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Effects of oral stimulus frequency spectra on the development of non-nutritive suck in preterm infants with respiratory distress syndrome or chronic lung disease, and preterm infants of diabetic mothers

Steven M. Barlow [a,*], Jaehoon Lee [b], Jingyan Wang [a], Austin Oder [a], Hyuntaek Oh [a], Sue Hall [c], Kendi Knox [c], Kathleen Weatherstone [d], Diane Thompson [d]

[a] SPLH, Programs in Neuroscience, Human Biology, and Bioengineering, University of Kansas, Lawrence, KS, USA
[b] Center for Research Methods and Data Analysis, University of Kansas, Lawrence, KS, USA
[c] Stormont-Vail HealthCare, Topeka, KS, USA
[d] Overland Park Regional Medical Center, Overland Park, KS, USA

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Abstract The precocial nature of orofacial sensorimotor control underscores the biological importance of establishing or orythmic activity in human infants. The purpose of this study was to assess the effects of comparable doses of three forms of orosensory experience, including a low-velocity spectrally reduced orocutaneous stimulus (NT1), a high-velocity broad spectrum orocutaneous stimulus (NT2), and a SHAM stimulus consisting of a blind pacifier. Each orosensory experience condition was paired with gavage feedings 3×/day for 10 days in the neonatal intensive care unit (NICU). Four groups of preterm infants ($N = 214$), including those with respiratory distress syndrome (RDS), chronic lung disease (CLD), infants of diabetic mothers (IDM), and healthy controls (HI) were randomized to the type of orosensory condition. Mixed modeling, adjusted for gender, gestational age, post-menstrual age, and birth weight, demonstrated the most significant gains in non-nutritive suck (NNS) development among CLD infants who were treated with the NT2 stimulus,

* Corresponding author. University of Nebraska, Barkley Memorial Center, Lincoln, NE 68583-0738, USA.
E-mail address: steven.barlow@unl.edu (S.M. Barlow).

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with smaller gains realized among RDS and IDM infants. The broader spectrum of the NT2 stimulus maps closely to known response properties of mechanoreceptors in lip, tongue, and oral mucosa and is more effective in promoting NNS development among preterm infants with impaired oromotor function compared to the low-velocity, spectrally reduced NT1 orosensory stimulus.

Introduction

The trigeminal and facial cranial nerve systems attain functionality well before term gestational age (GA) in humans. Toward the end of the 8th week post-menstrual age (PMA), light tactile stimulation of the lips and face evoke a rooting and orienting response (Humphrey, 1970). The precocial nature of orofacial touch sensitivity underscores the biological importance of establishing motor rhythms as evidenced by the presence of sucking, swallowing, and chest wall movements *in utero* (Popescu et al., 2008). In the infant's mouth and tongue, there are at least three known types of rapidly-conducting Aβ mechanoreceptors, including Merkelcells, Meissner's corpuscles, and Ruffini nerve endings which transmit touch, pressure, vibration and motion sense information along trigeminal pathways to the developing thalamus and sensorimotor cortex. Each mechanoreceptor type exhibits a unique response profile. For example, the Ruffini ending is most responsive to slow indentations of the lip and encode position, whereas the Meissner corpuscle is most responsive to rapid changes in skin indentation and pressure (e.g., vibration). Collectively, these mechanoreceptors make it possible for the infant to appreciate a wide range of oral experiences, some of which are presumed to be soothing (e.g., light touch from a caretaker's finger, stiffness of a pacifier, infant's fingers, mother's breast) whereas other unexpected orosensory experiences may lead to maladaptive oral aversion (e.g., orotracheal intubation, nasogastric feeding tube, ventilator, tape on the skin) at a critical period of brain development for ororhythmic pattern formation (Barlow, 2009a; Barlow et al., 2010; Shiao et al., 1995).

The central nervous system and oromotor pattern generation is vulnerable to delay and injury in RDS, CLD, and IDM infants (Barlow 2009b; Khaksar et al., 2012; Nold and Georgieff, 2004; de Regnier et al., 2007). For example, infants diagnosed with CLD often manifest oromotor dyscoordination, absent or weak suck, poor airway protection, dysphagia, and poor state control (Gewolb and Vice, 2006). Delayed development of NNS is well documented in preterm RDS infants (Poore et al., 2008; Stumm et al., 2008; Estep et al., 2008). The invasiveness of lengthy intubation, oxygen supplementation, and nasogastric feeding procedures associated with prematurity and lung disease cost the baby precious sensory and motor experiences during a critical period of brain development for oromotor pattern generation (Bosma, 1973). Preterm infants of diabetic mothers (IDM) babies exhibit macrosomia but are lethargic when attempting sucking and feeding (de Regnier et al., 2007). A common approach is to provide preterm infants with orotactile stimulation to promote sucking. The dose, skin site, stimulus features (slow vs fast touch, low vs high pacifier stiffness, etc.), vary widely among NICUs, including but not limited to a gloved finger, gentle stroking of the mouth using a finger or cotton swab, silicone pacifier, or a computerized oral entrainment system. Overall, controlled somatosensory stimulation strategies have proven beneficial in developing NNS and oral feeding skills in premature infants (Fucile et al., 2005, 2011; Rocha et al., 2007). Recently, a pressure-modulated pacifier was developed to provide tube-fed preterm infants with a pulsatile orosensory experience that closely mimics the expected spatiotemporal pattern of non-nutritive suck (Barlow et al., 2008).

Each form of oral somatosensory stimulation has a unique spectral 'frequency' signature (power spectrum) that will activate a subset of mechanoreceptor types while leaving other mechanoreceptors in a quiescent state. The relation between orocutaneous stimulus power spectrum and NNS development in preterm infants is unknown. In the present study, we systematically investigated the effects of comparable doses of 3 different types of orosensory experience, including a high-velocity broad spectrum orocutaneous stimulus, a low-velocity spectrally reduced orocutaneous stimulus, and a SHAM condition consisting of a silicone pacifier. Given the exquisite frequency sensitivity of trigeminal mechanoreceptors in orofacial tissues, it is hypothesized that the high-velocity broad spectrum orocutaneous stimulus (with