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Human Fetal and Neonatal Movement Patterns: Gender Differences and Fetal-to-Neonatal Continuity

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ABSTRACT: Longitudinal quantification of leg movements per minute for human subjects during both fetal and neonatal periods was accomplished from videotapings conducted antenatally (ultrasonography 30, 34, and 37 weeks gestational age) and postnatally (birth and 6 weeks of age). Fetal/neonatal subjects displayed decreasing numbers of leg movements per minute during antenatal development (30 to 37 weeks), followed by increasing numbers of leg movements per minute during postnatal development (birth to 6 weeks of age). Male subjects displayed greater numbers of leg movements per minute than female subjects during both antenatal and postnatal development. Fetal-to-neonatal continuity for numbers of leg movements per minute was found for comparisons between fetal (37 weeks gestational age) and neonatal (during sleep states at birth) measures, and females displayed a stronger and different movement continuity pattern than males. These results indicate a

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differential time course for neurobehavioral development of male and female fetuses/neonates, and the findings have implications for the clinical assessment of fetal neurobehavioral development and well-being. © 2001 John Wiley & Sons, Inc. *Dev Psychobiol* 38: 252–273, 2001

Keywords: *human; fetus; infant; leg movement; male; female; gender; antenatal; postnatal; birth; third trimester; neurobehavioral development*

The study of human fetal movements with ultrasonography or automated transduction systems is advancing our understanding of fetal neurobehavioral development; however, much remains to be learned (e.g., Birnholz, Stephens, & Faria, 1978; Ianniruberto & Tajani, 1981; Van Dongen & Goudie, 1980; de Vries, Visser, & Prechtl, 1982; Groome, Owen, Singh, Neely, & Gaudier, 1992; Swartjes, van Geijn, Mantel, van Woerden, & Schoemaker, 1990; Pillai & James, 1990a, 1990b; Nijhuis, Prechtl, Martin, & Bots, 1982; Robertson, 1985, 1987). For example, there is little known about potential gender influences on the development of fetal movement patterns, and, understanding of potential fetal-to-neonatal continuity for movement patterns is limited. Research on both of these issues is important for advancing knowledge of human neurobehavioral development during antenatal and antenatal-to-postnatal periods, and for determining the potential clinical usefulness of fetal movement measures for the assessment of fetal well-being and neurobehavioral development and dysfunction (e.g., Visser, Laurini, de Vries, Bekedam, & Prechtl, 1985; Bekedam, Visser, de Vries, & Prechtl, 1985; Sival, Visser, & Prechtl, 1992).

Many studies of human fetal movement do not report male-female comparisons. When gender comparisons are made, however, most studies report no differences for movement patterns between male and female fetuses regardless of gestational age. For example, using ultrasonography, de Vries, Visser, and Prechtl (1988) report no male-female differences for fetal movement patterns studied qualitatively at gestational ages ranging from 7 to 37 weeks, and Pillai and James (1990b) report no gender differences for eye, limb or body movements at gestational ages of 37 weeks and later. Using maternal counts of fetal movements, Valentine, Lofgren, Marsal, & Gullberg (1984) report no male-female movement differences at gestational ages of 34 weeks through term. However, while DiPietro, Hodgson, Costigan, Hilton, and Johnson (1996) report increased activity in fetal males compared to females (using actography), their group did not find gender differences for fetal activity in a later report using the same methodology (Pressman, DiPietro, Costigan, Shupe, & Johnson, 1998). The relative lacking of reports of gender differences

for fetal movement may be related to procedural issues, such as fetal ages studied and methods of movement analysis.

The preponderance of negative gender findings for fetal movement studies contrast with other antenatal studies reporting positive gender effects for a variety of biological and growth measures, and for neonatal studies showing gender differences for movement patterns. For example, antenatal studies of humans and other animals report gender differences for measures of hormones (Bayer, Green, & Hutchison, 1994; Hines, 1982), nervous system (Hutchison, Bayer, Green, & Wozniak, 1994; de Lacoste, Holloway, & Woodward, 1986), somatic growth (Ounsted, Scott, & Moar, 1981; Sumulian, Campbell, Rodis, Feeney, Fabbri, & Vintzileos, 1995), and lung development (Hanley, Rassner, Jiang, Vansomphone, Crumrine, Komuves, Elias, Feingold, & Williams, 1996; Nielsen & Torday, 1981), among others. Further, postnatal studies report gender differences for motility and sensorimotor behaviors for human infants (Aylward, Hatcher, Leavitt, Rao, Bauer, Brennan, & Gustafson, 1984; Buelke-Sam, Sullivan, Kimmel, & Nelson, 1984; Eaton & Enns, 1986; Phillips, King, & DuBois, 1978). Combined, the fetal hormone, nervous system and somatic growth research plus the neonatal movement studies indicate the potential for gender differences for fetal movement patterns.

There are relatively few repeated measures studies of human fetal-to-neonatal neurobehavioral continuity. However, the few available studies tend to agree that such continuity may exist for certain types of movements, or for certain neonatal behavioral states. Patrick, Campbell, Carmichael, Natale, and Richardson (1982) report that percentages of stretching-rolling movements of fetuses undergoing ultrasonography (i.e., 11.8% at 38–40 weeks GA) were similar to the percentages displayed by the subjects as neonates (i.e., 9.2% at 1–3 days after birth). Pillai and James (1990b) report that fetal behavioral state 1F (as based on ultrasonographic study of eye, limb, and body movements) was comparable to neonatal behavioral state S1 (quiet sleep), and similarly for behavioral states 2F and S2 (active sleep). However, they also report that fetal-to-neonatal continuity for waking states were less clear or non-existent. Finally,

Robertson (1985, 1987; based on strain gage measures of movement) reports that cyclic movement patterns were similar between fetuses (last months of gestation) and neonates (18–124 hr following birth) when the neonates were in active sleep states. Although few in number, the results of these studies suggest some degree of fetal-to-neonatal neurobehavioral continuity, and that this continuity may be preferentially expressed for neonatal sleep states.

These gender and fetal-to-neonatal continuity issues were addressed in the present quantitative study of movement patterns using a repeated measures design. Movement patterns of male and female fetuses were studied during the third trimester (gestational ages of 30, 34 and 37 weeks) and postnatally (at birth and 6 weeks of age) to test the hypothesis that males and females would differ for movement patterns during both antenatal and postnatal development, and to test the hypothesis that fetal-to-neonatal continuity exists for movement patterns measured between the late antenatal and early postnatal periods for both genders.

METHODS

Subjects

Pregnant women ($n = 43$) were recruited into the study from the greater St. Louis, MO region, including the patient population seen by the obstetrical ultrasound unit of Washington University Medical Center (St. Louis, MO). These women had their initial ultrasound (US) examination at gestational ages of 20–24 weeks, and completed a detailed questionnaire regarding demographics, and personal and medical history. Based on review of the US examination and questionnaire data and application of the Maternal and Fetal recruitment-exclusion criteria presented in Table 1, eligible subjects were recruited into the study. The Maternal and Fetal recruitment-exclusion criteria were continuously applied throughout gestation, and additional exclusion criteria were applied at Birth and during Infancy (i.e., from birth through 12 months postnatal) as shown in Table 1. Based on

Table 1. Antenatal and Postnatal Recruitment-Exclusion Factors for Mothers and Fetal/Infant Subjects

| |
|--|
| Maternal factors: Applied for history and during pregnancy |
| History of preterm delivery, hypertensive disorders of pregnancy, or isoimmunization |
| Absence of menstrual dating |
| Medical conditions |
| renal or cardiac disease |
| hypertension |
| collagen vascular disease |
| pre-gestational or gestational diabetes |
| seizure disorder |
| pulmonary disease |
| Chronic medication or drug use (e.g., antidepressants, tobacco, alcohol) |
| Fetal factors: Applied from 20–24 weeks through 36–38 weeks gestational age |
| Structural malformation |
| Aneuploidy |
| Multiple gestations |
| Growth disorders (e.g., SGA or LGA) |
| Abnormal amniotic fluid volume or placental location |
| Fetal distress |
| Birth-neonatal factors: Applied from delivery through 6 weeks of age postnatal |
| Delivery outside of hospital |
| Maternal general anesthesia |
| Preterm delivery at < 37 weeks gestational age |
| Infant/fetal/maternal distress (e.g., infant resuscitation) |
| Apgar scores < 8 at 1 or 5 min |
| Birth weight < 10th or > 90th percentiles |
| Abnormal or suspect medical or neurological exams |
| Infant factors: Applied from 6 months through 12 months of age postnatal |
| Missing follow-up studies |
| Atypical growth pattern |
| Major illness |
| Abnormal or suspect medical or neurological exams |
| Abnormal or suspect follow-up studies (e.g., Bayley and/or Vineland Scales) |

Table 2. Maternal History, Pregnancy and Delivery Demographics for Male and Female Subjects

| | Subjects | |
|--|------------------|--------------------|
| | Male (n = 17) | Female (n = 20) |
| Maternal: History and pregnancy ^a | | |
| Age (years) | 29 ± 4 | 30 ± 4 |
| Body Weight (kg) | 65.3 ± 8.2 | 62.1 ± 7.3 |
| Education (HS graduate+) | n = 17/17 (100%) | n = 20/20 (100%) |
| Primagravidas | n = 8/17 (47%) | n = 10/20 (50%) |
| Maternal: Labor and delivery ^a | | |
| Duration of labor (hours) | 15 ± 10 | 12 ± 8 |
| Anesthesia | | |
| Epidural/regional | n = 15/17 (88%) | n = 17/20 (85%) |
| None | n = 2/17 (12%) | n = 3/20 (15%) |
| Delivery mode | | |
| Vaginal | n = 15/17 (88%) | n = 18/20 (90%) |
| Cesarean (planned) | n = 2/17 (12%) | n = 2/20 (10%) |
| Fetal presentation | | |
| Vertex | n = 16/17 (94%) | n = 20/20 (100%) |
| Breech | n = 1/17 (6%) | n = 0/20 (0%) |
| Hospital stay (≤ 3 days) | n = 17/17 (100%) | n = 20/20 (100%) |

^aNo statistically significant differences between male and female subjects based on chi square or *t*-test analyses (all *p*'s > .05)

the recruitment-exclusion criteria, one subject was excluded due to the intrauterine development of a central nervous system abnormality (i.e., hydrocephaly as per US examination), four subjects were excluded based on their premature birth (i.e., at < 37 weeks gestational age), and one subject was excluded because the mother decided not to have the infant participate in the postnatal follow-up studies. Thus,

the results of this study are based on 37 fetal/infant subjects (17 male and 20 female). For the subjects of this study, maternal characteristics are shown in Table 2, neonatal/birth characteristics are shown in Table 3, and antenatal and postnatal gestational age and growth measures are shown in Table 4. Figure 1 presents antenatal and postnatal body weights of the subjects.

Table 3. Neonatal Status for Male and Female Subjects

| | Subjects | |
|----------------------------------|------------------|--------------------|
| | Male (n = 17) | Female (n = 20) |
| Birth ^a | | |
| Ethnicity: | | |
| White | n = 15/17 (88%) | n = 18/20 (90%) |
| Black | n = 1/17 (6%) | n = 1/20 (5%) |
| Asian | n = 1/17 (6%) | n = 0/20 (0%) |
| Hispanic | n = 0/17 (0%) | n = 1/20 (5%) |
| AGA (weight for gestational age) | n = 17/17 (100%) | n = 20/20 (100%) |
| Apgar scores: | | |
| 1 min = 8–10 | n = 17/17 (100%) | n = 20/20 (100%) |
| 5 min = 9–10 | n = 17/17 (100%) | n = 20/20 (100%) |

^aNo statistically significant distribution differences between male and female subjects based on χ^2 analyses (all *p*'s > .05).

Table 4. Gestational Age and Growth Measures of Male (n = 17) and Female (n = 20) Subjects During Antenatal and Postnatal Development

| | Testing gestational age (weeks) | | | | |
|---|---------------------------------|--------------------------|--------------------------|-------------------------|-------------------------|
| | Antenatal | | | Postnatal | |
| | 30 ± 1 | 34 ± 1 | 37 ± 1 | 40 ± 1 Birth | 46 ± 1 6-Weeks |
| Fetal+neonatal measures | | | | | |
| Age at testing (GA in weeks) ^a | | | | | |
| Males | 30.4 ± 0.2 | 34.0 ± 0.2 | 37.2 ± 0.2 | 39.5 ± 0.4 | 45.8 ± 0.6 |
| Females | 30.8 ± 0.2 | 33.7 ± 0.2 | 37.2 ± 0.2 | 39.7 ± 0.2 | 45.6 ± 0.3 |
| Head Circumference (cm) ^{a,b} | | | | | |
| Males | 29.4 ± 0.3 | 32.0 ± 0.2 ^d | 33.6 ± 0.2 ^d | 35.5 ± 0.4 ^d | 38.8 ± 0.3 ^d |
| Females | 28.8 ± 0.3 | 31.0 ± 0.3 | 32.6 ± 0.2 | 34.1 ± 0.3 | 37.7 ± 0.3 |
| Fetal Measures | | | | | |
| Amniotic fluid Index (mm) ^c | | | | | |
| Males | 143.2 ± 6.4 ^d | 150.0 ± 5.8 | 161.2 ± 5.8 ^d | | |
| Females | 163.2 ± 6.4 | 137.0 ± 5.7 | 123.3 ± 7.1 | | |
| Biparietal diameter (cm) ^{a,b} | | | | | |
| Males | 8.02 ± 0.08 | 8.86 ± 0.05 ^d | 9.38 ± 0.06 ^d | | |
| Females | 7.83 ± 0.08 | 8.47 ± 0.06 | 9.07 ± 0.07 | | |
| Abdominal circumference (cm) ^a | | | | | |
| Males | 26.9 ± 0.2 | 30.7 ± 0.3 | 34.1 ± 0.4 | | |
| Females | 27.0 ± 0.3 | 29.7 ± 0.5 | 33.6 ± 0.5 | | |
| Head/abdominal ratio ^a | | | | | |
| Males | 1.09 ± 0.01 | 1.04 ± 0.01 | 0.99 ± 0.01 | | |
| Females | 1.07 ± 0.01 | 1.05 ± 0.01 | 0.97 ± 0.02 | | |
| Cephalic index ^a | | | | | |
| Males | 78.4 ± 0.7 | 80.0 ± 0.7 | 80.8 ± 0.6 | | |
| Females | 78.1 ± 0.7 | 78.1 ± 0.7 | 80.5 ± 0.9 | | |
| AFI/EFW ratio ^{a,c} | | | | | |
| Males | 0.85 ± 0.05 ^d | 0.62 ± 0.03 | 0.50 ± 0.02 | | |
| Females | 0.97 ± 0.04 | 0.61 ± 0.03 | 0.41 ± 0.03 | | |

^aSignificant age effect.^bSignificant gender effect.^cSignificant age × gender interaction.^dSignificant post-testing gender effect (all *p*'s < .05).

This study was approved by the Institutional Review Board at Washington University Medical Center, and signed informed consent was obtained from each woman prior to the first ultrasound testing session.

Procedure

Fetal Movement Testing: Ultrasound Examinations.

The subjects underwent US examinations (60–70 min each) at gestational ages of 30 ± 1, 34 ± 1, and 37 ± 1 weeks. Examinations were performed using real-time ultrasound machines (Acuson 128 × p10/OB, Acuson Corp., Mountain View, CA) and curvilinear and linear 3.5 and 5 MHz frequency transducers.

US examinations were conducted in a quiet, dedicated ultrasound room at the Washington University Medical Center. The mother was in the left-lateral, semirecumbent position on a standard examination table. US examinations for all subjects were conducted between 0730–0900 hr or between 1600–1700 hr, and the morning-afternoon timing of the examinations across the three testing ages (i.e., 30, 34 and 37 weeks gestational ages) were counter-balanced between subjects.

The initial 30 min of each US examination included assessment of fetal anatomy and size, placental location and amniotic fluid volume (see Table 4 and Fig. 1). Multiple measurements of the following biometric parameters were performed: biparietal diameter, occipito-frontal diameter, abdominal circumference,

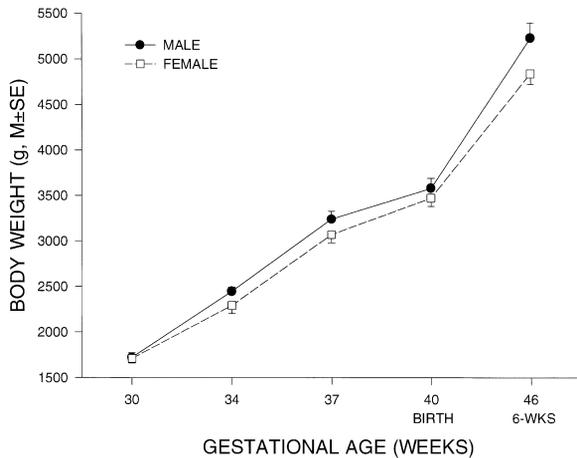


FIGURE 1 Mean (\pm SE) antenatal and postnatal body weights (g) of male and female subjects (fetuses/neonates) plotted as a function of gestational age in weeks. Body weights increased with gestational age ($p < .0001$), and there were no male-female differences ($p = .09$). Filled circles, males; and open squares, females.

femur length, and humerus length. A semi-quantitative assessment of the amniotic fluid volume was performed using a summation of the maximum vertical pockets of fluid in the four quadrants of the uterus, yielding an Amniotic Fluid Index (Phelan, Smith, Broussard, & Small, 1987). Using the fetal biometric measurements, estimated fetal weight was calculated based on head circumference, abdominal circumference, and femur length (Hadlock, Harrist, Sharman, Deter, & Park, 1985), and weight percentile was assigned using local prenatal growth curves generated at the Washington University Medical Center. A detailed anatomic survey was performed imaging the fetal intracranial contents, spine, face, thorax, heart, abdomen and contents, genitalia, cord insertion, as well as extremities.

The second 30 min of each US examination was conducted for quantification of fetal movements. A two-part "sweep" of the uterine cavity was performed; first a transverse section from caudad to cephalad was made, and then a longitudinal section from maternal right to maternal left was performed. This was recorded on videotape, so that on later review the position of the fetus could be assessed (e.g., right vs. left limbs). The fetal lower legs were then identified and scanned in cross section below the knee so that the tibia and fibula and surrounding soft tissue could be clearly seen. The transducer was held in such a position that movement of the lower legs could be easily identified, without the limbs moving out of the field of view of the transducer. Pilot studies were performed using the more traditional longitudinal

view of the lower legs, but it was found that this made "disappearance" of one or both legs more likely during leg movement. Once the appropriate transducer position was achieved, leg movements were continuously recorded on videotape for 30 min. The videotapes of spontaneous leg movements of the fetuses were quantified as described below.

The fetal US examinations (biometric and movement phases) were repeated at gestational ages of 30 ± 1 , 34 ± 1 , and 37 ± 1 weeks for each subject. At each US examination, the Maternal and Fetal recruitment-exclusion criteria shown in Table 1 were re-applied.

Postnatal Movement Testing: Birth and 6-Weeks of Age. Following birth of the fetuses, the newborn infants were tested within 48 hr of delivery (at between 1200–1700 hr), and re-tested at 6 weeks postnatal (at between 1200–1700 hr). Labor, delivery and growth data are presented in Tables 2, 3 and 4, and Figure 1.

During the birth testing at the hospital, the newborn infants were videotaped for quantitative analysis of their spontaneous leg movements (see below). The neonate was videotaped (whole body image) for 30 min with an S-VHS camcorder (Panasonic) while supine in a nursery bed in the maternal room. Labor (e.g., duration of labor), delivery (e.g., vaginal or cesarean section), and neonatal (e.g., birth weight) data were obtained at this time.

For the 6-weeks postnatal testing, the newborn infant and mother returned to the Washington University Medical Center (Developmental Neuropsychobiology Laboratory) for a 30-min videotaping of the supine infant in a crib (whole body image). Videotapes were analyzed off-line for quantification of leg movements. Growth and developmental measures of the infant were obtained (e.g., body weight, head circumference), and medical and sensorimotor screenings were performed (e.g., prior illnesses, vision, and hearing).

The Birth-Neonatal recruitment-exclusion factors shown in Table 1 were applied to the subjects at delivery and at 6 weeks postnatal.

Analysis of Fetal and Neonatal Leg Movements

The antenatal (i.e., 30, 34 and 37 weeks gestational age) and postnatal (birth and 6 weeks of age) videotapes of the fetal/neonatal subjects were scored for movements of the legs with an S-VHS playback system (Panasonic) that was temporally-linked with a computer-assisted movement analysis system (Developmental Neuropsychobiology Laboratory). One leg

at a time was scored with this system using specially developed software programs. While viewing one of the legs on a high-resolution video monitor (Sony), each movement of that leg was scored by pressing a computer key. Key depression was maintained for the duration of the leg movement, and the key was released when the movement stopped or paused for at least 1s. If the leg movement was continuous, but changed direction without pausing (e.g., flexion to extension), the key was quickly released at the change of direction and immediately re-pressed to be scored as another leg movement. For each subject, the computer output provided the numbers of leg movements per minute for the left leg and the right leg.

Three scorers, blind to subject data, conducted the movement scoring. An individual scorer only scored one of the legs for each of the fetal or infant tapings. Prior to quantification of antenatal and postnatal leg movements, the three scorers were trained to greater than .90 reliability for scoring movements, and that high level of reliability for scoring leg movements (simultaneously or independently) was maintained throughout the study. Calculation of Intraclass Correlation Coefficients (Shrout & Fleiss, 1979) revealed high levels of inter-scorer reliability ($r = 0.98$, $p < .0007$) and intra-scorer reliability (r 's = 0.96–0.98, $p < .001$) across subjects and antenatal-postnatal gestational ages.

Analysis of Postnatal Behavioral State

Behavioral states of infants tested at birth and at 6 weeks of age were classified according to the criteria of Prechtl (Prechtl, 1974; Prechtl & Beintema, 1964). The videotapes of the infants (30 min) were viewed separately for scoring of behavioral states by two scorers, both of whom were not involved in the movement scoring and were blinded to subject characteristics. Both scorers classified behavioral states for all subjects at the two postnatal ages. At birth and at 6 weeks of age, the infants were assigned to sleep states (States 1 and 2), awake states (States 3 and 4), or the distressed/crying state (State 5), based on the eyes being open or closed, with rapid, slow or no eye movements, respiration being regular or irregular, and relative amounts and types of body movements (Prechtl, 1974; Prechtl & Beintema, 1964). To be classified as a behavioral state, the state had to have a minimum duration of 3 min (otherwise the 'state' was classified as an indeterminate or transitional state). Kappa coefficient values across states 1 to 5 for both postnatal ages ranged from 0.92 to 0.97, indicating high inter-scorer and intra-scorer agreement (Cohen, 1968).

An overall behavioral state classification (i.e., sleep, awake or distressed/crying) was assigned to each infant at birth and at 6 weeks postnatal, and this classification was used for all data analyses. The overall behavioral state classification at each postnatal age was determined as the predominant behavioral state displayed by the infant on the videotape, i.e., the behavioral state in which the infant spent the greatest amount of time.

Follow-up Studies at 6 and 12 Months Postnatal

During follow-up studies at Washington University Medical Center (St. Louis Children's Hospital and Developmental Neuropsychobiology Laboratory), the infant received medical and neurological examinations and standardized developmental assessments [Bayley Scales of Infant Development-II (Bayley, 1993) and Vineland Adaptive Behavior Scales (Sparrow, Balla, & Cicchetti, 1984)]. In addition, the child's mother provided information on the family demographics (e.g., parents in the home, siblings, utilization of day care or special/therapy services), the home environment [Home Screening Questionnaire (Caldwell & Bradley, 1984)], family socio-economic status [Four Factor Index of Social Status (Hollingshead, 1975)], and maternal stress [Parent Stress Index (Abidin, 1990)]. Bayley and Vineland test results are shown in Table 5. The Infant recruitment-exclusion factors shown in Table 1 were applied to the results of the follow-up testing.

Data Analysis

Data analyses were accomplished with analysis of variance (ANOVA), t -tests, χ^2 and correlations (significance level of .05). Post-testing of significant ANOVA main effects or interactions were accomplished with simple main effects, Tukey, Newman-Keuls, and/or protected t -tests, as appropriate. For ANOVA interactions, only the statistically significant ones are presented in the Results section. Data presented in the text, tables and figures are means \pm standard errors ($M \pm SE$).

RESULTS

Maternal History, Pregnancy, and Birth Measures

Maternal History and Pregnancy Measures. Maternal history and pregnancy data were analyzed with independent t -tests or χ^2 and the maternal data for the

Table 5. Follow-Up Testing of Male (n = 17) and Female (n = 20) Infants at 6 and 12 Months of Age Postnatal

| | Age at postnatal follow-up testing | |
|---|------------------------------------|--------------|
| | 6 months | 12 months |
| Medical-Neurological Examinations ^a | | |
| Males | Normal | Normal |
| Females | Normal | Normal |
| Family demographics ^a | | |
| Males | Normal | Normal |
| Females | Normal | Normal |
| Home environment (Caldwell & Bradley, 1984) ^a | | |
| Males | Normal | Normal |
| Females | Normal | Normal |
| Socio-economic status (Hollingshead, 1975) ^a | | |
| Males | Levels III–V | Levels III–V |
| Female | Levels III–V | Levels III–V |
| Maternal stress (Abidin, 1990) ^a | | |
| Males | Normal | Normal |
| Females | Normal | Normal |
| Bayley scales of infant development-II (Bayley, 1993) ^a | | |
| Mental developmental index | | |
| Males | 107.6 ± 6.8 | 107.4 ± 5.2 |
| Females | 109.0 ± 7.6 | 110.5 ± 9.2 |
| Psychomotor developmental index | | |
| Males | 101.7 ± 11.4 | 100.9 ± 10.9 |
| Females | 104.8 ± 8.7 | 101.1 ± 8.1 |
| Vineland adaptive behavior scales (Sparrow et al., 1984) ^a | | |
| Males | 103.1 ± 9.5 | 106.5 ± 7.4 |
| Females | 107.1 ± 4.4 | 105.9 ± 4.9 |

^aNo statistically significant differences between male and female subjects, or between 6 and 12 month testing ages, based ANOVA or χ^2 analyses (all p 's > .05).

male and female subjects (fetal/infant) are presented in Table 2 (top). Prior to and throughout pregnancy, the mothers of male and female fetal/infant subjects did not statistically differ for age, body weight, education level (i.e., all at least high school graduates), gravidity (i.e., 1–3 pregnancies), or parity (i.e., 0–3 live births) (all p 's > .05).

Maternal Labor and Delivery Measures. Maternal labor and delivery data were analyzed with independent t -tests or χ^2 and are presented in Table 2 (bottom). The mothers of male and female subjects did not statistically differ for duration of labor (hours), use or type of delivery anesthesia (i.e., epidural, regional, none), fetal presentation (i.e., vertex, breech), delivery mode (i.e., vaginal, planned cesarean section), or length of hospital stay (i.e., 1–3 days) (all p 's > .05). The planned cesarean sections included two males (1 breech and 1 repeat/elective) and two females (1 cephalopelvic disproportion and one repeat/elective).

Birth Measures. Birth measures for male and female subjects were analyzed with χ^2 and are presented

in Table 3. The male and female subject distributions did not statistically differ for ethnicity (majority were white), birth weight relative to gestational age (all subjects were appropriate for gestational age throughout pregnancy and at birth), or Apgar scores at 1 or 5 min (all 8 or higher) (all p 's > .05).

Fetal-Neonatal Growth Measures

Gestational Age at Testing (Weeks). Gestational age at testing is shown in Table 4 (top), and the data were analyzed with a mixed design ANOVA with one between subjects factor (gender: male and female), and two within subjects factors (gestational age: 30, 34, 37, 40, and 46 weeks; measurement method for determining gestational age: menstrual dating and US examination dating). This ANOVA revealed no statistically significant gestational age differences at testing between males and females ($F[1,35] < 1.0$), or for measures of gestational age based on menstrual dating versus US examination dating ($F[1,35] < 1.0$). As

expected, gestational age of the subjects increased significantly during developmental testing from 30 to 46 weeks ($F[4,140] = 970.40, p < .0001$).

Body Weight (g and Percentile). Body weights of the male and female subjects are plotted as a function of gestational age at testing and are presented in Figure 1. ANOVA (between subject factor: gender; within subject factor: gestational age) revealed that body weight of the subjects significantly increased with gestational age ($F[4,140] = 563.62, p < .0001$), and that there was a non-significant trend for males to be slightly heavier than females ($F[1,35] = 3.04, p = .09$). A similar ANOVA was used to analyze body weight percentiles as a function of gestational age and gender. Weight percentiles ranged from the 60th to 84th percentiles across gestational age and gender, and there were no significant main effects for gestational age ($F[1,35] < 1.0$) or for gender ($F[1,35] < 1.0$).

Head Circumference (cm). The head circumference data for male and female subjects are presented in Table 4 (top). ANOVA (between subjects factor: gender; within subjects factor: gestational age) showed that head circumference increased as a function of gestational age ($F(4,140) = 502.31, p < .0001$), and that head circumference averaged approximately 1 cm greater for males than females ($F[1,35] = 13.68, p < .0008$). Simple main effects post-testing revealed that the gender difference for head circumference was found at all gestational ages (p 's $< .05$) except 30 weeks ($p = .12$).

Fetal Growth Measures

ANOVA's [between subjects factor: gender; within subjects factor: gestational age (30, 34 and 37 weeks)] were used for the following antenatal analyses [data shown in Table 4 (bottom)]:

The Amniotic Fluid Index (mm, AFI) did not significantly differ across gestational ages ($F[2,70] = 2.42, p = .10$) or between genders ($F[1,35] = 2.64, p = .11$), however, there was a significant gestational age \times gender interaction ($F[2,70] = 14.25, p < .0001$). Simple main effects post-testing of this interaction revealed that females had higher AFI's than males at 30 weeks, and that males had higher AFI's than females at 37 weeks (p 's $< .02$).

Biparietal diameter (cm, BPD) significantly increased as a function of gestational age ($F[2,70] = 252.67, p < .0001$), and there was a significant main effect for gender ($F[1,35] = 16.55, p < .0004$). Simple main effects post-testing of the gender effect showed that males had a greater BPD than females at 34 and 37 weeks (p 's $< .0001$), but no gender differences were found at 30 weeks ($p > .05$).

Abdominal circumference (cm) significantly increased as a function of gestational age from 30 to 37 weeks ($F[2,70] = 290.83, p < .0001$), with no gender differences ($F[1,35] = 1.00, p = .32$).

The ratio of head/abdominal circumference (HC/AC) significantly decreased from 30 to 37 weeks ($F[2,70] = 80.28, p < .0001$), and there were no differences in the HC/AC ratio between males and females ($F[1,35] = 1.25, p = .27$).

The Cephalic Index (ratio of biparietal/occipitofrontal diameter) significantly increased as a function of gestational age ($F[2,70] = 7.92, p < .0008$), without gender differences ($F[1,35] = 1.26, p = .26$).

The ratio of Amniotic Fluid Index/Estimated Fetal Weight (AFI/EFW) was calculated as an estimate of amniotic fluid volume relative to fetal size, i.e., an estimate of uterine free space relative to body size for each fetus and each gestational age (e.g., Phelan et al., 1987; Reinold, 1976). Analysis of the AFI/EFW ratio data revealed that there was a significant decrease in the ratio with increasing gestational age ($F[2,70] = 119.92, p < .0001$), no significant main effect for gender ($F[1,35] < 1.0$), but a significant gestational age \times gender interaction ($F[2,70] = 6.68, p < .002$). Simple main effects post-testing of this interaction showed that females had a higher AFI/EFW ratio (i.e., more relative free space) than males at 30 weeks ($p < .01$), and that males and females did not differ for the AFI/EFW ratio at either 34 or 37 weeks (p 's $> .05$).

Follow-Up Studies at 6 Weeks and 12 Months of Age

Postnatally, male and female subjects at 6 and 12 months of age did not statistically differ (all p 's $> .05$) for results of medical-neurological examinations (all subjects were normal), socio-economic status (all subjects were middle-to-upper class status), the home environment (all were normal), maternal stress (all mothers were at non-clinical levels of stress), family demographics (e.g., none of the subjects were using special or therapy services), or for Bayley Scales and Vineland Scales standard scores (all subjects were within 1 SD of the mean [100 ± 15] at both 6- and 12-month testing). Results of follow-up studies are presented in Table 5.

Antenatal and Postnatal Movement Analysis

Fetal-neonatal leg movements. For the overall analysis, number of leg movements per minute were analyzed with ANOVA with two within-subject factors (leg: left and right legs; gestational age: 30, 34, 37, 40, and 46 weeks) and one between-subject factor (gender:

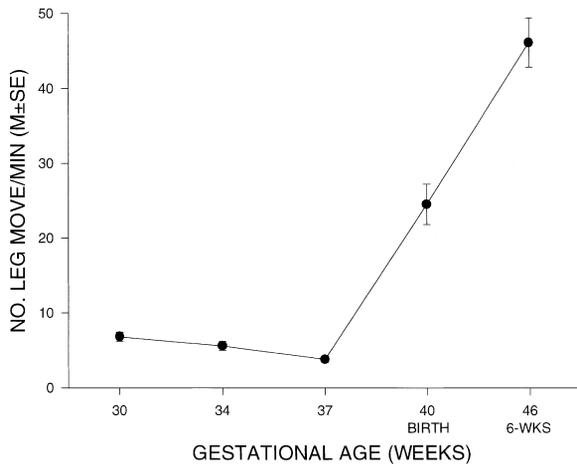


FIGURE 2 Mean (\pm SE) numbers of leg movements per minute plotted as a function of gestational age in weeks for subjects during fetal and neonatal development. Numbers of leg movements per minute decreased from 30 to 37 weeks gestational age, then increased from 37 to 40 weeks, then increased from 40 weeks (i.e., birth) to 46 weeks gestational age (i.e., 6 weeks of age) ($p < .0001$).

male and female). The number of leg movements per minute did not differ between the left and right legs ($F[1,35] < 1.0$). However, number of leg movements per minutes differed as a function of gestational age ($F[4,140] = 78.61$, $p < .0001$), and males displayed more leg movements per minute than females ($F[1,35] = 4.70$, $p < .03$). Because there were no significant differences between left leg and right leg movements per minute, or significant interactions with the left-right leg factor, the mean number of left-right leg movements per minute were computed for each subject, and this mean was used in all the figures, and for all subsequent data analyses. The significant main effects for gestational age and gender on leg movements per minute are described below.

Mean number of leg movements per minute are plotted as a function of gestational age in Figure 2. Newman-Keuls post-testing of the significant main effect for gestational age revealed that leg movements per minute decreased from 30 weeks to 37 weeks antenatal ($p < .04$), then increased from 37 weeks antenatal to 40 weeks (birth), then increased again from birth to 46 weeks postnatal (p 's $< .0001$), i.e., for leg movements per minute: $30 > 37 < 40 < 46$ weeks gestational age. Leg movements per minute did not differ between 30 and 34 weeks, or between 34 and 37 weeks (p 's $> .05$).

Fetal leg movements. Leg movements per minute for the significant antenatal gender effect are plotted as a function of gestational age (30, 34 and 37 weeks) in Figure 3. Simple main effects and protected t -test

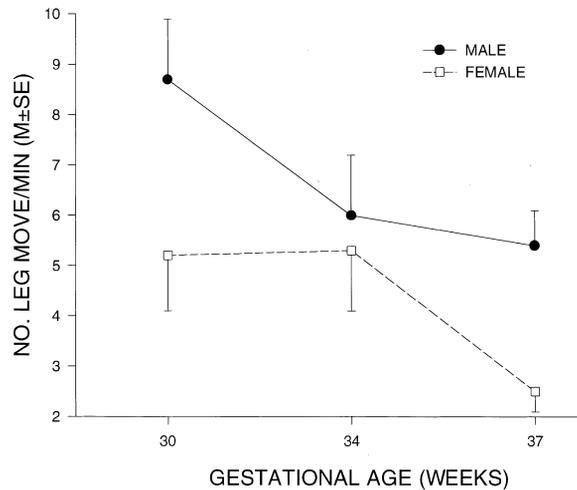


FIGURE 3 Mean (\pm SE) numbers of leg movements per minute plotted as a function of antenatal gestational ages for male and female fetuses. Numbers of leg movements per minute decreased with gestational age ($p < .0004$), and males moved their legs more than females ($p < .0004$). Filled circles, males; and open squares, females.

post-testing revealed that males displayed greater numbers of leg movement per minute than females at both 30 weeks ($p < .0009$) and 37 weeks ($p < .005$), but not at 34 weeks ($p > .05$). Males displayed their greatest number of leg movements per minute at 30 weeks, followed by a decrease to 34 weeks ($p < .01$), with no change between 34 and 37 weeks ($p > .05$). For females, leg movements per minute did not differ between 30 and 34 weeks ($p > .05$), but leg movements per minute decreased from 30/34 weeks to 37 weeks (p 's $< .005$). Thus, both male and female fetuses decreased their number of leg movements per minute between 30 and 37 weeks; however, the timing of the decreased leg movements differed with gender, i.e., leg movements of male fetuses decreased between 30 and 34 weeks, while leg movements of female fetuses decreased later, at between 34 and 37 weeks.

Neonatal leg movements. It was anticipated that postnatal leg movement per minute data and behavioral state classifications (i.e., sleep, awake or distressed/crying) might be associated because relative amount/type of body movement is one of the defining characteristics for classifying the different behavioral states (Prechtl, 1974; Prechtl & Beintema, 1964). Spearman correlations computed between behavioral states (coded as increasing levels of arousal: sleep = 1, awake = 2, and distressed/crying = 3) and leg movements per minute were statistically significant at birth testing (40 weeks GA: $r = +0.70$, $p < .0001$) and at 6-weeks postnatal testing (46 weeks GA: $r = +0.64$, $p < .0001$). Thus, numbers of leg movements per

minute increased as arousal levels increased from sleep through waking through distressed/crying behavioral states for infants (supine position) at both birth and 6-weeks postnatal testing. Because of the relatively strong postnatal associations between leg movements and behavioral states, two additional analyses were conducted and are described below.

The first analysis determined if there were differences in the proportions of male and female infants in the different behavioral states for testing at birth and at 6 weeks (χ^2 analysis). The proportions of male and female infants displaying the different behavioral states (sleep, awake, and distressed/crying) did not differ at birth ($X[2] < 1.0$) or at 6 weeks of age ($X[2] = 1.34, p > .05$). There was a difference, however, in the proportions of subjects in the different behavioral states at birth versus 6 weeks testing ($X[2] = 6.00, p < .05$). The highest proportions of both male and female subjects were in the sleep state at birth (overall = 56%: males = 52%, females = 60%), and in the awake state at 6 weeks of age (overall = 48%: males = 52%, females = 45%). These results show that male and female infants did not differ for their distributions of behavioral states at birth or at 6 weeks postnatal, and thereby justify analysis of the leg movement per minute data using behavioral state as an ANOVA factor.

For the second analysis, the ANOVA included a behavioral state factor (between subjects: sleep, awake, and distressed/crying), as well as gender (between subjects: male and female) and gestational age (between subjects: birth and 6 weeks of age) factors. For this ANOVA, gestational age was treated as a between subjects factor because too few of the subjects were in the *same* behavioral state at both birth and 6 weeks testing. For numbers of leg movement per minute, there were significant main effects for: gestational age [i.e., fewer movements at birth (24.46 ± 2.72) vs. 6 weeks (46.08 ± 3.38); $F[1,62] = 11.72, p < .001$], behavioral state [i.e., movements increased as a function of increasing arousal levels: sleep (19.68 ± 2.79), awake (42.99 ± 3.46), and distressed/crying (53.08 ± 4.09) states; $F[2,62] = 26.54, p < .0001$], and gender [i.e., more leg movements per minute for males (38.50 ± 3.27) vs. females (32.07 ± 3.73); $F[1,62] = 4.01, p < .05$]. The age \times behavioral state interaction was significant ($F[2,62] = 5.51, p < .006$), as was the all inclusive gender \times gestational age \times behavioral state interaction ($F[2,62] = 5.33, p < .007$).

The data for the statistically significant 3-way interaction are plotted in Figure 4, i.e., numbers of leg movements per minute for postnatal gestational age (birth and 6 weeks of age), gender (males and females) and behavioral state (sleep, awake, and distressed/

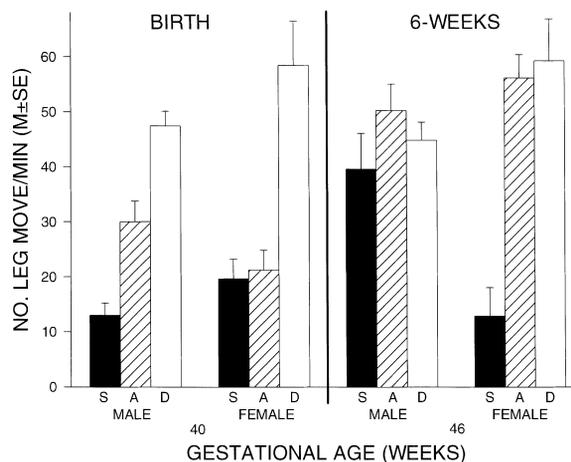


FIGURE 4 Mean (\pm SE) numbers of leg movements per minute plotted for male (left side of Birth and 6-Weeks panels) and female (right side of Birth and 6-Weeks panels) infants during sleep (S, filled bars), awake (A, cross-hatched bars) and distressed/crying (D, open bars) behavioral states at birth (40 weeks gestational age) and at 6 weeks of age (46 weeks gestational age).

crying). Post-testing of this interaction used 2-way ANOVA, simple main effects, and protected *t*-tests.

At birth: Females displayed greater numbers of leg movements per minute than males while in the sleep state, males moved more than females while in the awake state, and females moved more than males while in the distressed/crying state (p 's $< .05$). Males displayed their fewest leg movements during sleep, intermediate numbers of leg movements during the awake state, and the greatest numbers of leg movements during the distressed/crying state (i.e., sleep $<$ awake $<$ distressed/crying, p 's $< .001$). Females displayed their fewest leg movements during sleep and awake states (which did not differ, $p > .05$), and their greatest numbers of leg movements during the distressed/crying state (i.e., sleep = awake $<$ distressed/crying, $p < .001$).

At 6-weeks of age: males moved their legs more than females while in the sleep state, and females moved their legs more than males while in the distressed state (p 's $< .05$), however there were no gender differences in rate of leg movements during the awake state ($p > .05$). Males did not differ for numbers of leg movements per minute across the different behavioral states (i.e., sleep = awake = distressed/crying, p 's $> .05$), while females displayed their greatest leg movements during the awake and distressed/crying states (which did not differ, $p > .05$) compared to the sleep state (i.e., sleep $<$ awake = distressed/crying, p 's $< .0001$).

Comparisons between birth and 6-week postnatal revealed that during the sleep state, males moved their

legs less at birth compared to 6 weeks ($p < .005$), while females did the opposite, moving their legs more at birth than at 6 weeks during the sleep state ($p < .05$). For both the awake and distressed/crying states, the overall pattern of leg movements between birth and 6 weeks were not different between males and females, i.e., during the awake state both genders moved their legs more at 6 weeks than at birth (p 's $< .02$), and for the distressed/crying state neither gender differed for leg movements between birth and 6 weeks (p 's $> .05$).

Fetal-to-neonatal movement continuity/discontinuity. Research indicates that human fetuses are predominantly in some form of sleep or quiet behavioral states during the latter half of the third trimester (e.g., Nijhuis et al., 1982; van Vliet, Martin, Nijhuis, & Prechtl, 1985). In order to assess potential fetal-to-neonatal movement continuity/discontinuity, those newborn infants who were in sleep states at birth were selected, and their leg movement data at birth were compared to their fetal (i.e., 37 weeks) leg movement data using gender specific, paired t -tests. These analyses revealed that both males ($n = 8$) and females ($n = 11$) displayed greater numbers of leg movements per minute at birth (when known to be in sleep states) than they did as fetuses at 37 weeks, i.e., assumed to be in sleep states (p 's $< .02$). When neonates were selected specifically for the waking state or the distressed/crying state at birth, and their birth leg movement data compared to their fetal data, the fetal-to-neonatal increases in leg movements per minute for both genders were equal to or greater than the increases found for the sleep state (all p 's $< .03$). These results could be interpreted to indicate a lack of fetal-to-neonatal continuity for numbers of leg movements per minute because numbers of leg movements per minute were always greater for neonates than fetuses, regardless of the neonates behavioral state. However, fetal-to-neonatal continuity can be assessed in another way, namely, via a measure of strength of association.

Pearson correlation coefficients between fetal (37 weeks) and neonatal (birth) numbers of leg movements per minute were calculated separately for males ($n = 8$) and females ($n = 11$) in the neonatal sleep state, and for males ($n = 9$) and females ($n = 9$) in a combined neonatal awake-distressed/crying state group (awake and distressed/crying states were combined into a single group because the relatively low numbers of subjects in those neonatal states precluded meaningful correlational analyses). The results revealed a statistically significant, positive correlation between fetal and neonatal numbers of leg movements per minute for females when they were in the sleep

state neonatally ($r [10] = +0.73$, $p < .0007$), but the correlation was not significant for females in the waking-distressed/crying state group at birth ($p > .28$). For males, a negative correlation of borderline significance (trend) was obtained for antenatal-to-postnatal leg movements per minute for those males who were in sleep states as neonates ($r [7] = -0.47$, $p = .059$), and the correlations for males in the neonatal awake-distressed/crying group were not significant ($p > .23$). Also, there were no significant correlations (p 's $> .05$) between fetal movements at 37 weeks gestation and movements at 6 weeks postnatal for either males or females, regardless of behavioral state. These results show some degree of fetal-to-neonatal leg movement continuity when neonates were in the sleep state.

DISCUSSION

The present study of fetal and neonatal leg movement patterns shows that numbers of leg movements per minute decreased during the third trimester, followed by an increase at birth through 6 weeks postnatal. During both the antenatal and postnatal measurement periods, males moved their legs more than females. Postnatally, behavioral state had a strong impact on numbers of leg movements per minute for both males and females. Also, fetal-to-neonatal continuity for rates of leg movements were found during neonatal sleep states (stronger continuity for females than males), but not for neonates of either gender during waking-distressed/crying states.

Relations Among Leg Movements and Movements of Other Body Segments

Direct measurement of movements per minute of the head, arms, legs, and trunk for the postnatal subjects of this study (i.e., at birth and 6 weeks of age) revealed that the measure of leg movements per minute provided a relatively accurate index of overall infant motor activity (data not shown). For infants at birth and 6 weeks postnatal, numbers of leg movements per minute were highly correlated with movements per minute of the head, arms and trunk (at birth: r 's[35] = +0.89 to +0.97, $p < .0001$, at 6 weeks: r 's[35] = +0.86 to +0.97, $p < .0001$), indicating that infants displaying high numbers of leg movements per minute were also displaying relatively high numbers of head, arm and trunk movements per minute.

The evidence for potential relationships among movement levels of the different body segments for fetuses is more limited and indirect. For low-risk preterm infants (born at gestational ages ≤ 32 weeks and

studied at gestational ages of 28–40 weeks), relatively strong associations for numbers of movements among the head, arms, legs, and trunk (r 's $> +0.70$) have been found (Almli, 1993). Also, for leg and arm movements of human fetuses (gestational ages of 30–39 weeks), Almli, Mohr, Ball, and Bernhard (1995) report that rankings for fetal movement activity were the same whether based on measures of arm or leg movements. Similarly, other human fetal movement studies often sample multiple body segments for movement and behavioral state analyses (e.g., eye, trunk/abdomen, and/or limb) and show that movements of different body segments tend to co-occur, but not necessarily simultaneously (Arabin & Riedewald, 1992; Nijhuis et al., 1982; Pillai & James, 1990b; Pillai, James, & Parker, 1992; Roberts, Griffin, Mooney, Cooper, & Campbell, 1980).

Combined, these direct and indirect findings converge to indicate that measurement of numbers of leg movements per minute for both neonates and fetuses provides a relatively accurate estimate of overall body movement activity, i.e., fetal/neonatal subjects with high levels of leg movement activity are likely to be displaying relatively high levels of movement activity of the other body segments as well.

Fetal Movement Development: Gestational Age and Gender Effects

Fetal gestational age and movement. Fetal/embryonic leg movements have been reported as early as gestational ages of 8–12 weeks (Van Dongen & Goudie, 1980; Ianniruberto & Tajani, 1981; Natsuyama, 1991; de Vries et al., 1982; de Vries, Visser, & Precht, 1985), and the present results show that the rate of fetal leg movements per minute decreased during the third trimester from 30 to 37 weeks. The present finding of decreasing rates of fetal leg movements is consistent with previous studies (based on ultrasound or maternal report methods) showing that various types of fetal body movements (e.g., number and rate of trunk movements, duration of general movements, kicking counts, number of limb movements) tend to decrease during the third trimester (Minagawa, 1986; Roberts et al., 1980; Panattoni & Todros, 1989; de Vries et al., 1988; Arabin & Riedewald, 1992; Walters, 1964; Edwards & Edwards, 1970; Sadovsky, Laufer, & Allen, 1979). This decrease in fetal movements during the third trimester is paralleled by a report of decreasing movements of low-risk, preterm infants from 32/33 weeks to 36/37 weeks GA (Faienza, Capone, Galgano, & Sani, 1986).

The decrease in body movements as human fetuses approach term-age may be related to a variety of fetal,

maternal, and/or intrauterine environment factors. These factors may include, for example: fetal growth and relative changes in amniotic fluid volume (Sival, Visser, & Precht, 1990; Vintzileos, Campbell, Nochimson, Commolly, Fuenfer, & Hoehn, 1985), fetal nervous system and muscular system development (Almli & Mohr, 1995; Brooksbank, Atkinson, Balazs, 1981; Clandinin, Chappell, Heim, Swyer, & Chance, 1981; Dobbing & Sands, 1973; Foxall & Emery, 1975; Galaburda, LeMay, Kemper, & Geschwind, 1978; Hasegawa, Houdou, Mito, Takashima, Asanuma, & Ohno, 1992; Kaplan, Grumbach, & Aubert, 1976; Koop, Rilling, Herrmann, & Kretschmann, 1986; Meerman, van Bel, van Zwieten, Oepkes, & den Ouden, 1990; Neil, Shiran, McKinstry, Schefft, Snyder, Almli, Akbudak, Aronovitz, Miller, Lee, & Conturo, 1998; Panattoni & Todros, 1989; Schoenen, 1982), changes in maternal-fetal hormones (Bayer et al., 1994; Breedlove, 1986; Hines, 1982; Meyer-Bahlburg, Feldman, Cohen, & Ehrhardt, 1988; Reinisch, 1974; Toran-Allerand, 1984), changing fetal positions (e.g., to the cephalic/vertex position prior to birth; Suzuki & Yamamuro, 1985), and/or fetal behavioral development (de Vries et al., 1982; Groome et al., 1992; Pillai et al., 1992). Although any or all of these factors (among others) could be related to decreasing fetal leg movements with advancing third trimester gestational age, two of these issues (physical growth and neural-behavioral development as the fetus approaches term-age) are specifically addressed below.

It is possible that fetal movement may become more limited as body size increases to fill/stretch the uterus when approaching term. However, in the present study there were no significant associations between fetal weight (g) and fetal leg movements per minute ($r[109] = -0.18, p > .05$), or between amniotic fluid volume and fetal leg movements per minute ($r[109] = +0.13, p > .05$), at gestational ages from 30 to 37 weeks.

To investigate this issue further, a ratio of the Amniotic Fluid Index to Estimated Fetal Weight (AFI/EFW) was calculated (Phelan et al., 1987; Reinold, 1976). The AFI/EFW ratio was used to estimate uterine free space (amniotic fluid space) *relative* to fetal size, i.e., uterine space available for the fetus to move from 30 to 37 weeks. The AFI/EFW ratio was found to decrease from 30 to 34 to 37 weeks, indicating that uterine free space decreased relative to increasing fetal size during the third trimester, and a significant association was found between the AFI/EFW ratio and fetal leg movements per minute ($r[109] = +0.34, p < .002$). Although this finding indicates that decreasing uterine free space relative to increasing fetal size (a fetal swaddling effect?) may be

a contributing factor for the decrease in fetal leg movements/per minute during the third trimester, the proportion of the variance accounted for ($R^2 = 0.12$) was low. Further, animal studies show that fetal rat body movements decrease during late gestation, even when the fetus was externalized from the uterus and the amniotic membranes were removed, i.e., no potential for movement restriction by the uterus or membranes (Smotherman & Robinson, 1987). Thus, it appears that other factors, such as nervous system and behavioral development, may be important for the decrease in fetal leg movements per minute during the third trimester.

Research shows that the human fetus undergoes tremendous nervous system development (e.g., based on structural and functional measures: Almlil & Mohr, 1995; Brooksbank et al., 1981; Dobbing & Sands, 1973; Galaburda et al., 1978; Meerman et al., 1990; Neil et al., 1998) and behavioral development (e.g., spontaneous movements, movement cycles/rhythms and behavioral states: Birnholz et al., 1978; Dierker, Pillay, Sorokin, & Rosen, 1982; Groome & Watson, 1992; Groome et al., 1992; Ianniruberto & Tajani, 1981; Pillai & James, 1990a,b; Pillai et al., 1992; Robertson, 1985; Robertson, Dierker, Sorokin, & Rosen, 1982; Swartjes et al., 1990; Van Dongen & Goudie, 1980; de Vries et al., 1982; Nijhuis et al., 1982) during the third trimester. Based on these neural and behavioral developmental changes, it is important to determine potential inter-relationships between measures of nervous system and behavior during fetal development to gain a better understanding of the process of fetal neurobehavioral maturation. With regard to the present findings of decreasing fetal leg movements during the third trimester, for example, Meerman et al. (1990) report that fetal cerebral blood flow velocities (middle cerebral artery) increase during the third trimester, then drop during the first 5 days postnatal, and Neil et al. (1997) report that apparent diffusion coefficients of water decrease with gestational age in the brains of low risk preterm and full-term infants from 32 to 40 weeks gestational age. The pattern of both of these measures of brain development appear to be related to the present findings of decreasing leg movements during the third trimester, i.e., for third trimester gestational ages, leg movements and cerebral blood flow appear to be inversely related, and, leg movements and apparent diffusion coefficients of water in the brain appear to be positively related. Thus, decreasing fetal leg movements during the third trimester may be related to advancing nervous system and behavioral development of the fetus; and changes in cyclic movement patterns, behavioral states, and leg movements during the third

trimester may each be indicative of progressive neuro-behavioral maturation.

Fetal gender and movement. Reports of gender differences for fetal movement patterns are rare in the research literature. For example, de Vries et al. (1988) report no male–female differences for fetal movement patterns studied qualitatively with ultrasound at between gestational ages of 7–37 weeks, Pillai and James (1990b) report no gender differences for fetal eye, limb or body movements via ultrasound at 37 weeks and later, and Valentine et al. (1984) report no gender differences for fetal movements from 34 weeks to term based on maternal reports. The dearth of reported antenatal gender differences for human movement patterns contrasts with the relatively numerous human and animal research studies showing antenatal gender differences based on biological measures, and gender differences for newborn infants based on behavioral measures. Gender differences have been reported for antenatal studies of hormones (Bayer et al., 1994; Hines, 1982; Meyer-Bahlburg et al., 1988; Reinisch, 1974; Toran-Allerand, 1984), nervous system (Beaston-Wimmer & Smolen, 1991; Engele, Pilgrim, & Reiser, 1989; Hutchison et al., 1994; de Lacoste et al., 1986; Patchev, Hayashi, Orikasa, & Almeida, 1995; Schindler, 1975), surfactant production and lung development (Hanley et al., 1996; Neilsen & Torday, 1981), biochemistry and immunology (Romero, Gomez, Galasso, Mazor, Berry, Quintero, & Cotton, 1994), and somatic growth (Ounsted et al., 1981, Scott, Guardian, Angelus, & Backstrom, 1991; Sumulian et al., 1995). For newborn infants, there are reports of gender differences for motility and sensorimotor behaviors (Aylward et al., 1984; Buelke-Sam et al., 1984; Eaton & Enns, 1986; Phillips et al., 1978), as well as perinatal gender differences for the incidence of preterm birth (McGregor, Leff, Orleans, & Baron, 1992) and for perinatal mortality (Perelman, Palta, Kirby, & Farrell, 1986). The antenatal biological studies (particularly the hormonal, nervous system and growth studies) and the neonatal motor behavior studies converge to indicate that gender differences for antenatal movements might be expected, based on differential biological and behavioral developmental patterns for male and female fetuses and neonates.

The present study shows that male fetuses move their legs more than female fetuses at 30 and 37 weeks, but not at 34 weeks gestational age. Although there may be some (unknown) significance to the 34 weeks age period, the differential pattern of the decrease in leg movements between genders may be what is important during the third trimester. Males displayed their third trimester decrease in leg movements at

between 30 and 34 weeks, while females displayed a later decrease at 34 to 37 weeks. It is possible that the lack of gender differences for leg movements at 34 weeks is spurious, and merely due to the fact that males and females display a differential time course of decreasing leg movements during the third trimester. This differential time course of leg movement decrease between genders may therefore reflect a gender-specific, differential pattern of neurobehavioral development during the third trimester.

Although it is likely that the gender differences for antenatal leg movements reported here are related to gender differences in hormonal, nervous system and/or neurobehavioral development, there are a number of more specific factors that could have influenced the present results, for example, potential gender differences for fetal size, amniotic fluid volume, behavioral state, and/or movement cyclicality.

Fetal body weight/size. Male fetuses moved more than female fetuses at 30 and 37 weeks, yet male-female body weights did not significantly differ at those gestational ages. Also, leg movements per minute did not change between 34 and 37 weeks for males, although their body weights were increasing. Likewise, females displayed no change for numbers of leg movements per minute between 30 and 34 weeks when their body weights were increasing. In addition, males displayed their major decrease in leg movements at between 30 and 34 weeks, when they were at lower body weights than were females when they displayed their major decrease in leg movements at between 34 and 37 weeks (compare Fig. 1 and 3). Finally, if gender differences for fetal weight/size determined gender differences for leg movements per minute, then males should have moved less (not more) than females because males tended (non-significant) to be slightly heavier than females (see Fig. 1). Thus, the gender effect for antenatal leg movements per minute does not appear to be related to potential gender differences for fetal body weight/size.

Amniotic fluid volume. At 30 weeks gestational age, female fetuses moved less than males even though females had a greater amniotic fluid volume than males. Also, the AFI/EFW ratio (discussed above; Phelan et al., 1987; Reinold, 1976) calculated for male and female fetuses showed that females had greater uterine free space relative to body size than males at 30 weeks, yet males moved more than females. At 37 weeks, males again moved more than females, but there were no gender differences for uterine free space relative to body size at 37 weeks. Thus, uterine free space relative to body weight cannot account for the gender differences for numbers of fetal leg movements.

Behavioral state. Although our understanding of the development of fetal behavioral states is incomplete (Groome & Watson, 1992; Nijhuis et al., 1982; Pillai & James, 1990a,b), gender differences for leg movements per minute do not appear to be an artifact of potential behavioral state differences between males and females. First, there are no research reports describing gender differences for fetal behavioral state development during the third trimester. If potential gender differences in behavioral state development determined or accounted for the gender differences for fetal leg movements reported here, one might expect there to be reports of gender differences for the development of behavioral states. Second, it is generally agreed that well-organized, fetal behavioral states are not displayed until approximately 38–40 weeks gestational age (Groome & Watson, 1992; Nijhuis et al., 1982; Pillai & James, 1990a,b). Thus, the gender differences for leg movements found at 30 weeks actually precedes the development of organized fetal behavioral states, and the gender effect on leg movements found at 37 weeks is on the early fringe for the age at which a majority of normal fetuses are reported to begin displaying organized behavioral states [i.e., 38–40 weeks (Groome & Watson, 1992; Nijhuis et al., 1982; Pillai & James, 1990a,b)]. Thus, it does not appear that gender differences for fetal leg movements per minute during the third trimester can be simply explained by potential gender differences in behavioral state development, but this remains an open and unanswered question.

Movement cyclicality. Third trimester fetuses are described as displaying behavioral oscillations in the form of, for example, rest-activity rhythms and ultradian movement cycles (Groome & Watson, 1992; Nijhuis et al., 1982; Pillai & James, 1990a,b; Dierker et al., 1982; Robertson, 1985; Robertson et al., 1982). Although possible, it is not likely that biased sampling resulted in male fetuses being studied only during high activity phases, and female fetuses being studied only during low activity phases, based on our repeated measures design of 37 subjects studied over three gestational ages. Also, the videotapes of fetal leg movements would have cut across a number of potential rest-activity rhythms or ultradian movement cycles which generally have durations on the order of approximately 1–3 min (Groome & Watson, 1992; Nijhuis et al., 1982; Dierker et al., 1982; Robertson, 1985; Robertson et al., 1982). Finally, there do not appear to be any reports of gender differences for fetal activity rhythms or cyclicality. Thus, it is unlikely that biased sampling or movement oscillations could account for the gender differences for leg movements reported here.

The relative lack of studies reporting gender differences for human fetal movement patterns may be related to a number of methodological differences between the present study and previous studies. For example, other studies tend to use small numbers of subjects of both genders (e.g., often less than 10 subjects), to use potentially heterogeneous groups of fetal/maternal subjects (e.g., providing limited descriptions of fetal/maternal health status, using only short-term [birth] postnatal follow-up studies), and/or to use qualitative (i.e., categorical, classification) measures of movement (e.g., gross body movement) which may not be sufficiently sensitive to detect gender differences when they exist. In contrast, the present report of antenatal gender differences for leg movements was based on 37 subjects, used a repeated measures design, re-applied recruitment-exclusion factors from antenatal recruitment through 12 months of age postnatal (see Table 1), and used a relatively more precise methodology of continuously imaged fetal leg movements for quantification (i.e., cross-sectional view as opposed to the longitudinal view).

Neonatal Movement Development: Birth to 6 Weeks Postnatal

Studies of early human postnatal development report that general movements are a prominent and stereotyped feature of behavior (Prechtl, 1974, 1984; Hadders-Algra & Prechtl, 1992), that motor activity is relatively stable over 1–4-day periods immediately following birth (Campbell, Kuyek, Lang, & Partington, 1971; Cioni, Ferrari, & Prechtl, 1989; Korner, Hutchinson, Koperski, Kraemer, & Schneider, 1981), that levels of spontaneous motor activity of neonates are strongly influenced by behavioral state (Cioni et al., 1989; Hadders-Algra, Nakae, Van Eykern, Klip-Van den Nieuwendijk, & Prechtl, 1993; Prechtl, 1984; Wolff, 1966), and that leg movements are a major feature of movement patterns displayed by supine infants (Thelen, 1981). Further, newborn infants do not appear to display motor asymmetries for leg or arm movements (Butterworth and Hopkins, 1993; Provins, 1992), although for leg kicking movements, a favored leg might emerge at 4–6 weeks postnatal (Thelen, Bradshaw, & Ward, 1981).

In general agreement with those studies, the present findings for infants at birth and 6 weeks postnatal show that leg movements increase with postnatal age and are a prominent feature of supine infant behavior, that there were no left-right leg asymmetries for leg movement rates, and that infant leg movements per minute were influenced by behavioral state. There were relatively strong associations between leg move-

ment numbers and behavioral states (i.e., sleep, awake, and distressed/crying) at both birth ($r = +0.70$) and 6 weeks postnatal ($r = +0.64$), i.e., increasing numbers of leg movements per minute with increasing levels of arousal from sleep to awake to distressed/crying both at birth and 6 weeks postnatal. Further, there were no differences in numbers of leg movements per minute between the left and right legs at either birth or 6 weeks postnatal, indicating no evidence for infant movement asymmetries for the legs.

Leg movements have received considerable research attention for the newborn infant; however, much of this research has focused on a specific type of leg movement, namely kicking-like movements of the legs of supine infants (Irwin, 1930; Prechtl, 1977; Shirley, 1931; Stubbs & Irwin, 1933; Thelen, Fisher, & Ridley-Johnson, 1984; Thelen, Skala, & Delso, 1987; Touwen, 1976). Leg kicking-like movements are a predominant type of fetal movement detected by the mother, and these kicking movements may be important for aligning the fetus into the vertex presentation before birth (Illingworth, 1980; Oppenheim, 1981; Thelen, 1985). Further, fetal and neonatal kicking-like movements may reflect pattern generator functions (Grillner, 1975, 1981) which are likely to be important for the later development of locomotion.

In the present study, leg movements measured during the neonatal period consisted of all active leg movements, and included kicking-like movements, as well as less frequent, uni-directional leg movements of slower speed and shorter excursion. Because the predominant form of leg movements in the present study had the topography of kicking-like movements as described by others (Geerdink, Hopkins, Beek, & Heriza, 1996; Thelen, 1985; Thelen, Ridley-Johnson, & Fisher, 1983; Thelen et al., 1987), the leg movement per minute data for birth and 6 weeks postnatal were transformed [divided by 2 because a kick (flexion-extension) was scored as 2 movements] to get an estimate of the rate of kicking-like movements per minute for the present study. This transformation facilitates comparison of the present leg movement results with results reported in the kicking research literature.

Comparison of kicking rates between the present estimate of kicks and those reported by others indicates relatively good agreement for birth measures, but less agreement for 6 week measures. For birth (within 48 hr), 12.3 kicks/min were estimated for the present study and this kicking frequency compares favorably with the 14.3 kicks/min reported by Heirza (1988) for full-term neonates at 1–3 days postnatal. However, at 6 weeks postnatal, the frequency of 23.1 kicks/min for the present study is approximately twice

as high as the frequency of 11 kicks/min reported by Geerdink et al. (1996) for infants at the same age. The discrepancy between the 6-week measures of kicking rates may be related to methodological differences between studies, but not behavioral state differences (i.e., for the present study, the discrepancy remained even when only awake infants' data were used to estimate kick rates; see Fig. 4). More likely, the discrepancy at 6 weeks appears to be due to an increased proportion of leg movements that do not meet kicking criteria (i.e., slow, short excursion and unidirectional leg movements) for the 6-week results of the present study. This explanation of the discrepancy between the present 6-week kicking estimates and the results of other studies is supported by reports of no change in kicking rates between birth and 6 weeks postnatal (Heriza, 1988; Thelen & Fisher, 1982; Geerdink et al., 1996). It is possible that the increase in non-kicking types of leg movements between birth and 6 weeks postnatal may reflect advancing neurobehavioral development of the infant.

Neonatal gender and movement. The present study shows that males moved their legs more than females both at birth and at 6 weeks postnatal, and that this gender difference for leg movements interacted with behavioral state (see Fig. 4). Other studies have also reported neonatal gender differences for motility and sensorimotor behaviors, for example, low-intensity activity, patterns of activity development, and performance on neurological exams (Aylward et al., 1984; Buelke-Sam et al., 1984; Phillips et al., 1978). With advancing postnatal development from infant through adolescent ages, gender effects on motor behaviors are frequently reported (e.g., Aaron, Kriska, Dearwater, Anderson, Olsen, Cauley, & Laporte, 1993; Eaton & Enns, 1986; Gabriel, Chilla, & Kozielski, 1976; Johnson & Brody, 1977; Schwartz, Niman, & Gisel, 1984). For many postnatal gender studies, males are reported to be more active than females, as reported here for fetal and neonatal leg movements. The gender differences for postnatal motor development are likely to be related to differential patterns (potential or known) of human neural and behavioral development [e.g., motor cortex and pathways (Amunts, Istomin, Schleicher, & Zilles, 1995; Sarnat, 1989), development of functional hemispheric lateralization (Grattan, De Vos, Levy, & McClintock, 1992; Tan, Ors, Kurkcuoglu, Kutlu, & Cankaya, 1992)], as well as potential and known gender differences for somatic growth patterns which can strongly influence the biodynamic properties of body segments such as the legs (Thelen, 1985; Thelen et al., 1984). Nevertheless, other neonatal studies, including qualitative analysis of movement (e.g., Cioni et al., 1989;

Weggemann, Brown, Fulford, & Minns, 1987), or detailed analysis of specific types of movement, such as leg kicking (e.g., Heriza, 1988; Thelen & Fisher, 1982; Geerdink et al., 1996), have not reported gender effects for neonatal movements.

The present results show that the gender differences found for antenatal leg movements persisted into the early postnatal period, at least between birth and 6 weeks of age. The fact that the genders did not differ for birth weight and gestational age, health status, distributions of behavioral states at birth and 6 weeks postnatal, or for follow-up measures through 12 months of age postnatal indicates that those factors are unlikely to account for the gender effects on postnatal leg movements reported in the present study.

Fetal-to-Neonatal Movement Continuity

There are relatively few studies that have investigated potential antenatal-to-postnatal relationships for movements (or other behaviors) using repeated measures designs. However, the available studies generally indicate that some degree of continuity may exist between human fetal behavior during the late third trimester and behavior of the human neonate. In an ultrasound study of fetal gross body movements at 38–40 weeks, followed by study of neonatal gross body movements at 1–3 days postnatal, Patrick et al. (1982) have reported that the subjects displayed a similar percentage of rolling and stretching movements during both antenatal and postnatal measurement periods (fetus = 11.8%, neonate = 9.2%). Similarly, Pillai and James (1990b) have reported that fetal behavioral state 1F was comparable to neonatal behavioral state S1 (quiet sleep), and that fetal state 2F was comparable to neonatal state S2 (active sleep), based on ultrasound study of the frequency of eye, limb and body movements. However, they also report that relationships between fetal and neonatal movement measures for the waking states were less clear or non-existent (Pillai & James, 1990b). In addition, Robertson (1985, 1987) used strain gages to measure cyclic movement patterns for fetuses (during the last months of gestation) and for neonates (at 18–124 hr postnatal), and reported that cyclic movement patterns were similar between the antenatal and postnatal measurement periods for those neonatal subjects who were in active sleep states. The consensus of these few studies is that there may be some degree of continuity between fetal and neonatal behavior, and that this continuity may be preferentially manifest during the neonatal sleep state.

Although the studies above report similarities between fetal and neonatal behaviors, the similarities

reported were generally deduced from a lack of significant differences between antenatal and postnatal measures (i.e., accepting the null hypothesis). Using this same logic, the present results can be interpreted as not showing fetal-to-neonatal continuity, because the subjects moved their legs significantly more after birth than during the antenatal period (regardless of neonatal behavioral state). However, another way to assess the question of fetal-to-neonatal continuity is to calculate correlation coefficients to determine strengths of association between fetal and neonatal leg movement activity.

In the present study, relative continuity between fetal (37 weeks) and neonatal (within 48 hr after birth at 40 weeks) leg movement numbers was supported by results for both males and females. Females displayed positive associations between fetal and neonatal numbers of leg movements when in sleep states neonatally ($r(10) = +0.73, p < .007$), while males displayed a negative association (of borderline significance) for fetal and neonatal leg movements when in sleep states neonatally ($r(7) = -0.47, p = .059$). Neither gender displayed significant associations between fetal and neonatal leg movements when in the awake-distressed/crying state neonatally.

Thus, the present results agree with previous studies showing that fetal-to-neonatal behavioral continuity may be preferentially manifest during neonatal sleep states, and less so during neonatal awake and distressed/crying states (Pillai & James, 1990b; Robertson, 1985, 1987). Although there often is an age-gap of weeks between fetal and neonatal measures, and the antenatal and postnatal environments differ considerably, the agreement among studies of fetal-to-neonatal behavioral continuity indirectly indicates that late third trimester behavioral states of fetuses are predominantly sleep states, and that the higher levels of arousal associated with the awake and distressed/crying states of neonates may represent ontogenetic adaptations to the extra-uterine environment, as suggested by others (e.g., Pillai & James, 1990a,b; Oppenheim, 1981).

Final Comments and Implications

Overall, these results indicate gender specific patterns of relatively stable neurobehavioral development during late gestation and early neonatal periods. These findings are important for understanding antenatal and perinatal neurobehavioral development and for the potential use of movement measures in the clinical assessment of fetal neurobehavioral development and well-being. Other studies have shown stability of neurobehavioral development from the neonatal

period through childhood, for example, active neonates tend to more easily approach novel environments at 4–8 years of age (Korner, Zeanah, Linden, Berkowitz, Kraemer, & Agras, 1985), and irritable neonates tend to be distressed toddlers at 2 years of age (Reise, 1987). With regard to determining fetal–neonatal–childhood neurobehavioral relationships, studies are in progress to determine if and how fetal behaviors (i.e., quantitative analysis of movement patterns) may be related to normal and abnormal developmental variations of neurobehavioral functions such as activity levels, learning/memory, and temperament for male and female children. In addition, the present findings of gender-specific patterns of antenatal neurobehavioral development have implications for the clinical assessment of fetal well-being and the effects of fetal nervous system abnormalities. However, our understanding of neurobehavioral development of fetuses with nervous system involvement is limited because there are relatively few research studies available [e.g., fetal growth restriction (Beke-dam et al., 1985; Sival et al., 1992), anencephaly (Visser et al., 1985)]. Thus, studies of male and female fetuses are in progress to determine if and how antenatal neurobehavioral development (e.g., quantitative analysis of leg movements) may be impacted by different types of intrauterine central nervous system abnormalities.

NOTES

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REFERENCES

- Aaron, D. J., Kriska, A. M., Dearwater, S. R., Anderson, R. L., Olsen, T. L., Cauley, J. A., & Laporte, R. E. (1993). The epidemiology of leisure physical activity in an adolescent population. *Medicine & Science in Sports & Exercise*, 25, 847–853.
- Abidin, R. R. (1990). *Parenting stress index* (3rd ed.). Charlottesville, VA: Pediatric Psychology Press.

- Almlı, C. R. (1993). Influence of perinatal risk factors (preterm birth, low birth weight, and oxygen deficiency) on movement patterns: An animal model and premature human infants. In N. J. Anastasiow & S. Harel (Eds.), *At-risk infants: Interventions, families and research* (pp. 127–136). Baltimore, MD: Brooks Pub. Co.
- Almlı, C. R., & Mohr, N. M. (1995). Normal sequential behavioral and physiological changes throughout the developmental arc. In D. A. Umphred (Ed.), *Neurological rehabilitation* (3rd ed.) (pp. 33–65). St. Louis, MO: Mosby.
- Almlı, C. R., Mohr, N. M., Ball, R., & Bernhard, L. (1995). Human fetal and neonatal movement patterns and effects of CNS abnormality. *Neuroscience Abstracts*, 21, 1791.
- Amunts, K., Istomin, V., Schleicher, A., & Zilles, K. (1995). Postnatal development of the human primary motor cortex: A quantitative cytoarchitectonic analysis. *Anatomy & Embryology*, 192, 557–571.
- Arabin, B., & Riedewald, S. (1992). An attempt to quantify characteristics of behavioral states. *American Journal of Perinatology*, 9, 115–119.
- Aylward, G. P., Hatcher, R. P., Leavitt, L. A., Rao, V., Bauer, C. R., Brennan, M. J., & Gustafson, N. F. (1984). *Child Development*, 55, 1155–1165.
- Bayer, C., Green, S. J., & Hutchison, J. B. (1994). Androgens influence sexual differentiation of embryonic mouse hypothalamic aromatase neurons in vitro. *Endocrinology*, 135, 1220–1226.
- Bayley, N. (1993). *Bayley scales of infant development* (2nd ed.). San Antonio, TX: The Psychological Corporation, Harcourt Brace & Co.
- Beaston-Wimmer, P., & Smolen, A. J. (1991). Gender differences in neurotransmitter expression in the rat superior cervical ganglion. *Brain Research. Developmental Brain Research*, 58, 123–128.
- Bekedam, D. J., Visser, G. H. A., de Vries, J. J., & Prechtl, H. F. R. (1985). Motor behaviour in the growth retarded fetus. *Early Human Development*, 12, 155–165.
- Birnholz, J. C., Stephens, J. C., & Faria, M. (1978). Fetal movement patterns: A possible means of defining neurologic developmental milestones in utero. *American Journal of Roentgenology*, 130, 537–540.
- Breedlove, S. M. (1986). Cellular analyses of hormone influence on motoneuronal development and function. *Journal of Neurobiology*, 17, 157–176.
- Brooksbank, B. W., Atkinson, D. J., & Balazs, R. (1981). Biochemical development of the human brain. II. Some parameters of the GABA-ergic system. *Developmental Neuroscience*, 4, 188–200.
- Buelke-Sam, J., Sullivan, P. A., Kimmel, C. A., & Nelson, C. J. (1984). Sex and strain differences in the developmental activity profile of the rat tested over clean vs home cage bedding. *Developmental Psychobiology*, 17, 67–77.
- Butterworth, G., & Hopkins, B. (1993). Origins of handedness in human infants. *Developmental Medicine and Child Neurology*, 35, 177–184.
- Caldwell, B. M., & Bradley, R. H. (1984). *Home observation for measurement of the environment* (revised ed.). Little Rock, AK: University of Arkansas.
- Campbell, D., Kuyek, J., Lang, E., & Partington, M. N. (1971). Motor activity in early life, II. Daily motor output in the neonatal period. *Biology of the Neonate*, 18, 108–120.
- Cioni, G., Ferrari, F., & Prechtl, H. F. R. (1989). Posture and spontaneous motility in full term infants. *Early Human Development*, 18, 247–262.
- Clandinin, M. T., Chappell, J. E., Heim, T., Swyer, P. R., & Chance, G. W. (1981). Fatty acid accretion in the development of human spinal cord. *Early Human Development*, 5, 1–6.
- Cohen, J. (1968). Weighted kappa: Nominal scale agreement with provision for scaled disagreement or partial credit. *Psychological Bulletin*, 70, 213–220.
- de Lacoste, M. C., Holloway, R. L., & Woodward, D. J. (1986). Sex differences in the fetal human corpus callosum. *Human Neurobiology*, 5, 93–96.
- de Vries, J. I. P., Visser, G. H. A., & Prechtl, H. F. R. (1982). The emergence of fetal behaviour. I. Qualitative aspects. *Early Human Development*, 7, 301–322.
- de Vries, J. I. P., Visser, G. H. A., & Prechtl, H. F. R. (1985). The emergence of fetal behaviour. II. Quantitative aspects. *Early Human Development*, 12, 99–120.
- de Vries, J. I. P., Visser, G. H. A., & Prechtl, H. F. R. (1988). The emergence of fetal behaviour. III. Individual differences and consistencies. *Early Human Development*, 16, 85–103.
- Dierker Jr., L. J., Pillay, S. K., Sorokin, Y., & Rosen, M. G. (1982). Active and quiet periods in the preterm and term fetus. *Obstetrics & Gynecology*, 60, 65–70.
- DiPietro, J. A., Hodgson, D. M., Costigan, K., Hilton, S., & Johnson, T. R. (1996). Fetal neurobehavioral development. *Child Development*, 67, 2553–2567.
- Dobbing, J., & Sands, J. (1973). Quantitative growth and development of human brain. *Archives of Diseases of the Child*, 48, 757–767.
- Eaton, W. O., & Enns, L. R. (1986). Sex differences in human motor activity level. *Psychological Bulletin*, 100, 19–28.
- Edwards, D. D., & Edwards, J. S. (1970). Fetal movement: Development and time course. *Science*, 169, 95–97.
- Engele, J., Pilgrim, C., & Reiser, I. (1989). Sexual differentiation of mesencephalic neurons in vitro: Effects of sex and gonadal hormones. *International Journal of Developmental Neuroscience*, 7, 603–611.
- Faienza, C., Capone, C., Galgano, M. C., & Sani, E. (1986). The emergence of the sleep-wake cycle in infancy. *Italian Journal of Neurological Sciences*, 5, 37–42.
- Foxall, C. D., & Emery, A. E. (1975). Changes in creatine kinase and its isoenzymes in human fetal muscle during development. *Journal of the Neurological Sciences*, 24, 483–492.
- Gabriel, P., Chilla, R., & Kozielski, P. (1976). Speech development in preschool children. II. Sex differences in articulation and tongue motility. *Folia Phoniatrica*, 28, 26–33.
- Galaburda, A. M., LeMay, M., Kemper, T. L., & Geschwind, N. (1978). Right-left asymmetries in the brain. *Science*, 199, 852–856.

- Geerdink, J. J., Hopkins, B., Beek, W. J., & Heriza, C. B. (1996). The organization of leg movements in preterm and full-term infants after term age. *Developmental Psychobiology*, 29, 335–351.
- Grattan, M. P., De Vos, E., Levy, J., & McClintock, M. K. (1992). Asymmetric action in the human newborn: Sex differences in patterns of organization. *Child Development*, 63, 273–289.
- Grillner, S. (1975). Locomotion in vertebrates: Central mechanisms and reflex interaction. *Physiological Reviews*, 55, 247–304.
- Grillner, S. (1981). Control of locomotion in bipeds, tetrapods, and fish. In V. B. Brooks (Ed.), *Handbook of physiology: Sect. 1, The nervous system*, Vol. 2, Motor control (pp. 1179–1236). Bethesda, MD: American Physiological Society.
- Groome, L. J., Owen, J., Singh, K. P., Neely, C. L., & Gaudier, F. L. (1992). Spontaneous movement of the human fetus at 18 to 22 weeks of gestation: Evidence of early organization of the active-rest cycle. *Journal of Maternal Fetal Investigation*, 2, 27–32.
- Groome, L. J., & Watson, J. E. (1992). Assessment of in utero neurobehavioral development, I. Fetal behavioral states. *Journal of Maternal Fetal Investigation*, 2, 183–194.
- Hadders-Algra, M., Nakae, Y., Van Eykern, L. A., Klip-Van den Nieuwendijk, A. W. J., & Prechtl, H. F. R. (1993). The effect of behavioural state on general movements in healthy full-term newborns. A polymyographic study. *Early Human Development*, 35, 63–79.
- Hadders-Algra, M., & Prechtl, H. F. R. (1992). Developmental course of general movements in early infancy. I. Descriptive analysis of change in form. *Early Human Development*, 28, 201–213.
- Hadlock, F. P., Harrist, R. B., Sharman, R. S., Deter, R. L., & Park, S. K. (1985). Estimation of fetal weight with the use of head, body, and femur measurements—A prospective study. *American Journal of Obstetrics and Gynecology*, 151, 333–337.
- Hanley, K., Rassner, U., Jiang, Y., Vansomphone, D., Crumrine, D., Komuves, L., Elias, P. M., Feingold, K. R., & Williams, M. L. (1996). Hormonal basis for the gender difference in epidermal barrier formation in the fetal rat. Acceleration by estrogen and delay by testosterone. *Journal of Clinical Investigation*, 97, 2576–2584.
- Hasegawa, M., Houdou, S., Mito, T., Takashima, S., Asanuma, K., & Ohno, T. (1992). Development of myelination in the human fetal and infant cerebrum: A myelin basic protein immunohistochemical study. *Brain Development*, 14, 1–6.
- Heriza, C. B. (1988). Comparison of leg movements in preterm infants at term with healthy full-term infants. *Physical Therapy*, 68, 1687–1693.
- Hines, M. (1982). Prenatal gonadal hormones and sex differences in human behavior. *Psychological Bulletin*, 92, 56–80.
- Hollingshead, A. B. (1975). Four factor index of social status. New Haven, CN: Yale University.
- Hutchison, J. B., Beyer, C., Green, S., & Wozniak, A. (1994). Brain formation of estrogen in the mouse: Sex dimorphism in aromatase development. *Journal of Steroid Biochemistry & Molecular Biology*, 49, 407–415.
- Ianniruberto, A., & Tajani, E. (1981). Ultrasonographic study of fetal movements. *Seminars in Perinatology*, 5, 175–181.
- Illingworth, R. S. (1980). *The development of the infant and young child*. New York: Churchill Livingstone.
- Irwin, O. C. (1930). The amount and nature of activities of newborn infants under constant external stimulating conditions during the first ten days of life. *Genetic Psychology Monographs*, 8, 1–91.
- Johnson, D., & Brody, N. (1977). Visual habituation, sensorimotor development, and tempo of play in one-year-old infants. *Child Development*, 48, 315–319.
- Kaplan, S. L., Grumbach, M. M., & Aubert, M. L. (1976). The ontogenesis of pituitary hormones and hypothalamic factors in the human fetus: Maturation of central nervous system regulation of anterior pituitary function. *Recent Progress in Hormone Research*, 32, 161–243.
- Koop, M., Rilling, G., Herrmann, A., & Kretschmann, H. J. (1986). Volumetric development of the fetal telencephalon, cerebral cortex, diencephalon, and rhombencephalon including the cerebellum in man. *Bibliotheca Anatomical*, 28, 53–78.
- Korner, A. F., Hutchinson, C. A., Koperski, J. A., Kraemer, H. C., & Schneider, P. A. (1981). Stability of individual differences of neonatal motor and crying patterns. *Child Development*, 52, 83–90.
- Korner, A. F., Zeanah, C. H., Linden, J., Berkowitz, R. I., Kraemer, H. C., & Agras, W. S. (1985). The relation between neonatal and later activity and temperament. *Child Development*, 56, 38–42.
- McGregor, J. A., Leff, M., Orleans, M., & Baron, A. (1992). Fetal gender differences in preterm birth: Findings in a North American cohort. *American Journal of Perinatology*, 9, 43–48.
- Meerman, R. J., van Bel, F., van Zwielen, P. H., Oepkes, D., & den Ouden, L. (1990). Fetal and neonatal cerebral blood velocity in the normal fetus and neonate: A longitudinal Doppler ultrasound study. *Early Human Development*, 24, 209–217.
- Meyer-Bahlburg, H. F., Feldman, J. F., Cohen, P., & Ehrhardt, A. A. (1988). Perinatal factors in the development of gender-related play behavior: Sex hormones versus pregnancy complications. *Psychiatry*, 51, 260–271.
- Minagawa, Y. (1986). Evaluation of fetal development and well-being with the ultrasonic Doppler fetal actocardiograph. *Acta Obstetrica et Gynaecologica Japonica*, 38, 1569–1577.
- Natsuyama, E. (1991). In utero behavior of human embryos at the spinal-cord stage of development. *Biology of the Neonate*, 60, 11–29.
- Neil, J. J., Shiran, S. I., McKinstry, R. C., Schefft, G., Snyder, A. Z., Almlı, C. R., Akbudak, E., Aronovitz, J. A., Miller, J. P., Lee, B. C. P., & Conturo, T. E. (1998). Normal brain in human newborns: Apparent diffusion

- coefficient and diffusion anisotropy measured by using diffusion tensor MR imaging. *Radiology*, 209, 57–66.
- Nielsen, H. C., & Torday, J. S. (1981). Sex differences in fetal rabbit pulmonary surfactant production. *Pediatric Research*, 15, 1245–1247.
- Nijhuis J. G., Prechtl H. F. R., Martin C. B., & Bots R. S. (1982). Are there behavioural states in the human fetus? *Early Human Development*, 6, 177–195.
- Oppenheim, R. W. (1981). Ontogenetic adaptations and retrogressive processes in the development of the nervous system and behavior: A neuroembryological perspective. In K. J. Connelly & H. F. R. Prechtl (Eds.), *Maturation and development: Biological and psychological perspectives* (pp. 1–54). Philadelphia, PA: Lippincott.
- Ounsted, M., Scott, A., & Moar, V. (1981). Proportionality and gender in small-for-dates and large-for-dates babies. *Early Human Development*, 5, 289–298.
- Panattoni, G. L., & Todros, T. (1989). Fetal motor activity and spine development. *Panminerva Medica*, 31, 183–186.
- Patchev, V. K., Hayashi, S., Orikasa, C., & Almeida, O. F. (1995). Implications of estrogen-dependent brain organization for gender differences in hypothalamo-pituitary-adrenal regulation. *FASEB Journal*, 9, 419–423.
- Patrick, J., Campbell, K., Carmichael, L., Natale, R., & Richardson, B. (1982). Patterns of gross fetal body movements over 24-hour observation intervals during the last 10 weeks of pregnancy. *American Journal of Obstetrics and Gynecology*, 142, 363–371.
- Perelman, R. H., Palta, M., Kirby, R., & Farrell, P. M. (1986). Discordance between male and female deaths due to the respiratory distress syndrome. *Pediatrics*, 78, 238–244.
- Phelan, J. P., Smith, C. V., Broussard, P., & Small, M. (1987). Amniotic fluid volume assessment with the four-quadrant technique at 36–42 weeks' gestation. *Journal of Reproductive Medicine*, 32, 540–542.
- Phillips, S., King, S., & DuBois, L. (1978). Spontaneous activities of female versus male newborns. *Child Development*, 49, 590–597.
- Pillai, M., & James, D. (1990a). Development of human fetal behavior: A review. *Fetal Diagnosis & Therapy*, 5, 15–32.
- Pillai, M., & James, D. (1990b). Are the behavioural states of the newborn comparable to those of the fetus? *Early Human Development*, 22, 39–49.
- Pillai, M., James, D. K., & Parker, M. (1992). The development of ultradian rhythms in the human fetus. *American Journal of Obstetrics & Gynecology*, 167, 172–177.
- Prechtl, H. F. R. (1974). The behavioural states of the newborn infant (a review). *Brain Research*, 76, 185–212.
- Prechtl, H. F. R. (1977). *The neurological examination of the infant* (2nd ed.). London: S. I. M. P. and Heinemann.
- Prechtl, H. F. R. (1984). Continuity and change in early neural development. In H. F. R. Prechtl (Ed.), *Continuity on neural functions from prenatal to postnatal life. Clinics in developmental medicine*, (No. 94, pp. 1–15). Philadelphia, PA: Lippincott.
- Prechtl H. F. R. & Beintema D. J. (1964). The neurological examination of the full-term newborn infant. *Clinics in Developmental Medicine*, 12, 74–276.
- Pressman, E. K., DiPietro, J. A., Costigan, K. A., Shupe, A. K., & Johnson, T. R. B. (1998). Fetal neurobehavioral development: Associations with socioeconomic class and fetal sex. *Developmental Psychobiology*, 33, 79–91.
- Provins, K. A. (1992). Early infant motor asymmetries and handedness: A critical evaluation of the evidence. *Developmental Neuropsychology*, 8, 325–365.
- Reinisch, J. M. (1974). Fetal hormones, the brain, and human sex differences: A heuristic, integrative review of the recent literature. *Archives of Sexual Behavior*, 3, 51–90.
- Reinold, E. R. (1976). Fetal movements and fetal behavior. In P. J. Keller (Ed.), *Ultrasonics in early pregnancy* (pp. 102–129). Zürich: S. Karger.
- Riese, M. L. (1987). Temperament stability between the neonatal period and 24 months. *Developmental Psychology*, 23, 216–222.
- Roberts, A. B., Griffin, D., Mooney, R., Cooper, D. J., & Campbell, S. (1980). Fetal activity in 100 normal third trimester pregnancies. *British Journal of Obstetrics and Gynaecology*, 87, 480–484.
- Robertson, S. S. (1985). Cyclic motor activity in the human fetus after midgestation. *Developmental Psychobiology*, 18, 411–419.
- Robertson, S. S. (1987). Human cyclic motility: fetal-newborn continuities and newborn state differences. *Developmental Psychobiology*, 20, 425–442.
- Robertson, S. S., Dierker, L. J., Sorokin, Y., & Rosen, M. G. (1982). Human fetal movement: Spontaneous oscillations near one cycle per minute. *Science*, 218, 1327–1330.
- Romero, R., Gomez, R., Galasso, M., Mazor, M., Berry, S. M., Quintero, R. A., & Cotton, D. B. (1994). The natural interleukin-1 receptor antagonist in the fetal, maternal, and amniotic fluid compartments: The effect of gestational age, fetal gender, and intrauterine infection. *American Journal of Obstetrics & Gynecology*, 171, 912–921.
- Sadovsky, E., Laufer, N., & Allen, J. W. (1979). The incidence of different types of fetal movements during pregnancy. *British Journal of Obstetrics and Gynaecology*, 86, 10–14.
- Sarnat, H. B. (1989). Do the corticospinal and corticobulbar tracts mediate functions in the human newborn? *Canadian Journal of Neurological Sciences*, 16, 157–160.
- Schindler, A. E. (1975). Metabolism of androstenedione and testosterone in human fetal brain. *Progress in Brain Research*, 42, 330.
- Schoenen, J. (1982). Dendritic organization of the human spinal cord: The motor neurons. *Journal of Comparative Neurology*, 211, 226–247.
- Schwartz, J. L., Niman, C. W., & Gisel, E. G. (1984). Tongue movements in normal preschool children during eating. *American Journal of Occupational Therapy*, 38, 87–93.
- Scott, S. M., Guardian, C. M., Angelus, P., & Backstrom, C. (1991). Developmental pattern of urinary epidermal growth factor in the premature infant and the influence of gender. *Journal of Clinical Endocrinology & Metabolism*, 72, 588–593.

- Shirley, M. M. (1931). The first two years: A study of twenty-five babies: Vol. 1. Postural and locomotor development. Minneapolis, MN: University of Minnesota Press.
- Shrout, P. E., & Fleiss, J. L. (1979). Intraclass correlation: Uses in assessing rater reliability. *Psychological Bulletin*, 86, 420–428.
- Sival, D. A., Visser, G. H. A., & Prechtl, H. F. R. (1990). Does reduction of amniotic fluid affect fetal movements? *Early Human Development*, 23, 233–246.
- Sival, D. A., Visser, G. H. A., & Prechtl, H. F. R. (1992). The effect of intrauterine growth retardation on the quality of general movements in the human fetus. *Early Human Development*, 28, 119–132.
- Smotherman, W. P., & Robinson, S. R. (1987). Prenatal expression of species-typical action patterns in the rat fetus (*Rattus norvegicus*). *Journal of Comparative Psychology*, 101, 190–196.
- Sparrow, S. S., Balla, D. A., & Cicchetti, D. V. (1984). Vineland adaptive behavior scales (interview ed.). Circle Pines, MN: American Guidance Service.
- Stubbs, E. M., & Irwin, O. C. (1933). Laterality of limb movements of four newborn infants. *Child Development*, 4, 358–359.
- Sumulian, J. C., Campbell, W. A., Rodis, J. F., Feeney, L. D., Fabbri, E. L., & Vintzileos, A. M. (1995). Gender-specific second-trimester biometry. *American Journal of Obstetrics & Gynecology*, 173, 1195–1202.
- Suzuki, S., & Yamamuro, T. (1985). Fetal movement and fetal presentation. *Early Human Development*, 11, 255–263.
- Swartjes J. M., van Geijn H. P., Mantel R., van Woerden E. E., & Schoemaker H. C. (1990). Coincidence of behavioural state parameters in the human fetus at three gestational ages. *Early Human Development*, 23, 75–83.
- Tan, U., Ors, R., Kurkcuoglu, M., Kutlu, N., & Cankaya, A. (1992). Right-, left-dominance and ambidexterity in grasp reflex in human newborn: Importance of left brain in cerebral lateralization. *International Journal of Neuroscience*, 62, 197–205.
- Thelen, E. (1981). Kicking, rocking, and waving: Contextual analysis of rhythmical stereotypies in normal human infants. *Animal Behavior*, 29, 3–11.
- Thelen, E. (1985). Developmental origins of motor coordination: Leg movements in human infants. *Developmental Psychobiology*, 18, 1–22.
- Thelen, E., Bradshaw, G., & Ward, J. A. (1981). Spontaneous kicking in month-old infants: Manifestation of a human central locomotor program. *Behavioral & Neural Biology*, 32, 45–53.
- Thelen, E., & Fisher, D. M. (1982). Newborn stepping: An explanation for a “disappearing reflex.” *Developmental Psychology*, 18, 760–775.
- Thelen, E., Fisher, D. M., & Ridley-Johnson, R. (1984). The relationship physical growth and a newborn reflex. *Infant Behavior and Development*, 7, 479–493.
- Thelen, E., Ridley-Johnson, R., & Fisher, D. M. (1983). Shifting patterns of bilateral coordination and lateral dominance in the leg movements of young infants. *Developmental Psychobiology*, 16, 29–46.
- Thelen, E., Skala, K. D., & Kelso, J. A. S. (1987). The dynamic nature of early coordination: Evidence from bilateral leg movements in young infants. *Developmental Psychology*, 23, 179–186.
- Touwen, B. C. L. (1976). Neurological development in infancy. London: S. I. M. P. and Heinemann Medical; Philadelphia: Lippincott.
- Toran-Allerand, C. D. (1984). On the genesis of sexual differentiation of the central nervous system: Morphogenetic consequences of steroidal exposure and possible role of α -fetoprotein. *Progress in Brain Research*, 61, 63–98.
- Valentine, L., Lofgren, O., Marsal, K., & Gullberg, B. (1984). Subjective recording of fetal movements. I. Limits and acceptability in normal pregnancies. *Acta Obstetrica et Gynecologica Scandinavica*, 63, 223–228.
- Van Dongen, L. G. R., & Goudie, E. G. (1980). Fetal movement patterns in the first trimester of pregnancy. *British Journal of Obstetrics and Gynaecology*, 87, 191–193.
- van Vliet, M. A. T., Martin, C. B. Jr., Nijhuis, J. G. & Prechtl, H. F. R. (1985). Behavioural states in the fetuses of nulliparous women. *Early Human Development*, 12, 121–135.
- Vintzileos, A. M., Campbell, W. A., Nochimson, D. J., Commolly, M. E., Fuenfer, M. M., & Hoehn, G. J. (1985). The fetal biophysical profile in patients with premature rupture of the membranes: An early predictor of fetal infection. *American Journal of Obstetrics and Gynecology*, 152, 511–516.
- Visser, G. H. A., Laurini, R. N., de Vries, J. I. P., Bekedam, D. J., & Prechtl, H. F. R. (1985). Abnormal motor behaviour in anencephalic fetuses. *Early Human Development*, 12, 173–182.
- Walters, C. E. (1964). Reliability and comparison of four types of fetal activity and of total activity. *Child Development*, 35, 1249–1256.
- Weggemann, T., Brown, J. K., Fulford, G. E., & Minns, R. A. (1987). A study of normal baby movements. *Child: Care, Health & Development*, 13, 41–58.
- Wolff, P. H. (1966). The causes, controls, and organization of behavior in the neonate. *Psychological Issues*, 5, 1–105.