



The early stool patterns of young children with autistic spectrum disorder

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ABSTRACT

Aim: To investigate whether children with autistic spectrum disorder (ASD) have bowel symptoms consistent with underlying enterocolitis.

Methods: Information on children's stool patterns and gut symptoms collected by questionnaire at 4 weeks and at 6, 18, 30 and 42 months of age were available for 12 984 children from the Avon Longitudinal Study of Parents and Children (ALSPAC). Data on the 78 children identified by local health and/or education systems to have special educational provision for ASD were compared with the 12 906 remaining children in the cohort.

Results: Comparison of the ASD and control group during the first 3.5 years of life showed no major differences in stool colour or consistency, or in frequency of diarrhoea, constipation, bloody stools or abdominal pain. The ASD children had similar stool frequency up to 18 months, but there was a trend for ASD children to pass more stools at 30 months (OR 3.73, 95% CI 1.11 to 12.6; $p = 0.004$) and at 42 months (OR 6.46, 95% CI 1.83 to 22.7; $p < 0.001$), although only three children passed more than 4 stools/day. Repeating the analysis on only those cases diagnosed as having classical childhood autism resulted in very similar findings.

Conclusions: During the first 42 months of life, ASD children had a stool pattern that was very similar to that of other children, apart from a slight increase in stool frequency at 30 and 42 months. There were no symptoms to support the hypothesis that ASD children had enterocolitis.

There has been considerable debate following publication of a *Lancet* paper in 1998 describing 12 children with lymphoid hyperplasia, non-specific colitis and pervasive developmental disorder of sudden onset.¹ Wakefield and colleagues² suggested that a primary gastrointestinal pathology, an enterocolitis which they described as a new variant of inflammatory bowel disease, plays an important role in the onset and clinical expression of autism.

A number of studies have described gastrointestinal symptoms in children with autism,^{3,4} including oesophagitis,⁵ chronic gastritis,⁵ constipation⁶ and diarrhoea.⁷ Valicenti-McDermott *et al*⁸ compared the lifetime prevalence of gut symptoms in children with autistic spectrum disorder (ASD), children with developmental disability and those with normal development at a mean age of 7.6 years. A history of gut symptoms was elicited in 70%, 42% and 29% of children in the three groups. However, when the United Kingdom General Practice Database was used to investigate retrospectively the relationship between childhood

What is already known on this topic

- ▶ Older children with autistic spectrum disorder (ASD) have an increased prevalence of gut symptoms.
- ▶ It has been hypothesised that a non-specific enterocolitis is associated with the onset of ASD.
- ▶ Controversy exists whether gut symptoms are intrinsic to ASD, or are secondary to dietary and behavioural changes in these children.

What this study adds

- ▶ Children with ASD do not have symptoms suggestive of underlying enterocolitis and their stool pattern is very similar to that of typically developing children.
- ▶ From 30 months of age, they show a slight increase in stool frequency which may be a secondary phenomenon related to differences in diet.

gastrointestinal disorders and autism, nine of 96 (9%) autism cases and 41 of 449 (9%) matched controls had a history of gut symptoms before the date of the first recorded diagnosis of autism in the cases and the equivalent date for controls.⁹

Diseases involving chronic inflammation of the bowel (IBD) are well described with internationally agreed criteria for diagnosis (the Porto criteria¹⁰). Common symptoms include diarrhoea, abdominal pain and blood in the stool, but constipation is unusual.¹¹

To date no study has prospectively assessed the early bowel patterns and gut symptoms prior to a diagnosis of ASD using a geographically defined population. We have used longitudinal data on stool patterns and abdominal symptoms reported prospectively by mothers of children taking part in the Avon Longitudinal Study of Parents and Children (ALSPAC)¹² to test the hypothesis that the onset of ASD is preceded by symptoms of colitis, and to describe the stool patterns of ASD children compared to others of the same age.

METHODS

ALSPAC is a cohort study following the health and development of children who had an expected date of delivery between April 1991 and December 1992, and were resident in the Avon area of South West

England at the time of their birth. A total of 14 541 mothers enrolled in pregnancy, resulting in 14 062 live births of whom 13 971 survived the first 5 years.¹² Full details of the questionnaires used, the biological samples retained, the examinations and observations of the children are available on the ALSPAC website.¹³ Ethics approval for the study was obtained from the ALSPAC Law and Ethics Committee and the Local Research Ethics Committees.

Identification of cases of ASD

The children within ALSPAC with a diagnosis of ASD by age 11 were identified from two independent sources: (a) the clinical records of all children in the cohort investigated for a suspected developmental disorder by multi-disciplinary assessment, using standardised measures to diagnose ASD and (b) the national educational database in England (PLASC) which identifies all children in state schools (over 90% of children) who needed special educational provision because of ASD in 2003. Details of the methods used in the identification and characteristics of cases have previously been reported.¹⁴ A total of 86 children were identified, giving a prevalence of 62 per 10 000 children aged 11 years. The median age of diagnosis of childhood autism was 45 months, although many were showing symptoms of autism from early in infancy. Questionnaire data on stool patterns were available for 78 of the children with ASD.

Stool patterns

Questions on stool patterns of the children were included in structured questionnaires sent to the mother or main carer at 4 weeks and at 6, 18, 30 and 42 months after the birth of the child.¹⁵ The mothers were asked about the usual frequency of stool, the consistency and colour of the stools and history of diarrhoea. Options for response to stool frequency were: 4 or more per day, 2–3 per day, 1 per day, once in 2–4 days, 1 per week. In general the numbers were small in the last two categories, and they were combined. Options for colour of stools and consistency of stools were: usually, often, occasionally, never.

Bowel symptoms

The presence of abdominal pain was recorded at 18, 30 and 42 months. History of blood in stools was recorded at 6, 18, 30 and 42 months.

Statistical analyses

Logistic regression was used to analyse associations between ASD and stool patterns. Due to the strong association between male gender and ASD (OR 6.40, 95% CI 3.42 to 12.14), analyses were adjusted for gender. *p* Values were calculated for trend with frequency of each stool pattern. Although multiple comparisons were undertaken, we looked for consistent patterns of results. Isolated results, which may be chance events, were only considered important if significant at the 1% level. To assess the impact of the variable amounts of missing data at different time points, analyses were repeated on a restricted sample of children with a complete dataset.

RESULTS

The 78 children recognised as having ASD were compared with a control group of 12 905 other members of the cohort who had information on stool patterns and/or bowel symptoms. Table 1 compares the frequency of the stools of these children from 4 weeks to 42 months of age. There were no significant

differences at 4 weeks or at 6 or 18 months. At 30 months ($p = 0.002$) and 42 months ($p < 0.001$) the ASD children were more likely to defecate more frequently than controls, in particular to pass at least two motions a day. Only three children with ASD, less than 5% of the ASD population, passed more than 4 stools/day. The percentage of children who passed less than 1 stool/day was similar (around 6% at 42 months) in the two groups.

When the colours of the stools were compared, out of the 19 comparisons of frequency of green, brown, yellow or black stools, there were no significant differences at 4 weeks or at 6 or 18 months. The only differences were at 30 and 42 months, when ASD children passed yellow stools more often than non-ASD children. By 42 months over 90% of children in both groups usually passed brown stools.

There were no significant differences in the consistency of stools between the two groups at 4 weeks and at 6, 18 and 30 months. Stools became firmer with age with 20–28% of children usually passing a hard stool by age 30 and 42 months. There was only one significant difference between the two groups, which was liquid stools at 42 months: however, this was experienced by eight controls and a single child with ASD.

Table 2 shows the prevalence of diarrhoea in the two groups. The prevalence of diarrhoea increased with age, from around 3% at age 4 weeks to over 30% by 6 months and over 50% thereafter. There were no significant differences in the prevalence of diarrhoea in the two groups at 4 weeks or at 6, 18 or 30 months. After 30 months of age, ASD children were slightly more likely to have diarrhoea (58%) compared to controls (44%) ($p = 0.039$). There were no differences between the two groups as regards blood in stools or abdominal pain.

There was no association between age at identification of ASD and stool frequency at 42 months ($p = 0.975$) or diarrhoea at 42 months ($p = 0.609$).

At 57 months ASD children were six times more likely to be still wearing nappies: 11.7% (7) of the ASD children compared to 1.8% (164) of the controls.

Repeating the analysis on only those cases diagnosed as having classical childhood autism (excluding atypical autism and Asperger syndrome) resulted in very similar findings. Analysis of the restricted sample of children with a complete dataset also gave very similar results, confirming that the above findings are not an artefact of a changing sample.

DISCUSSION

This large population based study comparing prospectively collected longitudinal data from ASD and control children shows that there were very few differences in the stool patterns between the two groups of children. In particular, there was no increase in symptoms (abdominal pain or blood in the stools) suggestive of colitis in the ASD group. These findings do not support the hypothesis that the aetiology of ASD is associated with enterocolitis. Although children with ASD had more frequent defecation at 30 and 42 months, only four of these children passed more than 4 stools/day and the clinical significance of these differences is questionable. A history of diarrhoea in this population was quite high (around 50%) and the only difference between the two groups was between 30 and 42 months of age. The ASD children did not appear to have an increase in the frequency of constipation (passage of hard stool or less than 1 stool/day). Stools in normal children are known to change with age,^{16 17} becoming firmer, and the prevalence of constipation increases with age. The children in

Table 1 Comparison of frequency of stools at five different ages

Number of motions per day	ASD cases (n)	Rest of cohort (n)	OR (95% CI)	p Value
Characteristics at 4 weeks				
4+	37.5% (27)	27.6% (3316)	1.18 (0.71 to 1.96)	
2–3	45.8% (33)	41.4% (4967)	1.00 Reference	
1	11.1% (8)	24.4% (2921)	0.42 (0.19 to 0.91)	
<1	5.6% (4)	6.6% (791)	0.85 (0.30 to 2.41)	0.032
Characteristics at 6 months				
4+	1.4% (1)	3.0% (337)	0.45 (0.06 to 3.30)	
2–3	58.0% (40)	56.5% (6314)	1.00 Reference	
1	37.7% (26)	36.9% (4129)	1.01 (0.62 to 1.66)	
Once in 2–4 days or less	2.9% (2)	3.6% (399)	0.85 (0.20 to 3.54)	0.794
Characteristics at 18 months				
4+	2.7% (2)	1.4% (155)	1.52 (0.36 to 6.35)	
2–3	58.9% (43)	51.7% (5644)	1.00 Reference	
1	34.2% (25)	45.2% (4934)	0.76 (0.46 to 1.25)	
<1	4.1% (3)	1.6% (176)	2.74 (0.84 to 8.98)	0.602
Characteristics at 30 months				
4+	4.2% (3)	0.7% (74)	3.73 (1.11 to 12.55)	
2–3	45.1% (32)	29.7% (2974)	1.00 Reference	
1	47.9% (34)	64.7% (6468)	0.56 (0.34 to 0.91)	
<1	2.8% (2)	4.8% (484)	0.51 (0.12 to 2.13)	0.002
Characteristics at 42 months				
4+	4.6% (3)	0.4% (36)	6.46 (1.83 to 22.71)	
2–3	38.5% (25)	22.4% (2207)	1.00 Reference	
1	50.8% (33)	70.6% (6943)	0.42 (0.25 to 0.71)	
<1	6.2% (4)	6.6% (645)	0.61 (0.21 to 1.75)	<0.001

ASD, autistic spectrum disorder.

the Afzal study⁶ were older than 42 months and this may partially explain the difference in rates of constipation.

Although the ASD children appeared to pass yellow stools more often after 30 months of age, the vast majority of the children (around 90%) in both groups passed brown stools at 30 months and beyond. These colour changes in stools are known to be associated with dietary changes^{17–19} and may reflect differences in the diet of the two groups. The ASD children did not have an increased frequency of black stools.

The increase in stool frequency in ASD children may be a consequence of differences in diet, as stool pattern is known to vary with diet. As a function of the limited range of interests and difficulty in accepting change which characterises autism, children with ASD may show limited food preferences.^{20–21} Furthermore, once a child has been suspected of or diagnosed with ASD, the carer may put them on a diet that is very different (for example a dairy or/and gluten free diet), with consequent changes in stool pattern. Possible further explanations are that the increased frequency is a reflection of the developmental immaturity of the children with ASD (as stool frequency tends to reduce with age^{16–17}), or that these children have disordered gut motility (like other neurodevelopmental conditions such as cerebral palsy²²).

Table 2 Prevalence of diarrhoea in first 3.5 years of life

Age period	ASD cases (n)	Rest of cohort (n)	OR (95% CI)	p Value
0–4 weeks	2.7% (2)	3.2% (392)	0.82 (0.20 to 3.36)	0.784
0–6 months	33.3% (23)	33.4% (3808)	0.98 (0.59 to 1.62)	0.934
6–18 months	50.0% (37)	51.3% (5637)	0.91 (0.58 to 1.44)	0.697
18–30 months	56.3% (40)	55.1% (5648)	0.98 (0.61 to 1.57)	0.925
30–42 months	57.6% (38)	44.0% (4396)	1.68 (1.03 to 2.74)	0.039

Odds ratios are relevant to children with no history of diarrhoea in the particular period, after taking account of the sex of the child. ASD, autistic spectrum disorder.

The main strength of this study is that the data were collected prospectively before ASD was diagnosed. Limitations are that the cases were diagnosed by clinical teams rather than by structured research assessment, and that stool data were reported by the child's mother with no objective validation. It is possible that the reporting of stool symptoms by parents was affected by receiving a diagnosis of ASD, although against this there was no association between age at identification and reported stool frequency or diarrhoea at 42 months.

The study has also not differentiated between ASD children with and without regression. However, repeating the analysis on only those children with classical childhood autism did not change the results, so it is unlikely that splitting the ASD children into subgroups will reveal any differences between early stool patterns of the children with ASD who did and did not show signs of regression in the second year of life.

CONCLUSION

Children with ASD do not have symptoms suggestive of underlying enterocolitis. Their early stool patterns are not very different from those of typically developing children as regards frequency, colour or consistency, and there is also no difference in prevalence of diarrhoea. Some differences in stool frequency start to appear at 30 months and may be a secondary phenomenon related to differences in diet.

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