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Massage Improves Growth Quality by Decreasing Body Fat Deposition in Male Preterm Infants

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Objectives To assess the effect of massage on weight gain and body fat deposition in preterm infants.

Study design Preterm infants (29-32 weeks) were randomized to the massage group (n = 22, 12 girls, 10 boys) or the control group (n = 22, 12 girls, 10 boys). Treatment was masked with massage or control care administered twice-daily by licensed massage therapists (6 d/wk for 4 weeks). Body weight, length, Ponderal Index (PI), body circumferences, and skinfold thickness (triceps, mid-thigh, and subscapular [SSF]) were measured. Circulating insulin-like growth factor I, leptin, and adiponectin levels were determined by enzyme-linked immunosorbent assay. Daily dietary intake was collected.

Results Energy and protein intake as well as increase in weight, length, and body circumferences were similar. Male infants in the massage group had smaller PI, triceps skinfold thickness, mid-thigh skinfold thickness, and SSF and increases over time compared with control male infants ($P < .05$). Female infants in the massage group had larger SSF increases than control female infants ($P < .05$). Circulating adiponectin increased over time in control group male infants (group × time × sex interaction, $P < .01$) and was correlated to PI ($r = 0.39$, $P < .01$).

Conclusions Twice-daily massage did not promote greater weight gain in preterm infants. Massage did, however, limit body fat deposition in male preterm infants. Massage decreased circulating adiponectin over time in male infants with higher adiponectin concentrations associated with increased body fat. These findings suggest that massage may improve body fat deposition and, in turn, growth quality of preterm infants in a sex-specific manner. *(J Pediatr 2013;162:490-5)*.

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Massage therapy is advocated for stress attenuation in preterm infants (<37 weeks' postmenstrual age [PMA]).[1] Preterm infants admitted to the neonatal intensive care unit (NICU) are exposed to numerous stressful events.[2] Stressful events elicit neuroendocrine release of glucocorticoids, which suppress the insulin-like growth factor I (IGF-1) axis and, in turn, weight gain in preterm infants.[3,4] We found improved autonomic nervous system function, and in turn stress response, in male preterm infants who received twice-daily massage.[5] Infant massage is also reported to increase circulating IGF-1[6] and weight gain.[7] Stress attenuation by massage therapy, therefore, may help optimize weight gain of hospitalized, preterm infants.

Optimal weight gain is essential for survival and long-term health of preterm infants. Preterm infant weight gain alone, however, is a poor indicator of growth quality.[8] Growth encompasses simultaneous changes in body length, lean tissue, and fat mass. Fat tissue deposition may be abnormally higher in hospitalized, preterm infants. Excess endogenous glucocorticoid exposure, as a result of chronic stress, alters growth quality by promotion of fat storage.[4] Preterm infants are lighter and shorter at term (40 weeks' PMA) than term-born infants, but their total body[9,10] and interabdominal fat mass[11] is up to 70% greater. These alterations to body fat deposition impair growth quality and may result in part from the numerous stressful events associated with preterm birth.

To date, how stress attenuation by massage relates to growth quality of preterm infants is unknown. Therefore, we evaluated weight gain, body fat deposition, and circulating leptin and adiponectin levels in preterm infants randomized to receive a twice-daily massage program compared with preterm infants randomized to receive standard NICU care (control group). We hypothesized that massage would decrease body fat deposition in preterm infants. We also tested the relationships between massage, body fat deposition, and circulating leptin and adiponectin in preterm infants.

GEE	General estimating equation
IGF-1	Insulin-like growth factor I
IUGR	Intrauterine growth restricted
MTSF	Mid-thigh skinfold
NICU	Neonatal intensive care unit
PI	Ponderal Index
PMA	Postmenstrual age
SSF	Subscapular skinfold
TSF	Tricep skinfold

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Supported by grants from the National Institutes of Health (NCCAM R21 AT004185-01) and University of Utah Interdisciplinary Research. The authors declare no conflicts of interest.

Registered with ClinicalTrials.gov: NCT00722943.

 http://dx.doi.org/10.1016/j.jpeds.2012.08.033

Methods

Preterm infants admitted to the NICU at University of Utah Hospital or Intermountain Medical Center and born between 28 4/7 and 32 3/7 weeks' PMA confirmed by maternal dates, mid-pregnancy 2-dimensional fetal ultrasound, and physical examination at birth and with birth weight, length, and head circumference between the 10th and 90th percentiles for gestational age were eligible for study. At the time of informed parental consent, infants were stratified by sex and randomized to the massage or control group. Exclusion criteria included abnormal intrauterine growth, congenital anomalies, intravenous nutrition at 14 days of age, or other conditions known to affect growth. Infants entered the study protocol when tolerating enteral feeding volumes >100 mL/kg/d. This study was approved by the University of Utah Institutional Review Board for Human Subjects. This trial was registered with ClinicalTrials.gov (NCT00722943).

The massage and control treatments were performed for 20 minutes twice daily at 7:00 a.m. and 7:00 p.m., 6 d/wk (Monday through Saturday), for a maximum of 4 weeks. The massage and control treatments were performed behind a privacy screen by a licensed massage therapist. The massage treatment was modeled after the Infant Massage USA (Springfield, Virginia) protocol and modified for preterm infants by eliminating massage of the abdomen. Although there is no evidence that massage of the abdomen is associated with the development of necrotizing enterocolitis or other abdominal injury, we eliminated massage of the abdomen as a precautionary measure.[5] The massage protocol consisted of the application of 6 soft-tissue compression strokes to the following areas of the supine infant: (1) top of thighs to ankles and feet; (2) chest over ribcage; (3) shoulders down the arms to hands; (4) head from crown to neck; and (5) along the back from the neck to the waist.[5] Range of motion to the arms and legs as described was delivered following the massage. During the range-of-motion phase, each arm and each leg was moved away from (extension) and back toward (flexion) mid-line against the infant's own resistance. Extension/flexion movements were repeated 5 times for each arm and each leg. The control treatment required the licensed massage therapist to stand quietly by the infant's bedside for 20 minutes twice daily at 7:00 a.m. and 7:00 p.m.

Nine licensed massage therapists, certified in infant massage, provided all massage and control treatments. All massage therapists were trained to recognize clinical signs of distress. A rotation schedule assured equal distribution of the therapists' within study subjects and between treatments. The lead massage therapist (S.H.) randomly observed the treatment protocol every 20 treatments as administered by the massage therapists to ensure treatment fidelity.

Both massage and control procedures were administered behind a privacy screen to maintain "masking" of the infant's study assignment to parents and NICU clinical staff. In addition, study personnel responsible for anthropometric measurements or biochemical analyses (the clinical studies coordinator and 2 research assistants) were masked to the infant's study assignment to minimize bias during data collection. Only the massage therapists and the study principal investigator (L.M.-M.) were aware of the infant's study assignment.

Anthropometric measures included body weight, length, body circumferences (head, abdominal, mid-upper arm, and mid-thigh), and skinfold thickness at days 1, 8, 15, 22, and 29 (baseline through week 4). Body weight on an electronic infant scale (Air Shields, Vickers, Ohio) was recorded to the nearest gram. Body length (Infant Length Board, Ellard Instrumentation, Seattle, Washington) and body circumferences (head, abdomen, mid–upper arm, and mid-thigh) using a disposable paper tape were measured to the nearest 0.1 cm as described by Koo et al.[12] Measures of infants' body fat included skinfold thickness (triceps [TSF], mid-thigh [MTSF], and subscapular [SSF]; in mm)[13] by caliper (Lange, Beta Technologies, Santa Cruz, California) and Ponderal Index (PI; in g/cm^3). Enteral feeding volume was recorded daily. Calories (g/kg/d) and protein, fat, and carbohydrate (all g/kg/d) based on the feeding source (human milk + commercial fortifier or preterm infant formula) was determined.

Spot blood samples were collected onto filter paper using standard heelstick technique at baseline and 2 and 4 weeks. Samples were immediately processed and stored. IGF-1, leptin, and adiponectin were extracted[14] and concentrations determined in duplicate by enzyme-linked immunosorbent assay (Signosis, Sunnyvale, California). The intrarater and interrater coefficients of variation for all assays were <2% and <5%, respectively.

Statistical Analyses

The sample size of 5 infants per treatment group and sex to achieve a power of .80 with $\alpha \le 0.05$ was based on an expected +2.8 $\pm$ 1.6 g/kg/d average daily weight gain difference between massage and control groups at the completion of the 4-week study period.[7] Independent t test and χ^2 were used to test for differences between massage and control infants' characteristics at birth and study entry. The generalized estimating equation (GEE) procedure was used to determine the effect of treatment (massage or control) on anthropometric measures, growth rate, and serum measures for all infants. A random intercept for each infant and a random slope for study day were included in the model to estimate individual trajectories for change over time. Goodness of fit was achieved for the positively skewed independent variables using the γ distribution. The GEE test accommodates the dependent nature of repeated measures data. Similar to an ANOVA-derived F distribution, the GEE test uses the Wald χ^2 to test the true value of the measurement of interest. Sex was included in the modeling due to its known recognized influence on weight gain, body fat, and serum variables of interest. The 3-way interaction (treatment $\times$ study day $\times$ sex) was our primary effect of interest. Weekly average energy (Kcal/kg/d) and protein (g/kg/d) were cofactors for anthropometric comparisons, whereas biochemical measures were