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Size for Gestational Age and Neonatal Sleep Variables: Behavioral Indices of Risk in Fullterm Twins

M.L. Riese

Louisville Twin Study, Child Development Unit, Health Sciences Center, University of Louisville, Louisville, Kentucky USA.

Abstract. Neonatal sleep behaviors and behavioral state cycling were observed for 20 pairs of same-sex, fullterm twins in which one twin of the pair was appropriate-for-gestational-age (AGA) and the other twin was small-for-gestational-age (SGA). Time-sampling recordings were made in active sleep of number and vigor of limb movements, body and head movements, and mouth movements. No group differences were observed for time spent in first active sleep, first quiet sleep, or length of first sleep cycle. Examination of specific behaviors indicated a significantly higher incidence of vigorous limb movements and right hand-to-mouth movements, with a trend for more small limb movements and left hand-to-face movements, for AGA twins when compared with SGA twins. SGA twins had significantly more spontaneous smiles and a trend for more spontaneous startles than AGA twins. A stepwise discriminant analysis indicated that a composite of the variables smile, large limb movement, startle, and left hand-to-face significantly discriminated between the two groups, with 90% correct classification of the AGA twins and 75% correct classification of the SGA twins. The results demonstrated the utility of evaluating specific sleep behaviors, rather than state cycling only, to describe differences in neonatal sleep characteristics between AGA and SGA twins.

Key words: Size-for-gestational-age, Neonates, Sleep, Twins.

INTRODUCTION

When compared with appropriate-for-gestational-age (AGA) children, small-for-gestational-age (SGA) children have been described as being more likely to have a higher incidence of neurological, psychomotor, and behavioral abnormalities, poor scores on developmental tests, and learning difficulties in school [1,24,34]. Differences between AGA and SGA infants have been described in motor and reflex behavior in the first 10 days of life [2,20]; in habituation rates at 4 months [12]; in neurological integrity at 40 weeks [25]; and in psychomotor development at 18 months [23].

Several studies have suggested, however, that SGA children are not necessarily developmentally delayed. For example, failure to find differences between AGA and SGA children has been reported for mental development, language development, motor development, hearing and vision [1,4,23,25,34]. Thus, prediction of risk for developmental problems for SGA children as a group is difficult, and it is not clear at birth or in early infancy which SGA infants will be most at risk for problems [24].

One way of evaluating developmental integrity for possible early identification of infants at risk for developmental problems is by observation of neonatal sleep behaviors and behavioral state cycling, as the organization of states has been related to central nervous system (CNS) functioning [13,15,26,38]. State organization and the behavioral indices observed during neonatal sleep have been found to be predictive of later developmental problems [37]. Neonates who demonstrated poor organization of states, indicated by amount of time spent in different states, the appropriate behaviors observed in states and cycling of states, were likely to demonstrate poor organization of states at 8 months of age [35]. Poor consistency in state organization from 2 to 5 weeks of age was related to medical or behavioral dysfunction measured in the first 3 years of life [37]. In addition, neonatal disorganization in sleep patterns, particularly measured by time spent in active sleep and indeterminate sleep, has been related to poor regulation of attentional patterns and lower IQ scores at 12 years of age [32].

Neonatal sleep indices also have been suggested to be good indicators for detecting normal and abnormal CNS development [5,13]. Neonates with known abnormalities or brain damage have been found to differ from healthy fullterm neonates in state cycling and in the amount of time spent in the different behavioral states [22,26]. In-utero exposure to alcohol and to narcotics and other drugs has been shown to affect neonatal state regulation as well as the type and frequency of specific behaviors such as extended body movements and startles [6,30,31]. Premature infants have been found to differ from fullterm infants during sleep states in the occurrence of specific behaviors, such as startles, smiles, frowns, grimaces, mouth movements, large body movements and total body movements, as well as in state organization [5,8,9,11,29,33].

Although there is some literature on differences between fullterm and preterm infants in neonatal sleep characteristics, comparatively little research has been done in this area with SGA infants. In one such study [38], SGA infants were found to have a greater rate of state change and more active sleep without REMs than fullterm infants. However, the SGA group included both preterm and fullterm infants (groups for which previous studies have demonstrated differences in sleep behavior), and specific sleep behaviors were not studied.

In the present study, fullterm AGA and SGA twin neonates were observed for the frequency of occurrence of specific behaviors during active sleep, as well as for sleep cycling. The specific sleep behaviors recorded were those described as spontaneous behaviors observed in specific states in the neonatal period, and which define specific neonatal states [7,10,33,35,36,39]. Observation of twins allowed for the control of gross prenatal and obstetrical variables that may differentially influence neonatal behavior.

Although there clearly were some differences in the prenatal histories, since one twin was AGA and the other SGA, maternal variables such as age, diet, medical status and stress potentially would be the same for each infant of the twin pair.

METHOD

Subjects

The sample consisted of 20 pairs of same-sex, fullterm twins (10 female, 10 male) in which one twin of the pair was appropriate-for-gestational-age (AGA) and the other twin was small-for-gestational-age (SGA). Birth gestational age ranged from 38 to 41 weeks, with a mean of 39 weeks. Size for gestational age was determined by using the norms from Lubchenco et al [18] that define SGA infants as those in the lower 10th percentile of weight for gestational age. The National Institute of Child Health and Human Development has recommended the use of these criteria for both clinical and research purposes [27]. These criteria also have been recommended for use in the evaluation of intrauterine growth in twins [19].

Delivery route was the same for cotwins, except for one pair in which the first twin was delivered vaginally and the second by cesarean section because of fetal distress and failure to progress. Sixteen AGA infants were first-born. Although no analysis has been performed comparing first- and second-born twins in the larger sample on all of the specific behaviors observed in this study, previous analyses indicated that birth order was not related to number and vigor of limb movements in active sleep, or to other neonatal behavioral variables [28]. Seventeen AGA and 16 SGA twins presented in the vertex position; the balance were breech or shoulder presentation (information was not available for one SGA twin). These twins were participating in a larger study of infant development, and size for gestational age was not determined until after the behavioral assessment was completed. Zygosity determination was not available for all pairs because not all twins had been blood-typed.

Information on perinatal variables is presented in Table 1. As would be expected, there was a significant difference between the AGA and SGA groups on birth weight. Measures of neonatal status and complications also are listed and include scores on the Postnatal Complications Scale [17]. This scale assesses 10 areas of neonatal complications scored as "optimal" and "nonoptimal". Differences between groups on these measures would suggest initial differences between the AGA and SGA twins that might be related to differences in the behavioral measures of interest. It should be noted that, in the main, none of the twins in this study were seriously ill during the neonatal period. In the SGA group, 13 infants received the optimal score and 4 infants received the next level score. In the AGA group, 14 infants received the optimal score and 5 infants received the next level score. There were no significant differences between the AGA and SGA groups on any of the measures of neonatal status or complications.

Table 1 - Means and ranges of perinatal variables for AGA and SGA twins (N = 20 pairs)

Variable	AGA		SGA		t for Means
	Mean	Range	Mean	Range	
Birth weight (grams)	2887	2381–3558	2306	1673–2559	6.91, $p < 0.0001$
1-minute Apgar	7.6	4–9	7.2	4–9	ns.
5-minute Apgar	8.7	8–10	8.8	7–10	ns.
Postnatal Complications Scale [a]	142.4	87–160	137.4	77–160	ns.
Bilirubin (mg/dl; N: AGA = 7, SGA = 9)	8.36	0–11.1	9.0	0–11.1	ns.
Duration of phototherapy (days; N = 7 pairs) [b]	1.86	0–5	2.29	0–6	ns.
Test chronological age (days)	3.8	1–7	5.5	1–21	ns.

[a] 160 = optimal score
[b] at least one twin of pair had phototherapy
ns: not significant

Procedure

The twins were tested when they were ready for discharge from the hospital (Table 1). Immediately following a nursery-scheduled feeding, the infant was undressed except for a diaper and placed under a warmer with a temperature probe on the abdomen. Infants were supine but propped slightly to the right side because they had just been fed; complete mobility of body and limbs was possible.

Behavioral states were defined as described by Anders et al [3]. Observations were made for 10 minutes during the first active sleep period following the feeding, and began two minutes after the infant was in active sleep in order to confirm active sleep. Test order for the first- and second-born twins was counterbalanced for consecutive pairs. Time-sampling recordings, consisting of alternating 15-second observation and recording periods, were made of the occurrence of the following spontaneous behaviors: the number of limbs moved (0 to 4) and vigor of limb movement (slight, moderate, or large); body movements consisting of startles, stretches and head movements; movements of hands to face; mouth movements consisting of smiles, grimaces, sucks and other general mouth movements.

In addition, the entire first sleep cycle was observed to determine the length of the total cycle, and the length of the first active sleep period and the first quiet sleep period. Interrater reliabilities for sleep behaviors and behavioral states ranged from $r = 0.85$ to $r = 1.00$.

RESULTS

Etiology for Intrauterine Growth Retardation

Intrauterine growth retardation may result from genetic factors, congenital infections, maternal ingestions, maternal diseases and placental insufficiency, although the cause of growth retardation remains unknown in up to 50% of SGA infants [1,16,21]. In twin pregnancies, growth retardation can result from a suboptimal implantation site or, in the case of monochorionic twins, from abnormal vascular anastomoses [1,16]. The medical charts were reviewed to determine the presence of any of those variables known to be associated with small birth size. Of the possible maternal variables, 7 mothers had toxemia or preeclampsia. Of the other variables, there was one instance of twin transfusion syndrome and two instances of vascular anastomosis. (One pair of twins with vascular anastomosis was the offspring of a mother with preeclampsia). The medical charts for the remaining eleven pairs of twins indicated no prenatal complications. Thus, there was a suggestion of known etiology for intrauterine growth retardation for some infants. For more than half the sample, however, other than being a product of a multiple gestation, the specific etiology remains unknown. Furthermore, it is not known why the potential etiologic variables appeared to have a more adverse affect for one twin of the pair when compared with the cotwin.

AGA-SGA Differences in Sleep Variables

To determine if there were differences between the AGA and SGA twins in the sleep cycle or in ratings on the behaviors observed in active sleep, two-tailed *t* tests were computed between the groups for these variables which are listed in Table 2. There were no differences between the groups for latency to sleep after feeding, time spent in first active sleep, time spent in first quiet sleep, or length of the first sleep cycle (which also includes transitional, or indeterminate, sleep).

Significant differences were observed between the AGA and SGA twins on specific behaviors, as follows. AGA twins had more vigorous movements than SGA twins; AGA twins had more right hand-to-mouth movements than SGA twins; and SGA twins had more spontaneous smiles than AGA twins. In addition, certain trends were observed — AGA twins tended to have more small limb movements than SGA twins: SGA twins tended to startle more frequently than AGA twins; and AGA twins tended to have more left hand-to-face movements than SGA twins.

Intercorrelations of Sleep Variables

The interrelations among the variables that differentiated between the two groups were examined separately for the AGA and SGA twins. The results, presented in Table 3, indicated that for the AGA twins there two significant correlations between these variables. AGA twins who startled more frequently had more total large movements of one,

Table 2 Means and ranges of sleep variables for AGA and SGA twins (N = 20pairs)

Variable	AGA		SGA		*t* for Means
	Mean	Range	Mean	Range	
Latency to sleep after feeding (minutes)	4.25	0–16	4.35	0–20	ns.
Time in first active sleep (minutes)	26.7	16–45	23.8	13–66	ns.
Time in first quiet sleep (minutes)	15.5	0–30	16.5	0–32	ns.
Length of first sleep cycle (minutes)	44.0	16–68	42.5	18–66	ns.
Small movement of 3 or 4 limbs	2.4	0–10	1.4	0–4	1.77, $p<0.09$
Large movement of 1, 2, 3 or 4 limbs	0.45	0–2	0.10	0–1	2.08, $p<0.05$
Startle	0.45	0–2	0.80	0–2	-1.70, $p<0.10$
Stretch	2.1	0–5	1.6	0–5	ns.
Head movement	6.4	1–14	5.0	1–11	ns.
Right hand-to-face	3.4	0–8	3.0	0–10	ns.
Left hand-to-face	2.6	1–6	1.8	0–6	1.72, $p<0.10$
Right hand-to-mouth	0.65	0–3	0.15	0–1	2.23, $p<0.04$
Left hand-to-mouth	0.05	0–1	0.00	0	ns.
Smile	0.60	0–2	1.45	0–5	-2.08, $p<0.05$
Grimace	0.75	0–3	0.80	0–4	ns.
Suck	0.35	0–4	0.10	0–1	ns.
General mouth movements	12.6	5–17	11.0	3–19	ns.

Note: Means for behavioral variables refer to the number of 15-second intervals, out of a possible 20 intervals, in which the behavior was observed.

two, three or four limbs, and AGA twins who smiled more frequently during active sleep had more left hand-to-face movements than twins who smiled less frequently. There were no other significant correlations between the variables for the AGA group. For the SGA group, there were no significant correlations between the variables that had differentiated between the two groups. Therefore, the occurrence of these behaviors in sleep generally were independent of each other.

Statistical analyses then were performed to determine if the differences observed be-

Table 3 - Intercorrelations for sleep variables that differentiated between AGA and SGA twins, separately by group

Variables	Small movement	Large movement	Startle	Hand-to-face	Hand-to-mouth	Smile
AGA Correlations						
Small limb movement		−0.21	0.09	−0.06	0.06	0.07
Large limb movement			0.63**	−0.02	−0.07	0.06
Startle				0.04	−0.08	−0.04
Left hand-to-face					0.40	0.57**
Right hand-to-mouth						0.15
Smile						–
SGA Correlations						
Small limb movement		0.05	−0.26	−0.07	−0.28	0.09
Large limb movement			0.34	−0.05	−0.14	0.22
Startle				0.36	−0.09	−0.38
Left hand-to-face					0.32	−0.17
Right hand-to-mouth						0.14
Smile						–

** $p<0.01$

tween the sleep-variable correlations for the AGA and SGA twins represented significant group differences in the relations. For this purpose, the r to z transform was used, and statistical analyses were computed between the z coefficients [14] to compare the two correlations for which significant associations were found for the AGA twins but not for the SGA twins. The results indicated that there was a significant difference between the AGA and SGA groups, using a two-tailed test, for the correlation between smiling and left hand-to-face, $\mathrm{CR}=2.39$, $p<0.05$. There was no significant difference between the groups for the association between startles and large limb movements. Although the incidence of smiling was not high, the AGA group demonstrated a stronger relation between smiling and left hand-to-face movement than the SGA group, thus suggesting a possible common underlying association for these two sleep behaviors for AGA infants but not for SGA infants.

Stepwise Discriminant Analysis

To determine if the above sleep variables that were found to occur, or tended to occur, with different frequencies for the AGA and SGA twins might be used to differentiate

Table 4 - Stepwise discriminant analysis of sleep variables for AGA and SGA twins

Step No.	Variable Entered (E) or Removed (R)	*F* Value to Enter or Remove	No. of Variables Included	Approximate *F*-Statistic	Degrees of Freedom	
1	Right hand-to-mouth (E)	4.97	1	4.97*	1	38
2	Smile (E)	4.70	2	5.08*	2	37
3	Large limb movement (E)	4.83	3	5.34**	3	36
4	Startle (E)	11.40	4	8.02***	4	35
5	Right hand-to-mouth (R)	3.99	3	8.64***	3	36
6	Left hand-to-face (E)	6.18	4	8.96***	4	35

* $p<0.05$; ** $p<0.01$; *** $p<0.001$

between these two groups, a stepwise discriminant analysis was computed with the 6 variables. Use of the discriminant analysis could determine if a composite of the variables strengthened the differentiation between the two groups of infants while eliminating the potential redundancy of related variables. This is particularly meaningful because of the low frequency of occurrence of some of the behavioral variables. The summary of this analysis is presented in Table 4. Right hand-to-mouth best discriminated between the two groups and was the first variable entered. The variables smile, large limb movement, and startle, respectively, were entered next, as adding to the discrimination between the groups. At the next step, the variable right hand-to-mouth was removed; once the other three variables were entered, right hand-to-mouth no longer was necessary to add to the discrimination between the groups. Finally, at step 6, left hand-to-face was entered as the last variable to add to the discrimination between the AGA and SGA twins.

The discriminant analysis also predicts group membership on the basis of the composite discriminant scores (in this case, for smile, large limb movement, startle and left hand-to-face). The jackknifed classification indicated that 90% (18 of 20) of the AGA twins were placed correctly in the AGA group by these composite scores, and 75% (15 of 20) of the SGA twins were placed correctly in the SGA group by the composite scores. Examination of the canonical variables indicated that, for those twins who were misclassified, the misclassification margin was relatively small. Thus, the discriminant analysis demonstrated that the composite of 4 sleep variables was sensitive to differences between AGA and SGA fullterm twins.

DISCUSSION

Fullterm AGA and SGA twins have been found to differ from each other in neonatal sleep characteristics. As the frequency of neonatal complications was not different for the two groups (and the overall incidence of complications was low), the behavioral differences most likely were related to intrauterine factors associated with the growth retardation.

Some of the specific behaviors that entered the discriminant function previously have been evaluated as markers of risk for high-risk neonates. For example, the motor movements have been indicated to be related to the maturational process of the central nervous system (CNS) and have been suggested to be useful to detect abnormal CNS development [13]. In fact, differences in motor movements, as well as in the frequency of spontaneous sleep startles, during neonatal sleep have been observed for infants exposed to drugs and alcohol in utero [6,30,31], and for preterm infants [5,9] when compared with healthy fullterm infants. These motor movements were observed less frequently in the SGA twins than in the AGA twins. In contrast, startles, which typically occur in quiet sleep rather than in active sleep in healthy neonates [7,35], were observed more frequently in the SGA twins than in the AGA twins. Also, neonatal smiles, which have been related to spontaneous discharge of subcortical origin and previously have been observed more frequently in high-risk preterm infants than fullterm infants [7,8,33], occurred more frequently in the SGA group than in the AGA group. Thus, neonatal sleep variables that have differentiated other risk populations from healthy neonates also have differentiated between these AGA and SGA twin neonates.

Of interest, as well, was finding that there were no differences between the AGA and SGA twins in time spent in first active sleep or first quiet sleep, nor in the length of the first sleep cycle. Previous research had demonstrated that the first epoch of active sleep following feeding was longer for preterm infants than for fullterm infants, with the length of the first sleep cycle correspondingly longer for the preterm infants [11,29]. Neonatal state cycling also has been found to be related to in-utero drug and alcohol exposure [6,30,31]. Contrary to the findings for other risk groups, then, measures of neonatal state cycling did not differentiate between these AGA and SGA cotwins.

The results of the stepwise discriminant analysis indicated that a composite score can be created from behaviors observed in active sleep in order to assign individual infants to the low-risk AGA group or to the high-risk SGA group. A composite score clearly is more reliable than individual variable scores because it represents a pattern of behaviors, and because the occurrence of individual sleep behaviors may be relatively low. In this context, increasing the length of observation during acrive sleep may help to increase the power of the composite score so that prediction of group membership may become more accurate.

In any event, the percent of correct assignment for infants from each group appears to be not only logical, but useful in eliminating infants who may not be at risk. That is, finding 90% correct classification for AGA twins suggests that a specific pattern of behavior exists for twins who are not at risk in the neonatal period. Finding 75% correct classification for SGA twins not only is a high percentage for classification but may help to remove infants from the high-risk group when their behavior patterns are similar to those of the low-risk group. The discriminant analysis format allows not only for the classification of neonate twins at risk but also for the examination of scores through canonical variables in order to determine the degree of deviance from the scores of the overwhelming majority of low-risk neonate twins.

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Correspondence: Dr. Marilyn L. Riese, Ph.D, Child Development Unit, Health Sciences Center, University of Louisville, Louisville, Kentucky 40292-0001, USA.