Vibration-Induced Motor Responses of Infants With and Without Myelomeningocele

Sandra L. Saavedra, Caroline Teulier, Beth A. Smith, Byungji Kim, Benjamin D. Beutler, Bernard J. Martin, Beverly D. Ulrich

Background. The severity of myelomeningocele (MMC) stems both from a loss of neurons due to neural tube defect and a loss of function in viable neurons due to reduced movement experience during the first year after birth. In young infants with MMC, the challenge is to reinforce excitability and voluntary control of all available neurons. Muscle vibration paired with voluntary movement may increase motoneuron excitability and contribute to improvements in neural organization, responsiveness, and control.

Objectives. This study examined whether infants with or without MMC respond to vibration by altering their step or stance behavior when supported upright on a treadmill.

Design. This was a cross-sectional study.

Methods. Twenty-four 2- to 10-month-old infants, 12 with typical development (TD) and 12 with MMC (lumbar and sacral lesions), were tested. Infants were supported upright with their feet in contact with a stationary or moving treadmill during 30-second trials. Rhythmic alternating vibrations were applied to the right and left rectus femoris muscles, the lateral gastrocnemius muscle, or the sole of the foot. Two cameras and behavior coding were used to determine step count, step type, and motor response to vibration onset.

Results. Step count decreased and swing duration increased in infants with TD during vibration of the sole of the foot on a moving treadmill (FT-M trials). Across all groups the percentage of single steps increased during vibration of the lateral gastrocnemius muscle on a moving treadmill. Infants with MMC and younger infants with TD responded to onset of vibration with leg straightening during rectus femoris muscle stimulation and by stepping during FT-M trials more often than older infants with TD.

Conclusions. Vibration seems a viable option for increasing motor responsiveness in infants with MMC. Follow-up studies are needed to identify optimal methods of administering vibration to maximize step and stance behavior in infants.

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Myelomeningocele (MMC) is the most common neural tube defect with an incidence of 1,500 to 2,000 new cases per year in the United States.[1] Occurring in the first 4 weeks of gestation,[2] this disruption of the developmental processes leads to a partial spinal cord lesion. At birth, infants with MMC present varying degrees of sensory and motor loss at the level of the lesion and below.[3] Interestingly, infants with MMC or with typical development (TD) are equally active *in utero*,[4] but infants with MMC quickly fall behind in gross motor skills following birth. Compared with infants with TD, infants with MMC make fewer and less-vigorous spontaneous leg movements[5,6] and take fewer steps when one attempts to elicit newborn stepping.[7] Prenatally, infants are stimulated by movement of surrounding fluid systems, sporadic uterine contractions, and maternal motor activity.[8] Reduced extrinsic motor stimulation via the decreased pool of available motor units and recovery from neonatal spinal surgery are considered to be contributing factors to reduced movement in these infants postnatally.[9] Unfortunately, loss of sensory and motor nerve communication (from the neural lesion) combined with reduced movement creates a cascading constraint to motor skill development. Decreased motor activity during the first year of life has been shown to cause activity-dependent deficits in both sensory and motor function.[10,11]

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- eTable 1: Two-Way Interaction Statistical Results
- eTable 2: Three-Way Interaction Statistical Results

According to a maturational theory of motor development, the severity of the neural lesion may be considered as an impenetrable barrier to behavior change in children with MMC. A more current approach to motor development, dynamic systems theory, considers behavioral outcomes to be flexible, emergent properties that result from interaction of anatomical, physiological, and neurological components within specific task and environmental contexts. Not only the behavior, but also each subcomponent is considered to be a dynamic, multilevel, nonstationary process.[12] This theory is consistent with contemporary evidence of activity-dependent corticospinal plasticity.[10,11,13,14] Thus, providing a scaffold to support weak or missing components can release new patterns of behavior and allow the system greater opportunities for motor action. For example, treadmill-elicited stepping practice has been shown to increase movement control and step frequency in infants with TD and in those with Down syndrome.[15]

Infants with MMC respond to being supported on a treadmill by stepping,[7] but step frequency is significantly lower for them than for infants with TD. In general, infants with TD take more steps than infants with MMC when supported on a treadmill: at 2 to 5 months of age, infants with TD and those with MMC respond inconsistently to the treadmill, using a variety of step types, but by 7 months, infants with TD respond consistently with alternating steps, whereas infants with MMC do not begin increasing alternating steps until 9 to 10 months of age.[7,12] Altering the treadmill surface through use of a checkerboard visual pattern or Dycem nonslip material (Dycem Ltd, Warwick, Rhode Island) to increase leg displacement by friction can increase the step rate, but this result was more pronounced for older infants with MMC than for younger infants with MMC.[16] Vibration-induced sensory input offers a more direct option for enhancing neuroplasticity in these infants.

In adults post–spinal cord injury (SCI), vibration, applied on the skin directly over a muscle or a tendon, has been shown to increase recruitment and strength of the triceps brachii muscles during maximum voluntary contraction[17] and to improve the timing of quadriceps muscle activation for the stance phase during robot-assisted gait.[18] In adults who are healthy, continuous vibration of hamstring muscles can increase walking speed.[19] The application of muscle vibration during submaximal voluntary contraction may improve performance compared with training without vibration. For example, quadriceps muscle strength and power during jumping increased in elderly women who were healthy following 3 consecutive days with 30 minutes of concurrent quadriceps muscle contraction and vibration[20]; after a cerebrovascular accident, active dorsiflexion and heel-strike improved in adults who received therapy including 30 minutes of vibration applied to the dorsiflexor muscles 3 times per week for 4 weeks[21]; and overground walking speed increased in adults post–SCI after standing on a vibrating platform 3 minutes per day, 3 days per week, for 4 weeks.[22] If infants' neuromotor mechanisms are sufficiently similar to those of adults, application of vibration to infants' legs may improve the quality and frequency of treadmill-elicited stepping.

Neurophysiologically, vibration has been shown to facilitate motor responses through a complex set of mechanisms. Early studies on vibration focused on a reflexive muscular contraction induced primarily by the

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activation of muscle spindles[23] and, to a lesser extent, of cutaneous receptors.[24,25] High-frequency, low-amplitude vibratory input applied to a tendon or muscle belly evokes a slow but sustained increase in activity termed "tonic vibration response" (TVR) in the vibrated muscle and relaxation of its antagonists. This motor response, initially observed by Rood in 1860[26] and later called TVR,[23,27] is mediated by monosynaptic and polysynaptic pathways[25,28] and has been found in nearly every muscle in humans.[23] Although in adults the magnitude of the TVR fluctuates as a function of time, frequency, and location of stimulation, state of the muscle (active, passive and initial muscle length), and stimulus amplitude,[29–31] it was recently found that vibration-induced motor responses are less clearly defined in infants younger than 10 months of age[32]; stimulated muscles respond less frequently, and responses may be evoked simultaneously in agonist muscle groups, antagonists, and distal muscles. Thus, motor responses to vibration may be more variable in infants than in adults.

In other recent research, motor-evoked potentials resulting from transcranial magnetic stimulation have been used to explore vibration-induced changes within the central nervous system in adults. Tendon vibration alone was enough to increase corticospinal tract excitability when delivered at frequencies of 75 and 120 Hz but not at 20 Hz.[33] Combining submaximal voluntary contraction with tendon vibration at 60 Hz has been shown to increase excitability of the contralateral motor cortex during and for more than 30 minutes after vibration.[34] Although not tested in infants, these adult studies suggest that vibration may offer a noninvasive method to enhance and strengthen sensory and motor connections in infants with MMC.

The effectiveness of vibration stimulation to enhance motor activity in infants is largely unknown. Hence, the purpose of this study was to determine infant responses to localized vibration under conditions that enhanced muscle activity, muscle stretch, or stepping. For this purpose, infants were supported upright with their feet in contact with a stationary or moving treadmill belt while vibration was applied to different segments of the lower limb. We used the supported standing context because it is known to facilitate positive support and stepping responses in infants. Young infants with and without MMC do not yet have stable step responses to the treadmill; thus, we chose to alternate the vibratory stimulus between left and right legs in hopes of entraining alternating step behavior. We hypothesized that vibration would increase the step count, specifically the number of alternating steps, in young infants with TD and infants with MMC. Older infants with TD have robust step responses to the treadmill that may override vibration responses. We further hypothesized that stimulation applied to the shank (lateral gastrocnemius [LG] muscles) or thigh (rectus femoris [RF] muscles) would increase activity in these muscles, causing plantar flexion for the LG muscles and leg straightening for the RF muscles. Lastly, we hypothesized that infants would raise the foot in response to vibration of the sole of the foot, which could facilitate step initiation.

Method

Participants

We enrolled 24 infants, 12 with TD and 12 with MMC, in this cross-sectional study. We selected infants in 2 age ranges, 2 to 5 months and 7 to 10 months, giving us 4 sets of infants (younger infants with TD and MMC and older infants with TD and MMC). Infants with TD were recruited through local newspaper advertisements, fliers, and word-of-mouth communication. To qualify

The Bottom Line

What do we already know about this topic?

Vibration has been shown to enhance motor activity in adults with and without neurologic deficits. The effectiveness of vibration has not been previously investigated with regard to enhancing standing or stepping responses in infants.

What new information does this study offer?

The results of this study indicate that localized vibration seems a viable option for increasing motor responsiveness in young with typical development and in infants with myelomeningocele.

If you're a patient/caregiver, what might these findings mean for you?

This study provides basic information about how location and context (moving or stationary surface) can influence the type of motor response, which ultimately can have an impact on stepping and standing behavior. Further research is needed to identify techniques that could facilitate functional responses and improve the consistency of response.

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Table 1.
Participant Demographics[a]

Group	Sex	Age[b] (mo)	Body Length (cm)	Weight (kg)	Leg Length (cm)	Bayley Scales of Infant Development FM (Raw Score)	Bayley Scales of Infant Development GM (Raw Score)	Lesion Level	Clubfoot	Hydrocephalus	Sensorimotor Score
TD:Y (n=6)	2 male	3.3 (0.96)	60.5 (1.84)	5.82 (0.5)	21.6 (1.02)	7.8 (1.72)	14.5 (5.93)	N/A	N/A	N/A	N/A
MMC:Y (n=6)	3 male	3.5 (0.86)	59.03 (2.91)	6.25 (1.47)	21.8 (1.93)	8.5 (1.38)	12.8 (2.64)	1=L4–5	No	Shunt	8
								2=S1	L, R, casted	Shunt	4
								3=L2–4	L, R, casted	No	5
								4=L5–S2	No	Shunt	6
								5=S1	No	Shunt	7
								6=L2	L, R	Shunt	5
TD:O (n=6)	3 male	8.9 (1.1)	69.6 (1.14)	8.54 (0.79)	27.9 (2.71)	26.5 (0.84)	35.3 (4.55)	N/A	N/A	N/A	N/A
MMC:O (n=6)	5 male	9.36 (1.45)	70.5 (4.04)	9.64 (0.78)	28.1 (1.68)	26.4 (1.34)	27.6 (3.65)	1=L2–4	L, R, casted	Shunt	5
								2=L5–S1	No	Shunt	7
								3=S1	L, R, released	Shunt	4
								4=S1–2	No	No	8
								5=L5–S2	No	Shunt	6
								6=S1–4	No	Shunt	8

[a] Values shown are mean (SD). FM=fine motor, GM=gross motor, TD=typical development, MMC=myelomeningocele, Y=younger (2–5 mo), O=older (7–10 mo), N/A=not applicable. For clubfoot: L=left, R=right.
[b] Corrected age if infant born less than 36 weeks of gestation.

for the study, they needed to be born full term and have no known sensory or motor deficits. Infants with MMC were recruited through pediatric neurology clinics, pediatric therapists, special interest support groups, and word of mouth from southeastern Michigan and northwestern Ohio. To qualify for the study, they had to be affected by a lesion in the lumbar or sacral region of the spine (determined by a neurosurgeon), have a gestational age of at least 28 weeks, and have no complications beyond those common for infants with MMC (eg, hydrocephalus, clubfeet, Arnold-Chiari malformation). All parents gave informed consent prior to their infants' involvement in the study. Participant characteristics are listed in Table 1.

When examining the effectiveness of sensory enhancements, especially in infants with neuromotor deficits, it is important to contemplate, and test (if possible), the neural pathways that might be affected. In order to explore the contribution of proprioceptive and cutaneous sensorimotor pathways to motor behavior in infants, we accessed data from a companion study in which 15 infants from the current study (4 infants from each set, with the exception of 3 infants for the younger MMC set) participated.[32] The companion study was designed to evaluate the functioning of proprioceptive pathways. For the companion study, electromyographic (EMG) reflex responses to tendon tap (stretch reflex) and 80-Hz tendon vibration (TVR) were recorded in the LG and RF muscles of both legs during quiet sitting.[32] These data were used to enhance exploration of the relationships among functions of proprioceptive and cutaneous sensorimotor pathways and behavioral responses to vibration stimulation.

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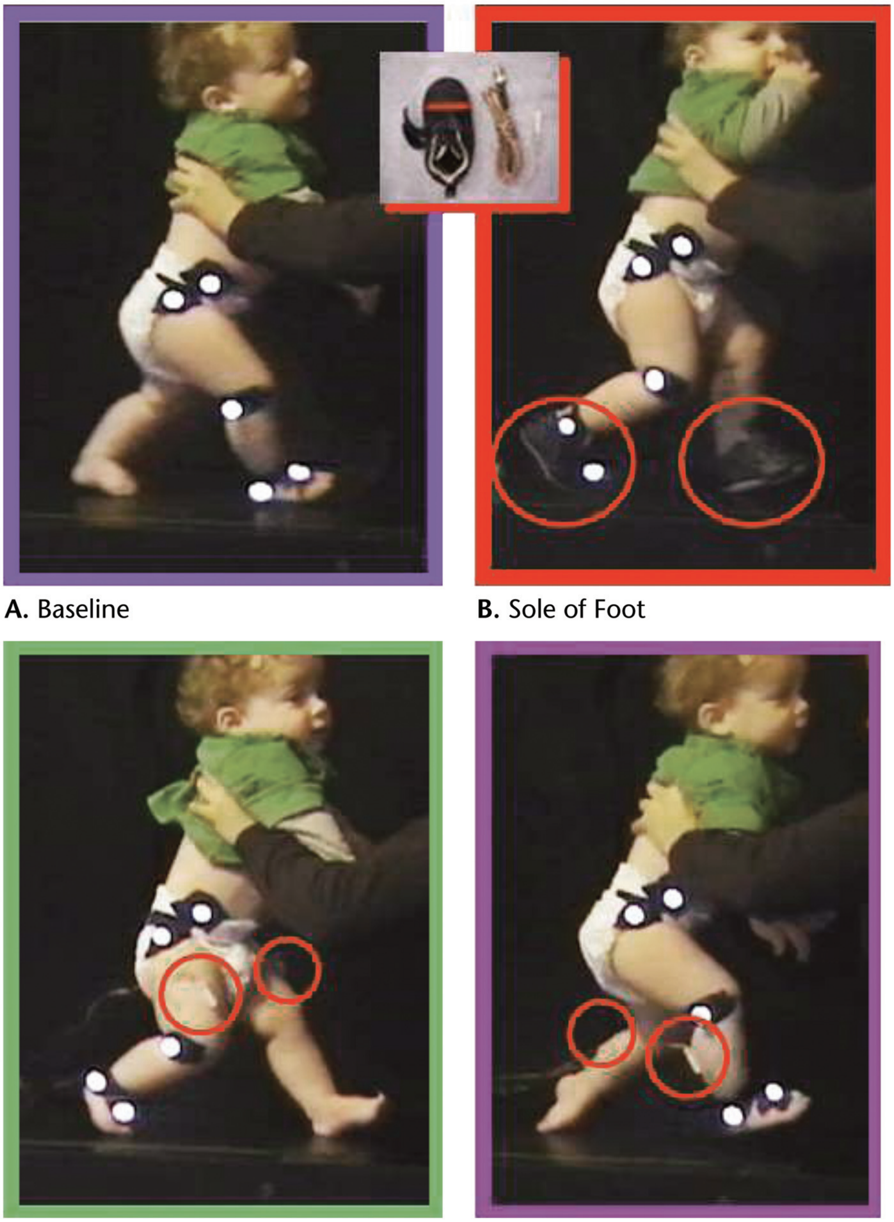

A. Baseline

B. Sole of Foot

C. Rectus Femoris Muscle

D. Lateral Gastrocnemius Muscle

Figure 1.
Seven trials were repeated twice for each infant. Trials consisted of a baseline (moving treadmill, no vibration, panel A) plus 3 vibration locations. Panel B shows vibration to the sole of foot. Inset shows the vibration location in the custom-designed shoe. Vibration location for the rectus femoris and lateral gastrocnemius muscles are shown in panels C and D, respectively. These vibration locations were the same for trials with moving or stationary belt.

Procedure

We tested infants in a quiet room using a pediatric treadmill (Carlin's Creations, Sturgis, Michigan), a 2-camera Peak Motus motion analysis system (Peak Motus-Vicon, Oxford Metrics Group, Oxford, United Kingdom), and a pair of small, custom-designed eccentric vibrators. Infants with TD were tested in the laboratory at the University of Michigan. Due to distances between the laboratory and infants' homes, all but 2 of the infants with MMC were tested in their homes. Vibration was applied to 1 of 3 locations on the lower extremities (soles of the right and left feet or the LG or RF muscles, as illustrated in Fig. 1) during 2 treadmill actions (moving or stationary) for a total of 6 experimental condi-

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tions. The addition of a baseline control trial (moving treadmill with no vibration) gave a total of 7 conditions. These 7 conditions, tested in a random order, were repeated twice for a total of fourteen 30-second trials.

The custom-designed vibration device consisted of a small DC motor with an eccentric rotating mass secured inside a plastic tube (3.2 cm long × 0.8 cm in diameter, about the size of a ballpoint pen barrel). A custom-designed LabVIEW program (National Instruments Corp, Austin, Texas) controlled the vibrators producing alternating 500-millisecond bursts of vibration (160 Hz sinusoid, 0.02–0.12 mm amplitude) in a regular work cycle.

To help entrain rhythmic step behavior, we adjusted vibration timing to reflect the mean step rate expected for infants with TD. To determine the lag between vibration stimulations, we used average step cycle duration produced by infants with TD in a previous longitudinal treadmill study[7] at the belt speed (0.146 m/s) that we used in the current study. This mean duration varied by age and leg length; thus, we measured leg length and inserted this value along with age to tailor vibration cycles for each infant. Therefore, the number of stimulations varied from 10 to 16 episodes per leg for each 30-second trial. Infants with shorter legs had shorter cycle durations and thus more stimuli per minute. For vibration applied to the foot, a set of custom-designed shoes (Preschoolians, Westport, Connecticut) were created (Fig. 1B inset). A split insole was made so the vibrator could be embedded at the same height as the insole. Vibrators and wires were threaded through a hole in the back of the shoe, and each vibrator was securely taped into the gap in the insole. Shoe size was selected to fit snugly to ensure contact of the vibrator with the forefoot. Six shoe sizes were available, ranging from 8.5 to 11.5 cm in length.

After we explained the study to the parents and they signed an informed consent statement, we prepared the infants for data collection. We removed all clothing except diapers; measured foot, thigh, and shank length; and placed reflective markers on the right leg at the mid-iliac crest, the greater trochanter, the knee at the lateral joint line, and the lateral malleolus and on top of the third metatarsophalangeal joint. Depending on the condition, we secured vibrators with tape over the RF or LG muscles or placed shoes with vibrators on the soles of the infants' feet. For all trials, we supported infants upright by holding them under their arms. Infants were given rest breaks as needed during the experiment. Remaining anthropometric measurements (body length, weight, thigh and calf circumference), standardized motor skill assessment (Bayley Scales of Infant Development III), and a brief sensorimotor assessment of infant response to touch on the lower extremities were completed at the end of the session. For the sensorimotor assessment, one point was given for each location at which a motor response could be elicited by touch when the infant was seated or positioned supine. Thus, the maximum sensorimotor score was 8 points (toes=2, ankles=2, knees=2, and hips=2). Table 1 shows scores for these items.

For in-home sessions, we created a data collection space in a room in the family's home. The same table, treadmill, and camera distance and angle were used for all data collections, whether in the home or in the laboratory. A black backdrop was set up behind the table, the treadmill was placed on the table, and a calibration frame was used to set camera distance and angle. Cameras were placed 200 cm lateral to the treadmill and were separated by 240 cm to form a 70-degree angle with the center of the treadmill. One laptop computer generated the vibration stimulus via a custom-designed LabVIEW program. A second laptop computer recorded vibration signals using Noraxon hardware and software (Noraxon USA Inc, Scottsdale, Arizona). An audio signal was used to trigger data collection onset and synchronize video recordings and vibration data. One researcher supported the infant while another researcher held vibrator wires out of the way and helped with vibration location changes.

Data Reduction

Step behavior. Step occurrence and the specific step type were determined for each leg according to the following criteria: alternating (step with one leg followed and preceded by step with the other leg), single (step with one leg not overlapped by a step with the other leg), parallel (both legs swing forward simultaneously), and double ("stutter step," one foot takes 2 steps within a series of alternating steps). Dependent variables for each infant included: total number of steps per trial, percentage of each step type per trial, and mean stance and swing duration of alternating steps for each trial. To determine the frequency and quality of steps, and infants' general level of motor activity, movements and behaviors were coded from the digital video recordings using Peak Motus software that allowed frame-by-frame review (1,800 frames per 30-second trial). All coders were trained and obtained a coefficient of agreement (*agreements/agreements+disagreements*) of 0.85 with previously validated behavior coders using a training set of data.

Responsiveness to vibration. To fully explore the effects of vibration,

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4 trained behavior coders conducted an additional level of behavioral analysis. Video data were examined frame by frame for 800 milliseconds of data (48 frames) following onset of vibratory stimulation. The phase of the step cycle (early, mid, or late stance; early, mid, or late swing) at stimulus onset was recorded. During stationary trials, onset was classified as early, mid, or late swing phase if an infant was in the process of picking up the leg when vibration stimulation occurred and early, mid, or late stance according to foot alignment: early if the foot was in front of the hip, mid if the foot was aligned beneath the hip, and late if the foot was behind the hip. Raters determined whether there was a visible motor response, and if a response occurred, a brief written description of the response was recorded. From the response descriptions, we extracted frequencies for the most common behaviors: leg flexed, straightened, or abducted; foot picked up; foot twisted; going up on toes; stepped forward; or shifted weight sideways. Dependent variables for each infant were: percentage of stimuli that elicited a motor response, percentage of onsets during each phase of the step cycle, and frequency of each type of motor response during different treadmill actions and vibration locations.

Data Analysis

We performed analyses of variance (ANOVAs) based on linear mixed models for repeated measures (SPSS version 17.0, SPSS Inc, Chicago, Illinois) for each of the dependent variables listed above. Age (younger, older) and group (TD, MMC) were between-subject fixed effects. Treadmill action and vibration location were repeated measures for each infant. We assessed main effects and interactions using 2 (treadmill action) × 2 (age) × 2 (group) × 3 (vibration location) ANOVAs. Step type analyses were not performed for stationary trials due to the very low number of steps taken during those trials. For analysis of moving belt trials, we had a baseline control trial with treadmill and no vibration. Thus, for examination of step type during moving belt trials, we used a 2 (age) × 2 (group) × 4 (baseline + 3 vibration locations) model. Multivariate analysis of variance (MANOVA) was used for step type because percentages in this variable were correlated. We used the UCLA Statistical Group method of exploring simple effects for interpretation of interactions.[35] Tukey honestly significant difference and Sidak corrections for multiple comparisons were used when *post hoc* or pair-wise comparisons were needed. Alpha was set at $P<.05$ for significance. Only those results that were significant are reported. Details of statistics used to interpret the interactions are presented in eTable 1 (2-way interactions) and eTable 2 (3-way interactions) (both available at ptjournal.apta.org).

We used Pearson correlation coefficients to examine the relationship among vibration responsiveness, reflex responsiveness (tendon tap and TVR from the companion study), sensorimotor assessment score, and step count.

Standard error for all figures was calculated for each set of infants

$$\left(\textit{Standard Error} = \frac{\textit{Standard Deviation of Sample}}{\sqrt{\textit{Number of Infants in Sample}}}\right)^{36}$$

We are providing this calculated standard error instead of the estimated mean standard error from the statistics program because we believe it allows the reader to better visualize the variability for each set of infants in our sample.

Results

Step Behavior

Step count. Figure 2 shows means for step count during each treadmill action and vibration location for each set of infants. Four 2-way interactions were significant and involved all independent variables. In response to the moving belt, older infants from both groups took more steps than younger infants (treadmill action × age), and infants with TD took more steps than infants with MMC (treadmill action × group). Across all infants, fewer steps were taken during vibration of the sole of the foot on a moving treadmill (FT-M trials) (mean=22.9 steps/trial) than during vibration of the LG muscles on a moving treadmill (LG-M trials) (mean=28.9) and vibration of the RF muscles on a moving treadmill (RF-M trials) (mean=30.4) (treadmill action × vibration location). Infants with TD took fewer steps during FT-M trials compared with LG-M and RF-M trials, whereas step count was not significantly different between vibration locations for infants with MMC (group × vibration location).

Step type. Figure 3 shows the percentage of each step type for each set of infants during moving belt trials. Results of the 2 (age) × 2 (group) × 4 (baseline + 3 vibration locations) MANOVA showed a main effect of vibration location (Wilks lambda, $F_{10,11}=4.6$, $P=.009$) and an age × group interaction. Across all infants, the percentage of single steps was greater during LG-M trials (mean=31%) compared with baseline (mean=25%) ($P=.048$). The age × group interaction was the result of different effects of age depending on group. For the TD group, older infants took more alternating steps (mean=97%) than younger infants (mean=59%). For the MMC group, younger infants took more single steps (mean=57%) than older infants (mean=31%).

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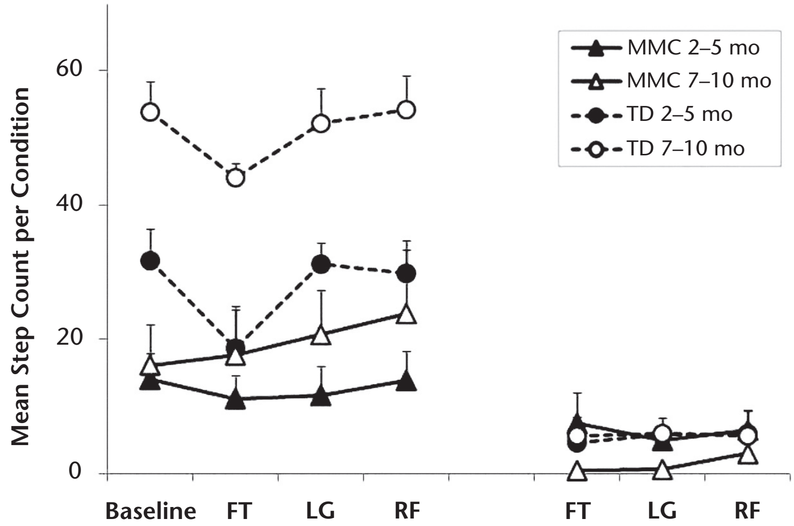

Figure 2.
Mean step count for each set of infants during each condition. All infants took more steps during moving belt trials. Infants with typical development (TD) but not those with myelomeningocele (MMC) had decreased steps during vibration applied to the sole of the foot (FT) on a moving treadmill belt. LG= lateral gastrocnemius muscle, RF= rectus femoris muscle. Error bars indicate standard error.

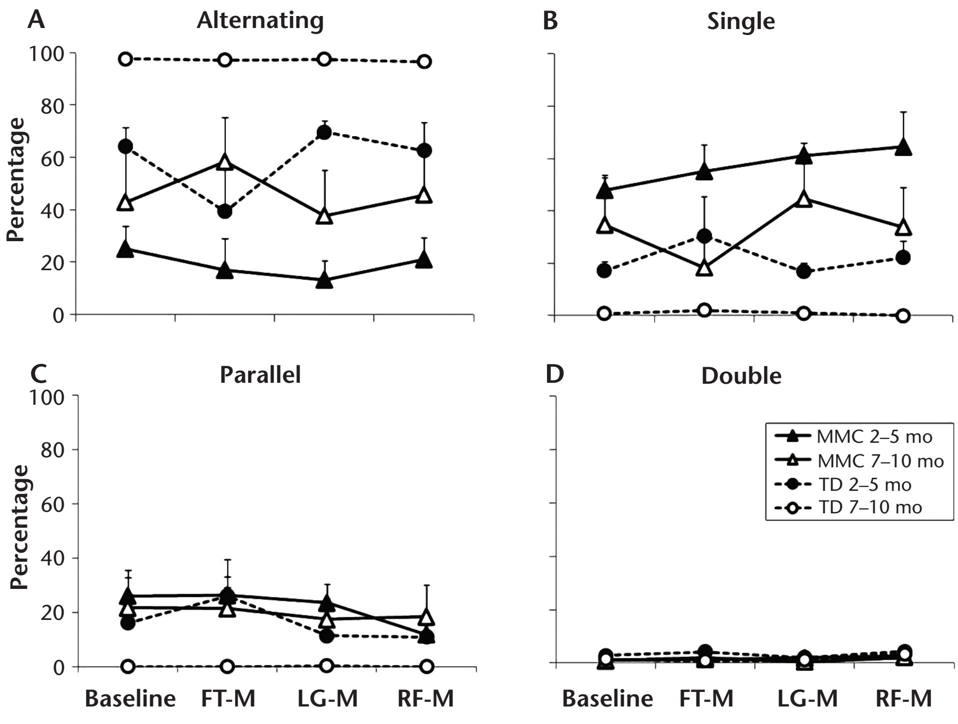

Figure 3.
Mean percentage of each step type for each set of infants and each vibration location (FT=sole of foot, LG=lateral gastrocnemius muscle, RF=rectus femoris muscle) during moving belt trials (-M). TD=infants with typical development, MMC=infants with myelomeningocele. Error bars indicate standard error.

Step cycle. To determine whether step behavior changed with vibration, we examined step cycle characteristics for a subset of infants who took 100 or more alternating steps across the 8 moving belt treadmill trials (FT-M, LG-M, RF-M, and baseline, twice each). This subset (n=10) included all older infants with TD, 2

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Table 2.
Step Cycle Duration by Condition for Subset of Infants (N=10) Who Stepped Consistently During Moving Belt Trials[a]

Variable	Baseline	FT	LG	RF
Stance duration (s)	1.3 (0.38)	1.4 (0.38)	1.4 (0.39)	1.2 (0.29)
Swing duration (s)	0.43 (0.15)	0.51 (0.10)	0.43 (0.15)	0.43 (0.15)
Swing percentage	25.5 (4.2)	27.2 (5.5)	24.4 (5.5)	26.0 (5.9)
Percentage of vibration onsets during swing	N/A	21.0 (9.4)	18.9 (6.9)	21.8 (8.9)

[a] Values presented as mean (SD). Vibration location: FT=foot sole, LG=lateral gastrocnemius muscle, RF=rectus femoris muscle. N/A=not applicable.

infants from the younger TD set, and 2 infants from the older MMC set. Infants who took more than 100 alternating steps were selected because they had adequate representation of alternating steps across all vibration conditions. The group included just 2 infants with MMC and 2 infants from the younger TD set, so we could not reasonably find an effect of age or group, or interactions that involved age or group. For statistical analysis, stance and swing durations (Tab. 2) were normalized for leg length.[37] A one-way repeated-measures ANOVA indicated a significant main effect of vibration location for swing duration ($F_{3,27}$=6.87, P=.001) and stance duration ($F_{3,27}$=2.95, P=.05). Swing duration was significantly longer during FT-M trials than during baseline (P=.046) and LG-M (P=.014) trials. Stance duration differences were not strong enough to remain significant under constraints of multiple comparison error correction. Thus, this subset of consistent steppers showed longer swing duration during FT-M trials than during baseline or LG-M trials.

In summary, a moving treadmill belt was more effective for older infants (TD and MMC groups) and younger infants with TD than for young infants with MMC. Infants with TD, but not those with MMC, took fewer steps when treadmill movement was combined with foot vibration. Infants who were consistent steppers exhibited longer swing duration during FT-M trials. Older infants with TD exhibited primarily alternating steps, whereas younger infants with MMC exhibited primarily single steps. Older infants with MMC did not differ significantly from younger infants with TD with regard to variety of step types. Across all sets of infants, single steps increased during LG-M trials.

Vibration Responsiveness

All infants showed some response to vibration. Mean vibration response rates did not vary significantly by treadmill action, vibration location, group, or age, and no interactions were indicated. The range of vibration responsiveness was 25.5% to 31.3% in younger infants with TD, 13.1% to 24.1% in older infants with TD, 17.3% to 25.9% in younger infants with MMC, and 14.6% to 22.4% in older infants with MMC. The highest (67.7%) and lowest (0%) individual trial response rates occurred in 2 young infants with MMC during RF-S trials.

Five types of responses (pick up foot, step, straighten leg, twist foot or ankle, and going up on toes) were observed across all infants and for both treadmill actions. These responses were investigated using 2 (treadmill action) × 2 (age) × 2 (group) × 3 (vibration location) ANOVAs. Figure 4 shows the mean number of responses for each set of infants, vibration location, and treadmill action for response types that had interactions.

Pick up foot. Across all vibration locations, younger infants (TD and MMC groups) responded more often (mean=4.1 responses/trial) than older infants (mean=1.6 responses/trial) by picking up their foot (main effect of age: $F_{1,20}$=4.616, P=.044), and all infants picked up their foot more often during stationary belt trials (mean=3.69) than during moving belt trials (mean=1.97) (main effect of treadmill action: $F_{1,20}$=5.229, P=.033).

Step (Fig. 4A). Younger infants (TD and MMC groups) responded to vibration by stepping more than older infants but only during moving belt trials (treadmill action × age). Infants with MMC had more step responses than infants with TD during moving belt trials but not stationary belt trials (treadmill action × group).

Straighten leg (Fig. 4B). Infants with MMC straightened their leg more than infants with TD in response to vibration of the RF muscles during stationary belt trials but not moving belt trials (treadmill action × group × vibration location). Younger infants responded by straightening their leg more often than older infants, and this response occurred during stationary belt trials (MMC group) and moving belt trials (TD group) (treadmill action × age × group).

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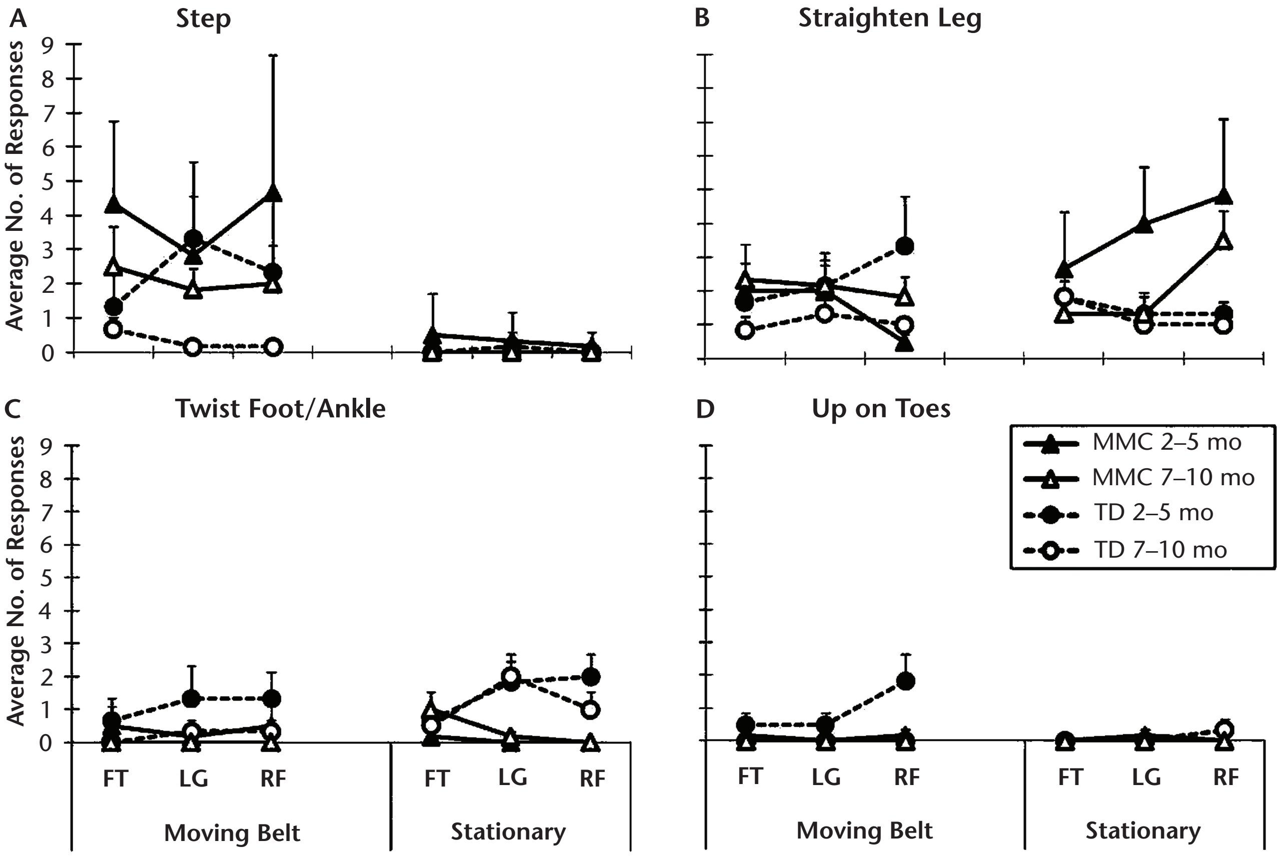

Figure 4.
Group means for the 4 types of vibration onset responses that resulted in significant interaction effects. FT=sole of the foot, LG=lateral gastrocnemius muscle, RF=rectus femoris muscle, TD=infants with typical development, MMC=infants with myelomeningocele. Error bars indicate standard error.

Twist foot or ankle (Fig. 4C). Infants with TD twisted their foot and ankle more than infants with MMC when vibration was applied to the LG and RF muscles (vibration location × group).

Up on toes (Fig. 4D). The up-on-toes response occurred more often in infants of both ages with TD than in those with MMC during stimulation of the RF muscles (vibration location × group). Young infants with TD responded more often than all other groups by going up on toes, and this response occurred more frequently during moving belt trials (treadmill action × age × group).

Overall, some responses to vibration onset were common across vibration locations, whereas other responses were location specific. The greatest variety of specific responses was observed for vibration applied to the rectus femoris muscles. Infants with TD more than those with MMC responded to onset of RF muscle vibration by twisting their foot and ankle or going up on their toes. Infants with MMC more than those with TD responded to RF vibration onset by straightening their leg more frequently during stationary belt trials than during moving belt trials. Infants with TD more than those with MMC also responded to onset of LG muscle vibration by twisting their foot or ankle. Across all vibration locations, younger infants more than older infants responded to stimulus onset by taking a step during moving belt trials, picking up their foot or straightening their leg during stationary belt trials, and going up on their toes with both treadmill conditions. Infants with MMC more than those with TD responded to vibration onset across all locations by straightening their leg during stationary belt trials and by taking a step during moving belt trials.

Sensorimotor Correlations

Infants with MMC had positive correlations between sensorimotor score and step count (n=12, r=.693, P=.012), and these findings were correlated with stretch reflex from the companion study (sensorimotor score: n=7, r=.821, P=.024; step count: n=7, r=.863, P=.012). Step count was negatively correlated with

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vibration responsiveness during LG-M trials ($r=-.709$, $P=.01$) and RF-M trials ($r=-.635$, $P=.027$) for infants with TD.

Thus, vibration responsiveness in this study was negatively correlated with step count in infants with TD but not those with MMC. Vibration responsiveness was not related to sensorimotor score, step count, or reflexes for infants with MMC.

Discussion

The purpose of this study was to determine whether and how infants with and without MMC produced leg movements in response to localized vibrations. The results showed that location of vibration and treadmill action do influence the specific responses and that these responses are stronger in infants with MMC and younger infants with TD.

Our hypothesis that step count, especially the percentage of alternating steps, would increase with cyclic vibration alternating between legs was not supported. Step count was reduced during FT-M trials in infants with TD, but not in infants with MMC (Fig. 2). When we examined specific responses to the onset of vibration, we found that infants with MMC responded by taking a step more often than infants with TD during moving belt trials (Fig. 4A).

Duysens and colleagues[38] evaluated EMG response to vibration of the sole of the foot during sitting and standing in adults who were healthy. Their results showed that vibratory stimulation to the foot can elicit short-latency EMG responses in ankle muscles as well as hamstring muscles. Thus, motor responses to foot vibration can extend through the entire leg. Verschueren and colleagues[39] documented reduced walking speed during eyes-closed walking overground with tendon vibration compared with no vibration in adults who were healthy. This reduced walking speed was attributed to the vibration-induced uncertainty of foot position. Based on the results of these 2 adult studies, and the understanding that sensory information is interpreted and used as a function of the context in which it is elicited,[40–43] we believe vibration was disruptive for infants with TD and constructive for infants with MMC due to relative differences in lower-extremity sensation. Infants with MMC, who have lumbar or sacral lesions, often have sensory deficits in the legs and feet. We believe vibration raised the overall sensory input beyond the threshold for eliciting a motor response for infants with MMC. Infants with TD, who have intact sensation, may have experienced uncertainty with regard to their foot position, and thus vibration was disruptive and decreased the step count.

Although there was variability across infants, our results suggest that some viable pathways may be accessed with vibration to produce motor responses in infants with MMC. Infants with MMC, more than infants with TD, showed leg straightening responses to the onset of stimulation during RF-S trials and step responses to the onset of stimulation across all 3 vibration locations during moving belt trials (Fig. 4). A study of adults using EMG and force measurements confirm that vibration can induce TVR and increase force in partially paralyzed triceps brachii muscles in people with cervical SCI.[17]

With regard to location-specific hypotheses, we found more leg straightening responses during vibration of the RF muscles, and this effect was strongest in stationary belt trials for infants with MMC and in younger infants. Infants with TD were more likely to go up on toes in response to RF muscle stimulation. Stimulation of the LG muscles increased the number of single steps across all infants during moving treadmill trials and resulted in increased foot and ankle twist in infants with TD during both treadmill actions. We predicted that infants would pick up the foot and step in response to vibration to the sole of the foot during moving belt trials. Isolated picking up of the foot was stronger during stationary belt trials, whereas step response was more common during moving belt trials; however, these responses occurred for all vibration locations. The subset of infants who were consistent steppers had increased swing duration during FT-M trials, suggesting that it encouraged infants to pick up the foot. Thus, the location of vibration does influence the type of response in infants with and without MMC.

We examined step responses at 2 levels of analysis: the overall step count across the full trial and specific examination of response to vibration onset. Younger infants and infants with MMC were more likely to step in response to onset of stimulation during moving belt trials and to pick up the foot or straighten the leg during stationary belt trials. We anticipated stronger vibration responses during moving belt trials because of the combination of muscle stretch and functional responses; however, it appears that muscle activity during stationary belt trials was adequate to enhance specific vibration responses. This differentiation of responses as a result of context suggests that, although patterns of movement are not yet clearly established in younger infants and infants with MMC, they do respond differently to vibration when it is combined with a moving versus a stationary treadmill, whereas older infants with TD consistently responded with alternating steps during moving belt trials and had fewer step and pick up foot

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responses during stationary belt trials. These findings support the concept that it may be easier to modify or induce motor responses at ages before they become consistent.

The absence of correlation between responses to localized vibration in this study and reflex responses in the companion study[32] suggests that responses observed during vibration could only be partially attributed to activity of muscle spindle primary endings. In adults, muscle spindle fibers can respond in 1-to-1 synchrony up to 220 Hz, depending on the length and tension of individual muscles,[29,44] whereas the harmonic response of cutaneous mechanoreceptors in the human foot and leg exists up to 200 Hz.[24,45] When frequency exceeds the optimal range for a specific muscle, spindle fibers continue firing at lower subharmonic frequencies. Optimal vibration frequency for adult lower-extremity muscles has been reported to be between 80 and 90 Hz.[38,43] Thus, it may be assumed that our stimulation frequency of 160 Hz induced subharmonic responses near 80 Hz in proprioceptive pathways and much stronger activation of cutaneous pathways. However, cutaneous pathways cannot be the sole mediators of vibration responses because infants with MMC who did not demonstrate response to tactile stimulation on the shank or foot had observable responses to vibration on the foot and LG muscles. Moreover, sensorimotor scores were not correlated with vibration responsiveness.

Many of the responses we documented (ie, picking up the leg, going up on toes, twisting the foot or ankle, and taking a step) support the strong influence of cutaneous afferents, as they contribute to the withdrawal reflex, which is modulated by skin vibration.[46] Furthermore, treadmill-elicited step responses and weight-bearing responses during standing, which are known to be stronger in the older group of infants, may have attenuated the tendency to withdraw from the stimulation in older infants. This interpretation is in agreement with results indicated above showing that the role of sensory information is a function of the context in which it is elicited.[39–42] Another possibility is that infants were more susceptible to the amplitude of vibration. Eklund and Hagbarth[23] found vibration amplitudes of 1 to 2 mm to be most efficient in adults and noted that amplitudes greater than 2 mm induced withdrawal reactions. Although our vibration amplitudes (0.8–0.12 mm) were much smaller, it is possible that this range was strong enough to induce withdrawal responses in infants.

Limitations

Our study had several limitations. We used intermittent vibrations, alternating at a preset frequency and duty cycle. Adapting the vibration timing as a function of infant position or movement might have been more effective in promoting continuous stepping. We did not have a control trial with no vibration for the stationary treadmill. Thus, we are unable to draw conclusions about the effect of stimulation compared with no stimulation for stationary conditions. We used behavioral measures of vibration responsiveness; thus, we may have missed more-subtle responses that could have been revealed by EMG recordings. Our sample size was small and heterogeneous. Overall, we believe this sample size and these behavioral methods were sufficient for a first analysis of vibration effectiveness in infants. We were interested in determining whether robust, functionally relevant effects could be demonstrated. The fact that we found significant results warrants future investigation with more-refined hypotheses that may require EMG or specific timing of vibration. Future empirical work will be necessary to confirm and expand these findings.

Recommendations for Future Studies

Now that we know motor activity can be facilitated in infants with diminished neuromotor systems with the use of vibration, the method of administration warrants further investigation. Ivanenko and colleagues[19] compared the effects of continuous and phasic muscle stimulation and found that continuous stimulation was more effective at increasing speed during treadmill stepping. Vibration of the sole of the foot has been shown to activate muscles throughout the leg, and we have seen that infants (including those with lower-leg sensory deficits) can respond to this stimulation. These findings suggest that it might be advantageous to stimulate muscle activity in infants with MMC through the use of a vibration platform or continued refinement of the vibrator on foot technique we used here. Investigations are under way in our laboratory to explore the effectiveness of brief exposure to a vibration platform for facilitating treadmill-elicited step responses in young infants with TD.

Recent work showing the neuroplastic effects of even brief exposure to vibration paired with voluntary muscle activation[20,33,34,47] makes this modality appealing for developmental work. Empirical studies are needed to determine the most effective frequency and amplitude of stimulation for infants and young children. During the first year of life, the corticospinal tract is actively developing[10,11,14] and stretch reflexes and TVR are variable and unstable.[32,48] It is unknown whether the ideal frequency for infants should target muscle spindle activa-

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tion or a combination of muscle and cutaneous receptors. The optimum frequency and amplitude to facilitate functional motor responses and avoid withdrawal reactions in infants is an important area of future research with strong clinical implications.

Based on our findings, younger infants (2–5 months of age) and those with MMC would benefit most from vibration combined with a moving treadmill. Once stepping responses become entrained, vibration does not appear to improve stepping. Vibration applied to the quadriceps muscle during stationary support in standing can be used to improve leg strengthening and thus weight bearing, but this was done only in infants with MMC in our study.

Conclusions

Overall, our study showed that infants with MMC and TD do respond to vibration applied to the lower limbs, and there is potential to facilitate specific functional responses. Some responses could be used to enhance stepping and standing behavior, whereas other responses interfered with stepping or standing behavior. Future studies are needed to explore the best methods of optimizing specific motor responses.

Dr Teulier, Dr Smith, Dr Martin, and Dr Ulrich provided concept/idea/research design. Dr Saavedra, Ms Kim, Mr Beutler, and Dr Ulrich provided writing and data analysis. Dr Saavedra, Dr Teulier, Dr Smith, Ms Kim, Mr Beutler, and Dr Ulrich provided data collection. Dr Saavedra, Dr Teulier, and Dr Ulrich provided project management. Dr Ulrich provided fund procurement, institutional liaisons, and clerical support. Dr Martin and Dr Ulrich provided facilities/equipment. Dr Teulier, Dr Smith, Ms Kim, Mr Beutler, Dr Martin, and Dr Ulrich provided consultation (including review of manuscript before submission.

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This study was approved by the University of Michigan Institutional Review Board.

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eTable 1.

Two-Way Interaction Statistical Results[a]

Step Count	F	*P*	1-Way Across Second Variable	F	*P*	Simple Effects	*P*	Confidence Interval: Lower Bound	Confidence Interval: Upper Bound
Grp × Loc $F_{2,40}$	3.32	.046	Loc: MMC	1.98	ns				
			Loc: TD	9.98	<.05	FT:LG	.034	−10.7	−0.42
						FT:RF	.013	−10.1	−1.27
						RF:LG	ns		
Grp × T-Act $F_{1,20}$	17.72	<.005	Grp: stationary	0.28	ns				
			Grp: moving	41.98	<.05	MMC:TD	.002	−34.62	−9.12
Age × T-Act $F_{1,20}$	14.81	.001	Age: stationary	0.48	ns				
			Age: moving	22.6	<.05	Young:old	.030	−30.38	−1.68
Loc × T-Act $F_{2,40}$	6.97	.003	Loc: stationary	0.22	ns				
			Loc: moving	15.48	<.05	FT:LG	.012	−10.89	−1.19
						FT:RF	.002	−12.34	−2.75
						RF:LG	ns		
Step Type	**F**	***P***	**1-Way Across Second Variable**	**F**	***P***	**Simple Effects**	***P***	**Confidence Interval: Lower Bound**	**Confidence Interval: Upper Bound**
Age × Grp $F_{4,17}$	4.34	.013	Alternating						
			Age: MMC	2.36	ns				
			Age: TD	7.04	<.05	Young:old	.001	−57%	−19.6%
			Single						
			Age: TD	4.21	ns				
			Age: MMC	6.61	<.05	Young:old	.082	−3.9%	55.8%
Vibration Response Type	**F**	***P***	**1-Way Across Second Variable**	**F**	***P***	**Simple Effects**	***P***	**Confidence Interval: Lower Bound**	**Confidence Interval: Upper Bound**
Step									
Age × T-Act	5.38	.031	Age: stationary	0.18	ns				
			Age: moving	13.34	<.05	Young:old	.28	0.22	3.61
Grp × T-Act	4.39	.049	Grp: stationary	0.07	ns				
			Grp: moving	10.42	<.05	MMC:TD	.056	−0.05	3.44
Twist foot/ankle									
Grp × Loc $F_{2,40}$	4.83	.013	Grp: FT	0.02	ns				
			Grp: LG	18.44	<.05	MMC:TD	.001	−1.99	−0.59
			Grp: RF	11.99	<.05	MMC:TD	.004	−1.71	−.37
Up on Toes									
Grp × Loc	3.91	.028	Grp:FT	0.26	ns				
			Grp:LG	0.26	ns				
			Grp:RF	13.00	<.05	MMC:TD	.048	−1.16	−0.004

[a] Grp=group (TD=infants with typical development, MMC=infants with myelomeningocele), Loc=vibration location (FT=foot sole, LG=lateral gastrocnemius muscle, RF=rectus femoris muscle), T-Act=treadmill action (S=stationary, M=moving), Age (young=2–5 mo, old=7–10 mo).

eTable 2.

Three-Way Interaction Statistical Results[a]

Vibration Response Type	F	*P*	2-Way Across Third Variable	F	*P*	1-Way Across Second Variable	F	*P*	Simple Effects	*P*	Confidence Interval	
											Lower Bound	Upper Bound
Straighten leg												
Grp × T-Act × Loc $F_{2,40}$	8.79	.001	Grp × T-Act: FT	0.86	ns							
			Grp × T-Act: LG	2.46	ns							
			Grp × T-Act: RF	24.6	<.05	Grp:M	3.08	ns				
						Grp:S	27.7	<.05	MMC:TD	.02	0.52	5.48
Grp × T-Act × Age $F_{1,40}$	4.45	.048	Grp × T-Act: Old	0.06	ns							
			Grp × T-Act: Young	7.54	<.05	Grp:M	1.15	ns				
						Grp:S	7.91	<.05	MMC:TD	.229	−1.72	6.39
Up on Toes												
Grp × T-Act × Age $F_{1,40}$	5.66	.027	Age × T-Act: MMC	0.04	ns							
			Age × T-Act: TD	12.8	<.05	T-Act:O	0.35	ns				
						T-Act:Y	19.9	<.05	S:M	.064	−0.07	1.74

[a] Grp=group (TD=infants with typical development, MMC=infants with myelomeningocele), Loc=vibration location (FT=foot sole, LG=lateral gastrocnemius muscle, RF=rectus femoris muscle), T-Act=treadmill action (S=stationary, M=moving), Age (young=2–5 mo, old=7–10 mo). Due to conservativeness of multiple comparisons, the final level of Grp × T-Act × Age interactions (straighten leg and up on toes) did not reach significance.

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