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The Effects of Vestibular Stimulation Rate and Magnitude of Acceleration on Central Pattern Generation for Chest Wall Kinematics in Preterm Infants

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Abstract

Objective—To examine the role of vestibular inputs on respiratory and oromotor systems in healthy preterm infants.

Study Design—27 preterm infants were quasi-randomly assigned to either the VestibuGlide treatment or control groups. VestibuGlide infants were held in a developmentally supportive position, given a pacifier and received a series of vestibular stimuli, counterbalanced across rate and acceleration conditions, 15 minutes 3x/day for 10 days. The control infants were also held in a developmentally supportive position, given a pacifier for 15 minutes 3x/day for 10 days but did not receive the VestibuGlide stimulation.

Result—A multi-level regression model revealed that treatment infants increased their respiratory rate in response to vestibular stimulus and that the highest level of vestibular acceleration delivered to the infants (0.51 m/s^2) resulted in a significant increase in breaths per minute.

Conclusion—Vestibular stimulation delivered to preterm infants prior to scheduled feeds effectively modulates respiratory rate and resets the respiratory central pattern generator.

Keywords

respiration; non-nutritive suck

Introduction

The development of the brain involves a complex temporal and sequential order of events that is initiated soon after conception and continues into the second decade of life.[1, 2] The NICU environment can disrupt the sequential order of events needed for brain development and is considered a rate-limiting environment that deprives infants of sensory stimulation they would otherwise receive *in utero*. Neonatal complications, invasive oxygen therapies,

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Conflict of interest
The authors have nothing to disclose and there are no conflicts of interest.

numerous daily medical procedures, and stationary confining isolettes all reduce the amount of vestibular, kinesthetic, tactile, auditory, and visual information available to the infant.[3] The duration of these maladaptive exposures can last from a few days to a few months depending on the stability and co-morbidities of the preterm infant. Unfortunately, premature infants receive these altered sensory inputs during a critical period where sensorimotor experience is hypothesized to plays a vital role in brain circuitry and development. [4]

With the number of preterm births increasing, experimental applications of supplemental sensory stimulation is a salient and needed research avenue to gain further knowledge on the relation between brain plasticity and the infant's environment.[5] Because the vestibular system is one of the first sensory systems to develop, the premature infant may be more receptive to stimulation in this modality than in any other. Morphogenesis of the vestibular apparatus in humans is complete by the 49th day *in utero* and the vestibular nerve is myelinated and functional between the 8th and 9th month of intrauterine life.[6, 7, 8] Response to vestibular stimulation has been observed as early as 25 weeks gestational age (GA).[9] Fetal buoyancy in amniotic fluid creates a whirlpool-like milieu rich in sensory cues, including potent and nearly continuous vestibular and cutaneous stimulation.[10, 11] Due to the early maturation of the vestibular system, it is one the best mechanisms for providing developmentally appropriate stimulation to the infant.[10]

Rocking is one way to generate vestibular stimulation that mimics certain features (rhythmicity) of maternal walking and infant movement *in utero.*[12] Rocking has been shown to facilitate later emerging sensory modalities including more accurate visual and auditory pursuits.[10, 13, 14] Rocking stimulation reduces the frequency of apneic attacks and decreases the need for respiratory therapies.[10, 15, 16] These findings show the potent effect vestibular stimulation can have on many physiological systems, including respiration. Presumably, the increased neural stability and discharge synchrony among vestibular afferents afforded by rocking, reduces the intensity on internal needs (crying and/or disorganized states) and allows the infant's focus to shift towards external events, such as responding to the local environment.[17]

Previous rocking studies have yielded important clues on the potential role of vestibular inputs in preterm infants, but significant limitations in instrumentation, experimental design, and physiological monitoring warrant further study to identify the salient features of vestibular inputs. Thus, the primary goal of this study was to provide highly controlled vestibular stimuli over a specified operating range to the preterm infant with clearly defined parameters in order to assess the effect of vestibular inputs on chest wall and oromotor patterning. To achieve precise stimulus control, a new stimulator and data acquisition platform was developed at the University of Kansas, known as the VestibuGlide system. For this first experiment, it was hypothesized that linear gliding stimuli in the horizontal plane, systematically varied in frequency and acceleration within the physiologic operating range, will encourage respiratory patterning and non-nutritive sucking, which in turn would facilitate feeding skills.

Materials and Methods

Patients

Control infants were enrolled from Stormont-Vail Regional HealthCare, Topeka, KS and Overland Park Regional Medical Center, Overland Park, KS. VestibuGlide infants were enrolled from Stormont-Vail Regional HealthCare. The Human Subjects Committee from both hospitals approved the research protocol for this study. Informed consent was obtained from the parents prior to the participants' enrollment into the study following consultation

with the attending physician and research nurse. A total of 27 healthy preterm infants (15 females, 12 males), were quasi-randomly assigned to either the VestibuGlide treatment or control groups. This experiment was quasi-randomized as infants in the control group were part of a larger randomized study and the VestibuGlide infants were specifically enrolled for this project.

General inclusion criteria for preterm infants in this study were born between 28 and 34 weeks GA, as determined by obstetric ultrasound and clinical examination, currently receiving tube feedings, minimal or no oxygen history (≤5 days of ventilator, CPAP, & nasal cannula), head circumference within 10–90th percentile of mean for PMA, neurological examination showing no anomalies for PMA (response to light, sound, and spontaneous movements of all extremities), stable vital signs (heart rate, blood pressure, age appropriate respiratory rate, baseline target SpO_2 range appropriate for PMA to allow for stimulation), and at least 32 weeks PMA at the initiation of study.

General exclusion criteria for preterm infants in this study were intraventricular hemorrhage grades III and IV, periventricular leukomalacia, necrotizing enterocolitis, neonatal seizures and culture-positive sepsis or meningitis at time of testing, chromosomal anomalies or craniofacial malformation, nervous system anomalies, cyanotic congenital heart disease, gastroschisis, omphalocele, mothers with diabetes, diaphragmatic hernia, and/or other major gastrointestinal anomalies, or not ready for oral feedings as determined by the health care team.

The control group included 15 premature infants (8 females, 7 males) with an average birth GA of 32.7(1.84), and mean birth weight of 1888.13 (538.11) grams. The VestibuGlide treatment group included 12 premature infants (7 females, 5 males) with an average birth GA of 32.84 (.96) days, and mean birth weight of 1927.92 (298.47) grams. Infants in the control and VestibuGlide treatment groups had similar oxygen supplementation histories, mean 1.47 (1.88) and 2.25 (1.76) days, respectively (see Table 1 for preterm details).

VestibuGlide System

The major components of the VestibuGlide system included a glider chair (Figure 1), custom non-commutated linear servo motor (H2W Technologies, Inc., Santa Clarita, California, USA), servo electronics, and PC-interfaced National Instruments cRIO FPGA (field programmable gate array) programmed as a motion control and data acquisition system. The PC-based data acquisition tablet microprocessor allowed for quick touchpad operation and real-time data display of the infant's chest wall, pulse-ox, and oromotor physiology during vestibular stimulation.

The chair began as a hospital-grade glider, upholstered in a moisture barrier vinyl material (Carolina Business Furniture, Inc., Archdale, North Carolina, USA). The Communication Neuroscience Laboratory Bioengineering group at KU-Lawrence modified and instrumented this glider chair with a special linear servomotor (H2W Technologies, San Clarita, California) and designed a control module to operate the chair (chair, tester, preterm infant) smoothly under position feedback. To accommodate the servo linear motor, the stock factory gliding assembly was removed and the tubular steel sub-frame of the glider chair was fit with a custom machined 0.25″ thick aluminum base in order to increase platform stability and load-bearing capacity (1000 lbs). The specially designed linear motor from H2W Technologies provided horizontal translation on a dual-track roller bearing stage instrumented with both a digital linear encoder and analog position sensor. The four hospital-grade antibacterial rubber wheels (load rated at 400 lbs each) bolted to the underside of the chair base platform made it possible to move the chair easily around the hospital and NICU. Stable positioning at crib side within the NICU was assured by engaging

each of the load bearing lift-locks which physically elevated the wheels and entire VestibuGlide System by 2″ from the floor (Fig. 1).

The servo controller was programmed to generate the control signal protocol to 'glide' the chair according to sinusoidal input functions at rates from 0.5 to 0.95 cycles per second at horizontal glide displacements ranging from 1.98 cm to 8.07 cm.

Respiratory Sampling

A battery-powered variable inductance plethysmograph, clinical Respitrace™, was used to measure chest wall kinematics. Soft cloth band transducers encircled the infant's chest wall (rib cage and abdomen) to sense changes in circumference (size). The upper band was placed around the axillae with its lower edge just below the nipples. The lower band was placed below the costal margin and its lower edge above the iliac crest[18, 19].

Non-Nutritive Suck (NNS) Sampling

NNS nipple compression pressure waveforms were digitized during every VestibuGlide and control session. A green Soothie™ silicone pacifier was coupled to a specially designed Delrin receiver (see Figure 2) which incorporated a lubricated spherical acetyl head instrumented with a Honeywell pressure transducer. In an effort to assess the acceleration the infant received during the gliding stimulus, a uniaxial accelerometer (PBS Piezotronics Model 3711B122G), was mounted to the infant's pacifier receiver (white arrow in Figure 2). A line bubble meter was also mounted on the receiver to ensure the accelerometer was maintained in the horizontal plane during vestibular stimulation.

VestibuGlide Stimulus

The VestibuGlide system provided linear horizontal motion stimuli to the infant. Many previous rocking studies have included stimuli that vary in rate or acceleration but have rarely controlled for both types of stimuli in their study. Our study included seven stimulus conditions that varied in rate and acceleration (see Table 2). Stimuli 1 through 4 varied in rate with acceleration held constant. These rates were based on previous rocking studies and also correspond to typically breathing rate for preterm infants. Stimuli 5 through 7 varied in three comfortable accelerations with rate held constant at 0.65 Hz.

Table 2 shows the 15-minute gliding protocol that the VestibuGlide infants received. This protocol alternated between baseline (B1–B8) and stimulus (S1–S7) conditions every minute. During the baseline conditions, the glider chair did not move and only respiration and non-nutritive suck were monitored. Overall, there were seven gliding stimuli and eight baseline conditions. Stimulus order among the baseline conditions was varied among participants and session by using 15 different stimulus sequences that were presented to the infants in a counterbalanced sequence.

VestibuGlide Treatment Sessions

Infants assigned to this group received the 15-minute gliding protocol 3x/ day for 10 days. Before the gliding protocol was initiated, infants were fitted with a dual-channel clinical Respitrace™ device. This involved the placement of two soft cloth inductance bands around the rib cage and abdomen. Pulse rate and oxygen saturation (SpO_2) signals were also measured throughout the gliding protocol with a neonate oxygen sensor placed around the infant's wrist. Infants remained connected to the usual NICU monitors at all times for observation of respiration, heartbeat, and oxygen saturation by their bedside nurse.

After the Respitrac™ bands and the oxygen sensor were placed on the infants; the infant was swaddled and placed on the researcher's lap, by either the nursing staff or the infant's

parent/caregiver, in a semi-inclined supportive position against a Boppy® Pillow. The infant was given a Soothie™ pacifier and NNS was monitored.

No-Treatment Control Sessions

Infants assigned to the control group did not receive the vestibular stimulus, but were held for 15-minutes and offered an instrumented Soothie™ pacifier 3x/day for 10 days.

Statistical Analysis

General mixed modeling was completed for the VestibuGlide group only for the dependent variables: rib cage breaths per minute (BPM), abdominal BPM, SpO_2, pulse, and NNS parameters. For each of the outcome variables, an individual growth model [20] was fitted in order to examine the day (level-1; e.g., linear or quadratic change over days) effect as well as stimulation condition (level-2) effect. When the day and/or stimulation condition effect(s) were significant, their interaction (cross-level) effect was further examined. Infants' birth weight, oxygen history, and caffeine intake (yes/no), were also included into the model as covariates to account for differences in these factors and thereby further increasing the power to detect significant effects. When the stimulation condition effect was significant, adjusted means were pair-wise compared using a Bonferroni-corrected *p*-value.

Oral feed results were compared between the VestibuGlide treatment infants and the control infants using an analysis of variance.

Results

VestibuGlide Results

Vestibular stimulation effectively modulates respiratory rate and resets the respiratory central pattern generator (rCPG) in healthy preterm infants. Stimulus condition had a significant effect for the rib cage [$F(7, 77) = 25.53$, $p < 0.01$] and abdominal [$F(7, 77) = 23.60$, $p < 0.01$] cycling expressed as breaths per minute (BPM) (see Table 3). Infants increased their respiratory rate in response to the VestibuGlide stimuli. Stimuli 2–7 were all significantly different than the average baseline condition (Table 4).

There were no significant differences in chest wall motor patterning among the four different vestibular stimulus rate conditions; however, there were significant differences in chest wall motor patterning in response to vestibular stimulus acceleration. Stimulus number 7 provided the highest acceleration to the infant and induced significantly higher BPM than stimuli 1, 4, and 5 for the rib cage and stimuli 1 and 4 for the abdomen (see Table 4). It is clear that vestibular acceleration has the largest influence over the rCPG and is capable of inducing significant changes in chest wall kinematics.

Pulse-oximetry

In spite of the increases in BPM during vestibular stimulation, infants maintained stable SpO_2 and pulse rate throughout the VestibuGlide study. In fact, stimulus condition had a significantly positive effect on SpO_2, $F(7, 77) = 2.57$, $p < .05$. Infants had higher SpO_2 during stimulus conditions 3, 4, and 6 compared to baseline conditions; however, after a Bonferroni-correction these differences did not reach statistical significance. Infants are able to modify their respiratory rate in response to vestibular stimulus while maintaining stable $SpO_2$and pulse. All infants were offered a Soothi™ pacifier during each VestibuGlide session; however, vestibular stimulation had no effect on within-burst NNS outcomes.

Oral Feed Growth Functions

A daily oral feed percentage extracted from the nursing care notes was calculated across the eight daily feeds for all VestibuGlide infants in the study and was compared to the feed profile among control infants. ANOVA revealed no difference in the oral feed growth slopes between the VestibuGlide treated infants and the control infants: $F(1, 22) = .25$, $p = 0.625$. On average, VestibuGlide infants advanced their oral feeds at 8.17% per day; whereas, control infants advanced their oral feeds at 9.47% per day.

Discussion

Respiratory Outcomes

The magnitude of vestibular acceleration in contrast to the cycle rate has the largest influence over the rCPG and is capable of inducing significant changes in chest wall kinematics. Vestibular otoliths respond best to linear acceleration [21]; thus, the highest peak acceleration provided by stimulus 7 at 0.51 m/s^2 presumably drove the otolith output maximally which resulted in strengthened sensorimotor coupling between the vestibular apparatus and the rCPG.

Salient sensory signals, such as linear acceleration, serve to regulate the magnitude of ongoing motor activity and dynamically adjust the sensitivity of reflexes, thereby providing an adaptive and flexible neural substrate with changes in task dynamics and environmental conditions.[22] Infants that are able to modify their chest wall kinematics in response to relevant linear acceleration are at an advantage for rapid control of their breathing mechanism. This type of adaptive response is vital for adjusting to various task demands, such as feeding and early vocalizations.

The increased neural drive of the rCPG afforded by gliding reduces the intensity on internal needs and allows the infant's focus to be more on external needs, such as responding to one's local environment.[17] Adapting to one's environment is a critical component for early learning. The richness of sensory experience offered by VestibuGlide stimulation offers a new and exciting neurotherapeutic application for pro-habilitation of the rCPG in preterm infants.

The increased rCPG activity evident in infants who received the VesibuGlide therapy likely reflects a global up-regulation of output which did not show evidence of entrainment. A coherence analysis was completed to assess the entrainment between the glider waveform and the abdominal waveform outputs. The highest coherence value between the glider and abdomen was.023 which was associated with stimulus 7 (highest acceleration). Overall, coherence outcomes were very low (<.023) providing negative evidence for entrainment between the glider and abdominal wall motion.

Pulse/SpO_2 Outcomes

In spite of the increases in BPM during vestibular stimulation, infants maintained stable SpO_2 and pulse rate throughout the VestibuGlide study. In fact, infants often had higher levels of oxygen saturation during the stimulus conditions compared to baseline. This finding is not surprising as vestibular stimulation can elicit respiratory changes that provide for stable blood oxygenation during movements and changes in posture.[23]

Many previous studies have shown that a rocking stimulus is correlated with a reduction in the frequency of apneic attacks and decreases the need for respiratory therapies. [10, 15, 16] Infants in the VestibuGlide group effectively modulated their rCPG in response to vestibular stimulation. Apnea is one result of non-integrated vestibular inputs to/from the rCPG.

Apnea of prematurity is the most common problem in preterm infants with 70% of infants born less than 34 weeks GA having significant apnea, bradycardia, or O_2 desaturations during their hospital stay.[24] Immaturity and depression of rCPG drive to the respiratory musculature are key factors in the pathogenesis of apnea of prematurity. [25] As a key premotor input, a neurally intact rCPG is essential for optimal respiration during the neonatal period. Therefore, therapeutic programs like the VestibuGlide system, aimed at accelerating and stabilizing the function of the rCPG are vital for this population.

Non-Nutritive Suck Outcomes

Overall, vestibular stimulation had no significant effect on within-burst NNS development when compared to the baseline conditions. In order to fully explore how the VestibuGlide stimulus alters suck, a larger sample size is needed.

Oral Feed Outcomes

There was no significant difference in the rate of attainment of oral feeds in the infants who received the vestibular stimulation compared to the control infants. More infants are needed in each group to explore this dependent measure further.

Speculative Outcomes

The length of stay in the NICU was measured from the admission date (birth date in the hospital) to the discharge date for the VestibuGlide treatment infants and the control infants. Infants in the VestibuGlide treatment group left the hospital on average nine days sooner than infants in the control group. We speculate that this outcome was likely the result of improved infant state control and respiratory pattern generation due to the VestibuGlide protocol. Improved state control likely allowed the VestibuGlide infants to be in active states longer and acquire more quiet sleep—both essential components for the growing and developing infant. State control was not quantitatively examined in this study. Therefore, a subsequent study using a larger randomized control trial needs to be completed to examine the length of stay outcome further.

Overall, results of this first study using a custom engineered vestibular glider chair increased our understanding of the salient operating range for vestibular stimulation rate and acceleration and provided new information on the role linear acceleration plays in modulating the rCPG. This information will be used to inform future studies and the development of new therapeutic interventions aimed at enhancing chest wall control to support respiration and physiologic stability among a variety of preterm infant populations, including those with various degrees of lung disease, and neurologic insult. Overall, vestibular stimulation delivered to preterm infants between 32 and 34 weeks PMA safely and effectively modulates respiratory rate and resets the rCPG.

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Figure 1.
Front view of VestibuGlide system.

Figure 2.
Infant sucking on Soothie™ pacifier during VestibuGlide stimulation. The infant's Soothie™ pacifier is attached to a Delrin receiver necessary to measure suck displacement. A uniaxial accelerometer (white arrow) was also attached to the Delrin receiver.

Table 1

Participant information

VESTIBUGLIDE INFANTS							
	Birth GA (wks;days)	**Birth weight (gms)**	**Birth Length (cm)**	**Birth Head Circumference (cm)**	**O_2Hx (days)**	**Study PMA (wks; days)**	**Number of VestibuGlide Sessions**
Mean	32; 6	1927.92	43.7	30.35	2.25	33;7	24.41
SD	0.96	298.47	2	1.78	1.76	0.82	4.44

CONTROL INFANTS							
	Birth GA (wks;days)	**Birth weight (gms)**	**Birth Length (cm)**	**Birth Head Circumference (cm)**	**O_2Hx (days)**	**Study PMA (wks; days)**	**Number of VestibuGlide Sessions**
Mean	32; 5	1888.13	43.28	30.05	1.47	34; 3	0
SD	1;6	538.11	3.53	2.42	1.88	1.5	0

Table 2

15 minute gliding protocol.

Condition	Freq (Hz)	RPM	Disp (cm)	Accel (m/s^2)	SP (m/s)
B1					
S1	**0.50**	30	8.07	0.36	1.08
B2					
S2	**0.65**	40	4.49	0.36	1.08
B3					
S3	**0.80**	49	2.87	0.36	1.08
B4					
S4	**0.95**	57	1.98	0.36	1.08
B5					
S5	0.65	40	2.59	**0.21**	1.08
B6					
S6	0.65	40	4.47	**0.36**	1.08
B7					
S7	0.65	40	6.40	**0.51**	1.08
B8					

B= baseline condition, S= stimulus condition.

S1–S4 varied in frequency and S5–S7 varied in acceleration. During the baseline condition, the chair did not move.

Table 3

Respiratory outcomes for infants in the Vestibuglide treatment group. This table includes the outcomes means prior to including the data into a hierarchical mixed model, the adjusted means after the model, stimulus condition effects, and effect sizes.

Respiratory Outcomes for VestibuGlide Infants					
Outcomes	**Condition**	**Means**	*** Estimated Means**	**Stimulus Condition Effect**	**Effect Size**
BPM Rib Cage	S1	60.75	60.42	$F(7, 77) = 25.53$, $p<0.01$	1.42
	S2	63.11	62.80		
	S3	62.86	62.55		
	S4	61.45	61.14		
	S5	60.44	61.57		
	S6	62.18	61.86		
	S7	64.40	64.11		
	Avg. Baseline	59.05	58.70		
BPM Abdomen	S1	60.91	60.72	$F(7, 77) = 23.60$, $p<0.01$	1.36
	S2	63.21	63.05		
	S3	62.96	62.78		
	S4	61.65	61.47		
	S5	60.69	62.09		
	S6	62.46	62.27		
	S7	64.46	64.31		
	Avg. Baseline	59.29	59.10		

* estimated means have been entered into a hierarchical mixed model to account for the covariates (birth weight, oxygen history, and caffeine intake)

Table 4

Due to the significant stimulus condition effects evident in the respiratory outcomes, adjusted means were pairwise compared.

Significant Pairwise Comparisons for VestibuGlide Infants		
Conditions Compared	**T score**	*** p value**
BPM Rib Cage		
S2. vs. Avg. Baseline	7.23	<0.001
S3. vs. Avg. Baseline	6.80	<0.001
S4. vs. Avg. Baseline	4.31	<0.001
S5. vs. Avg. Baseline	5.06	<0.001
S6. vs. Avg. Baseline	5.57	<0.001
S7. vs. Avg. Baseline	9.54	<0.001
S1 vs. S7	−4.88	<0.001
S4 vs. S7	−3.94	0.005
S5 vs. S7	−3.36	0.034
BPM Abdomen		
S2. vs. Avg. Baseline	6.88	<0.001
S3. vs. Avg. Baseline	6.44	<0.001
S4. vs. Avg. Baseline	4.14	0.002
S5. vs. Avg. Baseline	5.20	<0.001
S6. vs. Avg. Baseline	5.53	<0.001
S7. vs. Avg. Baseline	9.08	<0.001
S1 vs. S7	−4.71	<0.001
S4 vs. S7	−3.72	0.010

* All *p* values are based on a *Bonferroni Adjustment*