Discriminating ability of the *Infant Neurological International Battery* (Infanib) for the neurological outcome of high-risk infants in a cohort of 5857 low birth weight infants followed during their first year of corrected age in a Kangaroo Mother Care Program in Bogota, Colombia.

Ana María De la Hoz, Research asistant, Kangaroo Foundation
Nathalie Charpak, Pediatrician, Kangaroo Foundation
Fabián Gil, Biostatistician, Department of Epidemiology, Javeriana University
Juan Gabriel Ruiz, Pediatrician, Epidemiologist, Deparment of Epidemiology, Javeriana University

Introduction

At the Kangaroo Mother Care Program in Bogota, the *Neurological International Battery* (**Infanib**) has been used as a neuromotor integrity screening tool for nearly 20 years in order to make a timely intervention of possible neuromotor chronic disorders in premature/LBW infants.

Screening is performed at 3, 6, 9 and 12 moths of corrected age and, according to results, interventions including physical therapy, further testing and reference to pediatric neurology are performed.

Infanib is a practical and short time performing test that can be easily integrated into the periodic follow up evaluations of high risk infants by pediatricians and other health care professionals.

Infanib

Designed to provide information on age specific motor development impairment, and to identify patients and motor areas that could benefit from early intervention.

	Factor	Items
INFANIB	**Spasticity**	Asymmetric tonic neck reflex Tonic labyrinthine in prone Tonic labyrinthine in supine Hands held open or closed
	Head and trunk	Sitting Pulled to sitting All fours Body derotative
	Vestibular function	Backward parachute Forward parachute Sideway parachute Body rotative
	Legs	Standing Foot grasp Dorsiflexion of foot Positive support reflex
	French angles	scarf sign heel to ear popliteal angle abductor's angle

Classifies motor development as:

Normal
Transient
Abnormal

And also has the potential to identify some types of neurological abnormalities:

- **Spastic tetraparesis**
- **Spastic hemiparesis**
- **Spastic diplegia**
- **Hypotonia**

INFANIB **Name & Last name**

Review Date **Son**

	name	Chronological Age 0-1	1 2	2 3	Corrected Gestational Age 3 4	4 5	5 6	6 7	7 8	8 9	9 18 meses	FACTORS 3M 1 2 3 4 5	FACTORS 6M 1 2 3 4 5	FACTORS 9M 1 2 3 4 5	FACTORS 12M 1 2 3 4 5
1	Hands closed/open		closed	smtime	open							closed = 1 open = 5	closed = 1 open = 5	closed = 1 open = 5	closed = 1 open = 5
2	Scarf sign			0-15°		15-45°			45-60°		60-85°				
3	Heel to ear			100-90°		90-60°			60-40°		10°				
4	Popliteal angle			80-90°		90-110°			110-150°		150-170°	final asymmetry = 1	final asymmetry = 1	final asymmetry = 1	final asymmetry = 1
5	Leg abduction			40-70°		70-100°			100-130°		130-150°				
6	Dorsiflexion of Foot	0-10°		10-40°	40-70°				70-80°		80-90°				
7	Foot grasp		exaggerated = 1 other =5								absent =5 less pre=3				
8	Tonic labyrinthine supine		exaggerated = 1 other =5 absent=5 some =3 full =1												
9	Asymmetric tonic neck reflex		exaggerated = 1 other =5 absent=5 some =3 full =1												
10	Pull to sitting										full = 5 delayed cef partial or does not use arms = 3 full delay & does not use arms = 1				
11	Body derorative				Present to both sides = 5 Slow or slightly asymmetrical = 3 Absent or markedly asymmetrical = 1										
12	Body rotative										present = 5 poor= 3				
13	PRONE All fours	Lifts Head	Head up	Forearms only	Head up 90°		Bears weight on extended arms		Assumes all forus unsteadily	Assume s all fours	Stands up through plantígrade				
14	Tonic labyrinthine prone		exaggerated = 1 other = 5								absent = 5 full = 1				
15	SITTING Sitting position				L3		L5								
16	Sideways parachute						Present in both arms =5 Slow or midly asymetrical = 3 Absent or markedly asymetrical								
17	Backwards parachute										Present in both arms = 5 Slow or idly asymetrical = 3 Absent or markedly asymetrical = 1				
18	STANDING Weight bearing	Primitive reflex	No weight bearing	Poor weight bearing Breaks at knees (persistent more than 60°) =1				Unequal weight bearing							
19	Positive support reaction				Feet flat = 5 5 to 30sec. On toes then drop to feet flat = 3										
20	SUSPENDED Forward parachute								Present = 5 Slow or midly . Asimétrico = 3 ausente o muy asymétrical =1						

degree normality/abnormality based on local registration

LESS THAN 4 MONTHS	4 to 8 MONTHS	8 MONTHS OR MORE	Total:	Total:	Total:	Total:
Abnormal : 48 Transient 49-65 Normal= 66	Abormal <54 Transient 55-71 Normal >7	Abnormal < 56 Transient 59-82 Normal >83	Date:	Date:	Date:	Date:

abnormality category

Spastic Tetraparesis/dyskinesia ☐ Spastic Hemiparesis ☐ Spastic Diplegia ☐ Hypotonía ☐ ● according to age = 5 1 Step below = 3 2 step below = 1

Objective

To date, no comprehensive assessment of the test applied to preterm/LBW infants follow up program has been conducted

The objective of the study was to assess the discriminating ability of the INFANIB performed at 3, 6 and 9 months of CA for detecting neurological abnormal findings at one year CA in preterm and/or low birth weight infants.

Method

Observational analytic study in a non biased sample of infants from an historical cohort of 6481 infants with a complete follow up during their first year of life in a KMCP in Bogota between 1993 and 2009.

Inclusion criteria: complete information on neurological outcome at 1 year of corrected age (***Griffiths Mental Development Scale*** and **Infanib** evaluation) and information regarding at least 1 neuro developmental evaluation at 3, 6 or 9 months of corrected age with Infanib.

Neurological outcome at 1 year CA was the reference standard defined as the presence of neurological abnormality given by the results of ***Griffiths*** and **Infanib** (abnormality in any of the two tests, or transient result in both of them).

Method

The INFANIB test classifies any infant as abnormal, transient and normal. INFANIB result at 3,6 and 9 months was dichotomized as:

- Abnormal: any abnormal or transient result
- Normal.

Sensitivity, specificity, area under the ROC curve, PPV and NPP were calculated for Infanib evaluations at 3, 6 and 9 months of CA to determine the discriminating ability of Infanib on motor disorders or function at one year CA

Results

624 infants excluded due to incomplete or invalid information on neurological evaluation at 1 year of CA:

Final sample of 5857 infants included in the analysis.

Information of Infanib evaluation at :

3 months: 5812 (99.2%)

6 months: 5801 (99%)

9 months: 5833 (99.5%)

General characteristics of the population

Characteristic	No.	%	Mean	Min-max
Birth weight (g)	-	-	1795.5	500 - 2687
Categorical birth weight (g)				
Less than1000 g	269	4.6	-	-
1000 to 1500 g	1085	18.5	-	-
1501to 2000 gr.	2834	48.4	-	-
More than 2000 gr.	1668	28.5	-	-
Gestational age at birth (weeks)	-	-	33.75	25-41
Categorical gestational age at birth (weeks)				
30 or less	738	12.6	-	-
31 to 32	860	14.7	-	-
33 to 34	1748	29.8	-	-
35 to 36	1922	32.8	-	-
37 and more	534	9.1	-	-
C section	4448	75.9	-	-
Male	2878	49.1	-	-
Acute fetal distress	2044	34.9	-	-
Oxygen dependency	1293	22.1	-	-
NICU	1495	25.5	-	-
IUGR	1537	26.2		
Anoxia	759	32.9		
IVH	300	5.1		

Results

Neurodevelopmental Outcome at 1 year of corrected age

256/5857 (4.4%) infants with abnormal result in the neurological evaluation

Characterisation of adverse outcome at 1 year CA	No/total (%)
Abnormal result in both tests	45/256 (17.6)
Abnormal and a transient result	56/256 (21.9)
Abnormal and normal result	59/256 (23.0)
Griffiths abnormal - INFANIB normal Griffiths normal - INFANIB abnormal	50/256 (19.5) 9/256 (3.5)
Transient result in both tests	96/256 (37.5)

Results

INFANIB assessments

Age of assessment	Result	No./total (%)
3 months CA N=5812	Normal	4326/5812 (73.9)
	Transient	1438/5812 (24.6)
	Abnormal	48/5812 (0.8)
6 months CA N=5801	Normal	4185/5801 (71.5)
	Transient	1532/5801 (26.2)
	Abnormal	84/5801 (1.4)
9 months CA N=5833	Normal	5142/5833 (87.8)
	Transient	609/5833 (10.4)
	Abnormal	82/5833 (1.4)

	Neurological impairment at 1 year CA	
Characteristic	Present	Absent
GA at birth (weeks) N/total (%)		
30 or less	87 (34.5)	651 (11.7)
31-32	39 (15.5)	821 (14.8)
33-34	48 (19)	1700 (30.6)
35-36	56 (22.2)	56 (33.6)
More than 37	22 (8.7)	22 (9.2)
Birth weight (grams) N/total (%)		
Less than 1000	42 (16.4)	227 (4.1)
1001-1200	25 (9.8)	288 (5.1)
1201-1500	50 (19.5)	722 (12.9)
1501-1800	62 (24.2)	1336 (23.9)
1801-2000	26 (10.2)	1410 (25.2)
More than 2000	51 (19.9)	1617 (28.9)
NICU admission N/total (%)	116 (45.3)	1379 (24.6)
IVH N/total (%)	49 (19.8)	251 (4.7)
Oxygen dependency N/total (%)	131 (51.2)	1162 (20.7)
Neonatal anoxia N/total (%)	24 (54.4)	1635 (32)
Fetal distress N/total (%)	94 (36.7)	1950 (34.8)

Discriminative ability of Infanib

	Neurological outcome 1 year CA		Sensitivity	Specificity	ROC area	PPV	NPV
Infanib 3 months N= 5812	Abnormal	Normal					
Abnormal n=1486 (%)	156	1330	**62.2% (56-68%)**	**76.1% (75-77)**	0.69 (0.66;0.72)	10%	98%
Normal n=4326 (%)	95	4231					
Infanib 6 months N= 5801							
Abnormal (n=1616)	193	1423	**77.5% (71.8;82.5)**	**74.4% (73.2;75.5)**	0.76 (0.73;0.78)	12%	98%
Normal (n=4185)	56	4129					
Infanib 9 months N=5833							
Anormal (n=691)	196	495	**77.2% (71.5;82.2)**	**91.1% (90.4;91.9)**	0.84 (0.81;0.87)	28%	99%
Normal (n=5142)	58	5084					

Discussion

Results of the present study seem to confirm that early evaluation with Infanib may have an acceptable predictive validity to neurological outcome at one year of age.

Soleimani et al (2006): Evaluation of validity of Infanib in primary care. Infants 4 to 18 months. Sensitivity 90% Specificity 83% (General population)

Liao et al (2012): Predictive validity of a Chinese version of Infanib at 3, 7 and 10 months CA on neurological outcomes at 1 year CA. High risk premature and full-term infants

	Liao et al (2012) (high risk)			Our study (high risk)
	Preterm (n=55)	Full-term (n=49)		Preterm and/or LBW
3 months			**3 months** (n=5812)	
Sensitivity(95%CI)	76.9 (46.2;95)	76.9 (46.2;95)	Sensitivity (95%CI)	62.1 (56;68)
Specificity	57.1 (41;72.3)	41.7 (25.5;59.2)	Specificity	76.1 (75;77)
7 months			**6 months** (n=5801)	
Sensitivity	84.6 (54.6;98.1)	84.6 (54.6;98.1)	Sensitivity	77.5 (71.8; 82.5)
Specificity	57.1 (41;72.3)	72.2 (54.8;85.8)	Specificity	74.4 (73.2;75.5)
10 months			**9 months** (n=5833)	
Sensitivity	84.6 (54.6;98.1)	92.3 (64;99.8)	Sensitivity	77.2 (71.5; 82.2)
Specificity	81.0 (65.9; 91.4)	77.8 (60.8;89.9)	Specificity	91.1 (90.4;91.9)

Discussion

- Sensitivity of INFANIB is low at 3 months (62%), and statistically significantly different from sensitivities at 6 and 9 months.
- Sensitivities at 6 and 9 months are almost identical and non statistically different. The value is modest (77%) and not high enough for use as a screening test.
- Specificity increases steadily with age, the trend is clearly significant.

Discussion

- Overall discriminating ability (area under the ROC curve) also increases steadily with corrected age.
- These observations are consistent with the fact that abnormalities in neurodevelopment might be originated early (for instance at birth due to asphyxia) but manifestations become evident when the affected structures or functions should develop (maturation).
- In consequence, the more mature the infant when the evaluation is performed, the better the discriminant ability of the INFANIB test.

Discussion

- Ideal sensitivity of a screening test should be as close as possible to 100%
- According to this, INFANIB could be judged as insufficient.
- The issue is that one can not diagnose a problem that has not appeared yet. Neurodevelopment evolves in time, therefore there are abnormalities not present and impossible to detect at certain times, and a screening test or a confirmatory test will not detect them. (One cannot evaluate vocabulary and numerical reasoning or walking ability at 3 months of age).
- One should not confound diagnosis and prediction. Screening test do not predict but establish a preliminary diagnosis.

Discussion

- In summary although INFANIB at 9 month is not sensitive enough for diagnosis motor outcomes at one year, it detects those infants who do have a problem at 9 months. (Discriminate but do not necessarily predict). A normal Infanib means that the infant should continue under close clinical monitoring.
- Specificity at 9 months is very high (>90%). Meaning that an abnormal result is very likely to be a true positive finding.
- The other use of INFANIB is not to diagnose but to timely identify infants likely to benefit from early intervention.
- INFANIB at 3 and 6 months can help identifying infants in need for early intervention (physical therapy): reflected in a sharp decrease in number of abnormal Infanib results between 6 (1616) and 9 months (691)

Conclusion

- Periodic INFANIB testing can be informative and easily included in the routine physical exam made by the paediatrician in kangaroo follow-up programs.

- Should not be regarded as a screening test for future neuromotor impairment, given that sensitivity is not high enough. I.E. A negative result does not rule out future neuromotor impairment, and “normal” subjects should continue under close clinical surveillance, including periodic INFANIB testing.

Conclusion

- An abnormal INFANIB test particularly at 9 months should rise concern given the high specificity and prompt for aggressive and timely intervention.

- The quest for developing or identifying a better screening tool should continue.

Thank you