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

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Abstract

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 explored the possibility that motor, vision, hearing and cognitive impairments might contribute to this increase.

Results—Relative to children who could walk, the odds for screening positive on the M-CHAT was increased 23-fold for those unable to sit or stand independently and more than 7-fold for those needing assistance to walk. Compared with children without a CP diagnosis, those with quadriplegia were 13 times more likely 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 an MDI greater than 70, the odds for screening positive were increased 13-fold for those with an MDI below 55 and more than 4-fold for those with an MDI 55–69.

Conclusion—Major motor, cognitive, visual, and hearing impairments appear to account for more than half of the positive M-CHAT screens among extremely low gestational age newborns. Even after eliminating those with such impairments, 10% of children, or nearly double the expected rate, screened positive.

Keywords

Cerebral palsy; Neurodevelopmental outcomes

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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 the child's development [1]. One of the "ASD-specific screening tools" is the M-CHAT [2]. When the M-CHAT is used as a screen in unselected children during well-child care visits between 16 and 30 months of age, 5.7% screen positive [3]. In contrast, we have found that 21% of infants born before the 28th week of gestation screen positive for ASD on the M-CHAT [4]. Four studies found that children born preterm are at greater risk of an autism diagnosis than children born at term [5, [6], [7,8], and two other studies found that low birth weight was associated with increased risk of an autism diagnosis [9], [10]. One recent study reported an elevated rate of screening positive 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 autism spectrum disorders. The other is that developmental impairments other than ASD (for which ELGANs are at increased risk) [4,12–14] increase the frequency of screening positive. 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", two of the M-CHAT critical items, even though the child may show no language or social impairment. We evaluated to what extent developmental impairments contribute to the risk of screening positive 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 (the acronym for Extremely Low Gestational Age Newborns). During the years 2002–2004, women delivering before 28 weeks gestation at one of 14 participating institutions in 11 cities in 5 states were asked to enroll in the study. The enrollment and consent processes were approved by the individual institutional review boards.

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

24-month developmental assessment

Seventy-seven percent had developmental assessments within the range of 23.5–27.9 months; of the others, about half were assessed before 23.5 months and about half after 27.9 months. Of the 1200 children who survived to 24-months corrected age, 988 had a complete developmental assessment that included a neurological examination, the Gross Motor Functional Classification System (GMFCS), the Bayley Scales of Infant Development, Second edition (BSID-II), and several parent reported assessments, including the Modified-Checklist for Autism in Toddlers (M-CHAT) (Figure). The parent or other caregiver who brought the child for the 24 month developmental assessment was also interviewed in order to complete a standardized 60-item interval medical history form. One of the questions asked if the child had a hearing problem, and, if so, whether the child required a hearing aid or needed special services for hearing impairment. The parent or other caregiver was also asked if the child had a vision problem and if the child was considered to be legally blind.

Modified Checklist for Autism in Toddlers

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

Cerebral palsy

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

Bayley Scales of Infant Development – Second Edition (BSID-II) [16]

Certified examiners administered and scored the BSID-II [12]. All examiners had prior experience with the BSID-II and attended a one-day workshop at which the published guidelines for test administration and videotaped examinations were viewed and discussed. Examiners were aware of the infant’s enrollment in the ELGAN Study but were not informed of any specifics of the child’s medical history. Before testing, examiners were told the child’s corrected age; after completion of testing they were told 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 more than 2 items were omitted or judged to be ‘unscorable,’ the child was classified as non-testable on that scale. The Adaptive Behavioral Composite (ABC) of the Vineland Adaptive Behavior Scales (VABS) was obtained for 26 of 33 children who were considered non-testable with the BSID-II Mental Scale. Of the 38 infants unscorable with the BSID-II Psychomotor Scale, 32 were assessed with the VABS Motor Skills Domain. These children’s scores on the ABC and the VABS served as the basis for imputation of the BSID-II scores.

Data analysis

Among the candidate prematurity-associated dysfunctions that might account for the high rate of positive screens are those associated with motor, vision, hearing and cognitive impairments. We compared the rate of motor, vision, hearing and cognitive impairments among children screened positive on the M-CHAT with the rate among those who screened negative. We also evaluated the frequency with which items from the M-CHAT requiring intact motor, vision, and hearing were reported as abnormal in those who had motor handicap, vision difficulties, hearing limitations, and cognitive dysfunctions (by MDI).

Motor, vision, hearing and cognitive limitations tend to cluster in this sample. For example, children with quadriplegia were more than three times as likely to have an MDI below 70 as 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, we created a multivariate logistic regression model that retained one 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 children without motor, vision, hearing or cognitive impairment, 10% screened positive (Table II). Because two-thirds of children with an ASD are also cognitively impaired [5], excluding children from the referent group on the basis of cognitive limitations eliminates some who are at high risk of an ASD. Consequently, we created a second referent group that excludes children with motor, vision and hearing impairments, but includes children with the full range of MDI scores (Table II). Sixteen percent of children in this referent group still screened positive on the M-CHAT.

Association of positive M-CHAT with motor impairment

The more severe the motor limitation as assessed with the GMFCS, the more likely the child screened positive on the M-CHAT (Table II). For example, the rate was lowest in those who could walk (GMFCS <1: 17%), intermediate in those who needed 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 children not given a cerebral palsy (CP) diagnosis screened positive, those who had CP had rates that were considerably higher (diparesis: 29%; hemiparesis: 44%; quadriplegia: 73%). The lower the PDI, another indicator of motor ability, the higher the probability the child screened positive on the M-CHAT (PDI < 55: 57%; 56–69: 28%; ≥ 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 was increased 23-fold for those who could not sit or stand independently (GMFCS ≥ 2) and more than 7-fold for those who needed assistance to walk (GMFCS = 1) (Table III). Compared with children who were not given a CP diagnosis, those with quadriplegia were 13 times more likely and those with a hemiparesis were almost 4 times more likely to screen positive for ASD on the M-CHAT. The doubling of risk among diparetic infants was not statistically significant.

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

Association of positive M-CHAT with a history of neurosensory impairment

Of the 25 children deemed legally blind in at least one eye, 68% were M-CHAT positive, whereas 20% of their peers were M-CHAT positive (Table II). Of the 19 children who required a hearing aid or received specialized services for the hearing impaired, 68% were M-CHAT positive. In contrast, 21% of their peers were M-CHAT positive. Compared with children without their impairment, children considered blind and children with a hearing impairment had an odds ratio for screening positive of 8.4 (Table III).

Considering items that require relatively intact visual abilities, the median number of M-CHAT items marked abnormal, was 5 for those who were visually impaired and 0 for those who were not (data not shown). Considering items that require relatively intact hearing, the mean number of items marked abnormal, was 1 for those who were hearing impaired and 0 for those who were not.

Association of positive M-CHAT with neurocognitive impairment

The more severe the cognitive limitation, the more likely the child screened positive on the M-CHAT. For example, 61% of children whose MDI was less than 55 screened positive, compared

with 35% of children whose MDI was between 55 and 69, and 11% of children whose MDI was 70 or higher (Table II).

The M-CHAT was designed for screening of children between 18–30 months of age and has not been validated in children under 16 months of age [2], [3]. We re-evaluated the association of M-CHAT positivity with Bayley Scales separately for those whose adjusted MDI equivalent was over and under 16 months. Half of the 220 children with mental age less than 16 months screened positive on the M-CHAT in comparison to 13% of children with mental age above 16 months.

Relative to those who had an MDI of 70 or more, the odds for screening positive was increased 13-fold for those with an MDI below 55 and more than 4-fold for those with an MDI 55–69 (Table III). Excluding children who had a GMFCS of 1 or more, the odds for screening positive was still more than 6-fold for those with an MDI less than 55 and nearly 4-fold for an MDI of 56–69.

Multivariate models

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

Discussion

Among children who were born at an extremely low gestational age, those who have 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 autism-spectrum disorder at an older age, we do not know if these children with motor, vision, or hearing impairments really are at increased risk of an autism-spectrum disorder, or if 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 of screening positive on the M-CHAT appears to be related to motor and special sensory impairments, among children without such impairments, the rate of screening positive was still 16%, nearly three times higher than expected among 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 screen for ASD in toddlers aged 18 to 24 months with sensitivity of 0.87 and specificity of 0.99 in American children [2], [17]. More recent reports indicate that sensitivity, specificity, and positive predictive value (PPV) might be lower [3,18]. In unselected children, the PPV is 0.11, and in high-risk children it is 0.6 [3]. When adding telephone interview confirmation for the M-CHAT screens, something that was not done in the ELGAN study, 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 who should be given an autism-spectrum diagnosis (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 an autism-spectrum diagnosis [19,20], yet almost ten 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 predictive values of the MCHAT in our sample.

Children whose mental age was below 16 months equivalent were much more likely to be M-CHAT positive than the remainder of the cohort. Inclusion of children with mental age less than 16 months should not diminish the importance of our findings because two-thirds of children destined to have ASD have cognitive impairment [21].

Approximately 70% of children with autism have no identifiable medical or genetic cause and are morphologically normal [22]. Among such children with “idiopathic” autism, the ratio of boys to girls is close to 4 rather than the ratio of between 1 and 2 seen among children who have a medical or genetic cause or are morphologically abnormal. Fully 15% of children with idiopathic autism have macrocephaly, whereas microcephaly appears to be especially common among the children who have a syndrome or a medical- genetic basis for their ASD [22]. Finally, severe cognitive impairment is considerably more common among children with syndromic and otherwise explained autism than among 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 pattern seen in children who have syndromic/medical-genetic disorder-explained autism than in those with idiopathic autism.

If an appreciable proportion of the children in our sample are documented to have ASD, some of the increased rate might be attributable to prematurity-related antecedents. One study found that among 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 seen also in those with ASD [23]. These children had diminished right temporal lobe white matter size on MRI volumetric studies.

We raise the possibility that in its present form, the specificity of the M-CHAT may be low among children born extremely prematurely 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 only minimally or moderately increased among children who screen positive, however, then the M-CHAT might require modification for use in children born at extremely low gestational ages and for children who have physical and special sensory impairments.

Our cohort is at high risk for developmental impairments, whether or not they ultimately carry the 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 birth weight, efforts to minimize inter-observer disagreements about 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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Figure 1.
Sample description.

Table 1

The percent of children who screened positive and negative on the M-CHAT and were marked as abnormal on the items listed on the left. The items are ordered in 4 sets that group them functionally and items that require multiple capabilities are listed multiple times. Bolded italicized items are M-CHAT “critical 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
<i>7. Does not point to indicate interest</i>	50	1	115
8. Does not play with small toys	35	1	82
<i>9. Does not bring objects to you</i>	28	0	62
<i>13. Does not imitate you</i>	38	2	94
16. Does not walk	30	2	78
Vision items			
<i>2. Does not show interest in others</i>	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
<i>7. Does not point to indicate interest</i>	50	1	115
8. Does not play with small toys	35	1	82
<i>9. Does not bring objects to you</i>	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
<i>13. Does not imitate you</i>	38	2	94
<i>15. Does not follow when you point at a toy</i>	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
<i>14. Does not respond to name</i>	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

Table 2

The percent 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
	Cerebral palsy	Quadripareisis	73	55
		Hemiparesis	44	18
		Diparesis	29	34
		None	17	881
	PDI	< 55	57	152
		55–69	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
	Gender	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 with assistance

** by parent report (blind in one or both eyes; hearing aids or services for hearing impairment)

[†] No cerebral palsy diagnosis, MDI ≥ 70, PDI ≥ 70, no reported limitation of vision or hearing

^{††} No cerebral palsy diagnosis, no reported limitation of vision or hearing

Table 3

Odds ratios (and their 95% confidence intervals) for screening positive on the M-CHAT by the impairments listed in the left column. The referent group for each impairment is the unidentified group (GMFCS < 1, No CP, PDI $\geq$ 70, normal vision, normal hearing and MDI $\geq$ 70)

		Univariate odds ratios	Multivariate odds ratios
Motor	GMFCS: 2+	23 (11, 51)	8.7 (2.7, 20)
	GMFCS: 1	7.4 (3.7, 15)	3.4 (1.5, 7.8)
	Quadriparesis	13 (8.8, 23)	
	Hemiparesis	3.8 (1.5, 9.7)	
	Diparesis	2.0 (0.7, 4.2)	
	PDI: < 55	9.3 (6.3, 14)	
	PDI: 56–69	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: 56–69	4.3 (2.8, 6.8)	3.7 (2.3, 5.9)
	MDI: < 55**	6.7 (4.2, 11)	
	MDI: 56–69**	3.9 (2.4, 6.3)	

* By parent report (blind in one or both eyes; hearing aids or services for hearing impairment)

** Odds ratio among infants with GMFCS < 1