

The Prevalence of Migraine and Other Neurological Conditions Among Retired National Football League Players: A Pilot Study

Findings suggest that retired NFL players may be at increased risk for migraine, depression, anxiety, chronic pain, bedwetting, essential tremor, and Parkinson's disease.

By Randolph W. Evans, MD

Roughly four years have passed since the National Football League (NFL) reached a \$1 billion settlement with former players who had accused the League of failing to warn and protect players against long-term neurological risks of repetitive head trauma.

According to the settlement, which became effective on January 7, 2017, benefits include “monetary awards for diagnoses of Death with CTE before April 22, 2015 (the Final Approval Date), ALS, Parkinson's Disease, Alzheimer's Disease, Level 2 Neurocognitive Impairment (i.e., moderate Dementia) and Level 1.5 Neurocognitive Impairment (i.e., early Dementia) (see Injury Definitions). All valid claims under the Settlement, without limitation, will be paid in full throughout the 65-year life of the Settlement.”¹

Retired players seeking to qualify for monetary awards applied to the monetary award fund (MAF) and were directed to see a physician (i.e., a board-certified neurologist, neurosurgeon, or neurospecialist) authorized to make a qualifying diagnosis.

Little is known about the prevalence of migraine in retired NFL players. I conducted a retrospective pilot study to investigate the prevalence of migraine and co-morbidities using a convenience sample of 50 retired players seen in my practice. The average age for players in the study was 45.46 years

(range between 31 and 78 years). The average time spent in the league was 8.32 years (range of three to 21 years). Additionally, the average player in the study began playing tackle football at 12.1 years of age.

An independent review board exemption was obtained, including waiver of informed consent, and data extracted was de-identified. This article is neither endorsed nor authorized by the NFL Concussion Settlement Program, the parties to, or the administrators of that settlement.

Migraine and Concussion

The evaluation of headache and migraine in the pilot study began with a complete headache history. Participants were evaluated for the presence of light and noise sensitivity during headaches.² If they were not more sensitive to light and noise during a headache than without a headache, participants were asked the following two questions:

- During a headache, would you prefer to be in bright sunlight or in a dark room?
- During a headache, would you prefer to be in a room with loud music or in a quiet room?

In total, 92% of participants reported having headaches that met International Classification of Headache Disorders, 3rd edition (beta version) criteria for migraine.³



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Pilot Study: In Brief

Background: Little is known about the prevalence of migraine among retired National Football League (NFL) players.

Objectives: To evaluate the one-year prevalence of migraine in a pilot study using a convenience sample of retired NFL players.

Methods: A retrospective analysis was performed of 50 consecutive retired NFL players, and the prevalence of migraine, depression, anxiety, chronic non-headache pain, frequent opiate use, nocturnal enuresis, essential tremor, and Parkinson's disease was evaluated. Demographics were also analyzed, including number of concussions.

Results: The one-year prevalence of migraine among the retired players was 92% (56% with episodic and 36% with chronic migraine), which is much more than the 6% with episodic and 0.5% with chronic migraine in the general adult male population. Only 4% reported migraine onset before playing in the NFL; 48% had onset while playing, and 48% after retiring with a mean age of onset of 33.0 years. The number of reported concussions occurring in the NFL, college and high school was a mean of 18.5, median 8.5, and range of zero to 155. Current depression was reported by 78% and anxiety by 86%, which is

much greater than the prevalence in the general population and among migraineurs. Additionally, 88% reported chronic non-headache pain, similar to a prior survey with 25% of those having chronic pain citing chronic opioid use. A current history of nocturnal enuresis was reported by 78% of retired players compared to up to 7% of adult males in the general population. A total of 22% of participants have essential tremor, compared to 5% of adults in the general population, and 4% of subjects have Parkinson's disease, compared to about 1% over the age of 50 in the general population.

Conclusions: The cause of the greatly increased prevalence of migraine, depression, anxiety, nocturnal enuresis, and essential tremor in this pilot study is not known. Possible causes include brain injury and chronic non-headache pain. Confirmation of these findings in a population-based sample of the approximately 22,000 retired NFL players would be of interest. Further studies may also evaluate the prevalence of cognitive impairment with neuropsychological testing, sleep-disordered breathing documented by sleep studies, obesity, stressful life events, quality of life, and diffusion tensor MRI of the brain and their relationship to migraine.

A prior study evaluating 10 retired NFL players with an average age of 36.7 years found that 43% had chronic migraine.⁴

A total of 28 players had episodic migraine (56% of all players in the study), and 18 had chronic migraine (36%). Of note, only 6% of adult men in the general population report having episodic migraine,⁵ and 0.5% reported having chronic migraine.⁶ These data suggest a far greater prevalence of both types of migraine in retired NFL players.

Among the 28 players with episodic migraine, 23 had no aura, four had attacks of migraine with and without aura, and one had attacks of migraine without headache and migraine visual aura without headaches. Of the 18 chronic migraineurs, one had migraines without and with aura. The mean age of migraine onset was 33 years (range of 12-63 years); players' onsets were during their career (48%), after retiring (48%), or before playing in the NFL (4%).

To assess the impact of headaches on the lives of these retired players, they were given the Headache Impact Test-6 (HIT-6).⁷ The mean HIT-6 score was 58.9, indicating a substantial to severe impact of headaches on the lives of retired NFL players.⁸ Yet, only 35% of players with migraines reported having seen a physician for treatment. Similar to general population studies, most migraineurs are not seeing physicians, and many may benefit from consultation.⁹

There are a number of possible reasons why migraines may have an increased prevalence among retired NFL players. For example, subconcussive impacts (i.e., the transfer of mechanical energy to the brain at enough force to injure axonal or neuronal integrity but not cause clinical symptoms¹⁰) have been shown to cause long-term neurological injury.¹¹ It is not known, however, whether subconcussive impacts alone may be a risk factor for migraine.

According to the International Classification of Headache Disorders, 3rd edition (beta version) criteria, the onset of post-traumatic headache should be less than seven days after injury.¹² However, post-traumatic headache could have a latency of weeks or months.¹³ The upper limits of post-traumatic migraine onset is not known. It is possible that the latency could be many years, similar to the long latency of post-traumatic seizures after TBI. In a randomly chosen population sample, head and neck injury within two years of chronic daily headache onset was a significant risk factor and accounted for 15% of chronic daily headache, with lifetime risk increasing with the number of head and neck injuries.¹⁴

The causes of post-traumatic migraine remain poorly understood. Possible mechanisms include diffuse axonal injury, release of excitatory neurotransmitters, impairment in cerebral vascular autoregulation, and neuroinflammation. Chronic traumatic encephalopathy (CTE) may also be associated with headaches.¹⁵

Retired players in the pilot study were provided with a definition of concussion (i.e., “knocked unconscious,

knocked cold, dazed, saw stars, or had “your bell rung”) and asked about concussion history and frequency. Results showed that 92% of players reported concussions while playing in the NFL, 60% reported concussions while playing in college, and 44% reported concussions while playing in high school. The mean number of concussions players experienced while playing in the NFL was 13, as compared to 3.2 in college and 2.3 in college and high school, respectively. The median number of concussions was 5, 1, and 0, respectively.

In a previously reported survey of 512 former players, 20% reported having at least one to two concussions, 23% reported three to four concussions, 35% reported five or more, and 12% were unsure of the number of concussions they experienced.¹⁶

It is worth noting that reports regarding the number of concussions by retired NFL players may be inaccurate due to recall bias and not being familiar with the definition of concussion.¹⁷ Players often responded to the query by asking whether the author wanted to know how many concussions they had or the number actually reported at the time. Many older players stated that they didn't understand the definition of concussion while they were playing and just had “dings.” Because they were trying to obtain compensation from the settlement fund, it is possible that some players exaggerated the number, although they were advised that the number of concussions was not used to determine whether they had cognitive impairment.

Links to Other Neurological Conditions

Depression and anxiety. In the pilot study cohort, 78% of retired players reported having depression. Of those, 11 were administered the Mini International Neuropsychiatric Interview, which revealed that eight had major depression, two had moderate depression, and one had no depression. Among 11 individuals not endorsing depression, nine also had migraine.

In the US, the one-year prevalence of major depression is about 6%, while the prevalence of persistent depressive disorder is about 2%.¹⁸ Because most of the cohort have migraine, this prevalence is even greater than general population studies in which about 30% of those with chronic migraine and 17% with episodic migraine have depression.¹⁹ A prior study of 45 randomly selected retired NFL players found depression in 33% of participants.

Anxiety was endorsed by 43 players (86%) in the pilot cohort. Of the seven patients not reporting anxiety, six also had migraine. In the general population, 7.5% report anxiety, as compared to 25% of migraineurs.

Interestingly, evidence suggests that depression and anxiety predict more migraine days.²⁰ Moreover, depression and migraine may have a bidirectional relationship where the presence of one increases the risk of the other.²¹

Composite Case History

The following composite case history is illustrative of a typical retired NFL player presenting in practice.

A 35-year-old linebacker played in the NFL for six years. He reported having a history of perhaps 20 or more concussions as a professional (he asked me to clarify regarding concussions reported while playing or total experienced concussions; described as bell rung, dings, or seeing cobwebs), two in college, and none previously. He has had progressive cognitive symptoms and depression for three years. He has also had chronic daily pain in his shoulders, neck, back, wrists, knees, and ankles since retiring from football.

He has a four-year history of migraine without aura, which have increased from one to two per week to daily in the last year and no prior headaches. He takes ibuprofen or an aspirin/acetaminophen/caffeine combination tablet daily. He has not seen a physician for the headaches and does not know the cause.

—*Randolph W. Evans, MD*

Chronic pain. Retired players in the pilot cohort were asked about the presence of chronic non-headache pain, which was defined as having pain on most or all days. Findings revealed that 44 (88%) reported chronic pain in various locations, including the neck, back, joints, hands, and feet; all except one player experienced onset while playing. Moreover, all but one in the pilot cohort experienced onset of pain while playing in the NFL. These findings are similar to another study in which 89% of retired players reported aches and pains on a daily basis.¹²

Studies have shown that non-headache pain (from the face, neck or shoulders, back, arms or hands, legs or feet, chest, abdomen or pelvic, other) increases the risk of chronic migraine.²²

One study found that 58% of migraineurs reported chronic pain (arthritis, back or neck pain, or other pain), as compared to 36% of those without headache.²³ Possible explanations include changes in the brain in response to chronic pain such as central sensitization and genetic factors.

Opioid overuse (defined as use on eight or more days per month) was reported by 11 out of 44 (or 25%) of those with chronic pain in the pilot cohort, which contrasts with previous survey findings in which 7% of retired players reported opioid use at least once per week.²⁴

Additionally, there is an increased risk of medication overuse headache (headache occurring on 15 or more days per month) with opioid use of eight or more days per month.^{25,26}

Nocturnal enuresis. The Clinical Dementia Rating worksheet²⁷ asks whether nocturnal enuresis (or bedwetting) is present and, if so, whether the individual is occasionally, frequently, or doubly incontinent. In the pilot cohort, nocturnal enuresis was reported by 78% of individuals, as compared to 7% of the general adult male population.²⁸ Among those with nocturnal enuresis, 82% experienced it occasionally and 18% frequently. Often, a spouse or girlfriend would report this problem, which the patient would reluctantly confirm.

If an increased prevalence of nocturnal enuresis is confirmed in a randomized sample or subsets (such as those with cognitive impairment on neuropsychological testing) of retired players, there are a number of possible mechanisms. Bedwetting could result from psychological factors, hypnotic use, alcohol before bedtime, or sleep-disordered breathing. The prefrontal cortex has a predominantly inhibitory function on voiding.²⁹ Traumatic injury to the prefrontal cortex due to diffuse axonal injury³⁰ or CTE³¹ could also be a cause. Traumatic injury to the posterior pituitary could result in central diabetes insipidus and overproduction of urine at night.³²

Essential tremor and Parkinson's disease. The diagnosis of essential tremor in the pilot cohort was based on physical examination (the presence of an action and postural tremor of the hands) and confirmatory history. Those excluded included players on medications that can cause postural tremor. These include amphetamines, antiarrhythmics, bronchodilators, levothyroxine, lithium carbonate, metoclopramide, methylxanthines, neuroleptics, pseudoephedrine, serotonin-norepinephrine reuptake inhibitors, selective serotonin reuptake inhibitors, tricyclic antidepressants, and valproic acid.³³

Findings from the pilot cohort revealed that 22% of retired players had essential tremor, which compares to approximately 5% of adults in the general population.³⁴ The author is not aware of prior reports of an increased prevalence in retired football players. If a significantly increased prevalence were confirmed in a randomized sample of retired players, the cause would not be certain, however, damage to the prefrontal cortex is a consideration.³⁵

Neurological exam findings consistent with Parkinson's disease, as defined by the World Health Organization's International Classification of Disease, 10th edition (required as criteria by the Court settlement), were found in two retired players (4%). One player was in his early fifties, and the other was in his seventies. Neither was aware of having Parkinson's disease. Parkinson's disease is present in about 1% of those over the age of 50 in the general population. Antecedent head trauma is a significant risk factor for Parkinson's disease.³⁶

Conclusion

This pilot study finds an increased prevalence of episodic and chronic migraine, depression, non-headache pain, nocturnal enuresis, and essential tremor among retired NFL players, compared to the general population. The retired players were part of a biased, nonrandom sample and are probably not representative of all retired NFL players. Nonetheless, findings might suggest problems present in those more symptomatic. Because the participants in the study were applying for compensation, exaggeration or malingering is possible. However, compensation is based upon the presence of cognitive impairment on neuropsychological testing or the presence of Parkinson's disease or ALS and not any of the other symptoms or findings assessed in this study.

There are approximately 22,000 retired NFL players.³⁷ Further studies of a randomized sample of retired players would be of high interest. Future studies may wish to also evaluate sleep-disordered breathing (with an overnight sleep study), obesity, and stressful life events (not evaluated in this study) that could be risk factors for chronic migraine,³⁸ as well as quality of life and diffusion tensor MRI of the brain.^{39,40} The relationship of cognitive impairment on neuropsychological testing to migraine prevalence could also be investigated. Given efforts to reduce the number of concussions, the prevalence of these problems in current NFL players is not certain. ■

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1. NFL Concussion Settlement. In RE: National Football League Players' Concussion Litigation. No. 2:12-md-02323 (E.D. Pa). Available at <https://www.nflconcussionsettlement.com/Un-Secure/FAQDetails.aspx?q=2#2>. Accessed on August 1, 2017.
2. Evans RW, Seifert T, Kailasam J, Mathew NT. The use of questions to determine the presence of photophobia and phonophobia during migraine. *Headache*. 2008;48(3):395-397.
3. Headache Classification Committee of the International Headache Society (IHS). The international classification of headache disorders, 3rd edition (beta version) *Cephalalgia*. 2013;33:629-808.
4. Conidi F. Incidence of headache in retired NFL Players. Correlation with diffusion tensor MRI Imaging and neuropsychological testing. *Neurology* 2015;84(14), 527.004.
5. Lipton RB, Bigal ME, Diamond M, et al. AMPP Advisory Group. Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology*. 2007;68(5):343-349.
6. Buse DC, Manack AN, Fanning KM, et al. Chronic migraine prevalence, disability, and sociodemographic factors: results from the American Migraine Prevalence and Prevention Study. *Headache*. 2012;52(10):1456-1470.
7. QualityMetric and GlaxoSmith Kline. HIT-6. Headache Impact Test. Available at <http://neurohealth.info/wp-content/uploads/2010/10/hit6.pdf>. Accessed on August 1, 2017.
8. Yang M, Rendas-Baum R, Varon SF, Kosinski M. Validation of the Headache Impact Test (HIT-6™) across episodic and chronic migraine. *Cephalalgia*. 2011;31(3):357-367.

9. Lipton RB, Serrano D, Holland S, et al. Barriers to the diagnosis and treatment of migraine: effects of sex, income, and headache features. *Headache*. 2013;53(1):81-92.
10. Manley G, Gardner AJ, Schneider KJ, et al. A systematic review of potential long-term effects of sport-related concussion. *Br J Sports Med*. 2017;51(12):969-977.
11. Bailes JE, Petraglia AL, Omalu BI, et al. Role of subconcussion in repetitive mild traumatic brain injury. *J Neurosurg*. 2013 Nov;119(5):1235-1245.
12. Headache Classification Committee of the International Headache Society (IHS). The international classification of headache disorders, 3rd edition (beta version) *Cephalalgia*. 2013;33:629-808.
13. Evans RW. Posttraumatic headaches in civilians, soldiers, and athletes. *Neuro Clin*. 2014;32(2):283-303.
14. Couch JR, Lipton RB, Stewart WF, Scher AI. Head or neck injury increases the risk of chronic daily headache: a population-based study. *Neurology*. 2007;69(11):1169-1177.
15. McKee AC, Stern RA, Nowinski CJ, et al. The spectrum of disease in chronic traumatic encephalopathy. *Brain*. 2013;136(Pt 1):43-64.
16. The Washington Post. NFL Retired Players Survey. May 20, 2013. Available at https://www.washingtonpost.com/page/2010-2019/WashingtonPost/2013/05/17/National-Politics/Polling/release_236.xml. Accessed on August 1, 2017.
17. Alcoso ML, Jarnagin J, Tripodis Y, et al. Utility of providing a concussion definition in the assessment of concussion history in former NFL players. *Brain Inj*. 2017;4:1-8.
18. Karg RS, Bose J, Batts KR, et al. Past year mental disorders among adults in the United States: results from the 2008-2012 Mental Health Surveillance Study. Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality Data Review. October, 2014 <http://www.samhsa.gov/data/sites/default/files/NSDUH-DR-N2MentalDis-2014-1/Web/NSDUH-DR-N2MentalDis-2014.pdf>. Accessed August 1, 2017.
19. Buse DC, Silberstein SD, Manack AN, et al. Psychiatric comorbidities of episodic and chronic migraine. *J Neurol*. 2013;260(8):1960-1969.
20. Probyn K, Bowers H, Caldwell F, Mistry D, Underwood M, Matharu M, Pincus T; CHES Team. Prognostic factors for chronic headache: a systematic review. *Neurology*. 2017;89(3):291-301.
21. Breslau N, Davis GC, Schultz LR, Peterson EL. Joint 1994 Wolff Award presentation: migraine and major depression: a longitudinal study. *Headache* 1994;34:387-393.
22. Scher AI, Buse DC, Fanning KM, et al. Comorbid pain and migraine chronicity: The Chronic Migraine Epidemiology and Outcomes Study. *Neurology*. 2017 Jul 5. [E-pub ahead of print]
23. Saunders K, Merikangas K, Low N, et al. Impact of comorbidity on headache-related disability. *Neurology*. 2008;70:538-547.
24. Cottler LB, Ben Abdallah A, Cummings SM, et al. Injury, pain, and prescription opioid use among former National Football League (NFL) players. *Drug Alcohol Depend*. 2011;116(1-3):188-194.
25. Bigal ME, Lipton RB. Excessive acute migraine medication use and migraine progression. *Neurology*. 2008; 71(22):1821-1828.
26. Thorlund K, Sun-Edelstein C, Druyts E, et al. Risk of medication overuse headache across classes of treatments for acute migraine. *J Headache Pain*. 2016;17(1):107.
27. Morris JC. The Clinical Dementia Rating (CDR): Current version and scoring rules. *Neurology* 1993;43:2412-2414.
28. Buckley BS, Lipton MC. Prevalence of urinary and faecal incontinence and nocturnal enuresis and attitudes to treatment and help-seeking amongst a community-based representative sample of adults in the United Kingdom. *Int J Clin Pract*. 2009;63:568-573.
29. Michels L, Blok BF, Gregorini F, et al. Supraspinal Control of Urine Storage and Micturition in Men—An fMRI Study. *Cereb Cortex*. 2015;25(10):3369-3380.
30. Rabinowitz AR, Levin HS. Cognitive sequelae of traumatic brain injury. *Psychiatr Clin North Am*. 2014;37:1-11.
31. Mez J, Daneshvar DH, Kiernan PT, et al. Clinicopathological Evaluation of Chronic Traumatic Encephalopathy in Players of American Football. *JAMA*. 2017;318(4):360-370.
32. Silva PP, Bhatnagar S, Herman SD, et al. Predictors of Hypopituitarism in Patients with Traumatic Brain Injury. *J Neurotrauma*. 2015;32(22):1789-1795.
33. Hedera P, Cibulik F, Davis TL. Pharmacotherapy of essential tremor. *J Cent Nerv Syst Dis*. 2013;5:43-55.
34. Louis ED, Ottman R, Hauser WA. How common is the most common adult movement disorder? estimates of the prevalence of essential tremor throughout the world. *Mov Disord*. 1998;13(1):5-10.
35. Chunling W, Zheng X. Review on clinical update of essential tremor. *Neuro Sci*. 2016;37(4):495-502.
36. Nicoletti A, Vasta R, Mostile G, et al. Head trauma and Parkinson's disease: results from an Italian case-control study. *Neuro Sci*. 2017 Jul 26. [Epub ahead of print]
37. Dale, MD. Judge reminding NFL retirees of concussion settlement. U.S. New & World Report, February 8, 2017. Available at <https://www.usnews.com/news/us/articles/2017-02-08/nfl-concussion-hearing-wednesday-to-be-aired-live-online>. Accessed August 1, 2017.
38. May A, Schulte LH. Chronic migraine: risk factors, mechanisms and treatment. *Nat Rev Neurol*. 2016;12(8):455-464.
39. Casson IR, Viano DC, Haacke EM, et al. Is There Chronic Brain Damage in Retired NFL Players? *Neuroradiology, Neuropsychology, and Neurology Examinations of 45 Retired Players*. *Sports Health*. 2014;6(5):384-395.
40. American Academy of Neurology. Press release 4/11/16. More than 40% of retired NFL players had brain injury. Available at <https://www.aan.com/PressRoom/Home/PressRelease/1453>. Accessed August 1, 2017.