

A Neurobehavioral Intervention and Assessment Program in Very Low Birth Weight Infants: Outcome at 24 Months

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Objective To determine whether the Infant Behavioral Assessment and Intervention Program (IBAIP) improves development and behavior in very low birth weight (VLBW) infants at 24-month corrected age.

Study design In a multicenter, randomized, controlled trial 86 infants received postdischarge intervention until 6-month corrected age. The intervention consisted of supporting infants' self-regulation and development, and facilitating sensitive parent-infant interactions; 90 control infants received regular care. At 6 months, positive intervention effects were found. At 24 months, development and behavior were evaluated with the Bayley Scales of Infant Development-II (BSID-II) and the Child Behavior Check List (CBCL).

Results Eighty-three intervention and 78 control infants were available for follow-up. After adjustment for differences in perinatal characteristics, an intervention effect of 6.4 points (\pm standard error, 2.4) on the Psychomotor Developmental Index favored the intervention infants. Groups did not differ on the Mental Developmental Index, the Behavioral Rating Scale of the BSID-II, or on the CBCL. Subgroup analyses revealed improved motor as well as improved mental outcomes in intervention infants with bronchopulmonary dysplasia and with combined biological and social risk factors.

Conclusions The IBAIP shows sustained motor improvement in VLBW infants until 2-year corrected age. (*J Pediatr* 2010;156:359-65).

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Growing concern about the developmental, social-emotional, and health problems in very preterm infants that persist into early adulthood¹ have led to the design of various types of early postdischarge intervention programs that aim to improve the long-term outcome of these children. Recent meta-analyses^{2,3} reported a significant impact of postdischarge intervention on cognitive outcomes at infant and preschool age. There is heterogeneity of the programs, and further studies are needed to identify intervention components that are most effective. Apart from biological factors, the infant's self-regulatory competence^{4,5} as well as parental sensitivity and responsiveness⁵⁻⁷ were noted as crucial for the quality of parent-infant interactions. These, in turn, influenced the infant's developmental course after preterm birth.^{5,8-10} The Infant Behavioral Assessment and Intervention Program (IBAIP¹¹), based on the synactive theory by Als,¹² is designed to support infants with developmental risk from term to approximately 8 months of age. This program aims to support the infant's self-regulatory competence as well as the infant's multiple developmental functions in an integrative way, via responsive and positive parent-infant interactions. We conducted a randomized, controlled trial to study the effect of the IBAIP on very low birth weight infants (VLBW). At 6-month corrected age, we found that the program improved the mental, motor, and behavioral outcomes of VLBW infants.¹³ Neurobehavioral assessment demonstrated increased attention and engagement in interactions over time, accompanied by less stress behavior in the intervention infants compared with control infants. The principal outcome measures of our trial were child development at 6 months, shortly after termination of the intervention, and at 24 months. We report infant outcomes at 24-month corrected age.

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The trial is registered with controlled-trials.com, number ISRCTN65503576.

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VLBW	Very low birth weight	MDI	Mental Developmental Index
LBW	Low birth weight	PDI	Psychomotor Developmental Index
IBA	Infant Behavioral Assessment	CBCL	Child Behavior Check List
IBAIP	Infant Behavioral Assessment and Intervention Program	APIP	Avon Premature Infant Project
NIDCAP	Newborn Individualized Developmental Care and Assessment Program	MITP	Mother-Infant Transaction Program
BSID-II	Bayley Scales of Infant Development	BPD	Bronchopulmonary dysplasia
BRS	Behavioral Rating Scale	GA	Gestational age
		PMA	Post menstrual age

Methods

The Medical Ethics Committee of all hospitals involved approved the study design. We carried out a multicenter, randomized, controlled trial in 7 Amsterdam hospitals. Infants with gestational ages (GA) of <32 weeks and/or birth weights of <1500 g, with parents living in Amsterdam, were eligible for the study. Infants with severe congenital abnormalities, infants whose mothers had a documented history of illicit drug use or severe physical or mental illness, infants from non-Dutch-speaking families for whom an interpreter could not be arranged, and infants who participated in other trials on postdischarge management were excluded. Randomization into a control or intervention group was computer-generated, stratified for GA (<30 and \geq 30 weeks) and recruitment site. Interventions were carried out by 6 experienced pediatric physical therapists who had received 1 year of training in the IBAIP from the author of this program (Rodd Hedlund). IBAIP training involved the reliable assessment and support of neurobehavioral competence, the facilitation of affective, social, cognitive, and motor functioning of the infant in an integrated way, and the use of a strength and process-based approach to support the parent-infant relationship. A detailed written report with recommendations was provided to the parents after every session. These reports, along with regular contact with the supervisor (K.K.) and monthly reflection sessions, served to maintain the consistency of the intervention.

Intervention infants and their parents received 1 IBAIP session shortly before discharge and 6 to 8 home interventions until the baby was 6 months of corrected age. Control infants received standard care and, if required (non-IBAIP trained), pediatric physical therapy. Regular outpatient visits to the pediatrician were standard in both intervention and control groups.

The content of the IBAIP has been more extensively described elsewhere^{13,14} and is available from the Internet.¹¹ The implementation of the IBAIP by pediatric physical therapists resulted in a comprehensive intervention model in which “prevention” and “treatment” overlapped to a large extent, supporting the parents as well as the evolving infant-parent relationship and the infant’s emerging functions. Guided by the infant’s behavior, the interventionist provides suggestions to encourage parents to support their infant’s self-regulatory efforts and/or competence; to adjust the environment to their infant’s needs; to support positive parent-infant interactions; and to enhance postural control and successful infant explorations without distress. Parents were given detailed information about their infant’s development to guide parents along their infant’s next developmental steps and to support realistic expectations of their child’s functioning. Central to the IBAIP intervention is the support of the parent to raise their child. In addition, mindful attention to their infant’s behavioral expressions and development may enhance the parents’ emotional availability, intrinsic motivation, feelings of joy, and confidence in themselves and their child.

Neurobehavioral intervention focuses on overall developmental and behavioral support. In line with the outcome measures at 6 months, the Dutch version of the Bayley Scales of Infant Development-II (BSID-II) was used to assess infant development.¹⁵ A mental developmental index score (MDI) and a psychomotor developmental index score (PDI) were calculated for the corrected age of the child. MDI and PDI in the normal population have a mean of 100 (SD, 15). Observations of infants’ behavior during the developmental test administration were rated using the Behavior Rating Scale (BRS) of the BSID-II. According to the Dutch manual, the percentile scores of the “orientation/engagement and emotional regulation” factor and the “motor quality factor” were studied separately and summed up to a total score, with higher scores on the BRS reflecting more adequate testing behavior. A score of \geq 26 is classified as normal, 25 to 11 is questionable, and \leq 10 is nonoptimal test behavior.

The Dutch version of the Child Behavior Check List 1½ to 5 (CBCL)¹⁶ was used to evaluate the child’s behavioral and socio-emotional performance, as rated by the parent. It is a standardized questionnaire with good reliability and validity, containing 100 items on problem behavior occurring now or in the previous 2 months. An Internalizing, Externalizing, and a Total problem score can be calculated. Raw scores are transformed into T-scores, accounting for differences in sex and age. A T-score of <60 is classified as normal, 60 to 63 is borderline, and >63 is in the clinical range.¹⁶

The neurological examination according to Touwen¹⁷ was used to examine neurological functioning at 24 months. Abnormal development is severe abnormality of tone, posture, and movement leading to an impairment and/or delay in motor development. Mildly abnormal development is a moderate abnormality of tone, posture, and movement leading to a minor impairment and/or minor developmental delay.

Perinatal variables were taken from the medical records at discharge. GA was determined by maternal history and ultrasound examination in early pregnancy and confirmed postnatally with the Dubowitz-score if antepartum information was inconclusive.¹⁸ Bronchopulmonary dysplasia (BPD) was defined as moderate to severe BPD when the infant was oxygen dependent \geq 36 weeks.¹⁹ Sociodemographic data were obtained by a parent questionnaire. A multiple risk factor was created to explore the possible additive effect of biological and social risk, including low maternal education and abnormal cranial ultrasound and/or BPD.

Assessment Procedure

At 24-month corrected age, pediatric, neurological, and developmental assessment took place at the follow-up clinic of the Academic Medical Center and was carried out by an experienced pediatrician and psychologist, blinded for group assignment. Parents were aware of the group assignment and were instructed not to inform any of the outcome assessors. The CBCL was sent to the parents 2 weeks before the follow-up visit, to be completed by the parent that was most responsible for the care-taking of the child.

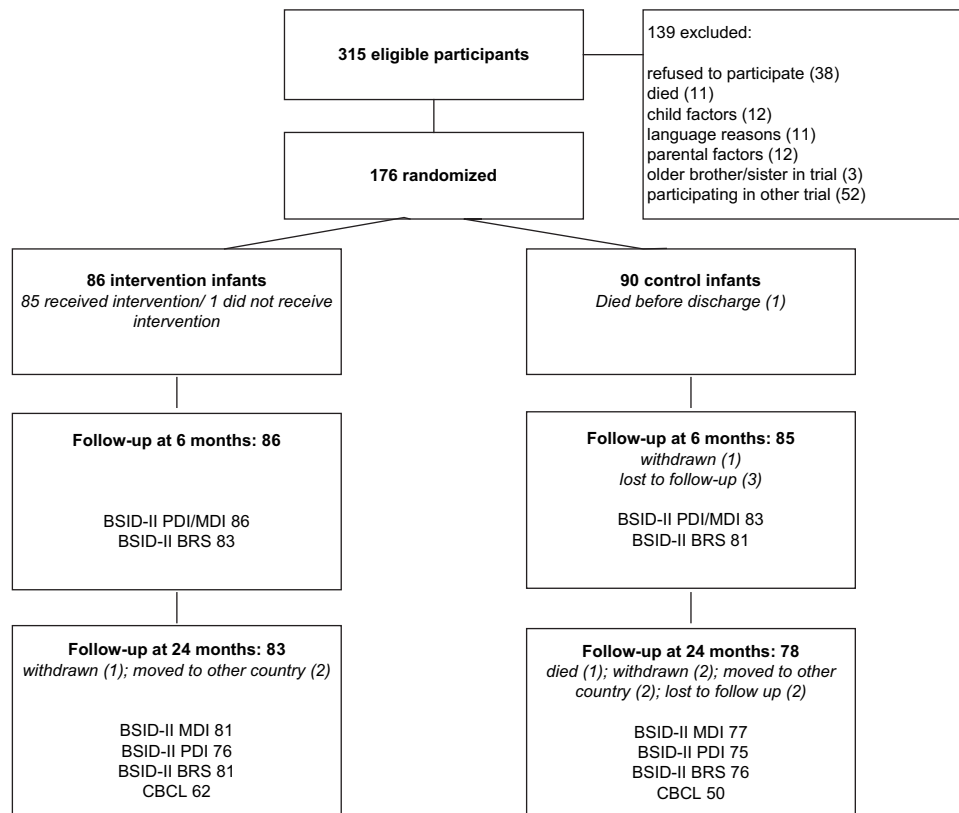


Figure. Patient flow and follow-up.

Outcome Measures

Primary outcome measures were the MDI and PDI of the BSID-II. Secondary outcomes were the BRS, CBCL, and neurologic measures.

Statistical Analysis

The sample size for this trial was selected to provide 90% power to detect a difference between intervention and control groups in BSID-II (PDI and/or MDI) at 6-month corrected age of 0.5 SD.¹³ With the initial sample size of 176 children and an assumed dropout rate at 24 months of 10%, the resultant sample size would provide slightly less than 90% power to detect a difference of 0.5 SD.

Data were analyzed using the SPSS 15.0 program (SPSS, Chicago, Illinois). Independent-samples *t* tests and χ^2 tests were performed to compare the 2 groups. Multivariate linear regression analyses were used to assess the effect of the intervention on the MDI, PDI, total-BRS, and CBCL scores, adjusting for baseline differences. Weeks of gestation, sex, cranial ultrasound abnormalities, and oxygen therapy ≥ 28 days were entered as fixed factors considering their potential influence on developmental and behavioral outcome. Although the number of low-educated mothers did not differ between the groups, the factor was added given its potential influence on infant developmental and behavioral outcome. Other factors associated with the primary outcomes, differ-

ing significantly between the intervention and control group (the use of indomethacin, dopamine, surfactant, and septic episodes), were entered stepwise.

Secondary analysis of the MDI and PDI were performed to explore the interaction between intervention and BPD, cranial ultrasound abnormality, gestational age, low maternal education, as well as multiple risk (low maternal education and abnormal cranial ultrasound and/or BPD). Post hoc *t* tests were performed to compare the outcomes of subgroups of infants with BPD and multiple risk. An α level of 0.05 was used for all tests of significance. All analyses were based on intention to treat. The trial is registered with controlled-trials.com, ISRCTN65503576.

Results

The 176 participating infants in this trial until 24-month corrected age are tabulated in the [Figure](#). One of 86 intervention infants did not receive the planned intervention because of severe psycho-social problems of the mother. According to the intention-to-treat principle, this infant was included in the intervention group. At 24 months, 83 (97%) intervention infants and 78 (89%) of the surviving control infants were available for follow-up. Perinatal and demographic characteristics of the group that was not available for follow-up did not differ from the group that was assessed at 24 months.

Table I. Sociodemographic and perinatal characteristics

	Intervention group (n = 83)	Control group (n = 78)	P
Social factors:			
Maternal age, mean (SD), y	32.4 (5.3)	32.2 (5.4)	.75
Paternal age, mean (SD), y	36.1 (7.1)	36.1 (6.5)	.96
Firstborn child (%)	59 (71)	49 (63)	.27
Family status of 2 parents (%)	68 (82)	70 (90)	.16
Mother born in The Netherlands (%)	49 (60)	47 (60)	.88
Father born in The Netherlands (%)	49 (60)	40 (51)	.32
Mother speaking Dutch (%)	75 (90)	62 (79)	.053
Maternal education (%)			
Not a high school graduate	30 (36)	29 (37)	
High school graduate	53 (64)	49 (63)	.89
Paternal education (%)			
Not a high school graduate	33 (40)	29 (37)	
High school graduate	46 (55)	49 (63)	.56
Perinatal factors			
Gestation (wk), mean (SD)	29.9 (2)	30.4 (2)	.16
Gestation <28 wk (%)	21 (25)	8 (10)	.013
Birth weight (g), mean (SD)	1238 (338)	1316 (321)	.14
Small for gestational age* (< -1 SD) (%)	21 (25)	15 (19)	.36
Sex: male/female	48/35	33/45	.049
Twins/triplets (%) [†]	27 (33)	23 (429)	.68
Antenatal steroid use, %	58 (70)	58 (73)	.53
Apgar score, at 5 min, mean (SD)	8.5 (1.6)	8.6 (1.4)	.70
Artificial ventilation, %	42 (51)	26 (33)	.027
Surfactant, %	34 (41)	16 (21)	.005
Oxygen therapy ≥28 d, %	33 (40)	14 (18)	.002
Oxygen therapy at 36-wk PMA, %	23 (28)	7 (9)	.002
Postnatal steroid use, %	5 (6)	2 (3)	.282
Indomethacin use, %	18 (22)	7 (9)	.026
Necrotizing enterocolitis, %	4 (5)	1 (1)	.196
Septic periods before discharge, %	51 (61)	30 (38)	.028
IVH grade I +II /III + IV [‡]	14/5	8/3	.96
PVL grade 1/ 2 + 3 [‡]	11/1	8/2	.43
Ventricular dilatation, %	2	3	.60
Cranial ultrasound normal/abnormal	52/31	59/19	.053
ROP grade ≥3, %	4	0	.050
At discharge			
PMA (wk), mean, SD	38 (16.9)	37.5 (16.6)	.24
Length of hospitalization (d), mean, SD	55.8 (25.8)	48.1 (21.4)	.04
Weight (g), mean, SD	2418 (448)	2364 (414)	.44
Breast milk at discharge, % [‡]	37 (45)	44 (56)	.15
Oxygen supply at discharge, %	5 (6)	3 (4)	.53

PMA, postmenstrual age. Numbers are given as number of infants unless otherwise stated. Independent-samples *t* tests and χ^2 tests.

*Small for gestational age was defined as <1 SD below the mean for Dutch reference data.

[†]At least 2 infants survived.

[‡]Either breast-fed or expressed milk.

[§]Cerebral hemorrhage (IVH) was defined according to Papile,²⁰ periventricular leukomalacia (PVL) according to de Vries.²¹

Children who could not complete the developmental assessment (>5 missing/incomplete items per scale) were excluded from the analyses (Figure). Parents of 62 intervention infants (75%) and of 50 control infants (64%) returned the CBCL questionnaires.

Sociodemographic factors were well-balanced (Table I).^{20,21} The child's parents were from various ethnic backgrounds; half of them were born in The Netherlands. Despite random assignment, more infants in the intervention group were <28 weeks GA than in the control group (21 vs 8; *P* = .013). In addition, there were more boys in the intervention group. More intervention infants had an abnormal cranial ultrasound, they had more septic episodes, and were oxygen dependent for a longer period ($O_2 \geq 28$ days and ≥ 36 weeks). Also, more intervention infants received indomethacin or surfactant and were hospitalized for a longer period of time.

Primary Outcomes

On the mental domain of the BSID-II, 69% intervention vs 63% control children were classified as normal (MDI >85); on the psychomotor domain, 50% intervention vs 45% control children were classified as normal (PDI >85).

The mean (\pm standard deviation [SD]) MDI scores were 91.7 ± 17 in the intervention group and 90.9 ± 18 in the control group (*P* = .72). Mean PDI scores were 87.5 ± 16 and 83.8 ± 14 , respectively (*P* = .12). After adjustment for perinatal and background variables a significant intervention effect was found on the motor scale of 6.4 ± 2.4 (*P* = .006). No intervention effect was found on the mental scale (2.4 ± 2.8 , *P* = .38). The effects of factors that independently influenced the primary outcomes and the adjusted means are summarized in Table II.

In total, there were 30 infants with BPD and 21 infants with multiple risk; 12 infants with BPD were included in the multiple risk group. Intervention children with BPD and with multiple risk had higher mental as well as higher motor scores compared with control children with these problems. In the children with BPD the mean \pm SD MDI scores were 88.5 ± 17.5 in the intervention children vs 73.0 ± 18 in the control children (*P* = .05, *n* = 23 vs 7); the mean PDI scores were 81.8 ± 17.6 in the intervention children vs 61.6 ± 10.0 in the control children (*P* = .009, *n* = 20 vs 7). In children with multiple risk, the mean MDI scores were 86.7 ± 17.1 in the intervention children vs 68.7 ± 11.0 in the control children (*P* = .029, *n* = 15 vs 6); the PDI mean scores were 85.7 ± 16.6 in the intervention children vs 63.8 ± 14.1 in the control children (*P* = .013, *n* = 13 vs 6).

Table III displays the multivariate linear regression analyses, which demonstrates the significant interaction between intervention and BPD and between intervention and multiple risk. No significant interaction was found between treatment and GA <28 and ≥ 28 weeks, cranial ultrasound abnormalities, or low maternal education. Performing the analyses with only 1 child per family in the case of multiples, to explore a possible nesting effect, did not change the results.

Table II. Multivariate regression models: Independent effect of factors on MDI, PDI, and BRS of the BSID-II at 24-month corrected age

MDI*				
Variable	Coefficient	SE	Standardized β	P
Gestation (wk)	-0.78	0.77	-0.09	.312
Male sex	-5.47	2.74	-0.16	.047
Abnormal ultrasound	+1.09	3.12	+0.29	.728
Oxygen therapy ≥ 28 d	-7.59	3.68	-0.20	.041
Low maternal education	-10.28	2.77	-0.29	.000
Intervention	+2.44	2.75	+0.07	.376
PDI†				
Variable	Coefficient	SE	Standardized β	P
Gestation (wk)	-0.30	0.68	-0.04	.653
Male sex	-1.48	2.41	-0.05	.541
Abnormal ultrasound	-3.25	2.73	-0.10	.236
Oxygen therapy ≥ 28 d	-11.03	3.22	-0.33	.001
Low maternal education	-0.09	2.47	-0.00	.972
Intervention	+6.40	2.40	+0.22	.009
BRS, total percentile score‡				
Variable	Coefficient	SE	Standardized β	P
Gestation (wk)	-1.10	1.40	-0.75	.428
Male sex	-2.36	4.77	-0.04	.622
Abnormal ultrasound	-0.07	5.48	-0.00	.990
Oxygen therapy ≥ 28 d	-15.06	6.61	-0.22	.024
Low maternal education	-19.77	4.82	-0.32	.000
Intervention	+2.92	4.80	+0.05	.543

Multivariate linear regression analyses: gestation, sex, abnormal ultrasound, $O_2 \geq 28$ days, and maternal education are included in the model as constant factors; the use of indomethacin, dopamine, surfactant, septic episodes, and intervention are entered stepwise. Intervention was included as fixed factor in which intervention was excluded from the model.

*The adjusted mean \pm SE MDI scores were 92.5 ± 2 in the intervention infants and 90 ± 2 in the control infants.

†The adjusted mean \pm SE PDI scores were 88.9 ± 2 in the intervention infants and 82.4 ± 2 in the control infants.

‡The adjusted mean \pm SE BRS total scores were 57.9 ± 3 in the intervention infants and 55 ± 4 in the control infants.

Secondary Outcomes

Behavioral. At 24 months, 84% of children in both intervention and control groups scored in the category normal test behavior on the BRS; 11% of the intervention, and 13% of the control children scored in the category questionable; 5% vs 3% scored nonoptimal. No statistically significant differences between the groups were found. The mean total percentile score \pm SD was 56.6 ± 31 in the intervention group and 56.3 ± 30 in the control group ($P = .89$). **Table II** shows the effects of factors that independently influenced the outcomes. No intervention effects were found. Also, no significant differences were found in problem behavior, as measured with the CBCL. The internalizing mean \pm SD T-score on the CBCL was 44.82 ± 9.4 in the intervention children and 46.2 ± 10.4 in the control children, the external-

izing mean \pm SD T-score was 48.0 ± 8.8 and 45.7 ± 9.7 , respectively, the total problem score was 45.81 ± 9.09 in intervention children and 45.2 ± 8.9 in control children. On the internalizing scale, 3 intervention children vs 4 control children scored above the borderline or clinical range; on the externalizing scale, 7 intervention versus vs 6 control children; on the total scale, 4 intervention vs 3 control children. No intervention effects were found after adjustment for differences in perinatal characteristics and low maternal education (not shown).

Neurological. No differences between the groups were found on neurological outcome measures. At 24 months, 5 intervention infants scored mildly abnormal and 3 intervention infants scored abnormal; in the control group, 3 infants scored mildly abnormal and 5 abnormal ($P = .24$). Between the end of the intervention at 6 months and the assessment at 24 months, significantly fewer intervention infants received paramedical support (pediatric physical therapy and/or occupational therapy and/or speech therapy) compared with control infants: 10 (13%) vs 21 (24%) infants, respectively ($P = .038$).

Discussion

IBAIP post discharge intervention, supporting VLBW infants until the corrected age of 6 months, improved the child's motor development at 24-month corrected age. We found a significantly better score on the psychomotor domain of the BSID-II after adjustment for perinatal factors and the influence of maternal education, which almost reached the preplanned half standard deviation. The positive intervention effect on mental and behavioral development that was found at 6 months was not seen at 24 months. However, in post hoc analyses, we found improved motor as well as improved mental development after IBAIP intervention in subgroups of children with BPD and children with multiple risk. Apart from the described outcomes, significantly fewer intervention infants received paramedical services after 6 months, and they were more compliant with follow-up, which underlines the positive effects of the intervention.

This study demonstrates motor improvement after postdischarge early intervention in VLBW infants at 24 months. Benefits on cognitive outcomes from age 2 on were reported earlier.^{2,3} The Infant Health and Development Program (IHDP) found a positive cognitive effect in LBW after 3 years of frequent home visits, attendance at a child development center, and parent group meetings.²² More recently, the APIP study²³ reported identical small cognitive gains of a developmental education program or a parent adviser program after supporting VLBW infants and families for 2 years. The most vulnerable VLBW infants (<1250 g and those with brain injuries) benefited most from the developmental curriculum. Both programs^{22,23} reported a strong relation between infant outcomes and social factors, such as the mother's educational level. We found only 1 short postdischarge early intervention

Table III. Multivariate regression models: Independent effect of factors, and interaction between BPD¹ and intervention, and a Multirisk factor² and intervention on MDI and PDI of the BSID-II at 24-month corrected age

Interaction between BPD and intervention								
Variable	MDI				PDI			
	Coefficient	SE	Standardized β	P	Coefficient	SE	Standardized β	P
Gestation (wk)	-0.562	0.695	-0.067	.420	0.198	0.609	0.028	.746
Male sex	-5.569	2.695	-0.161	.040	-1.538	2.387	-0.051	.520
Abnormal cranial ultrasound	2.414	3.124	0.064	.441	-2.193	2.754	-0.067	.427
BPD	-21.285	6.957	-0.482	.003	-22.379	6.039	-0.569	.000
Interaction BPD * intervention	16.222	7.740	0.330	.038	15.810	6.835	0.356	.022
Low maternal education	-9.520	2.724	-0.264	.001	1.036	2.436	0.033	.671
Intervention	0.234	2.935	0.007	.937	3.902	2.582	0.129	.133

Interaction between multiple risk and intervention								
Variable	MDI				PDI			
	Coefficient	SE	Standardized β	P	Coefficient	SE	Standardized β	P
Gestation (wk)	-0.604	0.667	-0.072	.366	0.162	0.645	0.022	.802
Male sex	-5.235	2.720	-0.152	.056	-2.493	2.404	-0.082	.301
Interaction multirisk * intervention	20.715	8.667	0.353	.018	17.566	7.638	0.327	.023
Multirisk	-25.881	7.225	-0.511	.000	-19.483	6.252	-0.129	.002
Intervention	0.170	2.910	0.005	.954	3.904	2.568	0.1290	.131
Indomethacin					-8.230	3.713	-0.196	.028

¹BPD: oxygen dependency ≥ 36 weeks. Multivariate linear regressions analyses: gestation, sex, abnormal cranial ultrasound, BPD, interaction BPD* intervention, low maternal education and intervention are included in the model as constant factors; the use of indomethacin, dopamine, surfactant, septic and septic episodes are entered stepwise.

²Multivariate linear regression analyses: gestation, sex, interaction multirisk* intervention, multirisk, and intervention are included in the model as constant factors; the use of indomethacin, dopamine, surfactant, and septic episodes are entered stepwise.

program²⁴ comparable in content to the IBAIP. It included infants <2000 g and ended at the corrected age of 3 months. This study applied a modified version of the Mother-Infant Transaction Program (MITP)²⁵ and found less parenting stress but no significant benefits in infant outcomes at age 2. The original version of the MITP reported increasing benefits in cognitive outcome from 3 years on, also preceded by enhanced parenting outcomes (maternal role satisfaction, maternal self-confidence and maternal perception of infant temperament), which suggests that intervention may have a delayed effect on cognitive outcome.

Improved motor outcome in the present study may be explained by the basic elements and timing of IBAIP implementation. Movement derives from the interactions between the individual, the task, and the environment in which the task is carried out.²⁶ We hypothesize that supporting both the infant's individual self-regulatory competencies as well as providing the environmental and task activities the infant expected and could handle, enhanced the infant's information processing and exploratory abilities. During early infancy, the sensory-motor system plays a key role in explorations as well as in self-regulation. Hence, these positive early experiences may have influenced the organization of the involved brain areas, on which the child could build after the intervention period.²⁷ Infants with BPD may have profited most from the intervention because they are particularly vulnerable to stress. Infants with BPD have difficulties in gaining homeostatic, postural, and state control. These problems make them more difficult to handle and harder to socially engage without physiological compromise,^{12,28}

which, in turn, may hinder their environmental explorations. The difference between intervention and control infants was stronger in those with multiple risk factors. This shows the need to support these often underserved groups with both adverse infant and parent characteristics.^{5,7,10} Unfortunately, these post hoc results are based on a small patient group, with fewer infants with BPD and multiple risk in the control group. Further studies are warranted to explore these promising effects of the IBAIP in high-risk infants.²⁹

Although better motor performance is expected to be intertwined with improvements in behavioral and cognitive development, this was not seen in the outcomes of all our children at 24 months. This may indicate the need of consistent and age-specific preventive interventions after 6 months to further boost the responsiveness of parents to their infant's development and self-regulation during increasingly complex skills (eg, social-emotional competencies and attention control, language, manipulation, and movement).^{4,30}

Given the impact of the IBAIP on motor development at 24 months and its encouraging effect on mental and motor development in the most vulnerable preterm infants, this neurobehavioral intervention program may contribute to the early resilience and developmental outcome of VLBW infants after discharge from hospital. We are now studying if the effect of the IBAIP sustains until early school age. ■

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References

- Saigal S, Doyle LW. An overview of mortality and sequelae of preterm birth from infancy to adulthood. *Lancet* 2008;371:261-9.
- Spittle AJ, Orton J, Doyle LW, Boyd R. Early developmental intervention programs post hospital discharge to prevent motor and cognitive impairments in preterm infants. *Cochrane Database Syst Rev* 2007;18(2):CD005495.
- VanderVeen JA, Bassler D, Robertson CM, Kirpalani H. Early interventions involving parents to improve neurodevelopmental outcomes of premature infants: a meta-analysis. *J Perinatol* 2009; Jan 15 (epub).
- Bronson M. Research to practice: supporting self-regulation in early childhood. In: Bronson M, editor. *Self-Regulation in Early Childhood: Nurture and Nature*. New York: Guilford Press; 2000. p. 167-98.
- Shonkoff JP, Phillips DA. Acquiring self-regulation. In: Shonkoff JP, Phillips DA, editors. *From Neurons to Neighbourhoods: The Science of Early Childhood Development*. Washington, DC: National Academy Press; 2001. p. 93-123.
- Gross SJ, Mettelman BB, Dye TD, Slagle TA. Impact of family structure and stability on academic outcome in preterm children at 10 years of age. *J Pediatr* 2001;138:169-75.
- National Scientific Council on the Developing Child, Young Children Develop in an Environment of Relationships. 2004 Working Paper No. 1. Retrieved December 8, 2008 from www.developingchild.net.
- Clark CAC, Woodward LJ, Horwood LJ, Moor S. Development of emotional and behavioural regulation in children born extremely preterm and very preterm: biological and social influences. *Child Dev* 2008;79:1444-62.
- Feeley N, Gottlieb L, Zekowitz P. Infant, mother and contextual predictors of mother-very low birth weight infant interaction at 9 months of age. *J Dev Behav Pediatr* 2005;26:24-33.
- Forcada-Guex M, Pierrehumbert B, Borghini A, Moessinger A, Muller-Nix C. Early dyadic patterns of mother-infant interactions and outcomes of prematurity at 18 months. *Pediatrics* 2006;118:e107-14.
- Hedlund R. The Infant Behavioral Assessment and Intervention Program. 1998. Available from: <http://www.ibaip.org>. Accessed February 9, 2009.
- Als H. A synactive model of neonatal behavioral organization. *Phys Occup Ther Pediatr* 1986;6:3-55.
- Koldewijn K, Wolf MJ, v Wassenaer A, Meijssen D, v Sonderen L, v Baar A, et al. The Infant Behavioral Assessment and Intervention Program for very low birth weight infants at 6 month corrected age. *J Pediatr* 2009;154:33-8.
- Koldewijn K, Wolf MJ, van Wassenaer A, Beelen A, Nolle F, Kok JH. The Infant Behavioral Assessment and Intervention Program to support preterm infants after hospital discharge: a pilot study. *Dev Med Child Neurol* 2005;47:105-12.
- Van der Meulen BF, Ruiter SAJ, Lutje Spelberg HC, Smrkovsky M. Bayley Scales of Infant Development-II. Netherlands version. Lisse: Swets Test Publishers; 2002.
- Achenbach TM, Rescorla. *LA Manual for the ASEBA Preschool Forms & Profiles*. Burlington, VT: University of Vermont, Research Center for Children, Youth, & Families; 2000.
- Touwen BCL. *Neurological Development in Infancy*. London: Spastics International Medical Publications/W. Heinemann Medical Books; 1976.
- Dubowitz L, Mercuri E, Dubowitz V. An optimal score for the neurological examination of the term infant. *J Pediatr* 1998;133:406-6.
- Jobe AL, Bancalari E. Bronchopulmonary dysplasia. *NICHD/NHLBI/ORD Workshop Summary*. *Am J Respir Crit Care Med* 2001;163:1723-9.
- Papile LA, Munsick-Bruno G, Schaefer A. Relationship of cerebral intraventricular hemorrhage and early childhood neurologic handicaps. *J Pediatr* 1983;103:273-7.
- de Vries LS, Eken P, Dubowitz LM. The spectrum of leukomalacia using cranial ultrasound. *Behav Brain Res* 1992;49:1-6.
- Brooks-Gunn J, Klebanov PK, Liaw F, Spiker D. Enhancing the development of low-birthweight, premature infants: changes in cognition and behavior over the first three years. *Child Dev* 1993;64:736-53.
- Johnson S, Ring W, Anderson P, Marlow N, Johnson S, Ring W, et al. Randomised trial of parental support for families with very preterm children: outcome at 5 years. *Arch Dis Child Fetal Neonatal Ed* 2005;90:909-15.
- Kaarens PI, Ronning JA, Tunby J, Nordhov SM, Ulvund SE, Dahl LB. A randomized controlled trial of an early intervention program in low birth weight children: outcome at 2 years. *Early Hum Dev* 2008;84:201-9.
- Achenbach TM, Howell CT, Aoki MF, Rauh VA. Nine-year outcome of the Vermont Intervention Program for Low-Birthweight Infants. *Pediatrics* 1993;91:45-55.
- Shumway-Cook A, Woollacott MH. Motor control: issues and theories. In: *Control Motor*, editor. *Theory and Practical Applications*. 2nd ed. Baltimore, MD: Lippincott, Williams & Wilkins; 2001. p. 1-26.
- Nelson CA. The neurobiological bases for early intervention. In: Shonkoff JP, Meissels SJ, editors. *Handbook of Early Childhood Intervention*. Cambridge: Cambridge University Press; 2000. p. 204-27.
- Brown NC, Doyle LW, Bear MJ, Inder TE. Alterations in neurobehavior at term reflect differing perinatal exposures in very preterm infants. *Pediatrics* 2006;118:2461-71.
- Anderson PJ, Doyle LW, FRACP. Neurodevelopmental outcome of bronchopulmonary dysplasia. *Semin Perinatol* 2006;30:227-32.
- National Scientific Council on the Developing Child. *The Timing and Quality of Early Experiences Combine to Shape Brain Architecture*. 2007 Working Paper 5. Retrieved February 18, 2009, from <http://www.developingchild.net>.