

Nutritive and non-nutritive swallowing apnea duration in term infants: Implications for neural control mechanisms

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Abstract

The impact of bolus ingestion and level of consciousness on swallowing apnea duration (SAD) in healthy term infants has not been adequately explored despite the likely contribution of swallowing apnea to upper airway protection against aspiration. SAD during wakefulness, sleep, and feeding (breast or bottle) of 10 term infants was measured 10 times from birth to 1 year of age. Nineteen thousand four hundred and two swallows were analyzed. Irrespective of age, SAD during feeding was significantly shorter than SAD of non-nutritive swallowing (during wakefulness and sleep). SAD did not change significantly within the first year of life in any of the three conditions and there was no change in the relative durations of nutritive, wake and sleep conditions with age. The absence of an age effect implies that the neural mechanisms controlling SAD are fundamentally brainstem-mediated and largely hard-wired at birth in healthy term neonates.

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1. Introduction

The oro-pharyngeal cavity is a conduit for both air and ingested materials and, hence, it is not surprising that breathing and swallowing cannot be performed

simultaneously. The breathing of human infants is suspended for a short period during swallowing (Hanlon et al., 1997). This swallowing-related apnea (cessation of respiratory airflow) is distinct from nondeglutitive apneic pauses in healthy term infants. Benign apneic pauses in normal healthy infants may be as short as 2 s (Hoppenbrouwers et al., 1980) or as long as 15 s (Hoppenbrouwers et al., 1977). Swallowing apnea (SA) is much shorter in duration, being 0.672 s for nutritive swallows in infants (Hanlon et al., 1997)

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and 1.03 s for non-nutritive swallows (Wilson et al., 1981).

Little information exists on swallowing apnea duration (SAD) of normally developing infants beyond 1 week of age (Hanlon et al., 1997). Much of the previously reported data were obtained, at least in part, from human preterm (e.g., Koenig et al., 1990) and other pediatric patient populations (e.g., Wilson et al., 1981). Normative data beyond the neonatal age is crucial for the identification of aberrant patterns in the patient population. Given the link between adequate cardiorespiratory control and efficient feeding (Pinnington et al., 2000), SAD may be a key component of successful integration of breathing and nutritive swallowing. Despite this, it seems the impact of feeding on SAD has not yet been directly compared to that of non-nutritive swallowing in healthy term infants.

The specifics of the neural control mechanisms of SAD are unknown although SA is thought to be “a central event with its occurrence receiving a dedicated neural command” (Hiss et al., 2003, p. 297). The potential that suprabulbar mechanisms may influence SAD appears not to have been previously suggested. Suprabulbar input is possible given that research indicates that pharyngeal activity may be influenced by the suppression of input from higher brain centers during sleep (review by Isono, 2000). It is therefore hypothesized that if SAD is influenced by descending input from higher brain centers, SAD will be altered during sleep when the relevant suprabulbar mechanisms are less influential. The present study aimed to investigate three features of infantile SAD: the influence of state of alertness, the influence of feeding-related sensory stimulation, and the maturation patterns of these influences from birth to 12 months of age.

2. Methods

2.1. Participants

Ten healthy term neonates (eight females, two males) were recruited to this study following the approval of the Canterbury Regional Health Ethics Committee. Written consent was obtained from a parent of each neonate. The neonates were born to mothers without prenatal maternal complications, were born above 38 weeks gestational age, presented with Apgar

scores at or above 7 at 5 min after birth. The neonates had no reported medical complications at birth, nor did they have nervous system or upper-body structural abnormalities. At each assessment, measures of normal development were documented: weight, head circumference, and the presence (or absence) of reflexes appropriate for chronological age (rooting, walking, grasp, moro, babinski, and tonic neck reflexes). From 1 month of age the Denver Developmental Screening Test II (DDST II) was also completed during each visit. All infants were found to be within normal limits on these measures.

2.2. Procedure and equipment

Breathing-swallowing coordination was monitored during unrestricted feeding from either the breast or bottle (as determined by the mothers) in a reclined position and then during sleep and wakefulness for as long as the infant slept or tolerated the procedure, respectively. Recording was momentarily halted if mouth-breathing was suspected (mouth opening). Sleep was subjectively monitored by the researcher and caregiver and confirmed by failure of the infant to respond to auditory and tactile stimuli. Attempts to keep a supine body position consistent across conditions and assessment ages were made given the known physiological effects of altered body position in infants (Chen et al., 1995). However, due to behavioral constraints this was not always possible particularly during wakefulness at 9 months and 1 year of age. Assessments were made within the first 48 h, at 1, 2, 3 and 4 weeks, 2, 3, 6, 9, and 12 months of age using simultaneous time-locked recordings of submental muscle activity (Wilson et al., 1981), presence or absence of nasal airflow (Hanlon et al., 1997) and thyroid acoustics (Pinnington et al., 2000). All recordings were captured by an integrated hardware-software system (Kay Elemetrics Swallowing Workstation). The collective submental muscle group was located by palpation and the bipolar surface EMG electrodes (Thought Technology Triode™) positioned over this muscle group with a reference electrode on the forehead. The rectified and averaged submental surface electromyography (SEMG) signals were sampled at 250 Hz. Nasal airflow was measured by an infant nasal canula to determine swallowing apnea duration. Nasal prongs were situated at the entrance to each nostril and secured firmly

around the head. Thyroid acoustics were measured by a laryngeal microphone and were used to rule out submental EMG artifact and confirm swallowing onset. The laryngeal microphone was a modified omnidirectional condenser microphone with a sensitivity of -62 ± 3 dB, an impedance of <2.0 k Ω , and a frequency response of 50–12,500 Hz. The microphone was connected to a preamplifier (Rolls mini-mic preamplifier MP13, gain of 6–50 dB). The signal from the preamplifier was sampled at 4000 Hz. The microphone was positioned lateral to the thyroid, which was located by palpation and held or taped in position with standard surgical tape. Body position was monitored using custom-made mercury switch position monitor secured to a soft elasticized band fitted around the chest with Velcro[®] at the level of the xiphisternum from 9 months of age. A change in body position resulted in a change in the output voltage which correlated to one of four body positions: side-lying (left = 1.02 V, right = .69 V), upright (1.55 V), supine (.35 V) and prone (1.33 V). The mercury switch position monitor was connected to a custom-made sensor box (which also acted as an external battery-operated power source) and the output fed into the auxiliary channel of the Kay Elemetrics Swallowing Workstation. The signal was sampled at 250 Hz.

2.3. Data processing and preparation

Swallows were identified by simultaneous bursts of SEMG and thyroid acoustic activity paired with a cessation in nasal airflow. The duration of swallowing apnea was measured manually using a computer cursor and the mean value for each infant in each condition at every assessment age was entered into the database. Mid-pause swallows were excluded. Swallows were classified as mid-pause if they occurred during an extended apneic pause of 2 s or greater (Hoppenbrouwers et al., 1980), and included consecutive swallows between which no respiration occurred. The duration of swallowing apnea could not be measured for mid-pause swallows since swallowing-specific apnea cannot be determined when imbedded in a prolonged respiratory pause. Similarly, the SAD of each swallow in consecutive swallow runs cannot be differentiated. Behavioral constraints prevented the collection of three data points, once during sleep and twice during wakefulness for three infants of differ-

ent ages. These missing samples were assigned the SAD value of their ‘closest match’ participant (Elliott and Hawthorne, 2005) at the appropriate assessment age and for the relevant condition. A random 20% of the data was reanalyzed by the primary rater and an independent rater in order to determine intraclass correlation coefficients for intra- and inter-rater reliability, respectively. The effects of age and condition on SAD were tested using repeated-measures analyses of variance (ANOVA), with both age and condition as repeated measures factors. All statistics were performed using the SPSS statistical software package (version 13.0, 2004), and a p -value $<.05$ was taken to indicate statistical significance.

3. Results

A total of 19,402 swallows were recorded and analyzed. Intraclass correlation coefficients demonstrated satisfactory interrater and intrarater reliability for SAD measurements ($r = .931$ and $r = .956$, respectively). The number of swallows obtained for sleep, wake, and feeding conditions for all assessment ages are shown in Table 1. The means and standard error scores of SAD for each assessment age for each condition and pooled over the three conditions are shown in Table 2. A repeated-measures ANOVA comparing the three conditions revealed a condition effect ($F = 93.7$, $d.f. = 2, 18$, $p < .001$) but no overall effect of age ($F = 0.46$, $d.f. = 3.54, 31.86$, $p = .74$) or any interaction of condition and age ($F = 0.84$, $d.f. = 18, 162$, $p = .65$); Fig. 1. The mean SADs for wake, sleep, and feeding

Table 1
Number of swallows for sleep, wake and feeding conditions for all assessment ages

Age	Wake	Sleep	Feeding	Total
48 h	540	982	1387	2909
1 week	249	215	1614	2078
2 weeks	297	250	1570	2117
3 weeks	315	184	1590	2089
4 weeks	236	251	1365	1852
2 months	368	100	1285	1753
3 months	360	90	1454	1904
6 months	288	78	1383	1749
9 months	218	72	1201	1491
1 year	157	39	1264	1460
Total	3028	2261	14113	19402

Table 2
Means and standard error scores of swallowing apnea durations (in ms) for each assessment age for each condition

Age	Wake		Sleep		Feeding	
	Mean	S.E.	Mean	S.E.	Mean	S.E.
48 h	709.1	31.6	768.8	44.1	498.1	22.0
1 week	833.6	42.5	843.3	57.0	508.7	20.4
2 weeks	806.6	52.4	814.7	57.4	527.5	22.9
3 weeks	754.5	42.4	830.8	35.0	486.8	15.6
4 weeks	785.5	56.9	731.4	51.3	504.9	15.7
2 months	764.8	45.3	751.4	36.4	538.8	24.0
3 months	819.4	87.9	764.0	38.5	508.5	24.4
6 months	779.6	38.7	869.6	67.9	481.0	20.8
9 months	846.8	91.8	757.7	35.9	503.2	29.6
1 year	742.8	67.6	827.6	118.1	498.7	37.6
Overall mean	784.1	29.4	795.8	26.9	505.6*	15.0

* Significantly different to the overall means of both wake and sleep ($p < .001$).

were 784.3 ms (± 182.7 ms), 795.9 ms (± 183.8 ms), and 506.6 ms (± 75.5 ms), respectively. The condition effect was further explored with the completion of two separate repeated-measures ANOVAs comparing feeding SAD to wake and sleep SAD. This showed that feeding SAD was shorter than wake ($F = 137$, d.f. = 1, 9, $p < .001$) and sleep SAD ($F = 145$, d.f. = 1, 9, $p < .001$).

A repeated-measures ANOVA for SAD during wakefulness revealed no age effect ($F = 0.64$, d.f. = 2.60, 23.40, $p = .576$). The maximum difference at any age during wakefulness was only 9.6% of the overall mean. A similar analysis for SAD during sleep also revealed no age effect of age on durations ($F = 0.71$, d.f. = 2.89, 26.02, $p = .55$). The maximum

difference at any age during sleep was only 8.12% of the overall mean. A repeated-measures ANOVA for SAD during feeding also revealed no age effect ($F = 0.75$, d.f. = 9, 81, $p = .66$). The maximum difference at any age during feeding was only 4.9% of the overall mean.

4. Discussion

This longitudinal study is the first to demonstrate three important features of infantile SAD. First, SAD soon after birth is shorter for nutritive swallows than for both wake and sleep non-nutritive swallows. Second, there is no difference in SAD between wake and sleep non-nutritive swallows. Third, SAD for all three types of swallows (nutritive, non-nutritive wakeful, and sleep) remain essentially unchanged through the first year of life.

The effect of nutritive swallowing on SAD may reflect the higher velocity of bolus propulsion through the pharynx during nutritive than non-nutritive swallowing. This argument is supported by evidence that adult tongue and pharyngeal pressure is greater (Cerenko et al., 1989) but the overall duration of oropharyngeal pressure is less (Perlman et al., 1993) during nutritive than non-nutritive swallows. Furthermore, bolus velocity during swallowing increases with increasing bolus volume (Ergun et al., 1993). If the same principles apply to infantile swallowing, the higher velocity of an ingested bolus may account for shorter nutritive swallow duration and subsequent shorter nutritive SAD.

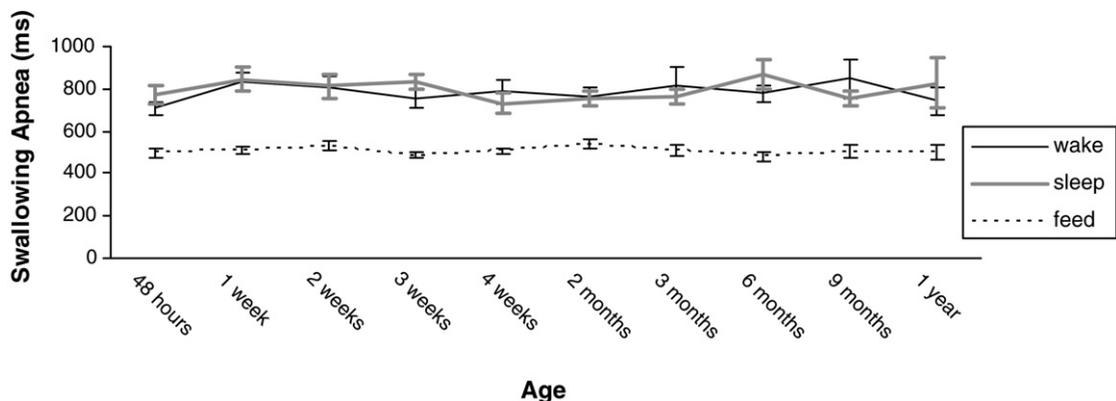


Fig. 1. The mean duration and standard error scores of swallowing apnea during wakefulness, sleep and feeding at each assessment age.

Both bolus size and chemical make-up differed between the feeding and saliva boluses, which may account for the differences between nutritive and non-nutritive SAD. Evidence from prior research suggests, however, that the chemical make-up may not be an independent variable in the present study. The latency of action potentials from the superior laryngeal nerve in mammals does not differ for saliva and milk boluses but does for water (Harding et al., 1978). Thus the condition effect observed in the present study is more likely due to the presence of the ingested bolus than the chemical characteristics thereof.

It is also important to note that respiration rate (Bamford et al., 1992) and ventilation (Mathew et al., 1985) of healthy human term neonates decreases during feeding. This may be in response to the rapid ingestion of fluids and subsequently result in shorter SAD as a means of compensating for ventilatory demands. Given that the cortex is involved in the modulation of ventilation in response to afferent respiratory input (Horn and Waldrop, 1998), increased ventilatory demands during feeding may have activated the cortex which in turn shortened SAD in order to compensate for the ventilatory demands.

However, there is greater support for brainstem mediation of SAD and, therefore, more independent SAD neural control. The fact that SAD was not altered by level of consciousness implies lower CNS or brainstem mediation. The transition from wakefulness to sleep, particularly non-rapid eye movement sleep, involves widespread cortical deactivation in adults (Braun et al., 1997) and alters respiration in infants (Hoppenbrouwers et al., 1977). The absence of a difference between sleep and wakeful SAD in the present study implies that SAD is impervious to the influences of the suprabulbar centers affected by sleep and, therefore, has neural substrates that are partially independent of those controlling respiration.

Brainstem mediation over SAD is further supported by the absence of a maturation effect in all conditions, particularly that of feeding, in the present study. The absence of maturation of SAD may reflect the relatively mature brainstem control. In general, the patterns of myelination coincide with developmental feeding milestones in the first year of life such as postnatal myelination of frontal regions and the emergence of voluntary feeding behaviors (review by Rogers and Arvedson, 2005). At birth, feeding is thought to be

reflexive and only involve higher central nervous system structures to a greater degree later in infancy (Stevenson and Allaire, 1991). If SAD was controlled by higher brain structures, a maturation effect would have at least been observed for nutritive swallowing as a result of brain development. As this was not observed, this suggests that SAD is primarily brainstem mediated and that there is minimal overlap between the neural control mechanisms involved in feeding and those involved in SAD.

Furthermore, SAD did not change with age despite postnatal maturation of similar respiratory- and swallowing-related phenomena: breathing (Rusconi et al., 1994), sleep-wake states (review by Peirano et al., 2003), airway protective responses to superior laryngeal nerve stimulation in mammals (Park et al., 2001), human pharyngeal anatomy (Sasaki et al., 1977) and human laryngeal morphology (Eckel et al., 1999). This offers further support for the previously purported SAD-specific neural control hypothesis, discussed above (Hiss et al., 2003).

The mature nature of SAD soon after birth probably indicated the importance of SA to survival. It seems appropriate that airway protection mechanisms and those controlling SAD are functional in term infants at birth given that feeding commences soon thereafter. This is supported by evidence that preterm infants demonstrate decreasing SAD with age to approximate their term controls (Hanlon et al., 1997). Thus, SAD may provide a useful marker of neurological immaturity or neural damage in the pediatric patient population and, therefore, may have important implications for clinical practice.

The fact that the nutritive versus non-nutritive condition effect on SAD exists soon after birth, is maintained throughout the first year of life, and is similar to the condition effect in adults (Shaker et al., 1992), indicates that it is an intrinsic robust feature of human physiology. The SAD of these infants is also remarkably similar to the SAD of healthy adults, suggesting that SAD, particularly for nutritive swallowing, is *fully* mature at birth. For example, the mean SAD of nutritive infantile swallows in the present study of 506 ms is similar to that reported for adult nutritive swallows of 550 ms (Issa and Porostocky, 1994). The mean SAD of 784 ms for non-nutritive swallows during wakefulness is only slightly shorter than reported mean of 860 ms for non-nutritive swallows in young female adults (Hiss

et al., 2001), which suggests slight maturation of non-nutritive SAD during childhood is possible but may not be detectable within the first year of life.

In conclusion, SAD is strongly influenced by feeding but not postnatal age or state of alertness in the first year of healthy human life. Although cortical afferent processing and subsequent efferent modulation of SAD is possible, it cannot account for absent sleep-wake and maturation effects on SAD. The fact that SAD appears largely mature soon after birth suggests that this feature of breathing and swallowing integration is hard-wired and robust. Following the confirmation of brainstem mediation, future comparison to the pediatric patient population may demonstrate that SAD is a useful indicator of brainstem impairment.

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