Autoantibodies in Autism Spectrum Disorders (ASD)

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ABSTRACT: Autism spectrum disorders (ASD) are a heterogeneous group of neurodevelopmental disorders defined behaviorally by abnormalities in social, verbal, and nonverbal communication. The etiologies of ASD are unknown, likely to be the result of a variety of numerous genetic, neurological, environmental, and immunological interactions that lead to a general behavioral phenotype defined as ASD. This review will focus on the various immune system anomalies, in particular, autoantibodies, which have been reported in subjects with ASD. In addition, we will discuss recent studies performed by our group concerning the presence of autoantibodies directed against neural antigens, which are observed in patients with ASD.

KEYWORDS: autism; ASD; immunity; autoantibodies; immune system; brain

INTRODUCTION

Autism spectrum disorders (ASD) are a heterogeneous group of neurodevelopmental disorders defined behaviorally by abnormalities in social, verbal, and nonverbal communication. They include Asperger's syndrome, autism, child disintegrative disorder, and pervasive developmental disorder, not otherwise specified (PDD–NOS).[1] Stereotypic and restricted behaviors and/or interests are often found in patients with ASD. Patients are diagnosed typically before the age of 36 months, males at a rate four times that of females.[2] The current prevalence is estimated at 1:150 in the total population.[3] There are likely to be

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Antibrain antibodies in children with autism and their unaffected siblings.

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Abstract

Serum autoantibodies to human brain, identified by ELISA and Western immunoblotting, were evaluated in 29 children with autism spectrum disorder (22 with autistic disorder), 9 non-autistic siblings and 13 controls. More autistic subjects than controls had bands at 100 kDa in caudate, putamen and prefrontal cortex ($p<0.01$) as well as larger peak heights of bands at 73 kDa in the cerebellum and cingulate gyrus. Both autistic disorder subjects and their matched non-autistic siblings had denser bands (peak height and/or area under the curve) at 73 kDa in the cerebellum and cingulate gyrus than did controls ($p<0.01$). Results suggest that children with autistic disorder and their siblings exhibit differences compared to controls in autoimmune reactivity to specific epitopes located in distinct brain regions.

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Maternal antibrain antibodies in autism.

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Abstract

Autism is a neurodevelopmental disorder of prenatal onset that is behaviorally defined. There is increasing evidence for systemic and neuroimmune mechanisms in children with autism. Although genetic factors are important, atypical prenatal maternal immune responses may also be linked to the pathogenesis of autism. We tested serum reactivity in 11 mothers and their autistic children, maternal controls, and several groups of control children, to prenatal, postnatal, and adult rat brain proteins, by immunoblotting. Similar patterns of reactivity to prenatal (gestational day 18), but not postnatal (day 8) or adult rat brain proteins were identified in autistic children, their mothers, and children with other neurodevelopmental disorders, and differed from mothers of normal children, normal siblings of children with autism and normal child controls. Specific patterns of antibody reactivity were present in sera from the autism mothers, from 2 to 18 years after the birth of their affected children and were unrelated to birth order. Immunoblotting using specific antigens for myelin basic protein (MBP) and glial acidic fibrillary protein (GFAP) suggests that these proteins were not targets of the maternal antibodies. The identification of specific serum antibodies in mothers of children with autism that recognize prenatally expressed brain antigens suggests that these autoantibodies could cross the placenta and alter fetal brain development.

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Maternal antibrain antibodies in autism ☆

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Abstract

Autism is a neurodevelopmental disorder of prenatal onset that is behaviorally defined. There is increasing evidence for systemic and neuroimmune mechanisms in children with autism. Although genetic factors are important, atypical prenatal maternal immune responses may also be linked to the pathogenesis of autism. We tested serum reactivity in 11 mothers and their autistic children, maternal controls, and several groups of control children, to prenatal, postnatal, and adult rat brain proteins, by immunoblotting. Similar patterns of reactivity to prenatal (gestational day 18), but not postnatal (day 8) or adult rat brain proteins were identified in autistic children, their mothers, and children with other neurodevelopmental disorders, and differed from mothers of normal children, normal siblings of children with autism and normal child controls. Specific patterns of antibody reactivity were present in sera from the autism mothers, from 2 to 18 years after the birth of their affected children and were unrelated to birth order. Immunoblotting using specific antigens for myelin basic protein (MBP) and glial acidic fibrillary protein (GFAP) suggests that these proteins were not targets of the maternal antibodies. The identification of specific serum antibodies in mothers of children with autism that recognize prenatally expressed brain antigens suggests that these autoantibodies could cross the placenta and alter fetal brain development.

Keywords: Autism; Maternal; Antibodies; Autoimmunity; Prenatal

1. Introduction

Autism is a disabling heterogeneous disorder affecting early child neurodevelopment, with deficits in language and social skills, and atypical behaviors (Rapin, 1997). Various abnormal systemic immune functions have been described in children with autism (reviewed by Zimmerman, 2005) and recently neuroinflammation was described in postmortem brain tissue (Vargas et al., 2005). In addition to important genetic influences underlying the autism spectrum disorders, "environmental factors" may also contribute to their apparently increasing incidence (Newschaffer and Curran, 2003).

There is growing recognition that the intrauterine environment is important for the fetus, because it can affect long-term health outcomes in childhood and adult life (Hampton, 2004). Maternal infections during pregnancy have been linked to autism and schizophrenia (Patterson, 2002), and relationships between antibody formation and CNS disease have been proposed in Sydenham chorea (Church et al., 2003) and Tourette syndrome (Singer

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treatment process of this sizable population.

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Right day, wrong century

Stanley Kubrick named his famous movie "2001, A Space Odyssey" for a very good reason: He wanted it to begin in the *next* century and he knew that the first century ran from A.D. 1 to the year 100, the second from 101 to 200, and the 21st from 2001 to 2100. This is because there was no year zero.

Therefore, your writer of "Rickover dead at 86" (SN:7/12/86,p.22) was incorrect in stating that Adm. Rickover "was born . . . on the 27th day of this century," since he was born on January 27, 1900, not 1901.

A lot of misinformed people are going to get drunk on the night of Dec. 31, 1999, thinking they are celebrating a new century and a new millennium. I don't suppose there's much hope you and other "esoteric" publications can make them understand their error, but please, don't perpetuate the error yourselves!

Bill White
Miami, Fla.

Autism and autoimmunity

Immunological abnormalities in autistic patients ("Immunology of autism," SN:7/26/86, p.58) were reported several years ago by Abraham Weizman et al. They demonstrated that many autistic children have an immune response to myelin basic protein, a component of the myelin sheath that covers many nerves. Myelin basic protein contains a serotonin (and LSD) binding site. Because serotonin levels are abnormally high in many autistic children, some of whom respond extremely well to the serotonin-lowering drug fenfluramine, it has been suggested that the abnormal serotonin levels are directly related to the autoimmune response to myelin basic protein. Serotonin, in turn, has a definite modulatory effect upon the stress peptide, ACTH, which in turn regulates corticosteroid production, which modifies immune responses.

Thus, Robert Moulias's suggestions that neurotransmitter disturbances in autism affect the immune system, and that autoimmunity may be a cause of autism, are probably both correct. Could immunosuppressants therefore alleviate some or all of the symptoms of autism?

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Moms with Autoimmune Diseases More Likely to Have Kids with Autism

By Jennifer Davis

7/21/09 Children of mothers who have autoimmune diseases, such as rheumatoid arthritis, celiac disease or type 1 diabetes, are at greater risk of having autism, a new study shows.

The study, published online in the journal *Pediatrics*, looked at more than 689,196 children born in Denmark between 1993 and 2003. Scientists found 3,325 of these children were diagnosed with autism spectrum disorders and discovered that many also had a family history of autoimmune diseases.

Autoimmune diseases develop when the body fails to recognize its own organs and tissues, attacking them as it would a dangerous invader.

In this study, for the first time, researchers discovered an increased risk of autism in children with a maternal history of celiac disease - a condition where people can't digest gluten, a protein found in wheat, rye and barley. Researchers also confirmed previous studies that found an increased risk of autism in children whose moms had rheumatoid arthritis or type 1 diabetes.

Children of mothers with celiac disease had a 197 percent increased risk of autism, while children of mothers with rheumatoid arthritis had a 56 percent increased risk. Those with moms who had type 1 diabetes had a 114 percent increased risk.

They also found a 78 percent increased risk of autism if the father had type 1 diabetes, but not if the father had arthritis or celiac disease.

Researchers say their results suggest a complex association between family history of certain autoimmune diseases and autism.

"A common genetic background could explain the results for diabetes, while for arthritis it is more possible it is caused by immune responses in the mother or factors in the fetal environment," says Hjördis Osk Atladottir, MD the lead author of the study done at the University of Aarhus in Aarhus, Denmark.

"We can't conclude anything based on only our results but our results are a part of a bigger puzzle of many studies, suggesting that autism and the immune system, and autoimmunity in particular, are connected," he adds.

The researchers also stress that current or future parents with an autoimmune diseases shouldn't worry too much about the study results because the large majority of people affected by these conditions do not have children with autism.

Paul Ashwood, PhD, is an immunologist at the University of California, Davis M.I.N.D. Institute in Sacramento who specializes in studying the role of the immune system in autism. He says this is an interesting and large study that supports existing research that shows autism often runs in families.