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ARTICLE

Neonatal State Organization, Neuromaturation, Mother-Infant Interaction, and Cognitive Development in Small-for-Gestational-Age Premature Infants

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ABSTRACT

OBJECTIVE. The purpose of this work was to examine the relations among neuromaturation, mother-infant relationship, and cognitive development in small-for-gestational-age premature infants and to assess the interactive effects of birth weight and intrauterine growth restriction on developmental outcomes.

METHODS. We studied 120 singleton premature infants (birth weight: 530–1790 g; gestational age: 25–35 weeks). In group 1, 40 small-for-gestational-age infants (22 girls) were case-matched with group 2 ($n = 40$) for birth weight (appropriate for gestational age matched for birth weight) and group 3 ($n = 40$) matched for gestational age (appropriate for gestational age matched for gestational age). Exclusion criteria included intraventricular hemorrhage grade 4, perinatal asphyxia, central nervous system infections, and genetic conditions. Infants were further divided into those born below and above 1000-g subgroups. Neonatal state organization was observed for 4 consecutive hours. Neuromaturation was assessed with the Neonatal Behavioral Assessment Scale. At 3 and 24 months' corrected age, mother-infant interaction was evaluated. At 1 and 2 years' corrected age, the infants' cognitive development was tested with the Bayley Scale of Infant Development, 2nd edition.

RESULTS. Small-for-gestational-age infants showed less organized state and less mature neurobehavioral profiles, particularly in the orientation and motor domains. Mother-infant interactions were characterized by maternal intrusiveness and miscoordination and negative infant engagement. Cognitive outcomes at 1 and 2 years were lower for the small-for-gestational-age group. Small-for-gestational-age infants born <1000 g showed the poorest neurodevelopmental, social, and cognitive development of all of the groups. Cognitive outcomes at 2 years were predicted by small-for-gestational-age status, the interaction of actual birth weight

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Key Words
SGA, small for gestational age, intrauterine growth restriction, IUGR, state organization, NBAS, premature infants, neurobehavioral maturation, cognitive development, mother-infant interaction

Abbreviations
IUGR—intrauterine growth restriction
SGA—small for gestational age
AGA—appropriate for gestational age
NBAS—Neonatal Behavioral Assessment Scale
GA—gestational age
CRIB—Clinical Risk Index for Babies
MANOVA—multivariate analysis of variance
MDI—mental developmental index
PDI—psychomotor development index

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and small-for-gestational-age status, neonatal state organization, and maternal intrusive behavior.

CONCLUSION. Small-for-gestational-age premature infants are at higher risk for developmental and cognitive delays, as well as difficulties in the mother-infant relationship across infancy. Those born at extremely low birth weight are at a double risk. This group should receive special clinical attention and care.

INTRAUTERINE GROWTH RESTRICTION (IUGR) is a multifaceted condition that results in the birth of a small-for-gestational-age infant ([SGA] <10% percentile) and has been associated with increased short- and long-term risk.[1–8] Although the underlying mechanisms for IUGR are heterogeneous,[9] the most common cause is uteroplacental dysfunction, which restricts the delivery of critical amounts of vital substrates to the fetus via the placenta.[10,11] In such affected fetuses, there may also be a chronic stress resulting in activation of the hypothalamic-pituitary axis, leading to excessive secretion of corticosteroids and catecholamines and decreased secretion of anabolic hormones.[12,13] Animal models of IUGR have documented a reduction in brain neuronal number, neuronal migration to the cortex, and abnormalities in neuronal arborization and dendritic growth,[14–17] whereas Tolsa et al[18] recently reported both structural and functional abnormalities of the cerebral cortex in human preterm IUGR infants. These findings clearly suggest that the condition of IUGR differs from prematurity per se, although both conditions often co-occur, and may explain the resulting poor outcome in such growth-compromised infants.

Delayed neurologic maturation has been reported for IUGR infants. Different response patterns of brainstem auditory evoked potential have been noted in preterm IUGR infants compared with appropriate-for-gestational-age (AGA) infants,[19] and preterm SGA infants also showed less mature spontaneous leg movements.[20] Term SGA infants have demonstrated less rhythmic patterns of heart rate,[21] lower amplitudes of heart-rate variability,[22] and lower coordination of sleep state, temperature, and heart rate,[23] including more frequent state changes and more active sleep without rapid eye movement.[24] On the Neonatal Behavior Assessment Scale (NBAS),[25] term SGA infants scored lower on the motor and reflex clusters[26] and showed immature profiles in the interactive processes including low orientation to external stimuli, poor defensive reaction, reduced social responsiveness, and higher negative reactivity.[27] The majority of longitudinal follow-up studies of infant development have shown that both term and preterm SGA infants fare worse than their AGA-matched peers, including lower cognitive skills, poor motor functioning, language delays, learning deficits, lower reading comprehension, and more behavior problems in later childhood and adolescence.[3,28–38]

However, in contrast to research on the neurologic and cognitive outcomes of SGA infants, very little is known about the caregiving environment of such infants or the postneonatal mother-infant relationship. SGA infants have been noted to have deficiencies in orientating to their social and nonsocial environment[26] and are often less rewarding social partners. SGA infants typically display higher levels of negative affect, smile and look at the mother's face less during interactions, and are described as less adaptive and rhythmic.[39,40] Interactions between mothers and term SGA infants were found to be less synchronous,[23] and mothers of SGA infants tend to show lower adaptation to the infant's signals during feeding.[41] Comparing interactions among mothers, fathers, and their 4-month-old firstborn child in 5 high-risk populations, it was found that infants in the SGA group displayed the highest levels of negative affect, and their parents showed the highest level of intrusive, uncoordinated behavior.[42] In addition, the associations among infant negative affect, lower maternal adaptation, and less optimal home environment with lower infant cognitive development at 6 months were especially strong among SGA infants.[43] Yet, given these observations it is of interest that no study to date has followed the development of the mother-infant relationship in SGA infants.

As such, the present study was designed to examine the development of premature SGA infants over a period of 2 years. We hypothesized that SGA infants would display lower organization of sleep and wake states and less mature neurobehavioral profiles in the neonatal period; that the SGA infants would show higher levels of negative engagement during social interactions, and their mothers would demonstrate more intrusive, uncoordinated behavior across infancy; and that the cognitive development of SGA infants would be less optimal at 1 and 2 years. It was further hypothesized that these neurobehavioral features of the SGA premature infant would be interrelated and would predict cognitive development at 2 years.

METHODS

Participants

Participants were 120 singleton premature infants (gestational age [GA] <36) born at the Shaare Zedek Medical Center in Jerusalem from February 1996 to February 1999. The study sample group 1 included 40 SGA infants (birth weight <10th percentile) who were matched to 2 control groups: group 2 (AGA-BW), 40 AGA infants matched for birth weight (±100 g), and group 3 (AGA-GA), 40 AGA infants matched for GA (within the same week). Each group included 22 girls and 18 boys.

Infants in the 3 groups were matched for gender, birth order (primiparous/multiparous), family demographics (including maternal and paternal age and education), and the family's self-reported level of social support. Exclusion criteria included intraventricular hemorrhage grade IV; perinatal asphyxia; metabolic, genetic, or syndromic disease; intrauterine infection; or postnatal central nervous system infection. All of the families were considered middle-class by Israeli standards[44]; mothers were ≥20 years old and married to the child's father. In all of the families, ≥1 parent was employed.

To further examine the effects of IUGR, all 3 of the groups were further divided for analysis to 2 subgroups according to birth weight: subgroup A included infants born with a birth weight of <1000 g, and subgroup B included those with a birth weight >1000 g. A convenience sample of consecutive mothers whose infants matched the study criteria was approached to enroll in a developmental follow-up study of premature infants. Eight mothers refused citing time constraints as the main reason. These mothers and infants did not differ from the participating families on any demographic or infant medical variables.

Procedure and Measures

Infant medical risk was quantitated according to the Clinical Risk Index for Babies (CRIB) score.[45] Infants' state organization and neurobehavioral status were observed in the NICU before discharge at 37 weeks' GA. Mother-infant interactions were observed at 3 months' corrected age during a home visit and at 24 months' corrected age during a laboratory visit. At 12 and 24 months' corrected age, infants' cognitive development was tested by trained professionals. The study was approved by the institutional review board, and all of the mothers signed an informed consent before enrolling in the study.

State Observation (37 Weeks' GA)

During 4 consecutive evening hours (7:00 PM to 11:00 PM), trained coders observed the infant's state in 10-second epochs and entered the data into a computerized program. Six states were observed and defined according to Holditch-Davis[46] and Brazelton,[25] including quiet sleep, active sleep, sleep-wake transition, unfocused alertness, alert wakefulness, and cry.

Neurodevelopmental Status (37 Weeks' GA)

At 37 weeks' GA, infants were examined with the NBAS by a trained neonatologist. Items were composited into 6 clusters,[26] and the habituation, orientation, and motor maturity clusters were compared

Mother-Infant Interaction (3 and 24 Months' Corrected Age)

Approximately 10 minutes of mother-infant interaction were videotaped during a home visit at 3 months and in a laboratory visit at 24 months. Coding of all of the tapes was conducted at a central university laboratory by trained observers. Interactions were coded with the Coding Interactive Behavior,[47] a global rating system of parent-infant interaction that includes 42 codes rated from 1 (low) to 5 (high). The system has been validated in numerous studies of healthy and at-risk infants and has shown sensitivity to infant age, interacting partner, cultural background, and developmental risk conditions.[48–52] Two factors were examined in the present study, as described below.

Maternal Intrusiveness

Maternal intrusiveness was measured based on 5 items: parent's physical manipulation of infant's body, interruption of infant's activities, breaking gaze while infant is looking, disregard of infant's signals, and parent leading the interaction (Cronbach α = .82 and .86 at 3 and 24 months, respectively).

Infant Negative Engagement

Infant negative engagement was calculated from 4 items at 3 months and from 5 items at 24 months. These included infant demonstrating signs of fatigue, emitting fuss-cry vocalization, averting gaze, or withdrawing and/or physically avoiding mother (Cronbach α = .87 and .83 at 3 and 24 months, respectively). Two coders, who did not participate in the testing and were not aware of the infant's group membership or medical risk, were trained to 90% agreement. Reliability was measured on 15 at each stage and reliability averaged 96% (κ = 0.86).

Cognitive Testing (12 and 24 Months' Corrected Age)

Trained psychologists assessed infant cognitive development with the Bayley Scale of Infant Development, 2nd edition.[53] Different psychologists were used for cognitive testing at each observation point to ensure unbiased evaluation.

Statistical Analyses

For each set of variables (state organization and neurodevelopmental status in the neonatal period, mother-infant interactions at 3 and at 24 months, and cognitive development at 12 and at 24 months) a multivariate analysis of variance (MANOVA) with group (SGA, AGA-BW, and AGA-GA) and birth weight subgroups as the between subject factors was computed. After significant findings, posthoc comparisons with Scheffé tests were conducted. Second, associations between variables within each age and across ages were examined with Pearson correlations. Third, 2 hierarchical multiple regressions examined the prediction of infants' mental and psychomotor development at 24 months from variables across the first 2 years of life. The sample provided enough power to detect medium effect size at power = .80 for α = .05 on all of the statistical tests.[54]

RESULTS

Family demographics and infant medical status for the 3 groups are summarized in Table 1. There was no difference between the 3 groups as to parental age, education, or social class. As expected, group 2 (AGA-BW) was significantly less mature than either group 1 or group 3. The CRIB score was significantly lower in group 3 (AGA-GA) as compared with groups 1 and 2. Figure 1 depicts the breakdown of each group and subgroup.

State Organization and Neurodevelopmental Status at 37 Weeks' GA

State Organization

A MANOVA with group (SGA, AGA-BW, and AGA-GA) and birth weight as the between-subject factors revealed an overall main effect for SGA group (Wilks' $F_{12,220}$ = 2.34; P = .042). Univariate tests (Table 2) showed significant differences for transition and cry. SGA infants spent more time in transitory states and cried more than the AGA-BW group, who showed more transition and cry than the AGA-GA group. As expected, main effects were also found for birth weight (Wilks' $F_{6,110}$ = 3.28; P = .044) with infants born <1000 g showing more transition and cry states. Most importantly, an overall interaction effect of SGA group and birth weight was found (Wilks' $F_{6,110}$ = 3.22; P = .043). Univariate tests showed significant differences in active sleep ($F_{1,110}$ = 8.03l P = .005) and transition ($F_{1,110}$ = 4.24; P = .041). Group 1A SGA infants showed the lowest proportions of active sleep states (mean: 0.26; SD: 0.19), whereas the group 1B SGA infants showed the highest proportions of active sleep states compared with all other groups (mean: 0.49; SD: 0.25; $F_{1,39}$ = 5.03; P = .031). Differences were also observed for transition and indicated that group 1A SGA infants, SGA infants born <1000 g, had the highest

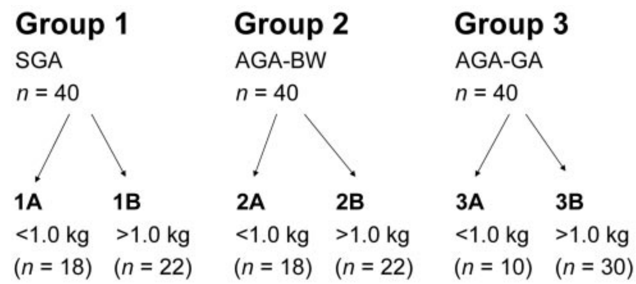

FIGURE 1
Study population and subgroups.

proportions of transition episodes compared with all of the other groups ($F_{1,119}$ = 4.65; P = .024; Fig 2).

Neurodevelopment Status

A MANOVA conducted for the 3 NBAS clusters (habituation, orientation, and motor maturity) with group and birth weight as the between-subject factors revealed an overall main effect for group (Wilks' $F_{6,226}$ = 2.94; P = .038). Univariate tests (Table 2) indicated that SGA infants scored lower than the other groups on orientation and motor maturity. Orientation was the least mature in the SGA group, AGA-BW showed higher orientation, and the AGA-GA scored the highest of the 3 groups. Overall main effects were also found for birth weight (Wilks' $F_{3,113}$ = 4.01; P = .018) and showed that all of the infants born <1000 g scored lower on habituation and motor maturity. In addition, an interaction of SGA and birth weight was also found (Wilks' $F_{6,226}$ = 2.69; P = .048), and univariate tests revealed differences in orientation ($F_{1,113}$ = 3.54; P = .049) and motor maturity ($F_{1,113}$ = 3.65; P = .031). Infants in group 1A (SGA with birth weight <1000 g) scored significantly lower on orientation (mean: 4.54; SD: 1.71) compared with all other groups (mean: 5.41; SD: 1.52; $F_{1,119}$ = 4.85; P = .026). Similarly, group 1A infants showed poorer motor maturity (mean: 3.42; SD: 0.83) compared with all other groups (mean: 4.61; SD: 0.57; $F_{1,119}$ = 5.64; P = .021).

TABLE 1 **Family Demographic and Infant Medical Variables**

Variable	A SGA (n = 40)		B AGA-BW (n = 40)		C AGA-GA (n = 40)	
	Mean	SD	Mean	SD	Mean	SD
Birth weight, g	1282.05	363.29	1278.56	318.49	1698.29	367.02
GA at birth, wk	33.19	3.12	30.12[a]	1.96	33.46	0.94
CRIB (score)	2.80	2.76	2.57	2.98	0.83[b]	0.28
Maternal age, y	28.63	5.35	29.08	6.14	29.87	5.79
Mother education, y	14.73	1.96	13.58	3.12	13.96	1.98
Paternal age, y	30.78	8.13	31.60	5.55	31.94	7.08
Father education, y	13.92	3.13	13.40	4.09	13.28	4.76
Male/female ratio	18:22		18:22		18:22	

[a] B < A, C; P < .05.
[b] C < A, B; P < .05.

TABLE 2 **Group Differences in State Organization and Neurodevelopmental Status**

Variable	A SGA		B AGA-BW		C AGA-GA		Univariate F
	Mean	SD	Mean	SD	Mean	SD	
State organization							
Quiet sleep	0.30	0.21	0.32	0.29	0.37	0.26	NS
Active sleep	0.38	0.25	0.38	0.21	0.41	0.17	NS
Transition	0.14	0.15	0.09	0.07	0.05	0.04	3.74 A>B>C[a]
Unfocused alertness	0.07	0.07	0.10	0.09	0.08	0.09	NS
Alert wakefulness	0.02	0.04	0.04	0.04	0.03	0.04	NS
Cry	0.09	0.06	0.05	0.05	0.03	0.03	3.62 A>B>C[a]
Neurodevelopmental status (NBAS)							
Habituation	6.02	1.13	6.27	0.88	6.50	0.97	NS
Orientation	4.96	0.96	5.16	0.91	5.60	0.86	3.54 A<B<C[a]
Motor maturity	4.03	0.79	4.63	0.74	4.75	0.68	3.65 A<B, C[a]

State organization variables are proportion of time out the 4-hour observation that the infant spent in each state. NS indicates not significant.
[a] $P < .05$.

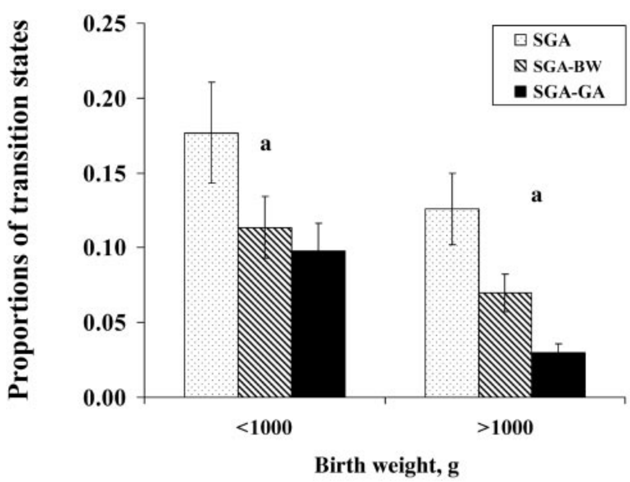

FIGURE 2
Proportions of transition episodes in the neonate's sleep measured across 4 consecutive hours in 10-second epochs in SGA, AGA-BW, and AGA-GA infants analyzed by birth weight. [a] A > B > C; $P < .05$.

Mother-Infant Interactions at 3 and 24 Months

3 Months

MANOVA conducted for the 2 mother-infant interaction variables at 3 months (maternal intrusiveness and infant negative engagement) with group and birth weight as the between-subject factors revealed a significant overall main effect for group (Wilks' $F_{4,230} = 2.48$; $P = .044$). Univariate tests (Table 3) indicated that mothers of SGA infants were significantly more intrusive than mothers of AGA-BW, and those were significantly more intrusive than mothers of AGA-GA. Consistent with our hypotheses, there was an interaction of SGA status and birth weight (Wilks' $F_{2,114} = 3.17$; $P = .045$), and univariate tests indicated differences in mother intrusiveness ($F_{1,114} = 4.20$; $P = .042$). Mothers of infants who were SGA and born <1000 g (group 1A) showed the highest level of intrusive behavior (mean: 2.89; SD: 1.16) compared with all of the other groups (mean: 2.32; SD: 1.13; $F_{1,119} = 3.98$; $P = .045$; Fig 3).

24 Months

A MANOVA conducted for the 2 mother-infant interaction variables at 24 months with group and birth weight as the between-subject factors showed a significant overall main effect for group (Wilks' $F_{4,230} = 2.73$; $P = .032$). Univariate tests (Table 3) showed that mothers of SGA infants were significantly more intrusive than mothers of AGA-BW who were more intrusive than mothers of AGA-GA. In addition, infants in the SGA and AGA-BW groups showed higher negative engagement than the AGA-GA group.

Correlations between mother intrusiveness and infant negative engagement were r at 0.25 ($P = .010$) at 3 months and r at 0.18 ($P = .041$) at 24 months. The correlation between maternal intrusiveness at 3 and 24 months was r at 0.22 ($P = .015$) and between infant negative engagement at 3 and 24 months was r at 0.23 ($P = .012$). Neonatal orientation was negatively related to higher maternal intrusiveness at 3 months ($r = -0.18$; $P = .041$).

Cognitive Development at 12 and 24 Months

12 Months

A MANOVA conducted for the 2 cognitive indices, mental developmental index (MDI) and psychomotor development index (PDI) at 12 months, with SGA group and birth weight as the between-subject factors showed a significant overall main effect for SGA group (Wilks' $F_{4,230} = 3.94$; $P = .026$). Univariate tests (Table 3) indicate that SGA infants scored lower than AGA-GA, but the differences between SGA and AGA-BW were not significant. An overall main effect was also found for birth weight (Wilks' $F_{2,114} = 2.75$; $P = .044$), with infants born <1000 g showing poorer cognitive development. No interaction effects were found at 1 year.

24 Months

A MANOVA conducted for the 2 cognitive indices, MDI and PDI, at 24 months with SGA group and birth weight

TABLE 3 **Group Differences in Mother-Infant Interaction and Cognitive Development**

Variable	A SGA		B AGA-BW		C AGA-GA		Univariate F
	M	SD	M	SD	M	SD	
Mother-infant interaction							
3 mo							
Maternal intrusiveness	2.92	1.02	2.40	1.17	2.18	1.11	3.74 A>B>C[a]
Infant negative engagement	1.50	0.97	1.37	0.78	1.30	0.77	NS
24 mo							
Maternal intrusiveness	2.04	1.08	1.71	0.86	1.40	0.82	3.81 A>B>C[a]
Infant negative engagement	1.96	0.97	1.78	0.93	1.45	0.96	3.92 A, B>C[a]
Cognitive development							
12 mo							
MDI	82.35	10.24	85.3	11.41	90.62	11.02	3.93 A<C[a]
PDI	87.04	14.32	88.31	12.28	91.28	10.14	NS
24 mo							
MDI	85.21	12.20	89.70	13.77	93.20	11.66	4.23 A<B<C[a]
PDI	84.52	10.85	88.25	12.66	90.03	11.58	3.68 A<B, C[a]

Mother-infant interaction variables are rated on a scale of 1 to 5; NS indicates not significant.
[a] $P < .05$.

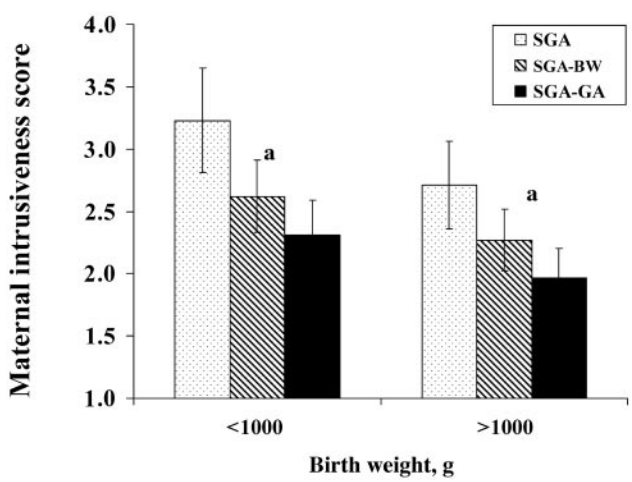

FIGURE 3
Mother intrusiveness score averaged from the 3- and 24-month observation in SGA, AGA-BW, and AGA-GA infants analyzed by birth weight. [a] A > B > C; $P < .05$.

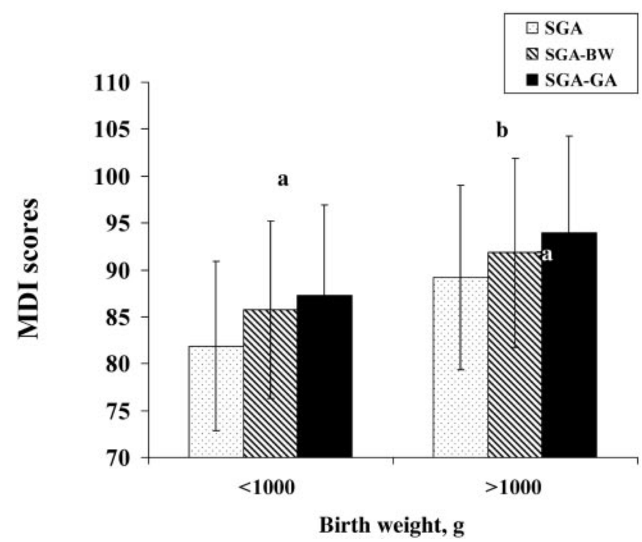

FIGURE 4
MDI scores at 2 years in SGA, AGA-BW, and AGA-GA infants analyzed by birth weight. [a] A < B < C; [b] A < C; $P < .05$.

as the between-subject factors showed a significant overall main effect for SGA group (Wilks' $F_{4,230} = 3.94$; $P = .026$). Univariate tests showed that SGA scored significantly lower than AGA-BW, who scored lower than the AGA-GA. As to PDI, the SGA group showed the poorest motor development compared with both the AGA-BW and AGA-GA groups. There was an interaction of SGA and birth weight (Wilks' $F_{2,114} = 2.78$; $P = .044$). Infants who were both SGA and born <1000 g showed the lowest MDI scores (mean: 81.88; SD: 14.8) compared with all of the other groups (mean: 90.7; SD: 13.71; $F_{1,119} = 5.98$; $P < .01$; Fig 4).

The correlation between infants' MDI scores at 12 and 24 months was r at 0.45 ($P < .001$) and between the 2 PDI scores was r at 0.41 ($P < .001$). Correlations between neonatal variables and cognitive development at 2 years were as follows: the proportion of transitory states was negatively related to MDI scores ($r = -0.19$; $P = .032$). Better habituation to sound and light was related to higher MDI scores ($r = 0.20$; $P = .022$), and motor maturity correlated with PDI ($r = 0.18$; $P = .037$). Mother intrusiveness was negatively related to MDI scores at 2 years ($r = -0.23$; $P = .010$).

Predicting Infants' Cognitive Development at 24 Months

Two hierarchical multiple regressions were computed for predicting infants' MDI and PDI scores at 24 months. Predictors were entered in 5 blocks. In the first block, 3 background variables were entered as dummy variables; the first variable was SGA versus AGA status, the second variable was birth weight below or above 1000 g, and the third was the interaction of SGA and birth weight. These variables were entered first, to partial out variance related to risk conditions. In the second block, the 2 states related to IUGR were entered, transition and cry. In the third block, the 3 NBAS variables, orientation, habituation, and motor maturity, were entered. The fourth block included mother intrusiveness and infant negative engagement, and each was the average of the 3- and 24-month variables. Finally, the fifth block included the infant's 12-month MDI score in predicting MDI or the 12-month PDI score in predicting PDI. Results of the regression models are presented in Table 4, including the standardized regression coefficients (β) from the final step, the increment in R^2 for each step, the F value for each step, and the F level for the entire model. All of the variables were normally distributed, and outliers were checked before analysis.

Significant independent predictors of MDI at 24 months included the 3 background variables, frequencies of transitory states, degree of maternal intrusiveness during interactions at 3 and 24 months, and MDI scores at 12 months. In combination, these variables explained 36% of the variability in infants' mental development at 24 months. Infants' PDI scores were predicted by SGA status, the interaction of SGA and birth weight, NBAS motor maturity, and 12-month PDI scores. In combination, these variables explained 32% of the variance in PDI scores.

DISCUSSION

Results of this study, the first to examine the neurobehavioral, social-relational, and cognitive development of premature SGA infants in comparison to both birth weight- and GA-matched controls in a single study, demonstrate that IUGR is associated with unfavorable outcomes in all 3 domains. SGA infants showed poor neurobehavioral maturation in the neonatal period, as expressed in state disorganization, poor motor maturity, and lower orientation to social and nonsocial stimuli. The caregiving environment of the SGA infants was less optimal, and their mothers displayed higher levels of intrusive behavior that was uncoordinated with the infant's state, level of social engagement, or communicative signals. Finally, SGA infants demonstrated lower cognitive outcomes at 24 months in both the mental and psychomotor domains. These 3 dimensions of development (neonatal neuromaturation, mother-infant relatedness, and infant cognitive development) were interrelated, and indices of poor maturation and intrusive mothering predicted poor cognitive functioning at 24 months. On most outcomes, SGA infants scored lower as compared with AGA infants matched for both birth weight and GA, supporting the conclusion that the outcome abnormalities in these infants are not fully explained by the degree of prematurity per se.

Our study criteria minimized contamination of the results by excluding cases of perinatal asphyxia, major intracranial hemorrhage, and/or intrauterine or central nervous system infection. It also should be emphasized that this study was not an attempt to correlate the degree or type of neurobehavior abnormality with the variety of medical complications that afflict small preterm infants. On the contrary, the uniqueness of this study was that it documented that SGA preterm infants, as a group, have a unique neurobehavioral pattern independent of their neurologic status. In turn, these distinct neurobehavioral features interfere and complicate the mothering process leading to dyadic mother-infant difficulties that correlate with poor cognitive outcome. This information is important for the clinical care of such infants. Furthermore, the AGA-BW group was more immature and had CRIB scores (a measure of medical risk) comparable to the SGA infants but still showed more favorable outcomes than the SGA group. The AGA-GA infants, who, by definition, had a comparable GA to the SGA group,

TABLE 4 **Predicting Infants' Cognitive Development at 2 Years**

Criterion Predictors	MDI			PDI			Degrees of Freedom
	β	R^2 Change	F Change	β	R^2 Change	F Change	
SGA group	.55[a]			47[a]			
Birth weight group	.64[b]			36			
SGA × birth weight	−.64[b]	0.17	8.16[b]	.54[b]	0.12	6.43[b]	3,115
Habituation	.11			.19			
Orientation	.15			.12			
Motor maturity	.09	0.03	2.21	.27[a]	0.06	4.12[a]	6,109
Transition	−.20[a]			−.06			
Cry	−.14	0.09	4.37[a]	−.04	0.01	1.03	8,107
Maternal intrusiveness	−.18[a]			−.10			
Infant negative engagement	−.10	0.04	3.76[a]	−.13	0.02	1.37	10,105
12-mo measure (MDI or PDI)	.38[b]	0.10	12.50[c]	.42[b]	0.11	13.06[c]	11,104
	R^2 total = 0.36; $F_{11,104}$ = 5.47; $P < .001$			R^2 total = 0.32: $F_{11,104}$ = 4.36; $P < .001$			

[a] $P < .05$.
[b] $P < .01$.
[c] $P < .001$.

showed more mature neurobehavioral profiles, more advanced cognitive development, and better interactive behavior. These observations support the conclusion that it is the IUGR and its interplay with premature birth that causes the poorer outcome and not any specific postnatal medical complication.

SGA infants who had a birth weight of <1000 g (group 1A) showed especially poor outcomes. These infants displayed the highest levels of transitory indeterminate sleep, a predictor of lower cognitive development in later childhood,[55] the highest levels of cry episodes, the lowest orientation to social and nonsocial stimuli, the poorest motor maturity, and the lowest cognitive outcomes as compared with all of the other groups. These findings extend and support our recently reported results in triplets,[56] which showed that the growth-retarded discordant infant of the triplet set received the lowest level of sensitive mothering and showed the slowest cognitive development across infancy. It is important to note that although Gortner et al[57] reported no significant differences in the neurodevelopmental status of SGA versus AGA preterm infants at 22 months, the study population included SGA infants with weights as high as 2205 g and higher GAs than our study population. Similarly the report by Scherjon et al[58] that, after adjusting for obstetrical variables, fetal growth per se was not independently associated with abnormal neurodevelopmental outcome was studied only in 19 SGA infants and included infants with birth weights as high as 2295 g, distinctly heavier than our study population.

Intrusive mothering was found to be highest in the SGA group, especially in the subgroup of SGA infants born at <1000 g, and was noted to predict lower cognitive outcomes. Mothers of premature infants tend to increase their intrusive behavior and often use didactic tactics that do not follow the infant's lead. Such behavior is thought to result from the mother's pressure to support the premature infant's cognitive growth and from the difficulty of responding to the premature infant's inconsistent social signals.[59–61] The mother's intrusive style has been associated with high maternal anxiety and low social support and was found to predict less optimal social-emotional development and lower maternal sensitivity.[47] These observations are consistent with the transactional model of early parent-infant relationships in normal and at-risk developmental contexts.[62] According to this model, the infant's biological dysregulation impacts on the caregiving context and extracts, in turn, less sensitive parenting from the mother. Moreover, intrusive mothering limits the infant's opportunities to experience synchronous social interactions, which are considered to be critical environmental inputs for the development of self-regulation, cognitive, and social-adaptive capacities.[63,64]

Interestingly, our data show that infant state organization and the mother-infant relationship were related to the child's mental, not motor, development at 2 years. It seems that the course of mental development is more open to inputs from the caregiving environment, and the parental style is more central in shaping the child's cognitive, as compared with motor, growth.[48] Our previous research has shown that the neurodevelopmental and cognitive skills of premature infants are influenced by a variety of maternal factors, including the provision of skin-to-skin contact, the frequency of maternal touch, or the degree of maternal postpartum depressive symptoms.[49,65] Mothers of SGA infants should, thus, be instructed of the need to wait for the infant's signals and to time their response accordingly, to tolerate the infant's unclear and often withdrawn social behavior, and to be aware of the need for a sensitive and synchronous maternal style for the infant's ultimate cognitive growth.

CONCLUSIONS

Using a case-matched longitudinal design in which premature SGA infants were matched for birth weight or GA, it was found that SGA as a group showed less favorable outcomes across infancy, including less mature orientation and motor behavior in the neonatal period, less organized state, less adaptive social behavior across infancy, and lower cognitive outcomes at 1 and 2 years. The group of infants who were both SGA and with a birth weight <1000 g were at an especially high risk and scored significantly poorer than all of the other groups, indicating a double risk for these infants. More research and clinical attention should be directed to this subgroup of premature infants and their special developmental needs.

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