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Congestive Heart Failure and Central Sleep Apnea

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I. Clinical Considerations

Historical perspective

An abnormal respiratory pattern has long been recognized as an ominous sign of congestive heart failure. The observations of three physicians who have lent their names to the pattern remain informative:

> "His breathing was very particular: he would cease breathing for twenty or thirty seconds, and then begin to breathe softly, which increased until he breathed extremely strong, or rather with violent strength, which gradually died away till we could not observe that he breathed at all. He could not lie down without running the risk of being suffocated, therefore he was obliged to sit up in his chair."
>
> John Hunter, 1781 (1)
>
> "The patient suddenly developed palpitations and displayed signs of severe congestive heart failure. The only particularity in the last period of his illness, which lasted eight or nine days, was in the state of respiration. For several days his breathing was irregular; it would entirely cease for a quarter of a minute, then it would become perceptible, though very low, then by degrees it became heaving and quick, and then it would gradually cease again. This revolution in the state of his breathing occupied about a minute, during which there were about thirty acts of respiration."

John Cheyne, 1818

"This symptom [periodic breathing], as occurring in its highest degree, I have only seen during a few weeks previous to the death of the patient."

William Stokes, 1854

The initial observations by Hunter, Cheyne and Stokes were made in patients close to death. They were the first to note the characteristic waxing and waning respiratory pattern of "Cheyne-Stokes respiration" (CSR), a common pattern of central sleep apnea (CSA) in patients with congestive heart failure (CHF). CSR is characterized by complete cessation of respiratory effort and airflow (apnea phase) alternating with profound hyperventilation (hyperventilation phase). Such patterns occur during wakefulness but are typically more prominent during sleep. (Figure 1) The apnea phase of Cheyne-Stokes respiration (CSR) causes arterial hypoxemia, and the hyperventilation phase produces surges in blood pressure, arousal from sleep and dyspnea. (2–5) (Figure 2). Typically CSR has a periodicity of 45–90 seconds, and occurs during non rapid eye movement (NREM) sleep stages 1 and 2. CSR severity is typically measured by quantifying the percent of total sleep time in CSR, and by the number of apneas and central hypopneas per hour of sleep (apnea-hypopnea index, AHI). (6) Despite advances in the treatment of congestive heart failure (e.g. beta-blockade, spironolactone), untreated CSR remains highly prevalent during sleep and retains its association with increased morbidity and mortality independent of heart failure severity (7–10). (Boxes 1–4)

Epidemiology in stable CHF

One of the first rigorous studies to use polysomnography by Javaheri and colleagues found a high prevalence (40%) of CSR in patients with systolic heart failure. (11) This prevalence has been a relatively consistent finding depending on the population studied (with increased prevalence with worsening heart failure) and the threshold and technology used to diagnosis sleep disordered breathing. (12–15) Although early epidemiological studies pre-dated the widespread use of advanced heart failure therapies, even the most recent studies continue to show a consistently high prevalence of CSR. (14, 16) CSR is also not limited to systolic heart failure; CSR is common in patients with symptomatic heart failure with preserved ejection fraction (17) (diastolic dysfunction), and is also common in patients with asymptomatic systolic dysfunction (18). Additional risk factors for CSR include male gender, older age, the presence of atrial fibrillation, nocturnal ventricular arrhythmias, low arterial PCO_2 ($PaCO_2$), dyspnea with minimal exertion (NYHA class ≥II), nocturnal dyspnea, very low ejection fraction (EF<20%), left atrial enlargement, and high NT-proBNP (5, 10, 12, 14, 15, 19, 20).

CHF in the ICU

Congestive heart failure is one of the most common causes of admission to hospitals in the United States, especially in those over 65 years of age, with over 1 million hospital admissions per year. (21) Approximately 10% of these patients will require ICU admission. (22) Despite the high number of hospital/ICU admissions, there are few data regarding the prevalence of CSR among hospitalized patients. Hoffman and colleagues noted CSR in 44%

of CHF patients after weaning from mechanical ventilation for cardiogenic pulmonary edema (23). More recently Padeletti and colleagues found moderate-severe CSR (AHI>15) in 75% of patients admitted for an acute exacerbation of systolic congestive heart failure, with an average of 51% of total sleep time spent exhibiting CSR. Thus, CSR appears to be more prevalent (~75%) in decompensated CHF in inpatients than in stable CHF outpatients (~40%).

Unfortunately, data on CSR prevalence in the ICU and effects on outcomes are lacking. Given the pathophysiological changes that occur in severe heart failure (that requires ICU admission for management) we might expect a very high rate of CSR. However, the most acutely ill patients may be on mechanical ventilation and sedated, often with narcotics. Mechanical ventilation will also provide ventilatory and cardiac support for the patient in heart failure, as both cardiac preload and afterload will be reduced while on positive end-expiratory pressure (PEEP). (24, 25) Thus, CSR is likely to be most relevant during the process of ventilator weaning (23) when such support is removed. It will be during the process of moving toward liberation from mechanical ventilation that sedatives will be decreased, PEEP and supplemental oxygen levels will be lowered, and patients will be placed on spontaneous modes (i.e. patient triggered) of ventilation.

II. Pathophysiological Considerations

Control of breathing

The physiological control of breathing is a negative feedback system that acts to regulate acid-base status and the partial pressure of arterial carbon dioxide ($PaCO_2$), and maintain adequate oxygenation. The primary components of the control of breathing system are chemoreceptor inputs located in the medulla which respond to changes in acid-base status and the peripheral chemoreceptors in the carotid bodies that are sensitive to both changes in PaO_2 and $PaCO_2$. Central and peripheral chemoreceptor inputs are integrated in the medulla and act to modulate breath amplitude (and timing to a lesser extent), ultimately resulting in a level of ventilation conducive to survival. Importantly, there are other sensors in the lungs and circulation whose inputs modify the behavior of the respiratory control system, including pulmonary stretch receptors, irritant receptors, and the “J” (juxta-capillary) receptors which may become important in disease states and which are discussed below. (26–30)

The concept of loop gain

The stability of the respiratory feedback loop has been quantified using the engineering criterion, loop gain. Briefly, loop gain is defined as the magnitude of the ventilatory response of the respiratory control system to a sinusoidal respiratory disturbance (at the frequency of CSR). Feedback loops with a value of loop gain which exceeds 1.0 (response is greater than the disturbance) are intrinsically *unstable* and periodic oscillations in breathing will inevitably occur (Figure 3). When loop gain is <1 (response<disturbance), transient oscillations are attenuated and thereby temporary. Detailed descriptions of loop gain have been given previously (31–33). Consider a period of hyperventilation (disturbance) which causes a reduction in $PaCO_2$. This reduction in PaCO2 is sensed by chemoreceptors after a

circulatory delay, which will in turn elicit a later reduction in ventilatory drive (response). In an unstable system, the drop in ventilatory drive will cause a greater degree of hypoventilation than the original hyperventilatory disturbance. Oscillations will be amplified and self-sustained with no specific initiating factor required. The concept of loop gain has been successfully applied to predict the occurrence of CSR (Figure 4). (34) and the resistance to its suppression with treatment (35, 36).

Detailed analyses of the control system consistently reveal four primary factors that contribute to loop gain (31, 34, 35, 37–39), according to the relationship:

$$\text{Loop gain} = G \frac{PaCO_2}{\text{Lung Volume}} T \quad \text{(Equation 1)}$$

where G is the *chemosensitivity*, defined as the change in ventilation in response to a change in $PaCO_2$; $PaCO_2$ is the arterial partial pressure of CO_2 (with the assumption here that inspired $PCO_2 = 0$); Lung volume is the end-expiratory lung volume (e.g. functional residual capacity); and T is a timing factor which incorporates the lung-chemoreceptor circulatory delay. A similar equation can be written for the ventilatory feedback control of arterial PO_2.

How CHF predisposes to CSR

Equation 1 provides the framework for identifying the factors that predispose an individual towards CSR. Indeed, there is evidence that each of these factors plays a role in the development or effective treatment of CSR.

Circulatory delay

Classically, an increased lung-to-chemoreceptor circulatory delay (T) has been implicated as the cause of CSR. Patients with heart failure can have elevated circulatory delay as a result of decreased cardiac output. CHF patients with a lower left ventricular ejection fraction, lower cardiac output, and elongated circulatory delays are at elevated risk of CSR (11, 19, 40, 41). Further evidence includes the observation that the lung-to-ear circulation delay (approximating the lung-to-chemoreceptor delay) is equal to the delay between the nadir CO_2 level and apnea during CSR (42). Raising cardiac output with exercise, pharmacological intervention, or cardiac resynchronization can also reduce the ventilatory oscillations in CHF (43–45). However, such interventions may also effect other factors (Eq. 1) contributing to stabilization. Moreover, many CHF patients with low LVEF and increased circulatory delays do not have CSR (34). Thus, the other factors identified in Eq. 1 are likely important as well.

Chemosensitivity

Increased chemosensitivity (G) is the most powerful determinant of CSR. (34, 46–48) Specifically, CHF-CSR severity is strongly associated with the dynamic ventilatory response to CO_2 (48), suggesting an essential role for elevated peripheral chemoreceptor (carotid bodies) activity in CSR. Increased chemosensitivity is thought to be due to increased left atrial pressure (Figure 5) (49). Additional evidence includes:

i. Raised PCWP is common in patients with CSR and is correlated with CSR severity (41, 45, 49).

ii. CSR is associated with elevated NT-proBNP (10, 50), a biomarker of left-ventricular stretch and elevated PCWP (51–54).

iii. Left atrial size is associated with CSR and chemosensitivity (55).

iv. PCWP is associated with hypocapnia (56), a marker of increased chemosensitivity (57) and predictor of CSR (12).

v. Raising left atrial pressure acutely increases chemosensitivity in dogs (58).

vi. CSR is associated with cardiogenic pulmonary edema in the form of reduced pulmonary diffusing capacity (59), presumably via increased pulmonary capillary pressure.

vii. CSR is linked with fluid status including the degree of overnight rostral fluid shift (60).

viii. The reduction in PCWP with vasodilator (nitroprusside) is linearly associated with the reduction in CSR (45).

Raised left atrial pressure is believed to increase chemosensitivity directly via stretch receptors in the left atrium or pulmonary vein (30, 61, 62) and indirectly through pulmonary edema via juxtapulmonary capillary receptors (J receptors, pulmonary C-fibers). It is important to note, however, that such vagal afferents may not entirely explain hypersensitive chemoreflexes in CHF-CSR given that CSR has been seen to persist despite lung transplantation (and hence vagal denervation) (63). Other factors that may raise chemosensitivity include reduced cardiac output via reduced carotid arterial blood flow (64) and hypoxemia (via pulmonary congestion). Hypoxemia raises chemosensitivity both acutely and over time (59, 65).

Lung volume

Reduced end-expiratory lung volume (EELV) is another factor that can raise loop gain, destabilize breathing and promote CSR (34, 35, 66). EELV is reduced in congestive heart failure as a result of lung edema and/or pleural effusions, cardiomegaly. Lowered lung volume acts to increase loop gain by lowering the lung gas volume for buffering ventilation-induced fluctuations in PCO_2 and PO_2 (35, 66). Lowered EELV, however, does not appear to differentiate between CHF patients and without CSR at baseline (34). Nonetheless, manipulating lung volume can have an important effect on improving CSR (35, 66). Szollosi et al (67) found that the lateral sleeping position attenuated the CSR severity (AHI) by ~60% compared with the supine position. Importantly, the lateral position attenuates apnea-associated oxygen desaturation without affecting event duration. The reduced desaturation speed in lateral versus supine positions is consistent with the known elevation in lung volume in the lateral position (68), and provides indirect evidence that lung volume might be of major importance in the pathogenesis of CSR. Whether the lateral position affects other factors including cardiac output or chemosensitivity in CHF patients is currently unknown.

Behavioral state effects

Behavioral state can also have a major effect on CSR severity. Although CSR can be observed during wakefulness, it is greatly exacerbated by the transition to sleep (69), which may appear counter-intuitive given the reduced chemosensitivity during sleep. (70–72) However, accompanying the transition from wake to sleep is an abrupt reduction in ventilatory drive (for any given $PaCO_2$); likewise accompanying the transition from sleep to wake (arousal) is an abrupt increase in ventilatory drive. Thus, any oscillation in ventilatory drive that is accompanied by transitions in state (73) will be enhanced and hence ventilation is further destabilized (74). CSR is most common in light non-REM sleep (stage 1) and is most powerfully suppressed in deep non-REM sleep (slow-wave) (67, 75). Deeper sleep presumably promotes stable breathing via increased arousal threshold (fewer arousals/awakenings) and reduced chemosensitivity compared to lighter sleep (70–72). The observation that a sedative (zolpidem) can greatly improve CSR in patients without CHF (76) further highlights the importance of behavioral state on ventilatory instability. CSR is also reduced but not always absent in REM sleep (35, 67, 75); while chemosensitivity is reduced in REM (77), the arousal threshold is similar in REM to stage 1 (78) and profound (non-CO_2 related) disturbances to ventilatory control are characteristic of this state. A final consideration is that sleep may promote CSR via the lowered end-expiratory lung volume that occurs with sleep onset (79).

III. Treatment of CSR

In patients with CHF, untreated but not treated CSR is associated with increased mortality (8, 80, 81) leading to the view that improving severe ventilatory oscillations of CSR may promote survival. Ongoing clinical trials are assessing whether CSR treatment improves mortality. In the meantime, clinicians treat symptomatic CSR to achieve improvements in quality of life, as well as nocturnal hypoxemia, sympathoexcitation, ventricular irritability, and for small improvements in cardiac function (82–89). Although no such data exist for CSR in the ICU, we review the treatment strategies below.

Treatment of heart failure

Based on the above, therapies for the treatment of CSR first focuses on improving CHF. It is expected that treatments that improve cardiac output, decrease left atrial pressure, and improve lung volume should improve CSR. For example, intensive medical therapy that included diuretics and afterload reduction can successfully lower PCWP and improve CSR (49) (Figure 5). Similarly, beta-blockers (90–92), cardiac resynchronization therapy (43, 93), left-ventricular assist devices (94) and transplantation (95–97) have been associated with improvements in CSR over time. Rapid changes in cardiac function, as might happen in the ICU, can quickly affect CSR severity. Kara and colleagues have shown that there are acute improvements/worsening in the CSR with acute administration/withdrawal of cardiac resynchronization. (98) Although CHF treatment can be effective at resolving CSR, in many patients CSR can persist despite the most aggressive therapies including cardiac resynchronization therapy (99), left-ventricular assist devices (100), and even heart transplantation (95). Thus, additional treatments are needed for CSR.

Positive airway pressure

Positive airway pressure, whether applied as PEEP from a mechanical ventilator or in noninvasive form as CPAP, has the potential to improve CSR acutely via multiple mechanisms:

- **i.** Acutely increasing lung volume, which increases the gas volume for buffering ventilation-induced changes in PCO_2 and PO_2 (35, 66, 101).
- **ii.** Stabilization of the upper airway, which may play a covert role in CSR in some patients (102).
- **iii.** Improved hypoxemia, which in turn reduces chemosensitivity both acutely and further over time (103, 104). CPAP may improve oxygenation by improving microatelectasis in cardiogenic pulmonary edema (105). CPAP also improves CSR-related desaturation independent of CSR resolution (35) presumably via increased lung volume.
- **iv.** Improved cardiac function by lowering cardiac preload and afterload. Such effects could theoretically raise cardiac output, decrease circulatory time, and lower PCWP (and chemosensitivity) (106). However, despite improvements in afterload, cardiac output and circulatory time do not typically change with CPAP. (25, 82). Long-term CPAP can improve chemosensitivity over time (82, 88, 103).

While variability in the mechanism of action may help to explain the variable effect size of CPAP in CSR (80, 83); it is those with the most unstable breathing pattern (the highest loop gain) that tend to respond insufficiently to CPAP (35). The majority of CPAP-related suppression of CSR is immediate (35, 87), consistent with major effects of CPAP acting via increased lung volume (35, 66, 101) and relief of hypoxemia. Smaller additional suppression of CSR can be observed over time (103), are presumably via improvements in cardiac function. Such improvements in cardiac function are seen exclusively in those in whom CPAP improves CSR, and not in those in whom CPAP fails to resolve CSR nor in those with CHF but without CSR (84, 107). Given that CPAP is only associated with beneficial outcomes when CSR is suppressed, the early use of more aggressive therapy for CSR may be warranted.

Given the variable CSR response to CPAP, there has been increasing interested in bi-level PAP and more advanced ventilation algorithms, such as adaptive-servo ventilation (ASV). Bi-level PAP offers the advantages of CPAP but when used in a spontaneous/timed mode can provide ventilation during periods of apnea. Importantly, bi-level PAP without any back up rate during periods of apnea may de-stabilize respiration further by augmenting hyperventilation (effectively raising chemosensitivity “G” in Equation 1), and can worsen central apneas during sleep (108). When applied to patients with CSR, bi-level PAP (with a backup rate) can show small further improvements in the CSR severity over CPAP. (109) ASV also provides PEEP, however, the amount of inspiratory pressure varies dynamically in order to prevent hypopneas and maintain constant minute ventilation. Inspiratory pressure increases as the patient’s inspiratory effort falls, but decreases as the patient augments their inspiratory effort. Preliminary data have been promising (81, 99, 110–118) and long term outcome data are pending (NCT01128816 and NCT00733343).

Oxygen

Supplemental inspired oxygen therapy maintains arterial oxygenation during CSR but can also effectively resolve CSR in many patients (116, 119–121). Relief of hypoxemia is expected to reduce chemosensitivity ("G" in Equation 1) and thereby reduce loop gain (104). However, the effect of supplemental oxygen on CSR is heterogeneous (unlike the uniform resolution of CSR when oxygen is used for altitude-induced central sleep apnea), demonstrating that hypoxemia alone is not sufficient to explain CSR.

Medications

Ventilatory stimulants have also been employed to improve CSR in CHF patients, including acetazolamide (69, 86) and theophylline (122). Stimulants act to lower $PaCO_2$ (see Equation 1) which lowers plant gain and acts to stabilize breathing (123). The administration of supplemental CO_2 has a similar effect on plant gain (36), and can powerfully suppress CSR (42, 124). As yet, a long-term therapeutic benefit of stimulants for CHF-CSR has not yet been proven. Alternatively, the use of sedatives/hypnotics can improve CSR in patients without CHF (76); the efficacy of this approach in HF patients is unknown. A mild dose of an opiate analgesic (e.g. dihydrocodeine), as routinely administered in the ICU, can lower chemosensitivity and improve CSR and dyspnea during wakefulness (125, 126); however, improvements in CSR during sleep and long term benefits have not been established. Judicious administration of medications on a case-by-case basis may be warranted to treat symptomatic CSR and associated sequelae in those who do not tolerate mask-pressure based therapies.

Lung volume manipulation

One of the simplest, yet under-recognized means to improve CSR is the manipulation of body position. Positional therapy via lateral positioning (67, 75, 127) and bed elevation (128) have potent effects on CSR severity. Given the low likelihood of "side-effects", manipulating body position to treat CSR may yield improved outcomes (Figure 6).

Novel and future therapies

Several new therapies are emerging for the treatment of CSR. Phrenic nerve stimulation, applied during the hypopnea phase of CSR, can resolve central events (129, 130). Dynamic CO_2 therapy, applied during the hyperventilation phase of CSR to prevent hypocapnia, can resolve CSR during wakefulness without considerably raising mean ventilation (131, 132). Finally, denervation of the carotid-body chemoreceptors has been shown in animal studies to improve survival in CHF, and a case patient with CHF improved sleep disordered breathing, exercise capacity and quality of life (133, 134).

IV. ICU Management

General Considerations

Although data are not available, CSR is most likely to occur during the period of ventilator weaning. When sufficient clinical progress provides for reduced sedation, and a switch to a spontaneous mode of breathing, the underlying respiratory pattern will be revealed.

Additionally, positive end expiratory pressure (PEEP) is frequently decreased as patients move toward liberation from mechanical ventilation. As PEEP is decreased, preload and afterload will both increase which may tend to exacerbate CHF and CSR.

Recognition

The first step in ICU management of CSR is recognition. Although apneas may be noted, especially by ventilator alarms, the initial management may be focused on 1) changing alarm settings to decrease alerts, or 2) changing ventilator modes from a spontaneous mode to an assist/control mode of ventilation. (An assist/control mode will assist all spontaneous respiratory efforts, but in the absence of patient effort and apnea the ventilator will control minute ventilation by delivering a breath from the ventilator.) Alternatively, depending on the ventilator and alarm settings, some ventilators will primarily alarm for a low minute ventilation (rather than apnea) when in a spontaneous mode of ventilation. The response may be to increase the amount of pressure support provided. As explained above, this will only increase hyperventilation and further increase apnea duration. (135) Only with proper recognition can appropriate steps be taken to treat underlying heart failure, and manage the patient correctly. Respiratory therapists as well as physicians need to be familiar with the recognition of CSR.

Differential diagnosis

For the patient not on mechanical ventilation, the differential for apnea includes obstructive sleep apnea (OSA). Although endotracheal intubation will stent the upper airway open, patients on NIPPV may still have upper airway obstruction if the airway pressure (expiratory positive airway pressure, EPAP) is inadequate to hold open the upper airway. OSA is extremely common, and is likely as prevalent in patients with CHF as CSR. It too, may even more likely in the acutely decompensated patient as a result of excess edema fluid and narrowing of the pharyngeal airway. (136) Bedside evaluation of the sleeping patient should focus on signs of flow limitation, such as snoring, as well as evidence of ongoing respiratory effort during the apnea, such as paradoxical movement of the thorax and abdomen. CHF patients may have both obstructive and central sleep apnea, such that both upper airway and ventilator control require interventions.

Another important consideration is central sleep apnea due to opioids, which are commonly used both for sedation while on mechanical ventilation, and for treatment of dyspnea in CHF. (137) Central sleep apnea due to narcotics is generally believed to exhibit an ataxic, irregular pattern with reduced respiratory rate and occasional missed breaths (138). However, many patients with narcotic-induced apneas exhibit a quasi-periodic or crescendo-decrescendo pattern similar to CSR (139). (FIGURE 6) The presence of CSR in the absence of hypocapnia may suggest opioid involvement.

Stroke (cerebral vascular accident, CVA) is another consideration. In fact the patient described by Dr. John Cheyne had both CHF and stroke (140). CSR is seen in ~20–50% of patients recovering from recent stroke (141–144). CSR is more common in patients with severe stroke, in those with concurrent CHF (low EF), and in those with longer hospital admissions (142–144). The mechanisms of stroke-related CSR are not well studied. Studies

over half a century ago illustrated that stroke, even in the absence of CHF, can cause an increase in chemosensitivity and CSR (145, 146). Likewise, more recent evidence suggests that CSR in stroke is caused by an increase in chemosensitivity (as indicated by observations of lower carbon dioxide) in stroke patients with CSR versus those without CSR (142). The role of high chemosensitivity (and high loop gain) is further confirmed by the case observation that medical agents which stabilize breathing can ameliorate CSR (147). Whether treating CSR has a beneficial effect on stroke outcomes remains unclear, but available observation data illustrate that stroke-related CSR and associated sleepiness can be effectively managed with ASV (148). Thus, the new appearance of central sleep apnea in a patient with improving CHF should prompt a neurological evaluation.

Treatment

As above, if possible, the best treatment would be further efforts at heart failure treatment, especially therapies designed to lower the left atrial/pulmonary capillary wedge pressure. Other medical therapies with respiratory stimulants may or may not be practical in critically ill patients.

Patient Positioning

Given the effects of lung volume on loop gain, proper patient positioning to maximize lung volumes may have an important clinical impact. Lung volumes are greater when sitting or laying lateral than when laying supine. (149) If possible, supine patients with CSR could be moved to a different position to improve lung volumes.

Ventilator Management

For patients with CSR manifest on a pressure support mode, it is worthwhile both diagnostically and therapeutically to decrease pressure support as much as possible to assess the underlying respiratory pattern. Again, a decrement in support may decrease apneic periods, which may be sufficiently brief (and without substantial oxygen desaturation) to consider moving toward liberation from the ventilator. The most robust stress test would be to monitor the patient in the absence of pressure support and PEEP, as this will mimic the additional stress that the heart will be under once liberated from mechanical ventilation. If prolonged apneas are noted, a spontaneous mode with a back-up rate (e.g. synchronized intermittent mandatory ventilation, SIMV). Most modern ventilators can also provide adaptive-servo ventilation (ASV).

Non-invasive positive pressure ventilation management

Once extubated, the treatment algorithm may not be substantially different then the list in Section III. NIPPV can be used to provide mechanical support to the left ventricle and limit CSR, especially during sleep. Again, CPAP, Bilevel PAP with a backup rate, and ASV could all be tried. Such therapy may be necessary not only in the ICU but during the remainder of hospitalization and after discharge.

IV. Conclusions

There are few data about the prevalence of CSR due to CHF in the intensive care unit. Nevertheless, CSR is expected to be highly prevalent amongst those with CHF, and treatment should focus on the underlying mechanisms by which CHF increases loop gain and promotes unstable breathing. Several important questions await further study: Does earlier recognition of CSR facilitate ventilator management and ultimately hasten weaning from mechanical ventilation? Does treatment of CSR during acute illness facilitate faster recovery? The answers to these questions could substantially impact a large number of ICU patients.

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Key Points

- Congestive heart failure (CHF) is a common clinical syndrome among patients in the intensive care unit (ICU), who frequently require non-invasive or mechanical ventilation.
- CHF affects control of breathing by increasing chemosensitivity and the circulatory delay, and thereby predisposes to central sleep apnea (CSA), most classically in a crescendo-decrescendo pattern of respiration known as Cheyne-Stokes respiration (CSR).
- Few data are available to determine prevalence of CSR in the ICU, or how CSR might affect clinical management and weaning from mechanical ventilation.

Box 1

Types/Causes of CSA in the ICU

- Cheyne-Stokes Respiration (CSR)
- Stroke/Neurological disease
- Narcotic Induced

Box 2

Features of Cheyne-Stokes Respiration

- Waxing and Waning respiratory pattern
- Baseline hyperventilation and hypocapnia is typical
- Periodicity of 45–90 seconds
- Improved in REM and slow-wave sleep

Box 3

Pathophysiology/Mechanisms of CSR in CHF

- Increased chemosensitivity, due to:
  - Elevated left atrial pressure
  - Hypoxemia
- Increased circulatory delay
- Low lung volumes

Box 4

Treatment of CSR

- Treat CHF
  - Improve cardiac function, left atrial pressure, and pulmonary congestion in order to decrease circulatory delay and lower chemosensitivity
- Position patient to improve lung volumes
  - Lateral
  - Bed elevation
- PAP therapy
  - Continuous PAP
  - Bilevel PAP with backup rate
  - Adaptive Servoventilation
- Supplemental oxygen therapy to reduce chemosensitivity
- Medication
  - Respiratory stimulants to *lower* CO_2
  - Sedatives to facilitate stable sleep
  - Low dose opioids to reduce chemosensitivity

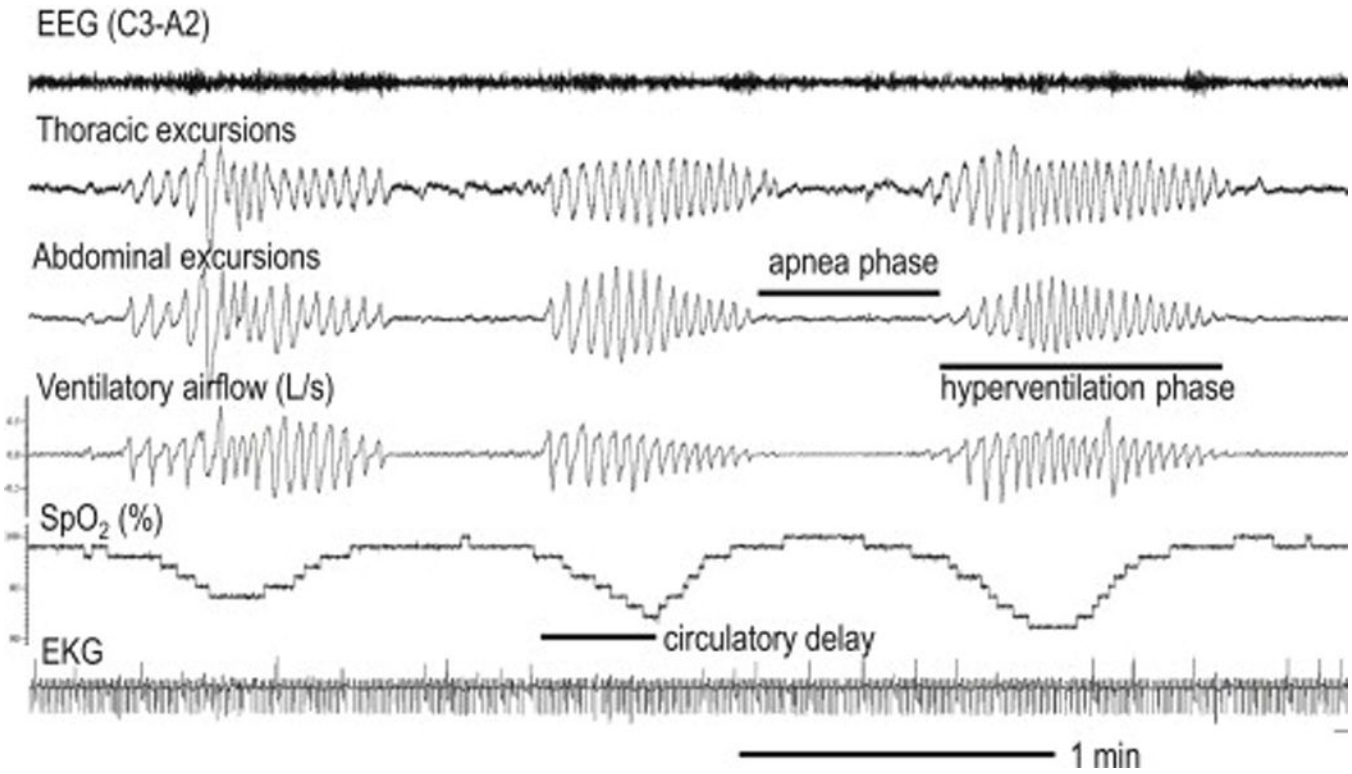

Figure 1.

Cheyne-Stokes respiration in a patient with congestive heart failure. Note crescendo-decrescendo pattern of respiratory effort and airflow. The lung-to-ear circulatory delay can be approximated by the time from resumption of airflow to the start of the rise in oxygen saturation. EEG=electroencephalogram, SpO_2=oxygen saturation, EKG=electrocardiogram.

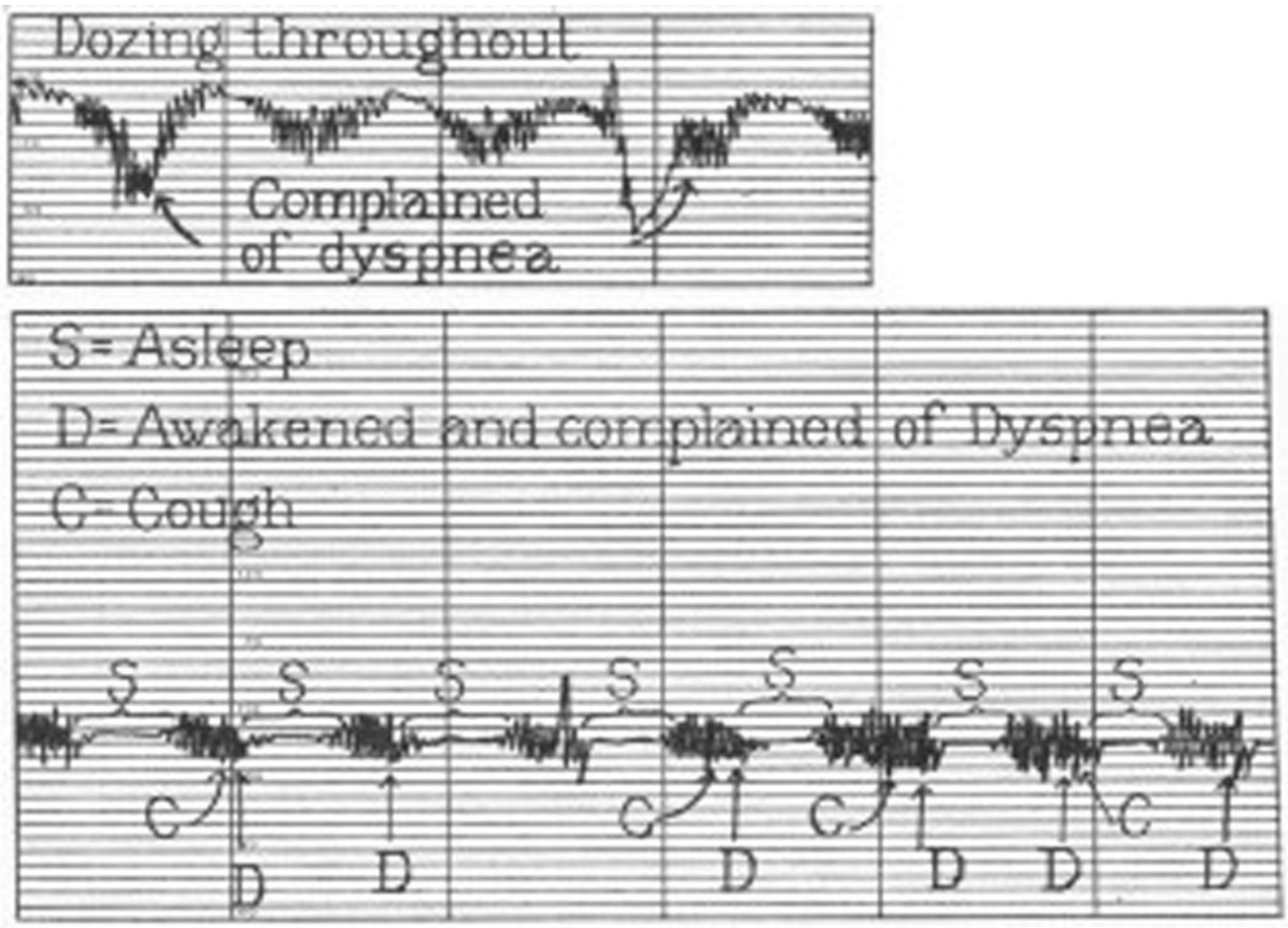

Figure 2.

Increased ventilatory drive during the hyperventilation phase of Cheyne-Stokes respiration results in dyspnea in a patient with heart failure.

Adapted from Harrison TR, King CE, Calhoun JA, Harrison WG, Jr. Congestive heart failure: Xx. Cheyne-Stokes respiration as the cause of paroxysmal dyspnea at the onset of sleep. Archives of Internal Medicine. 1934;53(6):891–910; with permission.

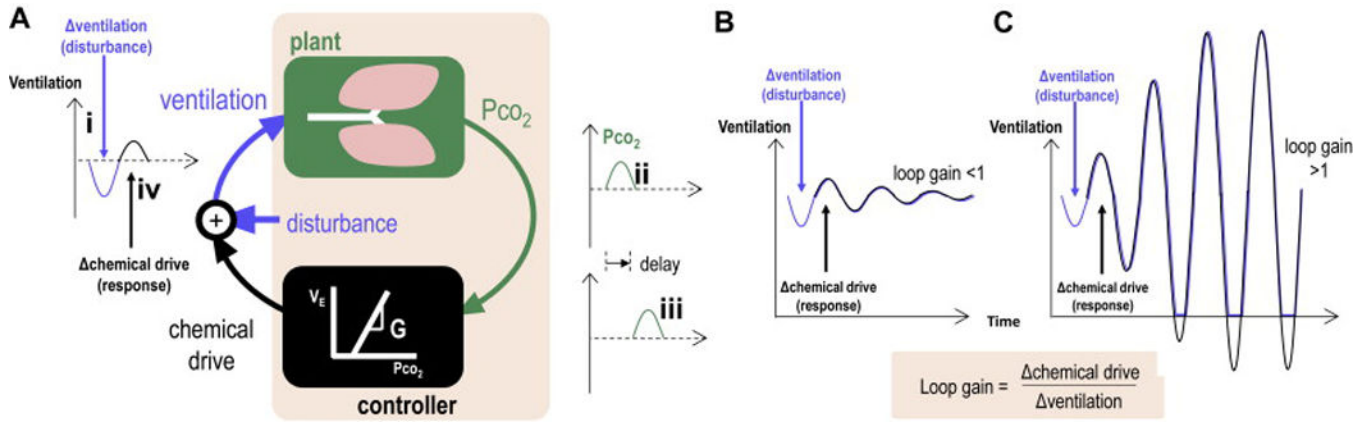

Figure 3.

Loop gain provides a framework to understand the pathophysiology of Cheyne-Stokes respiration. (A) Simplified conceptual block diagram of the respiratory control system. A disturbance to this system (i. hypoventilation) temporarily raises alveolar and arterial CO_2 (PCO_2) at the lungs (ii) as determined by the "plant". After a circulatory delay (iii) the controller perceives the blood gas change and increases its output to oppose the original disturbance (iv). Whether or not this oscillation grows and manifests CSR depends on the loop gain of the system. (B) If loop gain is below 1.0, each response is smaller than the prior disturbance and transient disturbances are damped away. (C) If loop gain exceeds 1.0, each response is greater than the prior disturbance, and oscillations grow until Cheyne-Stokes respiration is established.

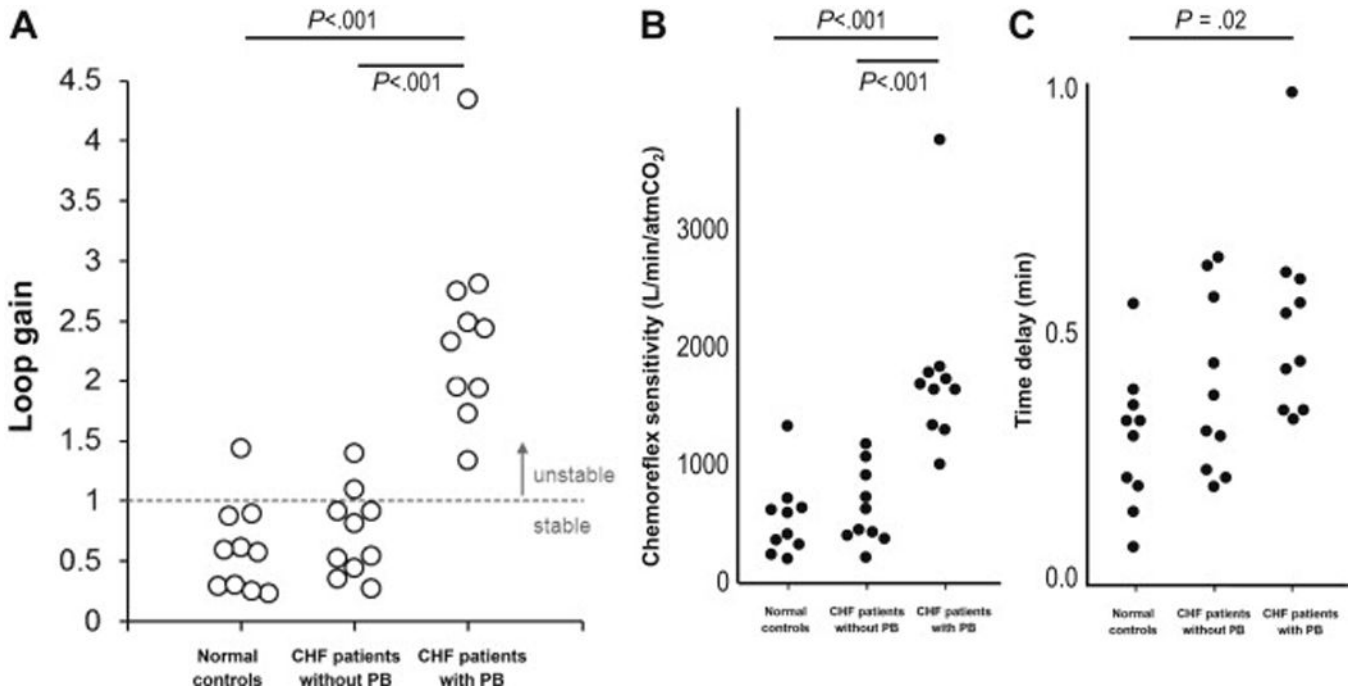

Figure 4.

Loop gain determines the presence or absence of Cheyne-Stokes respiration (periodic breathing, PB) during wakefulness. CHF patients with PB had higher loop gain compared to CHF patients without PB and healthy controls. Increased loop gain in CHF-PB was due to elevated chemosensitivity and increased circulatory delay.

Data from Francis DP, Willson K, Davies LC, Coats AJ, Piepoli M. Quantitative general theory for periodic breathing in chronic heart failure and its clinical implications. Circulation. 2000;102(18):2214-21 and Kee K, Sands SA, Edwards BA, Berger PJ, Naughton MT. Positive Airway Pressure in Congestive Heart Failure. Sleep Med Clin. 2010;5:393–405.

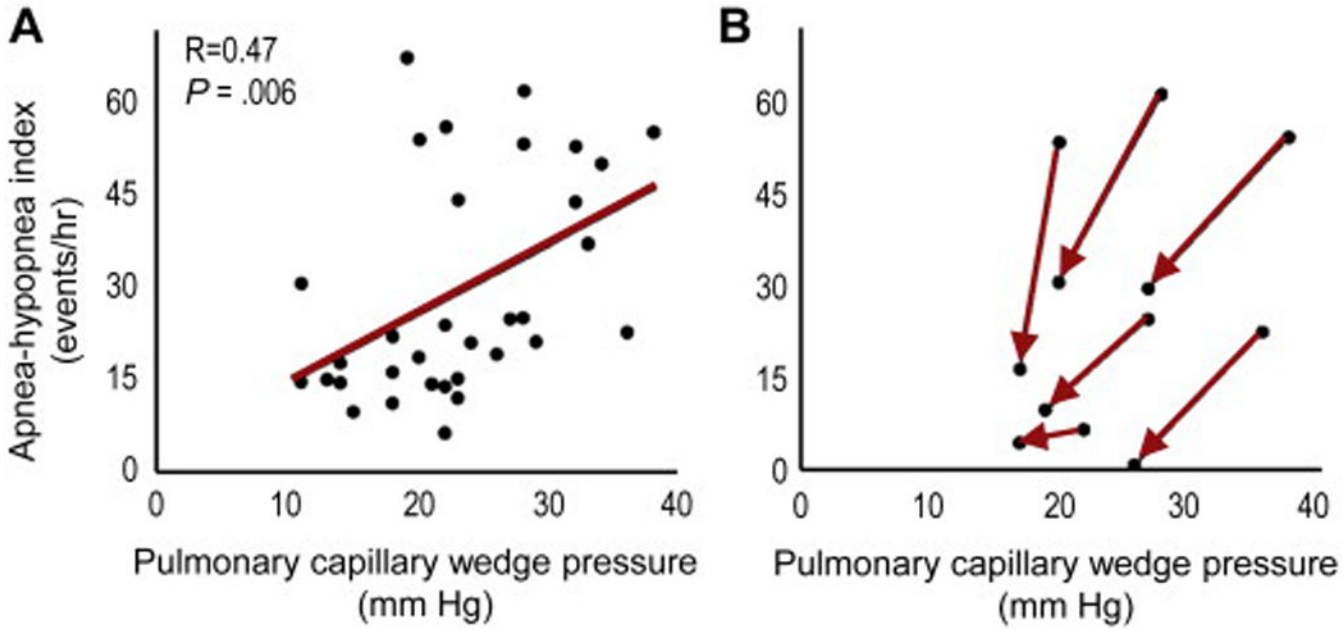

Figure 5.

Pulmonary capillary wedge pressure (PCWP) and Cheyne-Stokes respiration (CSR) during sleep. (A) Correlation between the pulmonary capillary wedge pressure and CSR severity (apnea-hypopnea index). (B) Reducing PCWP with medical intervention for heart failure improves CSR.

Adapted from Solin P, Bergin P, Richardson M, Kaye DM, Walters EH, Naughton MT. Influence of pulmonary capillary wedge pressure on central apnea in heart failure. Circulation. 1999;99(12):1574-9; with permission.

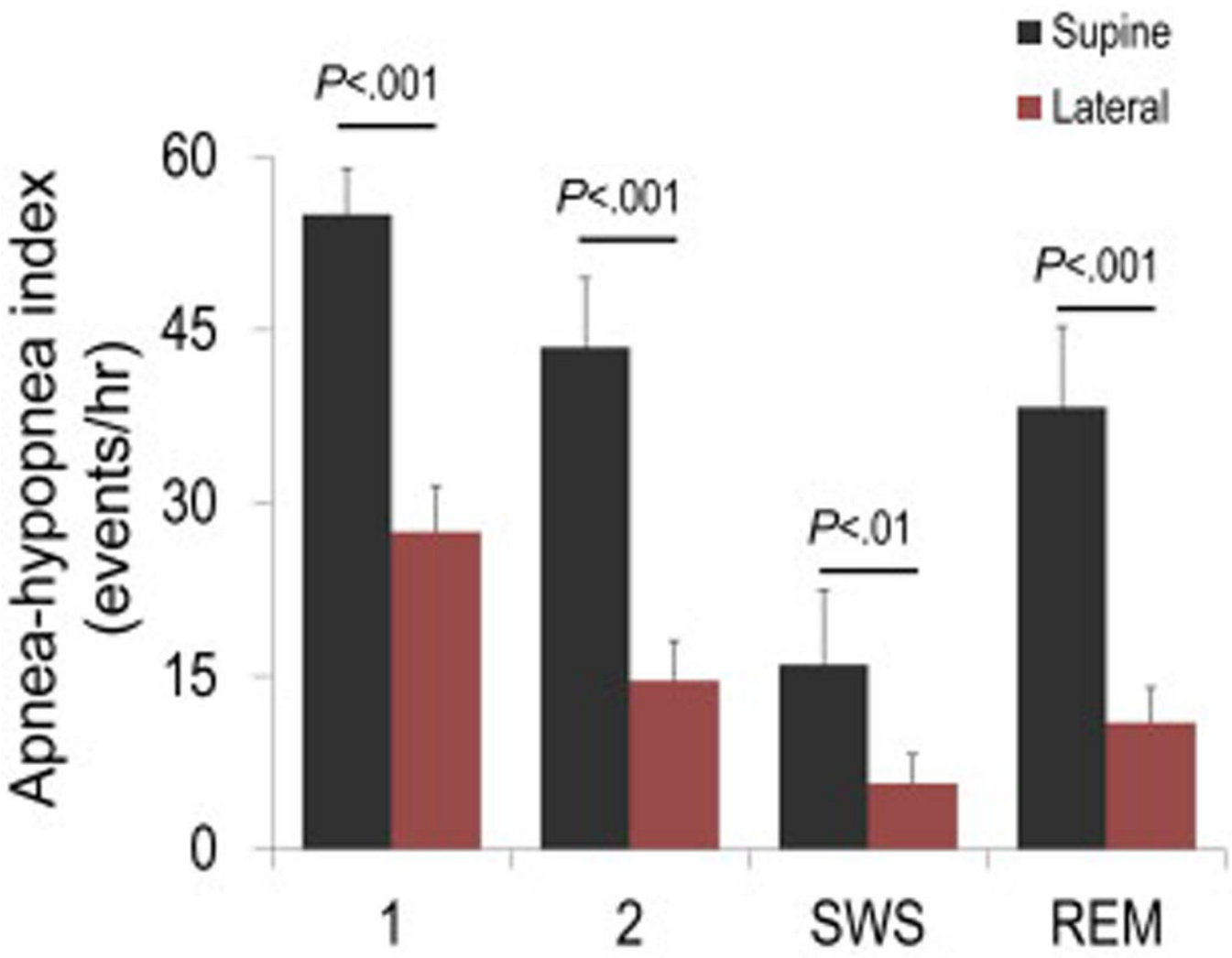

Figure 6.

Lateral position improves Cheyne-Stokes respiration (CSR) in patients with heart failure in all sleep stages. Note also that CSR severity is mild in slow wave sleep (SWS) and most severe in stage 1 non-REM.

Adapted from Szollosi I, Roebuck T, Thompson B, Naughton MT. Lateral sleeping position reduces severity of central sleep apnea / Cheyne-Stokes respiration. Sleep. 2006;29(8): 1045-51; with permission.