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Non-Nutritive Suck Parameter in Preterm Infants with RDS

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Abstract

Objective—To characterize the integrity of non-nutritive suck (NNS) parameters among three groups of preterm infants ranging from normal to those with progressive degrees of respiratory distress syndrome (RDS).

Study Design—NNS compression waveforms were sampled from 55 infants in the neonatal intensive care unit using a silicone pacifier electronically instrumented for intraluminal pressure. Seven select NNS parameters were measured at two different sessions, and statistically analyzed using a General Linear Model Analysis of Covariance.

Results and Conclusions—Preterm infants with a more extensive history of RDS and oxygen therapy manifest significantly ($p \leq 0.001$) degraded performance on six of the seven NNS measures. This trend was disproportionately amplified in preterm infants with moderate-to-severe RDS. Prolonged periods of RDS requiring oxygen therapy may cause maladaptive orosensory experiences, and restrict oral movements which may contribute to delayed NNS development.

Keywords

Preterm birth; Non-nutritive suck; Respiratory distress syndrome; Sensory deprivation

Introduction

The ontogeny of suck is marked by rhythmic bursts of fetal non-nutritive suck (NNS) activity and occurs at approximately 28–33 weeks gestational age (GA, i.e. the time elapsed between

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the first day of the last menstrual period and the day the infant is born) (Hack et al., 1985). The nutritive suck differs from NNS in that the expression of milk requires simultaneous coordination of suck, swallow and respiration (Medoff-Cooper, 2005), with slower suck cycles (1 Hz) and generally without inter-burst pauses (Wolff, 1968). Coordinated NNS is an important precursor to successful oral feeding and demonstrates remarkable stability by 34 weeks GA (Hack et al., 1985).

Infants who are born prematurely frequently exhibit oromotor dysfunction and are unable to suck and feed orally which can lead to an extended stay in the neonatal intensive care unit (NICU). An underdeveloped nervous system compounded by the necessity to face the environmental demands of extrauterine life presents a significant challenge to the formation of neural circuits which support adaptive sensorimotor control. The suck central pattern generator (sCPG) is one such highly adaptive neuromotor behavior that appears susceptible to prematurity. The sCPG is regulated by a bilateral neural network of pontine interneurons in the human infant which can be modulated by central descending inputs (sensorimotor cortex) and peripheral somatosensory inputs (Barlow & Estep, 2006).

Unstable neonatal conditions associated with lung disease or respiratory distress syndrome (RDS) require oxygen supplementation which means trussing the lower face with tubes and tape (Case-Smith, 1989). Unfortunately, these procedures produce unexpected tactile stimulation and movement restriction of the lower face that may negatively affect the development of the sCPG (Comrie & Helm, 1997; Finan & Barlow, 1996). In animal models, the combination of sensory deprivation and motor restriction has been shown to disrupt development of key brain structures involved in sensorimotor control, including motor cortex and cerebellum (Pascual & Figueroa, 1996; Pascual et al., 1993; Pascual et al., 1998). This is consistent with the notion of a *critical period* during early postnatal life, when manipulations in trigeminal sensory systems may significantly alter the structure and function of the developing brain (Bosma, 1973). Somatosensory information associated with oromotor behaviors is crucial in order for infants to integrate sensorimotor experiences in their environment, and such atypical oromotor experiences may significantly disturb the development of NNS and delay the transition to competent oral feeds.

Little is known about the motor dynamics of infant ororhythmic development, nor its response to rate limiting conditions such as the oral sensorimotor deprivation associated with RDS. Therefore, the purpose of this study was to characterize salient NNS parameters among three preterm groups, including healthy CONTROL (minimal oxygen history), RDS1 (mild oxygen history), and RDS2 (moderate-severe oxygen history) babies. We hypothesized the integrity of the NNS would be degraded as a function of RDS severity.

Patients & Methods

Patients

This study was approved by the human subjects committees of the University of Kansas Medical Center (Kansas City, KS) and Stormont-Vail Regional Medical Center (Topeka, KS) and written informed consent was obtained from the parents or guardians of the infants prior to study participation. Participants were 55 preterm infants (23 female, 32 male), with a mean GA of 30.06 weeks (SD 2.2) and mean birth weight of 1339.7 grams (SD 386.2). These infants were distributed among three groups based on oxygen supplementation history: CONTROL (no intubation, minimal or no oxygen history, range 0-4 days), RDS1 (Respiratory Distress Syndrome, mild oxygen history requiring endotracheal intubation and/or 5-7 days of oxygen therapy), and RDS2 (Respiratory Distress Syndrome, moderate-to-severe oxygen history requiring endotracheal intubation and more than 7 days of oxygen therapy). The clinical characteristics of each group are given in Table I.

Inclusion criteria for the study population were: head circumference within 10-90th percentile of mean for post-menstrual age (PMA, i.e. the time elapsed between the first day of the last menstrual period plus the time elapsed after birth), neurological examination showing no anomalies for PMA: response to light, sound, spontaneous movements of all extremities, and stable vital signs (heart rate, blood pressure, age appropriate respiratory rate, and oxygen saturation >92 SpO₂) to allow for NNS. All infants were extubated for >5 days at the time of testing. Exclusion criteria were: all grades of intracranial hemorrhage, periventricular leukomalacia, neonatal seizures and culture positive sepsis or meningitis at time of testing, chromosomal anomalies or craniofacial malformation.

Equipment and Data Collection

Infants were tested at the neonatal intensive care units over two sessions occurring approximately one week apart (mean = 6.8 days apart [SD = 2.5]), starting at 34 weeks PMA. Fifteen minutes before feeding, the mobile Actifier (Finan & Barlow, 1996) recording station, designed and developed in our laboratory, was positioned cribside. The Actifier was used to sample NNS compression waveforms with a sterile Soothie™ silicone pacifier (Children's Medical Ventures, Inc.) snapped onto a specially designed receiver, which included a lubricated spherical acetal head and stainless steel cannula with a Luer fitting coupled to a Honeywell pressure transducer. The Actifier was controlled by Neosuck RT®, a specialized software program developed in our laboratory for use in the NICU which communicates with the National Instruments PCI-6052E real time multifunction data acquisition card. Outputs from the Actifier's integrated pressure sensor were conditioned by a bridge amplifier (DC-coupled, Butterworth 3-pole LP filter @ 50 Hz), and digitized (3 kHz, 16 bits vertical resolution) in real time. A 2-point scale calibration of intraluminal air pressure for the Soothie™ pacifier was completed using water manometry and registered with each data file prior to digitization.

Following a brief examination of physiologic state, the infant was cradled in a supportive inclined posture, swaddled, with limbs positioned at midline, and background/overhead lighting dimmed in the isolette suites to promote eye contact with the tester. Sampling of NNS behavior was not initiated until the infant was in an optimal behavioral state, i.e., drowsy to quiet alert (stages 3 or 4 of the Preterm Infants Behavioral Scale, Newborn Individualized Developmental Care and Assessment Program; NIDCAP) (Als, 1995). The infant was presented the instrumented silicone pacifier to establish an oral latch on the nipple, and several minutes of NNS data were sampled. The infant remained connected to the NICU life support monitors at all times for observation of respiration, heartbeat and oxygen saturation. Physiological parameters of oxygen therapy requirement, PMA, and nurse's report of oral feeding ability were documented.

Data Analysis

Two minutes of continuous data were chosen based on the greatest number of pressure peaks, reflecting each infant's most active period of oromotor output. A specialized peak picking algorithm implemented in NeoSuck RT® utilized the first derivative of pressure and threshold intercepts to tag individual pressure cycles of a NNS burst. Peak pressure intercepts for time and amplitude were obtained by indexing each zero crossing of the derivative suck signal into the original suck signal data. This algorithm permitted objective identification of NNS activity occurring within the two-minute data sample associated with a single test session.

Seven dependent variables were quantitatively analyzed for each two-minute data sample. Waveform discrimination and threshold detection set to 1 cm H₂O was used for objective identification of nipple compression events. The minute-rate variables included: (1) **Total Mouthing Events** defined as the sum of all pressure events, (2) **Non-NNS Events** defined as

nipple compression pressure events that did not occur within an NNS burst sequence, (3) **Burst-related NNS Cycles** defined as suck compression cycles with cycle periods less than 1000 milliseconds and occurring within the NNS burst structure, and (4) **NNS Bursts** defined as the cumulative number of NNS bursts produced per minute. NNS bursts consisted of two or more compression cycles. The three remaining global measures included the (5) **Average Number of NNS Cycles/Burst**, and two ratiometric calculations which highlighted the proportions of organized ororhythmic activity produced among the preterm infant test groups, including (6) **NNS Cycles as a percentage of the Total Number of Mouthing Events** (Burst-related NNS cycles/Total Mouthing Events * 100), and its complement component, namely (7) **Non-NNS Events as a percentage of the Total Number of Mouthing Events** (Non-NNS Events/Total Mouthing Events * 100).

Statistical Analysis

A General Linear Model Analysis of Covariance (ANCOVA) was completed for each NNS variable measured at two different sessions. The purpose of the ANCOVA is to increase the sensitivity of the test of main and interaction effects by reducing the error variance. Since the NNS suck variables were measured twice at a one week interval there is a between-subject factor (i.e., mixed design). The major question for ANCOVA in the current study is whether or not there are group, measurement, and/or group by measurement differences in the mean NNS suck variable scores after they are adjusted for differences in the covariate scores. Thus, the between-subjects factor was preterm group (CONTROL, RDS1, and RDS2) and the repeated-measures factor was weekly session (session 1 and 2). Covariates included GA at birth, PMA at the first session, and birth weight. The mean differences were considered significant if $p < 0.05$, and the Bonferroni adjustment was used for multiple pairwise comparisons. Analyses were performed using SPSS v.15.

Results

An evaluation of assumptions of normality, linearity, homogeneity of variance-covariance matrices, multicollinearity, singularity, and sphericity were satisfactory. Repeated measures ANCOVA revealed a significant main effect of group ($p \leq 0.001$) for six of the seven dependent variables (Table II). The effects size, η^2 , ranged from 0.32 to 0.62 indicative of medium to large effects for the significant suck variables. Post hoc tests indicated the RDS2 group had significantly reduced oromotor output compared to the CONTROL and RDS1 groups on NNS variables. Although the minute-rate of non-NNS events did not significantly differ between groups, the proportion of non-NNS events of the total mouthing events was significantly greater in the RDS2 group compared to the CONTROL and RDS1 groups (Table III). This indicates differences in the minute-rate of total mouthing events between groups are primarily driven by the quantity of organized, burst-related NNS cycle activity. The absence of any significant interactions between session and group indicated the patterns observed in each oromotor variable were consistent between the two weekly sessions.

As shown in Figure 1, degradation of NNS structure appeared to follow a continuum with increasing severity of oxygen history from the CONTROL and RDS1 groups to the RDS2 group, with a disproportionate breakdown in oromotor control among RDS2 infants. The RDS2 group (average oxygen requirements: 37.4 days) endured longer periods of oxygen therapy compared to the CONTROL and RDS1 groups (average oxygen requirements: 1.4 days and 5.1 days, respectively). Of the three samples, the RDS2 group produced the highest non-NNS event percentage of total mouthing events (3.4 times greater than CONTROL), presumably indicating the output from a maladaptive neural circuitry underlying the sCPG. Such a lack of structured development highlighted by atypical oral movements clearly distinguished the RDS2 babies from the other groups.

Discussion

The potent nature of sensory input on development of motor systems is well documented in studies of cortical assembly. During early postnatal life, cortical layer 4 and thalamocortical pathways are very plastic allowing sensory-dependent development (Erzurumlu & Jhaveri, 1990). Cortical structure and function can be enhanced or impaired depending on characteristics of the activity in thalamocortical afferents (Miller et al., 1993). The extent of cortical reorganization points to the importance of correlated neural activity in the formation and maintenance of cortical representations of the body surface (Merzenich et al., 1984). Thus, sensory consequences associated with spontaneous and goal-directed movements provide the baby's brain with important cues for axonal guidance and synaptic reinforcement that are continually encoded, mapped in the brain, and encourage prompt development (Shatz, 1994). The status of the neural representation of orofacial systems is hypothesized to determine the behavioral output, and behavior itself changes the neuromotor system. Under these guiding principles, both spontaneous and patterned movements of the lips, tongue and jaw for suck, typically serve to provide the baby with a rich source of temporally salient somatosensory stimuli, which in turn reinforces the coordination of many muscle systems involved in producing the burst-pause pattern of NNS.

Feeding behavior in preterm infants matures significantly between 33-36 weeks PMA, and has been suggested to be predictive of future motor performance (Amiel-Tison & Gosselin, 2001). Preterm infants who show improvements in feeding patterns have been found to develop normally or with only minor neurodevelopmental delays at 18 months of age (Mizuno & Ueda, 2005). In comparison, premature infants who lack a functional suck or manifest oromotor dysfunction that persists well into early childhood are at significant risk for neurodevelopmental delay (Stoll et al., 2004). The lengthy intubation procedures cost the baby precious sensory and motor experiences during a critical period of brain development for oromotor pattern generation. The unusual orosensory environment resulting from the presence of the ventilator tube may influence perceptual-motor experience and interfere with movement pattern formation compared to non-intubated babies (Barnard & Bee, 1983; Bier et al., 1993). Bosma (1973) suggested that "appropriate oral experiences may be critical in the final weeks of gestation, and that their interruption may impair fragile syntheses of central neural representations of these functions." The importance of experience in brain development and plasticity is highlighted by the resultant physiological and cortical structural changes that modify motor and sensory system circuitry (Pascual et al., 1993; Pascual et al., 1998). Infants with perinatal distress and neurologic impairment compared to normal full-term infants manifest a significantly slower mean rate of NNS and a greater intra-individual variability of rate (Dreier & Wolff, 1972). This supports the hypothesis that NNS is indeed sensitive to perinatal distress and rhythmic oromotor activities could be sensitive indicators of minor disturbances of central nervous system (CNS) function in infants without any other obvious neurologic impairment (Medoff-Cooper & Ray, 1995). The usual activity-dependent associations reinforced through correlated sensorimotor activity in neurally organized babies are presumed to be degraded in infants who manifest oromotor dysfunction, a potential marker for discoordination within the CNS (Medoff-Cooper et al., 1993; Wolff, 1968).

In summary, NNS performance varies significantly as a function of RDS severity. In our view, RDS infants represent a test model of oral sensory and motor deprivation, depending upon the type and duration of oxygen therapy. The reduced opportunities for oromotor experiences, such as suck or autostimulation, in this sample are hypothesized to result in a delay in the development of brain circuits responsible for organized suck. Quantitative measures of the intraluminal pressure during NNS are designed to provide the clinician with a rapid, non-invasive and objective means to assess the integrity of the sCPG in the preterm infant. Repeated

measures in the NICU at weekly or even daily intervals may serve to guide therapeutic intervention and assess feeding readiness skills.

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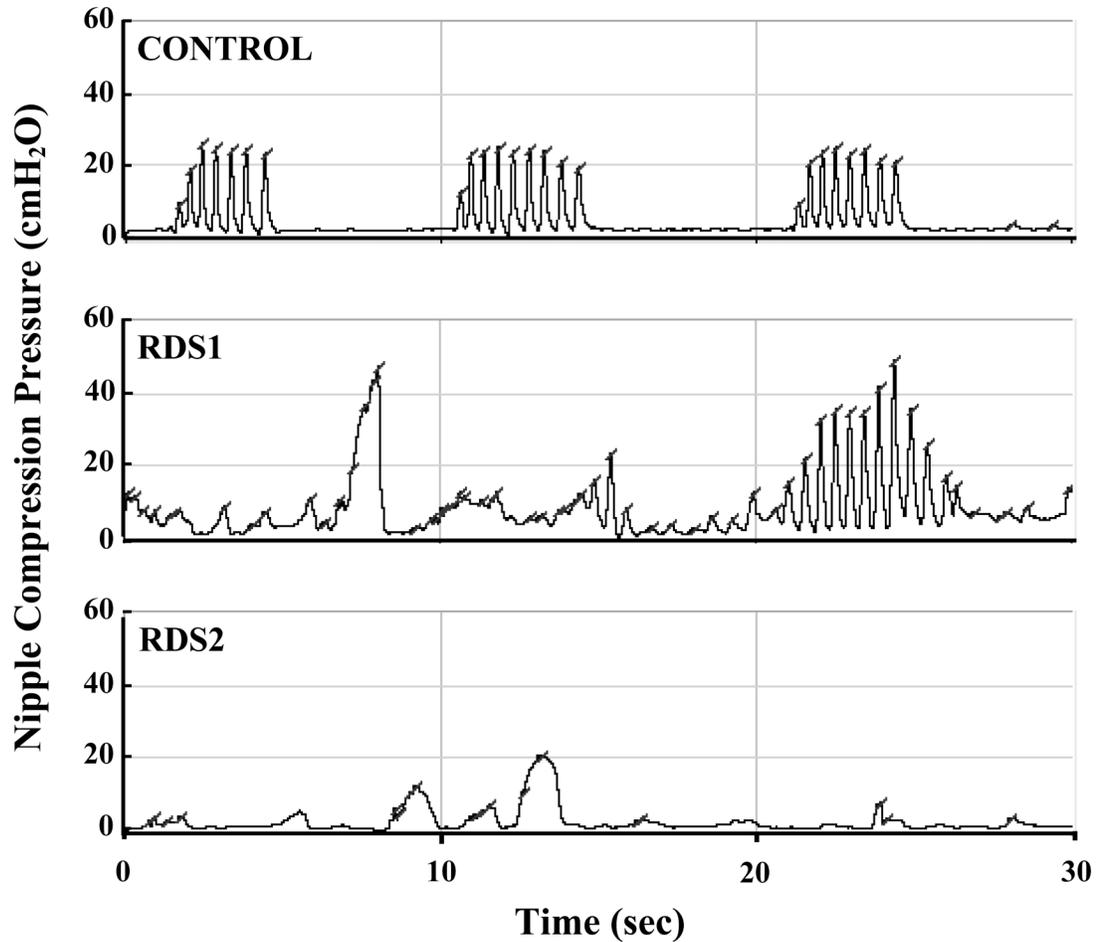


Figure 1. Oromotor Sample Profiles

Sample non-nutritive suck waveforms characteristic of healthy CONTROL, RDS1, and RDS2 infants. Three NNS bursts evident in CONTROL panel. One NNS burst and several non-NNS burst mouthings apparent in RDS1 record. No NNS burst structure in RDS2 panel.

Table I

Clinical Characteristics of Study Infants*

VARIABLE		CONTROL (n=17)	RDS1 (n=11)	RDS2 (n=27)
Gender (males : females)		8 : 9	7 : 4	17 : 10
Birth GA (weeks)		31.5 (1.4)	30.5 (2.1)	29.0 (2.2)
Birth Weight (grams)		1518.7 (318.6)	1442.4 (275.1)	1185.3 (409.9)
PMA @ Session (weeks)	Session 1	33.6 (1.7)	33.4 (1.3)	34.1 (2.2)
	Session 2	34.7 (1.6)	34.5 (1.1)	34.9 (2.1)
	Mean	34.2 (1.7)	34.0 (1.2)	34.5 (2.2)
% Oral Feeding	Session 1	13.2 (4.0)	9.4 (4.4)	3.4 (3.2)
	Session 2	35.0 (9.5)	40.6 (10.5)	10.4 (7.5)
	Mean	24.1 (6.8)	25.0 (7.5)	6.9 (5.4)
Oxygen Therapy History (days)	Ventilator	0.0 (0.0)	1.3 (1.3)	6.4 (11.0)
	CPAP	0.7 (1.1)	2.3 (2.2)	9.6 (10.2)
	Cannula	0.7 (1.3)	1.6 (1.6)	21.9 (15.2)
	Total	1.4 (1.7)	5.2 (1.8)	37.9 (26.0)

* Expressed as mean (sd)

Table II**ANCOVA Results**

Oromotor Variable	df	F	Sig	Eta²
Total Mouthing Events/min	2, 49	12.270	0.000	0.50
Non-NNS Events/min	2, 49	2.018	0.144	0.08
Burst Related NNS Cycles/min	2, 49	15.303	0.000	0.62
NNS Bursts/min	2, 49	9.527	0.000	0.39
Average Number of NNS Cycles/Burst	2, 49	7.952	0.001	0.32
NNS Cycle % of Total Mouthing Events	2, 49	12.166	0.000	0.50
Non-NNS Cycle % of Total Mouthing Events	2, 49	12.166	0.000	0.50

Table III

Outcome Variables

Oromotor Variable	CONTROL	RDS1	RDS2
Total Mouthing Events/min	41.4 (2.9)	44.4 (3.2)	25.5 (2.3) **
Non-NNS Events/min	5.3 (1.7)	5.8 (1.9)	9.7 (1.3) ***
Burst Related NNS Cycles/min	36.1 (3.2)	38.6 (3.5)	15.8 (2.5) **
NNS Bursts/min	5.4 (0.5)	5.6 (0.5)	2.9 (0.4) *
Average Number of NNS Cycles/Burst	7.2 (0.6)	7.5 (0.7)	4.4 (0.5) **
NNS Cycle % of Total Mouthing Events	89.4 (6.2)	86.3 (6.8)	50.8 (4.9) **
Non-NNS Cycle % of Total Mouthing Events	10.6 (6.2)	13.7 (6.8)	49.2 (4.9) **

RDS2 differs significantly from CONTROL and RDS1 groups at the $p = 0.01^*$, $p = 0.001^{**}$, and $p = 0.0001^{***}$ alpha levels.