

Positive Screening on the Modified Checklist for Autism in Toddlers (M-CHAT) in Extremely Low Gestational Age Newborns

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Objective To test the hypothesis that children born preterm are more likely to screen positive on the M-CHAT for an autism spectrum disorder.

Study design We compared the M-CHAT positive rate of those with cerebral palsy, cognitive impairment, and vision and hearing impairments to those without such deficits.

Results Relative to children who could walk, the odds for screening positive on the M-CHAT were increased 23-fold for those unable to sit or stand independently and more than 7-fold for those requiring assistance to walk. Compared with children without a diagnosis of cerebral palsy, those with quadriplegia were 13 times more likely to screen positive, and those with hemiparesis were 4 times more likely to screen positive. Children with major vision or hearing impairments were 8 times more likely to screen positive than those without such impairments. Relative to those with a Mental Development Index (MDI) of >70, the odds for screening positive were increased 13-fold for those with an MDI of <55 and more than 4-fold for those with an MDI of 55 to 69.

Conclusions Major motor, cognitive, visual, and hearing impairments appear to account for more than half of the positive M-CHAT screens in extremely low gestational age newborns. Even after those with such impairments were eliminated, 10% of children—nearly double the expected rate—screened positive. (*J Pediatr* 2009;154:535-40)

The Council on Children with Disabilities of the American Academy of Pediatrics recommends that pediatricians screen for an autism spectrum disorder (ASD) if there are concerns about a child's development.¹ One ASD-specific screening tool is the Modified Checklist for Autism in Toddlers (M-CHAT).² When the M-CHAT was used as a screen in unselected children during well-child care visits between age 16 and 30 months, 5.7% screened positive for ASD.³ In contrast, we found that 21% of infants born before the 28th week of gestation screened positive for ASD on the M-CHAT.⁴ Four previous studies found that children born preterm are at greater risk for an autism diagnosis than children born at term,⁵⁻⁸ and 2 other studies detected an association between low birth weight and increased risk of an autism diagnosis.^{9,10} A recent study reported an increased rate of positive screening for ASD on the M-CHAT in a selected low birth weight cohort.¹¹

Two compatible explanations for this apparently very high rate seem plausible. One is that extremely low gestational age newborns (ELGANs) are at increased risk for ASD. The other is that developmental impairments other than ASD (for which ELGANs are at increased risk)^{4,12-14} increase the frequency of positive screens. For example, the parent of a child with severe motor impairment might mark as abnormal such items on the M-CHAT screen as "does not point to indicate interest" or "does not bring objects to you," 2 of the critical items on the M-CHAT, even though the child may demonstrate no language or social impairment. In the present study, we evaluated the extent to which

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ASD	Autism spectrum disorder	M-CHAT	Modified Checklist for Autism in Toddlers
BSID-II	Bayley Scales of Infant Development, 2nd edition	MDI	Mental Development Index
CP	Cerebral palsy	PDI	Psychomotor Development Index
ELGAN	Extremely low gestational age newborn	PPV	Positive predictive value
GMFCS	Gross Motor Functional Classification System	VABS	Vineland Adaptive Behavior Scales

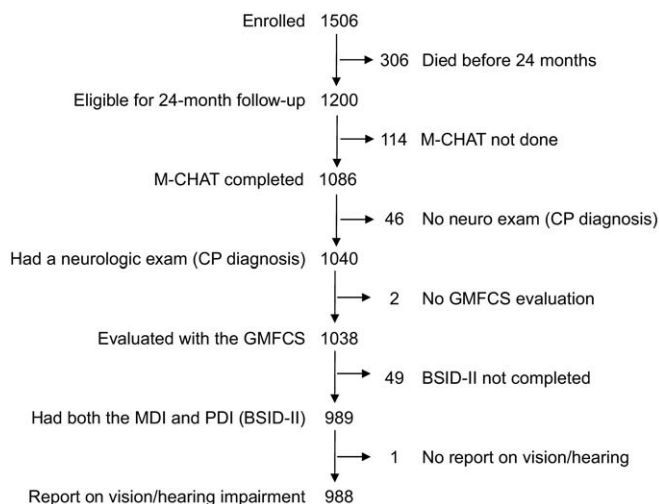


Figure. Sample description.

developmental impairments contribute to the risk of screening positive for ASD on the M-CHAT.

METHODS

The ELGAN Study

The ELGAN Study was designed to identify characteristics and exposures that increase the risk of structural and functional neurologic disorders in ELGANs. During the years 2002 to 2004, women delivering before 28 weeks gestation at 1 of 14 participating institutions in 11 cities in 5 states were invited to enroll in the study. The enrollment and consent processes were approved by the individual institutional review boards.

Mothers were approached for consent either on antenatal admission or shortly after delivery, depending on clinical circumstances and institutional preference. A total of 1249 mothers of 1506 infants consented; 257 women were either missed or did not consent to participate.

The 24-Month Developmental Assessment

Some 77% of the participants underwent developmental assessment within 23.5 to 27.9 months; of the others, about half were assessed before 23.5 months, and the other half were assessed after 27.9 months. Of the 1200 children who survived to 24 months corrected age, 988 underwent a complete developmental assessment that included a neurologic examination, a Gross Motor Functional Classification System (GMFCS) assessment, a Bayley Scales of Infant Development, 2nd edition (BSID-II) assessment, and several parent-reported assessments, including the M-CHAT (Figure). The parent or other caregiver who brought the child for the 24-month developmental assessment was also interviewed to complete a standardized 60-item interval medical history form. Questions included whether the child had a hearing problem and, if so, whether he or she needed a hearing aid or special services for hearing impairment, and whether the child had a vision problem or was considered legally blind.

M-CHAT

The M-CHAT asks the parent or other caregiver to report on 23 behaviors. A child was considered to screen positive if 2 of the 6 “critical” items (items 2, 7, 9, 13, 14, and 15) or 3 of any of the 23 total items were abnormal (Table I). Of the 23 items, 6 require a reasonably intact motor system (items 3, 6, 7, 9, 13, and 16), 13 require visual competence (items 2, 4, 5, 6, 7, 8, 10, 12, 13, 15, 17, 22, and 23), and 4 require intact hearing (items 11, 14, 20, and 21).

Cerebral Palsy

The clinicians who performed the neurologic examinations studied a manual, a data collection form, and an instructional CD designed to minimize examiner variability, and they demonstrated acceptably low variability.¹⁵ The topographic diagnosis of cerebral palsy (CP) (ie, quadriplegia, diparesis, or hemiparesis) was based on an algorithm.⁴ Those performing the neurologic examinations also completed the GMFCS form, assigning each child in the cohort to a level of gross motor function.

BSID-II

Certified examiners administered and scored the BSID-II.^{12,16} All of the examiners had previous experience with the BSID-II and attended a 1-day workshop, at which the published guidelines for test administration and videotaped examinations were viewed and discussed. The examiners were aware of the infants’ enrollment in the ELGAN Study but were not informed of any specifics of their medical history. Before testing, the examiner was informed of the child’s corrected age. After completion of testing, the examiner was informed of the child’s birth date, so that the unadjusted BSID-II Mental Development Index (MDI) and Psychomotor Development Index (PDI) scores could be obtained.

When a child’s impairments precluded administration of the BSID-II, or when more than 2 items were omitted or judged to be “unscorable,” the child was classified as nontestable on that scale. The Adaptive Behavioral Composite of the Vineland Adaptive Behavior Scales (VABS) was obtained for 26 of the 33 children who were considered nontestable with the BSID-II MDI. Of the 38 infants who were nontestable with the BSID-II PDI, 32 were assessed with the VABS Motor Skills domain. These children’s scores on the Adaptive Behavioral Composite and the VABS served as the basis for imputation of the BSID-II scores.

Data Analysis

Among the candidate preterm-associated dysfunctions that possibly may account for the high rate of positive screens are those associated with motor, vision, hearing, and cognitive impairments. We compared the rates of motor, vision, hearing, and cognitive impairments between the children who screened positive and those who screened negative on the M-CHAT. We also evaluated the frequency with which items from the M-CHAT requiring intact motor, vision, and

Table I. Percentage of children who screened positive and negative on the M-CHAT and were reported as abnormal on the individual M-CHAT items

	M-CHAT (column %)		Row n
	Positive	Negative	
Motor items			
3. Does not like climbing	18	1	46
6. Does not point to ask	48	2	117
7. Does not point to indicate interest	50	1	115
8. Does not play with small toys	35	1	82
9. Does not bring objects to you	28	0	62
13. Does not imitate you	38	2	94
16. Does not walk	30	2	78
Vision items			
2. Does not show interest in others	16	1	43
4. Does not enjoy peek a boo	10	1	26
5. Does not pretend	30	1	67
6. Does not point to ask	48	2	117
7. Does not point to indicate interest	50	1	115
8. Does not play with small toys	35	1	82
9. Does not bring objects to you	28	0	62
10. Does not look you in the eye	14	1	36
12. Does not smile in response to smile	4	0	9
13. Does not imitate you	38	2	94
15. Does not follow when you point at a toy	31	1	72
17. Does not look at things you look at	27	1	64
22. Stares at nothing or wanders with no purpose	42	8	153
23. Does not look at your face for reaction	34	5	109
Hearing items			
11. Is oversensitive to noise	48	17	232
14. Does not respond to name	9	0	21
20. Have you wondered if child is deaf	21	2	57
21. Does not understand what people say	19	0	42
Other items			
1. Does not enjoy being swung	8	1	26
18. Makes unusual finger movements	33	9	138
19. Does not try to attract your interest	30	4	91
Total	212	776	988

The items are ordered in 4 sets that group them functionally. Items that require multiple capabilities are listed multiple times. Boldface type indicates M-CHAT "critical items."

hearing were reported as abnormal in those who had motor handicaps, vision difficulties, hearing limitations, and cognitive dysfunctions as assessed by the MDI.

Motor, vision, hearing, and cognitive limitations tended to cluster in this sample. For example, children with quadriplegia were more than 3 times more likely to have an MDI <70 compared with those without CP.⁴ Thus, models for screening positive on the M-CHAT that include variables for motor, vision, hearing, and cognitive limitations are unlikely to truly reflect the contributions of each set of limitations. With that caveat in mind, we created a multivariate logistic regression model that retained 1 indicator for each of these limitations.

RESULTS

More than 21% (212/988) of all children screened positive for ASD on the M-CHAT (Table I). Among the children without motor, vision, hearing, or cognitive impairments, 10% screened positive (Table II). Because 2/3 of children with ASD also have cognitive impairment,⁵ excluding children from the referent group on the basis of cognitive limitations eliminates some who are at high risk for ASD. Consequently, we created a second referent group that excluded children with motor, vision, and hearing impairments but includes children with the full range of MDI scores (Table II); 16% of the children in this referent group still screened positive on the M-CHAT.

Association of Positive M-CHAT Screen with Motor Impairment

The more severe a child's motor limitation as assessed by the GMFCS, the more likely the child was to screen positive on the M-CHAT (Table II). For example, the rate of positive screening was lowest in those who could walk (GMFCS < 1, 17%), intermediate in those needing assistance to walk (GMFCS = 1, 60%), and highest in those who could not sit or walk even with assistance (GMFCS ≥ 2, 83%). Similarly, even though 17% of the children without a diagnosis of CP screened positive, those with a diagnosis of CP had considerably higher rates of positive screening (diparesis, 29%; hemiparesis, 44%; quadriplegia, 73%). Moreover, the lower a child's PDI (another indicator of motor ability), the more likely the child was to screen positive (PDI < 55, 57%; PDI 56 to 69, 28%; PDI ≥ 70, 12%).

We calculated point estimates of odds ratios of screening positive and their 95% confidence intervals for each of the individual impairments. Relative to children who could walk (GMFCS < 1), the odds for screening positive were increased 23-fold for those who could not sit or stand independently (GMFCS ≥ 2) and more than 7-fold for those needing assistance to walk (GMFCS = 1) (Table III). Compared with children without a diagnosis of CP, those with quadriplegia were 13 times more likely and those with hemiparesis were almost 4 times more likely to screen positive for ASD on the M-CHAT. The doubling of risk in diparetic infants was not statistically significant.

Table II. Percentage of children with the clinical characteristics identified on the left who screened positive on the M-CHAT

Characteristic	M-CHAT positive (row %)	Row n
Motor		
GMFCS*		
≥2	83	46
1	60	35
<1	17	907
CP		
Quadripareisis	73	55
Hemipareisis	44	18
Dipareisis	29	34
None	17	881
PDI		
<55	57	152
55 to 69	28	152
≥70	12	684
Sensory		
Vision†		
Yes	68	25
No	20	963
Hearing†		
Yes	68	19
No	21	969
Cognitive		
MDI		
<55	61	148
55-69	35	110
≥70	11	730
Other		
Mental age ≤ 16 months		
Yes	50	220
No	13	768
Sex		
Male	25	513
Female	18	475
Referent group		
Yes‡	10	572
Yes§	16	852

*GMFCS ≥ 2, cannot walk even with assistance; GMFCS = 1, cannot walk independently but can walk with assistance.

†By parent report (blind in one or both eyes; use of hearing aid or services for hearing impairment).

‡No CP diagnosis, MDI ≥ 70, PDI ≥ 70, no reported limitation of vision or hearing.

§No CP diagnosis, no reported limitation in vision or hearing.

Considering items that require relatively intact motor abilities, the median number of M-CHAT items noted as abnormal was 5 in children with a GMFCS of 2 or higher, 2 for those with a GMFCS of 1, and 0 for those with minimal or no motor impairment (data not shown).

Association of Positive M-CHAT Screen with a History of Neurosensory Impairment

Of the 25 children identified as legally blind in at least 1 eye, 68% screened positive on the M-CHAT, compared

Table III. Odds ratios (95% confidence intervals) for screening positive on the M-CHAT by impairment

	Univariate odds ratio	Multivariate odds ratio
Motor		
GMFCS = 2+	23 (11, 51)	8.7 (2.7, 20)
GMFCS = 1	7.4 (3.7, 15)	3.4 (1.5, 7.8)
Quadripareisis	13 (8.8, 23)	
Hemipareisis	3.8 (1.5, 9.7)	
Dipareisis	2.0 (0.7, 4.2)	
PDI < 55	9.3 (6.3, 14)	
PDI = 56 to 69	2.7 (1.8, 4.2)	
Sensory		
Vision limitation*	8.4 (3.6, 20)	3.3 (1.1, 9.6)
Hearing limitation*	8.4 (3.1, 22)	3.7 (1.1, 13)
Cognitive		
MDI < 55	13 (8.4, 19)	7.8 (5.0, 12)
MDI = 56 to 69	4.3 (2.8, 6.8)	3.7 (2.3, 5.9)
MDI < 55†	6.7 (4.2, 11)	
MDI = 56 to 69†	3.9 (2.4, 6.3)	

The referent group for each impairment is the unidentified group (GMFCS < 1, no CP, PDI ≥ 70, normal vision, normal hearing, and MDI ≥ 70).

*By parent report (blind in one or both eyes; use of hearing aid or services for hearing impairment).

†Odds ratio in infants with GMFCS < 1.

with 20% of their peers (Table II). Of the 19 children requiring a hearing aid or receiving specialized services for the hearing-impaired, 68% screened positive, compared with 21% of their peers. Compared with children without these impairments, the blind and hearing-impaired children had an odds ratio of 8.4 for screening positive on the M-CHAT (Table III).

Considering items that require relatively intact visual abilities, the median number of M-CHAT items reported as abnormal was 5 for those with visual impairment and 0 for those without visual impairment (data not shown). Considering items that require relatively intact hearing, the mean number of items reported as abnormal was 1 for those with hearing impairment and 0 for those without hearing impairment.

Association of Positive M-CHAT Screen with Neurocognitive Impairment

The more severe the cognitive limitation, the more likely the child was to screen positive on the M-CHAT. For example, 61% of children with an MDI of <55 screened positive, compared with 35% of children with an MDI of 55 to 69 and 11% of those with an MDI of ≥70 (Table II).

The M-CHAT was designed for screening of children age 18 to 30 months and has not been validated in children under age 16 months.^{2,3} We reevaluated the association of M-CHAT positivity with BSID-II score separately for those children with adjusted MDI equivalents of >16 months and <16 months. About 50% of the 220 children with a mental age of <16 months screened positive on the M-CHAT, compared with 13% of those with a mental age >16 months.

Relative to those children with an MDI of ≥ 70 , the odds for screening positive were increased 13-fold for those with an MDI < 55 and more than 4-fold for those with an MDI of 55 to 69 (Table III). Excluding children who had a GMFCS of ≥ 1 , the odds of screening positive were still more than 6 times greater in those with an MDI of < 55 and nearly 4 times greater in those with an MDI of 56 to 69.

Multivariate Models

We created a logistic regression model that simultaneously evaluated the contribution of multiple impairments, each in light of the others, to the risk of a positive M-CHAT screen. We found that motor impairment had the strongest association, but that cognitive, visual, and hearing impairments also were important (Table III).

DISCUSSION

In ELGAN children, those with motor, vision, or hearing impairments are much more likely than others to screen positive on the M-CHAT. Because we have yet to assess these children for an ASD at an older age, we do not know whether those children with motor, vision, or hearing impairments really are at increased risk for ASD or whether their visual, hearing, and motor deficits are equated with characteristics commonly seen in autism, such as visual avoidance, inconsistent response to voice, and failure to point or play with toys.

Although some of the risk for screening positive on the M-CHAT appears to be related to motor and special sensory impairments, in children without such impairments, the rate of positive screening was still 16%, nearly 3 times higher than expected in unselected populations. Even among children without cognitive impairment, 10% screened positive, nearly twice the rate expected.

The M-CHAT was developed in the late 1990s as a first-stage screening tool for ASD in toddlers age 18 to 24 months, with a sensitivity of 0.87 and a specificity of 0.99 in American children.^{2,17} More recent reports indicate that sensitivity, specificity, and positive predictive value (PPV) actually may be lower.^{3,18} The PPV is 0.11 in selected children and 0.6 in high-risk children.³ When adding telephone interview confirmation for the M-CHAT screens, which was not done in the ELGAN Study, the PPV increases to 0.65 in unselected children and to 0.76 in high-risk children. If the M-CHAT were an ideal screening tool, it would identify all children who should be given a diagnosis of ASD (high sensitivity) and a low number of others who should not be given this diagnosis (high specificity). Only 0.6% of children in the general population are given a diagnosis of ASD,^{19,20} yet almost 10 times that many (5.7%) screen positive.³ In contrast, however, 21% of our sample screened positive. We have not yet verified ASD in our sample and so cannot provide any information about sensitivity, specificity, and PPVs of the M-CHAT in our sample.

Children with a mental age of < 16 months equivalent were much more likely to screen positive on the M-CHAT

compared with the rest of the cohort. Inclusion of children with a mental age < 16 months should not diminish the importance of our findings, because 2/3 of children destined to have ASD have a cognitive impairment.²¹

Approximately 70% of children with autism have no identifiable medical or genetic cause and are morphologically normal.²² Among these children with “idiopathic” autism, the ratio of boys to girls is close to 4, compared with the ratio of between 1 and 2 seen in those children with an identified medical or genetic cause of autism or with a morphological abnormality. Fully 15% of children with idiopathic autism have macrocephaly, whereas microcephaly appears to be especially common in those children with a syndromic or a medical-genetic basis for ASD.²² Finally, severe cognitive impairment is considerably more common in children with syndromic and otherwise explained autism than in children with idiopathic autism.²² With a sex ratio of 1.4, an elevated rate of microcephaly (data not shown), and a high rate of severe cognitive impairment, the children who screened positive in our sample more closely resemble the children with syndromic/medical-genetic disorder-explained autism than those with idiopathic autism.

If an appreciable proportion of the children in our sample are documented to have ASD, then the increased rate may be attributable in part to preterm-related antecedents. A previous study found that in adolescents with normal IQ and vision, those diagnosed with periventricular leukomalacia were more likely than controls to have impairments in perceiving and understanding the actions of others, features also seen in children with ASD.²³ In those children, magnetic resonance imaging volumetric studies revealed decreased right temporal lobe white matter size.

We raise the possibility that in the M-CHAT’s present form, its specificity may be low in ELGAN children, because of associated developmental impairments and other unrecognized characteristics. Because this cohort did not undergo a diagnostic evaluation for autism, we cannot assess the false-positive rate for the M-CHAT screen. If the verified rate of ASD in our population is increased only minimally or moderately in those children who screen positive, however, then the M-CHAT might need to be modified for use in ELGAN children and in children with physical and special sensory impairments.

The children in our cohort are at high risk for developmental impairments whether or not they ultimately receive a diagnosis of ASD, because 23% of children with a false-positive M-CHAT have developmental language disabilities and/or global developmental disorders.¹⁸ Indeed, our data indicate that only 10% of ELGAN children who screen positive on the M-CHAT have a normal MDI and PDI.

Strengths of the current study include the large sample based on gestational age rather than on birth weight, efforts to minimize interobserver disagreements regarding motor findings, standardized administration of the BSID-II, and completion of the M-CHAT screen. A limitation of the M-CHAT screen in

this study is that telephone confirmation of results was not sought.

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