VAGAL ACTIVITY, GASTRIC MOTILITY, AND WEIGHT GAIN IN MASSAGED PRETERM NEONATES

Miguel A. Diego, MA, PhD, Tiffany Field, OTR, MS, PhD, and Maria Hernandez-Reif, MS, PhD

Objective **Multiple studies have documented an increase in weight gain after 5 to 10 days of massage therapy for preterm neonates. The massaged preterm neonates did not consume more calories than the control neonates. One potential mechanism for these effects might involve massage-induced increases in vagal activity, which in turn may lead to increased gastric motility and thereby weight gain.**

Study design **The present randomized study explored this potential underlying mechanism by assessing gastric motility and sympathetic and parasympathetic nervous system activity in response to massage therapy (moderate pressure) versus sham massage (light pressure) and control conditions in a group of preterm neonates.**

Results **Compared with preterm neonates receiving sham massage, preterm neonates receiving massage therapy exhibited greater weight gain and increased vagal tone and gastric motility during and immediately after treatment. Gastric motility and vagal tone during massage therapy were significantly related to weight gain.**

Conclusion **The weight gain experienced by preterm neonates receiving moderate-pressure massage therapy may be mediated by increased vagal activity and gastric motility.** ***(J Pediatr 2005;147:50-5)***

Randomized, controlled studies have consistently documented greater weight gain in preterm neonates receiving massage therapy (also known as tactile/ kinesthetic stimulation).[1-3] Preterm neonates receiving 5 to 10 days of massage therapy exhibited a 21% to 47% greater increase in weight gain during the study period and were hospitalized for 3 to 6 days less than control neonates receiving standard care. The question of how massage therapy facilitates weight gain in preterm neonates remains unanswered. One hypothesis was that massage leads neonates to consume more calories. However, preterm neonates who received massage did not consume more formula or calories than the control preterm neonates.[4-9] Another hypothesis was that massaged neonates conserved more calories by increasing sleeping time. However, the massaged neonates were more alert and spent more time in active awake states than control neonates, suggesting that enhanced weight gain was not achieved by decreased activity.[8]

A third hypothesis is that moderate-pressure massage stimulates vagal activity, leading to more efficient food absorption through increased gastric motility and the release of food absorption hormones, such as insulin.[10] This hypothesized mechanism is based on our work demonstrating increased vagal activity and insulin levels in preterm neonates after massage therapy,[10] on a rat model showing that moderate-pressure stroking is critical for stimulating the release of ornithine decarboxylase (an index of growth hormone),[11,12] and on both rat and human models showing that stimulation of pressure receptors in the intraoral cavity increases vagal activity and the release of food absorption hormones.[13]

We examined this potential mechanism by assessing indices of vagal activity and gastric motility in preterm neonates receiving moderate-pressure massage therapy. Based on previous findings and on our proposed pressure receptor stimulation model, we hypothesized that preterm neonates receiving moderate-pressure massage therapy would show greater weight gain and increased vagal activity and gastric motility, but not greater calorie intake than preterm neonates receiving light-pressure stimulation (sham/ placebo massage) or controls.

CSI	Cardiac sympathetic index	EGG	Electrogastrogram
CVI	Cardiac vagal index	IBI	Interbeat interval
ECG	Electrocardiogram		

From the Touch Research Institute, Department of Pediatrics, University of Miami School of Medicine, Miami, Florida.

Supported by an National Institutes of Mental Health Senior Research Scientist Award (MH00331) to T.F., an NCCAM research grant (AT00370) to M.H.-R., an NCCAM research supplement (AT00370-02S1) to M.D., and funding from Johnson & Johnson.

Submitted for publication Jul 30, 2004; last revision received Feb 4, 2005; accepted Feb 22, 2005.

Reprint requests: Miguel A. Diego, Touch Research Institute, University of Miami School of Medicine, P.O. Box 016820, Miami, FL 33101. E-mail: mdiego@med.miami.edu.

0022-3476/$ - see front matter

10.1016/j.jpeds.2005.02.023

METHODS

Participants

After approval by the institutional review board of the University of Miami School of Medicine and parental consent, medically stable preterm neonates were recruited from the University of Miami/Jackson Memorial Hospital Neonatal Intensive Care Unit. Neonates were excluded from this study if they (a) required surgery; (b) received respiratory support, antibiotics, or phototherapy; (c) had genetic anomalies, congenital heart malformations, and/or central nervous system dysfunction; or (d) were HIV-positive or immunocompromised or (e) if their mothers had a history of syphilis, hepatitis B, or alcohol/illicit drug use. At study entry, all neonates were gavage-fed. There were no systematic differences in diagnoses between treatment groups.

A total of 115 preterm neonates met our inclusion criteria. Of these, 61 had parents who could not be contacted (n = 55) or refused to participate in the study (n = 6). Due to equipment malfunctions and unusable data, 6 neonates (3 control, 2 massage, and 1 sham) were excluded from the study. Our final sample comprised 48 hospitalized preterm neonates who were assigned to a control (n = 16), massage therapy (n = 16), or sham massage therapy group (n = 16) based on stratified randomization based on birth weight and a permuted block design based on a computer-generated randomization list and a 1:1:1 allocation ratio implemented to attain equal treatment group sizes.

Data collection was done by researchers blind to the neonates' group assignments. Parents and clinical staff were also blind to the neonates' group assignments and to the hypotheses of the study. Massage therapists were blind to the hypotheses of the study. Power analyses based on our previous neonatal vagal tone study suggested that a minimum of 10 to 15 participants per group would be needed to detect vagal tone differences between groups (80% power; $P < .05$; 2-tailed test).

Throughout this 5-day massage therapy study, relevant medical history was gathered, and mean weight gain per day per neonate weight, mean calories consumed per day per neonate weight, and days from beginning of treatment to discharge (days to discharge) were recorded. Electrocardiograms (ECGs) and electrogastrograms (EGGs) were collected during the first treatment session (control/ massage/sham) of the study for a total of 45 minutes (15 minutes baseline, 15 minutes treatment, and 15 minutes posttreatment) at approximately the same time for all subjects (between 1:00 and 3:00 PM) 1 hour after feeding. All subjects continued to receive standard nursery care during the course of the study.

Treatment Groups

Treatment was provided for 3 15-minute periods per day for 5 days, 1 hour after feeding by massage therapists trained in the study protocol. Training involved presentation of a structured video treatment protocol followed by a series of observation and practice sessions. Reliability was assessed by the authors before study commencement and reevaluated throughout the study period to ensure protocol compliance, especially with respect to the amount of pressure provided. Each neonate received treatment from several therapists to ensure that treatment effects were the result of the treatment protocol and not from any one particular therapist. Therapists providing the light-pressure sham massage did not perform moderate-pressure massage therapy and vice versa.

The massage therapy consisted of the 15-minute preterm neonate massage therapy protocol used by Field et al.[5] The 15-minute stimulation sessions included 3 standardized 5-minute phases, with tactile stimulation in the first and third phases and kinesthetic stimulation in the middle phase. In the tactile stimulation phase, the neonate was placed in a prone position and stroked with moderate pressure (sufficient to produce a slight skin color change from pink to white in a Caucasian neonate or slight indentations in the skin for all neonates). The neonate is massaged for 5 1-minute periods (12 strokes at approximately 5 seconds per stroking motion) over each region in the following sequence: (1) from the top of the head to the neck and back to the top of the head, and back to the neck; (2) from the neck across the shoulders; (3) from the upper back to the waist and back to the upper back; (4) from the thigh to the foot to the thigh on both legs; and (5) from the shoulder to the hand to the shoulder on both arms. During the kinesthetic stimulation phase, the neonate is placed in a supine position and each arm, then each leg, and finally both legs together are flexed and extended (as in a bicycling motion). Each flexion/extension motion lasts 10 seconds, for a total of 5 1-minute segments.

The light-pressure sham massage followed the same Field et al[5] protocol. The scheduling and duration of the sham and massage therapy sessions were identical in the type, number, and rate of movements, with the exception that light-pressure stroking (producing no skin color change in a Caucasian neonate or skin indentation for all neonates) was used during the first and last 5-minute periods of the sham massage procedure. The middle 5-minute period of kinesthetic stimulation remained the same. The sham massage procedure served as a pressure stimulation control condition.

Physiological Measures

An ECG was obtained from each neonate using a UFI Model SRS2004/d-SP Electrophysiology Acquisition System (UFI, Morro Bay, CA) to derive measures of heart rate and autonomic nervous system function. ECGs were acquired by placing 3 disposable silver chloride electrodes on the neonate's chest and back. The signal was filtered between 1 Hz and 100 Hz, amplified using a gain of 2000, and sampled at a rate of 1000 Hz. After manual artifact correction, ECG data were converted to R-wave intervals (interbeat intervals [IBIs]) to the nearest millisecond using data acquisition and analysis software (Acq Knowledge software, version 3.5; Biopac Systems,). IBI data were then analyzed using CMETI software[14] (freeware written by J.J.B. Allen, Department of Psychology, University of Arizona, Tuscon, AZ) to obtain measures of sympathetic nervous system activity (cardiac

Table I. Means and standard deviations (range under means in parentheses) for demographics

	Control N = 16	Massage N = 16	Sham N = 16	df/F or χ^2, η^2	*P*
Gender*				$\chi^2(2) = 4.57$	NS
Male	62.5%	25.0%	43.8%		
Female	37.5%	75.0%	56.2%		
Ethnicity				$\chi^2(4) = 5.77$	NS
African-American	42.9%	56.3%	37.5%		
Hispanic	50.0%	43.8%	37.5%		
Caucasian	7.1%	0%	25.0%		
Birth weight (g)	1265 ± 333 (560-1800)	1091 ± 193 (790-1430)	1184 ± 205 (890-1525)	F(2,47) = 1.9, .08	NS
Gestational age	29.6 ± 2.7 (22-33)	29.8 ± 3.4 (25-37)	30.3 ± 1.7 (27-33)	F(2,47) = 0.27, .01	NS
Ponderal index	2.0 ± 0.4 (1.2-2.6)	2.1 ± 0.3 (1.4-2.6)	2.2 ± 0.2 (1.8-2.4)	F(2,47) = 0.94, .04	NS
Days since birth	29 ± 20 (9-76)	34 ± 18 (12-75)	32 ± 13 (13-56)	F(2,47) = 0.39, .02	NS
Day 1 weight (g)	1504 ± 224 (1115-1865)	1527 ± 236 (1085-1855)	1503 ± 189 (1220-1860)	F(2,47) = 0.06, .08	NS

NS, not significant.
*Exploratory analyses failed to reveal any gender differences in weight gain, vagal activity, or gastric motility responses to massage therapy.

Table II. Means (and standard deviations under means) for clinical outcomes

	Control	Massage	Sham	*F*, η^2, *P*
Days to discharge	25.5 ± 11.1	20.1 ± 11.2	24.4 ± 13.2	*F* = 0.93, .04, NS
Weight gain (kg/ day)*	15.5 ± 3.68	19.6 ± 3.96	16.2 ± 3.86	*F* = 5.13, .19, < .01
Caloric intake (kg/ day)	111 ± 12.4	111 ± 11.4	12^1 ± 9.2	*F* = 0.24, .01, NS

NS, not significant.
*Infants in the massage group gained significantly more weight than infants in the control or sham massage groups.

sympathetic index [CSI])[15] and vagal activity (cardiac vagal index [CVI][15] and vagal tone [respiratory sinus arrhythmia][14,16]).

EGGs were evaluated in each neonate using a UFI Model SRS2004/d-SP Electrophysiology Acquisition System (UFI) to assess gastric motility. EGGs were acquired by placing a ground electrode and 3 disposable silver chloride electrodes on the neonate's abdomen and back. The EGG signal was filtered between 1 Hz and 45 Hz, amplified using a gain of 3000, and sampled at a rate of 4.267 Hz. After manual artifact correction, the EGG data were spectrally analyzed using fast Fourier transforms on 15-minute epochs of EGG data using Matlab (version 6.0) to derive power density estimates in 0.5-cpm-wide bins from 1 to 15 cpm. Neonate EGG activity occurring between 2 and 4 cpm is considered normogastric activity, that occurring between 4 and 9 cpm is considered tachygastric activity, and that occurring between 1 and 2 cpm is considered bradygastric activity.[17] Inasmuch as each recording epoch lasted only 15 minutes, we could not obtain reliable bradygastric measurements.

Absolute EGG power comparisons between subjects are not reliable, because of the influence of several confounding factors (eg, abdominal wall thickness, skin preparation, electrode placement).[18] As such, relative rather than absolute EGG power was analyzed. Relative power in the 2- to 4-cpm band (representing normal gastric activity) was computed as %2 to 4 cpm activity = (2 to 4 cpm power/1 to 15 cpm power) $\times$ 100. Tachygastria (representing abnormally fast gastric activity) was computed as %4 to 9 cpm activity = (4 to 9 cpm power/1 to 15 cpm power) $\times$ 100.

Statistical Analyses

Analysis of variance (ANOVA) and χ^2 analyses were used to assess equivalence across groups on all demographic study entry variables. ANOVA was also used to assess for group differences in weight gain, calorie consumption, and days to discharge. Significant ANOVAs were followed by post hoc Bonferroni-corrected *t*-tests.

Group (control vs massage vs sham) by time (pre/during/post) repeated-measures ANOVAs were conducted on vagal (ie, CVI and vagal tone) and sympathetic activity and gastric motility (normal EGG and tachygastria) measures. Significant repeated-measures ANOVAs were followed by post hoc trend analyses to detect polynomial trend components, including positive or negative linear trends, suggesting an increase or decrease, respectively, in values during treatment and posttreatment periods, and U-shaped or inverted U-shaped quadratic trends, indicating an increase or decrease, respectively, of values during the treatment period. Finally, Pearson's *r* correlation analysis was used to assess the relationships between weight gain, vagal activity, and gastric motility.

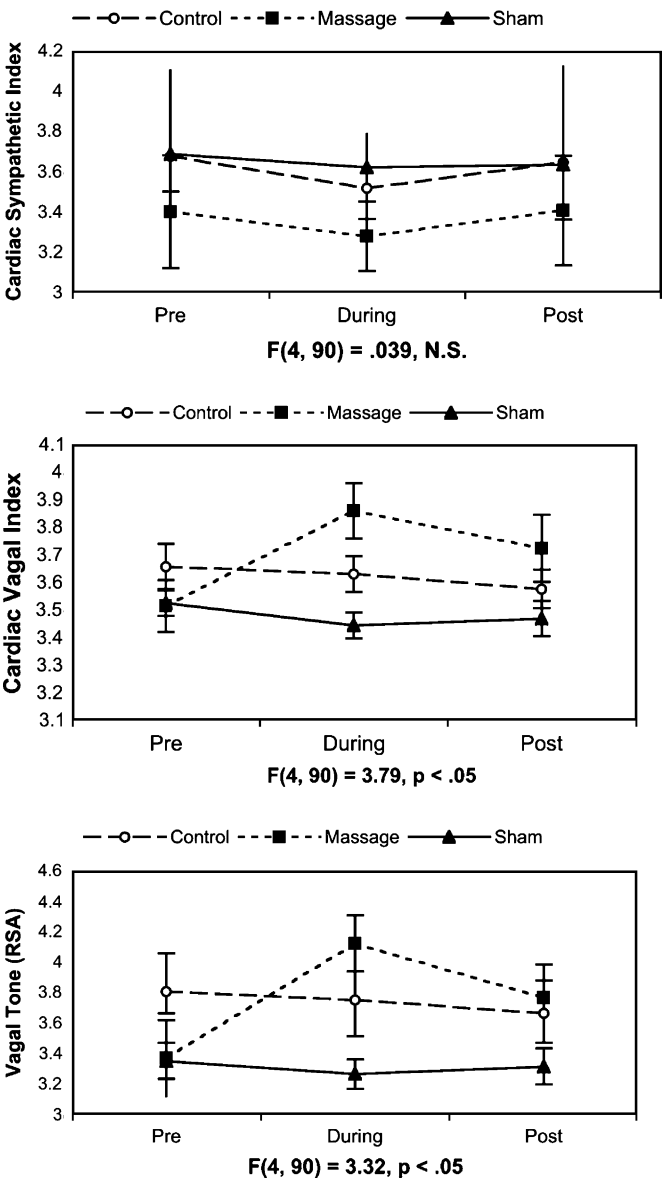

Figure 1. Mean sympathetic and parasympathetic activity 15 minutes before, during, and after treatment (error bars denote ± 2 standard errors). Group-by-time interaction statistics for each measurement are presented under each line plot.

RESULTS

Study Entry Variables

Maternal and neonate demographic and study entry characteristics did not differ between groups (Table I).

Outcome Variables

Control versus massage versus sham ANOVAs revealed that even though the preterm neonates in the massage therapy group gained significantly more weight than neonates in the control or sham massage groups, they did not consume more calories (Table II). Intent-to-treat analyses revealed that even with the inclusion of the 6 neonates with missing physiological data, the neonates in the massage therapy group gained significantly more weight than those in the control or sham massage groups (F (2, 15) = 6.93; $P < .01$; $\eta^2 = .21$), but did not consume any more calories (F (2, 15) = 0.10; P = not significant; $\eta^2 = .01$).

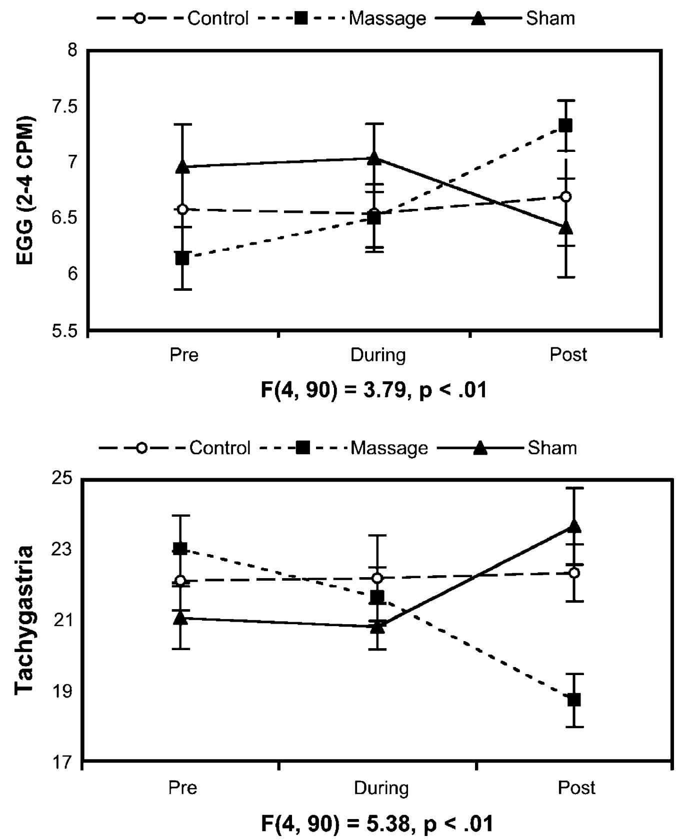

Figure 2. Mean gastric activity 15 minutes before, during, and after treatment (error bars denote ± 2 standard errors). Group-by-time interaction statistics for each measurement are presented under each line plot.

EKG and EGG Analyses

Group by time (pre/during/post) repeated-measures ANOVAs conducted on ECG and EGG measures revealed significant group-by-time interactions for CVI and vagal tone (Figure 1) and normal EGG activity and tachygastria (Figure 2). To better understand these interactions, post hoc trend analyses were conducted and revealed the following: (1) a significant increase in CVI (linear trend; $F(1, 15) = 8.42$; $P < .01$; $\eta^2 = .36$) that peaked marginally during the massage (quadratic trend; F (1, 15) = 3.13; $P < .1$; $\eta^2 = .17$) for only the massage therapy group; (2) a significant increase in vagal tone (linear trend; F (1, 15) = 5.62; $P < .05$; $\eta^2 = .27$) that peaked during the massage (quadratic trend; $F(1, 15) = 4.54$; $P < .05$; $\eta^2 = .23$) for only the massage therapy group; (3) a significant increase in gastric motility (linear trend; F (1, 15) = 10.66; $P < .01$, $\eta^2 = .42$) for only the massage therapy group; and (4) a significant decrease in tachygastria (linear trend; $F(1, 15) = 9.87$; $P < .01$; $\eta^2 = .39$) for only the massage therapy group.

Correlation Analyses

Correlation analyses revealed that relative weight gain was significantly related to changes in vagal tone during the massage (r (16) = .69, P < .01) and changes in gastric motility after the massage (r (16) = .55, P < .01). This finding suggests that neonates exhibiting the greatest increase in vagal activity during the massage and the greatest increase in gastric motility immediately after the massage on the first day of treatment gained the most weight during the 5-day treatment period.

DISCUSSION

Consistent with previous studies, preterm neonates receiving massage therapy gained 27% more weight than controls even though they did not consume more calories than controls.[1-10] Consistent with the model proposed by Field,[10] vagal activity peaked during massage therapy and remained significantly higher than baseline throughout the 15-minute poststimulation period. The consistent findings obtained using 2 independently derived estimates of vagal activity (CVI[15] and vagal tone[14,16]) support the validity of these metrics as noninvasive estimates of vagal activity. The preterm neonates receiving massage therapy did not exhibit increased CSI activity during or after the massage therapy procedure. As expected, gastric motility increased and tachygastria decreased during the treatment and posttreatment periods.

To our knowledge, this is the first study to examine gastric motility in response to massage therapy in neonates. Measures of vagal and gastric motility were measured only during the first treatment day. Future research should assess vagal activity and gastric motility throughout the 5-day treatment period.

Even though all of the preterm neonates in this study were medically stable and exhibited comparable diagnoses and severity of illness profiles, we did not account for any systematic differences in the types of medications administered throughout the study. This could have potentially confounded our weight gain, vagal activity, and gastric motility findings, because preterm neonates are commonly given medications that affect weight gain (eg, diuretics, steroids) and cardiovascular, respiratory (eg, methylxanthines), and gastrointestinal (eg, antacids, prokinetic agents) function.

The moderate-pressure massage group exhibited significantly (21%) greater weight gain during the treatment period than the sham massage therapy group. Like the standard care control group, the sham massage therapy group did not exhibit a significant change in vagal activity or gastric motility during the treatment or posttreatment phases of the study. These moderate- versus light-pressure massage therapy findings suggest the involvement of pressure receptors and/or baroreceptors. Animal studies also indicate that pressure receptor stimulation activates the vagus, in turn releasing food absorption hormones[13] and ornithine decarboxylase.[11,12] Further, a recent study indicated that compared with light-pressure stimulation, moderate-pressure stimulation reduced heart rate and central nervous system arousal in adults,[19] and a neonate massage study indicated more optimal growth (weight gain and length) and development (Brazelton Neonatal Behavior Assessment scores) after moderate- versus light-pressure massage during the first few months of life.[20]

Consistent with our model, the change in vagal activity elicited by massage therapy was significantly related to weight gain during the 5-day treatment period. This suggests that neonates who demonstrate increased vagal activity during massage are more likely to benefit from massage therapy. In fact, the 12 preterm neonates who demonstrated an increase rather than a decrease in vagal activity during the first massage gained 19% more weight than the 4 neonates who exhibited a decrease in vagal activity.

Taken together, these findings offer partial support for our hypothesized model indicating that moderate-pressure massage leads to greater weight gain through its effects on vagal activity and gastric motility. Further validation of this model will require assessing the effects of vagal activity and gastric motility on food absorption and digestive hormones during massage therapy while controlling for other potential mediating factors in a larger sample.

We thank the mothers and neonates who participated in this study and Julia Beutler, Larissa Feijo, Karla Gill, and Yanexy Vera for their help with participant recruitment and data collection. We also thank John Allen for his help with the ECG analysis software.

REFERENCES

1. Field T. Massage therapy facilitates weight gain in preterm infants. Curr Direct Psychol Sci 2001;10:51-4.

2. Field TM. Stimulation of preterm infants. Pediatr Rev 2003;24:4-11.

3. Vickers A, Ohlsson A, Lacy JB, Horsley A. Massage for promoting growth and development of preterm and/or low-birth-weight infants. Cochrane Database Syst Rev 2004;CD000390.

4. Dieter JN, Field T, Hernandez-Reif M, Emory EK, Redzepi M. Stable preterm infants gain more weight and sleep less after five days of massage therapy. J Pediatr Psychol 2003;28:403-11.

5. Field TM, Schanberg SM, Scafidi F, Bauer CR, Vega-Lahr N, Garcia R, et al. Tactile/kinesthetic stimulation effects on preterm neonates. Pediatrics 1986;77:654-8.

6. Ferber SG, Kuint J, Weller A, Feldman R, Dollberg S, Arbel E, et al. Massage therapy by mothers and trained professionals enhances weight gain in preterm infants. Early Hum Dev 2002;67:37-45.

7. Jinon S. The effect of infant massage on growth of the preterm infant. In: Yarbes-Almirante C, De Luma M, eds. Increasing safe and successful pregnancy. Amsterdam: Elsevier Science; 1996. p. 265-9.

8. Scafidi F, Field T, Schanberg S, Bauer CR, Tucci K, Roberts J, et al. Massage stimulates growth in preterm infants: a replication. Infant Behav Dev 1990;13:167-88.

9. Wheeden A, Scafidi FA, Field T, Ironson G, Bandstra E, Schanberg S, et al. Massage effects on cocaine-exposed preterm neonates. J Dev Behav Pediatr 1993;14:318-22.

10. Field T. Stimulation of preterm infants. Pediatr Rev 1988;10:149-54.

11. Pauk J, Kuhn CM, Field TM, Schanberg SM. Positive effects of tactile versus kinesthetic or vestibular stimulation on neuroendocrine and ODC activity in maternally-deprived rat pups. Life Sci 1986;39:2081-7.

12. Schanberg SM, Field TM. Sensory deprivation stress and supplemental stimulation in the rat pup and preterm human neonate. Child Dev 1987;58:1431-47.

13. Uvnas-Moberg K, Widstrom AM, Marchini G, Windberg J. Release of GI hormones in mother and infant by sensory stimulation. Acta Paediatr Scand 1987;76:851-60.

14. Allen JJB. Calculating metrics of cardiac chronotropy: a pragmatic overview. Psychophysiology 2002;39:S18.

15. Toichi M, Sugiura T, Murai T, Sengoku A. A new method of assessing cardiac autonomic function and its comparison with spectral analysis and coefficient of variation of R-R interval. J Autonom Nerv Syst 1997;62:79-84.
16. Porges SW. Vagal tone: a physiologic marker of stress vulnerability. Pediatrics 1992;90:498-504.
17. Tomomasa T, Miyazaki M, Nako Y, Kuroume T. Electrogastrography in neonates. J Perinatol 1994;14:417-21.
18. Verhagen MA, Van Schelven LJ, Samsom M, Smout AJ. Pitfalls in the analysis of electogastrographic recordings. Gastroenterology 1999;117:453-60.
19. Diego MA, Field T, Sanders C, Hernandez-Reif M. Massage therapy of moderate and light pressure and vibrator effects on EEG and heart rate. Int J Neurosci 2004;114:31-44.
20. Field T, Hernandez-Reif M, Diego M, Feijo L, Vera Y, Gil K. Massage therapy by parents improves early growth and development. Infant Behav Dev 2004;27:435-42.