Sequential arousal and airway-defensive behavior of infants in asphyxial sleep environments

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Lijowska, Anna S., Nevada W. Reed, Barbara A. Mertins Chiiodini, and Bradley T. Thach. Sequential arousal and airway-defensive behavior of infants in asphyxial sleep environments. J. Appl. Physiol. 83(1): 219–228, 1997.—Infants are prone to accidental asphyxiation. Therefore, we studied airway-defensive behaviors and their relationship to spontaneous arousal behavior in 41 healthy sleeping infants (2–26 wk old), using two protocols: 1) infant was rebreathing expired air, face covered by bedding material; and 2) infant was exposed to hypercarbia, face uncovered. Multiple measurements of respiratory and motor activities were recorded (video, polygraph). The infants’ response to increasing hypercarbia consisted of four highly stereotyped behaviors: sighs (augmented breaths), startles, thrashing limb movements, and full arousal (eyes open, cry). These behaviors occurred abruptly in self-limited clusters of activity and always in the same sequence: first a sigh coupled with a startle, then thrashing, then full arousal. Incomplete sequences (initial behaviors only) occurred far more frequently than the complete sequence and were variably effective in removing the bedding covering the airway. In both protocols, as inspired air (8). The rebreathing trial began either when the infant described technique to cause partial rebreathing of expired gas mixture. Our findings document the effectiveness and the limitations of these protective behaviors in relieving ventilatory compromise. Furthermore, our observations describe the particular pattern and sequence of these behaviors, which indicate their relationship to normal periodic respiratory and motor activity during sleep and to spontaneous as well as asphyxia-related arousals from sleep.

METHODS

Subjects. We studied 41 infants (age range 2 wk to 6 mo; mean age 14 ± 1.3 wk; 19 boys, 22 girls). Four infants were born prematurely, two at 34 wk gestation and two at 32 wk, but when studied they were >40 wk postconceptional age. This age range was chosen because it spans the period of peak vulnerability to accidental asphyxia and SIDS. All infants were healthy. Two infants (set of twins) born at 32 wk gestation had a history of respiratory distress syndrome treated with mechanical ventilation and surfactant with complete resolution with no residual lung disease. One term infant was briefly hospitalized for pneumonia at 1 wk of age but was fully recovered when studied at 2 mo. The other infants born at term had no history of any perinatal or neonatal complications. The study protocol was approved by the Washington University Human Study Committee, and informed consent was obtained from the parents of all infants. Parents were invited to be present during the study, and most chose to do so.

Rebreathing expired air protocol. Infants in this group were studied while sleeping prone, face down or were studied in other sleep postures with their face covered by cloth bedding (Table 1). For face-down infants, we employed a previously described technique to cause partial rebreathing of expired air (8). The rebreathing trial began either when the infant spontaneously positioned his head face straight down or when we turned his/her head toward midline so as to cause the infant’s nose to be covered by the mattress. As in a prior study, a soft sheepskin covered by a cotton sheet was beneath the infant (8). For a trial to be selected for analysis, first a
sustained elevation in percent inspired CO₂ (CO₂I) had to be achieved. The trial was concluded when spontaneous infant motor activity resulted in prompt and sustained reduction of CO₂I by >10% of the level immediately preceding the activity.

For supine or side-sleeping infants, the rebreathing trial began when we loosely draped a light-weight silk scarf over the sleeping infant’s face. This fabric was selected to minimize tactile stimulation. Additional cloths made of cotton or cotton-polyester blends were added every 1-2 min to increase expired air trapping so as to create a slow increase in CO₂I. The maximum combined thickness of added cloths ranged from 1 to 4 cm. The trial was concluded when any spontaneous body movement or combination of movements resulted in a prompt and sustained reduction in CO₂I by >10% of the preceding level.

Hypercapnia-hyperoxia protocol. The infants were placed in the crib in their normal sleep position, supine or prone. A Plexiglas hood was placed over their head when they fell asleep. Then a mixture of 10% CO₂-90% O₂ was introduced into the hood and blended with O₂ from a separate source so as to gradually increase the level of CO₂I in the hood to 8% over 10 min by using a protocol closely similar to that of van der Hal et al. (35). The trial was terminated when the infant opened his/her eyes and/or cried.

Spontaneous startles and arousals. Records were reviewed to find well-documented spontaneous sleep startles and/or arousals occurring before or after rebreathing trials. They were spontaneous in that no obvious external stimulus was present. In some cases, there was minimal rebreathing due to natural circumstances such as the infant’s hand against his/her face. Data from 15 infants in whom recordings of periods of undisturbed natural sleep were obtained were utilized.

Monitoring techniques. The studies were performed during the infants’ usual daytime nap after feeding. We recorded electrocardiogram (EKG) and, in most infants, an electromyogram of the right biceps muscle. A small silicone catheter (8 Fr) was taped to the skin immediately below nostrils for CO₂ detection (CO₂ monitor, Ohmeda, Englewood, CO). In most infants, we also recorded nasal airflow semiquantitatively using a second catheter taped to the skin to record pressure at the nares opening. When the infant’s face was covered with a cloth and narial pressure was measured against room pressure by using a differential pressure transducer, respiratory flow was linear over a range of 0-8 l/min. The pressure signal was integrated to provide a relative measure of tidal volume (VT) waveform. Oxygen saturation was measured at the right toe (Pulsoxymeter, Nellcor, Hayward, CA). Respiration was also recorded by using the inductive plethysmography technique with bands placed around the chest and abdomen (Respitrace system, Ambulatory Monitoring, Ardsley, NY). All of the parameters were recorded on a polygraph (Beckman). All infants were constantly monitored for activity by two or more observers, and notes were written directly onto the polygraph chart.

Nineteen of the 41 infants were videotaped (JVC Professional Products, Elmwod Park, N J) during the study (15 while face covered, 3 while face down, 8 while breathing CO₂). The infant was filmed with an infrared camera, and, simultaneously, the polygraph signal was filmed and displayed on a split-screen video monitor (Videonix, Campbell, CA). In these infants, respiratory sounds were recorded by using a small microphone taped directly to the lateral submandibular part of the infant’s neck.

State determination. Infants were studied during sleep as determined by the criteria of Precht for sleep and behavioral state determination. State 1: eyes closed, regular respiration, no movements. State 2: eyes closed, irregular respiration, no gross movements (30). Because increased respiratory drive reduced breath to breath variability in respiratory frequency and amplitude, state 1 was not differentiated from state 2 responses in the analysis of rebreathing and hypercapnic hypoxic trials.

Data analysis. The electromyographic signal and/or EKG baseline shift artifacts were used to more precisely determine exact onset of motor activity. The timing of these signals with infant movements was cross-correlated with the video record by using frame-by-frame replays of events. Because body movements might introduce artifacts in the Respitrace recording, we cross-correlated CO₂, respiratory flow, and neck sounds for determining occurrence of sighs (augmented breaths). During rebreathing trials, a prolonged inspiratory time, biphasic contour, and reduced CO₂I of the inspiratory component of the CO₂ trace were a particularly useful indication of a sigh (7). A cross-correlational “confidence score” was used to assess the strength of the evidence for simultaneous occurrence of a sigh and startle occurring as an isolated event or occurring immediately before other motor activity. A score of 3 was used when all recordings conclusively indicated cooccurrence of sigh and startle; a score of 2, when evidence for this was strong but one or more signals were indeterminate; and a score of 1, when evidence could be open to question because of absence of a second reliable respiratory recording to confirm the Respitrace recording or because of lack of confirmation of the Respitrace from one or more other reliable respiratory recordings. Often, the Respitrace recordings indicated multiple sighs occurring sequentially during generalized motor activity. However, occurrence of the second or third sigh following the initial sigh at onset of motor activity frequently could not be confirmed by the nasal flow or CO₂ recordings. This is probably because vigorous motor activity disturbed bedding near the infant’s face, thereby changing resistance to breathing at the nose and creating air currents that made CO₂ and flow recordings less reliable. For this reason, only the first sigh at onset of motor activity was counted in determining sigh frequencies.

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**Table 1. Subjects, trials, characteristics of protective events, and spontaneous arousal sequences**

<table>
<thead>
<tr>
<th>Trial</th>
<th>No. of Infants</th>
<th>No. of Protective Events or Spontaneous Arousal Sequences</th>
<th>CO₂I at Onset of Protective Event, %</th>
<th>Sequence of Behaviors During Protective Event or Spontaneous Arousal, % Total events</th>
<th>Cross-Correlation Confidence Score, %†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Face down</td>
<td>12</td>
<td>37</td>
<td>3.10 ± 0.22</td>
<td>15 (41%) + 16 (43%) – 6 (16%)</td>
<td>3</td>
</tr>
<tr>
<td>Face covered</td>
<td>25</td>
<td>42</td>
<td>3.80 ± 0.17</td>
<td>0 (0%) + 25 (60%) – 17 (40%)</td>
<td>7</td>
</tr>
<tr>
<td>CO₂-O₂ protocol</td>
<td>8</td>
<td>10</td>
<td>6.84 ± 0.25</td>
<td>30 (56%) + 17 (31%) – 7 (13%)</td>
<td>11</td>
</tr>
<tr>
<td>Spontaneous arousal</td>
<td>15</td>
<td>54</td>
<td></td>
<td>84 (13%) + 13 (3%) – 10 (10%)</td>
<td></td>
</tr>
</tbody>
</table>

Values for % inspired CO₂ (CO₂I) are means ± SE; total no. of subjects was 41, some infants were tested in 2 or more protocols. †Reflects repeat trials or occurrences in subjects. See Data analysis for explanation.
Definitions. We used the terms “augmented breath” and “sigh” interchangeably. The terms were used for breaths with the following characteristics: 1) an amplitude as indicated on Respitrace and VT tracings greater than those of the 10 consecutive preceding breaths; and 2) a biphasic pattern with phase I having an inspiratory time, volume, and flow pattern similar to preceding breaths and phase II consisting of one or more additional bursts of flow (34). The term “full arousal” was used when the infant’s eyes opened and/or he/she began to cry. The term “arousal sequence” was used for the sequence of behaviors immediately preceding full arousal. The term “protective event” was used for behavioral activity resulting in sustained lowering of CO₂I by >10% of the preceding level.

RESULTS

Character of airway-protective events during rebreathing and identification of arousal sequences. All but one infant (see below) successfully lowered CO₂I on one or more occasions, and oxygen saturation remained within the normal range during all trials in all infants. In both face-covered and face-down trials, the airway-protective activity that resulted in lowering CO₂I consisted of highly stereotyped behaviors (Table 1). These behaviors occurred sequentially, the initial event being a sigh (i.e., augmented breath) coupled with a startle (Fig. 1). A sigh-startle was either followed by prompt resumption of sleep or by generalized motor activity that we called “thrashing.” Thrashing then either spontaneously subsided or progressed without interruption to full arousal. Because of its repeated occurrence and consistent pattern, we called the sequence of sigh-startles, thrashing, and full arousal an “arousal sequence.” In 93–97% of instances, there was strong evidence for the simultaneous occurrence of sigh and startle at onset of arousal sequences (confidence score ≥2). Although in 3–7% of cases evidence was not absolutely convincing, in no single instance were components of the arousal sequence obviously missing or out of sequence (Table 1).

Sighs were similar to spontaneous sighs occurring before trials with respect to timing of the two phases and increased amplitude. Startle was characterized by a generalized sudden movement that included spreading of the fingers, a symmetric outward reaching movement of the arms, adduction of legs at the hip, and neck extension (Fig. 2). Startles varied greatly in magnitude, ranging from minimal arm flexion and finger spreading to completely outstretched arms. In face-down infants, the most prominent feature of startle was sudden neck extension resulting in the infant’s head being lifted above the mattress (Fig. 3). Head lifting was usually combined with head rotation, resulting in a coordinated postural change from face down to face to the side. Startle-associated arm and leg movements in prone sleeping infants were similar to those of supine sleeping infants, but due to the positional restriction of movement arm flexion consisted of brief downward...
pressure on the mattress, which appeared to facilitate head lifting. In contrast to startles, thrashing movements were slower repeated movements that were largely asymmetrical (Fig. 4). They were characterized by back-and-forth head turning, truncal torsion and arching, and flailing leg and arm movements, which often were interspersed with additional sighs and sigh-startles. Although thrashing seemed largely to be

Fig. 2. Single frame of a video recording showing infant during spontaneous startle. Arrows indicate direction of movement as indicated by prior and subsequent frames. Arms are moving outward, head backward, and left leg forward (right leg covered). Also, note characteristic wide-spread ing fingers.

Fig. 3. Polygraphic record of an airway-protective event in an infant sleeping in face-down position. Protective event begins with a sigh coupled with a startle (onset indicated by movement artifact in EKG trace) with associated head lifting and turning. Sigh is indicated by Respitrace and long inspiratory time in CO₂ trace (arrow). During startle, head position changes from head straight down to head angled to the side, causing improved access to fresh air (i.e., CO₂ is reduced). Respitrace tracing suggests that a 2nd sigh follows the 1st (see METHODS). Lack of further movement following startle indicates minimal sleep disturbance.
composed of random movements, most infants brought their hands up and brushed their faces during thrashing. Altogether, thrashing had a distinctive, stereotypic character.

Character of airway-protective events during CO₂-O₂ breathing. The arousal sequence culminating in full arousal that terminated these trials appeared to be identical in all respects to that observed during rebreathing trials (Fig. 5, Table 1).

Effectiveness of airway-protective behaviors. In 41% of airway-protective events in face-down infants, the behavior that effectively lowered CO₂ was the head repositioning component of startle (Table 1). In such instances, startle was followed by immediate resumption of sleep. When the initial startle-associated head lifting was not combined with effective head turning (59% of cases), the repeated sigh-startles and/or the side-to-side head movements of thrashing usually uncovered the infant’s nose and mouth.

In face-covered infants, access to fresh air was accomplished in two ways: 1) head and arm movement that jostled the face cloths, bringing currents of fresher air to the infant without permanently displacing the cloths; and 2) face-brushing movements that partially or completely removed the cloths. The sigh-startle at onset of arousal sequences was ineffective in reducing CO₂, and all infants proceeded to thrashing (60%) or then on to full arousal (40%) before CO₂ was substantially reduced (Table 1).

There was a wide range in degree of effectiveness in airway defense. The majority of face-down sleeping infants fully cleared their nose and mouth, whereas most face-covered infants partially lowered CO₂ but did not fully clear their airway spontaneously so that the face cloths had to be removed when the infants gave evidence of distress by continued thrashing or crying. In addition, although episodes of sigh-startle followed by thrashing ultimately were successful in lowering CO₂ in most face-covered infants, 40% of all thrashing episodes occurring in these infants spontaneously terminated without having any significant effect on CO₂. In fact, one face-covered infant failed to lower CO₂ despite repeated sigh-startles and a total of six sigh-startle-thrashing episodes. In this infant, thrashing activity was briefer and appeared to be less vigorous than that of other infants. We terminated this infant’s rebreathing trial because of its long duration (>30 min) without reduction in CO₂ (CO₂ was 4.8% at trial termination). It is also noteworthy that in eight instances, in four face-down infants, the infant’s airway was further

![Fig. 4. Two frames of a video recording illustrating characteristic movements during a spontaneous episode of thrashing. Arrows indicate direction of leg, arm, and trunk movements, as indicated by prior and subsequent frames during this brief episode. Legs flex, then extend repeatedly (frames A and B). Arm movements are asymmetric (frame A). Note right arm brushing across face (frame B). Note arching and twisting of trunk (arrow labeled “T”, frame B).](image-url)
compromised when a startle resulted in the infant’s head turning further down into the bedding, causing CO₂I to increase. In these instances, the CO₂I remained at increased levels for a period of time (several seconds to several minutes) until a repeat episode of sigh-startle, or sigh-startle-thrashing, uncovered the airway.

Occurrence of incomplete arousal sequences. Isolated sighs, sigh-startles, and sigh-startles followed by thrashing that were ineffective in reducing CO₂I were common during rebreathing trials. Such incomplete sequences also occurred before full arousal in CO₂-O₂ breathing trials. The occurrence frequency and the number of behaviors included in these incomplete sequences increased progressively as CO₂I increased during trials (Fig. 6). For example, during CO₂-O₂ breathing trials, sigh frequency progressively increased from 0.31 ± 0.13 sighs/min during the first quarter period of the trial to 2.97 ± 0.42 sighs/min during the last quarter. As CO₂I increased, recurring incomplete arousal sequences were characterized by abrupt onset and rapid spontaneous resolution. There were no indications at onset of an incomplete sequence to indicate whether it would progress to full arousal or succeed in effectively lowering CO₂I. Sleep rapidly resumed after incomplete sequences, whereas sleep resumption was usually delayed by a minute or more after full arousal (Figs. 1, 3, and 7).

Spontaneous startles and arousal sequences. During periods of sleep unassociated with rebreathing trials, we observed 54 spontaneous startles (Table 1). Although spontaneous sighs unassociated with startles were frequently observed, all startles occurred simultaneously with a sigh (Fig. 7). The confidence scores for cooccurrence of sigh and startle were somewhat lower than during rebreathing trials; however, this was primarily because the inspired CO₂ waveform and nasal flow trace were more often unavailable for confirming the Respitrace recording. Incomplete arousal sequences of varying length, some of which progressed to full arousal, were observed (Table 1). These arousal sequences were not preceded by identifiable stimuli and were episodic and self-limited occurrences. Similar to rebreathing trials, isolated sigh-startles were much more common than the more complete sequences. These sequences had the same characteristics as observed during rebreathing and CO₂-O₂ breathing trials, and as in such trials, in no case was it obvious that behavioral components were missing or out of sequence.

DISCUSSION
We have found that sleeping infants exposed to increased ambient CO₂ concentration, due to rebreathing expired air, protect their external airway by utilizing a highly stereotyped sequence of maneuvers. When the infant was face down, the effective protective movement was frequently the head lift and turn component of a sleep startle. When the infant’s head was in other positions and covered with a cloth, the startle was generally ineffective, and not until thrashing movements occurred was the airway effectively protected and access to fresh air obtained. Such highly stereotyped motor behaviors in infants are generally considered to be innate reflexes. Normal-appearing startles, sleeping, waking, and crying behavior can occur in infants congenitally lacking a cerebral cortex, indicating that these basic motor responses are not learned...
behavior (25). Our observation that seemingly identical behaviors, such as head lifting and turning, occur when ambient $\text{CO}_2$ is increased in the absence of bedding covering the nose and mouth suggests that these responses are stereotyped reflexes that, at this stage of the infant’s development, are not altered or modified to more effectively respond to different situations resulting in hypercapnia. The frequent failure of thrashing or even full arousal to completely eliminate rebreathing and remove bedding from the face of face-covered infants indicates that these innate reflex strategies are often only partially effective. Furthermore, we observed in face-down infants that startles occasionally resulted in head positions that actually increased rather than reduced $\text{CO}_2$. Hence, an inflexible reflex response can be disadvantageous. Were a sleeping infant’s head to overlie a narrow depression in the bed surface, it is conceivable that side-to-side head movements during thrashing might cause head entrapment, a circumstance termed wedging and a well-known cause of asphyxial death in infants (19).

We have described a sequence of behaviors that precede full arousal when the sleeping infant is exposed to increased environmental $\text{CO}_2$. The individual behaviors of this sequence have been previously described. The literature on infant sleep contains numerous references to sighs (30, 34), sleep startles (30, 37), and thrashing, also variously termed “writhing” “gross movements,” or “squirming” (1, 30, 37). Furthermore, some reports have noted that sighs and startles can at times accompany sleep arousal in infants (29, 30); however, no published report, to our knowledge, has shown the sequence of these behaviors to be as consistently and as temporally closely linked as our findings indicate. Although we did not systematically evaluate possible differences occurring in different sleep states, the few spontaneous arousal sequences that appeared to occur in state 2 did not obviously differ from those in state 1. We do not doubt, however, that a more systematic study of sleep state might have found subtle state-related differences in these responses.

Although the individual behaviors rarely occurred out of sequence, incomplete arousal sequences were common either as spontaneous occurrences or during hypercapnic exposure. Furthermore, the frequency with which incomplete arousal sequences occurred was inversely proportional to the number of responses in the sequence. That is to say, isolated sighs were more common than sighs plus startles, and sighs plus startles followed by thrashing were still less common. The entire sequence ending in full arousal was least common of all. Neural mechanisms that might produce such a sequence of behaviors are suggested by the work of Sherrington (33) and others, who noted that certain complex behaviors are composed of “chained reflexes” in which one reflex provides a stimulus for the next. Studies of periodic activity in sleeping cats suggest other potentially relevant neural mechanisms. Baker and McGinty (3) and McGinty et al. (23) studied a periodically occurring sequence of three behaviors in sleeping kittens: startle-like movement, then a sigh, then apnea. Similar to our observations in infants, partial sequences in the kittens occurred more commonly than the complete sequence. The authors suggested that the terminally occurring behaviors (i.e., sigh and apnea) might be suppressed by greater neural inhibition than the initial behavior (i.e., startle-like movements). Such differential inhibition would favor early termination of the sequence. Recurrent spontaneous behaviors require neural triggering mechanisms. McGinty et al. proposed that an “underlying excitatory process which occurs periodically” initiates the startle-like activity in kittens, using a concept similar to one previously invoked by Wolff (37) to explain spontaneous occurrence of startles in sleeping human infants. More recently, Orem and Trotter (26) observed that an augmented breath (sigh) usually occurs just before, or

![Fig. 6. Increase in $\text{CO}_2$ during face-covered rebreathing trials (top) and frequency of behaviors (bottom) (means ± SE). Data are from 12 randomly selected trials in 12 infants studied with complete assembly of monitoring techniques. Time from onset to termination of trial (i.e., fall in $\text{CO}_2$ caused by infant’s behavior) is divided into quarters, and data represent mean frequencies during each respective quarter. Sigh data represent both spontaneous sighs and sighs coupled with startle at onset of arousal sequences. Other behaviors are plotted individually, although they always occurred in conjunction with other behaviors during arousal sequences. $\text{CO}_2$ values were obtained just after onset of each quarter and just before termination of trial.](http://jap.physiology.org/DownloadedFrom/10.220.33.1/30.3.30.2017)
coincides with, awakening and other sleep state transitions in adult cats. They also, endorsed the concept of an underlying periodic excitatory process and suggested that this process is closely linked to neural mechanisms regulating both sighs and arousals. Noteworthy, in this context, is the similar association of sighs and arousals reported in dogs (28). By applying these concepts from animal studies to our infants, we can explain the increasing sigh frequency and progressive lengthening of arousal sequences during rebreathing if we assume that the CO₂ stimulus increases the frequency of the periodic underlying excitatory process and also decreases the differential inhibition of the terminal elements of the arousal sequence. Such a model would also explain the surprising abruptness of CO₂-stimulated arousals in infants, which occur without an immediate behavioral warning, as we here, and others previously, have noted (22). The concept that sighs reflect activity of arousal processes is not incompatible with the well-known importance of pulmonary vagal, chemoreceptor, and other afferent sources as stimuli for sighs, since the occurrence of sighs is believed to result from the summation of afferent stimuli from different sources (6, 12). An arousal-related stimulus could be additive with respiratory stimuli and could even be the dominant stimulus for sighs during sleep. Our observation that sighs occur as isolated events in sleeping infants and also appear in conjunction with a startle at the onset of most, if not all, episodes of increased behavioral activity appears to support Orem and Trotter’s (26) suggestion that sighs may be relatively sensitive indicators of increased activity in central arousal mechanisms. Additionally, our observations based on the Respitrace recordings suggest that multiple sighs can occur in rapid succession during arousal-related motor activity, whereas such repeated sighing is rare in the absence of arousal-related activity. This is similar to a previous observation in sleeping adults and appears to be additional evidence that activity in central arousal mechanisms can be a stimulus for sighing (27).

It is noteworthy that behavioral response to increasing CO₂ did not occur as gradual and uninterrupted augmentation of activity but rather as intermittent self-limited bursts of activity of increasing complexity. The several behaviors of the arousal sequence have important other functional roles in addition to airway protection. Periodic sighs have long been known to be crucial for preserving lung compliance (24). Moreover, the human fetus from 20 wk of gestation onward periodically startles and changes limb position in utero (31). Such postural movements are critical for normal limb and joint development (10). Similarly, periodic changes in head position are essential for symmetric head growth postnatally (14). Therefore, in the fetus and sleeping infant, there appears to be an underlying neural mechanism producing a periodic clustering of behaviors that are essential for respiratory homeostasis and normal growth. When the sleeping infant encounters rising environmental CO₂, accentuation of this normal cycle of activity is the means whereby he/she defends his/her external airway and, when
successful in this, summons assistance by crying. Considering the evidence that repeated sleep disruption retards infant growth and development (9), it is biologically appropriate that arousal occurs as a stepwise escalation of responses. Therefore, the infant’s initial responses to increased environmental CO₂ (sigh, startle, thrashing) disrupt his/her sleep less than the ultimate defense strategy, full arousal by crying.

We did not detect maturational differences in the responses of infants. This may be due to the concentration of subjects in a narrow age range. It is known that the frequency of sighs during sleep falls during the first weeks of life and that infant sleep startles disappear or are replaced by greatly diminished movements during the first year (29, 34, 38). However, some aspects of the arousal pathway appear to persist into adult life, given that sighs precede spontaneous arousal in the sleeping adult much more often than can be explained by chance association (20, 27). The relationship of spontaneous sleep startles in infants to the classic elicited startle response in awake adult humans and other species is unclear, although the observation that infant startles during sleep as well as in the awake state can be elicited by various exteroceptive stimuli suggests a close connection (21, 29).

Indirect evidence from several sources indicates that lethal asphyxiation is the immediate cause of death in a substantial number of infants diagnosed as SIDS who die in the face-down position (5, 15, 16). If asphyxia is presumed to be the cause of death in such cases, the present findings indicate that we must also assume that the airway-protective components of the infant’s arousal sequence of responses failed. Several recent studies suggest possible mechanisms that might result in failure of SIDS infants to protect their external airway. Anatomic studies of the brains of SIDS infants have revealed evidence of several kinds of neuronal abnormality in the brain stem (17). It has been suggested that certain of these abnormalities could interfere with CO₂ sensory mechanisms (18). Additionally, brain stem abnormalities might decrease occurrence or mechanical effectiveness of the brain stem-mediated reflexes, sigh, and startle, and, in fact, infants who subsequently died of SIDS have been observed to defend their oral and nasal airway less effectively than normal infants (2). Furthermore, two other independent polygraphic studies of infants who later succumbed to SIDS have shown that the frequency of normal periodic motor activity during sleep, or of artifacts presumably caused by such activity, is markedly reduced in SIDS infants compared with normal infants (13, 32). To the extent that our present studies indicate that such periodic motor activity reflects a primary arousal and airway defense mechanism, the finding of reduced motor activity in sleeping SIDS infants suggests that their airway defense mechanism may also have been impaired.

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