http://dx.doi.org/10.5665/sleep.1856

Respect for Muscle

Commentary on Frauscher et al. Normative EMG values during REM sleep for the diagnosis of REM sleep behavior disorder. SLEEP 2012;35:835-847.

Donald L. Bliwise, PhD; David B. Rye, MD, PhD

Department of Neurology, Sleep Program, Emory University School of Medicine Atlanta, GA

In considering the biological correlates that define sleep in the human polysomnogram (PSG), electromyographic activity is undeniably the least considered of electrophysiologic signals. The greatest value of the electromyogram (EMG) recorded above the surface of the mentalis traditionally derives from what its absence connotes (i.e., rapid eye movement [REM] sleep). Contrast this meager supporting role for EMG to sampling the spatiotemporal characteristics of thalamocortical excitability states evident in the electroencephalogram (EEG) recorded from the scalp surface. Electrode arrays of 128 or more sensors and signal processing that ranges from spectral analyses to period/amplitude analyses to non-linear dynamic approaches emerging from chaos theory speak to this fact. Even in those instances when molecular biological correlates of EMG signals have been revealed (e.g., periodic leg movements in sleep [PLMS] as an endophenotype for restless legs syndrome),[1] they are more often interpreted in light of other PSG signals presumed to have greater clinical significance. For example, PLMS are often portrayed as little more than epiphenomenal kicks, occurring at the end of more bona fide breathing events.[2]

This issue of *SLEEP* contains a study by Frauscher and colleagues[3] of motor activity during human sleep that could presage a change to this state of affairs. The activity of the vast majority of the over 600 skeletal muscles during sleep remains uncharted territory. Early researchers in the modern sleep research era[4] seemingly had more intuitive interest in the musculature during sleep, but focused largely on finding muscle groups that did or did not show REM atonia. Few muscle groups demonstrated atonia, and these observations[4] did not prompt much further work in this area. Perhaps the greatest boon to establish interest in EMG was the recognition of REM behavior disorder (RBD)[5] as an entity with potentially great prognostic significance for incident Parkinson disease,[6] at least as observed to date among selected clinical populations.

There are many practical considerations in approaching an examination of EMG during human sleep. First, there is the decision of what muscle groups to study and the concurrent recognition that time for electrode application and achieving low impedance signals taxes the precious commodities of both technologists' time and patients' patience. Frauscher et al.[3] sampled REM phasic activity both from flexors and extensors, the former typically demonstrating more activity in sleep, both in cats[7] and humans.[8] Additionally, examining muscles with innervations from different spinal cord segments allows some appreciation of whether higher nervous system input may operate uniformly within sleep, or as has been suggested by studies of some spinal cord lesion patients, whether generation and mediation of skeletal motor activity during sleep may be relatively independent of such supraspinal influences.[9]

The second choice-point revolves around how one quantifies muscle activity. Sleep Medicine does not have many precedents for how to do this, and with rare exception, most approaches are laborious and visually based. The system of visual quantification of phasic muscle activity described by Lapierre and Montplaisir 20 years ago[10] continues to serve as the default standard for several recent similar attempts, the majority of which invoke their approach with some variations, although computerized approaches may be in the offing.[11-13] Indeed, the current paper by Frauscher et al.[3] employed visual analyses for EMG measurements but embraces an innovative approach for simultaneity of EMG activity.[8]

A third issue in the study of muscle activity during human sleep involves a deceptively simple question: whom to record? Should everybody be recorded? The normative data presented here by Frauscher et al. certainly point to that direction. Given what is known about the apparently predictive nature of absence of REM atonia associated with later neurodegeneration,[6] should more comprehensive monitoring of the body's musculature enter the repertoire of routine PSG, much as breathing is now? If so, we should have a reasonable idea what patterns and levels of activity the general population might show. Here then is perhaps is the thorniest issue of all. When characterizing measurements on a case (i.e., patient) level, one implicitly invokes definitions of normality (i.e., at a population level). The tenets of the epidemiologic description of disease remind us that representativeness of the population under study is key for understanding not only the sensitivity and specificity of any putative measure of current or anticipated disease, but also its positive and negative predictive value. And it is here where the story begins to break down.

The study by Frauscher et al. is not unique in suggesting that quantification of muscle activity during human sleep may be clinically relevant. Earlier work[14-17] all suggested clinical utility for phasic activity discriminating between normality and disease using a somewhat more limited number of EMG recording sites. Unfortunately, neither these earlier studies, nor that of Frauscher

Submitted for publication April, 2012
Accepted for publication April, 2012

Address correspondence to: Donald L. Bliwise, PhD, Professor of Neurology, Psychiatry/Behavioral Sciences, and Nursing, Director, Program in Sleep, Aging and Chronobiology, Emory University School of Medicine, Wesley Woods Health Center, 1841 Clifton Road, Room 509, Atlanta, Georgia 30329; Tel: (404) 728-4751; Fax: (404) 728-4756; E-mail: dbliwis@emory.edu

et al.[3] can address the broader and more relevant issue of what prognostic value there is in finding high rates of phasic muscle activity in the human PSG. This is because those studies have not employed a population-based framework and have oversampled synucleinopathic patients using case control approaches. For example, Frauscher et al. employed equal numbers of patients and controls, whereas among other studies the corresponding ratios ranged from 2.8:1 (14) to 1.9:1 (15) to 1.5:1 (16) to 1:1.2 (17)—all potentially vastly overestimating the expected patient-to-control ratio of 1:50 that might be expected in a more representatively sampled population, assuming the self-reported data of violent behavior in sleep[18]—bear at least some relevance to EMG activation in RBD. Until the positive predictive value of the sleep EMG is determined in groups whose disease prevalence mirrors what is encountered in the general population, its ultimate prognostic significance will remain uncertain. Future population-based studies providing more careful examination of the skeletal muscles during sleep, much as we have now had for several decades for sleep disordered breathing,[19] would go a long ways toward determining under what circumstances EMG recordings offer diagnostic insights.

CITATION

Bliwise DL; Rye DB. Respect for muscle. *SLEEP* 2012;35(6):743-744.

ACKNOWLEDGMENT

This work was funded by NS-050595.

DISCLOSURE STATEMENT

Dr. Bliwise has consulted for Ferring Pharmaceuticals. Dr. Rye has consulted for UCB Pharma and is on the advisory board of UCB Pharma, Impax Laboratories, and Jazz Pharmaceuticals. He is on the External Data Monitoring Committee for Merck Inc.

REFERENCES

1. Stefansson H, Rye DB, Hicks A, et al. A genetic risk factor for periodic limb movements in sleep. N Engl J Med 2007;357:639-47.
2. Exar EN, Collop NA. The association of upper airway resistance with periodic limb movements. Sleep 2001;24:188-92.
3. Frauscher B, Iranzo A, Gaig C, et al. Normative EMG values during REM sleep for the diagnosis of REM sleep behavior disorder. Sleep 2012;35:835-47.
4. Jacobson A, Kales A, Lehmann D, Hoedemaker FS. Muscle tonus in human subjects during sleep and dreaming. Exp Neurol 1964:10:418-24.
5. Schenck CH, Bundlie SR, Ettinger MG, Mahowald MW. Chronic behavioral disorders of human REM sleep: a new category of parasomnia. Sleep 1986;9:293-308.
6. Iranzo A, Molinuevo JL, Santamaria J, et al. Rapid-eye-movement sleep behavior disorder as an early marker for a neurodegenerative disorder: a descriptive study. Lancet Neurol 2006;5:572-7.
7. Gassel MM, Marchiafava P, Pompeiano O. Phasic changes in muscular activity during desynchronized sleep in unrestrained cats. An analysis of the pattern and organization of myoclonic twitches. Arch Ital Biol 1964;102:449-70.
8. Frauscher B, Iranzo A, Hogl B, et al. Quantification of electromyographic activity during REM sleep in multiple muscles in REM sleep behavior disorder. Sleep 2008;31:724-31.
9. Provini F, Vetrugno R, Meletti S, et al. Motor pattern of periodic limb movements during sleep. Neurology 2001;57:300-4.
10. Lapierre O, Montplaisir J. Polysomnographic features of REM sleep behavior disorder: development of a scoring method. Neurology 1992;42:1371-4.
11. Ferri R, Manconi M, Plazzi G, et al. A quantitative statistical analysis of the submentalis muscle EMG amplitude during sleep in normal controls and patients with REM sleep behavior disorder. J Sleep Res 2008;17:89-100.
12. Fairley JA, Georgoulas G, Mehta NA, Gray AG, Bliwise DL. Computer detection approaches for the identification of phasic electromyographic (EMG) activity during human sleep. Biomed Signal Process Control 2012 http://dx.doi.org/10.1016/j.bspc2012.02.003.
13. Burns JW, Consens FB, Little RJ, Angell KJ, Gilman S, Chervin RD. EMG variance during polysomnography as an assessment for REM behavior disorder. Sleep 2007;30:1771-8.
14. Consens FB, Chervin RD, Koeppe RA, et al. Validation of a polysomnographic score for REM sleep behavior disorder. Sleep 2005;28:993-7.
15. Mayer G, Kesper K, Ploch T, et al. Quantification of tonic and phasic muscle activity in REM sleep behavior disorder. J Clin Neurophysiol 2008;25:48-55.
16. Ferri R, Rundo F, Manconi M, et al. Improved computation of the atonia index in normal controls and patients with REM sleep behavior disorder. Sleep Med 2010;11:947-9.
17. Bliwise DL, He L, Ansari FP, Rye DB. Quantification of electromyographic activity during sleep: a phasic electromyographic metric (PEM). J Clin Neurophysiol 2006; 3:59-67.
18. Ohayon M, Schenck C. Violent behavior in sleep: prevalence, comorbidity and consequences. Sleep Med 2010;11:941-6.
19. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993;328:1230-5.