

## FRÜHERKENNUNG: die ROLLE der STANDARDISEIERTEN KLINISCHEN UNTERSUCHUNG: GMA, SINDA und IMP



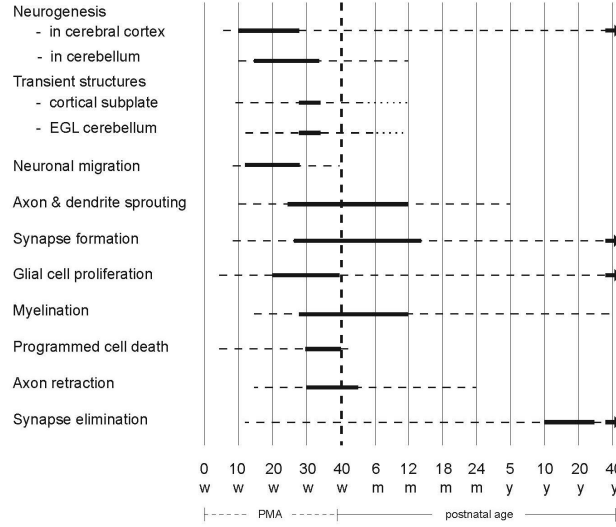
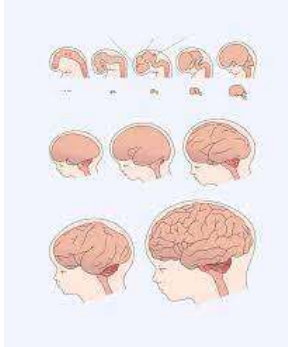
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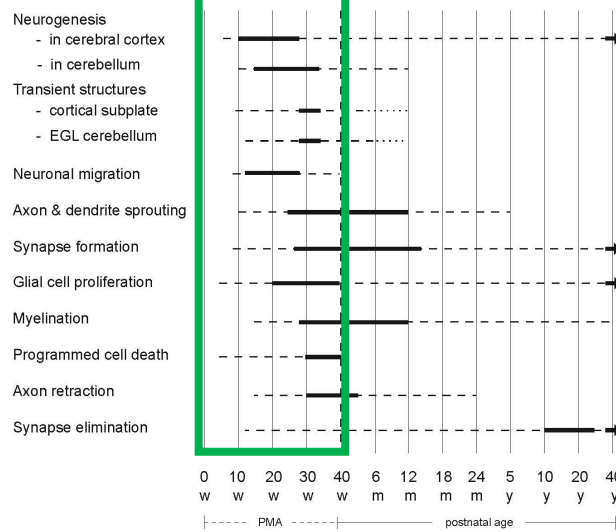
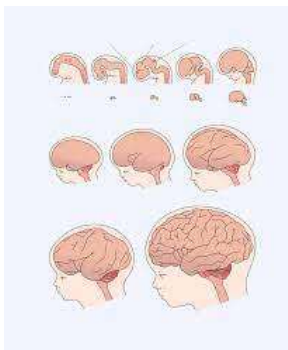
### Interessenskonflikte

- Ich versichere, meine Beiträge product- und firmenneutral zu halten
- Die Veranstalter nehmen auf den Inhalt meines Vortrags keine Einfluss
- Gegenüber den Teilnehmenden lege ich hiermit folgende Interessenskonflikte offen:
  - Ich versorge GMA-Kurse
  - Ich bin Ko-Autorin des SINDA-Manuals
  - Ich bin Ko-Autorin des IMP-Manuals und versorge IMP-Kurse

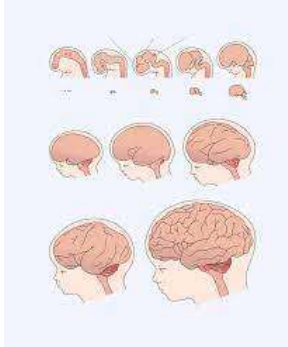
## NEURODEVELOPMENTAL PROCESSES DURING HUMAN ONTOGENY (Hadders-Algra, 2018, 2021)



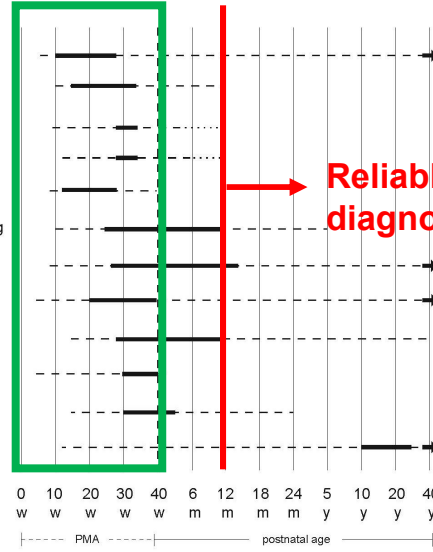
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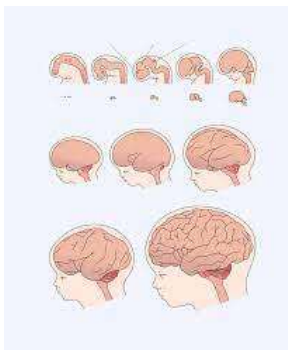


- Neurogenesis
  - in cerebral cortex
  - in cerebellum
- Transient structures
  - cortical subplate
  - EGL cerebellum
- Neuronal migration
- Axon & dendrite sprouting
- Synapse formation
- Glial cell proliferation
- Myelination
- Programmed cell death
- Axon retraction
- Synapse elimination

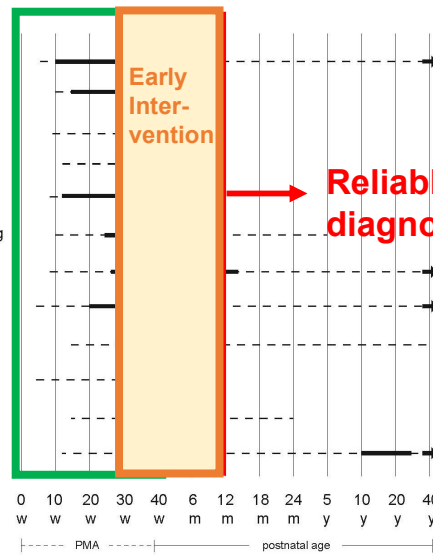


**Reliable diagnosis CP**

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**Early Intervention**

**Reliable diagnosis CP**

## EARLY DETECTION OF NEURODEVELOPMENTAL DISORDERS

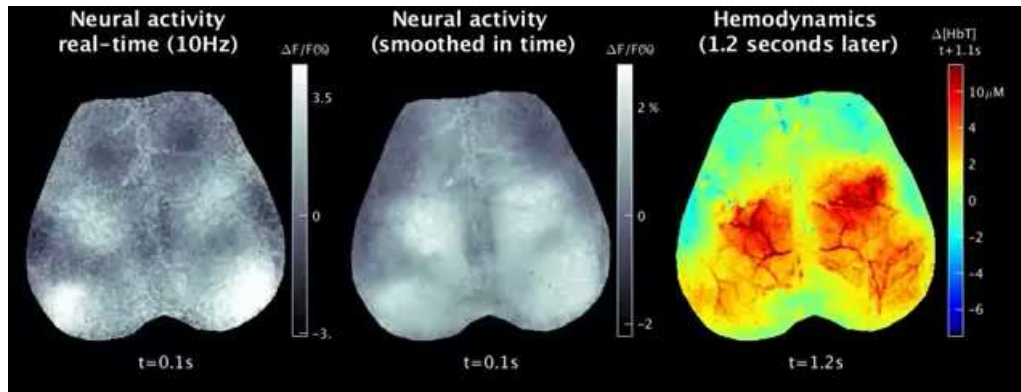


by means of  
neurological,  
neuromotor or  
developmental  
assessments

## CHANGING CONCEPTS in BRAIN FUNCTION and EARLY DIAGNOSTICS

- **Developmental milestones:**
  - Advantage: easy
  - Disadvantage: large variation; only significance when multiple milestones show delay
- **Neurological examination:**
  - Muscle tone
  - Reflexes and reactions
  - Quality of spontaneous movements → variation!

## SPONTANEOUS ACTIVITY HALLMARK OF NEURAL TISSUE



<https://youtu.be/G-4t0859db4>

## CHANGING CONCEPTS in BRAIN FUNCTION and EARLY DIAGNOSTICS

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  - Reflexes and reactions
  - Quality of spontaneous movements → variation!

## GENERAL MOVEMENTS (GMs)

- Movements involving head, trunk, arms and legs
- Present from early fetal life to 3-5 months CA: 3 phases
  - Fetal / preterm: 9-10 wk PMA – 36-38 wk PMA
  - Writhing: 36-38 wk PMA – 6-8 wk CA
  - Fidgety: 2-5 mo CA → emergence goal directed movements
- Typical GMs characterized by movement complexity and variation
  - Complexity = spatial variation
  - Variation = temporal variation



## GMA: VIDEO-BASED ASSESSMENT

- Video mandatory to evaluate **complexity and variation**
- At least 3 minutes of moving infant needed with infant in adequate behavioural state (i.e., not crying, not sucking)
- Reliability in experienced assessors good ( $\kappa > 0.80$ )

## GMs: TWO BASIC ASPECTS

1. At any GM-age: **complexity and variation** → reflecting integrity of cortical-subcortical connectivity
2. Age specific changes, the development via writhing to **fidgety movements** → maturation of the cortical networks

## Atypical General Movements

- **Predict outcome best at fidgety GM-age** (2-5 months CA)
- 2-5 mo CA: use of permanent networks in primary sensory, motor and visual cortices (cortical plate)
- Two aspects:
  - ↓↓ complexity & variation (definitely abnormal compl & var)
  - Absent fidgety movements
- In high risk infants with **both** signs:
  - Sensitivity CP: 98% (95% CI: 74-100%)
  - Specificity CP: 91% (95% CI: 83-93%)

## Standardized Infant NeuroDevelopmental Assessment (SINDA)

### • Three scales

- Neurological scale
- Developmental scale
- Socio-emotional scale



Uta Tacke



Joachim Pietz



Heike Philippi

### • Properties

- Age 6 weeks – 12 months
- Can be applied quickly and easily



## SINDA: no expensive toolkit required





# SINDA's NEUROLOGICAL SCALE

- 28 items, including 7 items on quality of spontaneous movements



Hadders-Algra et al. 2019, 2020, 2021



## SINDA Neurological Scale

**SINDA Neurological scale**

Behavioural state  awake, alert  sleepy, tired  noisy  crying  sub-acute illness

Facial events  absent  suspected  obvious

Head   cm  macrocephaly  microcephaly  plagiocephaly  atypical fontanel  atypical sutures

Additional  somatic symptoms  sex vs. impairment  dysmorphic signs  sex vs. impairment  atypical phonation

Name: \_\_\_\_\_  
 Birth date: \_\_\_\_\_ ♂ ♀  
 Corr. Age: \_\_\_\_\_  
 Date: \_\_\_\_\_  
 Examiner: \_\_\_\_\_  
 Hospital: \_\_\_\_\_

Additional clinical comments: \_\_\_\_\_

Pos*	Q.T*	Item	typical (T)	atypical (A)	score
<b>A1 Spontaneous movements (local)</b>					
1	A	Head & neck & trunk	varied & symmetric	absent/poor posture, asymmetric	R L
2	A	Arms	varied & symmetric	absent/poor posture, asymmetric	R L
3	A	Hands	varied & symmetric	absent/poor posture, asymmetric	R L
4	A	Legs	varied & symmetric	absent/poor posture, asymmetric	R L
5	A	Feet	varied & symmetric	absent/poor posture, asymmetric	R L
6	Su	ATNR	absent, occasionally present	frequently, robustly present, asymmetric	
<b>A2 Spontaneous movements (general)</b>					
7	A	Quality	varied & symmetric, & burst & isolated movements of limbs & face	absent/poor, jerky, erratic, hemiburst, sluggish, stiff, no isolated movements of fingers, toes, asymmetric	R L
8	A	Quantity	moderate & changing over time	predominantly hypokinetic, predominantly hyperkinetic	
<b>B Cranial features</b>					
9	A	Facial appearance	varied & symmetric	expressionless, asymmetric	R L
10	A	Oral motor behaviour	mouth mostly closed & large within the mouth & no obvious drooling	mouth mostly open, absent/large protrusion, functional, obvious drooling	
11	Su, St	Glabella reflex	moderate threshold & moderate intensity & symmetric	low, high threshold, low, high intensity, asymmetric	
12	Su, St	Eyeblink & eye movements	flexion & adduct position & evoked movement	no flexion, predominant dilation, unevoked movement, vertical midline, none, sylvianus	R L
13	Su, St	Optical blink reflex	absent & symmetric	absent, doubtful, delayed, asymmetric	R L
14	Su, St	Trigeminal reaction	absent & deep, normal & symmetric	absent, slow, toxic, asymmetric	R L
15	Su, St	Acoustic reaction to hearing	blink, facial reaction	absent, doubtful	
<b>C Motor reactions to postural stimulation</b>					
16	Su	Pubic-st	activation of neck & shoulder & arm muscles & symmetric arm, slight & delayed flexion	head/leg, active withdrawal, no, minimal muscle activation, asymmetric, isolated hyperflexion	R L
17	P	Head in prone	lifts head as reflexive action	does not lift head, stereotyped hyperextension	
18	VS	Prone suspension	head in air, across back head	head with floppy, stereotyped, apathetic	
19	VS	Vertical suspension	head upright & appropriate motor readiness & legs spread & symmetric	poor head control, flapping through, stereotyped leg movements, asymmetric	R L
20	VS	Feet touching the ground	varied head posture & movements & symmetric	absent/poor posture, asymmetric	R L
<b>D Muscle tone</b>					
21	Su, St	Tone of neck & trunk	moderate resistance against passive movements	over- or hypotonia, consistent hypotonia, sudden change in muscle tone	
22	Su, St	Resistance against passive movements, arm flexion	symmetric & moderate resistance against passive movements & slight elbow flexion	over- or hypotonia, consistent hypotonia, sudden change in muscle tone, asymmetric	R L
23	Su, St	Resistance against passive movements, hip flexion	symmetric & moderate resistance against passive movements & slight knee flexion	over- or hypotonia, consistent hypotonia, sudden change in muscle tone, asymmetric	R L
24	Su, St	Foot resistance against passive movements	symmetric & moderate resistance against passive movements	over- or hypotonia, consistent hypotonia, sudden change in muscle tone, ankle flexion, sudden catch phenomenon, asymmetric	R L
<b>E Reflexes and reactions</b>					
25	Su, St	Upper extremities: Moro reflex	symmetric positive response	asymmetric, asymmetric	R L
26	Su, St	Lower extremities: Head lift & ankle clonus	symmetric positive response	asymmetric, tonic response, clonus, asymmetric	R L
27	Su, St	Foot sole sensibility	withdrawal of legs & vertical toe movement & symmetric	no reaction, absent/poor toe movement, asymmetric	R L
28	Su, St	Foot sole response	vertical dorsiflexion for toe & toe spreading & symmetric	absent/poor, tonic, dorsiflexion or plantar flexion, no, weak response, asymmetric	R L

SINDA Neurological Score: \_\_\_\_\_

\* Pos: Position; A: All; P: Prone; VS: Vertical Suspension; S: Suspended Sitting; Su: Supine; SS: Supine Suspension; VS: Vertical Suspension; Q.T: Questionnaire Item; T: Typical.

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# SINDA's NEUROLOGICAL SCALE

- 5 domains:
  - Spontaneous movements (8 items)
  - Cranial nerves (7 items)
  - Motor reactions to postural stimulation (5 items)
  - Muscle tone (4 items)
  - Reflexes and reactions (4 items)
- 28 items: all scored dichotomously, typical or atypical



Hadders-Algra et al. 2019, 2020, 2021



## SINDA Neurological Scale

7/28 items (25%)  
quality spontaneous movements – variation

**SINDA Neurological scale**

Behavioural state:  awake, alert;  sleepy, tired;  fussy;  crying;  sub-acute illness

Facial events:  absent;  suspected;  obvious

Head:  normal;  microcephaly;  macrocephaly;  atypical fontanel;  atypical sutures

Additional:  somatic symptoms;  sex vs. impairment;  dysmorphic signs;  atypical phonation

Name: \_\_\_\_\_ Birth date: \_\_\_\_\_ Sex: ♂ ♀  
 Cort. Age: \_\_\_\_\_ Date: \_\_\_\_\_ Examiner: \_\_\_\_\_  
 Hospital: \_\_\_\_\_

Item	Item	typical (T)	atypical (A)	score
<b>A1 Spontaneous movements (focal)</b>				
A	Hand & neck & trunk	varied & symmetrical	stereotyped/abnormal, hyperflexion, hyperextension	R L
A	Arms	varied & symmetrical	stereotyped posture, asymmetric	R L
A	Hands	varied & symmetrical	stereotyped posture, asymmetric	R L
A	Legs	varied & symmetrical	stereotyped posture, asymmetric	R L
A	Feet	varied & symmetrical	stereotyped posture, asymmetric	R L
Su	ATNR	absent, occasionally present	frequently, continuously present, asymmetric	
<b>A2 Spontaneous movements (general)</b>				
A	Quality	varied & symmetrical & fluid & sustained	stereotyped, jerky, jittery, startles, tremulous, sluggish, stiff	R L
<b>B Cranial nerves</b>				
B	Facial appearance	varied & symmetrical	expressionless, asymmetric	R L
11	Oral motor behaviour	mouth mostly closed & tongue within the mouth & no obvious drooling	mouth mostly open, stereotyped tongue protrusion, fasciculations, drooling, drooling	
11	Glabella reflex	moderate threshold & moderate intensity & symmetric	low, high threshold, low, high intensity, asymmetric	
12	Eyeblink & eye movements	fluid & regular position & evoked movement	no fixation, predominant saccades, unevoked movement, variable media, saccade, saccades	R L
13	Optical blink reflex	absent & symmetric	absent, doubtful, delayed, asymmetric	R L
14	Palpebral reaction	absent & deep, normal & symmetric	absent, slow, late, asymmetric	R L
15	Accommodation reaction to blurring	absent, facial reaction	absent, doubtful	
<b>C Motor reactions to postural stimulation</b>				
16	Pubis-ast	activation of neck & shoulder & arm muscles & symmetric arm, slight & delayed flexion/extension	head/leg, active withdrawal, no, minimal muscle activation, asymmetric, bilateral, high/low	R L
17	Head in prone	lifts head as reflexive action	does not lift head, stereotyped hyperextension	
18	Prone suspension	head in the air, neck bent	head, neck floppy, developed, apathetic	
19	Vertical suspension	head upright & appropriate military readiness & legs spread & symmetric	poor head control, flapping through, stereotyped leg movements, asymmetric	R L
20	Feet touching the ground	varied foot postures & movements & symmetric	stereotyped foot postures, asymmetric	R L
<b>D Muscle tone</b>				
21	Tone of neck & trunk	moderate resistance against passive movements	over- or under-resistance, consistent hypertonia, sudden change in muscle tone	R L
22	Resistance against passive movements, arm flexion	symmetric & moderate resistance against passive movements & slight elbow flexion	over- or under-resistance, consistent hypertonia, sudden change in muscle tone, asymmetric	R L
23	Resistance against passive movements, hip flexion	symmetric & moderate resistance against passive movements & slight hip flexion	over- or under-resistance, consistent hypertonia, sudden change in muscle tone, asymmetric	R L
24	Feet resistance against passive movements	symmetric & moderate resistance against passive movements	over- or under-resistance, consistent hypertonia, sudden change in muscle tone, ankle flexion, sudden pronation, asymmetric	R L
<b>E Reflexes and reactions</b>				
25	Upper extremities: Babinski reflex	symmetric positive response	asymmetric, asymmetric	R L
26	Lower extremities: Babinski reflex & ankle clonus	symmetric positive response	asymmetric, tonic response, clonus, asymmetric	R L
27	Feet sole sensibility	sufficient of legs & varied toe movement & symmetric	no reaction, stereotyped toe movements, asymmetric	R L
28	Feet sole response	varied dorsiflexion for toe & toe spreading & symmetric	stereotyped, toes down or plantar flexion, no, weak response, asymmetric	R L

\* Pub: Pubis; A: All; P: Prone; DS: Prone Suspension; S: Supported Sitting; Su: Supine; SS: Supine Suspension; VS: Vertical Suspension; O: Observed/seen; T: Test item.

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## SINDA's NEUROLOGICAL SCALE

- 28 items, including 7 items on quality of spontaneous movements
- Criteria and cut-offs for dichotomous items independent of infant age
- Duration: < 10 minutes
- Relatively quick and easy to apply
- Good reliability



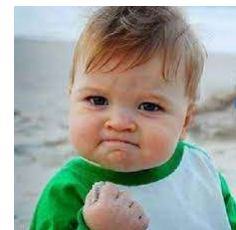
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## Predictive validity of at risk score ( $\leq 21$ ) of SINDA's neurological scale

- 2 studies in at risk populations (n=181 and n=223)
- Predictive values for CP and intellectual disability at age 2 yr:
  - CP: sensitivity: 91-100%  
specificity: 81-95%
  - Atypical: sensitivity: 83- 89%  
specificity: 94-96%
- **Very good prediction of neurodevelopmental disorders at the age of 2 years**



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# Developmental scale form 2-6 mo

Name: \_\_\_\_\_ First name: \_\_\_\_\_ Birth date: \_\_\_\_\_ Ass. date: \_\_\_\_\_ Corrected age (Mo): \_\_\_\_\_ Assessor: \_\_\_\_\_ Hospital: \_\_\_\_\_

Behavioural state:  awake, alert  sleepy, tired  fussy, moody  crying, cannot be assessed  ♂ / ♀

Additional clinical comments: \_\_\_\_\_

1 M 15 - 2 M 14	2 M 15 - 3 M 14	3 M 15 - 4 M 14	4 M 15 - 5 M 14	5 M 15 - 6 M 14
1 Smiles in response to smile of parent or assessor	16 Looks alternately from parent to assessor and vice versa	16 Looks alternately from parent to assessor and vice versa	27 Intended in environment and orientates in room	49 Inspects facial expression of assessor with sustained attention
2 Initiates contact with assessor, explores face and facial expression	4 Produces ≥ 2 different sounds (e.g., gash, ooh)	27 Interested in environment and orientates in room	28 Looks alternately from objects to persons and vice versa	50 Uses facial expression to communicate
3 Reacts to voice-like expressions of parent or assessor	5 Produces sounds as dialogue when being talked to	28 Looks alternately from objects to persons and vice versa	31 Produces sounds to express emotions, laughs loudly	30 Produces ≥ 3 consonant-vowel combinations
4 Produces ≥ 2 different sounds (e.g., gash, ooh)	17 Produces sounds with expression, expresses emotions	29 Produces ≥ 3 different sounds	39 Produces ≥ 3 consonant-vowel combinations	51 Produces sounds to draw attention to itself
5 Produces sounds as dialogue when being talked to	18 Smiles in response to optical approach of hand	30 Produces ≥ 1 labial consonant and one consonant-vowel combination	40 Localizes voices and directs visual attention to voice	52 Produces strings of syllables with speech melody
6 Reacts to sound	19 Turns eyes to sound producing object	31 Produces sounds to express emotions, laughs loudly	32 Searches visually to find object that disappeared	53 Turns eyes or head to soft sound, e.g., rustling of paper
7 Shortly fixates object at 30 cm distance	20 Turns visual attention away from one sound object to another	20 Turns visual attention away from one sound object to another	41 Looks ≥ 3 sec in direction of hidden object	41 Looks ≥ 3 sec in direction of hidden object
8 Follows object with eyes or head horizontally	21 Follows object with eyes or head, horizontally and vertically	32 Searches visually to find object that disappeared	42 Visually explores an object held in his hand	54 Visually searches falling and 'catching' object
9 Follows object with eyes or head vertically	11 Inspects own hand	12 Moves arm in direction of attractive object	43 Reaches across midline	55 Explores object with interest for details
10 Moves hand to mouth	22 Moves arm at appearance of object in visual field	33 Grasps object presented within visual fields with hand	44 Transfers object from one hand to the other	44 Transfers object from one hand to the other
11 Inspects own hand	12 Moves arm in direction of attractive object	34 Brings object to mouth, and explores with mouth and hand	45 Holds one object and reaches and touches a second object	45 Holds one object and reaches and touches a second object
12 Moves arm in direction of attractive object	23 Holds in midline and mutual touching of hands	35 Explores object with both hands	46 Plays with string	56 Shortly holds two grasped objects
13 Balances head for ≥ 3 sec in supported sitting	24 Balances head for ≥ 5 sec in supported sitting	36 Balances head for ≥ 10 sec in supported sitting, some wobbling allowed	37 Hand touches knee	57 Plays with feet (hand-foot contact)
14 Legs alternately on support surface and lifted bilaterally for ≥ 3 sec	25 Legs lifted from support surface & ≥ 3 sec foot-foot contact	37 Hand touches knee	47 Supported on two elbows and attempts to obtain object	58 Wiggling
15 Head lift, chin off support surface for ≥ 3 sec	26 Head lift > 45° for ≥ 3 sec	38 Head lift > 45° with elbow support ≥ 5 sec	48 Stable head position in supported sitting	59 Stands on hands, unilaterally or bilaterally
Σ	Σ	Σ	Σ	Σ



Interaction  Emotionality  Self-Regulation  React Position  React Visually  React Acoustically

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## SINDA's developmental & socio-emotional scale

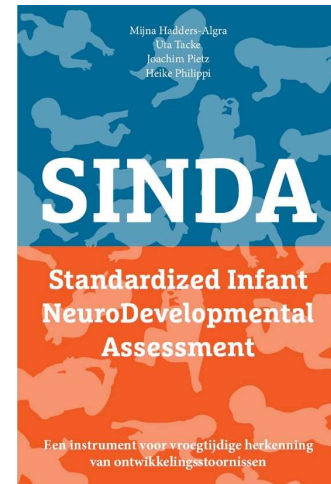
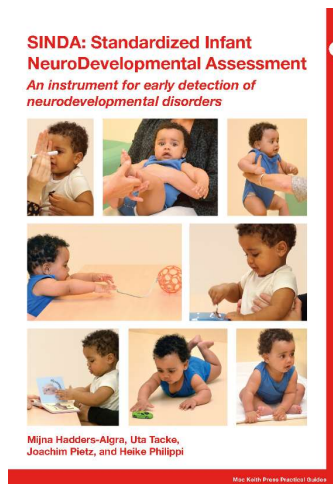
- Developmental scale:**
  - 15 items per month: pass or fail
  - cognition, communication, gross and fine motor domains
  - good reliability
  - primary goal: caregiver counselling
  - risk score (≤7) predicts intellectual disability: sens: 77%; spec: 92%
- Socio-emotional scale:**
  - 6 items → 4 behaviours
  - primarily goal: caregiver counselling; some assistance prediction behavioural disorders



Hadders-Algra et al. 2020, 2021, Hadders-Algra 2021, 2022



## SINDA's manual: richly illustrated, >160 videos



## Infant Motor Profile

- **Five domains**

1. Variation
2. Adaptability
3. Symmetry
4. Fluency
5. Performance

- **Properties**

- Age 3-18 mo (walking independently for some months)
- Video-based, self-produced movements
- Time needed: assessment 15 min, off-line scoring 10 min.
- Good reliability
- Prediction CP: sens 93%, spec 81%; ROC 0.89-0.99
- Excellent tool to design and evaluate early intervention



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Hadders-Algra & Heineman 2021, Hadders-Algra 2021



## Comparison GMA, SINDA and IMP

Property	GMA	SINDA neuro	IMP
Age range (CA)	≤ 5 mo	6 wk – 12 mo	3-18 mo
Video-based	Yes	No	yes
Time needed			
- video	5-10 min		15 min
- scoring	5 min	< 10 min	10 min
Prediction CP			
- sensitivity	98%	91-100%	93%
- specificity	91%	81-95%	81%



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## SUMMARIZING REMARKS EARLY DETECTION of INFANTS at HIGH RISK of CP

- Importance of quality of spontaneous movements (variation)
- Instruments using this principle: GMA, SINDA and IMP → proper detection of high risk of CP
- Prediction at early age is never perfect:
  - Be alert for false negatives
  - False positives do not exist: neurological deviancy at early age indicates the need of early intervention

