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ABSTRACT

This study examined whether cry acoustics enhance the prediction of developmental outcome in preterm infants, after accounting for medical and social variables. Selection criteria for 149 preterm subjects included being born at less than 35 weeks gestational age and less than 1,500 grams; for 25 term subjects, selection criteria included being born healthy at term age (38 to 41 weeks gestational age). At 40 weeks gestational age, both during and following a neurobehavioral examination, cries were elicited with a painful heel flick when infants were supine and awake. Cries were recorded for 30 seconds using standardized procedures, and 10 acoustical variables were measured using the Cry Research, Inc. (CRI) computer-aided automated cry analysis system. At 30 months, infants were administered the McCarthy Scales of Children's Abilities or the Bayley Scales of Infant Development. Results suggested that acoustical analysis of the cry at term conceptual age enhances the prediction of developmental outcome even after accounting for medical and demographic variables. The number of short cry utterances was the best predictor in infants with fewer short utterances doing more poorly. Data from this study supported the notion that cry analysis may have some diagnostic utility as a non-invasive technique for the early identification of infants at biological risk for developmental delay. (MM)

Predicting Developmental Delay From Cry Analysis in Preterm Infants*

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The current techniques that we have to identify which high risk premature infants are most likely to become mentally retarded, developmentally delayed or disabled are not adequate. Many attempts to predict outcome from known biological risk factors or from traditional tests of infant development have been made. However, it has become increasingly clear that these tests are not sufficiently sensitive or specific to differentiate infants who are at greater risk than the total group of high risk preterm infants.

There is a literature which suggests that the neurological status of the infant may be reflected by his or her cry characteristics. Infants at risk have been found to differ in cry acoustics from normal infants. For example, cry characteristics have been correlated with prematurity, low birthweight, intrauterine growth retardation, malnutrition and other obstetric risk factors. In a pilot study, Barry Lester and his colleagues found that the characteristics of the cries of a small sample of term and preterm infants were related to their developmental outcomes at both 18 months and 5 years of age.

In the present study, we hypothesized that the acoustical characteristics of the cry at 40 weeks gestational age predict developmental outcome at 30 months after medical and demographic variables are accounted for. Our objectives were to, first, determine if cry acoustics enhance the prediction of developmental outcome after medical and social variables are accounted for. We also planned to use cry, medical and demographic variables to develop a predictor equation which would identify infants with low developmental scores and to prospectively cross-validate the

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predictor equation on an independent sample. Infants at increased risk for developmental disabilities as a result of being born prematurely were studied. Two different samples were selected, a learning sample from Boston and a replication sample from Syracuse.

METHOD

Selection criteria included, for preterm infants, being born at less than 35 weeks gestational age and less than 1500 grams, and, for term infants, being born healthy at term age (38-41 weeks gestational age). At 40 weeks gestational age, both during and following a neurobehavioral exam, cries were elicited with a painful heel flick when the infants were supine and awake. Cries were recorded for 30 seconds using standardized procedures and 10 acoustical variables were measured using the C.R.I. computer-aided automated cry analysis system. At 30 months adjusted gestational age, the McCarthy Scales of Children's Abilities were administered. If the child could not do the McCarthy Scales either because of developmental delay or a difficult temperament, the Bayley Scales of Infant Development were administered.

One hundred seventy-four infants (25 term, 149 preterm) were recruited from 4 Boston hospitals as the test sample. 123 were seen at 30 months adjusted gestational age. 96 of these had cry recordings at 40 weeks. Characteristics of the sample can be seen in Table 1.

RESULTS

Multiple regressions. To answer the first question of whether cry adds anything more than medical and demographic information to the prediction of outcome, stepwise multiple regressions were performed on the 30 month scores. Since both the McCarthy General Cognitive Index and the Bayley Mental Developmental Index are standardized with a mean of 100 and standard deviation of 16, scores from Bayleys and McCarthys were equated to be used as a single outcome score at 30 months. Eighty percent of the Boston sample had McCarthys and 20% had Bayleys. The following medical and demographic variables were entered as predictors into the initial multiple regressions:

Medical	Demographic
Birthweight	Hollingshead socioeconomic score
5 minute Apgar score	Marital status
Days of hospitalization	Race
Days of oxygen therapy	Sex
Grade of intraventricular hemorrhage	
Necrotizing enterocolitis	

Based on the results of these regressions, the significant variables ($p<.05$) were chosen to be forced into the next multiple regressions before the cry variables. The stepwise procedure then selected cry predictors from the following list:

<u>Cry variables</u>

Number of utterances	% phonation
Number of short utterances	Fundamental frequency
Energy	First formant
Duration	Second formant
% nasalization	Amplitude fundamental frequency

The results can be seen in Table 2. Cry variables explained 12% of the variance in the 30 month outcome scores after variance due to medical and demographic variables was accounted for ($F(4,95)=15.53$, $p<.001$). The number of short cry utterances was chosen as the significant cry predictor by the stepwise procedure.

<u>Logistic regressions.</u> To develop a predictor equation from the medical, demographic and cry variables, we used logistic regression analyses. To predict low vs. normal scores, the sample was divided into infants with scores less than 1 standard deviation below average or less than 84 and 84 and above. Fifteen scored less than 84. As with the multiple regressions, the logistic regressions were first run with the medical and demographic variables. The significant variables were then forced into a logistic regression followed by the selection of significant cry variables. As shown in Table 3, using the variables, days of hospitalization, Hollingshead socioeconomic status (SES) score, race and number of short cry utterances, we were able to correctly predict 11 out of 15 infants with low scores and 71 out of 81 with high scores. This gave us a sensitivity, or the percentage of infants with true problems who were correctly detected by the cry test, of 73% and a specificity, or the percentage of infants without problems who were correctly detected, of 88%. The positive predictive value or the percentage of those infants who failed the cry test with true developmental problems was 52% and the negative predictive value or the percentage of infants who did not fail the cry test with a normal outcome was 95%. The overall hit rate was 85%.

Next, to strengthen our findings, we cross-validated the predictor equation by prospectively applying the same equation used with the Boston sample to an independent sample of preterm infants. Thus, we were able to greatly reduce the number of predictor variables by limiting them to the 4 that were significant in the previously developed predictor equation. Our replication sample included 64 preterm infants in Syracuse tested at 40 weeks gestational age and 30 months adjusted age, as in Boston. Characteristics of this sample are seen in Table 4. The McCarthy

Scales were administered to 62 infants and the Bayley Scales to 2. Eleven infants scored less than 84 on tests. As shown in Table 5, using our previously developed predictor equation, we correctly identified 8 of 11 low scoring infants and 42 of 53 high scoring infants giving us a sensitivity of 73% and specificity of 79%. The positive predictive value was 42%, the negative predictive value, 93%. The overall hit rate was 78%. The relative risk value of 6 is the percentage of infants with abnormal outcome who failed the cry test divided by the percentage of infants with abnormal outcomes who did not fail the cry test. In other words, the preterm infant's chances of being abnormal are 6 times greater with a positive cry test than with a negative cry test.

DISCUSSION

The results of this study suggest that acoustical analysis of the cry at term conceptual age enhances the prediction of developmental outcome even after accounting for medical and demographic variables. Although the amount of variance in the developmental scores accounted for by cry variables in the multiple regressions was low, we had already removed variance attributable to medical and demographic variables. Previous studies have shown that cry is correlated with the medical histories of infants. In fact, when medical and demographic predictors are ignored, cry variables accounted for approximately 20% of the variance in the Boston sample. Considering that we are predicting from a 30 second episode of crying in the newborn period to scores on a developmental test two and a half years later, we would not expect any more than this.

These findings are supported by the results of the logistic regressions. Using just a few medical, demographic and cry variables, we were able to predict which children would score low or high at 30 months with a high level of both sensitivity and specificity and, furthermore, we could replicate our prediction on a separate sample.

The number of short cry utterances was our best predictor with infants with fewer short utterances doing more poorly. This may reflect the poor respiratory control and lack of energy to sustain cries in the preterm infant.

There are a few reasons to be cautious of our findings. Our primary concern relates to the difficulties assessing developmental outcome at 30 months of age which made it necessary for us to use two developmental tests that may not be comparable. Additionally, relatively few infants scored in an abnormal range. We hope to be able to further test these children at school age which would allow us to substantially improve our confidence that each subject is accurately evaluated and classified with regard to outcome. It would also allow us to evaluate the use of cry to predict more subtle deficiencies such as learning disabilities which can not be identified at 30 months.

In conclusion, these data support the notion that the cry analysis may have some diagnostic utility as a non-invasive technique for the early identification of infants at biological risk for developmental delay. Improved ability to quantify perinatal insult based on medical histories and tests of measures such as the cry to identify at a very young age who is most in need of early intervention services could help improve the quality of life for infants graduating from neonatal intensive care units and their families.

Table 1.

Characteristics of the Boston Sample

Variable	Term (N=8)	Preterm (N=88)
Gestational age (weeks)	40 (1)*	29 (3)
Birthweight (grams)	3538 (246)	1134 (289)
5 min. Apgar score	9 (1)	7 (2)
Days of O2 therapy	0 (0)	24 (28)
Days of hospitalization	3 (1)	60 (30)
Hollingshead SES score	2.5 (2)	2.9 (1)
30 mos. MDI or GCI	111 (12)	99 (19)

* Mean (sd)

Table 2.

Prediction of 30 Month GCI/MDI

Significant Variables	Partial R^2	Model R^2
Medical/Demographic	.29	.29*
Cry		
No. short utterances	.12	.41*

* $p<.001$

Table 3.

Classification of Low (<84) Vs. High 30 Month Bayley/McCarthy Scores Based on Logistic Regression Analysis*

Boston Sample

	Low	High
Predicted Low	11	10
Predicted High	4	71

*Sensitivity = .73
Specificity = .88
Positive Predictive Value = .52
Negative Predictive Value = .95

Table 4.

Characteristics of the Syracuse Sample

Variable	Preterm Only (N=64)
Gestational age (weeks)	30 (3)*
Birthweight (grams)	1148 (281)
5 min. Apgar score	8 (2)
Days of O2 therapy	27 (34)
Days of hospitalization	60 (29)
Hollingshead SES score	3.1 (1)
30 mos. MDI or GCI	96 (19)

* Mean (sd)

Table 5.

Prospective Prediction of Low (<84) Vs. High 30 Month McCarthy GCI Scores*

Syracuse Sample

	Low	High
Predicted Low	8	11
Predicted High	3	42

*Sensitivity = .73
Specificity = .79
Positive Predictive Value = .42
Negative Predictive Value = .93
Relative Risk 6 (95% CI = 2 - 21)