

# Prenatal, Perinatal, and Neonatal Factors in Autism, Pervasive Developmental Disorder-Not Otherwise Specified, and the General Population

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**ABSTRACT.** *Objectives.* To examine various pre-, peri-, and neonatal factors in autistic participants and in pervasive developmental disorder-not otherwise specified (PDD-NOS) participants and to compare the incidence of each factor to that of the normal population.

*Methods.* Seventy-four participants (66 males, 8 females) were diagnosed with autism at 2.5 through 4 years of age using the most accurate and up-to-date methods, including the *Diagnostic and Statistical Manual of Mental Disorders* and the Autism Diagnostic Interview-Revised. At age 5, all participants were reevaluated using the *Diagnostic and Statistical Manual of Mental Disorders*, the Autism Diagnostic Interview-Revised, the Childhood Autism Rating Scale, and the Autism Diagnostic Observation Schedule-Revised, resulting in 61 autistic and 13 PDD-NOS participants. Twenty-eight pre-, peri-, and neonatal factors were examined in these 2 groups using both medical records and parental interviews. Incidences were compared with those of the US population as reported in the *Report of Final Natality Statistics, 1995*. This grand scale population group was used to closely approximate comparison to a normal, unbiased population. Results were analyzed using the binomial probability test, with a *P* value of <.05, constituting a significant difference in incidence. A Bonferroni correction was applied to the data to adjust for the number of factors investigated.

*Results.* Although most of the factors showed comparable incidences between the index and control groups, several factors showed statistically significant differences. Following the Bonferroni correction, the autism group was found to have a significantly higher incidence of uterine bleeding, a lower incidence of maternal vaginal infection, and less maternal use of contraceptives during conception when compared with the general population. Similarly, the PDD-NOS group showed a higher incidence of hyperbilirubinemia when compared with the general population.

*Conclusions.* The results of this study support previous findings suggesting a consistent association of unfavorable events in pregnancy, delivery, and the neonatal phase and the pervasive developmental disorders. However, interpretation of the meaningfulness of these results is difficult, as the specific complications that carried the highest risk of autism and PDD-NOS represented

various forms of pathologic processes with no presently apparent unifying feature. Additional studies are needed to corroborate and strengthen these associations, as well as to determine the possibility of an underlying unifying pathological process.

This study's analysis of obstetric and neonatal complications in combination with the use of participants diagnosed at an early age provides some interesting concepts to consider. Perhaps future research will confirm certain pre-, peri-, and neonatal associations that could be used to generate a high-risk historical profile with which to use in conjunction with currently employed diagnostic tools. This may, in turn, help to determine the reliability of a diagnosis of autism in younger children, leading to earlier intervention and assistance for an improved outcome in long-term functionality and quality of life. *Pediatrics* 2001;107(4). URL: <http://www.pediatrics.org/cgi/content/full/107/4/e63>; *autism, pervasive developmental disorder, pregnancy, delivery, risk factors, neonatal.*

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ABBREVIATIONS. PDD, pervasive developmental disorder; DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders, IV*; ADI-R, Autism Diagnostic Interview-Revised; PDD-NOS, pervasive developmental disorder-not otherwise specified.

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Autism is a behavioral syndrome with a reported prevalence of ~10 per 10 000 and an approximate 4:1 ratio of affected males to females.<sup>1</sup> It is classified under the category of pervasive developmental disorder (PDD) and results from a neurologic disorder affecting various functions of the brain. Autism is characterized by impairments in reciprocal social interaction, impairments in verbal and nonverbal communication, lack of imaginative play, and a pattern of repetitive, stereotypical behaviors and interests. Like most other behavioral syndromes, it seems to be a causally heterogeneous disorder. In the literature there is varying support for a wide spectrum of hypotheses regarding the cause of autism: from genetic studies showing a high concordance rate in monozygotic twins<sup>2</sup> to the relationship between environmental events and the development of autism.<sup>1</sup>

A number of studies have investigated the association between particular pre-, peri-, and neonatal factors and autism.<sup>3-5</sup> A summary of their findings is shown in Table 1. Nevertheless, no consistently identified factors have been shown. Other approaches, such as comparing composite scales, have been used with the argument that detection of liability is not dependent on specific items and that factors associ-

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