Are Sleep Disturbances a Risk for Chronic Traumatic Encephalopathy? Only the Shadow Knows

Stuart F. Quan, M.D., F.A.A.S.M.

Editor, *Journal of Clinical Sleep Medicine*; Division of Sleep Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, Arizona Respiratory Center, University of Arizona College of Medicine, Tucson, AZ

Junior Seau, Ollie Matson, John Mackey. What do these individuals have in common? History of National Football League (NFL) stardom? Enshrinement or possible induction into the Pro Football Hall of Fame? Both are true. Yet all share something much more ominous. Death related to the sequelae of chronic traumatic encephalopathy.¹ Chronic traumatic encephalopathy (CTE) is characterized by memory loss, depression, dementia and potentially premature death.² In some individuals, such as Junior Seau—and more recently major league baseball player Ryan Freel—it has been posited as the cause of their suicide.³ Pathologic examination of the brain of those with CTE reveals a degenerative neurologic process which is now attributed to repetitive concussive brain trauma.⁴ With the revelation that some living former NFL stars such as Brett Favre and Tony Dorsett are having symptoms suggestive of CTE,^{5,6} there is growing concern about the safety of all sports that can result in concussive brain injury. This level of concern has caused the NFL and college football to change their rules regarding tackling, leading to penalties and possible ejection for tackles that target the head. The NFL in cooperation with the National Institutes of Health also has begun funding research in this area with most of the emphasis on early detection using brain imaging techniques and further studies of the neuropathology.⁷ However, is repetitive concussive injury the only risk factor for CTE? Could obstructive sleep apnea (OSA) and other sleep disturbances be contributing or exacerbating factors?

Several recent studies document that many individuals who have suffered acute traumatic brain injury (TBI) are subsequently found to have a variety of sleep disturbances including OSA.⁸⁻¹⁰ In some of these studies, the prevalence of OSA and insomnia has been reported to be as high as 23% and 25% respectively.^{9,10} Furthermore, data suggest that cognitive function is worse in patients who have both OSA and previous TBI than in those with TBI alone.¹¹ In addition, treatment for sleep disturbances in the setting of chronic TBI may improve cognition and mood.¹² Studies of retired and active NFL football players have found that the prevalence of OSA ranges from 14% to 19%.^{13,14} However, the prevalence may be much higher in retired players.¹⁵ Awareness of the significance of OSA prompted NFL Charities to fund the development of a short online screening application for all players although there has been little interest in teams to use it.¹⁶ In addition to their respective adverse effects on sleep, both OSA and insomnia have been linked to the development of mood disturbances including depression

which are also observed with CTE.^{17,18} Recently, epidemiologic studies have identified a link between both OSA and insomnia, and subsequent development of dementia.^{19,20} With respect to OSA, a variety of neuroimaging studies suggest evidence of brain neuronal loss or dysfunction.²¹ Gray matter abnormalities also have been observed some,²²⁻²⁴ but not all studies of patients with chronic insomnia.²⁵

Given the interconnections among TBI, OSA, insomnia, mood disturbances, cognitive decline and neurodegeneration, one can speculate that OSA and insomnia may be additional risk factors or important modifying factors for the development of CTE. For example, could the development, severity or progression of CTE occurring after repetitive brain injury be worsened in the presence of insomnia or OSA? An interesting and provocative question? Hopefully so for sleep and brain injury investigators, parents, athletes and of course sports fans. Perhaps further research will provide enlightenment in this area. Until then, only the Shadow knows.

CITATION

Quan SF. Are sleep disturbances a risk for chronic traumatic encephalopathy? Only the shadow knows. *J Clin Sleep Med* 2014;10(3):241-242.

REFERENCES

1. Leahy MP. Junior Seau report highlights NFL's brain injury problem. *Breitbart News Network*. <http://www.breitbart.com/Breitbart-Sports/2013/01/12/Junior-Seau-Report-Highlights-NFL-s-Brain-Injury-Problem>. Published January 13, 2013. Accessed January 17, 2014.
2. Stern RA, Daneshvar DH, Baugh CM, et al. Clinical presentation of chronic traumatic encephalopathy. *Neurology* 2013;81:1122-9.
3. Report: Ryan Freel first major leaguer diagnosed with CTE. *MSN Fox Sports*. <http://msn.foxsports.com/mlb/story/report-ryan-freel-first-major-leaguer-diagnosed-with-cte-121613>. Published December 16, 2013. Accessed January 17, 2014.
4. McKee AC, Stern RA, Nowinski CJ, et al. The spectrum of disease in chronic traumatic encephalopathy. *Brain* 2013;136(Pt 1):43-64.
5. Boren C. Tony Dorsett diagnosed with signs of CTE. *Washington Post*. <http://www.washingtonpost.com/blogs/early-lead/wp/2013/11/07/tony-dorsett-diagnosed-with-signs-of-cte/>. Published November 7, 2013. Accessed January 17, 2014.
6. Greenberg C. Brett Favre believes concussions 'toll has got to be pretty high' would be 'leery' of son playing football. *The Huffington Post*. http://www.huffingtonpost.com/2013/11/18/brett-favre-concussions-nfl-memory-son_n_4297874.html. Published November 18, 2013. Accessed January 17, 2014.
7. NFL-backed concussion grants given. *ESPN NFL*. http://espn.go.com/nfl/story/_/id/10147890/nfl-nih-give-grants-concussion-studies. Published December 16, 2013. Updated 2013. Accessed January 17, 2014.
8. Viola-Saltzman M, Watson NF. Traumatic brain injury and sleep disorders. *Neurol Clin* 2012;30:1299-312.

9. Verma A, Anand V, Verma NP. Sleep disorders in chronic traumatic brain injury. *J Clin Sleep Med* 2007;3:357-62.
10. Castriotta RJ, Wilde MC, Lai JM, Atanasov S, Masel BE, Kuna ST. Prevalence and consequences of sleep disorders in traumatic brain injury. *J Clin Sleep Med* 2007;3:349-56.
11. Wilde MC, Castriotta RJ, Lai JM, Atanasov S, Masel BE, Kuna ST. Cognitive impairment in patients with traumatic brain injury and obstructive sleep apnea. *Arch Phys Med Rehabil* 2007;88:1284-8.
12. Wiseman-Hakes C, Murray B, Moineddin R, et al. Evaluating the impact of treatment for sleep/wake disorders on recovery of cognition and communication in adults with chronic TBI. *Brain Inj* 2013;27:1364-76.
13. George CF, Kab V, Kab P, Villa JJ, Levy AM. Sleep and breathing in professional football players. *Sleep Med* 2003;4:317-25.
14. Rice TB, Dunn RE, Lincoln AE, et al. Sleep-disordered breathing in the National Football League. *Sleep* 2010;33:819-24.
15. Albuquerque FN, Kuniyoshi FH, Calvin AD, et al. Sleep-disordered breathing, hypertension, and obesity in retired national football league players. *J Am Coll Cardiol* 2010;56:1432-3.
16. Czeisler CA, Quan SF, Barger LK, Lockley SW, Sullivan JP, Qadri S. Apnea: A resource for NFL players. <http://profootballapnearisk.com>. Published July 2013. Accessed January 17, 2014.
17. Chang PP, Ford DE, Mead LA, Cooper-Patrick L, Klag MJ. Insomnia in young men and subsequent depression. the Johns Hopkins Precursors Study. *Am J Epidemiol* 1997;146:105-14.
18. Chen YH, Keller JK, Kang JH, Hsieh HJ, Lin HC. Obstructive sleep apnea and the subsequent risk of depressive disorder: A population-based follow-up study. *J Clin Sleep Med* 2013;9:417-23.
19. Chen PL, Lee WJ, Sun WZ, Oyang YJ, Fuh JL. Risk of dementia in patients with insomnia and long-term use of hypnotics: A population-based retrospective cohort study. *PLoS One* 2012;7:e49113.
20. Chang WP, Liu ME, Chang WC, et al. Sleep apnea and the risk of dementia: A population-based 5-year follow-up study in Taiwan. *PLoS One* 2013;8:e78655.
21. Nowak M, Kornhuber J, Meyrer R. Daytime impairment and neurodegeneration in OSAS. *Sleep* 2006;29:1521-30.
22. Joo EY, Noh HJ, Kim JS, et al. Brain gray matter deficits in patients with chronic primary insomnia. *Sleep* 2013;36:999-1007.
23. Altena E, Vrenken H, Van Der Werf YD, van den Heuvel OA, Van Someren EJ. Reduced orbitofrontal and parietal gray matter in chronic insomnia: A voxel-based morphometric study. *Biol Psychiatry* 2010;67:182-5.
24. Harper DG, Plante DT, Jensen JE, et al. Energetic and cell membrane metabolic products in patients with primary insomnia: A 31-phosphorus magnetic resonance spectroscopy study at 4 tesla. *Sleep* 2013;36:493-500.
25. Spiegelhalter K, Regen W, Baglioni C, et al. Insomnia does not appear to be associated with substantial structural brain changes. *Sleep* 2013;36:731-7.

DISCLOSURE STATEMENT

Dr. Quan received support grant support from the National Football League Charities