Psychological Markers in the Detection of Autism in Infancy in a Large Population

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Background. Investigation to see if there are key psychological risk indicators for autism in a random population study of children at 18 months of age; and to assess how well these discriminate children who receive a diagnosis of autism from other forms of developmental delay.
Method. Sixteen thousand children in the southeast of England were screened for autism by their health visitor or GP, during their routine 18-month-old developmental check-up, using the CHAT (Checklist for Autism in Toddlers). From a previous high-risk study we predicted that children at 18 months of age who failed three items ('protodeclarative pointing', 'gaze-monitoring', and 'pretend play') would be at risk for receiving a diagnosis of autism. From other evidence, we further predicted that those 18-month-olds who failed one or two of the key items (either pretend play, or protodeclarative pointing and pretend play) would be at risk for developmental delay without autism.
Results: Twelve children out of the total population of 16 000 consistently failed the three key items. Of these, 10 (83.3%) received a diagnosis of autism. Thus, the false positive rate was 16.6% (2 out of 12 cases), and even these 2 cases were not normal. When the 10 children with autism were reassessed at 3.5 years of age, their diagnosis remained the same. Thus the false positive rate among the cases diagnosed with autism was zero. In contrast, of 22 children who consistently failed either protodeclarative pointing and/or pretend play, none received a diagnosis of autism, but 15 (68.2%) received a diagnosis of language delay.
Conclusions. Consistent failure of the three key items from the CHAT at 18 months of age carries an 83.3% risk of autism; and this pattern of risk indicator is specific to autism when compared to other forms of developmental delay.

Autism is regarded as the most severe psychiatric disorder of childhood. It is rarely diagnosed before 3 years old, and usually considerably later than this, despite the fact that in the majority of cases it has an onset during infancy (Gillberg, 1990). When examined at school-age, children with autism are impaired in three behaviours that are normally universally present by 14 months of age.

Protodeclarative pointing (PDP) (Bates *et al*, 1979): the normal 9–14-month-old infant points at an object in order to direct another person to look at the object, as an end in itself. This form of the pointing gesture is absent or severely impoverished in school-age children with autism (Wing, 1976; Baron-Cohen, 1989, 1995). This is a specific deficit, in that a related form of the pointing gesture (protoimperative pointing) in which the normal infant points at an object (usually out of reach) in order to try to obtain it, is not thought to be specifically impaired in autism.

Gaze-monitoring (GM) (Scaife & Bruner, 1975): the normal 9–14-month-old infant turns to look in the same direction that an adult is looking in. This behaviour is also absent in school age children with autism. Both PDP and GM are aspects of 'joint attention behaviours', which result in the convergence of the infant's and the adult's attentional foci onto the same object or event (Bruner, 1983).

Pretend play (PP): defined as play involving object-substitution, and/or the attribution of absent properties to objects or situations (Leslie, 1987). Across different cultures, it makes its earliest appearance in simple form by about 14 months of age (Bretherton, 1984). Again, in autism the deficit in pretend play is highly specific, in that functional play, in which the normal toddler uses a toy according to its conventional function, is not specifically impaired (Wing, 1977; Baron-Cohen, 1987).

If these three key behaviours are normally present by 14 months of age, and yet are absent or significantly impaired in school-age children with autism, they might serve as important indicators for the early detection of autism. Currently, none of

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these key behaviours are checked during routine developmental check-ups at 18 months of age. In an earlier study we therefore developed a new checklist, to test these predictions. The Checklist for Autism in Toddlers (CHAT) (see Fig. 1) was administered to a group of 41 children of 18 months of age, selected for being at raised genetic risk for developing autism. Of these only 4 failed on all three of the key items (PDP, GM, and PP), and at follow-up 12 months later, all 4 of these children had received a diagnosis of autism. None of the other 37 children failed more than one key item on the CHAT, and none developed autism. Equally, of 50 randomly selected 18-month-olds in a control group, none failed more than one key item, and none developed autism (Baron-Cohen et al, 1992).

We aimed to replicate the finding from the earlier study, and test the CHAT and the predictions on a random population study, in order to examine the generalisability of the earlier findings. In addition, since a delay in PDP or PP is associated with specific language or general developmental delay

(Medical Research Council Project)
To be used by GPs or Health Visitors during the 18 month developmental check up.

Child's Name: ....Date of Birth: ....Age: ....
Child's Address: ....Phone Number: ....

Section A: ask parent

1. Does your child enjoy being swung, bounced on your knee, etc?
2. Does your child take an interest in other children?
3. Does your child like climbing on things, such as up stairs?
4. Does your child enjoy playing peek-a-boo/hide-and-seek?
5. Does your child ever PRETEND, for example, to make a cup of tea using a toy cup and teapot, or pretend other things?
6. Does your child ever use his/her index finger to point, to ASK for something?
7. Does your child ever use his/her index finger to point, to indicate INTEREST in something?
8. Can your child play properly with small toys (eg: cars or bricks) without just mouthing, fiddling, or dropping them?
9. Does your child ever bring objects over to you (parent), to SHOW you something?

Section B: GP or HV observation

i. During the appointment, has the child made eye contact with you?
ii. Get child's attention, then point across the room at an interesting object and say "Oh look! There's a (name of toy)!" Watch the child's face. Does the child look across to see what you are pointing at?[1]
iii. Get the child's attention, then give child a miniature toy cup and teapot and say "Can you make a cup of tea?" Does the child pretend to pour out tea, drink it, etc?[2]
iv. Say to the child " where's the light?", or "Show me the light". Does the child POINT with his/her index finger at the light?[3]
v. Can the child build a tower of bricks? (If so, how many?) (Number of bricks:..........)

[1] (To record YES on this item, ensure the child has not simply looked at your hand, but has actually looked at the object you are pointing at).
[2] (If you can elicit an example of pretending in some other game, score a YES on this item).
[3] (Repeat this with "Where's the teddy?" or some other unreachable object; if child does not understand the word "light". To record a YES on this item, the child must have looked up at your face around the time of pointing).

Fig. 1 The CHAT (Reproduced from Baron-Cohen et al (1992)).

(Tomasello, 1988; Sigman et al, 1986), we aimed to test if absence of PDP, or absence of both PDP and PP, would distinguish children with developmental delay from autism.

Method

The overall design of the study involved screening a large general population of children at 18 months of age, identifying those consistently failing the CHAT (on two administrations), and then rescreening the whole population at age 3.5 years, to determine the sensitivity and specificity of the CHAT as a screening instrument. This paper is concerned with findings from the screen at 18 months.

Subjects

Nine districts in the southeast Thames Health Region took part in this study. Sixteen thousand children were screened using the CHAT, administered by health visitors or GPs. The mean age of the sample at screening was 18.7 months (s.d. = 1.1 month). The sex ratio of the total population was 1.05:1 (m:f). The social class distribution of the main caregiver of these children was broadly representative of the UK (*Economic Activity of Great Britain*, 1981). Children with severe developmental delay were not included, since such children are already clearly identified by 18 months of age, and because health visitors were reluctant to give additional assessments to parents whose children were likely to fail almost all items on the CHAT.

Screening

Each subject was screened using the CHAT (see Fig. 1), as close to their 18 month 'birthday' as was possible. In the majority of cases (n = 12 688, or 79.3%), this was administered by the family health visitor. In a proportion of cases (n = 771, or 4.8%) this was administered by the family GP. Finally, in another subgroup of cases (n = 2541, or 15.9%), the CHAT was administered by the main caregiver.[1] The CHAT form for each child was then sent back to our research centre, where all responses were entered into a computer database. The construction of the CHAT is described in detail elsewhere (Baron-Cohen et al, 1992). In structure, the CHAT has 2 sections: Questions in section A assess areas of development via parental report. In section B, the clinician checks the child's actual behaviour against the parental report given in section A. Like

1. In this latter subgroup, items Biii and Biv were omitted, since these would have been simply repeating questions A5 and A7.

most screening tests in public health surveillance, a positive case is identified if a child consistently fails on initial test and on a subsequent retest. In all cases, retest with the CHAT was done as soon as possible after the initial CHAT, and on average this was one month later. Our interest was only in those children who were consistently failing the key items, since this was likely to be due to significant developmental causes rather than situational causes (such as the child's current physical state), or very mild developmental delay. We searched for children whose scores met criteria for one of three risk groups:

(i) Autism risk group: Children who failed on PDP, GM, and PP (CHAT items A5, A7, Bii, Biii, and Biv). Note that a failure on Biii validated a fail on A5, and failure on Biv validated a fail on A7. Thus, children in this risk group failed 3 key items.

(ii) Developmental delay (without autism) risk group (henceforth developmental delay risk group): Children who failed PDP (A7 and Biv), or failed PDP and PP (A5, A7, Biii, and Biv). Critically, children in this group had to pass GM (Bii). Thus, children in this risk group failed either 1 or 2 key items.

(iii) Normal group: Children who passed all three key items; PDP, GM, and PP (A5, A7, Bii, Biii, and Biv).

Diagnostic groups

Children who met criteria for each of the risk groups were invited to our clinic in London for developmental and diagnostic assessments. These children were then given one of three diagnoses. These were:

(1) Autism[2]; children who met criteria for autism on at least 2 out of the following 3 diagnostic methods: (i) the Autism Diagnostic Interview – Revised (ADI-R[3]; Lord *et al*, 1994)

with the parents; (ii) ICD–10 criteria (World Health Organization, 1994) from interaction during assessment with the child in the clinic; and (ii) ICD–10 criteria as rated from videotapes of all 50 subjects. These three sets of diagnostic judgements were all strictly independent of each other, conducted by five independent judges (AC, GB, KM, AD, and SBC), and in all cases the judges were blind as to which of the three risk groups any given child was in. All judges were clinicians with considerable experience in the field of autism. The ADI–R was not used on its own, as it has not been used with this age-group before.

(2) Developmental delay: children who had (i) equal to or less than 5 words, according to parental report, as ascertained in the ADI. This is on the basis that less than 5% of children at 20-months-old have five or fewer words (Fenson *et al*, 1993); and/or (ii) a delay on the Griffiths Scale of Infant Development (Griffiths, 1986) of equal to or more than 4 months. This was administered by a psychologist in our team who remained blind to the autism diagnostic information. Given that children with severe developmental delay were not included in the population we screened, our aim was to assess if autism could be distinguished from mild to moderate developmental delay in language or cognition (without autism).

(3) Normal: those children who did not fall into the above two categories, and were free of other clinical diagnoses.

Following Wing & Gould (1979), we predicted that approximately 4 in 10 000 children in the population would have classic autism (Kanner, 1943), and as many as one per 1000 might have some form of autism (Gillberg, 1990). We therefore estimated there would be between 6 and 16 cases in a population of 16 000. We predicted that all of these cases would come from the autism risk group, as defined above. In contrast, we predicted that cases of developmental delay would come from the developmental delay risk group.

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2. The Autism diagnosis actually contains 2 subgroups: Autism (without any developmental delay), and Autism + Developmental Delay.

3. It should be noted however that with the judges who used the ADI-R (a parent-report measure only), criteria were slightly modified: To receive a diagnosis of autism, a child had to score above the traditional threshold on the first 2 axes (Reciprocal Social Interaction; and Communication), and score above a new threshold of 2 or more on the third axis (Repetitive Behaviour). This modification was made because many children scored above the traditional threshold on the first 2 axes, but just missed doing so on the third.

Results

From the total population of 16 000, just 12 children met criteria for the autism risk group (Failed A5, A7, Bii, Biii and Biv), 44 children met criteria for the developmental delay risk group (Passed Bii, but either failed A7 and Biv, or A7, Biv, A5 and Biii). Finally, more than 99.6% of the total

population met criteria for the normal group (estimate based on retesting approximately 20 cases in this group at the initial CHAT).

The number of children from each of the three risk groups who were given one of the three diagnoses is shown in Fig. 2, and summarised in Table 1. The following results are worth highlighting:

(i) Ten out of 12 (83.3%) of children in the autism risk group received an autism diagnosis, whilst the risk of receiving an autism diagnosis for a child in the developmental delay risk group was 0% (or 0/22). This odds ratio difference is highly significant ($\chi^2 = 7.99$, 1 d.f., $P = 0.005$).

(ii) None of the children in the autism risk group were diagnosed as normal. That is, the 2 cases in the autism risk group who did not receive a diagnosis of autism nevertheless received a diagnosis of developmental delay. Thus, the false positive rate for detection of autism is 16.6% (2/12), but even these cases are not normal.
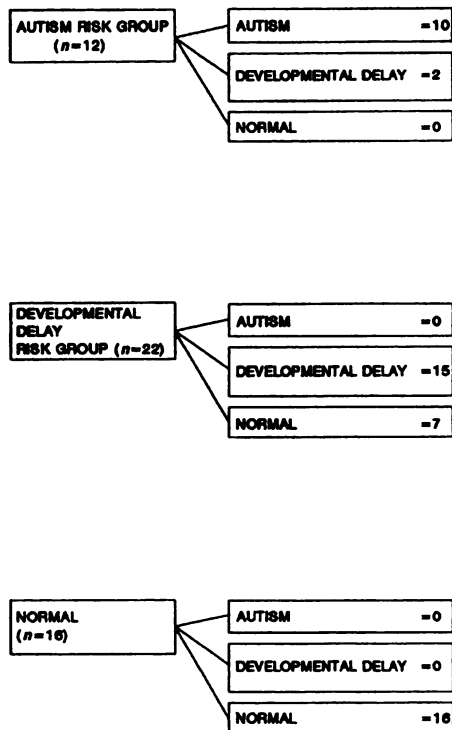

Fig. 2 Number of children from each of the three risk groups who received different diagnoses.

Table 1
Number of children failing all 3 key items, or only 1 or 2 of the key items, who were given different diagnoses

Key items failed (risk groups)	Diagnosis		
	Autism ($n=10$)	Developmental delay ($n=17$)	Normal ($n=23$)
Failed GP, PP, and PDP ($n=12$)	10	2	0
Failed PDP, or PDP and PP ($n=22$)	0	15	7
Fail 0 ($n=16$)	0	0	16

GM, gaze monitoring; PDP, protodeclarative pointing; PP, pretend play.

(iii) Thus, absence of PDP, GM, and PP in combination, carries a significant risk of autism (83.3%), while absence of PDP alone, or PDP plus PP, carries a zero risk of autism, when assessed at 18 months.

(iv) Absence of PDP alone, or of PDP plus PP, carries a 68.2% risk of the child receiving a diagnosis of developmental delay (based on 15 out of 22 children who were so diagnosed in the developmental delay risk group). That is, less than half of the children in the developmental delay risk group were diagnosed as normal.

(v) The finding of 10 cases of autism in a population of 16 000 (or 6.25 per 10 000) is within expected prevalence levels, given previous epidemiological studies (Wing & Gould, 1979). Note though that the number of cases of autism in the population is likely to be even higher than this, since there may have been some who passed on the CHAT and were therefore not detected at 18 months. Our follow-up study of this population (forthcoming) will therefore establish the final prevalence figure.

(vi) Nine of the 10 children who received a diagnosis of autism also had developmental delay (either in terms of language, or language plus non-verbal cognitive level). This implies that one of the children with autism had no developmental delay, and might therefore be diagnosed as Asperger's syndrome. However, we suspect Asperger's syndrome is more common than this, and our current work focuses on how to improve the detection of this related condition.

CHAT profile by diagnosis

CHAT scores for the children given each of the three diagnoses are shown in Table 2. Of the 10 cases of autism, A5, A7, Bii, Biii, and Biv were

failed by all of the group. Finally, 9 of the 10 cases also failed A6 (protoimperative pointing), which was not predicted from current theories, although this has been previously noted clinically. Of the 17 cases of children with developmental delay, none failed GM (Bii) in combination with the other key items. This combination of failure is therefore a powerful discriminator of autism from developmental delay.

Follow-up of the 10 children with autism

Since the diagnosis of autism at 18–20 months using the ADI-R has never been attempted before, we invited all 10 children who had received an autism diagnosis to be reassessed at 3.5 years of age. They were again given the ADI-R, as well as a clinical assessment by two members of our team with considerable experience in this field. In all cases, the diagnosis of autism was confirmed. Thus, diagnosis of autism using the ADI-R at 18–20 months produces no false positives.

Discussion

We predicted that undiagnosed toddlers with autism at age 18 months would fail to show three key behaviours: protodeclarative pointing (PDP), gaze-monitoring (GM), and pretend play (PP). In the majority of cases, this prediction was confirmed. Sixteen thousand children were screened, and of 12 children who fell into this pattern of failure on two administrations of the CHAT, 10 of these (83.3%)

received a diagnosis of autism. In contrast, of 22 children who failed PDP alone, or PDP and PP, none received a diagnosis of autism. This implies that absence of PDP, PP, and GM at 18 months carries a very high risk for autism. This study thus provides further evidence for the importance of these items in any screening method for the detection of autism at 18 months of age, and replicates earlier findings from a high-risk sample (Baron-Cohen et al, 1992).

Secondly, we predicted that children who lacked PDP, or PDP plus PP, at 18 months of age, would be at risk for developmental delay (without autism). This prediction was also supported: 15 out of 22 children (68.2%) who unambiguously lacked one or both of these behaviours received a diagnosis of developmental delay (without autism).

Consistent failure on the CHAT at 18 months indicates an 83.3% risk of autism; and at this stage, expert diagnosis should be sought. We stress that the CHAT should not be used as a diagnostic instrument, but it can alert the primary health professional to the need for an expert child psychiatric or paediatric referral. A follow-up study will be essential to establish the rate of false negatives, and will be reported separately in a further paper.

Table 2
Percentage of subjects consistently passing each item on the CHAT, by diagnosis

Item	Autism (n=10)	Developmental delay (n=17)	Normal (n=23)
A1	100	100	100
A2	50	94	91
A3	100	100	100
A4	90	100	96
A5 (PP)	0[1]	53	100
A6	10	53	87
A7 (PDP)	0[1]	0	70
A8	100	100	100
A9	60	65	91
Bi	70	100	100
Bii (GM)	0[1]	65	100
Biii (PP)	0[1]	65	100
Biv (PDP)	0[1]	0	70
Bv	90	82	91

1. This unique pattern identified 10 true positive cases of autism in 16 000, and 2 false positive cases of autism (they actually had developmental delay without autism).

Clinical implications

● Detection of autism is possible at 18 months of age.
● Early detection should lead to early support being available for families.
● Early detection should lead to treatment being started as soon after 18 months of age as possible.

Limitations of the study

● Until follow-up, the rate of false negatives will remain unknown.
● Diagnosis is not possible using the CHAT alone – only following a referral for expert assessment.
● Until early intervention studies have been tried and tested, the full value of early diagnosis will remain unknown.

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