Obstetric factors in Asperger syndrome: comparison with high-functioning autism

M. Ghaziuddin, J. Shakal & L. Tsai

University of Michigan, Ann Arbor, Michigan, USA

Abstract

Asperger syndrome (AS) is a pervasive developmental disorder widely regarded as a mild variant of autism. To investigate if AS is associated with a history of fewer obstetric insults compared to autism, we examined the developmental history and obstetric records of 10 males with AS (mean full scale IQ 95.3), and compared them with 10 autistic males with a full scale IQ of 70 or above (so-called high-functioning autism; mean full scale IQ 82.6). Males with AS showed a trend toward lower Apgar scores at one minute (chi-square=4; df=1; $P=0.04$) and were more likely to have been born to mothers outside the optimal age group of 20–30 years (chi-square=5; df=1; $P=0.02$). They were also less likely to have been irritable and floppy as infants (chi-square=3.8; df=1; $P=0.05$). However, the total optimality scores did not differ significantly between the two groups.

Introduction

Asperger syndrome (Asperger 1944; Wing 1981) is currently conceptualized as a pervasive developmental disorder with an overlap with autism. Although it is now included as a distinct category

Correspondence: Dr Mohammad Ghaziuddin, University of Michigan Medical Center, Box 0390, 1500 East Medical Center Drive, Ann Arbor, MI 48109-0390, USA.

within the pervasive developmental disorders both in the ICD-10 system of classification (WHO 1990) and in the DSM-IV (APA 1994), it is often regarded as a mild variant of autism. It has been proposed that Asperger syndrome (AS) is part of the autistic continuum with AS at the upper end, autism in the middle, and severely retarded children with the triad of language and social impairment at the lower end (Gillberg 1989). Despite the increasing interest in this disorder, it is not clear to what extent it differs from autism with normal intelligence, also referred to as high-functioning autism (HFA).

One manner in which patients with AS may differ from those with autism is in their obstetric histories. Mothers of autistic children have been shown to present with a variety of obstetric insults. Although no specific factors of aetiologic significance have been identified, compared to various control groups, studies have found an excess of first or midtrimester bleeding, advanced maternal age, and the use of medications (Tsai 1987). If AS is conceptualized as a mild form of autism, it is possible that patients with AS may present with a history of fewer obstetric insults than those with autism. However, little research has been done on the occurrence of pre-, peri- and neonatal deficits in the development of persons with AS. Wing (1981) commented that nearly half of her series of patients with AS had a history of pre-, peri- or postnatal conditions that could have caused cerebral damage. Subsequently,

in a study of 23 children with AS, Gillberg (1989) found that 10 children (43%) had 'contributory prenatal or perinatal factors that might have caused brain damage'. Eight patients (35%) had experienced toxemia or smallness for gestational age, one mother had been hypothyroid during pregnancy, and one boy had suffered from severe perinatal asphyxia. Compared to autistic controls, obstetric insults were indeed less common in AS patients. More recently, Rickarby *et al.* (1991) described biological factors in a group of 10 children with AS, based on the 'descriptive common characteristics set out by Asperger in 1944' (Rickarby *et al.* 1991, p. 342). Out of this group, two had a history of Caesarian section, four had been delivered by forceps, three by face presentation, and in the remaining three patients, labour was classified as normal.

None of the studies cited above used the ICD-10 criteria of AS since, with the exception of the study of Rickarby *et al.* (1991), these were published before the ICD-10 (1990). This is important because patients with mental retardation and speech delay are excluded from the ICD-10 definition of AS. Also, the ICD-10 criteria appear to be closer to the description given by Asperger in his original case series (Ghaziuddin *et al.* 1992). In brief, the ICD-10 criteria stipulate that persons with AS suffer from autistic social dysfunction without meeting the criteria for any pervasive developmental disorder including autism, and do not give a history of language delay or of mental retardation. Therefore, the present study was undertaken with the following aims:

(1) to document the occurrence of obstetric deficits in patients with AS diagnosed according to the ICD-10 (WHO 1990); and
(2) to investigate if AS is associated with fewer obstetric insults than a matched group of patients with high-functioning autism.

Method

Setting

The study was conducted at the University of Michigan Medical Center, Ann Arbor, Michigan, USA. Diagnosis of pervasive developmental

disorders (PDD) was made by one or both child psychiatrists (MG and LT) after a comprehensive multi-disciplinary evaluation which consisted of psychiatric examination of the child, speech and language evaluation, psychological testing, and behavioural assessment. A systematic developmental history was also obtained. Clinical information thus obtained was supplemented by data collected from the Autism Behaviour Checklist (Krug *et al.* 1980) and the Vineland Adaptive Behaviour Scales (Sparrow *et al.* 1984).

Subjects

Diagnosis of AS was based on the ICD-10 criteria (WHO 1990). In brief, patients with AS do not meet the criteria for autism or any other pervasive developmental disorder, but suffer from reciprocal social deficits as in autism. There is no significant speech or cognitive delay. Idiosyncratic interests and clumsiness may also be present (WHO 1990). In the present study, the diagnosis of AS was reached as follows: patients with pervasive developmental disorders who failed to meet the criteria for either DSM-III-R (APA 1987) autistic disorder or ICD-10 autism, and those who had a full-scale IQ over 70 on the WISC-R (Wechsler 1974) were identified. From this group, those who had a history of normal language development formed the ICD-10 AS subjects ($n=10$; mean age: $13.7+3.7$ years; mean full scale IQ: 95.3 ± 20.3). To eliminate the possible effect of gender on obstetric factors, females were excluded. Since there were two sets of siblings in the AS group, the number of mothers included in this group was seven.

Controls

Those patients who met the DSM-III-R/ICD-10 criteria for autism *and* had a full scale IQ over 70 formed the high-functioning autistic (HFA) control group ($n=10$; mean age: 14.3 ± 6.2 years; mean full scale IQ: 82.6 ± 8.0). As in the AS group, females were excluded.

All the AS and HFA patients were Caucasian and were born in North America. None suffered from any current seizure disorder or a diagnosed

neurologic condition (such as tuberous sclerosis) known to co-exist with autism. None of the subjects or controls met the clinical description of fragile-X syndrome.

Obstetric history

Details about obstetric history were collected from the parents based on a semi-structured interview. In addition, after obtaining consent, photocopies of original hospital records pertaining to the birth of the patient were examined. Optimality scores were allotted to each patient, based on the method of Gillberg & Gillberg (1983). According to this method, optimal scores are given for each event related to pregnancy and delivery. Any scores which fall above or below the optimum range are accorded points. The higher the points gained, the greater the history of obstetric deficits. Allotment of optimality scores was done by an investigator (JS) who was blind to the hypothesis and did not participate in the diagnostic evaluation. The method was modified so that delivery by forceps was categorized as an event. This was to allow comparison with the study by Rickarby et al. (1991) which commented on the use of forceps in their sample. Apgar scores were not available in one AS and one HFA patient; the score at one minute was taken into account because the 5-min score was not recorded in all cases.

Patient number	Maternal age	Parity	Bleeding in pregnancy	Infection in pregnancy	Generalized oedema	SGA	Vacuum extraction	Forceps	Epidural anaesthesia	Apgar score reduced	Cord complications	Amniotic fluid not clear	Hyperbilinubinemia	Irritable floppy infant	Total non-optimal score
Asperger syndrome group															
1	+	+						+	+	+				+	6
2	+	+					+			+					4
3	+									+		+			3
4					+			+		+					3
5						+							+		2
6	+														1
7										+					1
8										+					1
9															0
10															0
Total	4	2	0	0	1	1	1	2	1	6	0	1	1	1	21
Autism group															
11			+						+	+	+	+			5
12				+	+				+		+			+	4
13					+			+						+	3
14				+									+		2
15												+		+	2
16											+			+	2
17														+	1
18								+							1
19		+													1
20															0
Total	0	1	1	1	2	0	0	3	2	1	3	1	1	5	21

Significant difference versus control group: 0·02   0·04   0·05

Figure 1 Distribution of non-optimal factors in individual children

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Results

Eight AS patients gave a history of obstetric insults based on the optimality scale compared to nine in the HFA group. Four AS patients were born to women older than 30 years compared to none in the control group. Vacuum extraction or forceps were used in three subjects and three controls. Two AS patients had a history of one HFA control scored high on parity. One of the AS mothers had a history of generalized oedema in the first trimester compared to two in the HFA group. Six AS patients and one HFA patient scored outside the optimum range of Apgar score at one minute. The maternal age of four AS patients fell outside the optimum range of 20–30 years, compared to none in the HFA

Factors	Optimal	No. with reduced optimality		P
		AS (n=10)	HFA (n=10)	
Prenatal				
Maternal age (years)	20–30	4	0	0.02
Parity	1–2	2	1	
H/O abortion	0–2	0	0	
Bleeding in pregnancy	Absent	0	1	
Severe infections in pregnancy	Absent	0	1	
Generalized oedema	Absent	1	2	
Albuminuria	Absent	0	0	
Blood pressure	>140/95	0	0	
Psychiatric specialist care	No	0	0	
Maternal diabetes	No	0	0	
Maternal epilepsy	No	0	0	
Medication*	>1 week	0	0	
Gestational age (weeks)	36–41	0	0	
Small for gestational age†	No	1	0	
Intrapartum				
Twins or multiple birth	No	0	0	
Breech, foot or other	No	0	0	
Vacuum extraction	No	1	0	
Forceps	No	2	3	
Epidural anaesthesia	No	1	2	
Apgar score	9–10	6/9	1/9	0.04
Cord prolapse/around neck/knot	No	0	2	
Amniotic fluid	Clear	1	1	
Child severely traumatized (fractures, severe bruises)	No	0	1	
Neonatal				
Respiratory distress	Absent	0	0	
Septicemia/meningitis	Absent	0	0	
Hyperbilirubinemia‡	Absent	1	1	
Anaemia req transfusion	Absent	0	0	
Irritable/floppy infant	No	1	5	0.05
Convulsions	No	0	0	
Difficulties regulating temp	No	–	–	
Clinical dysmaturity (scaly skin, too large for body)	No	0	0	
Oxygen treatment >30%	No	0	0	

Table 1 Obstetric factors in Asperger syndrome and high-functioning autism

*Only medication with known or suspected negative effect on foetus.
†Weight <2 SD limit for gestational age.
‡Hyperbilirubinemia requiring treatment.

group (chi-square=5; df=1; P=0.02; Fig. 1). Patients with AS were less likely to give a history of having been irritable and floppy as infants; one AS patient gave such a history compared to five in the HFA group (chi square=3.8; df=1; P=0.05). They were more likely to give a history of lower Apgar scores at one minute (chi- square=4; df=1; P=0.04), and of higher mean maternal age (t=2.3; df=1; P=0.03). However, on the whole, no significant differences were found between the two groups so far as total optimality scores were concerned (Table 1).

Discussion

Obstetric abnormalities were present in eight out of 10 patients with AS; this high figure is consistent with the study of Rickarby *et al.* (1991), which found that seven out of a sample of 10 children with AS had a history of obstetric abnormalities. Obstetric insults sustained by our sample of AS patients appear to be milder qualitatively compared to those reported by Wing (1981) and Gillberg (1989). For example, in the Gillberg (1989) study, 35% of the AS group had experienced maternal toxemia, smallness for gestational age or both. Also, 30% of the 23 mothers of children with AS were over 30 years of age at the time of the child's birth. This may be because these studies used diagnostic criteria which did not exclude patients with mental retardation since there is some evidence that, compared to autistic patients, an IQ-matched group of mentally retarded patients may present with a history of more frequent perinatal complications (Levy *et al.* 1988).

The obstetric factors identified were of a wide range and severity. However, when compared with patients with high-functioning autism, no significant group differences were found. The total non-optimal score in both the groups was 21, and a history of obstetric insults was found in almost the same degree between the two groups: 80% in the AS group and 90% in the HFA group. However, the AS group differed significantly from the HFA group on some individual factors. More AS patients were likely to give a history of non-optimal Apgar score at one minute, and were less likely to have been irritable and floppy as infants.

Also, more mothers in the AS group were in the older range. It is not clear what significance should be attached to these findings at this stage.

In summary, a variety of obstetric insults may be found in the developmental histories of patients with AS. However, as in patients with autism, to what extent these factors contribute specifically to the aetiology of the disorder is not known. Also, the deficits do not appear any less severe than those associated with high-functioning autism, although some individual differences seem to occur between the two disorders. At the same time, the small size of the sample could have concealed real differences that may not have been detected in the present study. Therefore, large-scale population-based studies using operational diagnostic criteria are needed to further clarify the role of obstetric factors in the pathogenesis of AS.

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