

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39

7-31-08

Sucking Behavior of Pre-term Neonates
As a Predictor of Developmental Outcomes

Barbara Medoff-Cooper, Ph.D., FAAN
School of Nursing University of Pennsylvania
The Children’s Hospital of Philadelphia

Justine Shults, Ph.D.
Center for Clinical Epidemiology and Biostatistics
University of Pennsylvania

Joel Kaplan, Ph.D.

Corresponding Author:
Barbara Medoff-Cooper, Ph.D., FAAN
School of Nursing
University of Pennsylvania
Ruth M Colket Professor of Pediatric Nursing
Children’s Hospital of Philadelphia
420 Guardian Dr.
Philadelphia, PA 19004-6096
215-898-3399
Medoff@nursing.upenn.edu

Key works: infant, preterm, development, feeding

40 **Abstract**

41 The relationship between the pattern of sucking behavior of pre-term
42 infants during the early weeks of life and neurodevelopmental outcomes during
43 the first year of life were evaluated. The study sample consisted of 105 pre-term
44 infants (postmenstrual age [PMA] at birth = 30.5 ± 2.8 weeks [mean \pm SD]; birth
45 weight = 1476 ± 460 grams; mean length of hospital stay = 44.13 ± 32.6 days.)
46 All infants received a 5-minute sucking test at 34 and at 40 weeks PMA, with
47 outcomes evaluated at 6- and/or 12-months corrected gestational age (CGA) via
48 the Bayley Scales of Infant Development (BSID). As expected, 6- and 12-month
49 values for the Psychomotor Developmental Index (PDI) and Mental Development
50 Index (MDI) of the BSID fell significantly below the normative levels established
51 for infants delivered at term. A significant association between neonatal sucking
52 pattern at 40 weeks PMA and developmental outcome at 12 months CGA was
53 obtained.. Each of the three simple sucking parameters evaluated (number of
54 sucks, mean duration of sucking bursts, and mean sucking pressure peaks), as
55 well as a composite parameter (average of the respective parameter z-scores),
56 was significantly related to both PMI and MDI at 12 months. Multivariable
57 models, adjusting for PMA at birth, length of hospital stay, and other predictors,
58 affirmed that sucking performance at 40 weeks PMA was a significant,
59 independent predictor of developmental status 1 year later. Standardization of
60 an instrument for neonatal sucking assessment may offer a cost-effective early
61 screening strategy for pre-term infants at greatest risk for developmental delay.

62 Early identification of pre-term infants who are at risk for significant

63 cognitive and psychomotor delays remain a major concern for pediatric care
64 providers. It is estimated that approximately half of infants delivered prematurely
65 (< 37 weeks postmenstrual age [PMA]) will receive, or would otherwise benefit
66 from, remedial educational attention by the time they reach school age [1].
67 Neurodevelopmental delays in this population, in fact, become apparent during
68 the first year of life. For example, pre-term infants, on average, score about one
69 standard deviation below full-term norms for the mental and psychomotor
70 developmental indexes (MDI and PDI) of the Bayley Scales of Infant
71 Development (BSID) [2] . Close attention to developmental progress is indicated
72 for the most premature infants, those with very low birth weights, and infants with
73 salient pre-term comorbidities such as intraventricular hemorrhage [3], or
74 bronchopulmonary dysplasia [4]. Infants receiving such attention, however,
75 represent a modest fraction of more than 500,000 pre-term infants born each
76 year in the US [5] As a result, no early indication is available for a large number
77 of pre-term infants with apparently ‘uncomplicated’ courses of care and discharge
78 who, nevertheless, may experience significant delays in cognitive and
79 psychomotor development. At present, there is an urgent need for a clinically
80 useful and cost-effective instrument for stratification of developmental risk across
81 infants born prematurely [6].

82 In the present study, we explore the extent to which the pattern of nutritive
83 sucking of pre-term infants during the neonatal period can account for between-
84 infant variability in developmental outcomes evaluated at 6 and 12 months
85 corrected gestational age (CGA). Beginning with Wolff [7], a number of

86 researchers have shown that the character of sucking behavior provides an
87 indirect indicator of normal or abnormal brain function in the young infant [8-10].
88 Maturity of sucking organization parallels neurological development, as evaluated
89 over the first weeks after pre-term delivery [11, 12], and across groups of infants
90 born at different gestational ages [13]. These studies establish a clear
91 association between sucking organization and the contemporary neurological
92 status of preterm infants. Mizuno et al. [14] further indicated the prognostic
93 potential of a sucking assessment. They reported a significant association
94 between sucking performance of infants born prematurely and tested between 40
95 and 42 weeks PMA, and BSID measurements obtained when the same infants
96 reached 18 months CGA. The pattern of sucking was shown to be a better
97 predictor of developmental outcome than was perinatal cranial ultrasound and
98 other neonatal measurements taken in the study. This precedent encourages
99 further evaluation of the potential of a nutritive sucking assessment as part of a
100 standardized early screen for developmental risk, and further methodological
101 development. One limitation of the protocols used in the cited study was feeding
102 status assignments given in categorical terms (4 levels of 'feeding maturity'),
103 based on visual inspection of sucking pressure waveforms. In addition, the PMA
104 range of the study sample was narrow, with the infants best described as "near-
105 term" (mean PMA = 37.8 weeks), leaving open the relevance of the findings to
106 those infants born more prematurely and, in the aggregate, at greater risk for
107 developmental delays.

108 Here, we apply an automated analysis of the pattern of sucking of pre-
109 term infants (birth range: 28 – 34 weeks PMA) during separate 5-minute tests
110 delivered at 34 and 40 weeks PMA, and evaluate the association between
111 neonatal sucking performance and BSID outcomes evaluated at 6 and 12
112 months CGA. Sucking organization was characterized by three simple
113 parameters derived from each sucking record: the number of sucks emitted (SN),
114 the average number of sucks per burst (SBP), and the session-average of the
115 sucking pressure peaks (Pmax). These parameters have been shown to vary
116 consistently as a function of PMA at birth [12, 15, 16] and across other conditions
117 of clinical interest [10, 17]. We hypothesized that these parameters taken
118 individually, and as a composite “suck maturity index” (SMI), would be
119 independently and positively correlated with neurodevelopmental outcomes.

120 **Methods**

121 *Sample:* The study sample consisted of 105 subjects who had
122 developmental outcomes measured at 6 and or 12 months of age. Of these
123 subjects, 54 had measurements taken at both 6 and 12 months; 41 had
124 measurements only at visit one; and 10 had visits only at visit two. The infants
125 were predominantly African-American (65.9%) (28% Caucasian, 2% Hispanic,
126 2% Asian, and 2% other) and half (54%) were female. The mean maternal age
127 was 28.1 ± 6.9 years, with over 42% completing some college education. In
128 contrast, 26% of the mothers had less than a high school education, with the
129 remaining 32% having completed high school. Table 1 presents study sample

130 characteristics, including postmenstrual age at birth (PMA), length of hospital
131 stay (LOS), and birth weight.

132 *Apparatus:* Sucking performance was evaluated with a Nutritive Sucking
133 Apparatus (NSA), providing a continuous record of the negative sucking pressure
134 generated by the infant during the test session. The NSA incorporates a silicone
135 rubber-embedded calibrated capillary for metered flow of nutrient into an
136 otherwise ordinary nipple. The sucking signal is derived from a Cobe pressure
137 transducer embedded in a second tube. The volume delivered per suck
138 (consumption) is proportional to the pressure-time integral, or area under the
139 pressure-time curve, of the suck cycle. Flow is calibrated such that a sustained
140 100mg/Hg pressure yields a constant flow of 30 ml/min. All materials used in the
141 nipple set-up are non-toxic and easily sterilized. The pressure signal was fed
142 on-line to an IBM compatible computer, which displayed the pattern of sucks
143 throughout the session and stored the pressure waveform for off-line analysis.
144 Customized software was developed to detect each sucking event and to derive
145 the three session summary parameters selected for further analysis (below): the
146 number of sucks per session (SN); the average number of sucks per burst (SPB)
147 within the session (2-sec pause defined separation of 2 bursts), and the mean
148 maximum sucking pressure (Pmax) for all recorded sucks. In addition, a
149 composite parameter labeled the “suck maturity index” (SMI) was derived for
150 each session (see below).

151 *Bayley Scales of Infant Development:* The Bayley Scales of Infant
152 Development, Second Edition (BSID-II) are composed of 3 distinct scales which

153 measure mental acuities and abilities (mental developmental index- MDI), degree
154 of control of body coordination and fine motor skills (psychomotor developmental
155 index- PDI), and the child's social and objective orientation to the environment
156 (Infant Behavior Record). The Bayley scales have been used since 1958 and
157 remain one of the most accurate and sensitive ways to measure infant
158 development. The Bayley scales were standardized on 1262 children ranging in
159 age from 2 to 30 months. The standardization sample was stratified to control for
160 sex, race, socioeconomic status, and urban vs. rural home. The validity of the
161 Bayley scales is supported by the correspondence between scores on the Bayley
162 Mental Scale and the Stanford-Binet Intelligence Scale. Internal consistency
163 reliability of the Bayley scales range from .68 to .93. Test-retest reliability was
164 .76. The Bayley scales were administered by developmental experts who have
165 been trained in the administration of these scales. The BSID-II was completed at
166 6 and 12 months of age.

167 *Procedure:* The 5-minute sucking assessment was completed at 34 and
168 40 weeks post menstrual age (PMA) approximately 30 minutes prior to a late
169 morning scheduled feeding. Infants were picked up, swaddled and brought to a
170 quiet alert state prior to a feeding assessment. The 34 week measurement was
171 completed by a member of the research team. The 40 week measurement was
172 completed at an out-patient visit. The infant's parent was given instructions on
173 how to hold the infant and the feeding device. Infants were swaddled and held in
174 an upright position. Once the nipple was inserted into the infant's mouth, no
175 attempts were made to assist the infant sucking movements.

176 *Data Analysis:* Analyses were conducted with Stata 10.0 and SPSS, with
177 two-sided tests of hypotheses and a p-value < 0.05 as the criterion for statistical
178 significance. The primary variables of interest for the analysis were the sucking
179 parameters derived from the tests delivered at 34 and 40 weeks PMA: SN, SBP,
180 Pmax, and the SMI composite. SMI was calculated as the average of the z-
181 scores (parameter value minus mean, divided by standard deviation) of SN,
182 Pmax, and SBP. The primary developmental outcomes of interest were the MDI
183 and PDI subscales of the BSID, measured at 6 and 12 months of age. The
184 primary goal in the analysis was to identify significant correlates of increased MDI
185 and PDI, and in particular to test if sucking scores are significant independent
186 correlates of improved developmental outcomes. Initial analyses were
187 descriptive and included summarizing infant demographics and BSID outcomes
188 (Tables 1 and 2) via calculation of means, standard deviations (SDs), ranges,
189 and 95% confidence intervals for the means. Next, (Tables 3a and 3b) means,
190 SDs, and inter-correlations (with p-values for identification of correlations that
191 differed significantly from zero) were computed for the sucking parameters.

192

193 Multivariate analyses were then conducted to test the hypothesis that sucking
194 scores are significant correlates of MDI and PDI when the models are adjusted
195 for additional covariates. We constructed generalized estimating equation (GEE)
196 models (Tables 4 and 5) using the xtgee procedure in Stata 10.0 that considered
197 MDI and PDI simultaneously at 6 and 12 months. Implementation of GEE for
198 analysis of MDI and PDI was the same as conducting multivariable regression,

199 but with one additional step to account for the fact that two measurements (MDI
200 and PDI) were collected on each subject at each visit: This involved specifying a
201 regression model for expected MDI and PDI, but also specifying a 2 by 2
202 correlation matrix to describe the association between MDI and PDI at each visit.
203 The GEE approach could therefore be viewed as an extension of regression that
204 adjusted for the correlation between the MDI and PDI measurements that were
205 measured on subjects at each visit.[18] The first GEE models included SMI at 34
206 weeks, in addition to the variables Caucasian (that took value 1 for Caucasian
207 subjects and 0 otherwise), male (that took value 1 for male), PMA, and length of
208 stay in weeks. The subsequent GEE models then included SMI at 40 weeks, in
209 addition to the variables that were just mentioned. If the regression coefficients
210 for SMI differed significantly from zero, this would indicate that SMI was an
211 independent predictor for MDI and PDI.

212 A secondary analysis considered a binary outcome that considered both
213 MDI and PDI as simultaneous outcomes on each subject, to allow for improved
214 power for the lowest 10% of the combined outcomes. For this analysis, a logistic
215 GEE model was used to test the hypothesis that infants with lower SMI values at
216 40 weeks would be significantly more likely to be in the lowest 10% of subjects
217 with respect to 12-month MDI and PDI. Implementation of logistic GEE was the
218 same as conducting logistic regression, coupled with specification of a 2 by 2
219 correlation matrix to adjust for the correlation between MDI and PDI that were
220 collected on subjects at each visit.[18]) The logistic GEE regression models
221 considered a binary outcome on each infant that took value 1 if the infant was in

222 the lowest 10% with respect to MDI and PDI; and took value 0 otherwise; the
223 models included SMI as a covariate. This approach also allowed for adjustment
224 for the correlation between the two outcomes that were measured on each
225 subject at 12-months.

226 **Results**

227 *Developmental Outcomes:* Values for the MDI and PDI assessments at 6-
228 and 12-month CGA are shown in Table 2. For the group as a whole, each
229 outcome was significantly lower than the normative mean of 100 for infants
230 delivered at term [19, 20].

231 *Univariate analyses:*

232 *Sucking parameters:* Sucking performance values (mean \pm SD) derived
233 from tests delivered at 34 and 40 weeks PMA are shown in the left columns of
234 Table 3a and 3b, respectively. The three session summary parameters are
235 shown (total number of sucks emitted [SN], mean number of sucks per burst
236 [SPB], and the mean pressure maximum across all recorded sucks [Pmax]), as is
237 the composite score (SMI) given as the average z-score for the respective
238 parameters.

239 Pairwise correlations among the three primary parameters were significant for
240 both the 34- and 40-week sucking tests (Table 3). For the 40-week test, the
241 three session summary parameters as well as SMI were each significantly
242 associated with each BSID outcome (PDI and MDI) assessed at 12-months CGA
243 (Table 3b). A more limited set of significant associations was obtained between
244 34-week sucking performance and 12-month outcomes, excepting SPB as

245 related to MDI and Pmax as related to both MDI and PDI. By contrast, no
246 sucking parameter was correlated with BSID outcomes from the 6-month
247 assessment. The SMI was chosen for subsequent analyses for simplicity of
248 presentation, and for the statistical advantages of treating a single
249 (representative) sucking parameter in multivariable models. .

250 Multivariate Analyses:

251 A GEE models treating BSID outcomes (MDI and PDI) concurrently
252 provide a concise account of the predictive value of SMI taken alone, and when
253 the other predictor variables were included. The results were consistent with
254 those of respective GEE analyses treating the two outcome variables separately
255 (results not shown). As expected, the associations between MDI and PDI values
256 were significant ($r^2 = 0.56$, $p < 0.0005$).

257 *SMI at 40 weeks PMA and 12-month BSID outcomes:* An initial GEE
258 analysis evaluated the relationship between SMI and BSID outcomes, with an
259 included term representing the interaction between SMI and subscale type (PDI,
260 MDI). A significant association between SMI and outcomes was obtained (95%
261 confidence interval = 5.79, 16, 60; $p < 0.0005$). The interaction term was not
262 significant, indicating that the impact of sucking did not differ according to
263 whether the outcome was MDI or PDI. Importantly, SMI was still significantly
264 associated with 12-month outcomes after adjustment for additional covariates
265 (Table 4). SMI, in fact, was the only significant correlate when all potential
266 predictors were included. Thus, PMA and LOS, although individually correlated
267 with 12-month MDI and with PDI values, respectively, were not uniquely

268 associated with the outcomes in the inclusive GEE model (PMA: $p = 0.74$; LOS: p
269 $= 0.14$)

270 We sought to determine whether a low sucking score significantly
271 increased the likelihood that an infant's PDI or MDI outcome would be less than
272 70 (approximately at or below the 10th percentile for either). (Ten out of the 63
273 infants had at least one outcome that met this criterion.) The logistic GEE model
274 yielded a significant result ($p < 0.015$; odds ratio = 0.22; 95% CI = 0.07, 0.74).

275 *SMI at 34 weeks PMA and 12-month BSID outcomes:* An initial GEE
276 analysis showed a significant relationship between SMI and combined BSID
277 outcomes (95% CI = 2.09, 11.11; $p < 0.005$); the interaction term [SMI X outcome
278 type (MDI, PDI)] was not significant. The correlation between SMI and outcomes
279 was expected given the significant univariate correlations between 34-week SMI
280 and the respective MDI and PDI outcomes (see Table 3a). A significant overall
281 result was obtained for the inclusive GEE model treating SMI and other neonatal
282 variables, but no predictor was shown to be uniquely associated with the BSID
283 outcomes in this adjusted model (Table 5). This result speaks to the high degree
284 of intercorrelation among the three predictors (SMI, PMA and LOS) with
285 respectively significant univariate associations with the 12-monthly MDI and PDI.

286 **Discussion**

287 The present findings are consistent with the suggestion [14] that the
288 organization of sucking behavior during the neonatal period can provide an early
289 indicator of risk for emergent neurodevelopmental delays in infants born
290 prematurely. Based on manual inspection of suck-pressure records and

291 categorical ratings of feeding status, Mizuno et al. [14] demonstrated a significant
292 association between feeding performance of infants born near-term (mean PMA
293 at birth = 37.8 weeks PMA) and tested at 42 weeks PMA, and BSID outcomes
294 assessed at 18 months CGA. We also report a significant relationship between
295 neonatal sucking and BSID values, but with developmental outcomes evaluated
296 at an earlier age than in the study of Mizuno et al. (12 vs. 18 months CGA) and,
297 importantly, with a sample of infants that were considerably more premature at
298 birth (range 28 – 34 weeks PMA). The replication and extension of the earlier
299 indications are encouraging, particularly in light of the present methodological
300 developments. Here, the subjective elements of the sucking assessment were
301 eliminated through a fully automated analysis of the sucking pattern, yielding a
302 simple set of summary parameters expressed in ratio scale. The two studies
303 taken together commend further development of protocols for neonatal sucking
304 assessment. An optimized test delivered in clinical settings may help address
305 the largely unmet need for a simple, cost-effective screen for pre-term infants at
306 greatest risk for delayed cognitive and psychomotor development.

307 A significant association between neonatal sucking performance and
308 developmental outcomes was obtained here specifically with respect to the BSID
309 scoring performed when the infants reached 12 months CGA. Six-month
310 outcomes were not associated with sucking performance tested at either 34 or 40
311 weeks PMA. Univariate analyses revealed that SMI at each testing point was a
312 significant predictor of the 12-month MDI and PDI subscales of the BSID, with
313 strength of association on a par with that of PMA at birth and of length of hospital

314 stay (LOS). There was a high degree of intercorrelation among these
315 parameters, such that when 34-week SMI, PMA and LOS were evaluated
316 concurrently, neither of the three stood out uniquely as a predictor of
317 neurodevelopmental status. By contrast, when 40-week SMI was evaluated in
318 this manner, sucking performance was shown to be a significant, independent
319 predictor of MDI and PDI at 12-months. SMI, in fact, was the only neonatal
320 parameter in the adjusted model significantly related to 12-month outcomes. The
321 relatively stronger result derived from the latter sucking test may reflect sucking
322 that is more robust on average, with stable individual-infant differences in sucking
323 organization emerging as a function of increasing sucking experience.

324 Alternatively, the apparent contrast may have obtained by chance, given
325 variability in sucking performance under the present testing protocols (see below)
326 and the study's modest sample size. Clarification of the matter, relevant to
327 determining the optimal timing for delivery of a feeding-related screen for
328 developmental risk, requires further study.

329 The indicated association between neonatal sucking performance and
330 developmental outcomes may be noteworthy from a clinical perspective. With
331 respect to 40-week SMI and the 12-month outcomes, a decrease of one standard
332 deviation in the sucking score predicted a salient reduction in the BSID average
333 below the group mean (estimated declines of 9.5 and 6.4 points, as derived from
334 the initial and adjusted GEE models, respectively). Such a result would
335 represent an aggravated burden when viewed in relation to average scores for
336 pre-term infants that already fall well below the full-term norms [1, 21]. The

337 potential clinical utility of neonatal sucking evaluation was further indicated by the
338 GEE logistic model, where 40-week SMI was a significant predictor of whether an
339 infant's 12-month PDI or MDI values would fall in the lowest 10% of the sample
340 (here, with at least one subscale value below 70). Given the modest sample size
341 and the small number of subjects falling below the cutoff, however, this result
342 should be regarded as preliminary and in need of replication.

343 Further work may qualify the interpretation of the current findings. It is
344 also possible that the present results underestimate the prognostic potential of
345 neonatal sucking assessment. It should be emphasized, first, that each reported
346 associations with 12-month developmental outcomes was based on a single 5-
347 minute sucking test. The protocol was standardized such that tests were initiated
348 as closely as possible 30 minutes before the late morning, feeding.
349 Nevertheless, the inherent variability of infant sucking performance, arousal level
350 and temperament (day to day and meal to meal) is well known. Such within-
351 subject variability would have operated here to weaken the sensitivity of the
352 method for detecting real differences between infants in sucking organization. A
353 better estimate of an infant's maturational status may be derived from two or
354 more tests delivered the same day and/or over consecutive days. Separately, it
355 will be important to determine whether test sensitivity varies as a function of time
356 of day. Protocols optimized to capture reliable differences in sucking
357 organization between individual infants, therefore, may yield greater strength of
358 association between neonatal sucking and developmental outcomes than that

359 reported here. Empirical evaluation of this possibility must be provided in future
360 studies.

361 Given the present lack of clinical guidelines for early identification of pre-
362 term infants at greatest risk for developmental delays, and the scale of the
363 present “screening gap”, it is important that all potentially useful approaches –
364 analysis of neonatal feeding organization among them – be further explored. For
365 example, comprehensive neurobehavioral assessment regimes, such as the
366 Neurobehavioral Assessment of the Preterm Infant [NAPI][22], the Neonatal
367 Intensive Care Unit Network Neurobehavioral Scale [NNNS][23], and others,
368 have been shown to discriminate outcomes across groups of pre-term infants
369 with different risk profiles (e.g., between infants of very- versus extremely-low
370 birth weights; between pre-term infants with or without prenatal exposure to
371 cocaine or methamphetamine [24, 25]). Further work may indicate the (added)
372 value of such protocols for stratifying developmental risk across infants within
373 particular at-risk groups, such as otherwise healthy pre-term infants born within a
374 given PMA range. Assessments of brain morphology and function may reach
375 points of development suitable for discriminating between-infant differences in
376 developmental risk. At present, however, only between-group (e.g., pre-term vs.
377 control) sensitivities have been demonstrated [26, 27]. Another direction comes
378 from work on the organization of sleep patterns, where profiles were shown to
379 differ between pre-term and full-term neonates [28, 29] and to vary as a function
380 of PMA at birth and over time in pre-term infants [30, 31]. Importantly,
381 parameters related to sleep state organization of pre-term neonates have been

382 associated with individual differences in developmental outcomes assessed later
383 in infancy [32, 33]. The different approaches have yet to be compared and
384 contrasted systematically, and it may be determined that the strongest prognostic
385 models incorporate metrics derived from a combination of tests. Although future
386 clinical research may yield encouraging results, the 'cost factor' will be a
387 significant obstacle for widespread deployment of assessments, such as those
388 noted, that involve elaborate or expensive equipment and/or personnel with
389 specialized training. Therein lies a particular practical advantage of neonatal
390 feeding assessment as part of a screening instrument for developmental risk in
391 pre-term infants. With further evidence supporting its predictive value, cost
392 concerns may be mitigated by a recording device that should be inexpensive at
393 scale, and by an automated measurement and analysis system that would
394 minimize the need for specialized training in test delivery and interpretation [9].

395 In conclusion, evaluation of the sucking organization of pre-term infants
396 during the neonatal period offers a potentially useful and cost-effective approach
397 to developmental risk assessment. The link between early sucking performance
398 and risk for emergent developmental days is not likely a direct one; i.e., with
399 significant delays arising as a consequence of weak or poor quality feeds early in
400 life. Rather, poor sucking performance and elevated developmental risk would
401 appear to be epiphenomena of immature or compromised neurobehavioral
402 function in pre-term neonates. Further work is needed to verify and extend the
403 present findings, and to develop protocols with greater sensitivity for detection of
404 stable and reliable individual differences in neonatal sucking organization.

405

- 406 1. Sherlock, R.L., et al., *Neurodevelopmental sequelae of intraventricular haemorrhage at 8 years of*
407 *age in a regional cohort of ELBW/very preterm infants*. Early Human Development, 2005. **81**(11):
408 p. 909-16.
- 409 2. Bayley, N., *Manual for the Bayley Scales of Infant Development*. 1969, New York: Psychological
410 Corporation.
- 411 3. Inder, T.E., et al., *White matter injury in the premature infant: a comparison between serial*
412 *cranial sonographic and MR findings at term*. AJNR Am J Neuroradiol, 2003. **24**(5): p. 805-9.
- 413 4. Ambalavanan, N. and W.A. Carlo, *Bronchopulmonary dysplasia: new insights*. Clin Perinatol,
414 2004. **31**(3): p. 613-28.
- 415 5. Dimes, M.o. *Peristats*. 2008 [cited].
- 416 6. da Costa, S.P., L. van den Engel-Hoek, and A.F. Bos, *Sucking and swallowing in infants and*
417 *diagnostic tools*. J Perinatol, 2008. **28**(4): p. 247-57.
- 418 7. Wolff, P., *The serial organization of sucking in the young infant*. Pediatrics, 1968. **42**(6): p. 943-
419 956.
- 420 8. Als, H., F.H. Duffy, and G.B. McAnulty, *Behavioral differences between preterm and full-term*
421 *newborns as measured by the APiB systems scores: Part1*. Infant Behavior and Development,
422 1988. **11**: p. 305-318.
- 423 9. Mizuno, K. and A. Ueda, *The maturation and coordination of sucking, swallowing, and*
424 *respiration in preterm infants*. J Pediatr, 2003. **142**(1): p. 36-40.
- 425 10. Gewolb, I.H., et al., *Abnormal developmental patterns of suck and swallow rhythms during*
426 *feeding in preterm infants with bronchopulmonary dysplasia*. Dev Med Child Neurol, 2001. **43**(7):
427 p. 454-9.
- 428 11. Gewolb, I.H., Bosma, J., Reynolds, E., Vice, F., *Integration of suck swallow rhythms during*
429 *feeding in preterm infants with and without bronchopulmonary dysplasia*. Developmental and
430 Behavioral Pediatrics, 2003. **45**: p. 344-348.
- 431 12. Medoff-Cooper, B., Bilker, W., Kaplan, J., *Suckling behavior as a function of gestational age: A*
432 *cross-sectional study*. Infant Behavior and Development, 2001. **24**: p. 83-94.
- 433 13. Medoff-Cooper, B., W. Bilker, and J. Kaplan, *Suckling behavior as a function of gestational age:*
434 *A cross-sectional study*. Developmental and Behavioral Pediatrics, 2001. **24**: p. 83-94.
- 435 14. Mizuno, K. and A. Ueda, *Development of sucking behavior in infants who have not been fed for 2*
436 *months after birth*. Pediatr Int, 2001. **43**(3): p. 251-5.
- 437 15. Medoff-Cooper, B., *Changes in nutritive sucking patterns with increasing gestational age [see*
438 *comments]*. Nursing Research, 1991. **40**(4): p. 245-7.
- 439 16. Lau, C., Smith, E., Schandler, R., *Coordination of suck-swallow respiration in preterm infants*.
440 Acta Paediatr, 2003. **92**: p. 721-727.
- 441 17. Medoff-Cooper, B., J.M. McGrath, and J. Shults, *Feeding patterns of full-term and preterm*
442 *infants at forty weeks postconceptional age*. J Dev Behav Pediatr, 2002. **23**(4): p. 231-6.
- 443 18. Hardin, J.W. and M. Hilbe., *Generalized Estimating Equations*. 2003, Boca Raton, FL: Chapman
444 & Hall/CRC.
- 445 19. La Pine, T.R., J.C. Jackson, and F.C. Bennett, *Outcomes of infants weighing less than 800 grams*
446 *at birth: 15 years' experience*. Pediatrics, 1995. **96**(3 part 1): p. 479-83.
- 447 20. McCarton, C.M., et al., *Cognitive and neurologic development of the premature, small for*
448 *gestation infant through age 6: Comparison by birth weight and gestational age*. Pediatrics, 1996.
449 **98**(6): p. 1167-1177.
- 450 21. Holditch-Davis, D., Schwartz, T., & Scher, M. . *Prediction of development outcomes of*
451 *prematures from biological and social risk measures in infancy*. In B. Medoff-Cooper (Chair),
452 *New perspectives on behavioral organization in the preterm infant*. in *International Conference on*
453 *Infant Studies*. 2006. Kyoto, Japan.
- 454 22. Constantinou, J., et al., *Neurobehavioral assessment predicts differential outcome between VLBW*
455 *and ELBW preterm infants*. J Perinatol, 2005 **25**(12): p. 788-793.
- 456 23. Lester, B.M. and E.Z. Tronick, *History and description of the Neonatal Intensive Care Unit*
457 *Network Neurobehavioral Scale*. Pediatrics, 2004. **113**(3 Pt 2): p. 634-40.
- 458 24. Salisbury, A., et al., *Prenatal cocaine use and maternal depression: effects on infant*
459 *neurobehavior*. Neurotoxicol Teratol, 2007. **29**(3): p. 331-340.
- 460 25. Smith, L., et al., *Prenatal methamphetamine use and neonatal neurobehavioral outcome*.
461 Neurotoxicol Teratol., 2008. **30**(1): p. 20-28.

462 26. Peterson BS, et al., *Regional brain volume abnormalities and long-term cognitive outcome in*
463 *preterm infants*. JAMA, 2000. **284**(15): p. 1939-1947.

464 27. Arditi, H., et al., *Cerebral blood flow velocity asymmetry, neurobehavioral maturation, and the*
465 *cognitive development of premature infants across the first two years*. J Dev Behav Pediatr, 2007.
466 **28**(5): p. 362-368.

467 28. Scher, M.S., et al., *Functional brain maturation in neonates as measured by EEG-sleep analyses*.
468 Clin Neurophysiol, 2003. **114**(5): p. 875-82.

469 29. Hoppenbrouwers, T., et al., *Sleep architecture in term and preterm infants beyond the neonatal*
470 *period: the influence of gestational age, steroids, and ventilatory support*. Sleep, 2005. **28**(11): p.
471 1428-36.

472 30. Holditch-Davis, D., et al., *Sleeping and waking state development in preterm infants*. Early Hum
473 Dev, 2004. **80**(1): p. 43-64.

474 31. Curzi-Dascalova, L., et al., *Sleep state organization in premature infants of less than 35 weeks'*
475 *gestational age*. Pediatric Research, 1993. **34**(5): p. 624-8.

476 32. Holditch-Davis, D., Belyea, M. & Edwards, L. , *Prediction of 3-year developmental outcomes*
477 *from sleep development over the preterm period*. Infant Behavior and Development, 2005. **28**(2):
478 p. 118-131.

479 33. Borghese, I.F., K.L. Minard, and E.B. Thoman, *Sleep rhythmicity in premature infants:*
480 *implications for development status*. Sleep, 1995. **18**(7): p. 523-30.

481

482

483

484

485

486

487

488

489

490

491

492

493

494

495

496

497

498

499

500

501
502

Table 1: Infant Demographics

Study Sample	N = 105
Birth weight (mean ± SD)	1476.1 ± 459.6 grams (mean ± SD)
Gestational age at birth	30.5 ± 2.8 weeks (range 28 – 34 weeks)
Male	46.1%
White	28.6%
Maternal age	28.1 ± 6.9 weeks
Length of stay	41.6 ± 31.4 days
IVH *	11% (n = 16; n = 3 with grade III or III-IV)
BPD *	13% (none requiring O ₂ supplementation at time of hospital discharge)

503
504
505
506
507
508
509
510
511

- = Diagnosed at birth
- IVH- Intraventricular Hemorrhage
- BPD Bronchopulmonary Displasia

Table 2: Bayley Scales of Infant Development Scales: PDI and MDI Subscales

Bayley Subscales	Mean ± SD	95% Confidence Interval
6-Month Assessment (N = 95)		
MDI	89.4 ± 10.7	87.4, 91.5
PDI	84.7 ± 17.8	81.3, 88.2
12-Month Assessment (N = 63)		
MDI	91.2 ± 13.2	88.1, 94.3
PDI	88.7 ± 17.0	84.7, 92.7

512
513
514
515
516
517
518
519
520
521
522
523
524
525
526
527
528
529
530
531
532
533
534

MDI- Mental Developmental Index
PDI- Psychomotor Developmental Index

535
536
537
538
539
540
541

Table 3a: 34-Week Sucking Parameters: Inter-correlations and Relation to 6- and 12-Month Developmental Outcomes

<u>Feeding Parameter</u> mean ± SD	SN (p)	SPB (p)	Pmax (p)	PDI6 (p)	MDI6 (p)	PDI12 (p)	MDI12 (p)
<u>SN</u> 115.8 ± 78.1	1.00			0.17 (0.11)	0.05 (0.60)	0.32 (0.01)	0.28 (0.03)
<u>SPB</u> 6.85 ± 6.07	0.75 (0.00)	1.00		0.11 (0.31)	0.07 (0.47)	0.26 (0.04)	0.16 (0.22)
<u>Pmax</u> 61.30 ± 33.4	0.26 (0.003)	0.26 (0.013)	1.00	-0.04 (0.67)	-0.02 (0.86)	0.05 (0.72)	0.05 (0.70)
<u>SMI</u> 0.029 ± 0.79	0.87 (*)	0.85 (*)	0.64 (*)	-0.09 (0.38)	-0.10 (0.35)	0.42 (0.000)	0.37 (0.002)

542
543
544
545
546
547
548

* = <0.0005

Table 3b: 40-Week Sucking Parameters: Inter-correlations and Relation to 6- and 12-Month Developmental Outcomes

<u>Feeding Parameter</u> mean ± SD	SN (p)	SPB (p)	Pmax (p)	PDI6 (p)	MDI6 (p)	PDI12 (p)	MDI12 (p)
<u>SN</u> 241.3 ± 76.8	1.00			-0.06 (0.57)	-0.09 (0.39)	0.29 (0.02)	0.25 (0.05)
<u>SPB</u> 13.9 ± 13.0	0.49 (0.0000)	1.00		-0.11 (0.29)	-0.17 (0.11)	0.43 (0.001)	0.38 (0.002)
<u>Pmax</u> 117.5 ± 41.3	0.23 (0.03)	0.24 (0.02)	1.0000	-0.02 (0.85)	0.06 (0.54)	0.30 (0.017)	0.28 (0.028)
<u>SMI</u> [-0.05 ± 0.63]	0.78 (*)	0.78 (*)	0.60 (*)	-0.09 (0.29)	-0.19 (0.35)	0.42 (0.001)	0.38 (0.002)

549
550
551
552
553
554
555
556
557
558
559
560
561
562
563
564
565
566
567

• = <0.0005

- **SN** Suck Number
- **SPB** Sucks Per Burst
- **PMax** Mean Maximum Pressure
- **SMI** Sucking Maturity Index

568
569
570

Table 4: Generalized Estimating Equations Analysis of 34 Week Sucking Maturity Index at 12 Months

Outcome	Coefficient	Std. Error	z	P > z	[95% Conf. Interval]
SMI 34	3.367693	2.036807	1.65	0.098	-.6243762, 7.359762
Gestational Age	-.2121059	1.105186	-0.19	0.848	-2.37823, 1.954018
Male	-1.680172	3.0252	-0.56	0.579	-7.609455, 4.249111
LOS week	-1.291921	.7140157	-1.81	0.070	-2.691366, .1075243
White	.8120479	3.211843	0.25	0.800	-5.48305, 7.107145
Cons	104.1657	37.26191	2.80	0.005	31.13369, 177.1977

571
572
573
574
575
576
577
578

SMI 34 Sucking Maturity Index at 34 Weeks Post Menstrual Age
LOS Length of Stay

579
580
581

Table 5: Generalized Estimating Equations Analysis with 40 Week Sucking Maturity Index at 12 Months

Outcome	Coefficient	Std. Error	z	P > z	[95% Conf. Interval]
SMI 40	6.444341	2.988561	2.16	0.031	.5868694, 12.30181
Gestational Age	-.904588	1.156309	-0.34	0.736	-2.656782, 1.875864
Male	-4.106641	3.113005	-1.32	0.187	-10.20802, 1.994736
LOS week	-1.088891	.7439668	-1.46	0.143	-2.547039, .3692573
White	.3595041	3.273896	0.11	0.913	-6.057214, 6.776223
Cons	110.2118	38.80872	2.84	0.005	34.14812, 186.2755

582
583
584
585

SMI 40 Sucking Maturity Index at 40 Weeks Post Menstrual Age
LOS Length of Stay