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RESEARCH ARTICLE

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Multisystem afflictions in former National Football League players

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Abstract

Background: The long-term health consequences of participation in American style football (ASF) are not well understood.

Methods: We conducted a retrospective cohort study of men who had played in the NFL after 1960. Participants were studied using a standardized self-administered questionnaire designed to determine both the exposure history to ASF and the prevalence of chronic pain, sleep apnea, cardiometabolic disease, and neurocognitive impairment. Logistic regression and negative binomial regression models were used to assess associations between age, ethnicity, body-mass index during professional football career, field position, and football career duration with individual and multiple afflictions.

Results: In this cohort of former NFL players (n = 3745), approximately one quarter of the eligible former players (27%) reported two or more medical afflictions (chronic pain, cardiometabolic disease, sleep apnea, or neurocognitive impairment). Career duration was significantly associated with an increase in the number of comorbidities. Age, race, and body-mass index were associated with all affliction categories, other than neurocognitive impairment, which was similarly prevalent in middle-aged players and older players. Earlier age when first playing the sport was protective against cardiometabolic affliction.

Conclusions: Former NFL players report significant combinations of cross-system afflictions. Future work will be required to determine mechanistic underpinnings. However, attention to the whole player, rather than specific organ systems seems critical to improve long-term health outcomes in former ASF professional athletes.

KEYWORDS
aging athlete, epidemiology, football (American), medical aspects of sport

1 | INTRODUCTION

The long-term health implications of participation in American style football (ASF) is under significant debate. Previous research has described arthritis,[1] cardiometabolic abnormalities,[2] pain,[3] sleep apnea,[4] and neurological issues.[5] High profile cases of prominent former ASF athletes and their health burdens are reported on mainstream media outlets, which have furthered both the public and scientific discourse. There is a prevalent notion that former ASF players have poorer long-term health outcomes despite the understanding that early participation in sport and exercise can predict later-life behaviors [6] and protect against certain medical afflictions.[7]

Body-mass index (BMI), age, race and sex are all well-established risk factors for conditions such as cardiometabolic disease, sleep apnea and dementia in the general population,[8,9] and may represent predictive risk factors in former ASF players. Furthermore, the unique demands of participation in professional ASF may place players at greater risk for certain medical conditions later in life, whereby football-specific variables such as position, career injuries, and age at first participation in the sport have been associated with certain medical conditions.[10-12]

A large majority of previous research on the health of former ASF players has been limited to the study of a single condition. Our previous work has demonstrated that former NFL players report afflictions in specific categories of medical conditions, including pain, sleep apnea, cardiometabolic disease, and neurocognitive impairment.[13] Emerging evidence suggests that cross-correlations between certain medical conditions, such as sleep apnea and cardiovascular pathology (impaired vascular and left ventricular diastolic function),[14] may occur in ASF players also. Thus, the study of individual medical conditions in isolation may not capture the full extent to which ASF participation can affect long-term health and affliction in former players.

The aim of this study was two-fold: to quantify multisystem afflictions in former NFL players and to assess the impact of player characteristics and career history on the presence of both single and multisystem conditions. We hypothesized that former ASF players would show afflictions in more than one biological system, and that the characteristics of football exposure would be linked to single and multisystem comorbidities in cardiometabolic disease, sleep apnea, chronic pain, and neurocognitive impairment.

2 | METHODS

2.1 | Study design

The present study collected and analyzed questionnaire data from a cohort of former National Football League (NFL) players. Questionnaires asked players to self-report their demographics, exposure to the game, and medical diagnoses. An attempt was made to contact all living former players who participated in the American or National Football League from 1960 to present. Before 1960, there were substantial changes to the rules and equipment used by players. Specifically, the transition to the helmet with a hard, plastic shell was complete and well-established by 1960, although changes to the interior padding and facemask continue until the present day. Former players were defined as any player that touched the NFL (training camp, rookie camp, practice squad, or drafted by an NFL team), and were no longer playing in the NFL. After testing that there was no difference in response pattern to email or paper mailed questionnaires, we sent email or paper surveys to 13 200 former players with either a home or email address that did not return as undeliverable. Any duplicate responses (those who returned both a paper and electronic survey) were removed. Of the 13 200 reachable players (as of 2015), 3745 completed the survey (March 2017; ~28% response rate). To estimate the representativeness of our sample in regard to the wider former NFL player population (who did not respond to our questionnaire) we calculated the difference in our study variables from our sample compared to the nonresponders via data available from *Pro-Football Reference (PFR), an online source for historical data regarding NFL teams, players, scores and leaders*.[15] The study was approved by an institutional review board.

2.2 | Player characteristics

We categorized age (reported in years) into groups of 34 or younger (24-34), 35 to 54, and 55 or older. Race was divided into three categories; White, Black and other, where other includes American Indian/Alaskan Native, Native Hawaiian/Pacific Islander, Asian, Hispanic, and other. Professional body-mass index (BMI) was calculated (body weight [average annual during professional playing time] in kilograms divided by height [current] in meters squared).

2.3 | Football exposure

Football exposures examined included position played, number of seasons played in NFL, and age at which first began to play organized ASF. Position played was categorized as linemen (offensive and defensive) and nonlinemen (all other positions). Linemen were those participants who had exclusively played this position during their career. Position was categorized this way based on expected differences in body habitus and composition, as well as hit frequency/type. This categorization is consistent with the literature suggesting linemen may be at higher risk of a number of medical conditions.[1,16] The number of professional seasons played was reviewed for outliers, anyone reporting more than 15 years of professional play (N = 100), not exclusive to the NFL, was verified using *PFR*. Where there was a discrepancy of over or under three professional years self-reported from public records reviewed (*PFR*) the item was set to missing (N = 40). The age at which players first

began organized football was restricted to ages 4 to 25 to remove outliers (N = 10).

2.4 | Affliction categories

Four affliction categories were created based on the medical conditions highlighted via former player advisors and the medical and scientific literature. These were: sleep apnea, chronic pain, cardiometabolic disease, and neurocognitive impairment. These affliction categories were assessed via self-reported answers to the questionnaire regarding medical diagnoses. As misconceptions about health and disease are common,[17] we attempted to avoid misclassification of medical conditions by asking a player if they had ever been prescribed a medication for a given condition. For medical conditions less likely to be susceptible to misconceptions, such as Alzheimer disease, heart attack, or stroke, we asked "Has a health care provider ever told you that you have any of the following diagnoses or health outcomes?". The affliction categories were defined as follows: Sleep affliction was defined as having been diagnosed with sleep apnea. Pain affliction was defined as reporting that pain medication for chronic pain was prescribed by a medical provider and was still being taken at the time of survey response. Cardiometabolic affliction was defined as either being diagnosed with a heart attack or stroke by a medical provider, or currently taking medication for at least two of the following three medical conditions: diabetes, hypertension, and high cholesterol. Neurocognitive affliction was defined as being diagnosed by a medical provider with dementia or chronic traumatic encephalopathy (CTE) or having ever been prescribed by a physician medication for memory loss. Examination of multisystem comorbidity was characterized by assessing those players who met the criteria for one, two, three, or all four affliction categories.

2.5 | Statistical analysis

Analysis of individual affliction types were compared using logistic regression to assess the independent associations of player characteristics and football exposure, adjusting for all covariates, with affliction (afflicted or not afflicted). Results are reported as odds ratios where significance of $P < 0.05$ is measured by a confidence interval that does not include one. Due to overdispersion in the affliction count, a negative binomial regression model was used to assess the relationship of player characteristics and the number of simultaneous afflictions. Regression coefficients represent the log of the expected count of the dependent variable for each one-unit change in the predictor variables. We present the exponentiated coefficients (called mean ratio [MR]), which indicates the fold change in the count as the exposure variable increases by one unit. We used χ^2 statistics and t tests to test the difference in study variables between our responders and nonresponders (from *PFR*) as an estimate of sample representativeness. For this representativeness estimation, age from *PFR* (where only date of birth is provided) was calculated by assuming that the nonresponders filled out the questionnaire on the last date a responder did. Statistical analyses were performed in Stata, version 14 (Statacorp LLC, TX).

TABLE 1 Player sample characteristics

Age (y), n/N (%)	
34 or younger	465/3743 (12)
35-54	1528/3743 (41)
55 or older	1750/3743 (47)
Race,[a] n/N (%)	
White	2183/3698 (59)
Black	1370/3698 (37)
Other[b]	145/3698 (4)
Position, n/N (%)	
Linemen[c]	1093/3733 (29)
Nonlineman	2640/3733 (71)
Number of afflictions, n/N (%)	
0	1561/3669 (43)
1	1132 (31)
2	623/3669 (17)
3-4	353/3669 (9)
Professional BMI, mean (SD), kg/m^2	30.4 (4.2)
Number of seasons played, mean (SD)	6.7 (3.8)
Age when started football, mean (SD), y	11.8 (3.1)

[a]Subjects had the option to select more than one category.
[b]Other includes American Indian/Alaskan Native, Native Hawaiian/Pacific Islander, Asian, Hispanic, other, and multirace.
[c]Only played the offensive or defensive line. Special teams were classified as nonlinemen.

3 | RESULTS

3.1 | Player demographics

At the time of analysis, a total of 3745 former players had responded to our questionnaire. Most respondents were White (59%), with Black players representing 37% and "other" representing 4% of the total cohort. Linemen (offensive and defensive) represented 30% of respondents. The mean age ± standard deviation of the respondents was 52 ± 14 years. Average weight during professional play was 239 ± 42 lbs; the mean BMI during professional play was 30 ± 4. Respondents played an average of 7 ± 4 years professionally and were 12 ± 3-years of age when they first played organized football (Table 1).

3.2 | Individual affliction associations

A quantification of individual medical conditions reported by our cohort of former players is reported elsewhere.[13] Age was significantly associated with greater odds of sleep apnea, chronic pain, and cardiometabolic affliction, in which older players (55 years and above) were significantly more likely to be afflicted in these categories compared to younger players (Table 2). Players over 35 years of age, however, had similar odds of neurocognitive affliction compared to younger players. Race and BMI were also predictive of afflictions in all categories (Table 2). Black players were approximately one and a half times more likely to report afflictions in all categories compared to White players, and those

TABLE 2 Logistic regression coefficients for player characteristics on individual health domains

	Sleep affliction OR (95% CI)[c]	Pain affliction OR (95% CI)[c]	Cardiac affliction OR (95% CI)[c]	Neurocognitive affliction OR (95% CI)[c]
Age, y				
34 & under	Referent group	Referent group	Referent group	Referent group
35-54	2.99 (2.09-4.27)	1.76 (1.32-2.36)	3.33 (2.20-5.06)	2.16 (1.50-3.11)
55 and above	5.64 (3.91-8.15)	3.44 (2.56-4.63)	13.03 (8.57-19.82)	2.75 (1.89-3.99)
Ethnicity[a]				
White	Referent group	Referent group	Referent group	Referent group
Black	1.56 (1.30-1.86)	1.67 (1.42-1.97)	1.57 (1.32-1.86)	1.70 (1.41-2.05)
Other[b]	1.94 (1.33-2.83)	0.87 (0.59-1.30)	0.87 (0.57-1.33)	1.20 (0.77-1.86)
Position				
Nonlinemen	Referent group	Referent group	Referent group	Referent group
Linemen	1.10 (0.88-1.39)	1.05 (0.85-1.30)	0.88 (0.70-1.10)	0.99 (0.77-1.28)
Professional BMI (5-unit increase), kg/m^2	1.67 (1.46-1.92)	1.26 (1.11-1.42)	1.38 (1.21-1.58)	1.05 (0.91-1.21)
Per professional season played	1.00 (0.98-1.03)	1.02 (0.99-1.04)	0.99 (0.96-1.01)	1.01 (0.99-1.04)
Per year of age when started football	1.01 (0.99-1.04)	0.99 (0.96-1.01)	1.04 (1.01-1.07)	1.02 (0.99-1.05)

Abbreviations: BMI, body-mass index; CI, confidence interval; OR, odds ratio.
[a]Subjects had the option to select more than one category.
[b]Other includes American Indian/Alaskan Native, Native Hawaiian/Pacific Islander, Asian, Hispanic and other.
[c]Adjusted (for all other covariates) odds ratio; 95% CIs are significant in those which do not include 1.0.

who listed "other" for ethnicity were almost twice as likely to report sleep apnea compared to White players. Number of seasons played was essentially unrelated to any of the afflictions. However, older the age when participation in organized ASF first began increased the odds of cardiometabolic affliction significantly but marginally by 4% (Table 2).

3.3 | Multisystem afflictions

Approximately 27% of players were categorized as having more than one affliction and 9% had more than two, (Figure 1A). Figure 1B illustrates the combinations of afflictions reported by those

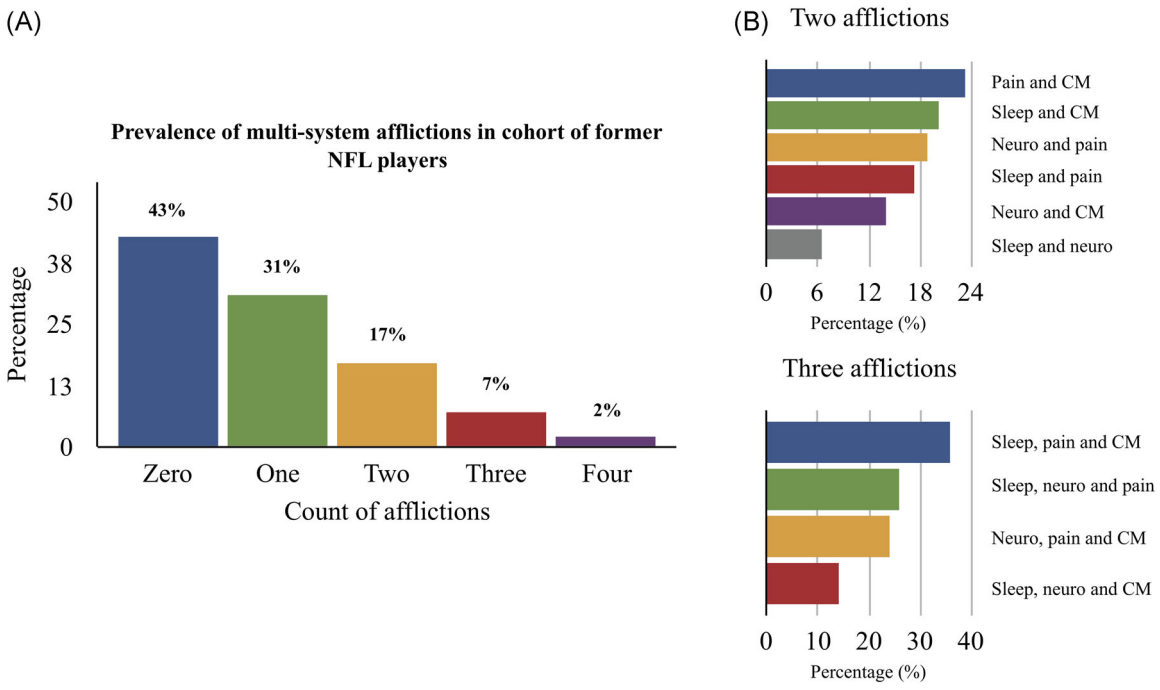

FIGURE 1 Prevalence of multiple afflictions within the cohort of former ASF players. A greater numerical proportion of players reported at least one affliction than none (A). The combinations of multisystem afflictions for those who report two and three afflictions, respectively, are shown in (B). The most common coupling of multisystem afflictions were pain, cardiometabolic (CM), and sleep apnea. ASF, American style football; NFL, National Football League [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 3 Player characteristics and number of health domain afflictions (0-3)[a]

	Mean Ratio (95% CI)[d]	*P*
Age, y		
34 and under	Referent group	
35-54	2.03 (1.73-2.39)	<.001
55 and above	3.38 (2.88-3.97)	<.001
Race[b]		
White	Referent group	
Black	1.36 (1.27-1.47)	<.001
Other[c]	1.10 (0.92-1.31)	.67
Position		
Nonlinemen	Referent group	
Linemen	1.03 (0.94-1.13)	.49
Professional BMI (5-unit increase), kg/m^2	1.19 (1.13-1.25)	<.001
Per season played	1.01 (1.00-1.02)	.01
Per year of age when started football	1.01 (1.00-1.02)	.06

Abbreviations: BMI, body-mass index; CI, confidence interval.
[a]3 = 3+ due to small cell issues in the four categories.
[b]Subjects had the option to select more than one category.
[c]Other includes American Indian/Alaskan Native, Native Hawaiian/Pacific Islander, Asian, Hispanic and other.
[d]Adjusted mean ratio; 95% CIs.

with two and three afflictions, respectively. Cardiometabolic and pain afflictions were the most common comorbid afflictions for those with two types of afflictions (23%), whereas for those reporting three afflictions, cardiometabolic, pain, and sleep apnea (36%) were the most common.

The MR of multisystem afflictions was significantly higher in middle-aged players and older players compared to players aged 34 or younger after adjusting all other variables in the model (Table 3). That is, players aged over 54 years were found to have a mean fold increase in the number of multisystem afflictions roughly three times greater than those aged 34 and under. Black players were also significantly more likely to have more afflictions compared to White players. Linemen did not have a greater fold increase in multiple afflictions compared to nonlinemen, but for every 5-unit increase in professional BMI, a 19% increase in multisystem afflictions was found. In contrast to the individual afflictions not being associated with the number of professional seasons played, having multiple afflictions was significantly associated with professional seasons played. While an older age at which players began to play organized football was associated with more afflictions, this did not reach statistical significance at the 0.05 level.

4 | DISCUSSION

More than half of the former NFL players in our cohort reported having at least one affliction, either sleep apnea, chronic pain, cardiometabolic disease, or neurocognitive impairment. Age was a significant predictor of all afflictions apart from neurocognitive afflictions. Middle-aged former players were just as likely to report neurocognitive impairment as older players, a finding which contributes to the growing understanding of an association between ASF participation and neurocognitive impairment that is above and beyond that which can be explained by aging alone. Multisystem afflictions were prevalent among our cohort with just over a quarter of former players reporting two or more afflictions. This prevalence of multisystem afflictions is higher than the one reported in the general population (21%).[18,19] Career duration was marginally predictive of multiple afflictions, whereas earlier age when first starting organized ASF appeared to be protective against cardiovascular affliction.

Previous research on the health of former and current ASF players has mostly been limited to the study of single system afflictions.[1,2,4,20] While our previous work[13] confirmed the presence of chronic health conditions (pain, cardiometabolic disease, sleep apnea, and neurocognitive impairment) previously described in the literature,[1-5] the results of this paper are novel and notable. We found that more than one-quarter of former players reported afflictions in multiple cross-system morbidities. Multisystem afflictions are key contributors to overall morbidity, long-term disability, poorer functional quality of life, treatment complications, and mortality.[18] Emerging evidence suggests that coupling of cross-system comorbidities within ASF players may be particularly prevalent from a rather early age.[14] Our results reveal the most common coupling of multisystem afflictions between cardiometabolic, sleep apnea, and pain. This is consistent with a recent study of collegiate ASF athletes that found impairments in measures of arterial stiffness and left ventricular diastolic function in those with sleep disordered breathing (defined as ≥5 on the apnea-hypopnea index), compared to those without sleep disordered breathing.[14] The understanding that cross-system comorbidities are present in former ASF players emphasizes the importance of targeted screening for multiple afflictions as well as the importance of future work to identify linking pathobiological processes.

The etiology of the development of multisystem comorbidity in former ASF players is unknown and the physiological correlates are likely to be complex, an understanding of which may lead to novel risk factors for postretirement diseases. In the general population age, race, and body habitus are common risk factors for individual afflictions [8,21-23] and our results suggest these are similar in former players. ASF participation is associated with atypical player phenotypes unique to the game that may also contribute to the development of multisystem afflictions. High training-associated static hemodynamic stress and low aerobic conditioning (especially in linemen) is common,[24] as is deliberate body-mass gain[13] and high-calorie diets,[25] routine use of nonsteroidal anti-inflammatory drugs,[26] and the use and misuse of opioids.[3] Repetitive blunt trauma to both the body and head is also an inherent aspect of participation in ASF caused by player-player impacts and the culminative effect of more years of this type of exposure appears to increase the number of later-life multisystem afflictions.

Whereas older age predicted cardiometabolic, pain and sleep apnea afflictions, it was not predictive of neurocognitive impairment. Younger (35-54years) and older (≥55 years) players had similar odds of reporting this affliction. An assumed link between football exposure and cognitive impairment in the public eye may cause bias regarding memory loss medication usage among former players (for which ~70% met the fulfillment criteria for this affliction category) and a potential selection bias in our study (those players who are more impaired/more concerned) may have increased the prevalence rate of this affliction category. Nevertheless, given that the age-standardized prevalence of all cause dementia in over 60-year-olds is between 5% and 7%,[27] the proportion of players who reported neurocognitive affliction in our cohort (17%; see Churchil et al[13]) is significantly large enough to still be a concern even if neurocognitive affliction is absent in all of the eligible former players not recruited into this study. Neurocognitive impairment associated with repetitive head trauma [5] and a trend towards early onset of Alzheimer's disease compared to the US general population[11] have previously been reported in former NFL players. While longitudinal studies are required to fully establish the incidence rate of dementia diagnosis, our results further corroborate the associations between ASF participation and neurocognitive issues, especially among younger former players. In this context, the finding of high prevalence of multisystem comorbidities is potentially particularly relevant since, for example, sleep apnea can accelerate the progression of dementia.[28]

Previous research has suggested that prognostic implications of certain risk factors for cardiometabolic disease in the general population, such as obesity,[29] hypertension,[30] and arterial stiffness[31] are comparable in ASF players.[2,4] Certain protective factors for cardiometabolic afflictions however, such as adherence to sport and exercise, are likely to be present in athletes, and especially present in those who begin playing ASF earlier. Early-life patterns can predict later-life behaviors, such as physical exercise,[6] which is associated with a 20% to 30% reduction in cardiovascular disease.[7] Our results suggest that those players who avoided early-life comorbidities and who began ASF participation earlier were less likely to develop cardiometabolic afflictions in later life. Consequently, while certain factors associated with the game are related to other comorbidities, early participation in ASF may promote certain lifestyle factors, or be related to certain body habitus (larger players who may have been drafted into the game later, purely based on body size), which are ultimately protective against the development of cardiometabolic afflictions.

The findings here should be interpreted in light of their limitations. While we attempted to minimize misclassification of medical conditions with our survey questions, accuracy of reporting health conditions is subject to the limitations of self-reported data. Nonetheless, accuracy in the reporting of certain health conditions through this type of survey study design has been reported in other populations.[32] The selection bias regarding the type of former player who enrolls in the study is also a limitation. It is not possible to know whether players more or less afflicted in the medical conditions studied were more or less likely to enroll. We had a response rate of ~28%. When we compared our participants to the contacted nonparticipants using data publicly available on *ProReference Football*, we found the mean age was likely to be representative of the overall population (53.3 ± 14.1 for responders compared to 51 ± 12.1 for nonresponders). Although significant differences in weight (232.8 ± 38.3 pounds for responders, 229.8 ± 39.9 pounds for nonresponders), years played (6 ± 3.6 for responders, 5.2 ± 3.5 for nonresponders), and the proportion of linemen compared to nonlinemen (28.5% linemen in the responders group, 20.8% linemen in the nonresponders group) existed. As such, because of these differences we must view the quantification of overall prevalence of the medical conditions among our sample of former NFL players with caution. We believe that the exposure-outcome relationships are less likely to have been affected based on selection bias as this would require former players to be more or less likely to enter the study based on both their affliction status and a certain demographic or football exposure status. Longitudinal follow-up studies and biological mechanistic insights are necessary to unveil the true extent of these afflictions in former NFL players and to develop strategies to mitigate the burden of affliction.

In summary, we show that former NFL players report both individual as well as comorbid afflictions across multiple domains. We found that while some factors inherent in those players who start the game earlier seem protective against cardiometabolic afflictions, other factors present a clear risk to early neurocognitive issues. Most relevant for long-term wellbeing, we found a high prevalence of multisystem afflictions. Quantification of intricate, multisystem afflictions and the understanding of cross-system correlates of comorbidity in former ASF players ought to lead to enhanced targeted screening and treatment.

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CONFLICTS OF INTEREST

All of the other authors named on this study are either partially or fully supported by the Football Players Health Study at Harvard University which is, in turn, sponsored by the NFLPA . The NFLPA had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication. Other authors report no potential or actual conflicts of interest.

Dr. A. Pascual-Leone serves on the scientific advisory boards for Neosync, Neuronix, Starlab Neuroscience, Neuroelectrics, Magstim Inc, Constant Therapy, and Cognito; and is listed as an inventor on several issued and pending patents on the real-time integration of transcranial magnetic stimulation with

electroencephalography and magnetic resonance imaging. He also serves on the editorial board for Circulation, and serves as an associate editor for Medicine Science Sports & Exercise. Dr. Zafonte serves on the Scientific Advisory Board of Myomo, Oxeia Biopharma, ElMINDA and Biodirection. He also evaluates patients in the MGH Brain and Body-TRUST Program, which is funded by the NFL Players Association.

AUTHOR CONTRIBUTIONS

APL, FS, LN, HT, RZ, MW, and AB participated in the conception of the study and its design. CM contributed to the data acquisition and CM and MW performed the data analysis. TM, CM, MW, AB, and APL contributed to the interpretation of the work. TM drafted the manuscript and CM, MW, AB, FS, and APL critically revised the work. All authors gave final approval for the work.

DISCLOSURE BY AJIM EDITOR OF RECORD

John Meyer declares that he has no conflict of interest in the review and publication decision regarding this article.

ETHICS APPROVAL AND INFORMED CONSENT

The institutional review board of Beth Israel Deaconess Medical Center, Boston, approved this study and all participants provided written consent before participating in the research.

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