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Child Behavior Check List 1½–5 as a tool to identify toddlers with Autism Spectrum Disorders: A case-control study

Antonio Narzisi [a,b,*], Sara Calderoni [a], Sandra Maestro [a], Simona Calugi [a], Emanuela Mottes [a,b], Filippo Muratori [a,b]

[a] Division of Child Neurology and Psychiatry, Stella Maris Scientific Institute, Pisa, Italy
[b] University of Pisa, Italy

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ABSTRACT

Tools to identify toddlers with autism in clinical settings have been recently developed. This study evaluated the sensitivity and specificity of the Child Behavior Check List 1½–5 (CBCL 1½–5) in the detection of toddlers subsequently diagnosed with an Autism Spectrum Disorder (ASD), ages 18–36 months. The CBCL of 47 children with ASD were compared to the CBCL of 47 toddlers with Other Psychiatric Disorders (OPD) as well as the CBCL of 47 toddlers with Typical Development (TD) in a case control study. One-way analysis of variance (ANOVA) and logistic regression with odds ratio (OR) analyses were performed. In order to establish the optimal threshold able to discriminate children with ASD from children with OPD and TD, Receiver Operating Characteristic (ROC) analyses were performed. One-way ANOVA revealed significant differences between the three groups. Logistic regression analysis showed that the Withdrawn and the Pervasive Developmental Problems (PDP) subscales can recognize toddlers subsequently identified as ASD from both children with TD ($p < 0.001$) and OPD ($p < 0.001$). ROC analyses showed very high sensitivity and specificity for the PDP (0.98 and 0.91) and Withdrawn (0.92 and 0.97) subscales when ASD was compared to TD. Sensitivity and specificity of Withdrawn (0.90 and 0.83) and PDP (0.85 and 0.83) remained high when comparing ASD versus OPD. In conclusion, the CBCL 1½–5 seemed to be able to identify toddlers subsequently diagnosed with ASD from children with TD and OPD. Its high sensitivity and specificity, coupled with its efficiency in terms of time and cost, suggest this broadband tool should be tested in a pilot screening survey of toddlers in the general population.

1. Introduction

Autism Spectrum Disorders (ASD) are a heterogeneous group of neurodevelopmental pathologies with a strong genetic basis and early altered neuroanatomical correlates whose diagnosis is still based on behavioral symptoms (Wolff et al., 2012). Early identification has become an essential step in clinical management of ASD for at least two reasons. First, autism is not a rare disorder; according to the Centers for Disease Control and Prevention (CDC, 2012), the incidence of ASD is 1 in 88 children in the U.S.A. Second, evidence suggests that children with ASD may benefit from intervention at a young age, when

* Corresponding author at: Division of Child Neurology and Psychiatry, University of Pisa, Stella Maris Scientific Institute, Via dei Giacinti, 2, I-56018 Calambrone, Pisa, Italy. Tel.: +39 050 886111/886308; fax: +39 050 886247.
E-mail addresses: antonio.narzisi@inpe.unipi.it, anarzisi@inpe.unipi.it (A. Narzisi).

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brain plasticity is maximal and environmental variables may have major effects on neurodevelopment (Dawson et al., 2010; Fernell et al., 2011; Green et al., 2010; Strauss et al., 2012). Even if a decreased frequency of nonverbal social–communication skills (e.g., social orienting, joint attention and imitation) has been described by the child's first birthday in toddlers subsequently diagnosed with an ASD (Maestro et al., 2005; Zwaigenbaum et al., 2009), the identification and diagnosis of ASD children before the age of 24 months are still hampered by the fact that ASD symptomatology usually emerges gradually over time and social–communication abnormalities are often non-specific (Ozonoff, Heung, Byrd, Hansen, & Hertz-Picciotto, 2008). The early identification of children with ASD is further complicated by the low specificity of the internationally recognized diagnostic instrument for ASD, such as the Autism Diagnostic Observation Schedule-Generic (ADOS-G, Lord et al., 2000), in toddlers and by the difficulty in adapting Diagnostic and Statistical Manual, Fourth Edition (DSM-IV; American Psychiatric Association, 1994) ASD criteria to very young children. Hence, it can be hard to distinguish ASD from typically developing children or children with other disorders. For these reasons, the validity of screening methods before the child's second birthday has been questioned (Al-Qabandi, Gorter, & Rosenbaum, 2011).

Longitudinal studies, however, have shown that the majority of ASD diagnoses made around the second birthday are stable when children are re-evaluated at age 4 or older (Chawarska, Klin, Paul, Macari, & Volkmar, 2009). However, instruments for diagnosis of autism, such as ADOS-G (Lord et al., 2000), Autism Diagnostic Interview-Revised (ADI-R) (Rutter, Le Couteur, & Lord, 2003) and the Screening tool for autism in two-year-olds (STAT) (Stone, Coonrod, & Ousley, 2000), are lengthy and require extensive training to be administered; thus, they must be considered second level instruments (Filipek et al., 2000; Matson, Rieske, & Turek, 2011).

Because the diagnosis of ASD can be reliably made by the second year of age, the American Academy of Pediatrics (Committee on Children With Disabilities, 2001) recommends the development of instruments for routine screening for autism risk at their 18- and 24-month well-baby visits. In fact, screening offers the opportunity to alert primary care providers to recommend further clinical evaluation and eventually early intervention (Ghuman, Leone, Lecavalier, & Landa, 2011; Nygren et al., 2012).

Instruments to evaluate the lack of social–communication skills and the presence of autistic symptoms in children who are at least 18 months are available. Among these ASD-specific instruments, the Checklist for Autism in Toddlers (CHAT et al., 1992) and the Modified Checklist for Autism in Toddlers (M-CHAT et al., 2001) are more often mentioned. The CHAT (Baron-Cohen, Allen, & Gillberg, 1992), directed to children 18–24 months of age, is a unique instrument that has been studied in a large first level sample with long term follow-up data (Baird et al., 2000); in that study it showed a sensitivity of only 0.40 and a specificity of 0.98, with a positive predictive value (PPV) of 0.26. Rescreening using the same instrument at 19 months for those who failed the 18-month screening, yielded a higher PPV of 0.75 (Baird et al., 2000). Because the CHAT can identify clinical features indicative of increased risk, but should not be used to rule out ASD, the same research group is developing a revised version, the Quantitative-Checklist for Autism in Toddlers (Q-CHAT) (Allison et al., 2008).

A modification of the CHAT (M-CHAT), a questionnaire filled out by parents, was first applied to a mixed sample of children from primary care settings and early intervention sites (Robins, Fein, Barton, & Green, 2001), and then as a level 1 instrument in a population aged 18–24-months (Robins, 2008). The moderate Positive Predictive Power (PPP) of 0.36 (sensitivity of 0.97, specificity of 0.95, negative predictive power (NPP) of 0.99) and the high number of false positive cases make it difficult to propose the M-CHAT as a screening questionnaire without a follow-up phone interview to confirm the risk and the need for a deeper evaluation. After the phone interview, the sensitivity remains at 0.97 and the specificity rises to 0.99 with a NPP at 0.99 and PPP at 0.68 (Robins, 2008).

Ghuman et al. (2011) reported preliminary validity and utility of the Ghuman–Folstein Screen for Social Interaction-Younger (SSI-Y), a measure of social interaction that can serve to screen for ASD in clinical samples of young high-risk children. Caregivers of 350 children – aged 24–42 months – with ASD, non-ASD developmental and/or psychiatric disorders, and without developmental concerns completed the 21 item SSI-Y. Sensitivity and specificity values for discriminating ASD from non-ASD clinical participants were 0.87 and 0.71.

The Baby and Infant Screen for Children with aUtIsm Traits (BISCUIT) scale conducted with baby present showed a sensitivity of 0.90 and specificity of 0.83 for PDD-NOS versus no diagnosis in at risk children and a sensitivity of 0.94 and a specificity of 0.71 for autism versus no diagnosis (Matson, Boisjoli, Rojahn, & Hess, 2009; Matson, Fodstad, & Mahan, 2009; Matson, Fodstad, Mahan, & Sevin, 2009; Matson, Wilkins, et al., 2009; Matson, Boisjoli, Hess, & Wilkins, 2010; Matson, Fodstad, Mahan, & Rojahn, 2010; Matson, Boisjoli, Hess, & Wilkins, 2011; Rojahn et al., 2009). A subset of BISCUIT items was found to be most effective in predicting autism versus PDD-NOS, or children without these diagnoses (Horovitz & Matson, 2010; Matson, Fodstad, & Dempsey, 2009).

Matson, Rieske, et al. (2011) in a review paper have described other screening and diagnostic tools (see Table A1 for their list which also includes the tools mentioned in the text).

The Child Behavior Check List (CBCL, Achenbach & Rescorla, 2000) is the most widely used parent report checklist that measures a broad range of behavioral and emotional problems, especially for applied epidemiological research or longitudinal studies (Crijen, Achenbach, & Verhulst, 1999). Its strength lies on a guided description of the child from the parents whose fidelity in reporting symptoms is also widely recognized for ASD symptoms (So et al., 2012). Different studies have provided support for the CBCL in identifying subjects with ASD at different ages. Bölte, Dickhut, and Poustka (1999) found that children and adolescents (4–18 years) with autism showed higher scores on the CBCL scales measuring attention problems, social problems and thought problems, and lower scores on the scale for somatic complaints. Duarte, Bordin, De Oliveira, and Bird (2003), using the CBCL 4–18 in school aged children, found a CBCL factor called Autistic/Bizarre that was

able to differentiate autistic conditions from Other Psychiatric Disorders (with a sensitivity of 0.89 and a specificity of 0.80) and from typical schoolchildren (with a sensitivity of 0.94 and a specificity of 0.94).

Biederman et al. (2010) evaluated the properties of CBCL in discriminating referred children with ASD from psychiatrically referred children without ASD. Their study showed that the Withdrawn, Social Problems, and Thought Problems scores were the best independent predictors of ASD conditions. In their study, Receiver Operating Characteristic (ROC) analyses showed that Withdrawn + Social + Thought Problems scores yielded an area under the curve of 0.86, indicating an 86% chance that a randomly selected sample of children with ASD will have abnormal scores on these scales. These findings suggested that a new CBCL-ASD profile consisting of the Withdrawn, Social, and Thought Problems scales could serve as a rapid and cost-effective screening instrument to identify school aged children likely to meet criteria for ASD in the clinical setting. Ooi, Rescorla, Ang, Woo, and Fung (2011) tested the ability of the CBCL to discriminate among children with ASD, children with Attention Deficit and Hyperactivity Disorder (ADHD), clinically referred children who did not receive a diagnosis, and typically developing (TD) children. Ooi et al. (2011) showed that Withdrawn, Social Problems, and Thought Problems scales significantly discriminated the ASD sample from other groups. In their study, an ASD cluster composed of nine CBCL items demonstrated moderate to high sensitivity (0.68–0.78) and specificity (0.73–0.92). All these studies provide strong support for the CBCL as a screening tool for older children with ASD. The recent CBCL form for preschoolers (Achenbach & Rescorla, 2000) has identified a specific DSM-Oriented scale named Pervasive Developmental Problems (PDP), which is supposed to be useful in identifying children under the age of 6 at risk for ASD. Two studies have shown a good predictive validity of the PDP scale (with both sensitivity and specificity above 0.80) in identifying preschoolers with an ASD diagnosis (Muratori et al., 2011; Sikora, Hall, Hartley, Gerrard-Morris, & Cagle, 2008). Nevertheless, until now, no study has taken into account its capacity in identifying ASD in children ages 18–36 months.

The main aim of this paper is to investigate the capacity of the CBCL 1½–5 to detect children 18–36 months of age (hereafter referred to as toddlers) subsequently diagnosed with an ASD. We have conducted a case-control study which must be considered a mandatory preliminary step to propose CBCL utilization as a first-level tool to identify children at risk of autism in primary care settings.

2. Methods

2.1. Participants

Participants were 141 children aged 18–36 months (mean age: 29.4 months; *SD* = 4.6 months) divided into three groups matched by gender, age, race, and socioeconomic status (SES). The first group consisted of 47 children with ASD (34 males and 13 females) recruited at the Autism division of the Scientific Institute Stella Maris and rigorously diagnosed according to the DSM-IV-TR criteria (American Psychiatric Association, 2000) by a multidisciplinary team including a senior child psychiatrist, an experienced clinical child psychologist and a speech–language pathologist during a 5-day extensive evaluation, and confirmed by the ADOS-G (Lord et al., 2000). All cases were selected from referred toddlers over a two-year period. The mean age was 29.5 months (*SD* = 4.7 months; range: 19–36 months).

Exclusion criteria were: (a) neurological syndromes or focal neurological signs; (b) significant sensory impairment (e.g., blindness, deafness); (c) anamnesis of birth asphyxia, premature birth, head injury or epilepsy; (d) use of any psychotropic medication; and (e) potential secondary causes of ASD determined by high-resolution karyotyping, DNA analysis of Fragile-X, or screening tests for inborn errors of metabolism. The second group consisted of 47 children (34 males and 13 females) with Other Psychiatric Disorders (OPD), recruited at the same hospital during the same period. In this group, both language and moderate/severe cognitive impairment were actively ruled out through the administration of Griffiths Mental Development Scales (Griffiths, 1984). For these children, an ASD diagnosis was actively excluded by a senior child psychiatrist, with more than 20 years of experience in assessing youth with child psychiatric problems, and supported by a score under 20 on the Childhood Autism Rating Scale (CARS; Schopler, Reichler, & Rochen Renner, 1986). Moreover, children with a Disorder of Relating and Communicating, according to Diagnostic Classification 0-3R criteria (Zero to Three, 2005), were not included in the OPD sample. Final diagnoses of the OPD children were: affective disorders (*n* = 31) and mixed disorders (*n* = 16). The mean age was 29.5 months (*SD* = 4.7 months; range: 19–36 months). A third group consisted of 47 children (34 males and 13 females) with Typical Development (TD) was recruited in two kindergartens of Pisa. The inclusion criteria for this group were: (1) frequency of regular kindergarten without support teacher (the Italian law provides teacher support for children with developmental/clinical problems); (2) no parent or teacher concern about child development as noted in both of the two following descriptive questions of the CBCL: '*Does the child have any illness or disability (either physical or mental)?*' and '*What concerns you most about the child?*'; (3) a CBCL Total Problems T score lower than 60. The mean age was 29.5 months (*SD* = 4.7 months; range: 18–36 months).

The OPD and TD groups met the same (a), (b), (c), and (d) exclusionary criteria as the ASD group with the further requirement of no family history of an ASD.

The whole group was composed of Caucasian children belonging mostly to middle/upper middle class families according to the Hollingshead and Redlich (1958) criteria.

2.2. Measures

The CBCL 1½–5 (Achenbach & Rescorla, 2000; Frigerio et al., 2009) is a 100 item parent-report measure designed to record the behavioral peculiarities of preschoolers. Each item describes a specific behavior and the parent is asked to rate the frequency of each behavior on a three-point Likert scale (0, not true; 1, somewhat or sometimes true; 2, very true or often true). The measure provides scores for three summary scales (i.e., Internalizing, Externalizing and Total Problems), seven syndrome scales (i.e., Emotionally Reactive, Anxious/Depressed, Somatic Complaints, Withdrawn, Sleep Problems, Attention Problems, and Aggressive Behavior), and five DSM-Oriented scales (i.e., Affective Problems, Anxiety Problems, Pervasive Developmental Problems, Attention Deficit/Hyperactive Problems and Oppositional Defiant Problems). A *T*-score of 63 and above for summary scales, and 70 and above for syndrome and DSM-Oriented scales, are generally considered clinically significant. Values between 60 and 63 for summary scales, or between 65 and 70 for syndrome and DSM-Oriented scales, identify a borderline clinical range. Values under 60 for the summary scales or under 65 for other scales are not considered clinically significant. For what concern psychometric property of CBCL, the test–retest reliability was supported by a mean test–retest $r = 0.085$ for CBCL scales over periods averaging 8 days. The commonly found tendency for problem scores to decline over brief rating intervals was evident in the scale scores, but it accounted for a mean of only 0.9% of the variance in the CBCL. For interparent agreement on the CBCL, the mean r was 0.61. The differences between mother's and father's mean scales scores did not exceed chance expectations, indicating that there was no significant tendency for parent of one gender to report more problems than parent of other gender. Odds ratios showed that large proportions of children classified as deviant on the basis of mother's ratings were also classified as deviant on the basis of father's ratings (Achenbach & Rescorla, 2000).

The ADOS-G (Lord et al., 2000) is a semi-structured observation measure. The ADOS attempts to set a 'social world' in which reciprocal social interaction and communication, play, and use of imagination are assessed (Lord et al., 2000). The observational schedule consists of four 30–45 min modules, each designed to be administered to different individuals according to their level of expressive language. In our study, only Modules 1 were used. Regarding this last module Lord et al. (2000) reported the following sensitivity: 0.97 (for Autism and PDD versus No Spectrum); 100% (for Autism versus PDD and No Spectrum); 0.94 (for PDD versus No Spectrum); 1.0 (for Autism versus No Spectrum). The Specificity was: 0.95 (for Autism and PDD versus No Spectrum); 0.79 (for Autism versus PDD and No Spectrum); 0.94 (for PDD versus No Spectrum); 1.0 (for Autism versus No Spectrum) (Lord et al., 2000).

The CARS (Schopler et al., 1986) is an observation instrument and was developed to identify children with autism compared to children with other developmental disabilities and determine symptoms severity (Schopler et al., 1986). The CARS was developed for children over the age of two years. The CARS consists of 15 four-point scales (or seven-point scale if half points values are used) where a child's behavior is rated for chronological age. Specific descriptive examples are provided for each of the behaviors being assessed. The scores are then summated to categorize a child on a continuum from 'non-autistic' to 'mild to moderate' to 'severe autism'. Nebel-Scwalm and Matson (2008) summarize reliability and validity research for the CARS. Internal consistency reliability (0.94), test–retest for CARS diagnoses (0.64) and for CARS scores (0.81), and inter-rater reliability (0.71), are all acceptable. Rellini, Tortolani, Trillo, Carbone, and Montecchi (2004) compared the CARS with DSM-IV criteria and found 100% sensitivity for children with autism.

2.3. Procedures

The study was carried out according to the standards for good ethical practice of the IRCCS Stella Maris Foundation. Written informed consent from a parent or guardian of each patient was obtained. Parents in the ASD and OPD groups filled out the CBCL before of the comprehensive clinical evaluation when they were unaware of the diagnosis of their child. Parents in the TD group filled out the CBCL in an anonymous way at kindergarten.

2.4. Data analysis

The CBCL scales were examined for normality using skewness tests and Kolmogorov–Smirnov testing. All scales met criteria for normal distributions. A chi-square test was used to compare categorical variables among the three groups. A one-way analysis of variance (ANOVA) was performed to test potential differences on age and the CBCL Total score among ASD, OPD and TD groups. Multivariate analyses of variance (MANOVA) were used to evaluate differences among the three groups on CBCL scales. We performed three different MANOVAs according to the different CBCL scales. The first MANOVA was carried out including Internalizing and Externalizing scores as dependent variables, the second including syndrome scores as dependent variables and the third including DSM-Oriented scores. Logistic regression analysis with odds ratios (ORs) was performed to identify CBCL scales discriminating among the three groups. We used separate logistic regression models to compare ASD versus TD and ASD versus OPD. In Model 1, the independent variable was the CBCL Total score; in Model 2, the independent variables were the Internalizing and Externalizing scores; in Model 3 the independent variables were the syndrome scores; in Model 4, the independent variables were the DSM-Oriented scores. The CBCL scales that were identified as predictors of an ASD diagnosis in the logistic regression analysis at $p < 0.001$ in both comparison (ASD versus TD and ASD versus OPD) were used in a ROC analysis, in order to determine their optimal cut-offs that differentiate children with ASD from children with TD or OPD. In the ROC analysis, sensitivity and specificity were plotted over the range of cut-off points.

The area under the curve (AUC) represents the accuracy of the instrument in predicting children who will or will not have ASD. The interpretation of the AUC values is traditionally as follows: an AUC < 0.7 suggests 'low' diagnostic accuracy; an AUC from 0.7 to 0.9 suggests 'moderate' diagnostic accuracy, and an AUC ≥ 0.9 suggests 'high' diagnostic accuracy (Swets & Pickett, 1982). Analyses were carried out using SPSS version 15.0 for Windows (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Preliminary analyses

The chi-square analysis showed no significant differences for male/female ratio (chi-square = 0.23, $p = 0.762$) and socio-economic status (chi-square = 0.33, $p = 0.867$) in the whole sample. The one-way ANOVA indicated no significant difference in age among the groups ($F[2,310] = 0.04$, $p = 0.996$).

3.2. Clinical characteristics (Table 1)

The multivariate ANOVAs revealed significant differences ($p < 0.001$) between groups on almost all CBCL scales except for the Anxious/Depressed, Sleep Problems, and Aggressive Behavior scales. Post hoc tests showed: (1) significantly higher scores for the ASD group compared to the TD group on all CBCL scales; and (2) significantly higher scores for the ASD group compared to the OPD group on all CBCL summary scales (i.e., Internalizing, Externalizing, Total Problems), on the Emotionally Reactive, Withdrawn and Attention problems syndrome scales, and on the Affective Problems, Anxiety Problems, Pervasive Developmental Problems (PDP) and Oppositional Defiant Problems DSM-Oriented scales.

In the logistic regression analysis, only the Withdrawn and PDP scales predicted the presence of an ASD over both the TD and OPD groups at a p level <0.001.

3.3. ROC analyses

Because Withdrawn and PDP scales have been identified as the best predictors of the presence of ASD in the logistic regression analysis, we used ROC analyses to estimate the best cut-offs for these scales. Table 2 reports sensitivity, specificity and AUC at the optimal cutoffs for the two scales in discriminating ASD from TD and OPD.

3.3.1. ASD versus TD

ROC analysis indicated that the optimal compromise between sensitivity and specificity to discriminate between ASD and TD was achieved at a score of 65 for both PDP scale (AUC = 0.988; 95% CI 0.973–1.003) and Withdrawn scale (AUC = 0.991;

Table 1
Multivariate ANOVA and logistic regression on CBCL *T*-scores (means and standard deviations) for ASD, OPD and TD groups.

CBCL scales	ASD ($n = 47$) M (*SD*)	OPD ($n = 47$) M (*SD*)	TD ($n = 47$) M(*SD*)	MANOVA		Logistic regression with odds ratio and 95% CI					
				F	*p*	ASD versus OPD			ASD versus TD		
						p	OR	95%CI	*p*	OR	95%CI
Total score	65.57 (11.56)[a,b]	56.77 (9.56)[c]	47.04 (10.48)	36.17	<0.001	0.001	0.92	0.87–0.96	0.000	0.83	0.77–0.90
Internalizing	66.13 (10.20)[a,b]	56.96 (9.48)[c]	46.70 (10.72)	43.08	<0.001	0.001	0.89	0.84–0.95	0.000	0.82	0.74–0.90
Externalizing	59.98 (10.21)[a,b]	54.55 (10.13)[c]	46.77 (9.64)	20.31	<0.001	0.788	1.00	0.95–1.06	0.073	0.98	0.89–1.08
Emotionally Reactive	61.83 (11.25)[a,b]	56.17 (7.51)	53.28 (4.92)	12.87	<0.001	0.732	1.02	0.88–1.18	0.884	1.02	0.77–1.34
Anxious/Depressed	58.89 (8.95)[a]	56.83 (8.47)[c]	53.43 (5.15)	6.02	0.003	0.054	1.12	0.99–1.26	0.673	0.93	0.69–1.26
Somatic Complaints	61.32 (11.89)[a]	58.66 (7.72)[c]	53.40 (5.64)	9.82	<0.001	0.324	1.04	0.95–1.15	0.423	1.10	0.86–1.42
Withdrawn	76.26 (9.42)[a,b]	57.74 (7.92)[c]	52.49 (4.67)	126.71	<0.001	0.000	0.69	0.59–0.82	0.000	0.57	0.40–0.82
Sleep Problems	59.32 (9.39)[a]	58.60 (10.46)[c]	53.62 (4.38)	6.27	0.002	0.391	0.94	0.81–1.08	0.454	1.15	0.79–1.68
Attention Problems	63.77 (8.07)[a,b]	57.43 (6.77)[c]	52.51 (5.25)	32.34	<0.001	0.266	0.91	0.78–1.06	0.085	0.72	0.50–1.04
Aggressive Behavior	59.09 (10.63)[a]	56.94 (8.45)[c]	52.55 (4.42)	7.68	0.001	0.170	1.10	0.95–1.27	0.504	1.18	0.72–1.94
Affective Problems	62.53 (11.40)[a]	57.60 (7.33)[c]	52.64 (4.15)	17.16	<0.001	0.746	1.01	0.92–1.12	0.182	0.80	0.58–1.10
Anxiety Problems	59.40 (9.86)[a]	56.36 (6.73)[c]	53.06 (4.62)	8.64	<0.001	0.032	1.15	1.01–1.30	0.048	1.54	1–2.37
PDP	75.72 (7.33)[a,b]	60.02 (9.01)[c]	53.28 (5.31)	114.57	<0.001	0.000	0.70	0.60–0.81	0.000	0.57	0.40–0.80
ADHD	59.72 (7.44)[a,b]	57.64 (7.87)[c]	52.98 (3.89)	12.68	<0.001	0.372	1.04	0.94–1.15	0.302	0.84	0.60–1.16
Oppositional Defiant Problems	57.26 (8.15)[a]	54.43 (6.33)[c]	51.45 (2.98)	10.29	<0.001	0.752	1.02	0.90–1.15	0.513	0.83	0.48–1.43

ASD: Autism Spectrum Disorder; OPD: Other Psychiatric Disorders; TD: Typical Development; CBCL: Child Behavior Check List; OR: odds ratio; CI: confidence interval.

[a] ASD significantly higher versus TD ($p < 0.01$).

[b] ASD significantly higher versus OPD ($p < 0.01$).

[c] OPD significantly higher versus TD ($p < 0.01$).

Table 2
Sensitivity, specificity, positive predictive values (PPV) and negative predictive values (NPV) at the best cutoff points on Withdrawn and PDP scales when comparing ASD versus TD children or versus OPD. AUC (area under the curve) represents the accuracy in predicting children who will have or will not have ASD.

	ASD versus TD		ASD versus OPD	
	Withdrawn (cutoff = 65)	PDP (cutoff = 65)	Withdrawn (cutoff = 65)	PDP (cutoff = 69)
Sensitivity	0.92	0.98	0.90	0.85
Specificity	0.97	0.91	0.83	0.83
PPV	0.98	0.92	0.84	0.83
NPV	0.92	0.98	0.88	0.85
AUC	0.991	0.988	0.939	0.914
Sweet and Picket criteria for AUC accuracy	High	High	High	High

95% CI 0.979–1.003). For the PDP scale, the sensitivity was 0.98, and the specificity was 0.91. For the Withdrawn scale, sensitivity was 0.92 and specificity was 0.97.

3.3.2. *ASD versus OPD*

In order to discriminate ASD from OPD, the optimal cut-off for the PDP scale was 69 (AUC = 0.914; 95% CI 0.854–0.975). Using this cut-off, the proportion of subjects with ASD who were correctly diagnosed was 0.85 (sensitivity) and the proportion of cases with OPD who were correctly diagnosed was 0.83 (specificity). For the Withdrawn scale, the optimal compromise between sensitivity (0.90) and specificity (0.83) was achieved at a score of 65 (AUC = 0.939; 95% CI 0.890–0.988). Following Sweet and Picket (1982) criteria, all the obtained AUC values can be considered high (Fig. 1).

4. Discussion

Motivated by prior reports on CBCL ability to detect for behaviors associated with ASD in preschoolers (Muratori et al., 2011; Rescorla, 1988; Sikora et al., 2008), in children (Duarte et al., 2003) and in adolescents (Bölte et al., 1999; So et al., 2012), we studied the CBCL profile in a group of toddlers with ASD.

The main result was that the CBCL was able to reliably discriminate toddlers subsequently diagnosed with ASD not only from typical children, but also from children with Other Psychiatric Disorders. This result is important because even though most parents report concerns about their child's development as early as the second year of life or even earlier (Frith & Soares, 1993; Horovitz, Matson, & Sipes, 2011; Wiggins, Baio, & Rice, 2006), these toddlers are usually diagnosed between 36 and 70 months of age (Maestro, Casella, Milone, Muratori, & Palacio-Espasa, 1999). Parental concerns usually first arise during routine health visits, and, as providing a thorough evaluation in this setting is challenging, brief tools with good sensitivity and specificity are needed to determine referrals for a specialized evaluation. Thanks to the evidence that parents are reliable informants (Glascoe, 1999) and rightly aware of the abnormal quality of social–communicative interaction of their children, checklists filled out by parents can be used to help clinicians to point out the actual risk for autism. To highlight the risk of ASD can, in its turn, reduce the time lag between first parental concerns, referral, diagnosis, and finally the beginning of treatment. The present study examined the CBCL's ability to identify toddlers at risk for ASD, with the aim of providing a sensible and specific instrument for primary care settings.

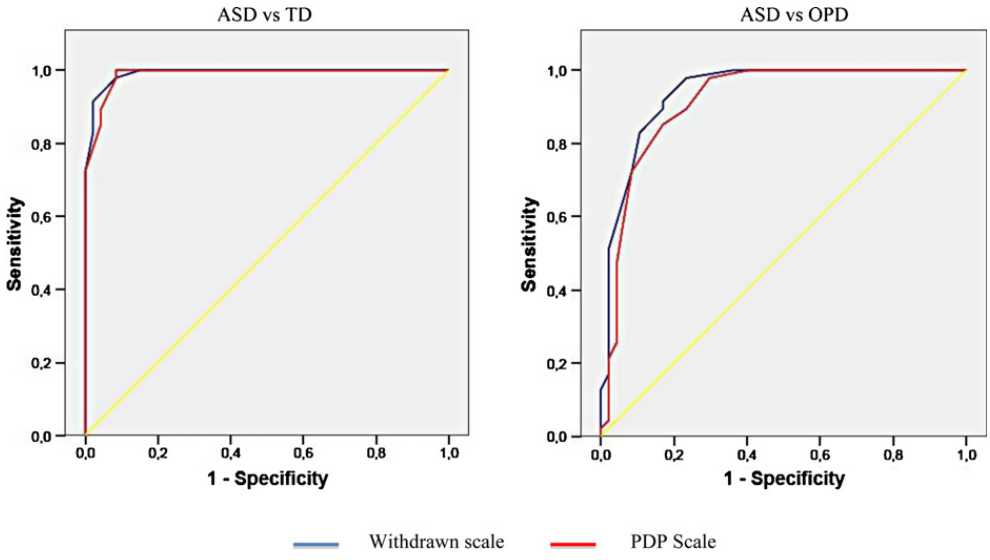
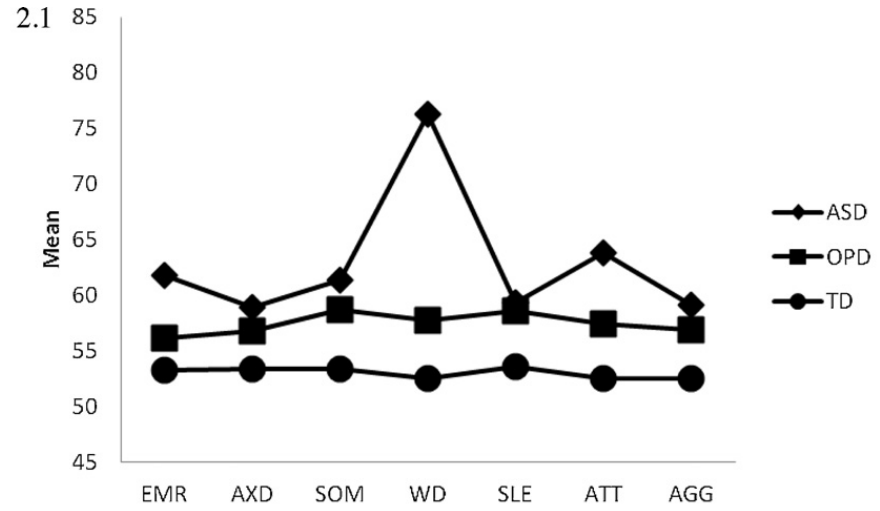
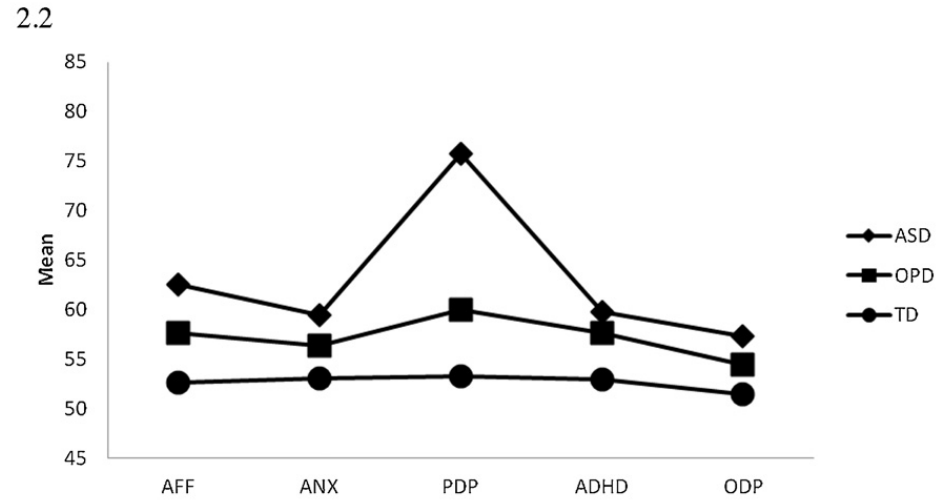


Fig. 1. Receiver operating curve (ROC) for Withdrawn and PDP scales.



EMR Emotionally Reactive, AXD Anxious/Depressed, SOM Somatic Complaints,
WD Withdrawn, SLE Sleep Problems, ATT Attention Problems,
AGG Aggressive Behavior.



AFF Affective Problems, ANX Anxiety Problems, PDP Pervasive developmental Problems,
ADHD Attention Deficit and Hyperactivity Disorder,
ODP Oppositional Defiant Problems.

Fig. 2. (a) Mean values of CBCL *T*-scores for syndrome scales in the three groups. EMR, Emotionally Reactive; AXD, Anxious/Depressed; SOM, Somatic Complaints; WD, Withdrawn; SLE, Sleep Problems; ATT, Attention Problems; AGG, Aggressive Behavior. (b) Mean values of CBCL *T*-scores for DSM-Oriented scales in the three groups. AFF, Affective Problems; ANX, Anxiety Problems; PDP, Pervasive developmental Problems; ADHD, Attention Deficit and Hyperactivity Disorder; ODP, Oppositional Defiant Problems.

First of all, our findings indicate that the Withdrawn and Pervasive Developmental Problem scales do a good job in differentiating children with ASD from both TD and OPD children. This finding is consistent with previous studies on children under-six years of age (Muratori et al., 2011; Sikora et al., 2008) and confirms similar CBCL profiles in toddlers with ASD (Fig. 2a and b).

Elevation on the Withdrawn cluster of symptoms was among the autistic/bizarre factor originally identified by Rescorla (1988), and it was more recently reported in school-aged children affected by ASD (Biederman et al., 2010). This consistent finding across different age groups suggests that the Withdrawn CBCL symptom cluster has a stable strength in recognizing autism. The present study suggests that when this cluster has a very high score (>70), it should be considered as an index of social difficulties specific to ASD rather than an affective disorder, even at this young age.

The present study also suggests that high scores on the Withdrawn scale are indicative of autism when associated with a similar high score on the PDP scale. The double profile shown in Fig. 2a (Syndrome scales) and in Fig. 2b (DSM-Oriented

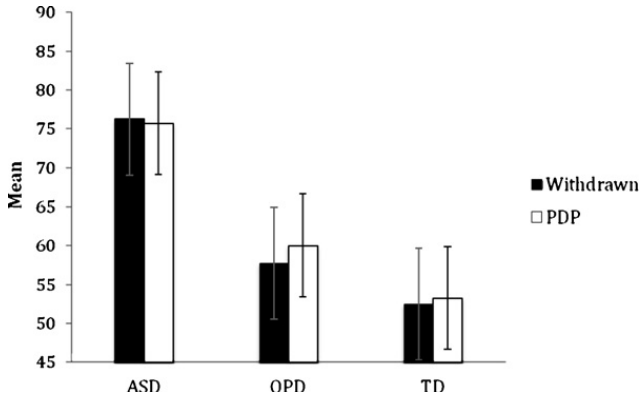


Fig. 3. Bar graphs with error bars of means of CBCL *T*-scores for Withdrawn and PDP scales in the three groups.

scales) should be considered together to enhance the ability of the CBCL to recognize toddlers subsequently diagnosed with autism. Thus, very high scores on both the PDP and Withdrawn scales could represent a criterion for the pediatrician to decide the appropriateness of a thorough ASD evaluation. Withdrawn and PDP scores are visualized through bar graphs with error bars in Fig. 3 which indicates that the probability of an overlap between samples is very unlikely. Only a minority of the OPD toddlers may actually turn out to be an ASD patient, and the high scores on the CBCL scales suggest that some other diagnoses may be formulated, so that these children are only "false" positives because they are not ASD, but they are positives from a larger clinical perspective.

The low number of false positive is important because it means that when applied as a screening instrument, the CBCL could avoid a worthless concern for parents of typically developing children.

Using the appropriate cutoff, sensitivity and specificity were always above 80% which is the recommended cutoff for screening instruments (Meisels, 1989), and above 90% when ASD are compared to TD. It is interesting that the sensitivity and specificity in the present younger sample are even better than that described in our previous paper on preschoolers (Muratori et al., 2011). We hypothesize that the explanation of this increased sensitivity and specificity of the Withdrawn and PDP scales with younger children may be twofold. First, parents of older children are probably more accustomed to the autistic behavior of their children and are much less able to perceive atypicality of behaviors than parents of younger children. Second, the items on the CBCL 1½–5 may be more appropriate for children aged 2–3 years because this version of CBCL (Achenbach & Rescorla, 2000) is identical (except for the replacement of two items) to the previous version CBCL 2–3 (Achenbach, 1992) that was designed specifically for toddlers.

Finally, we could suggest the CBCL as efficacious to substantiate parents' concerns regarding social–communication skills. To our knowledge, this is the first study describing the good power efficacy of the CBCL in recognizing ASD in toddlers at an age when the detection of ASD is often challenging. Our findings suggest that high value on both the Withdrawn scale (which is derived from factor analysis) and on the PDP scale (which is derived by expert judgment) could perform an excellent job in detecting toddlers at risk for ASD during a well baby visit. For this reason, we are planning to investigate whether the high sensitivity and specificity will be maintained in a pilot screening survey of toddlers derived from the general population, instead of a clinical sample of young patients with suspected ASD who were referred at a tertiary university hospital, as in the present study.

4.1. Limitations

We acknowledge some limitations in our paper. The data do not definitively answer the question of whether the CBCL profile is specific of ASD or at least partly due to their presumably different cognitive functioning from OPD and TD. To avoid this bias, a future study with carefully matched IQ scores between groups is needed, as well as the inclusion of a control group of toddlers with language and/or cognitive impairments. Second, the use of ADOS-G in the assessment process of toddlers could be questioned because it shows low specificity (0.79) for this young population (i.e., the tool could over-include in the ASD group young children with other neurodevelopmental disorders, including intellectual disabilities and/or language impairments). However, this limitation is lessened by the presence of a judgment performed by clinicians that had extensive experience in working with young children at risk for, and identified with, ASD. This high level of experience in working with the ASD population is extremely important for the validity of final clinical judgment, since the ADOS is only one component of a diagnostic decision (Chawarska et al., 2007).

Moreover, in a future study, the ADOS-2, which includes a new module for toddlers, may be used in order to enhance its reliability in toddlers and/or in children with a low cognitive level (Luyster et al., 2009). Third, ASD toddlers included in this study may not reflect the huge heterogeneity of ASD patients, since children diagnosed at an early age could probably belong to the most severe end of the spectrum, while less impaired ASD subjects tend to be identified later in life.

Fourth, the equal numbers of children in the ASD, OPD and TD groups do not reflect a population estimate, where we would expect many more children to have OPD and far more children to have Typical Development. For this reason, PPV and NPV, that are very dependent on the sample studied, might not be replicated in a population study.

Fifth, the inclusion of only Caucasian toddlers makes us cautious about the generalizability of our findings to other cultural contexts. For this reason, future studies should investigate the permanence of our results with non-Caucasian toddlers. However, some studies confirmed the multicultural robustness of the CBCL (Rescorla et al., 2007; Viola, Garrido, & Rescorla, 2011).

Finally, some doubts can arise about the administration of a broadband instrument to detect autism. Nevertheless, compared to instruments that are specific to ASD, a broadband instrument like the CBCL can offer several advantages: (a) it allows an immediate comparison of the scores with normative data, limiting mistakes in the interpretation of results that might be made by non-specialists; (b) it summarizes in a unique impressive profile single behaviors pointed out by parents; and (c) it requires minimal time commitment and cost. All these strengths, together with the high sensitivity and specificity, indicate the CBCL is a tool that can integrate pediatric observations while maximizing the role of the family in the detection of ASD.

5. Conclusions

These results indicate that information helpful for the early ASD diagnostic process may be obtained by parents through a well-known general measure of child behavior problems such as the CBCL 1½–5, an easy and quick instrument that allows professionals to identify the profile suggestive of a child with an ASD, as detected by the present study. A multidisciplinary team approach and ASD-specific diagnostic instruments are undoubtedly required to make an ASD diagnosis; however, pediatricians are very often the first professionals to see toddlers with social–communication impairments and such evaluations are carried out in settings bereft of multidisciplinary support. In these cases, data derived from the CBCL profiles can be useful in deciding when to recommend a more in-depth and specialized assessment. CBCL administration in a pediatric setting should help speed up ASD diagnoses and can earlier orient toddlers with ASD toward more focused, tailored intervention, which is known to be associated with improved developmental outcomes.

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Appendix A

Table A1

Table A1
Screening and diagnostic tools mentioned in the text.

Authors	Tools	Type of study[a]	Sample	Age[b]	Psychometric values[c]	LoI[d]
Baird et al. (2000)	CHAT *Checklist for Autism in Toddlers*	*S.P.*	$n = 16{,}235$	17–20 *mo*	Se. 0.40; Sp. 0.98	1
Robins et al. (2001)	MCHAT *Modified Checklist for Autism in Toddlers*	*S.P.*	$n = 1293$	18–30 *mo*	Se. 0.87–0.97; Sp. 0.95–0.99	1
Wetherby and Prizant (2002)	CSBS-DP *Communication and Symbolic Behavior Scales Developmental Profile*	*S.P.*	$n = 2188$	6–24 *mo*	Se. 0.78; Sp. 0.84	1
Siegel (2004)	PDDST-II *Pervasive, developmental disorders screening test II*	*S.P.*	$n \geq 1000$	12–48 *mo*	Se. 0.92; Sp. 0.91	1
Honda et al. (2009)	YACHT-18 *Young Autism and other developmental disorders CHeckup Tool*	*S.P.*	$n = 2814$	18 *mo*	Se. 0.83; Sp. 0.86	1
Matson, Wilkins, et al. (2009)	BISCUIT *The Baby and Infant Screen for children with aUtIsm Traits*	*S.P.*	$n = > 1000$	17–37 *mo*	Se. 0.90–0.94; Sp. 0.71–0.83	1–2
Dereu et al. (2010)	CESDD *Checklist for Early Signs of Developmental Disorders*	*S.P.*	$n = 6808$	3–39 *mo*	Se. 0.80; Sp. 0.94	1
Lord et al. (2000)	ADOS-G (Module 1) *Autism Diagnostic Observation Schedule -Generic*	*G.C.*	$n = 54$	3–4 *yr*	Se. 0.94–1.0; Sp. 0.79–1.0	2
Watson et al. (2007)	FYI-R *First Year Inventory*	*G.C.*	$n = 38$	14–75 *mo*	Se. 0.71–0.92; Sp. 0.78–0.89	1
Corsello et al. (2007)	SCQ *Social Communication Questionnaire*	*G.C.*	$n = 590$	2–16 *yr*	Se. 0.71; Sp. 0.71	1

Table A1 (*Continued*)

Authors	Tools	Type of study[a]	Sample	Age[b]	Psychometric values[c]	LoI[d]
Stone, McMahon, and Henderson (2008)	STAT *Screening tool for autism in two-year-olds*	*G.C.*	*n* = 71	12–23 *mo*	Se. 0.95; Sp. 0.73	2
Ward and Gilmore (2010)	ABII *Autistic Behavioural Indicators Instrument*	*G.C.*	*n* = 60	2–6 *yr*	Se. 1.0	1
Ghuman et al. (2011)	SSI *Screen for Social Interaction*	*G.C.*	*n* = 524	24–61 *mo*	Se. 0.81–0.87; Sp. 0.70–0.71	1
Rellini et al. (2004)	CARS *Childhood Autism Rating Scale*	*C.S.*	*n* = 65	18 *mo* to 11 *yr*	Se. 1.0	2
Swinkels et al. (2006)	ESAT *Early Screening of Autistic Traits Questionnaire*	*C.S.*	*n* = 34	16–48 *mo*	Se. >0.90	1

[a] *S.P.*, screening population (general population; samples could include low and high risk children); *G.C.*, group control (ASD already diagnosed versus other developmental problems and/or typical groups); *C.S.*, clinical study (only ASD group already diagnosed).

[b] mo, months; yr, years.

[c] Se., sensitivity; Sp., specificity.

[d] LoI, level of investigation; 1, routine developmental surveillance and screening specifically for autism; 2, diagnosis and evaluation of autism (based on Filipek et al., 2000).

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