covers of major news magazines. Much of the credit for the increased research is due to the dedicated advocacy efforts of parents of children with autism throughout the world. One early example of this was the late Bernard Rimland, Ph.D., a psychologist and father of a son with autism. His influential book entitled *Infantile Autism: The Syndrome and Its Implications for a Neural Theory of Behavior* (which had a forward by Leo Kanner) published in 1964, dismissed the myth that early psychodynamic influences, the "refrigerator mother," caused autism. Rimland reasoned that, if some of the co-morbid conditions of autism, such as epilepsy, were due to neural dysfunction, there was no reason not to think that the core features of autism might also be due to dysfunction of the nervous system.

Major impetus for the expansion of autism research in the United States came from the founding, in the mid 1990s, of two parent advocacy organizations, the National Alliance for Autism Research (NAAR) and Cure Autism Now (CAN), that promoted not only the awareness of autism spectrum disorders but also the need for research into the biological bases of autism. With the merger of these fund raising and advocacy groups into Autism Speaks in 2005, a highly strategic program for worldwide autism research has been developed that has greatly expanded the scope and intensity of all levels of research concerning autism spectrum disorders. More recently, the Simons Foundation, which is focused heavily on genetic and neurobiological investigations, has also had a significant impact on the funding of basic science research in autism. A 2009 study by Singh et al., found that funding for autism research from the National Institutes of Health increased fivefold between 1997 and 2006, from $22 to $108 million. Moreover, the number of autism research grants funded in the United States increased 15% each year from 1997 to 2006, with the majority of grants focused on genetics and neuroscience. Based on an analysis conducted by the NIH Interagency Autism Coordinating Committee (IACC), by 2008, the United States was spending over $222 million on autism research with 35% of the funding coming from private foundations (http://iacc.hhs.gov/portfolio-analysis/2008/index.shtml). In addition to basic science funding, there have also been efforts to increase support in the areas of translational and clinical research. This has been fostered, in part, through strategic planning by the IACC which has increasingly endeavored to encourage research directed at reducing disability now for persons with autism.

What this surge in interest and support for autism research has achieved is a wealth of new data into the biological features of autism. Gains in knowledge are both dramatic, given the need for many new autism centers and researchers to first establish the "infrastructure" to carry out autism research and, at the same time, frustrating for families who yearn for answers to the question *how do I solve the problem of autism for my child—now*.

As pointed out by speakers at the recent Brain Research symposium, *The Emerging Neuroscience of Autism Spectrum Disorders: Etiologic Insights; Treatment Opportunities*, achieving consensus on the biological features of autism has been difficult though a number of areas of agreement are emerging. There is now substantial consensus, for example, that portions of the brain undergo precocious growth in children with autism spectrum disorder (Carper and Courchesne, 2005; Courchesne et al., 2003; Hazlett et al., 2005). The causes for this regionally specific, rapid growth are not yet known but appear to lead to a cascade of aberrant connection formation and dysfunction of networks that underlie the behavioral symptoms of autism. This aspect of autism research was highlighted in presentations by Coruchesne, Pierce, and Murphy.

Microscopic analyses that might inform cellular processes leading to aberrant growth in the autistic brain are making progress but have not yet led to coherent theories of underlying mechanisms. In the amygdala, for example, there is consistent MRI data across several laboratories that, on average, the amygdala reaches an adult size earlier in children with autism than in typically developing controls (Munson et al., 2006; Schumann et al., 2004). Yet, as Schumann reviewed at the symposium, when postmortem studies of brains from older individuals with autism are carried out, there are actually significantly fewer neurons (Schumann and Amaral, 2006). Hof provided additional insight into the location and types of cortical pathology in autism. Interestingly, the only other stereological study published to date has also shown fewer neurons in the fusiform gyrus (van Kooten et al., 2008), a portion of the temporal lobe which is associated with face processing. This raises the question of whether there were fewer neurons in the amygdala and fusiform gyrus from birth or whether a neurodegenerative process takes place in autism. This won't be known until similar stereological studies can be carried out on the brains of much younger individuals with autism. Even the common findings, such as the enlarged amygdala in children with autism, do not appear to apply to all individuals with the diagnosis. In a large scale, longitudinal