

PERINATAL COMPLICATIONS AS PREDICTORS OF INFANTILE AUTISM

DIANA SUE WILKERSON
ALESSANDRA G. VOLPE
RAYMOND S. DEAN
JEFFREY B. TITUS

Neuropsychology Laboratory
Ball State University
Muncie, Indiana, USA

This study investigated the relationship between reported perinatal complications and autism. The biological mothers of 183 autistic children and 209 normals completed the Maternal Perinatal Scale (MPS), a maternal self-report that surveys complications of pregnancies and medical conditions of the mother. Previous research in this area has been limited, with no definitive conclusions. A discriminant analysis was performed to consider perinatal complications as predictors between the autistic and normal subjects. Using the MPS, 65% of the autistic cases were correctly grouped. The results further indicated significant differences on 3 of the 10 factors of the MPS, in particular, Gestational Age, Maternal Morphology, and Intrauterine Stress. When considered in an item by item fashion, 5 items were found to significantly predict group membership (prescriptions taken during pregnancy, length of labor, viral infection, abnormal presentation at delivery, and low birth weight). Finally, 3 maternal medical conditions were found to be highly significant and contribute to the separation between groups, including urinary infection, high temperatures, and depression.

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Address correspondence to Raymond S. Dean, PhD, Neuropsychology Laboratory, Ball State University, 1407 Marsh Street, Muncie, IN 47306, USA. E-mail: rdean@bsu.edu

Infantile autism is a pervasive developmental disorder characterized by disturbances in social and language development prior to 36 months of age (*DSM-IV*, 1996). The etiology of this disorder has been the subject of considerable study and debate. Hypotheses ranging from "cold, distant parenting" (Kanner, 1934) to genetic transmission (Fisch et al., 1986; Lee-Dukes, 1986; Wahlstrom, Gillberg, Gustavson, & Holmgren, 1986) have been offered. However, because perinatal complications have been demonstrated to place an infant at risk for significant neurological, mental, and behavioral disorders (Commeys & Fitzhardinge, 1979; Fitzhardinge & Steven, 1972; Hunt, 1981; Lillienfield & Pasamanick, 1954, 1955, 1956; Pfeiffer, Heffernan, & Pfeifer, 1985; Pollack & Woerner, 1966; Rutter, 1982; Yahraes & Prestwich, 1979), their relationship to infantile autism has also been investigated (Finegan & Quarrington, 1979; Nunn, Lak, & Cohen, 1986). Although research findings highlight consistent perinatal complications in the histories of autistic children (e.g., bleeding during pregnancy, viral infections, prescription drug usage during pregnancy), conclusions are compromised by the lack of a standardized assessment tool in gathering data on perinatal complications. Consequently, this study sought to evaluate the role of perinatal complications in the onset of infantile autism utilizing the Maternal Perinatal Scale (MPS), a psychometrically sound self-report measure. Specifically, the goals of this study were to 1) identify whether normal and autistic children significantly differed when evaluating the presence of perinatal complications as measured by the 10 factors of the MPS; 2) explore the degree of consistency between these research findings and their predecessors; and 3) evaluate the role of maternal medical conditions in placing children at risk for autism.

Perinatal complications, deviations from the expected course of events during pregnancy, labor, and delivery in the first 28 days of life, have been associated with a number of neuropsychological disorders, including cerebral palsy, mental retardation, epilepsy, childhood tic disorders, behavior disorders, speech disorders, and reading disabilities (Commeys & Fitzhardinge, 1979; Fitzhardinge & Steren, 1972; Hunt, 1981; Lillienfield & Pasamanick, 1954, 1955, 1956; Pfeiffer et al., 1985; Pollack & Woerner, 1966; Rutter, 1982; Yahraes & Prestwich, 1979). Research highlighting the role of perinatal complications in infantile autism is also significant (i.e., Deykin & McMahon,

1980; Finegan & Quarrington, 1979; Mason-Brothers et al., 1987). For example, Finegan and Quarrington (1979) found the length of labor to be shorter and "spontaneous" in their autistic sample's histories. In addition, obstetrical factors such as a higher incidence of bleeding during pregnancy and consumption of prescription medication by the autistic subjects' mothers were found to contribute. Others have reported a significant relationship between maternal viral infections and autism (Nunn et al., 1986). As a group, however, their research has been compromised by the use of nonstandardized measures (medical chart review and/or unstructured maternal interviews) to assess the role of perinatal complication. As a result, this has rendered the relationship between perinatal complications and infantile autism inconclusive, and highlights the need for this study.

METHODS

Participants

The participants ($N = 392$) of the study were a nationwide sample of 183 autistic and 209 normal subjects. The autistic subjects were obtained through two avenues. The first one was advertisement in *The Advocate*, a newsletter published by the Autism Society of America (ASA) that is sent to members nationwide. ASA members include parents of autistic children, as well as professionals who are involved in the diagnosis and treatment of autistic patients. They received a packet of material including the MPS, a cover letter, and a self-addressed, stamped envelope in which to return the protocol. Out of 94 responses to the advertisement, 84 returned the materials and are included in the study.

The second method of obtaining subjects was through contact with presidents of Midwestern chapters of the ASA. Those who agreed to participate in the study were mailed a requested number of packets of materials. Out of 177 packets sent to 6 ASA chapters from Indiana, Illinois, and Michigan, 99 were completed and returned, bringing the total number of subjects participating in the study to 183. The socioeconomic status (SES) of the respondents

tended to be primarily middle and upper-middle class, with few responses from lower middle and lower class families. The respondents were predominantly Caucasian.

The autistic subjects ranged in age from 28 months (2 years, 4 months) to 489 months (40 years, 9 months). There were 147 males and 36 females, resulting in a 4:1 male-to-female ratio. This sample is consistent with that of the general autistic population (4:1). The preponderance of responses was from parents of preschool and school-age children. Data were complete for all subjects included in the study. The comparative sex distribution of the sample population to that of the general autistic population and the fact that the autistic subjects were acquired from various geographic locations throughout the United States, led the principal investigator to believe that, with the exception of SES, the study sample was a fair representation of the whole population of autistic patients.

Data on normal control subjects ($N = 209$) were obtained from archival data collected by Gray, Dean, Strom, Wheeler, and Brockley (1987) in their study of perinatal complications and developmental disability. Normal status was determined by regular educational placement. None of the subjects in the control group was receiving any type of special education services at the time of data collection.

Instrumentation

The Maternal Perinatal Scale (MPS; Dean & Gray, 1985) is a maternal self-report form intended to reveal those factors that place a fetus at risk for perinatal complications. Validity and reliability studies (Gray, Dean, & Rattan, 1985) have demonstrated that the MPS is an accurate assessment measure of perinatal events and that responses are stable over time. Factor analysis of the first 216 items yielded 10 factors accounting for 58% of the variance (Gray, Dean, Rattan, & Bechtel, 1988). The items on it were demonstrated to be particularly pertinent to mothers and recognizable (Gray et al., 1985). Further, when compared to hospital charts of the delivery and 5-min APGAR scores, the mothers' responses were accurate and consistent (Gray et al., 1985). Additionally, the MPS has been determined to be an accurate predictor of later deficits in cognitive and intellectual functioning (Gray et al., 1987).

The MPS contains 47 items. In general, it requires each mother to recognize, from multiple responses, complications during the period of pregnancy and birth through the first 28 days of the neonate's life. It is divided into three sections. The first relates to a wide range of factors that occurred during the pregnancy and birth of the infant such as a vaginal bleeding, infant birth weight, status of the infant following birth, anesthesia used, maternal weight gain, edema, etc. The second section is a checklist of medical factors experienced by the mother during pregnancy such as viral infections, high blood pressure, maternal-fetal Rh blood differences, diabetes, etc. The third section contains a childhood checklist that describes behavioral characteristics of the child in question. The fourth grade reading level of the MPS makes the scale accessible to the broad population (Dean & Gray, 1985).

RESULTS

Descriptive Statistics

The autistic subjects ($N = 183$) were comprised of 147 males and 36 females. Means were established relative to the child's age in months, mother's age in years, mother's race, father's age in years, father's race, and occupation of the major wage earner of the family. Parents' ages were based on age at the time of response to the MPS. The mean age of the subjects in the autistic group was 135.48 months, or approximately 11 years, 4 months. By subtracting the age of the subjects from the age of the parents, it was determined that the average age of the parents at the time of the birth of the children was 28 years for the mothers and 30 years for the fathers. The parents' occupations fell primarily in the professional-technical and management-sales categories. There were a few responses from laborers, craftsmen, service workers, and unemployed individuals.

Means were calculated for the normal subjects ($N = 209$) in the same manner as for the autistic subjects. The average age of the children in the sample was 115.02 months, or approximately 9 years, 7 months. In this group, the mothers' average age was some 27 years. Primarily, the responses came from middle class individuals

with some lower socioeconomic families represented. With regard to the mean age of the children, mean age of the parents, and mean socioeconomic status, the autistic and normal groups were fairly similar. The male to female ratio of normal subjects was 3:1, as compared to the 4:1 ratio in the autistic group.

Multivariate Analysis of the Two Groups on the Factors of the MPS

Previously, Gray et al. (1988) established a 10 factor structure for the MPS (see Table 2 for a listing of the factors). Using this factor structure, a multivariate analysis was performed. As can be seen in Table 1, all of the multivariate tests were highly significant ($p > .000$), indicating that the autistic and normal groups differed overall on the 10 factors.

The MANOVA was followed up with univariate contrasts of the factors (see Table 2). This analysis revealed the two groups differed significantly on three specific factors of the MPS. The first of these was Factor 2, Gestational Age ($p < .02$). The items contributing to this factor were the child's weight at birth and months of pregnancy that passed prior to birth. Results indicated that autistic children tended to have lower birth weights than normal children, with the mean birth weight of children in the autistic sample falling between 5 lbs., 1 oz. and 6 lbs.

The second significant difference between groups was on Factor 4, Maternal Morphology ($p < .000$). The items contributing most heavily to this factor were the mother's weight just prior to pregnancy and her height at the time of pregnancy. Mothers of autistic children tended to be taller and weigh more prior to pregnancy than mothers of normal children. The mean weight of mothers of normal children fell between 111 and 120 lbs. Their mean height fell be-

TABLE 1. Multivariate tests of significance on the 10 factors of the MPS

<i>Tests</i>	<i>Value</i>	<i>Exact F</i>	<i>Hypothesized DF</i>	<i>Error DF</i>	<i>Significance</i>
Pillais	.10325	4.26021	10.0	370.00	.000
Hotellings	.11514	4.26021	10.0	370.00	.000
Wilks	.89675	4.26021	10.0	370.00	.000

TABLE 2. Univariate F-tests on factors 1 through 10 of the MPS

<i>Variable</i>	<i>F</i>	<i>Significance</i>
Factor 1		
Obstetric History	1.55751	.213
Factor 2		
Gestational Age	4.86666	.028
Factor 3		
Psychosocial	1.08162	.299
Factor 4		
Maternal Morphology	19.77033	.000
Factor 5		
Labor	.64601	.422
Factor 6		
Delivery	.09418	.759
Factor 7		
Maternal Weight Gain	.62872	.428
Factor 8		
Intrauterine Stress	14.00205	.000
Factor 9		
Teratogenic Stress	.10904	.741
Factor 10		
Fetal Oxygenation	2.24196	.135

tween 5'1" and 5'3". In contrast, the mean weight of mothers of autistic children prior to pregnancy fell between 121 and 130 lbs. Their mean height fell between 5'4" and 5'5".

The third significant factor was Factor 8, Intrauterine Stress ($p < .00$). The items contributing to this factor were the amount of bleeding during pregnancy, amount of stress experienced by the mother, medication taken by the mother, and type of previous gynecological surgery. Examination of Factor 8 revealed that while bleeding during pregnancy was not statistically significant ($p < .19$), it did occur more frequently in the autistic sample than in the normal control group. Similarly, stress during pregnancy occurred at a higher rate in the autistic sample than in the normal control group, though it was not statistically significant. Medications taken during pregnancy were significantly more common in the autistic group ($p < .05$) as were more serious forms of previous gynecological surgery (i.e., prior abortions; $p < .05$).

To consider the interaction between individual items of the MPS in predicting autism, a discriminant analysis was performed using items of the perinatal factors thought to be related to autism in

TABLE 3. Discriminant analysis of six high probability items using Wilks' Lambda

<i>Variable</i>	<i>Wilks' Lambda</i>	<i>F</i>	<i>Significance</i>
Bleeding	0.99550	1.75	0.1869
Medication	0.90970	38.41	0.0000
Labor (time)	0.96224	15.18	0.0001
Viral infections	0.89805	43.94	0.0000
Delivery	0.98846	4.52	0.0342
Child's weight	0.98916	4.24	0.0401

previous literature (see Table 3). The six individual items were bleeding during pregnancy, prescription medication taken during pregnancy, spontaneous labor, flu-like symptoms during pregnancy, breech delivery, and low birth weight. These items were entered into the equation relative to their theoretical importance. The results, using the Wilks Lambda Chi Square transformation, yielded one significant discriminant function ($p < .05$), with five of the items yielding a significant result ($p < .05$). As shown in Table 3, the items found to be significant were length of labor ($p < .0001$); breech or other abnormal delivery ($p < .03$); low birth weight ($p < .04$); prescription medication taken during pregnancy ($p < .0000$); and viral infections ($p < .00$).

Review of the group means and standard deviations for items in Table 3 revealed that, of the five significant items, four were in the expected direction, consistent with previous research (see Table 4).

Data were next organized via computer so that all items of the MPS were arranged in hierarchical order, with lower numbered responses indicating less or no risk, and higher numbered responses indicating greater risk. The first identified item, bleeding during

TABLE 4. Group means and standard deviations of the six high probability items

<i>Variable</i>	<i>Normal</i>		<i>Autistic</i>	
	<i>x</i>	<i>SD</i>	<i>x</i>	<i>SD</i>
Bleeding	1.34135	0.74459	1.44751	0.83915
Medication	1.52601	1.06509	2.43398	1.77792
Labor	2.48077	1.28898	2.99448	1.30596
Viral infection	1.97115	0.16778	1.75691	0.43014
Presentation	1.49683	0.87187	1.70856	1.09148
Child's weight	4.89423	0.41513	4.78453	0.62626

pregnancy was not significant, although it did occur at a higher rate in the histories of the autistic sample than the normal sample. In regard to prescribed medications taken during pregnancy, mothers of the autistic group took significantly more. The mothers of autistic children also experienced viral infections at a level significantly higher when compared to mothers in the normal group. Of note, the responses were coded "1" if the response was "yes" and "2" if the response was "no," rendering the lower mean indicative of the presence of viral infections. Breech or other abnormal delivery was also highly significant. Results indicated the presence of more difficult deliveries in the autistic group.

In terms of the child's weight at birth, the higher mean for the normal group indicates a higher birth weight. These results reveal that the autistic group tended to be composed of infants who had lower birth weights.

Prior research had shown spontaneous labor in the histories of autistic samples (i.e., Finegan & Quarrington, 1979). Contrary to these expectations, length of labor was significant in this study but in the reverse direction. The normal sample obtained a mean length of labor in the 3- to 5-h range, while the autistic sample's mean length of labor was closer to 6 to 10 h.

Review of the covariance matrix for the autistic group showed a high correlation between length of labor and presentation of the fetus at birth ($r = .90$). Small to moderate correlations were found for taking prescribed medication during pregnancy and presentation of the fetus at delivery ($r = .27$), and viral infection and child's weight at birth ($r = .25$). These correlations distinguished the autistic group from the normal group.

Following this exploration of the data, a stepwise discriminate analysis was performed on the items relating to the mother's medical conditions prior to and during pregnancy. Three items were found to discriminate significantly between groups. These items included urinary infection ($p = .0271$), high temperatures ($p = .0261$), and depression ($p = .0318$). The statistics for this analysis are presented in Table 5. The results for each were in the expected direction, though not identified in previous research.

Pooled within-group correlations between discriminating variables and canonical discriminant functions revealed that of the significant

TABLE 5. Discriminant analysis of maternal medical conditions

Variable	Wilks' Lambda	F	Significance
High blood pressure	0.99988	0.4763	0.8273
Anemia	0.99786	0.8339	0.3617
Emotional problems	0.99162	3.280	0.0709
Urinary infection	0.98748	4.921	0.0271
Mother/baby blood dif.	0.99996	0.1394	0.9061
Viral infections	0.89905	43.56	0.0000
High temperature	0.98732	4.984	0.0261
Parasitic infection	0.99789	0.8202	0.3657
Depression	0.98818	4.643	0.0318

items in this analysis, viral infection was determined to contribute the most to separation between groups ($r = .94$). Moderate correlations were also found for depression ($r = .30$), high temperatures ($r = .26$), and urinary infection ($r = .24$). Emotional problems ($r = .16$) approached significance ($p < .07$). This item is similar in nature to Item 46 (depression) but allows more latitude in response. The nature of individual emotional problems, aside from depression, was not revealed by the MPS. Anemia, parasitic infections, mother-baby blood differences, and high blood pressure did not contribute significantly to separation between groups. There was some overlap in terms of those items that correlated in both groups. Since those correlations did not contribute to the understanding of the differences between groups, they were not included in the discussion. The items that did contribute to group membership and were correlated within the autistic group, but not in the normal control group, were anemia and urinary infection ($r = .67$), emotional problems and high temperatures ($r = .77$), emotional problems and parasitic infection ($r = .38$), and urinary infection and depression ($r = .38$). Correlations between the remaining combinations of variables were either very low or in the negative range.

DISCUSSION

The etiology of infantile autism has been the subject of considerable study and debate. One significant area of study has involved the relationship of perinatal complications to the development of

infantile autism. Previous research highlighted the possible roles of bleeding during pregnancy, use of prescription medication, spontaneous labor, flu-like symptoms during pregnancy, breech delivery, and low birth weight. The conclusiveness of this body of research, though, was hindered by the lack of a standardized tool for assessing perinatal complications. Consequently, the current research utilized a standardized measure, the MPS, to evaluate the role of perinatal difficulties in the histories of autistic individuals, compare findings with those from previous research, and evaluate specific maternal health issues as possible risk factors for the development of autism.

Results revealed that 65% of the cases were correctly grouped (autistic/normal) utilizing the MPS. Of the 10 factors of the MPS, 3 were most significant: gestational age, maternal morphology, and intrauterine stress (bleeding during pregnancy, stress experienced by mother, prescribed medications consumed by mother, and previous gynecological surgery). In general, these findings add credence to the results of earlier research with the exception of Maternal Morphology (weight and height of mother). The reasoning behind this finding is unclear and complicated by the fact that neither the mothers' weight nor height was overtly excessive, thereby undermining any notion of physiological stress. Thus, it seems important that this factor be further evaluated.

Of the six factors noted in previous research (listed above), five also contributed significantly in separating the autistic from normal samples. These include labor, breech or other abnormal delivery, low birth weight, use of prescription medications during pregnancy, and viral infections. Of these, all but length of labor were in the expected direction. Previous research indicated that spontaneous labor was frequently present in the histories of autistic individuals. In this research, though, the mean length of labor ranged from 6 to 10 h, longer than that of normal individuals. Although not deemed excessive in terms of perinatal complications, this longer length of labor may have provided more time for other delivery complications and intrauterine stress. Perhaps length of labor on either side (spontaneous or longer) of that experienced by normal mothers highlights risk. In fact, further research might uncover an optimum range, beyond which is considered a risk factor.

The one item that was not fully supported by this research was bleeding during pregnancy. While uterine bleeding occurred more frequently in the autistic population in this research, the difference was not statistically significant. This difference may be secondary to an artifact of sample size or selection.

Analysis of maternal medical conditions also highlighted some divergency in this and previous research. Specifically, we found that urinary infections, high temperatures, and depression were experienced significantly more by the mothers of autistic individuals. This variance may reflect the fact that such information was not noted in medical charts or spontaneously reported by mothers. It is possible that the highly pertinent nature of the items of the MPS and its reliance on recognition versus recall allowed for a broader assessment of maternal conditions. Of note, although "emotional problems" did not reach a level of significance, it did approach it. The content of this category is likely broader than that of depression, suggesting that other psychological states may contribute to the mothers' emotional and physical health. The general negative impact of maternal stress on the developing fetus has been demonstrated (i.e., Annis, 1978). Its specific contribution to the development of autism needs additional evaluation.

The maternal medical condition that contributed most to the separation of the groups was viral infections. Ironically, this risk factor is one of the most difficult to avoid and treat. But, future research may want to focus on differentiating the type/types of viruses that occur in the histories of autistic mothers, thereby identifying key strains that possibly may be averted with mild to moderate behavior change on the part of the mothers.

As a result of this research, a number of perinatal complications have been highlighted as likely contributors to the development of infantile autism. Credence to much of the previous research was provided, suggesting that low birth weight, prescribed medication taken during pregnancy, viral infections, and abnormal delivery are indeed factors which place an infant at risk for developing autism. The specific contributions and interactions of each of these factors needs further research. Factors indicated as risk-related by this research, but not previously identified, include maternal morphology, longer (though not excessive) length of labor, depression, urinary

infections, and high temperatures. These, too, need further evaluation. Such evaluation of the risk factors found in this research study will one day help us reduce the incidence of autism.

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