Individualized Developmental Care for the Very Low-Birth-Weight Preterm Infant

Medical and Neurofunctional Effects

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Objective.—To investigate the effectiveness of individualized developmental care in reducing medical and neurodevelopmental sequelae for very low-birth-weight infants.

Design.—Randomized controlled trial.

Setting.—Newborn intensive care unit.

Patients.—Thirty-eight singleton preterm infants, free of known congenital abnormalities, weighing less than 1250 g, born before 30 weeks' gestation, mechanically ventilated within 3 hours of delivery and for more than 24 hours in the first 48 hours, randomly assigned to a control or an experimental group.

Intervention.—Caregiving by nurses specifically trained in individualized developmental care; observation and documentation of the infants' behavior within 12 hours of admission, and subsequently every 10th day; developmental care recommendations and ongoing clinical support for the nurses and parents based on regular observation of the infant by developmental specialists; and the availability of special caregiving accessories.

Main Outcome Measures.—Medical outcome, including average daily weight gain; number of days the infant required mechanical ventilation, oxygen, gavage tube feeding, and hospitalization; severity of retinopathy of prematurity, bronchopulmonary dysplasia, pneumothorax, and intraventricular hemorrhage; pediatric complications; age at discharge; and hospital charges. Neurodevelopmental outcome, including Assessment of Preterm Infants' Behavior scale and quantified electroencephalography (2 weeks after due date); and Bayley Scales of Infant Development and Kangaroo Box Paradigm (9 months after due date).

Results.—The infants in the experimental group had a significantly shorter duration of mechanical ventilation and supplemental oxygen support; earlier oral feeding; reduced incidence of intraventricular hemorrhage, pneumothorax, and severe bronchopulmonary dysplasia; improved daily weight gain; shorter hospital stays; younger ages at hospital discharge; and reduced hospital charges compared with the infants in the control group. At 2 weeks after their due dates, these infants also showed improved autonomic regulation, motor system functioning, self-regulatory abilities, and visual evoked potential measures; and at 9 months, they had improved Bayley Mental and Psychomotor Developmental Index scores, as well as Kangaroo Box Paradigm scores.

Conclusion.—Very low-birth-weight preterm infants may benefit from individualized developmental care in the neonatal intensive care unit in terms of medical and neurodevelopmental outcome.

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VERY LOW-BIRTH-WEIGHT infants who need mechanical ventilation are at high risk for bronchopulmonary dysplasia (BPD), intraventricular hemorrhage (IVH), and retinopathy of prematurity. These conditions are frequently associated with long-term pulmonary, neurological, cognitive, behavioral, and emotional compromise. They produce high costs in newborn intensive care and ambulatory care after discharge.[1] Reducing such costs is a top priority for current neonatal intensive care.

Current neonatal intensive care unit (NICU) environments, with their constant noise, lights, and procedures, have been found to influence infants' arterial oxygen saturations directly and contribute to the development of chronic lung disease.[2] Concerns have also been raised that unexpected activation of the premature infant's immature brain, as occurs in the NICU environment, may inhibit developing neuronal pathways and interfere with full differentiation.[3]

For editorial comment see p 890.

Changing the NICU environment to reduce stress to the infant may help improve these outcomes. An approach to intensive care has been developed that is geared to support the individual infant's own efforts toward self-regulation and competent functioning. Since even very immature infants display reliably observable behaviors in the form of autonomic and visceral responses, movement patterns, postures, tone fluctuation, and levels of awakeness,[4,5] repeated systematic observation of the infants' behavior before, during, and after provision of care is used to identify the infants' current behavioral goals, strengths, and vulnerabilities. Trained staff then deliver care in a way that makes use of and enhances the infants'

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Dr Als holds a patent for the bunting, one of the special caregiving accessories available for the infants in the experimental group. She has a royalty arrangement with the manufacturer and a contract with the coinventor for profit sharing.

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specific strengths and diminishes their vulnerabilities. The approach is referred to as individualized, developmentally focused intensive care[6] and is increasingly advocated clinically. So far, however, only two investigations have tested its effectiveness. Both used phase-lag historical designs.[7,8] The purpose of the current study was to test the impact of individualized developmental care, with the use of a more rigorous design with random assignment and initiation of the intervention at the time of admission.

PATIENTS AND METHODS

The study was conducted at the Brigham and Women's Hospital in Boston, Mass, in a 46-bed, level III NICU, with a 98% inborn population, and with primary care nursing.

Patients

The study population was derived from a group of 43 eligible infants consecutively admitted in a 21-month period, who met the following criteria: (1) inborn; (2) birth weight less than 1250 g; (3) less than 30 weeks and more than 24 weeks of estimated gestational age at birth[9]; (4) mechanical ventilation starting within the first 3 hours after birth and (5) lasting longer than 24 hours in the first 48 hours; (6) alive at 48 hours; (7) absence of chromosomal or other major genetic anomalies, congenital infections, and known fetal exposure to drugs of addiction; (8) singleton; (9) at least one family member with some English-language facility; (10) telephone access; and (11) living within the greater Boston area.

On admission to the NICU, infants were screened for meeting selection criteria 1 through 4 and 7 through 11. Informed consent was obtained in accordance with the study hospital's guidelines. Group status was determined by means of a sealed-envelope random assignment procedure. Experimental primary care teams were assigned to the care of infants in the experimental group within 3 hours. Control group status was not revealed to staff, nor was staffing for infants in the control group influenced in any way. Four infants were judged not viable by the admitting physician; all four of these died. One family refused participation.

Experimental Intervention

The experimental treatment consisted of staffing by specially educated nurses; regular evaluation of the infants' behavior with suggestions for ways to support their development, performed by a developmental psychologist (H.A.) and/or a developmentally trained clinical nurse specialist (G.L.); and the availability of special caregiving accessories.

Forty of 160 nurses volunteered for education in developmental care. This education was conducted by the psychologist and the nurse specialist before the start of the experimental component of the project. It was geared to bring about a shift from protocol-dependent to strategic thinking, with focus on the recognition of infants as being competent and as actively participating in their own care and shaping their own development. Extensive training[5,6] in the systematic observation of each infant's unique repertoire of behaviors, and in the understanding of the opportunities these behaviors offer for care provision, constituted the core of this education, as described elsewhere.[2] For the infants in the experimental group, at least one shift in a 24-hour cycle from admission on was staffed by a nurse specifically educated in this approach.

The psychologist and clinical nurse specialist provided ongoing support for the care teams and parents of the infants in the experimental group in jointly planning and implementing individually supportive care and environments. To this end, they conducted formal observations of each infant's behavior, starting during the acute phase of initial stabilization within 12 hours of admission, and subsequently every 10th day until hospital discharge. For each observation, the infants' responses were systematically recorded for approximately 20 minutes before a necessary medical or nursing caregiving activity, throughout the duration of the caregiving, and for approximately 20 minutes after the caregiving activity.

Ninety-one behaviors, including autonomic (respiration, heart rate, color changes, visceral signs), motor (postures, muscle tone fluctuations, movements), and state organization behaviors (levels of arousal, patterns of transitions between states, clarity and robustness of sleep and awake states), were monitored every 2 minutes.[5,7] Interrater reliability was established at greater than 85% accuracy. Behaviors were conceptualized as stress (eg, flaccidity, agitated or frantic movements, hyperextensions, duskiness, respiratory pauses, gagging, spitting up, finger splaying, arching, gaze aversion) and regulatory behaviors (eg, hand to mouth, hand clasping, grasping, efforts to suck, tucking) and interpreted as indexes of the infants' current vulnerabilities and strengths, respectively.

The observations were then used to formulate descriptive neurobehavioral reports, including specific suggestions for ways to promote the infants' stability and competence in regulating themselves. Suggestions included, for instance, gently placing the infant in a flexed position to promote restfulness; encouraging supportive holding during and after procedures and taxing manipulations; structuring sleep and feeding in synchronization with the infant's sleep and wake cycles; instituting dark and quietness; and, from admission on, supporting the parents in assisting as well as in nurturing and caring for their infants. Several accessories specifically designed to support the experimental group infants could be used as indicated, including a terry cloth bunting, a hammock, and a soft nipple sewn into a long, soft terry cloth band. The behavioral reports were used by the parents and primary care teams, with support by the psychologist and nurse specialist, to formulate specific individualized developmental care plans for the infants in the experimental group.

Control Group Treatment

Control group infants received the standard care practiced throughout the Brigham and Women's Hospital NICU. This included primary care nursing and a standard developmental protocol, involving uniform shielding of incubators with blanket covers, use of clothing, as well as a 24-hour visiting policy for the parents.

Background and Outcome Assessment

The effectiveness of the individualized, developmentally based approach to intensive care was assessed in terms of medical and developmental outcome at 2 weeks and 9 months after the expected date of confinement (EDC). After discharge, the infants' medical records, after removal of the neurobehavioral reports, were reviewed by trained research staff who were unaware of the group status of the infants and the goals of the study. Medical background variables assessed included birth weight; gestational age at birth[9]; Apgar scores[10] at 1 and 5 minutes; mean and maximum levels of fractions of inspired oxygen in the first 48 hours and first 10 days; the presence of patent ductus arteriosus; mode of delivery; obstetric complications[11]; and antenatal corticosteroid treatment, all known to influence outcome. Demographic background variables included maternal age, social class,[12] marital status, child's gender, birth order, and ethnic background. The interaction of gender and ethnic background with the mean and maximum levels of fraction of inspired oxygen in the first 48 hours and to day 10, and with patent ductus arteriosus, were also assessed.

Medical outcome variables included days of mechanical ventilator support, ie,

Table 1.—Medical and Demographic Background Variables*

Variable	Control Group (n=18)	Experimental Group (n=20)	df	F	χ^2	P
Birth weight, g	862±145	872±173	1, 36	0.04	...	.85
Gestational age at birth, wk	26.5±1.4	27.1±1.6	1, 36	1.90	...	.18
Apgar score						
1 min	2.9±1.7	3.8±2.3	1, 36	1.88	...	.18
5 min	5.5±1.8	5.6±2.5	1, 36	0.02	...	.89
Fraction of inspired oxygen						
1st 48 h						
Mean	0.55±0.19	0.48±0.17	1, 36	1.20	...	.28
Maximum	0.85±0.23	0.80±0.24	1, 36	0.42	...	.52
Day 1-day 10						
Mean	0.38±0.11	0.33±0.08	1, 36	2.77	...	.11
Maximum	0.86±0.22	0.81±0.24	1, 36	0.39	...	.53
Maternal age, y	28.33±5.18	27.65±5.63	1, 36	0.15	...	.70
Obstetric Complications Scale scores (mean, 100; SD, 20)	58.72±11.45	59.10±11.85	1, 36	0.01	...	.92
Patent ductus arteriosus, No. yes/no	9/9	8/12	1	...	0.38	.54
Prenatal corticosteroids, No. yes/no	1/17	3/17	1	...	0.90	.34
Parents married or attached, No. yes/no	16/2	18/2	1	...	0.01	.91
No. firstborn/later born	9/9	9/11	1	...	0.10	.76
Sex, No. M/F	11/7	9/11	1	...	0.99	.32
Race, No. black/other	3/15	8/12	1	...	2.51	.11
Race of female infants, No. black/other	2/5	4/7	1	...	0.12	.73
Vaginal deliveries, No. yes/no	7/11	7/13	1	...	0.06	.80
Social class, No. I and II/III/IV and V	10/3/5	9/4/7	2	...	0.43	.81

*Results are mean±SD except as otherwise stated. One-way analysis of variance: F, two tailed; χ^2 test, two tailed.

Table 2.—Medical Outcome Variables*

Variable	Control Group (n=18)	Experimental Group (n=20)	df	F	χ^2	P
Average daily weight gain from birth to 2 wk after EDC, g	20±6	24±7	1, 36	3.18	...	.08
Age after LMP at discharge, wk	48.3±17.3	39.7±3.1	1, 18	4.27	...	.05
No. of days in hospital	151±120	87±26	1, 18	4.78	...	.04
No. of days of mechanical ventilation	63.8±72.9	28.3±23.3	1, 20	3.93	...	.06
No. of days of oxygen	139.4±166.1	56.8±39.3	1, 19	4.25	...	.05
No. of days before bottle feeding	104.1±85.8	59.2±25.8	1, 18	4.33	...	.05
Pediatric Complications Scale scores (mean, 100; SD, 20)	53.1±2.5	55.5±4.4	1, 31	4.43	...	.04
Hospital charges, $1000s	189±174	98±37	1, 18	4.72	...	.04
Retinopathy of prematurity, No.						
None	5	10				
Mild (stages I and II)	10	8	2	...	1.99	.37
Moderate (stage III)	3	2				
Severe (stages IV and V)	0	0				
Bronchopulmonary dysplasia, No.						
None	3	2				
Mild (stage I)	7	13	3	...	9.21	.03
Moderate (stage II)	2	5				
Severe (stage III)	6	0				
Pneumothorax, No.						
No	12	19				
Mild	1	1	3	...	6.49	.09
Moderate	3	0				
Severe	2	0				
Intraventricular hemorrhage, No.						
None	8	19				
Grade I	3	0				
Grade II	1	0	4	...	12.75	.01
Grade III	2	1				
Grade IV	4	0				

*Results are mean±SD except as otherwise stated. Brown-Forsythe one-way analysis of variance: F, two tailed; χ^2, two tailed. EDC indicates expected date of confinement; LMP, last menstrual period.

endotracheal intubation; days of oxygen therapy; incidence and severity of pneumothorax and of BPD assessed by double-blind review of chest roentgenograms (J.G.B.),[13] of IVH assessed by double-blind review of cranial ultrasound scans by a consultant senior radiologist,[14] and of retinopathy of prematurity assessed by the NICU pediatric ophthalmologist[15]; days of intravenous and gavage tube feeding; average daily weight gain to 2 weeks after EDC; gestational age at discharge; number of days of hospital stay; pediatric complications[16]; and hospital charges from admission to discharge. Developmental outcome evaluation included, at 2 weeks after EDC, the Assessment of Preterm Infants' Behavior (APIB) using the 32 standard a priori variables,[1] as well as quantified electroencephalography and evoked potentials with topographic mapping.[3] At 9 months after EDC, it included the Bayley Scales of Infant Development[17] and a videotaped 15-minute play observation (Kangaroo Box Paradigm).[18] Weight, height, and head circumference were measured at both age points. All developmental outcome assessments were conducted at the Enders Pediatric Research Laboratories, Children's Hospital, Boston, Mass, by trained examiners not familiar with the goals of the study or the group membership of the infants.

Analyses

At a probability level of $<.05$, two tailed, the sample size chosen ensures the detection of medium to large effects accounting for between 23% and 69% of the variance.[19] For those outcome variables that showed significant group differences in terms of variance, instead of the one-way analysis of variance test (F), the conservative Brown-Forsythe Equality of Means Test (F^*)[20,21] was used, which does not assume equivalence of variances between groups. For categorical variables, the χ^2 test with Yates' correction was used. Canonical correlation analysis,[22] which defines covariation for two groups of variables, was performed to test the relationship of the behavioral findings from the newborn to 9-month testing. Path analysis[23,24] was used to investigate the influence of IVH and BPD on the other significant outcome findings. The technique was used as a way of describing partial associations within the structure of the data. It does not imply completeness of the model.

RESULTS

None of the background measures showed significant differences (Table 1), nor did any of the interactions tested, supporting the assumption of comparability of the control and experimental groups on admission to the study.

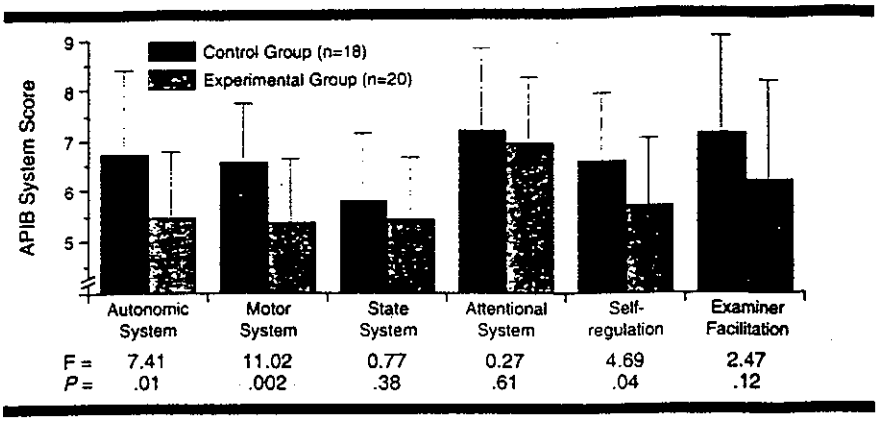

Figure 1.—Assessment of Preterm Infants' Behavior (APIB) system scores 2 weeks after expected date of confinement (mean±SD). Higher scores represent more poorly organized performance. Scores for autonomic, motor, state, and self-regulation systems are based on 18 scores per infant; for the attentional system, three scores; and for examiner facilitation, six scores. Significant F scores for the autonomic, motor, and self-regulation systems indicate that infants in the experimental group had better functioning of these systems.

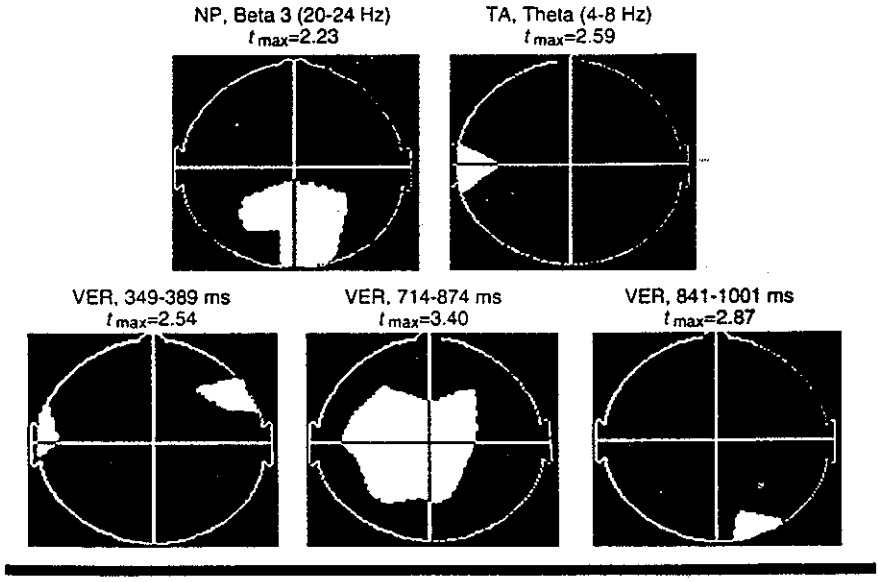

Figure 2.—Electrophysiological group differences 2 weeks after expected date of confinement. Schematic outlines show the nose at the top, the left ear to the left, and the right ear to the right. The white areas represent regions of significant between-group differences ($P<.05$, two tailed). The state of brain activation and the maximum t value (t_{max}) are as follows: nonprocessing awake (NP), in the electroencephalographic beta 3 range of 20 to 24 Hz; tracé alternant (TA), or quiet sleep, in the electroencephalographic theta range of 4 to 8 Hz; and visual-evoked response (VER) in quiet sleep from the times indicated. There were 14 infants in the control group and 17 in the experimental group.

Medical Outcome

Of the 12 medical outcome variables, eight were statistically significantly different, favoring the experimental group (Table 2). Although severity of lung disease and incidence of pneumothorax were significantly lower for the experimental group, there was no significant correlation between them (r=.17; P>.50). The earliest pneumothorax occurred on day 3 and the latest on day 21, ie, all well beyond the time of treatment onset for the experimental group.

Significantly more infants in the control group developed IVH, again after the time of treatment onset for the experimental group. Of the 10 infants in the control group with IVH, eight had normal ultrasound studies of the head on days 1 and/or 2, with the day of birth counted as day 0. One infant had a questionable grade II IVH on the first ultrasound performed on day 1, and one had a grade IV IVH by day 2, when the first ultrasound was performed. The one infant in the experimental group with IVH showed a grade II IVH on the first ultrasound performed on day 1, which developed into a grade III IVH by day 2. Although IVH was significantly more common in the control group, the correlation of IVH with severity of lung disease (r=−.009; P>.50) was not significant. Thus, the experimental group appeared to show an independent reduction in lung and in brain morbidity.

Developmental Outcome

Age at developmental outcome assessment was similar for the two groups at both outcome points (mean±SD, 18±5 vs 16±4 days after EDC and 9.2±0.6 vs 9.4±0.5 months after EDC). Growth variables measured did not show group differences at either outcome point. However, at 2 weeks after EDC, three of the six APIB system scores, ie, more than expected by chance, were significantly different, all favoring the infants in the experimental group. Figure 1 shows the APIB system score comparisons. Infants in the experimental group were better modulated in autonomic and motor system regulation, as well as in self-regulation. Furthermore, four of the 18 APIB summary variables[25]—symmetry of orientation (P<.003), autonomic stability (P<.0002), modulation of tone, movement, and posture (P<.03), and symmetry of motor performance (P<.02)—showed differences, favoring the experimental group, which also showed a significantly lower number of abnormal reflexes (P<.002) as assessed on the APIB.

Results of the neuroelectrophysiological evaluation in the brain activation states of alert processing, awake and not processing, quiet sleep, and flash visual-evoked response during quiet sleep for 14 infants in the control group and 17 in the experimental group identified five regions of significant differences between groups (Figure 2). These involved the parieto-occipital regions, the left midtemporal region, the right frontal and occipital regions, and a large bilateral central region. Two-group stepwise discriminant function analysis entering all five variables numerically representing the regions depicted yielded a Wilks' Λ of 0.476 (P<.0003), implying a large difference between the groups. Classification was 83.9% successful.

By 9 months after EDC, two infants in the control group were unavailable for study. On assessment with the Bayley Scales of Infant Development, the experimental group compared with the control group showed a significantly higher Mental Developmental Index (118.30±17.35 vs 94.38±23.31; F=12.47; df=1, 34; P≤.001) and Psychomotor Developmental Index (100.60±20.19 vs 83.56±17.97; F=6.97; df=1, 34; P≤.01).

Furthermore, of 20 infant variables measured in the 6-minute Kangaroo Box Paradigm Play Episode, 17 showed differences favoring the experimental group. They ranged in significance level

from <.03 to <.0001. The largest differences were found in gross and fine motor modulation, overflow postures and associated movements, complexity and modulation of combining object and social play, ability to stay engaged in the task, and degree of facilitation necessary. In the 6-minute Stillface Episode, 12 of 19 infant variables showed significant group differences ($P<.04$ to $<.0001$), again favoring the experimental group. None of the 14 parent variables assessed showed a significant group difference, yet three interaction variables (turntaking, overall synchrony of the interaction, and overall quality of the interaction [all $P<.0004$]) favored the experimental group. Thus, the infants in the experimental group appeared significantly more well organized, well differentiated, and well modulated than the infants in the control group. Canonical correlation between the factors derived from the APIB variables and the factors derived from the Kangaroo Box variables was significant (canonical $r=.84367$; $\chi^2=50.77$; $df=20$; $P<.0002$). This indicates a strong relationship between overall behavioral regulation at 2 weeks, as measured with the APIB, and overall regulation at 9 months, as measured with the Kangaroo Box Paradigm.

Influence of IVH and BPD

Neither IVH nor BPD had significant indirect effects on any of the medical outcome variables (Table 3). In terms of electrophysiological outcome, IVH had a significant indirect effect on only one variable. However, the direct intervention effect was stronger. The presence of BPD had no indirect effect on any of the electrophysiological findings. Neither IVH nor BPD had any significant indirect effects on any of the APIB or Bayley outcome measures. Furthermore, only two of the 32 Kangaroo Box measures showed significant indirect IVH effects, and none showed indirect BPD effects. Thus, the direct effects of the intervention appeared to go beyond the indirect contribution from reduction in IVH and BPD on the other outcomes.

Table 3.—Path Analysis to Medical, Electrophysiologic, and Behavioral Outcome Measures via IVH and BPD*

Variable	Direct Effect (P_{14})	Indirect Effect IVH ($P_{24}\times P_{12}$)	Indirect Effect BPD ($P_{34}\times P_{13}$)	r
Medical outcome measures (n=38)				
Age after LMP at discharge	−0.32†	0.12	−0.14	−.34†
No. of days in hospital	−0.32†	0.11	−0.15	−.36†
No. of days of oxygen	−0.31†	0.13	−0.16	−.34†
No. of days before bottle feeding	−0.27	0.08	−0.14	−.35†
Pediatric Complications Scale scores	0.24	0.02	0.07	.32
Hospital charges	−0.27	0.07	−0.16	−.36†
Electrophysiological outcome (n=31)				
Awake nonprocessing, beta 3 (20-24 Hz)	0.18	0.23	−0.01	.41†
Quiet sleep, theta (4-8 Hz)	−0.28	−0.16	0.01	−.44†
VER				
From 349-389 ms	0.25	0.19	−0.00	.44†
From 714-874 ms	−0.32†	−0.29†	−0.01	−.61‡
From 841-1001 ms	0.15	0.30	−0.00	.44†
Behavioral outcome: APIB (n=38)				
Autonomic system	−0.31†	0.01	−0.12	−.41†
Motor system	−0.45†	0.02	−0.05	−.48§
Self-regulation system	−0.36	0.07	−0.05	−.34†
Symmetry of orientation	0.53§	−0.02	−0.02	.49§
Autonomic stability	0.36†	0.00	0.13	.48§
Modulation of tone, movement, and posture	0.19	0.06	0.10	.35†
Symmetry of motor performance	0.38	0.03	−0.03	.39†
No. of abnormal reflexes	−0.50§	0.09	−0.07	−.49§
Behavioral outcome: Bayley Scales (n=36)				
Mental Developmental Index	0.41†	0.04	0.08	.52§
Psychomotor Developmental Index	0.24	0.07	0.10	.41†

*The path analysis tests the relationship of the independent variable, namely, the experimental treatment, to each of the dependent variables, namely, the outcome variables, taking the two intervening variables, intraventricular hemorrhage (IVH) and bronchopulmonary dysplasia (BPD), into account. The direct effect (P_{14}) and the two indirect effects ($P_{24}\times P_{12}$ and $P_{34}\times P_{13}$) sum to yield Pearson product moment correlations (r) between the experimental treatment and the outcome variables. LMP indicates last menstrual period; VER, visual-evoked response; and APIB, Assessment of Preterm Infants' Behavior.

†$P\leq.05$, two tailed.

‡$P\leq.005$, two tailed.

§$P\leq.01$, two tailed.

COMMENT

This study shows significant effects of a developmentally based, individualized approach to newborn intensive care, in terms of improved medical status and developmental outcome. Chance cannot account for the findings, since the number of effects was significantly larger than would be expected.[19] The pattern of the results was orderly and in keeping with the theory underlying the approach tested, which sees infants in the NICU as actively seeking behavioral support of their initial stabilization, ongoing differentiation, and developmental progression. Support to the infants' behavioral organizational efforts and competencies from the initial acute phase on may yield calmer infants, resulting in reduced cerebral blood flow velocity changes and fewer IVHs.[26] Since eight of 10 IVHs in the control group definitely occurred after the onset of the study, only two may potentially have occurred in utero, as did possibly the one IVH in the experimental group.[27] When these three instances of possibly intrauterine hemorrhages were excluded, the difference in incidence between the two groups was still significant ($P<.002$). Calmer infants also may require less supplemental oxygen and therewith develop less severe lung disease. This is in keeping with accepted mechanisms of lung disease.[28] The relatively low overall incidence of retinopathy of prematurity in both groups may in part be attributable to the covering of incubators in the study nursery for all infants,[29] and perhaps the closer attention to oxygenation levels.

Given the reduction in severity of lung disease and in incidence of IVHs, one would expect better neurobehavioral outcomes. The reduction in IVH did indeed contribute to some extent to improved neurobehavioral functioning and especially to improved neuroelectrophysiological functioning. The large bilateral central region found in the control group on the quantified electroencephalogram is consistent with data from positron emission tomographic studies,[30] suggesting broad regions of hypometabolism associated with extensive IVH. Yet a large number of outcome differences do not appear to be attributable to increased IVH and BPD in the control group, as the lack of correlation between IVH and BPD and the results of the path analysis showed. In fact, of the six infants in the control group with severe IVH (grade III and IV), only one showed severe chronic lung disease. Of the other five infants with severe BPD, three had no IVH and two had a grade I IVH only. The direct effect of the intervention may in part be associated with a reduction in progressive central nervous system injury from chronic hypoxemia[31] or might also reflect differences in sensory environmental experience,[3] leading to im-

proved brain development and neurobehavioral functioning. The strong correlation of improved neuroregulation in the newborn period and at 9 months appears to support the postulation of improved brain development.

Despite the encouraging results of this study, caution in interpretation is nevertheless indicated for several reasons. Although none of the background measures available showed significant group differences, other measures of initial severity of respiratory illness, such as mean airway pressure, will need to be evaluated in a future study. Furthermore, one might want to evaluate the developmental approach for a very low-birth-weight population treated with surfactant,[32] although to date, no significant surfactant effects on health and development at 1 and 2 years of age have been reported.[33]

A further factor to be considered in interpreting the results of this study is the possible differential skill, maturity, previous NICU experience, and motivation of the nursing staff who volunteered for developmental education, which might have accounted for the improved outcome in the intervention group. However, the nurses who volunteered were significantly younger (29.4±3.5 vs 32.3±4.5 years; $P<.002$) and had fewer years of NICU experience (4.7±3 vs 7.1±4.3 years; $P<.005$). Motivation is harder to measure. It will be important to study the success of developmental education for staff who are required to obtain such education, rather than who volunteer to do so. Since the study was conducted in one unit, it is probable that spillover of developmental care principles to control infants occurred. This is not of concern, however, since it would work against finding an effect.

A possible confounding factor on outcome at 9 months might be the effect of early intervention after hospital discharge. However, there was no difference in the number of infants in the control group who received early intervention after discharge compared with infants in the experimental group (14 of 16 vs 11 of 20; $P<.08$). Although information on outcome beyond 9 months is not available at this point, other studies have indicated predictive validity of the APIB and Kangaroo Box Paradigm assessments to ages 5 and 8 years.[34,35]

In summary, this highly controlled, randomized trial suggests that for very low-birth-weight, initially very ill, and early born infants, individualized, developmentally based intensive care improves outcomes medically and developmentally. The results validate and extend the findings of initial studies. Provision of expert intensive medical care within an individualized, developmental framework is not only feasible but necessary to enhance the effectiveness of NICU care.

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Individualized Developmental Care

An Emerging New Standard for Neonatal Intensive Care Units?

Many factors have improved the infant and neonatal mortality in this country. The evolution of nurseries for premature newborns into modern neonatal intensive care units (NICUs) and technological advances used in NICUs have certainly contributed to the reduction in mortality for all birth-weight/gestational-age categories. This reduction in mortality has been most dramatic in recent years for very low-birth-weight (<1500 g) and extremely low-birth-weight (<1000 g) infants. Mortality has traditionally been the tool used to evaluate the success of NICUs with these small infants. However, today both short-term and long-term morbidity and neurodevelopmental outcome must be evaluated when assessing any new intervention used in the NICU.

See also p 853.

The acceptance of new innovations in care in perinatal medicine has an unfortunate history. Unproven therapies or therapies with inappropriate risks have been adopted, while proven therapies remain underused. In the 1940s and 1950s, an epidemic of blindness, due to retinopathy of prematurity, was associated with the widespread use of oxygen to treat periodic breathing in infants. Many causes were suspected, but a multicenter randomized controlled trial confirmed the relationship between high oxygen concentrations and retinopathy of prematurity.[1] Subsequently, when oxygen was restricted, there was an increase in mortality and spastic diplegia. Better understanding of the risks and benefits of oxygen therapy, along with technological advances allowing for close monitoring of oxygen, has led to reductions in retinopathy of prematurity, spastic diplegia, and mortality. Conversely, in controlled trials as early as 1972, maternal steroids were shown to decrease the incidence and severity of respiratory distress syndrome in premature infants.[2] Yet the National Institutes of Health found it necessary to hold a consensus conference in 1994 because of the extremely low usage rate for maternal corticosteroids in eligible patients (<20%) throughout the country. After reviewing the available data, the consensus conference recommended maternal corticosteroids for nearly all mothers whose premature infants would be at risk for respiratory distress syndrome.[3]

In this issue of THE JOURNAL, Als and colleagues[4] present a carefully designed and executed randomized controlled trial of individualized developmental care for very low-birth-weight infants. Although previous work suggests that the individualized developmental care approach is beneficial, Als et al recognized the importance of a randomized controlled trial to minimize the effects of bias on their evaluation. They appropriately evaluated the effects of their proposed new therapy on both neonatal medical morbidities and neurodevelopmental outcome. As noted previously, these critical measures are necessary before the widespread use of any new intervention in NICUs.

Als et al demonstrated a significantly shorter duration of mechanical ventilation and supplemental oxygen use and a reduced incidence of pneumothorax and severe bronchopulmonary dysplasia in the experimental group. The experimental group also fed earlier, had better daily weight gain, and had a shorter hospital stay. They also had a reduced incidence of intraventricular hemorrhage and reduced hospital charges. In addition, at 2 weeks and at 9 months, the infants cared for with the individualized developmental care approach had better neurodevelopmental outcomes when compared with the control infants. Thus, their randomized controlled trial showed clear benefits without significant adverse effects.

The study is not without problems. The incidence of intraventricular hemorrhage is higher in the control group than in many other NICUs; the study was conducted before the widespread use of surfactant; the study was conducted in a single nursery with volunteer nurses for the experimental group. Despite these shortcomings, the clear differences in medical morbidity and neurodevelopmental outcome cannot be ignored. It is time that nurseries implement this type of care for ventilated, very low-birth-weight infants. Here is a "therapy" that reduces the most common and serious medical morbidities, improves neurodevelopmental outcome, and reduces overall hospital charges. Despite initial costs for changes in the physical environment of the NICUs and for the training

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of the professional staff in the newborn individualized developmental care and assessment program, shorter periods of ventilator dependence and hospital stay should save money.[5] Should third-party payers consider favoring nurseries that use individualized neurodevelopmental care to save money, while improving both medical and neurodevelopmental outcome? The NICUs choosing not to implement this form of therapy should have clear reasons and should consider their own randomized trial to attempt to disprove this work.

This is not a glamorous, high-technology form of neonatal intensive care. It does not dramatically rescue babies who are at immediate risk of death, as high-frequency ventilation, inhaled nitric oxide, or extracorporeal membrane oxygenation do. These high-technology interventions are widely used despite lack of well-controlled trials demonstrating their efficacy and safety. Will individualized developmental care for the very low-birth-weight infant be as widely accepted and implemented?

It is time for the American Academy of Pediatrics Committee on the Fetus and Newborn to critically evaluate this approach and make recommendations regarding the appropriateness of its use in NICUs. Unresolved questions should be addressed so that an appropriate research agenda can be recommended for study and funding. In particular, it will be crucial to study whether individual components of the nursery environment are important, or if they should be considered in the context of an individualized developmental care approach to the infant, as recommendations for levels of lighting, sound, and so on are developed or revised. Since the joint American Academy of Pediatrics and American College of Obstetricians and Gynecologists publication, *Guidelines for Perinatal Care*,[6] is currently being revised for a fourth edition, consideration should be given to making recommendations relative to individualized developmental care for very low-birth-weight infants.

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