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Early screening for Autism Spectrum Disorder: can we predict the diagnosis?

A prospective longitudinal study

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Early screening for Autism Spectrum Disorder: can we predict the diagnosis?

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ABSTRACT

The present study aimed to evaluate how well two specific screening measures, the Modified Checklist for Autism in Toddlers (M-CHAT) and the Social Communication Questionnaire (SCQ), or which specific items within them, work in prospectively identifying Autism Spectrum Disorder (ASD) cases from a sample of 201 at-risk preschooler children. Participants were referred to the Neurodevelopment and Autism Unit (UNDA) of Hospital Pediátrico (HP) from Centro Hospitalar e Universitário de Coimbra (CHUC) (Tertiary Pediatric Hospital – Central Region of Portugal) due to neurodevelopmental disorders suspicion. Between 2009 and 2015, all children were extensively and longitudinally evaluated in outpatient basis by the same expert and multidisciplinary clinical team for ASD diagnosis. Two assessments were performed at the median age of three (Time 1, T1) and five years old (Time 2, T2), comprising both positive and negative screening subjects. Final diagnoses (ASD, n=135, *versus* Other Neurodevelopmental Disorders (OND)/Non-ASD, n=66) were rigorously made using not only clinical judgement but also well stablished, objective measures, following gold standard procedures. The M-CHAT and the SCQ scores were analyzed for both assessments and their psychometric properties were compared. Considering the original cut-off score values, the SCQ yielded the highest specificity (98.5% at T2, AUC [0.854, 0.937], 51.1% sensitivity), while the M-CHAT was found to be more sensitive (94.1% at T1, AUC [0.913, 0.972], 65.2% specificity) allowing a lower number of ASD children incorrectly categorized as OND/Non-ASD. Therefore, both the M-CHAT and the SCQ revealed reliable and prospective agreement with final diagnosis. For better diagnostic accuracy, based on our sample, we recommend a cut-off score of failing two M-CHAT critical items when assessing at-risk children around the age of three (sensitivity of 80.0%,

specificity of 92.4%, AUC [0.847, 0.936]). Screening criteria adjustment to clinical setting and purpose may provide even better results. At the light of our findings, our study valuably contributes for screening practice in toddlerhood, highlighting the feasibility of ASD screening at early ages. This is of major clinical relevance, as early identification enhances accurate access to specialized diagnostic referrals and to specific intervention programs, improving prognosis and mitigating the substantial burden of ASD for both patients and families affected by this complex disorder.

Keywords: Autism Spectrum Disorder (ASD), Early detection, Prospective screening.

INTRODUCTION

Autism Spectrum Disorder (ASD) is a lifelong, heterogeneous and complex neurodevelopmental disorder characterized by wide impairments in social and communication skills, as well as by patterns of restrictive, repetitive and stereotyped behaviors (1–4). Once regarded as rare, it is now almost an epidemic disorder (5), partially as a consequence of the increasingly public and professional awareness, recognition and understanding of ASD in the past decades (2,3,5), and also a result of the marked changes in description and diagnostic criteria (2,5). Nowadays, the worldwide prevalence of ASD is 0.62–0.70% (2), 1-2% from largest scale-surveys (2,3). In Portugal, the prevalence at school age was estimated to be close to 10 per 10.000 children (6).

Although multiple risk factors have been identified (2), the exact etiology of ASD is still not known, and it is now broadly recognized that it is a multifactorial disorder resulting from both genetic and non-genetic factors and their interaction (3,7).

Different possible etiologies are likely associated with ASD's phenotypic heterogeneity (8). In fact, there is a tremendous variability not only in the etiology and neurobiology of ASD, but also in the clinical onset, course and severity of symptoms across cases (9,10). Even the same individual may experience significant changes regarding symptoms and diagnostic criteria met over time (10). Despite these variations in severity, all ASD manifestations are associated with significant impairments in communicative and social functioning and with pronounced risk for failure to adapt at the educational and social adaptive level, requiring some form of specialized support along life (7,11). Beyond the clinical and daily living challenges faced by patients and their families, ASD represents a heavy burden for societies (11), with an estimated cost of 7.7 million DALYs across the

world (DALYs=6.2 million) (12). The substantial impact of ASD across lifespan has important public health and policy implications (12), thus, finding reliable methods for early diagnosis is a key priority.

The early diagnosis and subsequent early and specific intervention in ASD's patients are two of the most important factors for improving lifetime prognosis for children affected by the disorder (11), leading to better language, social and functioning outcomes and fewer maladaptive behaviors (13).

ASD's specific signs are not reliably present at birth or first months of life, but emerge over time (14). Atypical, diminished or delayed social-communication behavior usually appear to begin in the second half of the first year and continue to develop for several years (2,14). Signs of ASD are generally evident by twelve to eighteen months (15), and parents typically report their initial concerns about their children development around eighteen to twenty-four months (6,9,11). However, the average age of diagnosis is significantly later, often at about four years (15,16), preventing an early access to specific intervention. As stated above, it has been reported that an appropriate intervention at an early age can maximize children's developmental outcomes. Understanding the stability of an early ASD diagnosis is also important clinically, given that it may affect decisions related to treatment planning, feedback to families and access to public services. Therefore, it is crucial to minimize this research-practice gap by identifying the earliest age at which a stable and reliable diagnosis is possible (15,17).

Screening for ASD enhances early identification and referral for a proper diagnostic evaluation. Both the Modified Checklist for Autism in Toddlers (M-CHAT) (18) (Annex 1) and the Social Communication Questionnaire (SCQ) (19,20) (Annex 2) are written parent

questionnaires to endorse (yes/no) symptoms descriptions of reciprocal social interaction, language and communication, and repetitive, stereotyped patterns of behavior (21). As screening measures, they were designed to identify young children with an increased likelihood of ASD (22,23), in order to appropriately refer them for diagnosis and early intervention (23). They are useful in gathering structured information about signs and symptoms, but they are not diagnostic nor should be used to rule out a diagnosis of ASD (22).

The M–CHAT was developed from the Checklist for Autism in Toddlers (CHAT) (24), which was the first attempt to develop a prospective screening instrument for ASD by primary health care providers (17,23). The M-CHAT includes the first nine items from the CHAT (the parent-report section), but was expanded to be a twenty-three items, simple questionnaire given to parents in physician's waiting room. The fourteen questions added allow a broad assessment of sensory and motor impairment, social referencing, imitation and orientation to name. Six of the total items are "critical", as they were considered to be the most predictive of an ASD diagnosis. Scoring the M-CHAT is simply converting the yes/no answers to pass/fail scores. A child fails the screen if failing two or more of the six critical items or when any three of the total items are failed (18,23,25,26).

The M-CHAT does not require examiner's training nor observation of the child, but physicians may "flag" an M-CHAT when suspecting of possible ASD, regardless of the given responses (18,26). In Portugal, the current National Child Health and Youth Program actually recommends the Portuguese version of this questionnaire for ASD routine screening during primary care, well-child assessments at the ages of eighteen and twenty-four months (4,27).

The Social Communication Questionnaire (SCQ) is a forty-items yes/no parent-report measure based on the more extended Autism Diagnostic Interview-Revised (ADI-R) (28).

Caregivers can complete the SCQ in generally less than ten minutes, and scoring takes no longer than five. There are two versions of this questionnaire: the lifetime form, suitable for diagnostic use of screening, and the current form, which should be used for assessment of change in diagnosis, as well as with young children (19,25).

The first item of the SCQ is about the current language level of the child and is not included in the final score. It allows to differentiate verbal and non-verbal children, as they are six inapplicable items for the latter. For each one of the applicable items is given a value of 1 or 0, according to the presence or absence of abnormal behavior, respectively. The total score ranges from 0 to 33 for the non-verbal subjects and from 0 to 39 for the verbal ones, higher score means more clinical severity. A cut-off of 15 for both verbal and non-verbal children is used to identify those who should receive a more thorough expert clinical assessment, as they are more likely of having ASD (19,20,23,25).

Both the M-CHAT and the SCQ are among the most widely screening instruments in the ASD field (21). However, it is important to characterize their effectiveness in the clinical setting, where they are likely to be used to differentiate ASD and non-ASD children (25). The waiting time for specialist ASD assessments may be considerable, so reducing inappropriate referral through an accurate screening process would be benefic for children, families and local services. Moreover, it would also reduce the distress of unnecessary referrals and the burden of delayed diagnostic evaluations (21).

The present study aimed to evaluate how well two specific neurodevelopmental and behavioral screening measures, the M-CHAT and the SCQ, or which specific items within them, work in prospectively identifying ASD cases from a sample of two-hundred and one at--risk young children. These children were referred to the Neurodevelopment and Autism Unit

(UNDA) of Hospital Pediátrico (HP) from Centro Hospitalar e Universitário de Coimbra (CHUC) (Tertiary Pediatric Hospital – Central Region of Portugal) because of neurodevelopmental disorders suspicion, where they were longitudinally evaluated by an expert and multidisciplinary clinical team for ASD diagnosis. Our approach was innovative because we applied those previously well described behavioral screening measures to assess their discriminative power for ASD and non-ASD children, considering their clinical outcome in a longitudinal evaluation of both positive and negative screening subjects. Importantly, this is the first study appraising the diagnostic value of the Portuguese version of the M-CHAT when screening for ASD in a large and well characterized cohort of at-risk, young Portuguese children.

POPULATION AND METHODS

1. SUBJECTS AND PROCEDURE

Participants were 201 children [168 (83.6%) males] under the age of four referred to the UNDA/HP/CHUC because of neurodevelopmental problems suspicion. Participants were seen as part of an outpatient clinic specialized in neurodevelopmental disorder, especially ASD, between 2009 and 2015.

This study is part of the project "Identifying the early signs of Autism Spectrum Disorder - integration of behavioral and genetic information for early autism detection in an at-risk population" (PTDC/SAU-SAP/119161/2010), approved and financed by the Portuguese Foundation for Science and Technology (FCT).

During the first evaluation (Time 1, T1), all children were screened for ASD using the M-CHAT and the SCQ. They also went through a current extensive clinical and functional evaluation by an expert multidisciplinary clinical team coordinated by a neurodevelopmental pediatrician for ASD and Other Neurodevelopmental Disorders (OND) diagnosis. The assessment included comprehensive caregiver interview containing questions related to background information, such as age of acquisition for neurodevelopmental milestones (first meaningful words, first phrases, walking age, daytime and night-time control of bladder sphincter) and areas of first and main concerns (descriptions and age of caregiver's first complaints about their child development and behavior). In addition, gold standard instruments designed specifically for ASD diagnosis (11), the Autism Diagnostic Interview-Revised (ADI-R) (28) and the Autism Diagnostic Observation Schedule (ADOS) (29), were applied. Adaptive functioning was assessed with the Vineland Adaptive Behavior Scales

(VABS) (30) and developmental assessment (development quotient - DQ) was measured with the Griffith Mental Development Scales (GMDS) (31).

Eighteen months after the first evaluation (Time 2, T2), the same children were again assessed to document their neurodevelopmental and behavioral trajectory. Autistic signs progression was monitored with the M-CHAT and the SCQ and diagnostic consistency was analyzed considering clinical judgement, in addition with the application of the ADI-R and the ADOS scales again. As part of the functional evaluation, the VABS and the GMDS were once more administered for the final and definitive neurodevelopmental diagnosis.

Only children with two full evaluations were included in the study.

The final diagnosis was made on the basis of the gold standard instruments: the ADI-R, the ADOS and clinical examination performed by a multidisciplinary team coordinated by experienced neurodevelopmental pediatricians, in accordance with the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5) criteria (1). The diagnostic decision did not rely solely on the cut-off scores of the instruments applied, as research has consistently found that clinical judgement by experienced clinicians using developmentally adequate tools is the most stable and reliable way of diagnosing ASD (15). As so, final diagnosis at T2 was made by the same team taking all the aforementioned information into account, splitting children in two diagnostic groups: ASD *versu*s OND/Non-ASD.

2. STATISTICAL ANALYSIS

Statistical analysis was performed by the version for Microsoft Windows® of the Statistical Package for Social Sciences software (SPSS®, Chicago, IL, USA). Assessment of normality was made resorting to Shapiro Wilks tests. We assessed the significance of the differences between groups using t-Student tests for quantitative variables with normal distribution and Mann-Whitney U tests for those who were not. The association between qualitative variables was assessed resorting to Fisher tests. Receiver Operator Characteristic (ROC) analyses were undertaken to evaluate the predictive value of the M-CHAT and the SCQ. Both sensitivity and specificity were determined for each variable, not only for the original cut-off score, but also for the optimal cut-off score value in this sample, defined as the one that maximised the sum of the sensitivity and the specificity. The level of significance adopted was 0.05.

3. ETHICS STATEMENT

This study and all the procedures were reviewed and approved by the Ethics Commission of HP/CHUC and were conducted in accordance with the standards of the Declaration of Helsinki. Informed consent was obtained from parents/caregivers of all participants.

RESULTS

1. SAMPLE CHARACTERIZATION

Table 1 summarizes demographic data for the whole sample and for each diagnostic group (ASD *versus* OND/Non-ASD).

The ASD group (n=135) consisted of 117 males (86.7%) and 18 females. The median age at the first and second assessments was 3 and 5 years, respectively. The median age of parental first concerns about their child's development was 18 months. As displayed in Table 2, these concerns were deficits in communication skills (language delay or regression, n=79, 59.0%), social interaction skills (n=34, 25.4%), stereotyped or obsessive behaviors (n=11, 8.2%) and developmental delay or regression (n=10, 7.5%). The information about caregiver's first concern was not reported for one child.

The OND/Non-ASD group (n=66) consisted of 51 males (77.3%) and 15 females who ultimately were found not to have ASD. The final diagnoses were language delay (n=35, 53.0%), global developmental delay (n=18, 27.3%), unspecified behavioral problems (n=8, 12.1%) and motor delay (n=1, 1.5%). Four children (6.1%) did not meet criteria for any of the clinical specific conditions assessed. The median age at each evaluation was 3 and 5 years. Among the parents of these children, first concerns were reported at the median age of 24 months, regarding deficits in communication skills (language delay or regression, articulation, n=40, 60.6%), challenging behaviors (n=13, 19.7%), developmental delay (n=9, 13.6%), social interaction skills (n=3, 4.6%) and motor delay (n=1, 1.5%) (Table 2).

There were no statistically significant differences between the two groups in respect to gender (p=0.106), median age at the first evaluation (p=0.164) nor at the second evaluation (p=0.248). First concerns arose significantly earlier among parents whose children were

diagnosed as having ASD. (p=<0.05) (Table 1). Only two areas of first concern were reported to differ significantly between ASD and OND/Non-ASD groups: social interaction deficits (p<0.001) and atypical behaviors (p=0.035).

Table 1 – Demographics for total sample and each diagnostic group.

	Total sample (n=201)	**ASD group (n=135)**	**OND/ Non-ASD group (n=66)**	***p-value***
Gender (Male: Female)	168: 33	117: 18	51: 15	0.106
Age (years) at Time 1 evaluation	3 (2; 4)	3 (2; 4)	3 (2; 4)	0.164
Age (years) at Time 2 evaluation	5 (4; 5)	5 (4; 5)	5 (4; 6)	0.248
Age of first concerns (months)	18 (18; 24)	18 (18; 24)	24 (18; 36)	**0.011**

Note: ASD – Autism Spectrum Disorder; OND – Other Neurodevelopmental Disorders.

Data presented as median (25^{th} percentile; $75t^{h}$ percentile). The p-values correspond to a comparison between children with ASD and children without ASD and were computed with Fisher tests, t-Student tests or with Mann-Whitney U tests, as applicable.

Table 2 – Neurodevelopmental areas of first concern.

Neurodevelopmental areas	**Total sample (n=200)**	**ASD group (n=134)**	**OND/ Non-ASD group (n=66)**	***p-value***
Communication	119 (59.5%)	79 (59.0%)	40 (60.6%)	0.879
Social Interaction	37 (18.5%)	34 (25.4%)	3 (4.6%)	**<0.001**
Behaviors	24 (12.0%)	11 (8.2%)	13 (19.7%)	**0.035**
Global development	19 (9.5%)	10 (7.5%)	9 (13.6%)	0.200
Motor development	1 (0.5%)	-	1 (1.5%)	-

Note: ASD – Autism Spectrum Disorder; OND – Other Neurodevelopmental Disorders.

Data presented as n (%). The p-values correspond to a comparison between children with ASD and children without ASD and were computed with Fisher tests.

The developmental and adaptive functioning profile of the whole sample, ASD and OND/Non-ASD groups were compared (Tables 3 and 4). At both assessments, children from the ASD group had significantly lower developmental and adaptive functioning scores comparing to those of the OND/Non-ASD group ($p<0.001$ for all variables except for GMDS Performance Subscale at T2, $p=0.002$, and VABS Motor Skills Domain at T1, $p=0.009$).

Table 3 – Developmental functioning assessment scores at each evaluation time.

Development Quotient	**Total sample (n=201)**	**ASD group (n=135)**	**OND/ Non-ASD group (n=66)**	***p-value***
T1				
GMDS Global DQ	86 (71; 98)	78 (65; 94)	93 (86; 106)	**<0.001**
GMDS Language Subscale	71 (51; 96)	64 (46; 89)	84 (67; 108)	**<0.001**
GMDS Performance Subscale	97 (77; 115)	93 (74; 112)	104 (94; 125)	**<0.001**
T2				
GMDS Global DQ	94 (76; 106)	86 (63; 104)	102 (92; 109)	**<0.001**
GMDS Language Subscale	92 (64; 110)	80 (47; 108)	97 (89; 118)	**<0.001**
GMDS Performance Subscale	100 (82; 116)	96 (78; 111)	107 (93; 121)	**0.002**

Note: ASD – Autism Spectrum Disorder; OND – Other Neurodevelopmental Disorders; T1 – Time 1; T2 – Time 2; GMDS – Griffith Mental Development Scales; DQ – Development Quotient.

Data presented as median (25^{th} percentile; 75^{th} percentile). The p-values correspond to a comparison between children with ASD and children without ASD and were computed with t-Student tests or with Mann-Whitney U tests, as applicable.

Table 4 – Adaptive functioning assessment scores at each evaluation time.

Adaptive functioning	**Total sample (n=201)**	**ASD group (n=135)**	**OND/ Non-ASD group (n=66)**	***p-value***
T1				
VABS Global Score	68 (61; 77)	65 (58; 72)	76 (70; 82)	**<0.001**
VABS Communication Domain	68 (61; 80)	66 (58; 74)	78 (69; 84)	**<0.001**
VABS Daily Living Skills Domain	72 (65; 81)	69 (64; 78)	80 (71; 87)	**<0.001**
VABS Social Skills Domain	72 (63; 81)	67 (61; 75)	81 (75; 88)	**<0.001**
VABS Motor Skills Domain	81 (70; 91)	77 (67; 90)	85 (77; 93)	**0.009**
T2				
VABS Global Score	71 (57; 79)	66 (54; 76)	76 (70; 83)	**<0.001**
VABS Communication Domain	73 (57; 83)	67 (54; 81)	78 (71; 86)	**<0.001**
VABS Daily Living Skills Domain	72 (61; 80)	66 (56; 76)	79 (72; 84)	**<0.001**
VABS Social Skills Domain	76 (65; 86)	70 (59; 82)	84 (76; 89)	**<0.001**
VABS Motor Skills Domain	85 (65; 96)	82 (62; 91)	93 (83; 100)	**<0.001**

Note: ASD – Autism Spectrum Disorder, OND – Other Neurodevelopmental Disorders; T1 – Time 1; T2 – Time 2; VABS – Vineland Adaptive Behavior Scales.

Data presented as median (25^{th} percentile; 75^{th} percentile). The p-values correspond to a comparison between children with ASD and children without ASD and were computed with t-Student tests or with Mann-Whitney U tests, as applicable.

Among the six neurodevelopmental milestones assessed (Table 5), there were significant differences in the age of acquisition of "first words", "first phrases", "night-time control of bladder sphincter" and "daytime control of bladder sphincter" (in all cases $p<0.05$). In the latter, the median age of acquisition did not differ between groups, but its distribution did, with the ASD group showing delayed daytime control of bladder sphincter. ASD children and OND/Non-ASD children did not differ significantly in the age of walking ($p=0.118$).

Table 5 – Median age (months) of acquisition of main neurodevelopmental milestones.

Neurodevelopmental milestone	**Total sample (n=201)**	**ASD group (n=135)**	**OND/ Non-ASD group (n=66)**	***p-value***
First words	24 (18; 30)	24 (18; 30)	18 (18; 24)	**0.002**
First phrases	36 (36; 48)	40 (36; 48)	36 (30; 36)	**0.000**
Walking age	14 (12; 16)	14 (12; 16)	14 (12; 15)	0.118
Daytime control of bladder sphincter	36 (30; 48)	36 (36; 48)	36 (24; 36)	**0.000**
Night-time control of bladder sphincter	41 (36; 48)	48 (36; 48)	36 (36; 42)	**0.001**

Note: ASD – Autism Spectrum Disorder; OND – Other Neurodevelopmental Disorders.

Data presented as median (25^{th} percentile; 75^{th} percentile). The p-values correspond to a comparison between children with ASD and children without ASD and were computed with t-Student tests or with Mann-Whitney U tests, as applicable.

2. M-CHAT AND SCQ SCORES

Table 6 illustrates median total scores for the M-CHAT and the SCQ at the first (T1) and second (T2) assessments. The ASD group failed significantly more items in both screening measures at each time. Noticeably, these children also presented a wider range of scores.

Table 6 – Median scores for the M-CHAT and the SCQ at the first and second evaluations.

	Total sample (n=201)	**ASD group (n=135)**	**OND/ Non-ASD group (n=66)**	***p-value***
M-CHAT T1				
Total items failed	7 (0-20)	11 (0-20)	1 (0-10)	**<0.001**
CI failed	2 (0-6)	3 (0-6)	0 (0-4)	**<0.001**
M-CHAT T2				
Total items failed	3 (0-20)	6 (0-20)	0 (0-10)	**<0.001**
CI failed	0 (0-6)	1 (0-6)	0 (0-2)	**<0.001**
SCQ T1				
Total items failed	16 (0-36)	21 (3-36)	5 (0-16)	**<0.001**
SCQ T2				
Total items failed	9 (0-36)	15 (0-36)	2 (0-16)	**<0.001**

Note: ASD – Autism Spectrum Disorder; OND – Other Neurodevelopmental Disorders; M-CHAT – Modified Checklist for Autism in Toddlers; CI – Critical Items; SCQ – Social Communication Questionnaire. T1 – Time 1; T2 – Time 2.

Data presented as median (minimum-maximum). The p-values correspond to a comparison between children with ASD and children without ASD and were computed with t-Student tests or with Mann-Whitney U tests, as applicable.

3. ROC ANALYSES

The predictive values of both the M-CHAT and the SCQ results were assessed with ROC analyses. For each variable, the cut-off value that optimised the sum of the sensitivity and specificity was also determined.

TIME 1

M-CHAT

As seen in Table 7 and in Figure 1, at T1, using the original criterion of failing any three items, the sensitivity and specificity were 94.1% and 65.2%, respectively. The optimal cut-off for this sample was failing six or more of the twenty-three total items. Using this cut-off score, the sensitivity was 83.7% and specificity was 92.4%. The area under the ROC curve (AUC) was CI 95% [0.913-0.972].

Using the M-CHAT authors criterion of failing two of the six critical items, the sensitivity was 80.0% and the specificity was 92.4%. This was also the optimal cut-off score for our sample at the first evaluation time. The AUC was CI 95% [0.847-0.936].

SCQ

Using the fifteen cut-off score proposed by the SCQ authors, sensitivity was 79.3% and specificity was 97.0%. For the current sample at the baseline evaluation, the optimal cut-off score was thirteen, with a sensitivity of 86.7% and a specificity of 93.9%. The AUC was CI 95% [0.930-0.980] (Table 7, Figure 1).

Table 7 – ROC analysis for the M-CHAT and the SCQ scores at Time 1 assessment.

Variable	Cut-off	Sensitivity	Specificity	95% CI for AUC	*p-value*
M-CHAT total items failed	≥3[a] ≥6[b]	94.1% 83.7%	65.2% 92.4%	[0.913, 0.972]	**<0.001**
M-CHAT CI failed	≥2 [a,b]	80.0%	92.4%	[0.847, 0.936]	**<0.001**
SCQ total items failed	≥15[a] ≥13[b]	79.3% 86.7%	97.0% 93.9%	[0.930, 0.980]	**<0.001**

Note: M-CHAT – Modified Checklist for Autism in Toddlers; M-CHAT CI – M-CHAT Critical Items; SCQ – Social Communication Questionnaire; AUC – Area Under Curve.

[a] Original cut-off score proposed by the M-CHAT/ the SCQ authors.

[b] Optimal cut-off score in the current sample, chosen to maximise the sum of the sensitivity and the specificity. The p-value was obtained using ROC analysis.

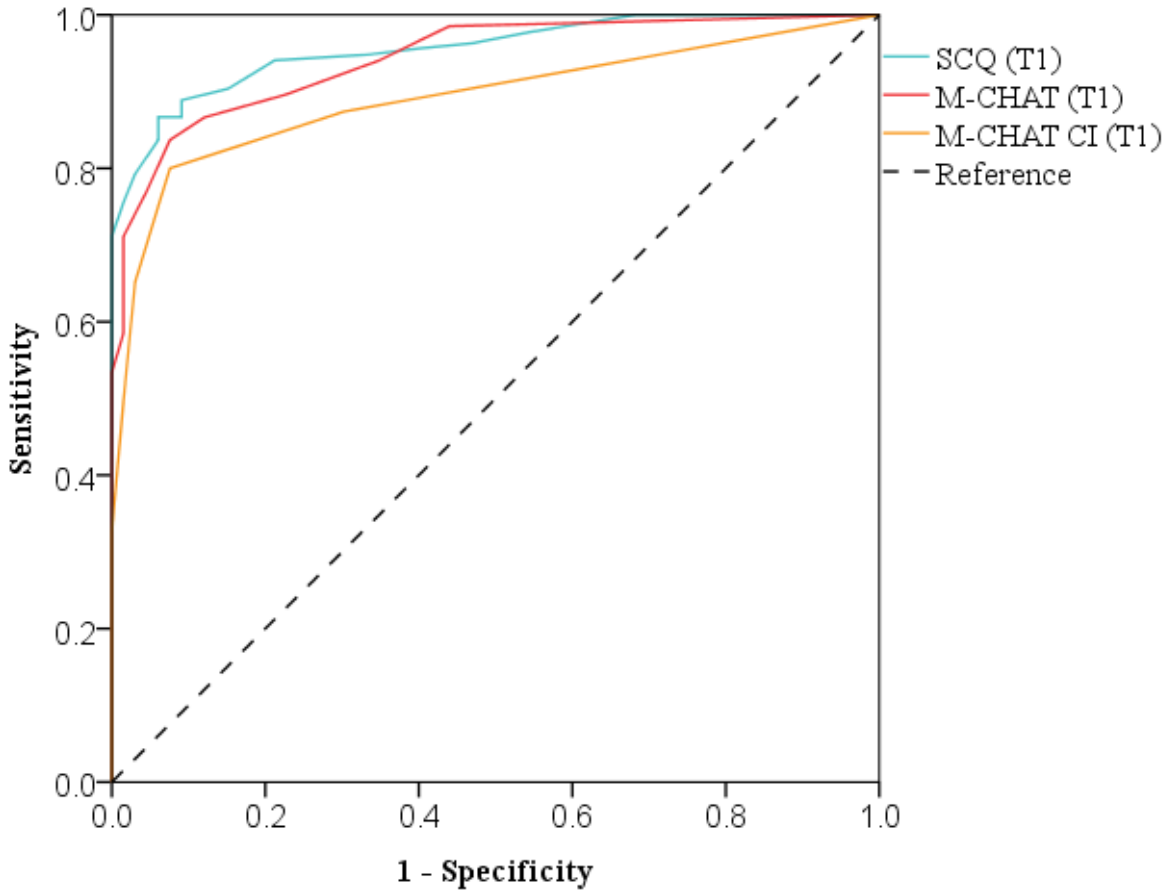

Figure 1 – ROC curve for the M-CHAT and the SCQ scores at Time 1 (T1) assessment.

Note: SCQ – Social Communication Questionnaire; M-CHAT – Modified Checklist for Autism in Toddlers; M-CHAT CI – M-CHAT Critical Items.

Table 8 – ROC analysis for the M-CHAT and the SCQ scores at Time 2 assessment.

Variable	Cut-off	Sensitivity	Specificity	95% CI for AUC	*p-value*
M-CHAT total items failed	≥3[a, b]	74.8%	83.3%	[0.829, 0.925]	**<0.001**
M-CHAT CI failed	≥2[a] ≥1[b]	47.4% 59.3%	96.7% 89.4%	[0.702, 0.829]	**<0.001**
SCQ total items failed	≥15[a] ≥10[b]	51.1% 70.4%	98.5% 95.5%	[0.854, 0.937]	**<0.001**

Note: M-CHAT – Modified Checklist for Autism in Toddlers; M-CHAT CI – M-CHAT Critical Items; SCQ – Social Communication Questionnaire; AUC – Area Under Curve.

[a] Original cut-off score proposed by the M-CHAT/ the SCQ authors.

[b] Optimal cut-off score in the current sample, chosen to maximise the sum of the sensitivity and the specificity. The p-value was obtained using ROC analysis.

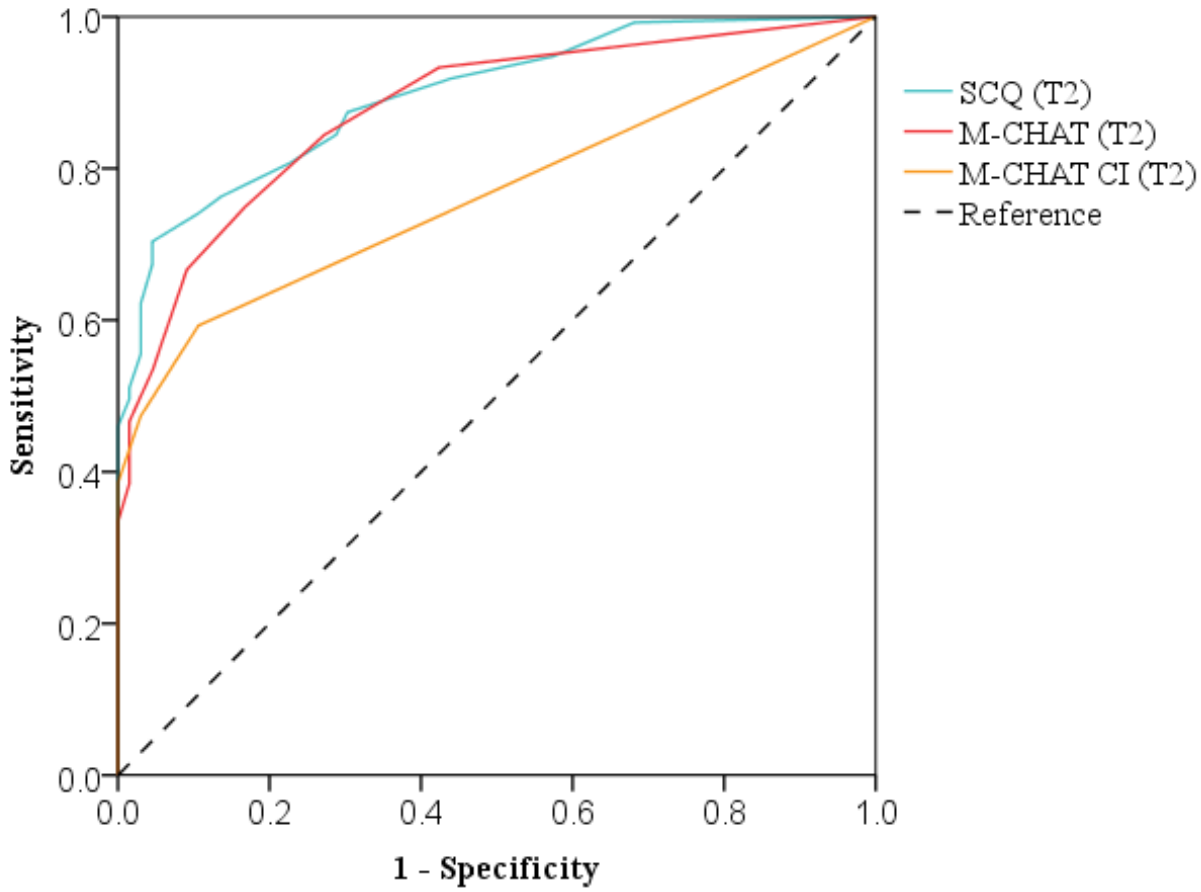

Figure 2 – ROC curve for the M-CHAT and the SCQ scores at Time 2 (T2) assessment.

Note: SCQ – Social Communication Questionnaire; M-CHAT – Modified Checklist for Autism in Toddlers; M-CHAT CI – M-CHAT Critical Items.

TIME 2

M-CHAT

At T2 (Table 8, Figure 2), the original criterion of failing three of the total items was the optimal cut-off for this sample as well, allowing a sensitivity of 74.8% and a specificity of 83.3%. The AUC was CI 95% [0.829-0.925].

Employing the recommended cut-off score of failing two M-CHAT critical items, the sensitivity and specificity were 47.4% and 96.7%, respectively. The optimal cut-off for this sample was failing any of the six critical items, with a sensitivity of 59.3% and a specificity of 89.4%. The AUC was CI 95% [0.702-0.829].

SCQ

Considering the fifteen original cut-off score, sensitivity and specificity were 51.1% and 98.5%, respectively. The optimal cut-off score was 10, yielding a sensitivity of 70.4% and a specificity of 95.5%. The AUC was CI 95% [0.854-0.937] (Table 8, Figure 2).

4. ITEM ANALYSES

M-CHAT

At the first evaluation time (Table 9, supplemental data), all items but “Enjoy climbing on things” (p=0.174) and “Walking” (p=0.550) were able to properly distinguish ASD subjects from those who were later diagnosed as OND/Non-ASD, with ASD children presenting higher failure rates for twenty-one out of the twenty-three M-CHAT items.

At T2 evaluation (Table 10, supplemental data), three items were not significantly different between groups: “Enjoy being swung, bounced on knee” (p=0.098), “Enjoy climbing on things” (p=0.552) and “Walking” (p=0.328).

SCQ

Both at T1 (Table 11, supplemental data) and T2 (Table 12, supplemental data) assessments, the ASD group had significantly higher failure rates in thirty-six out of forty SCQ items. As so, only four questions did not discriminate ASD from OND/Non-ASD children: “Inappropriate questions” (p=0.151 at T1, p=0.321 at T2), “Neologisms” (p=0.237 at T1, p=0.211 at T2), “Self-injury” (p=0.559 at T1, p=0.096 at T2) and “Unusual attachment to objects” (p=0.666 at T1, p=1.000 at T2).

DISCUSSION

1. SAMPLE CHARACTERIZATION

In our sample, there was a clear male predominance among ASD children, with a distribution of seven males to one female, a ratio even higher than the one previously reported by Oliveira G. (6), but still in agreement with epidemiological studies, in which male predominance is a consistent finding (2,3).

In accordance with previous studies, caregivers reports of first concerns about their children development occurred around the age of eighteen to twenty-four months (6,9,11), being earlier among ASD parents (32). Communication impairments meaning language delay acquisition were the main area of parental first concerns, worrying over half of the caregivers of both ASD and OND/Non-ASD children. Our findings were similar to those reported by Kozlowski et al. (32), who stated that communication impairments/ language delay are not ASD-specific, although their early recognition is still important, as they may warrant a global assessment for developmental delay. The presence of deficits in social interaction skills was also a noteworthy and distinctive first concern expressed by parents of ASD children, which is not surprising, since it is known that social referencing deficits are specific of ASD (4,18). Challenging behaviors, already found to be an important area of first concern within OND/Non-ASD toddlers, were significantly more frequent among these children. Despite significant differentiation between groups regarding social and behavioral concerns, which did not occur in Kozlowski et al. analysis, we do agree with author's statement about the need of an accurate and comprehensive assessment for ASD or OND children, considering the unlikeliness of a single trait or deficit to provide a reliable diagnosis (32).

As expected by previous research, ASD children in our sample had significantly lower developmental and adaptive functioning scores comparing to those of the OND/Non-ASD group. Mouga et al. (33) found that VABS Social Skills Domain was an independent and distinctive factor of ASD. In our sample, besides the adaptive behavior in domain of socialization skills impairment, ASD children also displayed significantly poorer motor and daily living skills and more serious social communication deficits than those diagnosed as OND/Non-ASD.

Attending to the clinical utility of knowing early psychomotor developmental profiles in ASD children (34), we also analyzed the age of acquisition for six neurodevelopmental milestones: first meaningful words, first phrases, walking age, daytime and night-time control of bladder sphincter. ASD children said their first words and first phrases significantly later than OND/Non-ASD children and had delayed daytime and night-time control of bladder sphincter, supporting the findings of Ferreira et al. (34).

2. M-CHAT AND SCQ – ORIGINAL *VERSUS* OPTIMAL CUT-OFF SCORES

M-CHAT

Time 1

Using the original cut-off score of failing any three of the M-CHAT items, we found a similarly high sensitivity (94.1%) as the originally reported by Robins et al. (97%), although the specificity was lower (65.2% in our sample *versus* 95%) (18). When comparing other studies focused in samples of young children referred with neurodevelopmental concerns as well, we slightly overcame the sensitivity stated by Eaves et al. (92%) (23) and by Snow and

Lecavalier (88%) (25) with a much higher specificity (65.2% in our study *versus* 27% by Eaves et al. and 38% by Snow and Lecavalier).

When equal weight was given to sensitivity and specificity, a cut-off score of six out of twenty-three items was found to be the optimal one for our sample, lowering the sensitivity but improving the specificity. When considering three items more than originally proposed by Robins et al. (18), the ability of the M-CHAT to properly identify those one hundred and thirty-five children with ASD was slightly lower, but eighteen more subjects may have been accurately identified as OND/Non-ASD (sensitivity improved from 65.2% to 92.4%). Thus, a slightly higher cut-off score would potentially lower the rate of unnecessary referrals of children not likely to receive an ASD diagnosis (false positives).

Our study confirmed the cut-off score of failing two critical items proposed by the M-CHAT authors (18), yielding a sensitivity and a specificity higher than previously reported by Eaves et al. (sensitivity of 77%, specificity of 43%) (23) and by Snow and Lecavalier (70% sensitivity, 38% specificity) (25).

Time 2

At the second evaluation time, the original cut-off score of failing any three M-CHAT items, although considered the optimal one, did not perform as well. Apart from the improved specificity, the sensitivity was lower than the assessed in the first evaluation time and than reported in the abovementioned studies (18,23,25). Having a decreased sensitivity, the second M-CHAT failed in properly identifying twenty-six five-year-old ASD children who were correctly screened at the age of three (false negatives).

Considering the cut-off score of failing two critical items, the sensitivity was quite low and the specificity was high compared with Eaves et al. and Snow and Lecavalier (23,25). The sensitivity was much lower than the one found by Robins et al., as seventy-one ASD children were considered not likely to be within autism spectrum, although the specificity was equally high (18). So, relying exclusively on the critical items score when screening older children led to an unacceptably high rate of false negatives, with more than half of ASD children passing the screen. Failing just one critical item yielded a slightly higher sensitivity, but a lower specificity – using this cut-off score, the M-CHAT would have excluded only fifty-five ASD children, but seven OND/Non-ASD children would be flagged as likely to have ASD, requiring further specialized assessment.

In both T1 and T2 evaluations, the cut-off scores of failing any three or six items were more sensitive than failing one or two of the six critical items. When considering the whole M-CHAT questionnaire, it might be required failing only a few items from a larger number of questions, improving the ability to detect atypical patterns of behavior.

SCQ

Time 1

At the first assessment, by scoring the SCQ as originally proposed, we found a sensitivity higher than reported by Charman et al. (64%) (21), Snow and Lecavalier (70%) (25), Wiggins et al. (47%) (35) and Eaves et al. (71-74%) (23,36), but lower than the 85%-sensitivity achieved by Berument (20). Specificity was higher than previous stated (97% *versus* 52%-89%) (20,21,23,25,35,36), with the SCQ providing early and accurate

identification of almost all the children who were later found not to have ASD (true negatives).

The usefulness of the SCQ as a well stablished, highly effective screening measure has been extensively reported by previous research (37), but our findings are particular relevant attending to the age range of our sample at the first evaluation time. Although the SCQ may be given to parents or caregivers at any time, it was designed for subjects since their fifth year of life (above two years of mental age) and it may not be as effective in categorizing younger ASD children when the recommended cut-off of fifteen is employed (35,37). However, in our sample, it properly identified one-hundred and seven ASD cases at the median age of three (true positives), a better outcome than already stated, supporting the SCQ utility in young children with neurodevelopmental concerns.

As expected by previous research (35), lowering the cut-off score in two points (failing thirteen SCQ items), leaded to better sensitivity without compromising specificity. Comparing to the standard cut-off score, ten ASD three-year old children were additionally flagged, at the cost of missing two other OND/Non-ASD cases. The cut-off score of thirteen was also the optimal one found by Snow and Lecavalier (25), however, it provided a lower specificity in their sample (40% *versus* 93.9%), despite the similar sensitivity (85% *versus* 86.7% in our study) .

Time 2

By the time of the second assessment, the original score of failing fifteen SCQ items yielded a much lower sensitivity comparing to the first results, meaning a large increase in ASD children passing the screen as probably not within autism spectrum (false negatives).

This was a surprising finding, as half of the SCQ items are focused on behavioral symptoms that might be more apparent when subjects are around the age of four to five years old (25), approaching the age range of our sample at the final evaluation. As so, it would be expected a higher number of five-year old ASD children scoring fifteen or more on the second SCQ applied.

The 98.5% specificity was more encouraging, being higher than previously reported – only one five-year-old OND/Non-ASD child would be inappropriately flagged as ASD. Once again, and similar to previous research (25,35), a lower cut-off score of failing ten items was found to be the optimal one, allowing proper categorization of ninety-five ASD children (higher sensitivity and low rate of false negatives) while misclassifying just three of the sixty-six OND/Non-ASD cases (low rate of false positives).

As sensitivity and specificity are influenced by the sample, our results may reflect sample differences. Screening results are always sample dependent and their utility is yoked to the impact of misleading diagnosis (25). As so, we presented our findings using different cut-off scores, allowing adjustment according to the purpose and setting of screening.

It is interesting to compare results between assessments. For both the M-CHAT and the SCQ, there was a decrease in the sensitivity from T1 assessment (around the age of three years old) to T2 assessment (around the age of five years old). When evaluating older children, there was an increased number of ASD subjects not reaching criteria for failing the screen (false negatives). Between both evaluation times, ASD children may have achieved better developmental outcomes, or they may have demonstrated atypically behaviors in a less consistent way, compromising the ability of being properly identified through these screening measures. Moreover, as written questionnaires to endorse (yes/no) symptom descriptions,

they might be more insensitive due to behavioral development in slightly older ASD children (23).

Sensitivity and specificity are estimated probabilities of accurately screening ASD and OND/Non-ASD children, respectively. In primary care setting, the sensitivity (children screened as likely to have ASD who received ASD diagnosis) may be more important than specificity, as the burden of false negatives outweighs the inconvenience of false positives (23,25). In this setting, the M-CHAT performed better than SCQ in both assessments, particularly when evaluating younger children, missing only eight out of one-hundred and thirty-five three-year old subjects who were later diagnosed with ASD. In terms of specificity, which can be though as the ability of properly identify children both screened and diagnosed as not having ASD, the SCQ was the most accurate tool, misclassifying just one OND/Non-ASD child at the second evaluation time. Thus, this highly specific SCQ performed around the age of five successfully screened out OND/Non-ASD children.

When assessing subjects already determined to have neurodevelopmental problems suspicion, however, sensitivity and specificity are equally important to maximize diagnostic accuracy (25). Taking previously validated cut-off scores into account, when evaluating three-year-old children, failing two M-CHAT critical items was found to be the most appropriated screening measure to our sample. Eighteen months later, at the median age of five years old, applying the whole M-CHAT questionnaire was more accurate in properly identifying both ASD and OND/Non-ASD subjects. Overall accuracy of both screening tools, evaluated with ROC analyses, was good to excellent.

3. ITEM ANALYSES

Being a prospective study, it is possible to look back at the first assessment data to compare descriptions of early social, behavior and communication development in children later diagnosed as having or not having ASD. Considering time constraints in clinical care setting, briefing screening measures would facilitate ASD-specific screening. An instrument with a limited number of items would also be easier to administrate and would elicit greater caregiver cooperation, allowing direct discussion about the significance of the test and potential parental concerns (38).

Twenty-one items on the first M-CHAT (T1) and twenty items on the second M-CHAT applied (T2) showed significant differentiation between ASD and OND/Non-ASD groups. These included the six critical items identified by Robins et al. ("Interest in other children", "Pointing to indicate interest in something", "Bringing objects to show", "Imitation of caregiver's action", "Response to name when called", "Following a point") (18), the two items reported by Snow and Lecavalier ("Unusual finger movements" and "Caregiver's referencing in novel situation") (25) and all of the six items selected by Kamio et al. in their analysis of the Japanese version of the M-CHAT ("Pretend play", "Pointing to ask for something", "Bringing objects to show", "Imitation of caregiver's action", "Following a point", "Speech comprehension") (38).

"Enjoy being swung, bounced on knee" was a discriminator item only at the first assessment. Differently from ASD subjects, all OND/Non-ASD children enjoyed being swinging, bouncing on knee regardless their age. They also liked climbing since they were about three years old, but this was never significantly different between cases. At the age of three, almost all children were already able to walk regardless their diagnostic group, as

expected by neurodevelopmental milestones assessment ("walking age" at fourteen months). Among the discriminator items in our sample, it is worth mentioning that, since first assessment, all children who were later diagnosed as having OND were able to look at a toy across the room ("Following a point"), while ASD children were not. Moreover, at the age of five, all OND/Non-ASD children responded to their name when called, what did not occur among ASD children. Indeed, there is some evidence upon reduced orienting to name as a later discriminator finding between ASD and OND, being already considered an early and prospective diagnostic marker among at-risk infants (9).

Thirty-six SCQ items (90%) showed statistically significant differentiation between the two groups across assessments, and included those identified by Snow and Lecavalier (25) as the best discriminators items ("Phrase speech", "Pronoun reversal", "Hand and finger mannerisms", "Social chat", "Pointing to indicate interest", "Nodding to indicate "yes"", "Shaking head to indicate "no""). Moreover, our results approached those of the SCQ standardization sample (20), where 94% of the items distinguished ASD from OND/Non-ASD subjects. Different from ASD cases, all OND/Non-ASD children soon looked at their caregivers and called attention when needed something ("Quality of social overtures"). Eighteen months later, none expressed "Verbal rituals" and all pointed to indicate interest, behaviors not verified among same-aged ASD subjects. However, two verbal items, "Inappropriate questions" and "Neologisms", along with "Self-injury" and "Unusual attachment to objects" were never useful in differentiating our sample. None of these questions addressed symptoms expected to develop around four years of chronological age, so, the SCQ had great ability to accurately differentiate both groups in our sample since their first assessment.

Further investigation is needed to confirm if our "critical items" as a group discriminate ASD children from others with OND/Non-ASD. If these items are shown to yield similar screening results as the full version of the questionnaires, then it may be possible to use them as a shorter form of ASD screening in clinical setting, where time constraints are usually a major problem.

STRENGHTS AND POTENTIAL LIMITATIONS

To our knowledge, this is the first prospective study comparing two screening measures for ASD in a large and well characterized cohort of at-risk children longitudinally assessed for neurodevelopmental disorders suspicion. Being a follow-up study of both positive and negative screening subjects, it was possible to evaluate the true sensitivity and specificity of the M-CHAT and the SCQ, as well as the behavioral and neurodevelopmental profile among cases, considering the final diagnosis reliably made eighteen months after the first evaluation.

We were interested in realize the performance of the M-CHAT and the SCQ in preschoolers suspected of ASD or OND, in accordance with current, real-life clinical applicability of ASD screening. Although the age range of our sample differed from those originally recommended for these measures (18,19), our findings indicate that both questionnaires are very useful when evaluating three to five-year old children. However, as sixty-seven percent of our sample was found to have ASD, there was a great chance for screening to agree with final diagnosis. As so, it may be highlighted that our results respect to a high-risk sample and not to subjects generally evaluated at well-child primary care assessments.

We did not match ASD and OND/Non-ASD groups on cognitive or adaptive functioning levels, nor differentiated verbal from non-verbal children. Knowing the impact of these variables on the scores achieved by both groups would be important, providing a more accurate evaluation of screening effectiveness. As there are six fewer SCQ items suitable for non-verbal children, including four that we found to distinguish ASD from OND diagnosis, using the same cut-off score for both verbal and non-verbal subjects may have biased results, potentially lowering the SCQ sensitivity.

Although the lack of blind assessments may be seen as a potential source of diagnostic bias, ASD final diagnosis was rigorously made using not only clinical judgement, but also well stablished, objective measures, following gold standard procedures. Moreover, we did not attempt to perform blind assessments as longitudinal observation of neurodevelopmental profiles of at-risk children by the same expert and multidisciplinary team allowed a better understanding and comparison of behavioral trajectories and clinical outcomes.

CLINICAL IMPLICATIONS

Having the majority of items as potential discriminators between ASD and OND/Non-ASD children, our study reinforces the strong psychometric properties of two widely screening measures in this field, the M-CHAT and the SCQ, when assessing preschoolers suspected of having neurodevelopmental disorders. This is of major clinical relevance, as ASD screening is most likely to be performed among this subset of at-risk children (36).

Both the M-CHAT and the SCQ performed well at properly identifying three-year old subjects who went on to meet ASD diagnostic criteria at the age of five. The M-CHAT was found to be more sensitive than the SCQ, allowing a lower number of ASD children

incorrectly screened as OND/Non-ASD (false negatives). Therefore, it would be of greatest interest at primary care setting, minimizing the costs of potential missed diagnosis. The M-CHAT also provided the best diagnostic accuracy, allowing the highest number of both ASD and OND/Non-ASD cases correctly screened as so. Based on our sample, and considering the originally proposed screening criteria, we recommend a cut-off score of failing two of the six critical items ("Interest in other children", "Pointing to indicate interest in something", "Bringing objects to show", "Imitation of caregiver's action", "Response to name when called" and/or "Following a point") when assessing at-risk three-year-old children, being more appropriate to apply the whole M-CHAT questionnaire when evaluating five-year-old subjects. Hence, our results are very meaningful, since they indicate that the M-CHAT is an accurate instrument for early detection of ASD among Portuguese toddlers, similarly to previous reported across the globe. Screening criteria adjustment to clinical setting and purpose may provide even better results, but care should be taken when selecting different cut-off scores from those originally proposed, as variability across samples greatly influences screening outcomes (2).

At the light of our findings, considering the strong and prospective agreement of early screening with final diagnosis, we encourage prompt referral of screen-positive three-year old children for early specialized ASD assessments. Altogether, our results provide valuable contribute for differential diagnosis and clinical decision making regarding feedback to families, access to public services and treatment planning, particularly when evaluating at-risk toddlers. This is of crucial importance, as early specialized referrals enhance early specific intervention, improving lifetime prognosis and mitigating the substantial impact of ASD for both patients and families affected by the disorder.

Reproducing this study with even younger children would be of greatest interest, to identify the earliest age at which a reliable and predictive screening for ASD is possible and, through suitable intervention programs, to promote even better developmental outcomes.

Finally, as previously noticed, we would like to highlight that screening measures are not designed for diagnostic purposes nor replace the need for further and comprehensive evaluations. Therefore, despite our encouraging results, the importance of clinical judgement cannot be overemphasized, and it must be combined with appropriated tests and assessments to accurately and reliably discriminate whether a child is on the autism spectrum, has other neurodevelopmental disorder or is within boundaries of typical development.

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ANNEX 1 – The Modified Checklist for Autism in Toddlers (M-CHAT),

Portuguese version

Nome: _____ Preenchido por: _____

Data de Nascimento: _____ Parentesco do informador: _____

Data: _____

Modified Checklist for Autism in Toddlers (M-CHAT)

Diana Robins, Deborah Fein & Marianne Barton, 1999

Por favor, preencha este questionário sobre o comportamento usual da criança. Responda a todas as questões. Se o comportamento descrito for raro (ex. foi observado uma ou duas vezes), responda como se a criança não o apresente. Faça um círculo à volta da resposta "Sim" ou "Não".

1	Gosta de brincar ao colo fazendo de "cavalinho", etc.?	Sim	Não
2	Interessa-se pelas outras crianças?	Sim	Não
3	Gosta de subir objectos, como por exemplo, cadeiras, mesas?	Sim	Não
4	Gosta de jogar às escondidas?	Sim	Não
5	Brinca ao faz-de-conta, por exemplo, falar ao telefone ou dar de comer a uma boneca, etc.?	Sim	Não
6	Aponta com o indicador para pedir alguma coisa?	Sim	Não
7	Aponta com o indicador para mostrar interesse em alguma coisa?	Sim	Não
8	Brinca apropriadamente com brinquedos (carros ou Legos) sem levá-los à boca, abanar ou deitá-los ao chão?	Sim	Não
9	Alguma vez lhe trouxe objectos (brinquedos) para lhe mostrar alguma coisa?	Sim	Não
10	A criança mantém contacto visual por mais de um ou dois segundos?	Sim	Não
11	É muito sensível aos ruídos (ex. tapa os ouvidos)?	Sim	Não
12	Sorri como resposta às suas expressões faciais ou ao seu sorriso?	Sim	Não
13	Imita o adulto (ex. faz uma careta e ela imita)?	Sim	Não
14	Responde/olha quando o(a) chamam pelo nome?	Sim	Não
15	Se apontar para um brinquedo do outro lado da sala, a criança acompanha com o olhar?	Sim	Não
16	Já anda?	Sim	Não
17	Olha para as coisas para as quais o adulto está a olhar?	Sim	Não
18	Faz movimentos estranhos com as mãos/dedos próximo da cara?	Sim	Não
19	Tenta chamar a sua atenção para o que está a fazer?	Sim	Não
20	Alguma vez se preocupou quanto à sua audição?	Sim	Não
21	Compreende o que as pessoas lhe dizem?	Sim	Não
22	Por vezes fica a olhar para o vazio ou deambula ao acaso pelos espaços?	Sim	Não
23	Procura a sua reacção facial quando se vê confrontada com situações desconhecidas?	Sim	Não

Traduzido pela Unidade de Autismo
Centro de Desenvolvimento da Criança – Hospital Pediátrico de Coimbra
Autorização Diana Robins

Modified Checklist for Autism in Toddlers (M-CHAT)

Diana Robins, Deborah Fein & Marianne Barton, 1999

O (M-CHAT) é um breve questionário referente ao desenvolvimento e comportamento utilizado em crianças dos 16 aos 30 meses, com o objectivo de rastrear as perturbações do espectro do autismo (PEA). Pode ser aplicado tanto numa avaliação periódica de rotina (cuidados primários de saúde), como por profissionais especializados em casos de suspeita. Como na maioria dos testes de rastreio poderá existir um grande número de falsos positivos, indicando que nem todas as crianças que cotam neste questionário irão ser diagnosticadas com esta perturbação. No entanto estes resultados podem apontar para a existência de outras anomalias do desenvolvimento, sendo por isso necessária a avaliação por profissionais desta área.

Cotação:

A cotação do **M-CHAT** leva menos de dois minutos. Resultados superiores a **3 (falha em 3 itens no total)** ou em **2 dos itens considerados críticos (2,7,9,13,14,15),** após confirmação, justificam uma avaliação formal por técnicos de neurodesenvolvimento.

As respostas Sim/Não são convertidas em passa/falha. A tabela que se segue, regista as repostas consideradas **Falha** para cada um dos items do M-CHAT. As questões a "**Negrito**" representam os **itens CRITICOS.**

1. Não	6. Não	11. Sim	16. Não	21. Não
2. Não	**7. Não**	12. Não	17. Não	22. Sim
3. Não	8. Não	**13. Não**	18. Sim	23. Não
4. Não	**9. Não**	**14. Não**	19. Não	
5. Não	10. Não	**15. Não**	20. Sim	

Referências bibliográficas:

• http://www2.gsu.edu/~psydlr

• Kleinman et al. (2008) 'The Modified Checklist for Autism in Toddlers: a Follow-up Study Investigating the Early Detection of Autism Spectrum Disorders', *Journal of Autism and Developmental Disorders*, 38:827-839.

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ANNEX 2 – The Social Communication Questionnaire (SCQ),

Portuguese version

Social Communication Questionnaire

AutoScore™ Form

Michael Rutter, M.D., F.R.S., Anthony Bailey, M.D.,
Sibel Kazak Berument, Ph.D., Catherine Lord, Ph.D. and Andrew Pickles, Ph.D.

Publicado por WESTERN PSYCHOLOGICAL SERVICES

Data: _____ / _____ / _____

Nome: _____

Data de Nascimento: _____ / _____ / _____

Idade Cronológica: _____ Y _____ M Género ☐ F ☐ M

Preenchido por: _____

Grau de Parentesco: _____

Local da Avaliação: _____

Examinador: _____

Instruções

Obrigada por ter disponibilizado o seu tempo para responder a este questionário. Por favor responda a cada uma das questões fazendo um círculo à volta do **SIM** ou do **NÃO**.

Algumas das questões colocadas descrevem vários padrões de comportamento que se relacionam entre si. Faça um círculo à volta do **SIM** nestas questões sempre que **QUALQUER UM** dos comportamentos referidos se encontrou presente NÃO seu/vosso filho/a nos **ÚLTIMOS 3 MESES**.

Mesmo que não tenha a certeza se determinado comportamento se encontrou presente ou não no período de tempo referido, não deixe de responder **SIM** ou **NÃO** a todas as questões, de acordo com o que pensa.

1. Tem frases? SE **NÃO** avance para a questão 8	SIM	NÃO
2. É capaz de manter um diálogo adequado (i.é, uma conversa que envolva uma discussão e uma troca de ideias)?	SIM	NÃO
3 Alguma vez utilizou ou repetiu palavras/frases estranhas de uma forma exaustiva e repetitiva (sempre da mesma maneira), fossem palavras/frases que tivesse ouvido dizer ou que tivesse inventado?	SIM	NÃO
4 Alguma vez fez perguntas ou afirmações socialmente inapropriadas (ex. fazer perguntas de foro pessoal/íntimo ou comentários constrangedores a/sobre alguém)?	SIM	NÃO
5 Alguma vez inverteu a utilização dos pronomes numa frase (i.é, dizer *tu* ou *ele/ela* em vez de *eu*)?	SIM	NÃO
6 Alguma vez utilizou palavras aparentemente inventadas por si ou utilizou uma forma metafórica de dizer as coisas (ex. referir-se a *vapor* como *chuva quente*)?	SIM	NÃO
7 Alguma vez repetiu a mesma palavra/frase de modo exaustivo e repetitivo (sempre da mesma maneira) ou lhe pediu para o fazer?	SIM	NÃO

8 Alguma vez realizou uma actividade ou tarefa de um modo particular ou numa determinada ordem ou insistiu que outras pessoas realizassem determinados rituais (ex. insistir que alguém abrisse e fechasse a porta repetidamente)?	SIM	NÃO
9 Considera que ele/ela revela uma expressão facial adequada a determinada situação?	SIM	NÃO
10 Alguma vez utilizou a mão de outras pessoas para segurar ou alcançar objectos ou como se fosse um prolongamento do seu próprio corpo (ex. utilizar o dedo de outra pessoa para apontar ou colocar a mão de outra pessoa NÃO puxador da porta para a abrir)?	SIM	NÃO
11 Alguma vez manifestou interesse por algo ou por alguma actividade que considerasse estranha ou que parecesse estranha aos olhos de outras pessoas (ex. marcas de automóveis, canos de esgoto ou horários)?	SIM	NÃO
12 Alguma vez lhe pareceu estar mais interessado/a em partes de um brinquedo ou objecto do que propriamente em utilizá-lo ou em brincar com ele do modo que seria esperado (ex. girar as rodas de um carro em vez de brincar com ele)?	SIM	NÃO
13 Alguma vez manifestou um interesse que tivesse considerado ser de uma intensidade invulgar, embora fosse algo apropriado à sua idade e aos gostos do seu grupo de pares (ex. dinossauros, comboios)?	SIM	NÃO
14 Alguma vez revelou um interesse invulgar em fixar o olhar, tocar, ouvir, lamber ou cheirar objectos ou pessoas?	SIM	NÃO
15 Alguma vez manifestou maneirismos motores ou fez movimentos estranhos com as mãos ou dedos (ex. fazer *flapping* (“abanar as mãos”) ou abanar os dedos ou as mãos à frente dos olhos)?	SIM	NÃO
16 Alguma vez manifestou movimentos estranhos como, por exemplo, andar às voltas ou pular repetidamente?	SIM	NÃO
17 Alguma vez se auto-agrediu de forma deliberada (ex. morder-se, bater com a cabeça na parede)?	SIM	NÃO
18 Tem um objecto que insiste em levar sempre consigo, que considere invulgar?	SIM	NÃO
19 Tem algum amigo/a preferido/a ou um/a melhor amigo/a?	SIM	NÃO

Nos comportamentos seguintes, tenha em conta o período de tempo entre os 4 e os 5 anos de idade. Pode facilitar recordar-se de eventos chave, como o início de frequência no jardim de infância, mudanças de casa, época natalícia ou outros eventos que são particularmente marcantes para a sua/vossa família.
Se o seu/vosso filho/a ainda não tiver 4 anos de idade cronológica, refira-se ao seu comportamento nos últimos 12 meses.

20. Quando tinha 4-5 anos, alguma vez falou consigo só para ser amável (em vez de ser para pedir algo)?	SIM	NÃO
21. Quando tinha 4-5 anos, alguma vez o/a imitou espontaneamente ou a outras pessoas ou as vossas acções (ex. aspirar, jardinagem, consertar coisas)?	SIM	NÃO
22. Quando tinha 4-5 anos, alguma vez apontou espontaneamente para as coisas à sua volta para as mostrar (ou apontava apenas como forma de pedir algo)?	SIM	NÃO
23. Quando tinha 4-5 anos, alguma vez usou gestos, para além do apontar ou puxar pela sua mão, de forma a demonstrar o que queria?	SIM	NÃO
24. Quando tinha 4-5 anos, acenava com a cabeça para dizer que “sim”?	SIM	NÃO
25. Quando tinha 4-5 anos, acenava com a cabeça para dizer que “não”?	SIM	NÃO
26. Quando tinha 4-5 anos, costumava olhar directamente para sua cara enquanto fazia coisas ou falava para si?	SIM	NÃO
27. Quando tinha 4-5 anos, sorria em resposta ao sorriso de outra pessoa?	SIM	NÃO
28. Quando tinha 4-5 anos, alguma vez ele/ela lhe mostrava coisas de forma a obter a sua atenção?	SIM	NÃO
29. Quando tinha 4-5 anos, costumava partilhar coisas consigo, sem ser comida?	SIM	NÃO
30. Quando tinha 4-5 anos, alguma vez procurava partilhar consigo a alegria de estar a fazer algo que lhe provocava prazer?	SIM	NÃO
31. Quando tinha 4-5 anos, alguma vez procurou confortá-lo/a quando estava triste, magoado/a ou doente?	SIM	NÃO
32. Quando ele/ela tinha 4-5 anos, quando queria alguma coisa ou precisava de algo, olhava para si e usava sons ou palavras acompanhadas por gestos para obter a sua atenção?	SIM	NÃO
33. Quando tinha 4-5 anos, apresentava uma variedade normal de expressões faciais?	SIM	NÃO
34. Quando tinha 4-5 anos, participava espontaneamente e tentava imitar acções em jogos sociais (ex. brincar à roda ou brincar à apanhada)?	SIM	NÃO
35. Quando tinha 4-5 anos, tinha jogo simbólico, ou seja, brincava ao *faz-de-conta*?	SIM	NÃO
36. Quando tinha 4-5 anos, interessava-se por outras crianças aproximadamente da mesma idade, que não conhecia?	SIM	NÃO

37. Quando tinha 4-5 anos, reagia positivamente quando outras crianças se aproximavam dele/dela?	SIM	NÃO
38. Quando tinha 4-5 anos, se chegasse a uma divisão da casa e começasse a falar para ele/ela, sem o/a chamar pelo nome, costumava olhar para si ou prestar atenção ao que lhe estava a dizer?	SIM	NÃO
39. Quando tinha 4-5 anos, alguma vez brincou de forma imaginativa com outra criança de uma maneira que o/a pai/mãe conseguia perceber que as crianças compreendiam o que cada uma estava a imaginar?	SIM	NÃO
40. Quando tinha 4-5 anos, participava cooperativamente em jogos de grupo (ex. escondidas, mata)?	SIM	NÃO

SUPPLEMENTAL DATA

Table 9 – M-CHAT item analyses at T1 assessment.

Item	ASD group (n=135) (Pass: Fail)	OND/ Non-ASD group (n=66) (Pass: Fail)	*p-value*
1 Enjoy being swung, bounced on knee	124 (91.9%): 11 (8.1%)	66 (100%): 0 (0%)	**0.017**
2 Interest in other children	49 (36.3%): 86 (63.7%)	56 (84.8%): 10 (15.2%)	**<0.001**
3 Enjoy climbing on things	130 (96.3%): 5 (3.7%)	66 (100%): 0 (0%)	0.174
4 Enjoy peek-a-boo/hide-and-seek	82 (60.7%): 53 (39.3%)	63 (95.5%): 3 (4.5%)	**<0.001**
5 Pretend play	61 (45.2%): 74 (54.8%)	62 (93.9%): 4 (6.1%)	**<0.001**
6 Pointing to ask for something	69 (51.1%): 66 (48.9%)	63 (95.5%): 3 (4.5%)	**<0.001**
7 Pointing to indicate interest in something	43 (31.9%): 92 (68.1%)	58 (87.9%): 8 (12.1%)	**<0.001**
8 Play properly with toys	96 (71.1%): 39 (28.9%)	64 (97%): 2 (3%)	**<0.001**
9 Bringing objects to show	56 (41.5%): 79 (58.5%)	64 (97%): 2 (3%)	**<0.001**
10 Eye contact	70 (51.9%): 65 (48.1%)	62 (93.9%): 4 (6.1%)	**<0.001**
11 Oversensitivity to noise	81 (60%): 54 (40%)	55 (83.3%): 11 (16.7%)	**0.001**
12 Smile in response to caregiver's smile	63 (46.7%): 72 (53.3%)	65 (98.5%): 1 (1.5%)	**<0.001**
13 Imitation of caregiver's action	77 (57%): 58 (43%)	61 (92.4%): 5 (7.6%)	**<0.001**
14 Response to name when called	63 (46.7%): 72 (53.3%)	63 (95.5%): 3 (4.5%)	**<0.001**

Table 9 (continued).

Item	ASD group (n=135) (Pass: Fail)	OND/ Non-ASD group (n=66) (Pass: Fail)	*p-value*
15 Following a point	80 (59.3%): 55 (40.7%)	66 (100%): 0 (0%)	**<0.001**
16 Walking	134 (99.3%): 1 (0.7%)	65 (98.5%): 1 (1.5%)	0.550
17 Look at what caregiver is looking at	32 (23.7%): 103 (76.3%)	59 (89.4%): 7 (10.6%)	**<0.001**
18 Unusual finger movements	79 (58.5%): 56 (41.5%)	57 (86.4%): 9 (13.6%)	**<0.001**
19 Attract caregiver's attention	41 (30.4%): 94 (69.6%)	63 (95.5%): 3 (4.5%)	**<0.001**
20 Concern about deafness	58 (43%): 77 (57%)	43 (65.2%): 23 (34.8%)	**0.004**
21 Speech comprehension	77 (57%): 58 (43%)	56 (84.8%): 10 (15.2%)	**<0.001**
22 Wander with no purpose	37 (27.4%): 98 (72.6%)	53 (80.3%): 13 (19.7%)	**<0.001**
23 Caregiver's referencing in novel situation	36 (26.7%): 99 (73.3%)	54 (81.8%): 12 (18.2%)	**<0.001**

Note: M-CHAT – Modified Checklist for Autism in Toddlers; T1 – Time 1; ASD – Autism Spectrum Disorder; OND – Other Neurodevelopmental Disorders;

Data is presented as n (%). The p-values were computed using Fisher exact test.

Table 10 – M-CHAT item analyses at T2 assessment.

Item	ASD group (n=135) (Pass: Fail)	OND/ Non-ASD group (n=66) (Pass: Fail)	*p-value*
1 Enjoy being swung, bounced on knee	128 (94.8%): 7 (5.2%)	66 (100%): 0 (0%)	0.098
2 Interest in other children	86 (63.7%): 49 (36.3%)	62 (93.9%): 4 (6.1%)	**<0.001**
3 Enjoy climbing on things	132 (97.8%): 3 (2.2%)	66 (100%): 0 (0%)	0.552
4 Enjoy peek-a-boo/hide-and-seek	97 (71.9%): 38 (28.1%)	65 (98.5%): 1 (1.5%)	**<0.001**
5 Pretend play	91 (67.4%): 44 (32.6%)	62 (93.9%): 4 (6.1%)	**<0.001**
6 Pointing to ask for something	98 (72.6%): 37 (27.4%)	65 (98.5%): 1 (1.5%)	**<0.001**
7 Pointing to indicate interest in something	73 (54.1%): 62 (45.9%)	63 (95.5%): 3 (4.5%)	**<0.001**
8 Play properly with toys	115 (85.2%): 20 (14.8%)	64 (97%): 2 (3%)	**0.014**
9 Bringing objects to show	84 (62.2%): 51 (37.8%)	65 (98.5%): 1 (1.5%)	**<0.001**
10 Eye contact	92 (68.1%): 43 (31.9%)	63 (95.5%): 3 (4.5%)	**<0.001**
11 Oversensitivity to noise	91 (67.4%): 44 (32.6%)	57 (86.4%): 9 (13.6%)	**0.004**
12 Smile in response to caregiver's smile	80 (59.3%): 55 (40.7%)	65 (98.5%): 1 (1.5%)	**<0.001**
13 Imitation of caregiver's action	89 (65.9%): 46 (34.,1%)	65 (98.5%): 1 (1.5%)	**<0.001**
14 Response to name when called	93 (68.9%): 42 (31.1%)	66 (100%): 0 (0%)	**<0.001**

Table 10 (continued).

Item	ASD group (n=135) (Pass: Fail)	OND/ Non-ASD group (n=66) (Pass: Fail)	*p-value*
15 Following a point	107 (79.3%): 28 (20.7%)	66 (100%): 0 (0%)	**<0.001**
16 Walking	135 (100%): 0 (0%)	65 (98.5%): 1 (1.5%)	0.328
17 Look at what caregiver is looking at	49 (36.3%): 86 (63.7%)	62 (93.9%): 4 (6.1%)	**<0.001**
18 Unusual finger movements	86 (63.7%): 49 (36.3%)	60 (90.9%): 6 (9.1%)	**<0.001**
19 Attract caregiver's attention	58 (43%): 77 (57%)	64 (97%): 2 (3%)	**<0.001**
20 Concern about deafness	90 (66.7%): 45 (33.3%)	57 (86.4%): 9 (13.6%)	**0.004**
21 Speech comprehension	91 (67.4%): 44 (32.6%)	59 (89.4%): 7 (10.6%)	**0.001**
22 Wander with no purpose	47 (34.8%): 88 (65.2%)	55 (83.3%): 11 (16.7%)	**<0.001**
23 Caregiver's referencing in novel situation	48 (35.6%): 87 (64.4%)	62 (93.9%): 4 (6.1%)	**<0.001**

Note: M-CHAT – Modified Checklist for Autism in Toddlers; T2 – Time 2; ASD – Autism Spectrum Disorder; OND – Other Neurodevelopmental Disorders.

Data is presented as n (%). The p-values were computed using Fisher exact test.

Table 11 – SCQ item analyses at T1 assessment.

Item	ASD group (n=135) (Pass: Fail)	OND/ Non-ASD group (n=66) (Pass: Fail)	*p-value*
1 Phrase speech	48 (35.6%): 87 (64.4%)	44 (66.7%): 22 (33.3%)	**<0.001**
2 Conversation	9 (18.8%): 39 (81.3%)	21 (47.7%): 23 (52.3%)	**0.004**
3 Stereotyped utterances	20 (41.7%): 28 (58.3%)	38 (86.4%): 6 (13.6%)	**<0.001**
4 Inappropriate questions	38 (79.2%): 10 (20.8%)	40 (90.0%): 4 (9.1%)	0.151
5 Pronoun reversal	18 (37.5%): 30 (62.5%)	30 (68.2%): 14 (31.8%)	**0.004**
6 Neologisms	39 (81.3%): 9 (18.8%)	40 (90.0%): 4 (9.1%)	0.237
7 Verbal rituals	26 (54.2%): 22 (45.8%)	38 (86.4%): 6 (13.6%)	**0.001**
8 Compulsions and rituals	59 (43.7%): 76 (56.3%)	58 (87.9%): 8 (12.1%)	**<0.001**
9 Inappropriate facial expression	69 (51.1%): 66 (48.9%)	59 (89.4%): 7 (10.6%)	**<0.001**
10 Use of other's body	26 (19.3%): 109 (80.7%)	53 (80.3%): 13 (19.7%)	**<0.001**
11 Unusual preoccupations	75 (55.6%): 60 (44.4%)	61 (92.4%): 5 (7.6%)	**<0.001**
12 Repetitive use of objects	60 (44.4%): 75 (55.6%)	58 (87.9%): 8 (12.1%)	**<0.001**
13 Circumscribed interests	90 (66.7%): 45 (33.3%)	60 (90.9%): 6 (9.1%)	**<0.001**
14 Unusual sensory interests	77 (57%): 58 (43%)	58 (87.9%): 8 (12.1%)	**<0.001**

Table 11 (continued).

Item	ASD group (n=135) (Pass: Fail)	OND/ Non-ASD group (n=66) (Pass: Fail)	*p-value*
15 Hand and finger mannerisms	58 (43%): 77 (57%)	56 (84.8%): 10 (15.2%)	<**0.001**
16 Complex body mannerisms	42 (31.1%): 93 (68.9%)	55 (83.3%): 11 (16.7%)	<**0.001**
17 Self-injury	109 (80.7%): 26 (19.3%)	56 (84.8%): 10 (15.2%)	0.559
18 Unusual attachment to objects	130 (96.3%): 5 (3.7%)	65 (98.5%): 1 (1.5%)	0.666
19 Friends	14 (10.4%): 121 (89.6%)	26 (39.4%): 40 (60.6%)	<**0.001**
20 Social chat	27 (20%): 108 (80%)	53 (80.3%): 13 (19.7%)	<**0.001**
21 Imitation	77 (57%): 58 (43%)	64 (97%): 2 (3%)	<**0.001**
22 Pointing to indicate interest	46 (34.1%): 89 (65.9%)	63 (95.5%): 3 (4.5%)	<**0.001**
23 Gesture to request objects	49 (36.3%): 86 (63.7%)	62 (93.9%): 4 (6.1%)	<**0.001**
24 Nodding to indicate “yes”	52 (38.5%): 83 (61.5%)	56 (84.8%): 10 (15.2%)	<**0.001**
25 Shaking head to indicate “no”	91 (67.4%): 44 (32.6%)	62 (93.9%): 4 (6.1%)	<**0.001**
26 Eye gaze	43 (31.9%): 92 (68.1%)	62 (93.9%): 4 (6.1%)	<**0.001**
27 Social smiling	61 (45.2%): 74 (54.8%)	65 (98.5%): 1 (1.5%)	<**0.001**
28 Showing and directing attention	61 (45.2%): 74 (54.8%)	64 (97%): 2 (3%)	<**0.001**

Table 11 (continued).

Item	ASD group (n=135) (Pass: Fail)	OND/ Non-ASD group (n=66) (Pass: Fail)	*p-value*
29 Offering to share	44 (32.6%): 91 (67.4%)	56 (84.8%): 10 (15.2%)	**<0.001**
30 Seeking to share enjoyment	37 (27.4%): 98 (72.6%)	57 (86.4%): 9 (13.6%)	**<0.001**
31 Offering comfort	47 (34.8%): 88 (65.2%)	57 (86.4%): 9 (13.6%)	**<0.001**
32 Quality of social overtures	58 (43%): 77 (57%)	66 (100%): 0 (0%)	**<0.001**
33 Range of facial expression	70 (51.9%): 65 (48.1%)	64 (97%): 2 (3%)	**<0.001**
34 Imitative social play	35 (25.9%): 100 (74.1%)	54 (81.8%): 12 (18.2%)	**<0.001**
35 Imaginative play	53 (39.3%): 82 (60.7%)	60 (90.9%): 6 (9.1%)	**<0.001**
36 Interest in children	39 (28.9%): 96 (71.1%)	54 (81.8%): 12 (18.2%)	**<0.001**
37 Response to other children	81 (60%): 54 (40%)	56 (84.8%): 10 (15.2%)	**<0.001**
38 Attention to voice	36 (26.7%): 99 (73.3%)	57 (86.4%): 9 (13.6%)	**<0.001**
39 Imaginative play with peers	19 (14.1%): 116 (85.9%)	40 (60.6%): 26 (39.4%)	**<0.001**
40 Group play	17 (12.6%): 118 (87.4%)	29 (43.9%): 37 (56.1%)	**<0.001**

Note: SCQ – Social Communication Questionnaire; T1 – Time 1; ASD – Autism Spectrum Disorder; OND – Other Neurodevelopmental Disorders.

Data is presented as n (%). The p-values were computed using Fisher exact test.

Table 12 – SCQ item analyses at T2 assessment.

Item	ASD group (n=135) (Pass: Fail)	OND/ Non-ASD group (n=66) (Pass: Fail)	*p-value*
1 Phrase speech	94 (69.6%): 41 (30.4%)	56 (84.8%): 10 (15.2%)	**0.024**
2 Conversation	22 (23.4%): 72 (76.6%)	39 (69.6%): 17 (30.4%)	**<0.001**
3 Stereotyped utterances	66 (70.2%): 28 (29.8%)	53 (94.6%): 3 (5.4%)	**<0.001**
4 Inappropriate questions	79 (84%): 15 (16%)	51 (91.1%): 5 (8.9%)	0.321
5 Pronoun reversal	38 (40.4%): 56 (59.6%)	49 (87.5%): 7 (12.5%)	**<0.001**
6 Neologisms	85 (90.4%): 9 (9.6%)	54 (96.4%): 2 (3.6%)	0.211
7 Verbal rituals	69 (73.4%): 25 (26.6%)	56 (100%): 0 (0%)	**<0.001**
8 Compulsions and rituals	76 (56.3%): 59 (43.7%)	64 (97%): 2 (3%)	**<0.001**
9 Inappropriate facial expression	75 (55.6%): 60 (44.4%)	62 (93.9%): 4 (6.1%)	**<0.001**
10 Use of other's body	74 (54.8%): 61 (45.2%)	63 (95.5%): 3 (4.5%)	**<0.001**
11 Unusual preoccupations	93 (68.9%): 42 (31.1%)	63 (95.5%): 3 (4.5%)	**<0.001**
12 Repetitive use of objects	94 (69.6%): 41 (30.4%)	59 (89.4%): 7 (10.6%)	**0.002**
13 Circumscribed interests	95 (70.4%): 40 (29.6%)	59 (89.4%): 7 (10.6%)	**0.002**
14 Unusual sensory interests	96 (71.1%): 39 (28.9%)	64 (97%): 2 (3%)	**<0.001**

Table 12 (continued).

Item	ASD group (n=135) (Pass: Fail)	OND/ Non-ASD group (n=66) (Pass: Fail)	*p-value*
15 Hand and finger mannerisms	67 (49.6%): 68 (50.4%)	61 (92.4%): 5 (7.6%)	**<0.001**
16 Complex body mannerisms	56 (41.5%): 79 (58.5%)	57 (86.4%): 9 (13.6%)	**<0.001**
17 Self-injury	121 (89.6%): 14 (10.4%)	64 (97%): 2 (3%)	0.096
18 Unusual attachment to objects	132 (97.8%): 3 (2.2%)	65 (98.5%): 1 (1.5%)	1.000
19 Friends	39 (28.9%): 96 (71.1%)	41 (62.1%): 25 (37.9%)	**<0.001**
20 Social chat	51 (37.8%): 84 (62.2%)	59 (89.4%): 7 (10.6%)	**<0.001**
21 Imitation	96 (71.1%): 39 (28.9%)	63 (95.5%): 3 (4.5%)	**<0.001**
22 Pointing to indicate interest	76 (56.3%): 59 (43.7%)	66 (100%): 0 (0%)	**<0.001**
23 Gesture to request objects	70 (51.9%): 65 (48.1%)	65 (98.5%): 1 (1.5%)	**<0.001**
24 Nodding to indicate “yes”	79 (58.5%): 56 (41.5%)	61 (92.4%): 5 (7.6%)	**<0.001**
25 Shaking head to indicate “no”	108 (80%): 27 (20%)	64 (97%): 2 (3%)	**0.001**
26 Eye gaze	66 (48.9%): 69 (51.1%)	65 (98.5%): 1 (1.5%)	**<0.001**
27 Social smiling	78 (57.8%): 57 (42.2%)	64 (97%): 2 (3%)	**<0.001**
28 Showing and directing attention	77 (57%): 58 (43%)	64 (97%): 2 (3%)	**<0.001**

Table 12 (continued).

Item	ASD group (n=135) (Pass: Fail)	OND/ Non-ASD group (n=66) (Pass: Fail)	*p-value*
29 Offering to share	65 (48.1%): 70 (51.9%)	63 (95.5%): 3 (4.5%)	**<0.001**
30 Seeking to share enjoyment	58 (43%): 77 (57%)	61 (92.4%): 5 (7.6%)	**<0.001**
31 Offering comfort	76 (56.3%): 59 (43.7%)	59 (89.4%): 7 (10.6%)	**<0.001**
32 Quality of social overtures	85 (63%): 50 (37%)	66 (100%): 0 (0%)	**<0.001**
33 Range of facial expression	86 (63.7%): 49 (36.3%)	64 (97%): 2 (3%)	**<0.001**
34 Imitative social play	53 (39.3%): 82 (60.7%)	58 (87.9%): 8 (12.1%)	**<0.001**
35 Imaginative play	87 (64.4%): 48 (35.6%)	61 (92.4%): 5 (7.6%)	**<0.001**
36 Interest in children	78 (57.8%): 57 (42.2%)	61 (92.4%): 5 (7.6%)	**<0.001**
37 Response to other children	107 (79.3%): 28 (20.7%)	64 (97%): 2 (3%)	**0.001**
38 Attention to voice	65 (48.1%): 70 (51.9%)	59 (89.4%): 7 (10.6%)	**<0.001**
39 Imaginative play with peers	36 (26.7%): 99 (73.3%)	49 (74.2%): 17 (25.8%)	**<0.001**
40 Group play	38 (28.1%): 97 (71.9%)	47 (71.2%): 19 (28.8%)	**<0.001**

Note: SCQ – Social Communication Questionnaire; T2 – Time 2; ASD – Autism Spectrum Disorder; OND – Other Neurodevelopmental Disorders.

Data is presented as n (%). The p-values were computed using Fisher exact test.

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