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SCIENTIFIC INVESTIGATIONS

Ventilatory Cycle Measurements and Loop Gain in Central Apnea in Mining Drivers Exposed to Intermittent Altitude

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Study Objectives: By measuring the apnea length, ventilatory phase, respiratory cycle length, and loop gain, we can further characterize the central apneas of high altitude (CAHA).

Methods: Sixty-three drivers of all-terrain vehicles, working in a Peruvian mine located at 2,020 meters above sea level (MASL), were evaluated. A respiratory polygraph was performed in the first night they slept at high altitude. None of the subjects were exposed to oxygen during the test or acetazolamide in the preceding days of the test.

Results: Sixty-three respiratory polygraphs were performed, and 59 were considered for analysis. Forty-six (78%) were normal, 6 (10%) had OSA, and 7 (12%) had CAHA. Key data from subjects include: residing altitude: 341 ± 828 MASL, Lake Louise scoring: 0.4 ± 0.8, Epworth score: 3.4 ± 2.7, apnea-hypopnea index: 35.7 ± 19.3, CA index: 13.4 ± 14.2, CA length: 14.4 ± 3.6 sec, ventilatory length: 13.5 ± 2.9 sec, cycle length: 26.5 ± 4.0 sec, ventilatory length/CA length ratio 0.9 ± 0.3 and circulatory delay 13.3 ± 2.9 sec. Duty ratio media [ventilatory duration/cycle duration] was 0.522 ± 0 0.128 [0.308–0.700] and loop gain was calculated from the duty ratio utilizing this formula: $LG = 2\pi / [(2\pi DR - \sin(2\pi DR)]$. All subjects have a high loop gain media 2.415 ± 1.761 [1.175–6.260]. Multiple correlations were established with loop gain values, but the only significant correlation detected was between central apnea index and loop gain.

Conclusions: Twelve percent of the studied population had CAHA. Measurements of respiratory cycle in workers with CAHA are more similar to idiopathic central apneas rather than Hunter-Cheyne-Stokes respiration. Also, there was a high degree of correlation between severity of central apnea and the degree of loop gain. The abnormal breathing patterns in those subjects could affect the sleep quality and potentially increase the risk for work accidents.

Keywords: driver, sleep, central apnea, high altitude, loop gain

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INTRODUCTION

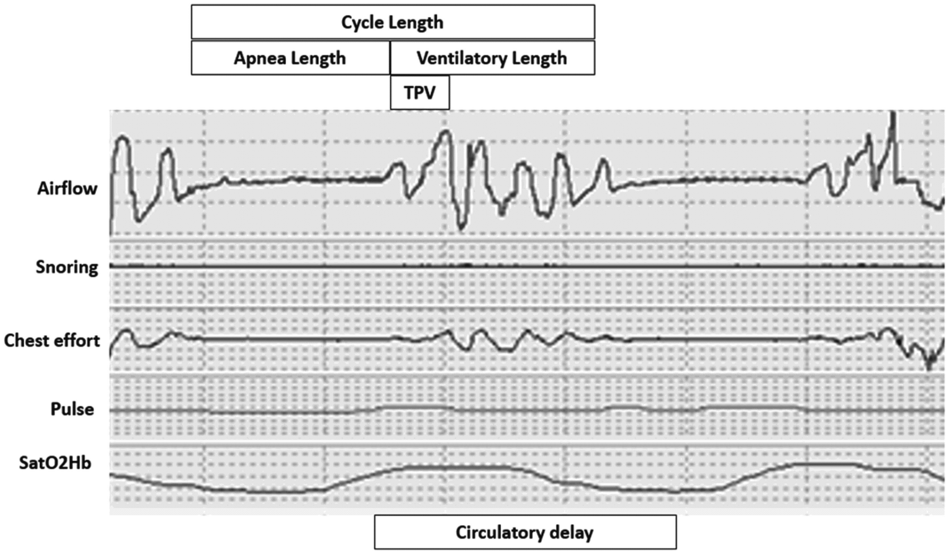
John Tyndall, an Irish physicist interested in the glaciation phenomena, described an abnormal breathing pattern associated with sleep during his first ascent of Mont Blanc in 1857.[1] The first description of periodic breathing at altitude is attributed to Mosso in 1898.[2] The pattern of periodic breathing is a common phenomenon in healthy adults exposed to altitude. It is considered that decrease of partial pressure of CO_2 plays an important role in the genesis of this phenomenon, and intermittent desaturation occurs due to the alternation of apneas or hypopneas of central origin.[3,4] The notable increase in mining activity in Peru over the last two decades has generated a need for human and technological resources at high altitudes areas of the Andes. Sixty-seven percent (67%) of the Peruvian extractive mining industry is concentrated in regions located above 2,000 MASL.[5] The development of the mining industry demands that more workers be exposed to altitude levels in an intermittent fashion; workers stay at high altitude on work days and return to hometowns at low altitudes during their days off. This work schedule arrangement exposes them intermittently to high altitude.[6] In 1995, Jalil et al.[7] recognized three types of exposures to high altitude: acute exposure to altitude, chronic exposure to altitude, and the intermittent exposure to altitude. Intermittent exposure is considered a *third situation*, a term coined by the investigators. The aim of this paper was to measure the variables of the breathing cycle to further characterize central apneas in workers exposed intermittently to high altitude.

BRIEF SUMMARY

Current Knowledge/Study Rationale: A respiratory polygraph was done on miners working at 2,020 meters' altitude. The prevalence of central sleep apnea in those workers was higher than expected for that level of altitude. We hypothesize that the intermittent exposure to a higher working altitude and residing in a lower altitude area preclude the acquisition of acclimatization, which may predispose to developing high altitude central sleep apnea.

Study Impact: These central apneas have the characteristics of idiopathic central apnea (non-cardiogenic) and have a high loop gain; also, there was a significant direct correlation between the central apnea severity and the loop gain values.

Figure 1—Cycle measurements in Type III device.



METHODS

The study was cross-sectional and descriptive. Probability sampling was used. It was implemented in drivers of all-terrain vehicles who work in the mining camp *La Granja* located in Cajamarca, Peru, at 2,020 meters above sea level (MASL). The characteristics of the population, rotation, and shift systems have been described previously.[8] We used the respiratory polygraph (RP) Apnea Link Plus (ResMed), a type III device according to the classification of the American Academy of Sleep Medicine (AASM).[9] Recordings were made on the first night that the drivers slept at the mining camp. A total time registration (TTR) over 420 minutes was considered adequate for the analysis. Drivers answered the Epworth Sleepiness Scale (ESS) and the Lake Louise Scoring System (LLSS) for Acute Mountain Sickness.[10,11] They did not receive nocturnal oxygen therapy and/or acetazolamide 4 weeks prior to the recording date.

Variables Defined from the Respiratory Polygraph

In order to qualify a RP test as central apnea at high altitude (CAHA), the following criteria had to be met:

1. $\geq$ 3 consecutive central apneas and/or central hypopneas separated by a crescendo and decrescendo change in breathing amplitude. Central hypopnea was defined as a decrease in the signal amplitude of the nasal cannula without flow flattening, snoring, and simultaneous reduction in thoracic effort.
2. Central apnea index of $\geq$ 5 or in TTR, and
3. More than 50% of events were central apneas and/or central hypopneas.

Criteria (1) and (2) were taken from the Task Force AASM paper,[12] and (3) was considered by the authors.

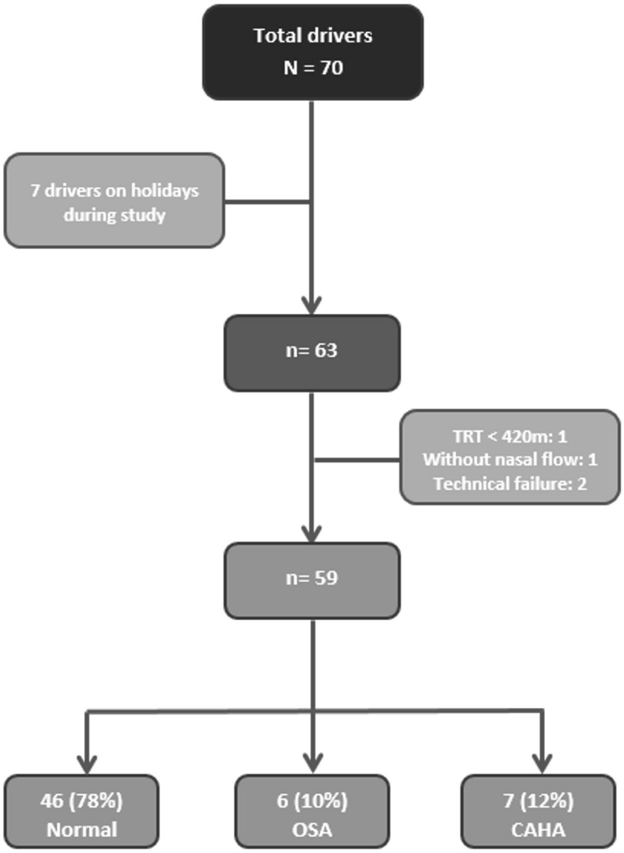
Respiratory Cycle Measurement

Wedewardt criteria[13] were used for respiratory cycle measurements. Central apnea length (CAL) in sec, ventilatory length (VL) in sec: time period hyperventilation (TPV) cycle length (CL) in sec: CAL + VL, ventilatory length/central apnea length ratio (VL/CAL), breath/hyperventilation (B/H): number of times breathing during ventilation phase, time to peak ventilation (TPV) in secs: period measured from the beginning to peak ventilation, circulation delay (CD) in secs: time between the completion of the central apnea and the nadir of SatO2Hb and Duty-ratio: ventilatory length/cycle length (**Figure 1**). The estimated loop gain was calculated according to Sands et al. from the formula $LG = 2\pi / [(2\pi DR-\sin(2\pi DR)]$.[14] The duty ratio has been assessed experimentally in lambs by Edwards et al. in 2008 by using a modified mathematical linearization model of the oscillatory breathing pattern of periodic breathing and the apneic threshold where an increase in loop gain results in a decrease in DR.[15] The same "duty ratio" [DR] method has also been used by Sands et al.[14] to calculate loop gain in the context of the periodic breathing of heart failure. Thus, an increase or decrease in loop gain in the respiratory control cycle can be determined by calculating the DR. According to the criteria described, measurements were taken from 3 complete cycles of periodic breathing in each of the following hours registration: from 22:00 hours to 00:00 (Period A), 00:00 to 02:00 (Period B), 02:00 to 04:00 (Period C), and 04:00 to 06:00 (Period D). The measurements were performed using an 18.5-inch flat screen with a resolution of 1,360 × 768 pixels. The final results were calculated as a media and standard deviation in each case considering periods A to D.

Statistical Analysis

Statistical analysis was performed in Stata 11.1 program (STATA Corp, College Station, TX). The descriptive analysis was performed for quantitative variables (mean, standard deviation, minimum and maximum value) and for categorical variables (frequency). We used the covariance on two variables with the Pearson correlation coefficient.

Figure 2—Drive mine workers flow chart.



Ethical Issues

Drivers that participated in the study signed an informed consent. The study was approved by the Committee on Bioethics from the British American Hospital of Lima. Independently, the Ethic Committee of Biomedical Research of the Hospital Nacional Dos de Mayo approved and authorized this study (Evaluation number 042-2012-CEIB-AI-OACDI-HNDM).

RESULTS

The total population were 70 drivers, 63 (90%) had a RP test. Four studies were excluded, two due to technical failures, one due to short recording time (less than 420 minutes), and one due to inadvertent removal of the nasal cannula during acquisition. There were 59 records that were valid, representing 84% of the population. Forty-six (78%) were normal test, 6 (10%) were consistent with obstructive sleep apnea (OSA), and 7 (12%) with respiratory CAHA pattern. These 7 cases entered into the final analysis (**Figure 2**).

The demographic characteristics are presented in **Table 1**. Drivers were male with a BMI in the overweight range. The score of the ESS and LLSS were between normal ranges. The RP variables obtained from the 7 cases are presented in **Table 2**. The apnea-hypopnea index (AHI) media values were in severe range,[16] and the events were predominantly central according to the criteria described with high T90 (percent of record time with oxygen saturation ≤ 90%) and T85 (percent of record time with oxygen saturation ≤ 85%) values. The oxygen saturation ($SatO_2$) media and nadir $SatO_2$ were low.

The ventilatory cycle measurement obtained in drivers with HACA are presented in **Table 3**. They had short CAL, VL, CD, and the VL/CAL ratio was < 1. Duty ratio media was 0.522 ± 0.128 (0.308–0.700), and all subjects have a high loop gain media 2.41 ± 1.76 (1.17–6.26). Correlation between duty ratio and loop gain is presented in

Table 1—Demographic description in 7 cases with high altitude central apnea.

Age (years)	37.3 ± 5.4
Body mass index (kg/m^2)	28.7 ± 3.2
Cervical perimeter (cm)	42.1 ± 4.0
Epworth Sleepiness Scale	3.4 ± 2.7
Lake Louise acute mountain sickness scoring system	0.4 ± 0.8
Meters above sea level birth	2,371 ± 259
Meters above sea level home	341 ± 828

Data presented as mean ± standard deviation.

Table 2—Respiratory polygraph type III variables in 7 drive mine workers with high altitude central apnea.

Total registered time (minutes)	473.7 ± 22.7
Apnea-hypopnea index	35.7 ± 19.3
Apnea index	20.4 ± 16.3
Obstructive apnea index	5.3 ± 6.4
Central apnea index	13.4 ± 14.2
Mixed apnea index	1.9 ± 2.5
Central hypopnea index	15.3 ± 10.0
Oxygen desaturation index	33.6 ± 17.2
Basal oxygen saturation	94.4 ± 1.6
Media oxygen saturation	90.9 ± 2.1
Maximal oxygen desaturation value	79.9 ± 5.7
Percent time registered with oxygen saturation ≤ 90%	43.7 ± 31.1
Percent time registered with oxygen saturation ≤ 85%	4.9 ± 6.7
Percent time registered with oxygen saturation ≤ 80%	1.0 ± 2.6
Pulse rate media	62.6 ± 6.9

Data presented as mean ± standard deviation.

Table 3—Ventilatory measurement in 7 drive mine workers with high altitude central apnea.

Central apnea length	14.4 ± 3.6
Ventilatory length	13.5 ± 2.9
Cycle length	26.5 ± 4.0
Ventilatory length/central apnea ratio	0.9 ± 0.3
Breathing number during hyperventilation	4.3 ± 0.6
Time to peak ventilation period	5.2 ± 1.1
Circulatory delay	13.3 ± 2.9
Loop gain	2.41 ± 1.76

Data presented as mean ± standard deviation.

Figure 3—Correlation between duty ratio and lop gain.

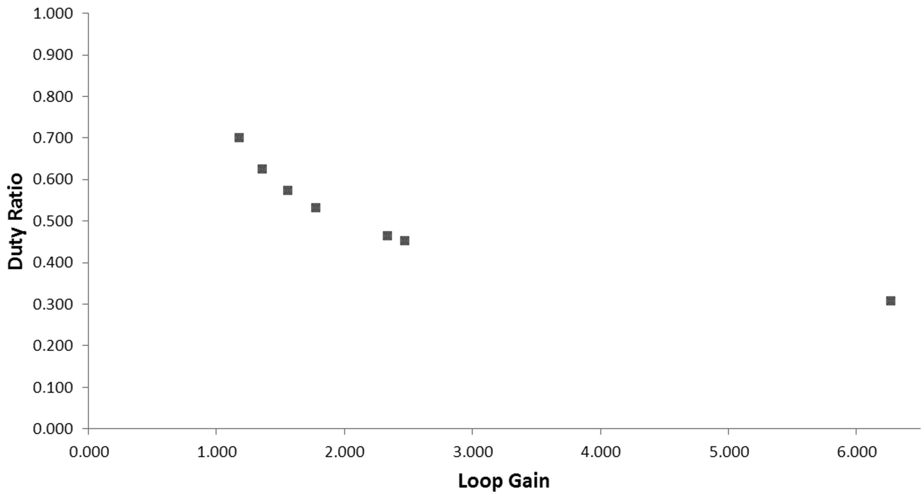


Figure 4—Correlation loop gain and central apnea index.

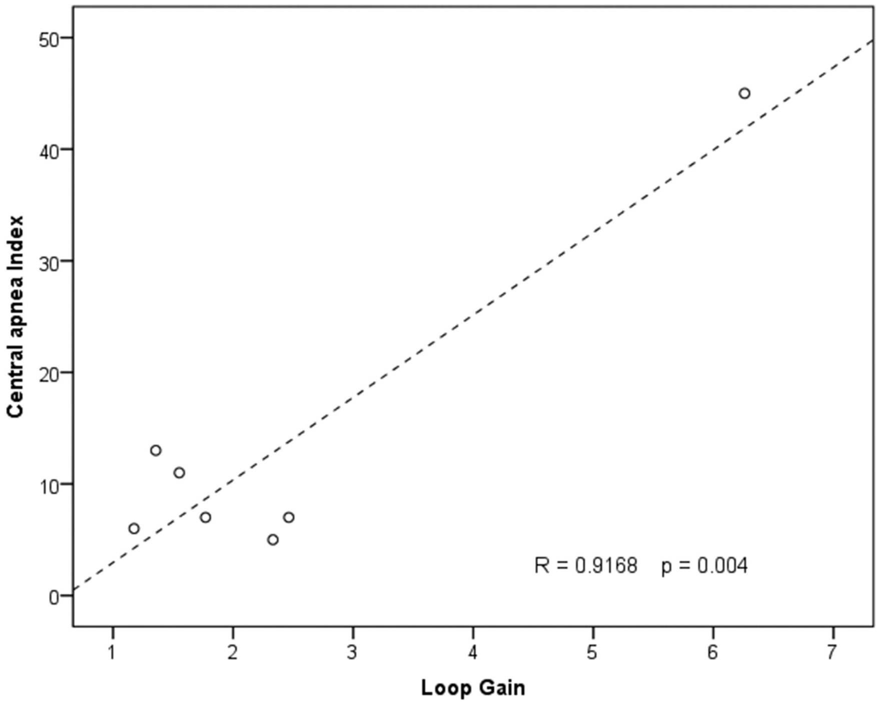


Figure 3. The r correlation between CAI and loop gain was high (r = +0.9168) (**Figure 4**).

DISCUSSION

As has been described by Berssenbrugge, Wickramasinghe, Nussbaumer-Ochner, and Ainslie, the sleep pattern at high altitude is different from sea level and is characterized by poor sleep quality, increased arousals, insomnia, remarkable hypoxemia, increase of light sleep stages, decrease in delta and REM sleep stages, and the appearance of high altitude periodic breathing.[17–20] In our research, we concentrated on the breathing abnormalities occurring in patients exposed to high altitude. The following variables CAL, VL, and CD were short in duration. The VL/CAL was less than one; in addition, the circulation time was not prolonged and the cycle length was short. The previous findings are compatible with Solin's description of non-cardiogenic central apnea.[21]

Using the ventilatory duration and the cycle duration, we were able to apply the formula published by Sands et al. to calculate the loop gain $LG = 2\pi / [(2\pi DR - \sin(2\pi DR)]$,[14] where duty ratio was defined as a quotient between the ventilatory phase (ventilatory duration) divided by the duration of each cycle of apnea plus recovery breaths (cycle duration). Although there have been multiple and more sophisticated techniques to measure loop gain,[22,23] we have used the Sand formula that can be calculated readily from the sleep parameters collected by portable monitoring technology.[24]

As was published by Ainslie et al., the central apnea duration tends to shorten as the altitude increases.[20] Moreover, Lombardi et al. found that males had more central apneas regardless of the level of altitude when compared to female subjects.[25] In our sample population, the apnea duration and severity were higher than expected for the level of altitude. We would presume it is related to our study population having only male subjects and also the sleep study being performed on the first night of reaching higher altitude. We are hypothesizing that a contributing factor to the increased likelihood of CAHA, could be the intermittent exposure to higher altitude that occur in the majority of our workers. The development of the mining industry demands that more workers are intermittently exposed to altitude levels above sea level. In our population, workers stay at high altitude exclusively worked day shifts with variable rotations alternating work and return to hometowns at lower altitudes during their days off for 5–7 days. This intermittent exposure is being commonly seen in our country. In 2013, the formal labor force in Peruvian mining sector was 230,000 workers, and 60% worked in mining camps over 3,000 MASL. Therefore, a significant proportion of workers are exposed intermittently to high altitude.[6] Approximately 5% of GNP in Bolivia and 19.5% of the income for exports is generated by mining activities.[26] Investments in mining activity increased by 120% in Argentina in 2006.[27] Also in Ecuador, investments in mining activity have increased during the last 10 years.[28] Chile is the first copper world producer, and mining activities generate the 14.2% of GNP.[29] In South America the main mining centers are located at high altitudes.

Andrews et al.[30] indicated that an increased loop gain that occurs with hypobaric hypoxia in the altitude could be explained by enhanced peripheral chemo-sensitivity and increased control gain secondary to low oxygen stores, leading to overall hyperventilation and ventilation instability. We were able to demonstrate in our sample population an increase in the loop gain, and to our knowledge, we are the first to describe a very significant correlation between the loop gain and the central apnea index.

The report has some limitations. The number of cases included with CAHA is low; nevertheless, the final sample is representative of the of the entire driver population in this mine. The applied questionnaires have limitations related to their subjective character, recall bias, and defensive attitude adopted by the workers in order to protect their labor position. It should also be noted that ventilatory cycle measurements were performed with type III device, and the original descriptions[13] used polysomnography. In the studies by Hall[31] and Ryan,[32] the pulse oximetry probe was placed on the ear; while in the Wedeward[13] and our study, the probe was placed on the finger, which could lead to different CL measurements. The oximetry sampling rate in our device was 1 per second that was below the ideal sampling rate 3 per second as was described by Davila et al.[33,34] A recent abstract published compared a set of 10 patients with obstructive sleep apnea who had polysomnography and home sleep testing on different days and they concluded that loop gain calculated by home sleep testing devices may not be as accurate as the one obtained by PSG technology.[35]

Although it was not part of our protocol, it would have been helpful to repeat the recording after 5–10 days of exposure to this level of high altitude to assess the role of acclimatization on the events characteristics particularly on the loop gain changes if they ever occur. Although it was not an objective of our study, it is important to mention that one out of ten drivers had OSA. It is well known and published by Pagel et al.,[36] that the high loop gain has been associated with CPAP titration failures.

In conclusion, the incidence of central sleep apnea is higher than expected for the level of altitude which could be due to multifactorial causes: all the subjects in our research were males, the study was recorded early in the acclimatization process, and the potential role of intermittent exposure to high and low altitude in a short frame of time. Oxygen stores in high altitude are low and this can be the cause of increased loop gain that was found in workers. In our sample population a very significant correlation was established between loop gain level and the central apnea index. The presence of CAHA may affect the sleep integrity and quality with day time consequences in the life of miners-drivers.

ABBREVIATIONS

AHI, apnea-hypopnea index
AI, apnea index
B/H, number of times breathing during ventilation phase
BMI, body mass index
CAHA, central apneas of high altitude
CAI, central apnea index
CAL, central apnea length
CD, circulation delay
CL, cycle length
CP, cervical perimeter
DR, duty ratio
ESS, Epworth Sleepiness Scale
LG, loop gain
LLSS, Lake Louise Scoring System
MASL, meters above sea level
MAI, mixed apnea index
OSA, obstructive sleep apnea
ODI, oxigen desaturation index
PR media, pulse rate media
PSG, polysomnography
RP, respiratory polygraph
SatO2Hb basal, basal oxigen saturation
SatO2Hb media, media oxigen saturation
TTR, total time registration
T90, percent of record time with oxygen saturation ≤ 90%
T85, percent of record time with oxygen saturation ≤ 85%
T80 % percent of record time with oxygen saturation ≤ 80
TPV, time to peak ventilation period
VL, ventilatory length

REFERENCES

1. John Tyndall Historical Report. SummitPost Web site. http://www.summitpost.org/john-tyndall-first-ascent-of-mont-blanc-1857/680872. Accessed August 15, 2012.
2. Mosso A. *Life of Man on the High Alps*. London, UK: Fisher Unwin; 1898.
3. Dong F. Langford WF. Models of Cheyne-Stokes respiration with cardiovascular pathogenesis. *J Math Biol*. 2008;57(4):497–519.
4. Vearrier D, Greenberg MI. Occupational health of miners at altitude: adverse health effects, toxic exposures, pre-placement screening, acclimatization, and worker surveillance. *Clin Toxicol (Phila)*. 2011;49(7):629–640.
5. Cuatro regiones concentran el 67% de megaproyectos mineros en el Perú. El Economista América Web site. http://www.eleconomistaamerica.pe/economia-eAm-peru/noticias/5186450/10/13/Cuatro-regiones-concentran-el-67-de-megaproyectos-mineros-en-el-Peru.html#.Kku8F6K4hs3I0DX. Published September 30, 2013. Accessed December 14, 2014.
6. Seguridad Minera Web site. http://revistaseguridadminera.com/eventos/seminario-internacional-de-salud-ocupacional-en-operaciones-mineras/. Accessed March 5, 2015.
7. Jalil J, Braun S, Chamorro G, et al. Cardiovascular response to exercise at high altitude in workers chronically exposed to intermittent hypobaric hypoxia. *Rev Med Chil*. 1994;122(10):1120–1125.
8. Rey de Castro J, Ortiz O, Rosales-Mayor E, Ferreyra J, Liendo A, Liendo CH. Prevalence of sleep-disorders breathing in truck drivers at a mine located at high altitude. *Sleep Sci*. 2013;6(2):59–65
9. Practice parameters for the use of portable recording in the assessment of obstructive sleep apnea. Standards of Practice Committee of the American Sleep Disorders Association. *Sleep*. 1994;17(4):372–377.
10. Roach RC, Bartch P, Hackett PH, Oelz O. Lake Louise acute mountain sickness scoring system. In: Sutton JR, Coates G, Houston CH, eds. *Hypoxia and Molecular Medicine*. Burlington, VT: Queen City Press; 1993:272–274.
11. Leandro S. Mal Agudo de Montañas. http://www.italiantrek.com/Montanismo_Altura.htm. Accessed September 17, 2012.
12. Berry RB, Budhiraja R, Gottlieb DJ, et al. Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the scoring of sleep and associated events. Deliberations of the sleep apnea definitions Task Force of the American Academy of Sleep Medicine. *J Clin Sleep Med*. 2012;8(5):597–619.
13. Wedewardt J, Bitter T, Prinz C, Faber L, Horskotte D, Oldenburg O. Cheyne-Stokes respiration in heart failure: cycle length is dependent on left ventricular ejection fraction. *Sleep Med*. 2010;11(2):137–142.
14. Sands SA, Edwards BA, Kirk Kee K, et al. Loop gain as a means to predict a positive airway pressure suppression of Cheyne-Stokes respiration in patients with heart failure. *Am J Respir Crit Care Med*. 2011;184(9):1067–1075.
15. Edwards BA, Sands S, Skuza EM, Brodecky V, Wilkonson MH, Berger PJ. Increased peripheral chemosensitivity via dopaminergic manipulation promotes respiratory instability in lambs. *Respir Physiol Neurobiol*. 2008;164(3):419–428.
16. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques on clinical research. The report or an American Sleep Academy and Sleep Medicine Task Force. *Sleep*. 1999;22(5):667–689.
17. Berssenbrugge AD, Dempsey JA, Skatrud J. Hypoxic versus hypocapnic effects on periodic breathing. In: West JB, Lahiri S, eds. *High Altitude and Man*. Bethesda, MD: American Physiological Society; 1984:115–128.
18. Wickmanasinghe H, Anholm JD. Sleep and breathing at high altitude. *Sleep Breath*. 1999;3(3):89–101.
19. Nussbaumer-Ochsner Y, Schuepfer N, Bloch KE. Exacerbation of sleep apnea syndrome at altitude: a randomized trial. *Thorax*. 2010:65(5):429–435.
20. Ainslie PN, Lucas SJ, Burgess KR. Breathing and sleep at high altitude. *Respir Physiol Neurobiol*. 2013;188(3):233–256.
21. Solin P, Roebuck T, Swieca J, Walters EH, Naughton MT. Effects of cardiac dysfunction on non-hypercapnic central sleep apnea. *Chest*. 1998;113(1):104–110.
22. Terrill PI, Edwards BA, Nemati S, et al. Quantifying the ventilatory control contribution to sleep apnoea using polysomnography. *Eur Respir J*. 2015;45(2):408–418.
23. Gederi E, Nemati S, Edwards BA, Clifford GD, Malhotra A, Wellman A. Model-based estimation of loop gain using spontaneous breathing: a validation study. *Respir Physiol Neurobiol*. 2014;201:84–92.
24. Stanchina M, Robinson K, Corrao W, Donat W, Sands S, Malhotra A. Clinical use of loop gain measures to determine continuous positive airway pressure efficacy in patients with complex sleep apnea. a pilot study. *Ann Am Thorac Soc*. 2015;12(9):1351–1357.
25. Lombardi C, Miriggi P, Agostoni P, et al. High-altitude hypoxia and periodic breathing: gender-related differences. *J Sleep Res*. 2013;22(3):322–330.
26. Camara Oficial Española de Industria y Comercio en Bolivia Web site. http://www.camara.com.bo/. Accessed May 3, 2016
27. Sarudiansky R, Nielson H. Minería en la República Argentina. Asociacion Argentina Para el Progreso de las Ciencias Web site. http://aargentinapciencias.org/2/index.php/grandes-temas-ambientales/mineria-y-ambiente/76-mineria-en-la-republica-argentina. Accessed June 25, 2016.
28. La reserva minera de Ecuador llega a $ 217.000 millones. El Telégrafo Web site. http://www.eltelegrafo.com.ec/noticias/economia/8/la-reserva-minera-de-ecuador-llega-a-217-000-millones. Published June 12, 2013. Accessed June 25, 2016
29. Indicadores de Comercio Exterior: Cuarto trimestre 2012. Banco Central de Chile. http://web.archive.org/web/20130626220422/http://www.bcentral.cl/publicaciones/estadisticas/sector-externo/pdf/ice042012.pdf. Accessed June 25, 2016.
30. Andrews G, Ainslie PN, Shepherd K, Dawson A, Swart M, Lucas S, Burgess KR. The effect of partial acclimatization to high altitude on loop gain and central sleep apnoea severity. *Respirology*. 2012;17(5):835–840.
31. Hall MJ, Xie A, Rutherford R, Ando SI, Floras JS, Bradley D. Cycle length of periodic breathing in patients with and without heart failure. *Am J Respir Crit Care Med*. 1996;154(2 Pt 1):376–381.
32. Ryan CM, Bradley TD. Periodicity of obstructive sleep apnea in patients with and without heart failure. *Chest*. 2005;127(2):536–542.
33. Davila DG, Richards KC, Marshall BL, et al. Oximeter performance: the influence of acquisition parameters. *Chest*. 2002;122(5):1654–1660.
34. Davila DG, Richards KC, Marshall BL, et al. JC. Oximeter's acquisition parameter influences the profile of respiratory disturbances. *Sleep*. 2003;26(1):91–95.
35. Orr JE, Sands SA, Edwards BA. Loop gain measurements from home sleep testing in obstructive sleep apnea. Poster presented at: American Thoracic Society 2016 International Conference; May 15, 2016; San Francisco, CA.
36. Pagel JF, Kwiatkowski C, Parnes BJ. The effects of altitude associated central apnea on the diagnosis and treatment of obstructive sleep apnea: comparative data from three different altitude locations in the mountain west. *J Clin Sleep Med*. 2011;7(6):610–615.

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