pii: jc-00109-16 http://dx.doi.org/10.5664/jcsm.5952

JCSM
Journal of Clinical Sleep Medicine

SLEEP MEDICINE PEARLS

A 16-Year-Old Boy with Refractory Epilepsy and Sleep-Disordered Breathing

Lourdes M. DelRosso, MD[1,2]; Romy Hoque, MD[3]; Mary B. Contreras, RPSGT[1]; Ngoc P. Ly, MD, MPH[1,2]

[1]University of California San Francisco, School of Medicine, San Francisco, CA; [2]Division of Pulmonary Medicine, Department of Pediatrics, University of California, San Francisco, CA; [3]Emory Sleep Center, Atlanta, GA

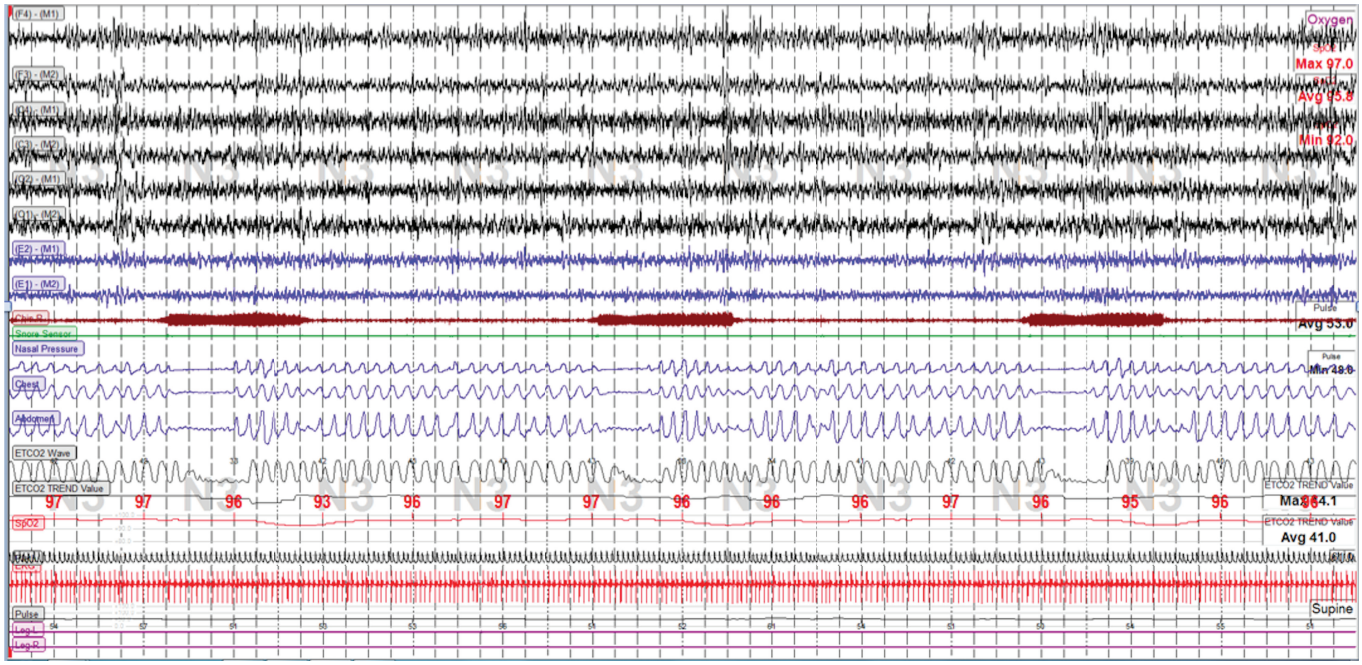
The patient is a 16-year-old boy referred for overnight polysomnography due to parental concern for apnea. The parents witnessed breathing pauses of up to 40 seconds that occur during sleep noted only in the past two years. He did not snore and did not appear to struggle to breathe. He slept for 12 hours at night and still was very difficult to wake up in morning. The parents noticed that he was fatigued during the day but did not take naps. His past medical history was significant for refractory generalized epilepsy diagnosed soon after birth requiring multiple antiepileptic medications and vagus nerve stimulator (VNS) placement at age 12 years. He was born at 34 weeks gestational age via normal spontaneous vaginal delivery. His medications included levetiracetam 600 mg twice a day, valproic acid 250 mg three times a day, and gabapentin 300 mg twice a day.

Physical exam revealed a non-cooperative, non-verbal child. His weight was at the 20th percentile, height was at the 11th percentile, and vital signs were within normal range. Oropharyngeal exam showed modified Mallampati I and Brodsky palatine tonsil size 1+. Cardiovascular, respiratory and gastrointestinal exam were normal. He had normal gait, decreased muscle bulk, and mild scoliosis.

Magnetic resonance imaging of the brain with and without contrast was normal. Diagnostic polysomnogram (PSG) revealed a total sleep time (TST) of 359 minutes; sleep efficiency was 87%; sleep latency was 0 minutes. The central apnea-hypopnea index (AHI) was 22 events per hour. The obstructive AHI was 0. The saturation nadir was 89%. There was no nocturnal hypoxemia or hypercapnia. Typical central events are shown in **Figure 1** and **Figure 2**.

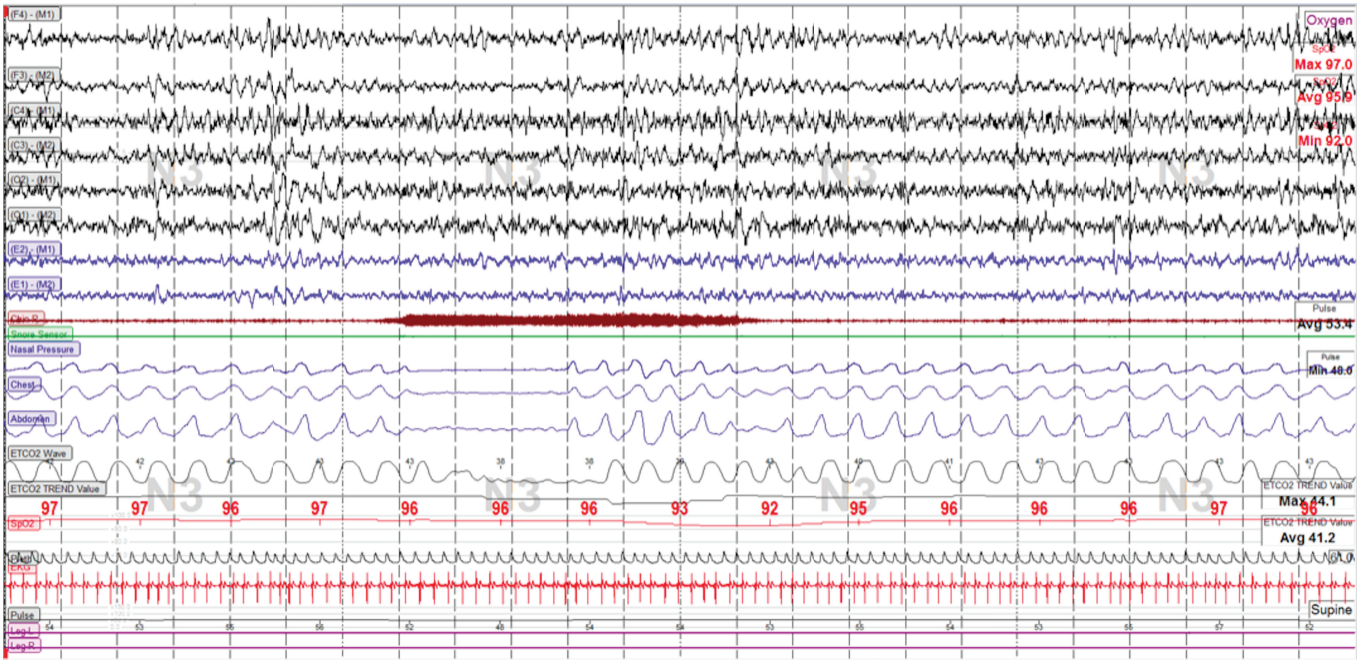
QUESTION: What two respiratory phenomena are seen during each VNS discharge?

Figure 1—Five-minute epoch.



Electroencephalogram leads (F4-M1, F3-M2, C3-M2, C4-M1, O1-M2, O2-M1); Electromyogram leads (chin, LEGL, LEGR), Ocular leads (E1-M2, E2-M1), Respiratory sensors (Nasal Pressure) EKG leads, SpO2 (oxyhemoglobin saturation), PWF (pulse wave form).

Figure 2—Thirty-second epoch.



Electroencephalogram leads (F4-M1, F3-M2, C3-M2, C4-M1, O1-M2, O2-M1); Electromyogram leads (chin, LEGL, LEGR), Ocular leads (E1-M2, E2-M1), Respiratory sensors (Nasal Pressure) EKG leads, SpO2 (oxyhemoglobin saturation), PWF (pulse wave form).

ANSWER: VNS activation is visualized by increased tone on the chin EMG channel. Simultaneous with each VNS discharge is a central apnea, followed by a period of hyperventilation, which ceases at the end of the VNS discharge. During the hyperventilation transient drop in end-tidal capnography (ETCO2) trend is noted. With the end of the VNS discharge, hyperventilation ceases, and ETCO2 increases. Both the central apnea and the hyperventilation may be in part due to VNS stimulation of medial pontine/medullary reticular formation brainstem respiratory centers.

DISCUSSION

VNS is approved for the treatment of refractory epilepsy. The vagus nerve consists of parasympathetic efferent fibers that innervate the neck, thorax and abdomen, and afferent fibers that go to the nucleus of the tractus solitarius and to the cortex.[1] Side effects of VNS are produced by anterograde stimulation (recurrent laryngeal nerve) and include voice changes in up to 66% of patients, cough in up to 45%, pharyngitis (35%), throat pain (28%), and dyspnea (25%), or retrograde effect on the brainstem respiratory centers.[1]

Sleep-disordered breathing has been shown in children with VNS as demonstrated by apneas and hypopneas that occur simultaneously with VNS activation, which may be visualized on PSG as periodic elevation of chin EMG tone. Our case demonstrates two often under-appreciated VNS associated phenomenon—central apneas, and hyperventilation with hypocapnia. One case report to date has reported the emergence of central apneas with VNS activation.[2] VNS induced hyperventilation with hypocapnia assessed with ETCO2 has been shown in a single case series of 10 patients.[3] Our case demonstrates that VNS associated apnea and hyperventilation may be seen in the same patient. The hyperventilation seen in our case is not simply a post-apnea phenomenon, in that the hyperventilation always ceased with the end of the VNS discharge.

Treatment options for patients with sleep-disordered breathing secondary to VNS include adjustment of VNS parameters or adding positive airway pressure. VNS discontinuation is often not a preferred option, given that the device is indicated for those with pharmacologically refractory epilepsy.

SLEEP MEDICINE PEARLS

1. VNS activation may be visualized on PSG with periodic elevation of chin EMG tone.
2. VNS can produce central apneas and hyperventilation during device discharge.
3. The hyperventilation seen in our case is not simply a post-apnea phenomenon, in that the hyperventilation always ceased with the end of the VNS discharge.

CITATION

DelRosso LM, Hoque R, Contreras MB, Ly NP. A 16-year-old boy with refractory epilepsy and sleep-disordered breathing. *J Clin Sleep Med* 2016;12(7):1062–1064.

REFERENCES

1. Hsieh T, Chen M, McAfee A, Kifle Y. Sleep-related breathing disorder in children with vagal nerve stimulators. Pediatr Neurol 2008;38:99–103.
2. Papacostas SS, Myrianthopoulou P, Dietis A, Papathanasiou ES. Induction of central-type sleep apnea by vagus nerve stimulation. Electromyogr Clin Neurophysiol 2007;47:61–3.
3. Holmes MD, Miller JW, Voipio J, Kaila K, Vanhatalo S. Vagal nerve stimulation induces intermittent hypocapnia. Epilepsia 2003;44:1588–91.

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication March, 2016
Accepted for publication March, 2016
Address correspondence to: Lourdes M. DelRosso, University of California San Francisco, School of Medicine, San Francisco, CA; Email: Lourdes.delrosso@ucsf.edu

DISCLOSURE STATEMENT

This was not an industry supported study. The authors have indicated no financial conflicts of interest.