Standardized Infant NeuroDevelopmental Assessment developmental and socio-emotional scales: reliability and predictive value in an at-risk population

MIJNA HADDERS-ALGRA[1] | UTA TACKE[2] | JOACHIM PIETZ[3] | ANDRÉ RUPP[4] | HEIKE PHILIPPI[5]

1 University of Groningen, University Medical Center Groningen, Department of Paediatrics, Division of Developmental Neurology, Groningen, the Netherlands. **2** University Children's Hospital (UKBB), Basel, Switzerland. **3** Palliative Care Team for Children and Adolescents, Frankfurt, Germany. **4** Department of Neurology, Section of Biomagnetism, University of Heidelberg, Heidelberg; **5** Centre for Child Neurology, Goethe University, Frankfurt am Main, Germany.

Correspondence to Mijna Hadders-Algra, University Medical Center Groningen, Developmental Neurology, Hanzeplein 1, 9713 GZ Groningen, the Netherlands.
E-mail: m.hadders-algra@umcg.nl

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ABBREVIATIONS

BSID	Bayley Scales of Infant Development
MDI	Mental Development Index
SINDA	Standardized Infant NeuroDevelopmental Assessment
SPZ	Sozial Pädiatrisches Zentrum

AIM To assess the reliability and predictive validity of the developmental and socio-emotional scales of the Standardized Infant NeuroDevelopmental Assessment (SINDA).
METHOD To assess reliability, two sets of three assessors forming eight assessor-pairs independently rated the developmental and socio-emotional scales of 60 infants. To evaluate predictive validity, 223 infants (gestational age 30wks [range 23–41wks]; 117 males, 106 females) attending a non-academic outpatient clinic were assessed by different assessors with SINDA's neurological, developmental, and socio-emotional scales. Atypical neurodevelopmental outcome at a corrected age of 24 months or older implied a Bayley Mental or Psychomotor Developmental Index score of less than 70 or neurological disorder (including cerebral palsy). Behavioural and emotional disorders were classified according to the International Classification of Diseases, 10th Revision. Predictive values were calculated from SINDA (2–12mo corrected age, median 7mo) and typical versus atypical outcome, and for intellectual disability only (Mental Developmental Index <70).
RESULTS Assessors highly agreed on the developmental and socio-emotional assessments (developmental scores: Spearman's rank correlation coefficient ρ=0.972; single socio-emotional behaviour items: Cohen's κ=0.783–0.896). At 24 months or older, 65 children had atypical outcome. Atypical neurological scores predicted atypical outcome (sensitivity 83%, specificity 96%); atypical developmental scores predicted intellectual disability (sensitivity 77%, specificity 92%). Atypical emotionality and atypical self-regulation were associated with behavioural and emotional disorders.
INTERPRETATION SINDA's three scales are reliable, and have a satisfactory predictive validity for atypical developmental outcome at 24 months or older in a non-academic outpatient setting. SINDA's developmental scale has promising predictive validity for intellectual disability. SINDA's socio-emotional scale is a tool for caregiver counselling.

Infant neurodevelopmental assessments have two goals. First, they aim to assess the infant's current condition. Knowledge of the infant's present condition allows the professional to inform caregivers about their infant's characteristics and how they can best promote their infant's development—with or without professional early intervention.[1,2] Second, neurodevelopmental assessments are used to predict developmental disorders. Until recently, most research on prediction of developmental disorders focused on the prediction of cerebral palsy (CP);[3,4] however, recently, increasing scientific attention has been paid to the early precursors of autism spectrum disorder and attention-deficit/hyperactivity disorder.[5,6] Prediction of intellectual disability in the absence of CP has been investigated less extensively, most probably because it has been relatively hard to predict cognitive outcome on the basis of infant assessments.[7–10] The difficulty of predicting intellectual disability on the basis of assessments at early age may be explained by the large developmental changes that occur from infancy onwards in the cortico–cortical and cortical–subcortical networks subserving cognitive abilities. These developmental changes result from a continuous interaction between these functional networks and the environment.[11,12]

We recently embarked on the development of the Standardized Infant NeuroDevelopmental Assessment (SINDA). SINDA aims to be an instrument that: (1) can be relatively easily and quickly applied in infants at 6 weeks to 12 months corrected age; (2) provides paediatricians with information on (a) the infant's current developmental and

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socio-emotional status and (b) the infant's risk of developmental disorders, such as CP, intellectual disability, or behavioural disorder. SINDA has three scales: neurological, developmental, and socio-emotional. The psychometric properties of the neurological scale (28 items, with a special focus on the quality of spontaneous motility; maximum score 28 points) were recently evaluated in a non-academic outpatient setting.[13] The study demonstrated that the neurological scale is a reliable method that can be performed in about 10 minutes. Predictive validity for atypical developmental outcome at 24 months or older was good: atypical neurological scores of the infant (below the 25th centile, ≤21) predicted atypical outcome and CP with sensitivities of 89% and 100%, and specificities of 94% and 81% respectively.[13] The current paper introduces the developmental and socio-emotional scales and aims to assess the psychometric properties of them. Major differences between the developmental and socio-emotional scales of SINDA and commonly used full developmental scales, such as the Bayley Scales of Infant and Toddler Development,[14] the Griffiths Mental Development Scales,[15] and the Mullen Scales of Early Learning,[16] are related to the fact that SINDA aims to screen—and not fully assess—the infant's developmental and socio-emotional condition. This means that SINDA, compared with the full developmental tests: (1) has the shortest age span—it focuses on the first year of life; (2) is the quickest to complete; (3) is easier to learn; (4) is cheapest as its testing material consists of common toys and objects that can be easily purchased (for details see Table S1, online supporting information).

SINDA's developmental scale has been designed as a screening tool that: (1) provides information on the infant's developmental status and is applicable from 6 weeks to 12 months corrected age; (2) covers cognition, communication, fine and gross motor development; (3) consists of 15 standardized items per month of age; (4) results in an age-specific score that is largely independent of the infant's age; (5) is easy to apply by general paediatricians and takes relatively little time to perform (including recording of the scores; infants aged 2–3mo: 5–7min; 4–9mo: 7–10min; 10–12mo: 10–15min); (6) assists the prediction of developmental outcome at older age.

The developmental scale consists of 113 items that are ordered age-wise with 15 items for each month of age, starting at 2 months and ending at 12 months (each month ±2wks). Some items are tested at adjacent ages. The 15 items cover the domains of cognition, communication, fine and gross motor function (see the two score forms in Appendices S1 and S2 [online supporting information] and some examples of items in Appendix S3 [online supporting information]). The 15 age-specific items are scored as pass (1) or fail (0). The number of passed items is added; this forms the infant's developmental score with a maximum of 15.

Performing the developmental scale means that only the 15 items corresponding to the infant's corrected age are tested. Care is taken that the infant is in an adequate behavioural state, namely that infants are not assessed while crying, drowsy, or tired. The assessment requires some attractive objects that can be purchased in any toyshop, for instance a small Mickey Mouse puppet, a rattle, and a ball (see Fig. S1, online supporting information).

If the infant does not meet the criteria (determined in the present study) of the age-specific set of 15 items at the level consistent with typical development, items belonging to younger ages may be tested to obtain an impression of the infant's developmental status. Likewise, the assessor may move up to items belonging to older ages in infants that perform very well for age.

The socio-emotional scale uses six items to evaluate four types of behaviour: interaction, emotionality, self-regulation, and reactivity. The assessment of the interaction between infant and adult (caregiver or assessor) is based on the age-specific cognitive and communication items of the developmental scale that are indicated by a red dot (see Appendices S1 and S2). If the infant scores 'pass' on at least half of the interaction items, the interaction item of the socio-emotional scale is classified as typical (happy smiley icon), otherwise the item is classified as atypical (sad smiley icon). The items of emotionality, self-regulation, reactivity in response to change of position, and reactivity to visual and acoustic stimuli are scored at the end of the developmental assessment. Emotionality evaluates the infant's mood during the assessment and is especially based on the infant's facial expressions and vocalizations. Self-regulation is the capacity to maintain attention, motor activity, and emotional state at a medium level to be able to explore, learn, and interact with the environment. The reactivity items evaluate the global impression of the latency and the intensity of the infant's responses to stimuli. Scoring of the emotionality, self-regulation, and reactivity items is based on the clinical impression of the infant's behaviour during the assessment, and consists of a classification as typical (happy smiley icon) or atypical (sad smiley icon). The three reactivity items are used to generate a single reactivity classification, which is atypical when at least two of the three reactivity items have been scored as atypical. This means that the six items of SINDA's socio-emotional scale result in a dichotomous score on four types of specific behaviour: interaction, emotionality, self-regulation, and reactivity. The socio-emotional scale does not result in a total score.

The aim of the present study was to assess the value of SINDA's developmental and socio-emotional scales as add-ons to SINDA's neurological scale in a sample of infants at risk of motor and mental developmental disorders in a population at risk of developmental disorders. To this end, we determined the following properties of both scales: (1)

What this paper adds

- Standardized Infant NeuroDevelopmental Assessment (SINDA)'s developmental and socio-emotional scales have excellent interrater reliability.
- Replication of the satisfactory validity of SINDA's neurological scale for atypical outcome.

interrater reliability; (2) dependency on infant age; (3) the validity of the developmental scale to predict intellectual disability at a corrected age of 24 months or older; (4) the validity of the four behaviours of the socio-emotional scale to predict behavioural and emotional disorders at a corrected age of 24 months or older. In addition, we determined (5) the capacity of the developmental scale to improve predictive validity of the neurological scale for atypical developmental outcome at a corrected age of 24 months or older; and (6) whether in a group of infants with trisomy 21 the developmental scale would assist the prediction of cognitive outcome.

METHOD

Participants

The study was a centre-based longitudinal case series, consisting of 240 infants (124 males, 116 females) who had been admitted to the Centre for Child Neurology in Frankfurt, Germany (Sozial Pädiatrisches Zentrum [SPZ] Frankfurt-Mitte). The SPZs in Germany are tertiary specialized outpatient clinics for infants at risk of, or with, a neurodevelopmental or neurological disorder. Infants are referred to the SPZ by general paediatric practitioners for a large variety of reasons including paroxysmal events, clinical signs of sensory deficits, atypical motor patterns (hypertonia, floppiness, asymmetry), somatic findings such as microcephaly and developmental delay. In addition, infants at risk of neurodevelopmental disorders, such as very preterm and newborn infants with neonatal complications, are followed by SPZs. We previously[13] reported that SINDA's neurological scale had been incorporated in the clinical routine of SPZs from May 2012 onwards, the developmental scale followed in January 2013, and that of the socio-emotional scale in October 2013. In the present study, infants were consecutively included when they had their first visit in SINDA's age range between January 2013 and October 2016, and had detailed outcome data reported in the medical records at a corrected age of 24 months or older. The latter included a neurological examination and a standardized neurodevelopmental assessment. Infants were excluded if they had: (1) a known progressive neurological disorder (*n*=4: early onset myotonic dystrophy; genetic refractory epileptic encephalopathy, *CDLK5*; refractory focal epilepsy, multiple side effects of antiepileptic drugs; structural West syndrome, cortical malformation) and (2) a behavioural state incompatible with SINDA (*n*=2). Also excluded were infants who had a SINDA, but no follow-up assessment at 24 months or older. The exclusion of these infants was mostly due to their clinical status requiring no or less specialized follow-up. Of the sample of 240 infants, 17 (seven males) had trisomy 21; their findings were analysed separately to evaluate the value of SINDA's developmental scale to assist prediction of cognitive outcome at preschool age in this specific group of infants. The remaining 223 infants formed our main study group. The items of the socio-emotional scale were completely documented in 165 infants. One hundred and fifty-one of the 223 infants had also been included in the previous study.[10] Table 1 summarizes the background characteristics of the 223 infants. The study was approved by the ethical committee of the Medical Faculty of Heidelberg University (S-021/2017).

SINDA

SINDA assessments were performed by the seven general paediatricians (of whom three were in training for paediatric neurology) of the SPZ. These paediatricians had

Table 1: Characteristics of the study samples

General 'at risk' sample (*n*=223)	
Sex (male/female)	117/106
Median age at SINDA assessment in months corrected age (25th; 75th centiles), *n*=223	7 (3; 10)
Maternal education,[a] *n*=192, high; middle; low	87 (45); 71 (37); 34 (18)
Paternal education,[a] *n*=189, high; middle; low	85 (45); 68 (36); 36 (19)
Median gestational age, wks (25th; 75th centiles)	30 (28; 34)
Median birthweight (g), (25th; 75th centiles)	1350 (950; 2005)
Small for gestational age[b]	38 (17)
Preterm (<37wks gestation)	180 (81)
Artificial ventilation	75 (34)
Bronchopulmonary dysplasia	25 (11)
Brain lesions in children with CP	
Intraventricular haemorrhage grade 3–4	8 (3.5)
Periventricular leukomalacia	10 (4.5)
Enlarged/asymmetric ventricular system	6 (3)
Other[c]	11 (5)
Developmental outcome ≥24mo	35 (15.5)
CP	
Bilateral spastic cerebral palsy	24 (11)
Unilateral spastic cerebral palsy	11 (5)
Distribution GMFCS I/II/III/IV/V, *n*	9/5/4/10/7
Distribution CFCS I/II/III/IV/V, *n*	12/5/5/4/9
Other neurological diagnoses[d]	4 (2)
Intellectual and/or motor disability (MDI/PDI<70)	54 (24)
Intellectual disability as single diagnosis	24 (11)
Behavioural or emotional disorder, *n*=165[e]	25 (15)

Infants with trisomy 21 (*n*=17)	
Sex (male/female)	10/7
Median age at SINDA assessment in months corrected age (25th; 75th centiles)	7 (6; 9)
Intellectual disability (MDI<70)[f]	16

Data are *n* (%) unless otherwise stated. [a]Parental education: high – university or vocational college; middle – low or middle level of vocational education; low – not exceeding elementary school. [b]Small for gestational age, birthweight <10th centile. [c]Examples of other brain lesions are pachygyria, cortical atrophy, subdural bleeding. [d]Diagnoses were septo-optic dysplasia, Aicardi–Goutieres syndrome, *CASK* gene mutation, and dystonia. [e]Diagnoses according to the International Classification of Diseases, 10th Revision, chapter V (F); behavioural and emotional disorders are only reported in infants for whom data on the Standardized Infant NeuroDevelopmental Assessment (SINDA) socio-emotional scores were available (*n*=165). [f]One child with trisomy 21 had typical mental development (Mental Developmental Index [MDI] at 24mo 102). CP, cerebral palsy; GMFCS, Gross Motor Function Classification System; CFCS, Communication Function Classification System; PDI, Psychomotor Developmental Index.

received the SINDA manual (unpublished material) and been trained in using SINDA through video sessions and attending 'life' assessments performed by one of SINDA's developers (HP). The training consisted of studying the manual, watching and discussing several videos of SINDA assessments, and attending three to five 'life' assessments.

The 28 items of the neurological scale are scored as pass (1) or fail (0). The number of passed items is added to form SINDA's neurological score; a score of no more than 21 indicates 'at risk' of atypical developmental outcome.[13] As described previously, the infant's developmental score is formed by the addition of the number of passed items, with a maximum score of 15 points. The socio-emotional scale results in scores of four types of behaviour: interaction, emotionality, self-regulation, and reactivity (see previous description). Each of the four behaviours was classified as typical (1) or atypical (0).

Neurodevelopmental assessment at 24 months or older

At a median corrected age of 27 months (range 24–57mo), the children had a follow-up assessment by the clinical team of the SPZ. The paediatrician in charge of the follow-up assessment knew the medical history of the child and the child's SINDA scores. However, the paediatrician was not aware of the significance of the SINDA scores, as it still had to be determined at that time. The follow-up assessment consisted of a neurological, neurobehavioural, and physical examination by one of the paediatricians, and a standardized developmental assessment by one of the two psychologists. Children were neurologically assessed according to the design and requirements specified by Michaelis and Berger.[17,18] The diagnosis of CP was based on this assessment, according to the criteria of the Surveillance of Cerebral Palsy in Europe.[19] The classification of behavioural and emotional disorders according to the International Classification of Diseases, 10th Revision (ICD-10)[20] was based on the assessments of the paediatrician, the psychologist, and parental report. In most children (95%; age <43mo) the developmental assessment consisted of the Bayley Scales of Infant Development, Second Edition (BSID-II) assessment;[21] in two older children other standardized tests were used for mental development (Snijders-Oomen Non-Verbal Intelligence Test revised version[22] and the Developmental Test ET6-6 [Petermann and Macha[23]]), and in two children for motor development (Movement Assessment Battery for Children, Second Edition [Henderson et al.[24]] and ET6-6). In another seven children, whose neurological examination showed typical function, developmental outcome was based on developmental screening by the paediatrician. This screening showed average or above-average performance. The BSID-II instead of the Third Edition (BSID-III) was used, as at the time of our study the German norms of the BSID-III were not available and application of the US norms of the BSID-III was associated with problems.[25] The BSID-II results in two outcome scores: the Psychomotor Development Index and the Mental Development Index (MDI). General outcome was classified as typical or atypical, with atypical implying the presence of a clear neurological syndrome such as CP or the presence of an MDI and/or Psychomotor Development Index less than 70 or its equivalent. Intellectual disability was defined as the presence of an MDI less than 70 or its equivalent.

Interrater reliability assessment

Interrater reliability of the developmental and socio-emotional scales was determined in a group of infants not included in the main study on the predictive properties of the SINDA scales. The interrater reliability was assessed on the basis of the 60 consecutively recruited infants of 6 weeks to 12 months corrected age, who were assessed from October to December 2018 in the framework of the IMP-SINDA project. In the Groningen IMP-SINDA project we recently collected norm data for the Infant Motor Profile and SINDA. Each infant was assessed by two assessors, an active assessor (who assessed the infant; assessors A, B, and C), and a passive assessor (who observed the assessment and provided an independent assessment based on this observation; assessors a, b, and c). The combination of persons forming the assessor pair depended on the part-time availability of the assessors. Both assessors independently scored SINDA's developmental and socio-emotional scales in the 60 infants (age 6wks–12mo; median 7mo). To determine interrater agreement of the developmental scores, Spearman's rank correlation coefficient (rho, ρ) was used. As the correlation coefficients would only indicate how well the scores generally agreed, we also provide a Bland–Altman plot to illustrate the agreement between the individual pairs of assessors.[26] Interrater agreement of the four socio-emotional behaviours was calculated with Cohen's kappa (κ). According to Fleiss,[27] κ values of 0.40 to 0.75 are rated as fair to good, and values greater than 0.75 as excellent.

Statistical analysis of other psychometric properties

To assess whether the developmental and socio-emotional scores were largely independent of age, the association between the infant's corrected age at assessment and the developmental score was evaluated with ρ as the data of the developmental scores were not normally distributed; that between the infant's corrected age and the socio-emotional behaviours with Pearson's point-biserial correlation.

To assess SINDA's predictive validity, we first replicated in our main study group the evaluation of the predictive validity of SINDA's neurological score of no greater than 21 for atypical outcome at a corrected age of 24 months or older.[13] Second, we assessed the predictive validity of an atypical ('at risk') developmental score, namely a score below the 25th centile of the study group, for intellectual disability at a corrected age of 24 months or older, both in the main study group of 223 infants and in the group of 17 infants with trisomy 21. Third, we assessed the

predictive validity of the four socio-emotional behaviours for behavioural and emotional disorders at a corrected age of 24 months or older in the main study group. Finally, we evaluated whether the developmental scale would assist the prediction of outcome in the infants who were classified as false positives and false negatives by SINDA's neurological score.

Predictive validity was reported in terms of sensitivity, specificity, and positive and negative predictive values. The associations between low SINDA developmental scores and outcome were also evaluated with a χ^2 test and Fisher's exact test where appropriate. To analyse the association of SINDA's socio-emotional behaviours with the presence or absence of behavioural or emotional disorder at follow-up, logistic regression analysis was performed. The associations are expressed by means of their odds ratios (ORs) and 95% confidence intervals (CIs). For the SINDA behaviours that were associated with follow-up, predictive validity was determined.

RESULTS

Interrater reliability

The 60 infants who participated in the interrater reliability study had been assessed by different pairs of assessors (A–a: n=23; B–b: n=11; B–a: n=10; B–c: n=5; A–b: n=4; C–b: n=4; A–c: n=2; C–a: n=1). The correlation between the developmental scores of the two assessors of the 60 infants was high: ρ=0.972 (p<0.001). Also, agreement on the developmental scores of the three pairs that rated most infants was high (A–a: ρ=0.968, p<0.001; B–a: ρ=0.910, p<0.001; B–b: ρ=0.970, p<0.001). The highly consistent results on the interrater agreement, also among the different pairs of assessors, are illustrated with a Bland–Altman plot in Figure S2 (online supporting information).

The agreement between the two assessors on the four behaviours of the socio-emotional scale of the 60 infants was excellent (interaction κ=0.896, emotionality κ=0.880, and self-regulation κ=0.783). For the item reactivity, κ could not be calculated as all assessors agreed that reactivity was typical. The high κ values of all assessor pairs indicated that the individual pairs also highly agreed.

Age-dependency

The infant's developmental score showed a negative correlation with age at assessment (ρ=−0.329; p<0.001), namely with increasing age the developmental scores decreased. Inspection of the data revealed that this significant correlation was brought about by the referral pattern to the SPZ: infants referred at a corrected age of 6 months or older had an atypical outcome significantly more often (50 out of 130; 38%) than the infants who were referred before the age of 6 months (15 out of 93; 16%; χ^2_1=12.034, p<0.001). As the developmental score is related to later outcome (see next sections), this explains the negative correlation between age and developmental score. When we tested the correlation between the infant's corrected age and developmental score separately in the subgroups of the 93 infants aged 6 weeks to 5 months and the 130 infants aged 6 to 12 months, the association between testing age and developmental score was no longer statistically significant (ρ=−0.042; p<0.691 and ρ=−0.012; p<0.896, respectively).

Three of the four socio-emotional behaviours were not correlated to age at assessment (emotionality: r=−0.0.16; p=0.839), self-regulation (r=−0.151; p=0.053), and reactivity (r=0.026; p=0.741). Interaction, which depends on performance on the developmental scale, was, like the developmental scale, correlated with age (r=−0.343; p<0.001). When the bias induced by the referral pattern was taken into account, the correlation between interaction and age disappeared (infants aged 6wks–5mo: r=0.048; p=0.690; infants aged 6–12mo: r=−0.195; p=0.061).

Predictive validity of the SINDA scales

At the follow-up at a corrected age of 24 months or older, 65 children were diagnosed with an atypical outcome (n=35 with CP; Table 1). An atypical SINDA neurological score (≤21) predicted atypical outcome well (Table 2): sensitivity was 0.831, specificity 0.956, positive predictive value 0.885, and negative predictive value 0.932.

The SINDA developmental scores ranged from 0 to the maximum of 15. Preliminary analysis indicated that the lowest 25th centile implied a score no greater than 7 points (≤7), which was considered as atypical. At follow-up at a corrected age of 24 months or older, 52 infants were diagnosed with intellectual disability (with or without other neurodevelopmental impairments). An atypical developmental score predicted intellectual disability well (Table 3): sensitivity was 0.769, specificity 0.923, positive predictive value 0.755, and negative predictive value 0.929. In the subgroup of 17 children with trisomy 21, one child had an MDI score greater than 70 at a corrected age of 24 months or older; the developmental score of this child (10 points) had rightly predicted his good cognitive outcome (MDI 102). On the other hand, two other infants with trisomy 21 scored greater than 7 on SINDA's developmental scale but were diagnosed with intellectual disability (Table 3).

Thirty-two infants showed atypical interaction (of the 165 infants: 19%), 11 (7%) atypical emotionality, 13 (8%) atypical self-regulation, and eight (5%) atypical reactivity. At follow-up at a corrected age of 24 months or older, 25 infants (of the 165) were diagnosed with a behavioural or emotional disorder, including seven with a social anxiety disorder (ICD-10 sF93.2), five with atypical autism (F84.1), and four with an adjustment disorder (F43.2). The logistic regression analysis demonstrated that emotionality and self-regulation were associated with a behavioural or emotional disorder at a corrected age of 24 months or older (OR 12.99, 95% CI 2.60–64.85; OR 21.11, 95% CI 4.74–93.75 respectively). SINDA's interaction and reactivity did not contribute to the prediction of later behavioural and emotional disorders. The predictive values of SINDA's emotionality and self-regulation are presented in Table 3.

Table 2: Association between atypical Standardized Infant NeuroDevelopmental Assessment (SINDA) neurological score and atypical outcome at follow-up at ≥24mo

	Outcome at ≥24mo					
		Atypical				
		Neurological syndromes				
SINDA neurological score	Total typical	CP	Other neurological diagnoses (no CP)[a]	Intellectual disability, no neurological syndrome[b]	Total atypical[c]	Total
>21 (typical)	151	3	—	7	11	162
≤21 (atypical)	7	32	4	17	54	61
Total	158	35	4	24	65	223

[a]Four children with other neurological diagnoses had intellectual disability and a movement disorder mimicking cerebral palsy (CP), e.g. Aicardi–Goutieres syndrome, septo-optic dysplasia. [b]Intellectual disability, no CP, no other neurological pathology. [c]The total number of atypical cases included two additional children who had a Psychomotor Development Index score <70 in combination with Mental Development Index >70; one had a neurological score >21, the other a score ≤21. Atypical vs typical outcome (n=223): χ^2_1=143.35, p<0.001; sensitivity 0.831, specificity 0.956, positive predictive value 0.885, negative predictive value 0.932. CP (n=35) vs no CP (n=188): χ^2_1=85.77, p<0.001. Intellectual disability (n=52) vs no intellectual disability (n=171): χ^2_1=25.59, p<0.001.

Table 3: Prediction of atypical scores of the Standardized Infant NeuroDevelopmental Assessment (SINDA) at ≥24mo corrected age: (a) developmental scale for intellectual disability; (b) socio-emotional scale for behavioural and emotional disorder

	General at-risk sample (n=223)			Infants with trisomy 21 (n=17)			All SPZ infants studied (n=240)		
	Intellectual disability			Intellectual disability			Intellectual disability		
(a) Developmental score	No	Yes	Total	No	Yes	Total	No	Yes	Total
>7	158	12	170	1	2	3	159	14	173
≤7	13	40	53	0	14	14	13	54	67
Total	171	52	223	1	16	17	172	68	240

(b) Atypical emotionality	Behavioural disorder			Atypical self-regulation	Behavioural disorder			Atypical emotionality and/or atypical self-regulation	Behavioural disorder		
	No	Yes	Total		No	Yes	Total		No	Yes	Total
No	137	17	154	No	137	15	152	No	134	12	146
Yes	3	8	11	Yes	3	10	13	Yes	6	13	19
Total	140	25	165	Total	140	25	165	Total	140	25	165

Predictive values of an atypical (≤7) developmental score in the general at-risk sample (n=223): χ^2_1=105.76, p<0.001, sensitivity 0.769, specificity 0.923, positive predictive value 0.755, negative predictive value 0.929; predictive values in all Sozial Pädiatrisches Zentrum (SPZ) infants studied: χ^2_1=125.03, p<0.001; sensitivity 0.794, specificity 0.924, positive predictive value 0.806, negative predictive value 0.919. Predictive values of atypical emotionality: sensitivity 0.320, specificity 0.849, positive predictive value 0.727, negative predictive value 0.890; predictive values of atypical self-regulation: sensitivity 0.400, specificity 0.979, positive predictive value 0.769, negative predictive value 0.901; predictive values of the presence of atypical emotionality and/or atypical self-regulation: sensitivity 0.520, specificity 0.957, positive predictive value 0.684, negative predictive value 0.812.

The specificity of both early behaviours to predict a later behavioural or emotional disorder was high (0.849 and 0.979 respectively); however, their sensitivity was relatively low (0.320 and 0.400 respectively).

Table 4 illustrates that the information of the developmental score in children with a typical neurological score did not improve prediction of atypical outcome. Nevertheless, it is noteworthy that the three children with a false-negative neurological SINDA score were all diagnosed with CP in Gross Motor Function Classification System (GMFCS) level I. In the children with an atypical neurological score, addition of the developmental score did improve prediction: 13 of the 19 infants with a developmental score greater than 7 had an atypical outcome (68%) compared with 41 of the 42 infants with an atypical developmental score (≤7; 98%).

DISCUSSION

The present study indicated that SINDA's developmental and socio-emotional scales have an excellent interrater reliability and that their scores are independent of the infant's age. In addition, the study replicated the good predictive validity of SINDA's neurological scale for atypical outcome at 24 months or older. It demonstrated the good predictive validity of SINDA's developmental scale for intellectual disability at 24 months or older, and the capacity of this scale to improve prediction of atypical outcome in children with an atypical neurological score. Finally, two infant socio-emotional behaviours (emotionality and self-regulation) had a high specificity to predict a behavioural or emotional disorder at 24 months or older.

SINDA's developmental and socio-emotional scales were independent of the infant's testing age, at least when the

Table 4: Prediction of atypical scores of the Standardized Infant Neuro-Developmental Assessment neurological and developmental scales for CP and intellectual disability at ≥24mo corrected age

Neurological score	Developmental score	*n*	Outcome at ≥24mo			
			Atypical	CP	OND	ID
>21	>7	141	No	—	—	—
		9 (1)[a]	Yes	3[b]	—	6
>21	≤7 (atypical)	10	No	—	—	—
		1	Yes	—	—	1
≤21 (atypical)	>7	6	No	—	—	—
		13	Yes	11	—	2
≤21 (atypical)	≤7 (atypical)	1	No	—	—	—
		40 (1)[a]	Yes	21	4	15
Total		223		35	4	24

[a]The total number of atypical cases included two additional children who had a Psychomotor Development Index score <70 combined with a Mental Development Index score >70, one with neurological score >21 and one with score ≤21. [b]The function of three children with CP was classified in Gross Motor Function Classification System level I and they had a Mental Development Index score >70. Atypical outcome: in children with a neurological score >21 (with or without an atypical developmental score), 11 out of 162 (7%); in children with an atypical neurological score (≤21) and a developmental score >7, 13 out of 19 (68%); and in children with an atypical neurological (≤21) and atypical developmental score (≤7), 41 out of 42 (98%); χ^2_2=150.08, p<0.001. CP, cerebral palsy with or without intellectual disability; OND, other neurological diagnoses: four infants with severe disability including intellectual disability and a movement disorder mimicking CP; ID, intellectual disability, no CP, no other neurological pathology.

referral pattern to the SPZ was taken into account. Nevertheless, it should be noted that the item 'interaction' tended to be negatively related to age. This may reflect the emergence of impairments in interactional skills at the end of the first year, which is the period in life during which social interactional skills show a rapid development, including the development of joint attention.[28]

The predictive value of SINDA's developmental scale for intellectual disorder is better than that reported for the Bayley Infant Neurodevelopmental Screener (sensitivity 0.57–0.68, specificity 0.49–0.50).[8] The predictive validity for intellectual disorder is comparable to that of the Griffiths Mental Development Scales performed at 6 to 12 months corrected age,[29] and to that of the MDI of the BSID performed at 12 months corrected age.[30] Yet, its predictive validity is better than that of the MDI measured at 4 and 8 months, as the latter predicts cognitive outcome to a limited extent.[30] Our limited data on infants with trisomy 21 indicated that SINDA's developmental scale may also to some extent guide the expectations of the later cognitive abilities in these infants—abilities that are known to be heterogeneous.[31]

SINDA's neurological scale predicted atypical outcome very well, but not perfectly. Addition of the developmental scale did not improve prediction in the infants with a typical neurological score (>21). Most of the 'false negatives'—the infants with a typical neurological score and an atypical outcome—also had a typical developmental score (>7). Yet, it is noteworthy that the three children with CP, who were classified as false negative, had a unilateral spastic CP and were functioning well in daily life (GMFCS level I and no intellectual disability). This means that the SINDA scales had correctly predicted their good outcome in terms of activities and participation at 24 months or older. The addition of the developmental scale did improve prediction of outcome in the infants with an atypical neurological score (≤21); infants who had an atypical score on both the neurological and developmental scales virtually all had an atypical outcome.

Two of the infant socio-emotional behaviours (emotionality and self-regulation) were associated with a behavioural or emotional disorder at follow-up; both behaviours paired high specificities with low sensitivities. In other words, if the infants showed atypical emotionality or atypical self-regulation, the chance was high that they were diagnosed later with a behavioural or emotional disorder. However, the absence of atypical emotionality or atypical self-regulation did not preclude the development of a behavioural or emotional disorder. This corresponds to the significant but moderate associations between infant temperament and attachment and later behavioural outcome reported in the literature, which can be explained by the multifactorial origin of behavioural disorders.[32]

This brings us back to the two-fold aim of a neurodevelopmental assessment in infancy. Its first aim is to counsel caregivers on the capacities and the challenges of their infant. The presence of an atypical neurological score indicates the need for additional diagnostics, professional early intervention, and careful monitoring of the infant's developmental progress.[1] The presence of an atypical developmental score may be used to explain to caregivers the developmental profile of the infant: which domains are easy for the child, and which are more difficult and would benefit from developmental stimulation by the caregivers.[33] The presence of atypical socio-emotional behaviour provides the professional with clues for specific caregiver counselling. The counselling aims at increasing the resilience of the caregivers and infant by means of promotion of: (1) positive caregiver–infant interactions; (2) caregiver support of the infant's emotionality and self-regulation; and (3) a positive caregiver–infant relationship.[34,35]

The strength of this study is the development of a neurodevelopmental screening instrument consisting of three scales for infants aged 6 weeks to 12 months. An additional strength is that we tested the predictive validity of SINDA in a non-academic setting, namely in a typical German SPZ setting. The setting was, however, not that of the general paediatricians for whom SINDA is designed, but a specialized outpatient clinic for infants at high risk of, or with, neurodevelopmental disorders—a risk that was reflected by the relatively high proportion of children diagnosed with CP or trisomy 21. This means that future research needs to address the reliability and predictive validity of SINDA in a general paediatric setting. The specific setting of the current study was also associated with some limitations. First, follow-up was performed in

clinical routines, inducing some variation in age at assessment (but in all: ≥24mo). The clinical routines also implied that a significant proportion of infants who were doing relatively well were not included in the study, as they had no follow-up at the SPZ outpatient clinic. This may have slightly affected SINDA's sensitivity, as we may have underestimated the number of false negatives. Yet, SINDA's specificity would not have been affected. Second, the clinical setting meant that the paediatricians in charge of the follow-up examinations knew the infant's SINDA scores, namely they had a clinical bias. On the other hand, the psychologists in charge of the BSID-II were not aware of the SINDA scores. Third, the setting also implied that a relatively large proportion (29%) of the infants had an atypical outcome, which increased the a priori chance of getting satisfactory predictive values. On the other hand, it should be realized that the predictive validity of novel developmental tests is almost always tested in groups with a comparable composition.[36,37] Finally, the design of the reliability part of the study with its different setting and eight pairs of assessors may be regarded as a limitation. Yet, the data on the relatively large sample of infants included in the interrater reliability part of the study clearly demonstrated highly consistent scoring across the pairs of assessors. This emphasizes the interrater reliability of the developmental and socio-emotional scales.

In conclusion, the present and previous study[13] indicated that the three SINDA scales can be reliably assessed in 15 to 20 minutes (youngest infants) or 20 to 25 minutes (oldest infants) and that its scores are independent of infant age. In a specialized non-academic outpatient setting: (1) the neurological scale was associated with a satisfactory predictive validity for atypical developmental outcome, including CP, at 24 months or older; (2) the developmental scale was associated with satisfactory prediction of intellectual disability at 24 months or older and with improved prediction of atypical outcome of infants with an at-risk neurological score; (3) two infant behaviours of the socio-emotional scale had a high specificity but low sensitivity to predict later behavioural and emotional disorders.

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SUPPORTING INFORMATION

The following additional material may be found online:

Table S1: Properties of various developmental assessments

Appendix S1: SINDA developmental and socio-emotional scale assessment form for the ages 6 weeks to 6.5 months.

Appendix S2: SINDA developmental and socio-emotional scale assessment form for the ages 6.5 months to 12.5 months.

Appendix S3: Some examples of items of the developmental scale.

Figure S1: Example of the testing material used in SINDA.

Figure S2: Bland–Altman Plot on interrater agreement of the developmental scale.

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RESUMEN

Evaluación estandarizada del neurodesarrollo infantil (SINDA) Escalas de desarrollo y socioemocionales: confiabilidad y valor predictivo en una población en riesgo

OBJETIVO

Evaluar la fiabilidad y la validez predictiva de las escalas de desarrollo y socioemocionales de la Evaluación estandarizada de neurodesarrollo infantil (SINDA, siglas en ingles).

METODO

Para evaluar la confiabilidad, dos conjuntos de tres evaluadores que forman ocho pares de evaluadores calificaron independientemente las escalas de desarrollo y socioemocionales de 60 niños. Para evaluar la validez predictiva, 223 lactantes (edad gestacional 30 semanas [rango 23-41 semanas]; 117 varones, 106 mujeres) que asistían a una clínica ambulatoria no académica fueron evaluados por diferentes evaluadores con las escalas neurológica, de desarrollo y socioemocional de SINDA. El resultado anormal del desarrollo neurológico a una edad corregida de 24 meses o más implicaba un puntaje del índice de desarrollo mental o psicomotor Bayley de menos de 70 o un trastorno neurológico (incluida la parálisis cerebral). Los trastornos conductuales y emocionales se clasificaron de acuerdo con la Clasificación Internacional de Enfermedades, Décima Revisión. Los valores predictivos se calcularon a partir de SINDA (edad corregida de 2 a 12 meses, mediana de 7 meses) y resultados típicos versus atípicos, y solo para discapacidad intelectual (Índice de desarrollo mental <70).

RESULTADOS

Los evaluadores estuvieron muy de acuerdo con las evaluaciones de desarrollo y socioemocionales (puntajes de desarrollo: coeficiente de correlación de rango de Spearman ρ = 0.972; ítems individuales de comportamiento socioemocional: κ de Cohen = 0.783–0.896). A los 24 meses o más, 65 niños tuvieron resultados atípicos. Las puntuaciones neurológicas atípicas predijeron resultados atípicos (sensibilidad 83%, especificidad 96%); puntajes de desarrollo atípicos predijeron discapacidad intelectual (sensibilidad 77%, especificidad 92%). La emocionalidad y la autorregulación atípicas se asociaron con trastornos conductuales y emocionales.

INTERPRETACION

Las tres escalas de SINDA son confiables y tienen una validez predictiva satisfactoria para un resultado de desarrollo atípico a los 24 meses o más en un entorno ambulatorio no académico. La escala de desarrollo de SINDA tiene una prometedora validez predictiva para la discapacidad intelectual. La escala socioemocional de SINDA es una herramienta para el asesoramiento del cuidador.

RESUMO

Escalas desenvolvimental e sócio emocional da Avaliação Neurodesenvolvimental Padronizada do Lactente (SINDA): confiabilidade e valor preditivo em uma população de risco

OBJETIVO

Avaliar a confiabilidade e validade preditiva das escalas desenvolvimental e sócio emocional da Avaliação Neurodesenvolvimental Padronizada do Lactente (SINDA).

MÉTODO

Para avaliar a confiabilidade, dois grupos de três avaliadores formando oito pares de availadores pontuaram independentemente as escalas desenvolvimental e sócio emocional de 60 lactentes. Para avaliar a validade preditiva, 223 lactentes (idade gestacional 30sem [variação 23–sem]; 117 do sexo masculino, 106 do sexo feminino) atendidos em uma clínica não-acadêmica foram avaliados por diferentes avaliadores com as escalas neurológica, desenvolvimental e sócio emocional da SINDA. Resultados neurodesenvolvimentais atípicos na idade corrigida de 24 meses ou mais implicaram um Índice Desenvolvimental Mental ou Psicomotor segundo a Bayley de menos de 70 ou uma desordem neurológica (incluindo paralisia cerebral). Transtornos comportamentais e emocionais foram classificados de acordo com a Classificação Internacional de Doenças, 10a edição. Valores preditivos foram calculados a partir da SINDA (2-12 mess de idade corrigida, mediana 7 meses) e também o resultado típico versus atípico, e para deficiência intelectual apenas (Índice de Desenvolvimento mental <70).

RESULTADOS

Os avaliadores concordaram fortemente quanto às avaliações desenvolvimental e sócio emocional (escores desenvolvimentais: coeficiente de correlação de Spearman ρ=0,972; itens isolados do comportamento sócio-emocional κ de Cohen =0,783–0,896). Aos 24 meses ou mais, 65 crianças tiveram resultado atípico. Escores neurológicos atípicos predizeram resultado atípico (sensibilidade 83%, especificidade 96%); escores desenvolvimentais atípicos predizeram deficiência intelectual (sensibilidade 77%, especificidade 92%). Emocionalidade atípica e auto-regulação atípica foram associados com transtornos comportamentais e emocionais.

INTERPRETAÇÃO

As três escalas da SINDA são confiáveis, e têm validade preditiva satisfatória para resultado desenvolvimental atípico aos 24 meses ou mais em um ambiente clínico não-acadêmico. A escala desenvolvimental da SINDA tem validade preditiva promissora para deficiência intellectual. A escala sócio-emocional da SINDA é uma ferramenta para aconselhamento dos cuidadores.