Recurrent Concussion and Risk of Depression in Retired Professional Football Players

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Departments of [1]Exercise and Sport Science, [2]Orthopedics, and [3]Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill, NC; [4]Department of Neurosurgery, West Virginia University School of Medicine, Morgantown, WV; [5]Neuroscience Center, Waukesha Memorial Hospital, Waukesha, WI; [6]Department of Neurology, Medical College of Wisconsin, Milwaukee, WI; [7]Department of Psychiatry, Florida State University College of Medicine, Tallahassee, FL; [8]Neurosurgery Service, Emerson Hospital, Concord, MA; and [9]Neurological Sports Injury Center, Brigham and Women's Hospital, Boston, MA

ABSTRACT

GUSKIEWICZ, K. M., S. W. MARSHALL, J. BAILES, M. MCCREA, H. P. HARDING JR, A. MATTHEWS, J. R. MIHALIK, and R. C. CANTU. Recurrent Concussion and Risk of Depression in Retired Professional Football Players. *Med. Sci. Sports Exerc.*, Vol. 39, No. 6, pp. 903–909, 2007. **Purpose:** The purpose of our study was to investigate the association between prior head injury and the likelihood of being diagnosed with clinical depression among retired professional football players with prior head injury exposure. **Methods:** A general health questionnaire, including information about prior injuries, the SF-36 (Short Form 36), and other markers for depression, was completed by 2552 retired professional football players with an average age of 53.8 (± 13.4) yr and an average professional football-playing career of 6.6 (± 3.6) yr. A second questionnaire focusing on mild cognitive impairment (MCI)-related issues was completed by a subset of 758 retired professional football players (50 yr and older). **Results:** Two hundred sixty-nine (11.1%) of all respondents reported having prior or current diagnosis of clinical depression. There was an association between recurrent concussion and diagnosis of lifetime depression (χ^2 = 71.21, *df* = 2, $P < 0.005$), suggesting that the prevalence increases with increasing concussion history. Compared with retired players with no history of concussion, retired players reporting three or more previous concussions (24.4%) were three times more likely to be diagnosed with depression; those with a history of one or two previous concussions (36.3%) were 1.5 times more likely to be diagnosed with depression. The analyses controlled for age, number of years since retirement, number of years played, physical component score on the SF-36, and diagnosed comorbidities such as osteoarthritis, coronary heart disease, stroke, cancer, and diabetes. **Conclusion:** Our findings suggest a possible link between recurrent sport-related concussion and increased risk of clinical depression. The findings emphasize the importance of understanding potential neurological consequences of recurrent concussion. **Key Words:** CONCUSSION, HEAD INJURY, NEUROLOGIC, DEMENTIA, PSYCHIATRIC, NEUROLOGICAL RISK FACTORS

Traumatic brain injury (TBI) is an important public health concern; the Centers for Disease Control report that each year, more than 1.2 million Americans suffer head injury. Varying degrees of severity exist, with the majority of these injuries classified as mild. Still, over 50,000 head-related injuries result in fatalities each year, and many others result in mild to severe physical, cognitive, and psychosocial disability. The psychological sequelae are often debilitating and costly (10) and include short-term or acute, and sometimes lifelong, consequences. Depression is the most cited psychological disturbance after TBI, with prevalence rates from 6% in cases of mild traumatic brain injury (31) to 77% in more severe TBI (20) within the first year after injury. Recently, TBI has been identified as a risk factor for chronic depression, as evidenced by a prospective cohort of retired World War II veterans that were assessed for prevalence of depression several decades after the initial injury. After accounting for age, education, and health conditions, an 18.5% lifetime prevalence of depression was observed in veterans who suffered a head injury in their 20s, which was significantly

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higher than the observed 13.4% lifetime prevalence for those without a history of head injury (16).

TBI has also been identified as a potential risk factor for the occurrence (or early expression) of neurodegenerative dementing disorders, including mild cognitive impairment (MCI), Alzheimer disease, and Parkinson syndrome (1,11,13,28,29,36). Although the formal diagnosis of major depression (2) is not common among patients with Alzheimer disease (39), a depressed mood is frequent and can precede the development of Alzheimer disease. Devanand et al. (9) have reported that even a persistently depressed mood increases in parallel with cognitive failure, and that depressed mood alone was associated with increased risk of incident dementia in a study of elderly individuals. However, the presence of depressed mood also increased with increasing cognitive difficulty, suggesting that it was probably an early manifestation of disease (8).

Much of the research studying the long-term consequences of TBI has focused on severe TBI, whereas studies addressing outcomes of recurrent mild TBI on neuropsychiatric disorders have been overlooked. Despite the recent study by Holsinger et al. (16) reporting that the risk of depression was highest for those with severe head injury, researchers have generated inconsistent findings regarding the distinguishing features and factors associated with depression after TBI, especially *mild* TBI.

The high rate of cerebral concussion, or mild TBI, in certain contact sports affords a unique opportunity to examine the immediate and long-term effects of this injury. The purpose of this study was to gain a better understanding of the long-term consequences of recurrent mild TBI in a group of retired professional football players. More specifically, we investigated the relationship between sport-related concussion and prevalence of lifetime clinical depression.

METHODS

A diverse group of retired professional football players were studied, including recent retirees and those who had played professional football before World War II. All participants played for a minimum of two seasons at the professional level. A general health questionnaire was sent to all living members of the National Football League Player's Association–Retired Section (N = 3683) through the Center for the Study of Retired Athletes. The questionnaire involved a variety of items about musculoskeletal, cardiovascular, and neurological conditions that each retired player had experienced during and after his football career. The section on neurological conditions, which was the focus of this paper, included questions about the number of concussions sustained as a player (concussion history) and the prevalence of physician diagnosed psychological and medical conditions, including depression, Parkinson disease, Alzheimer disease, and schizophrenia. The questionnaire included the Short Form 36 Measurement Model for Functional Assessment of Health and Well-Being (SF-36), which assesses health status and estimates how well a retired athlete functions with activities of daily living. From the SF-36, we calculated a physical health composite score (PCS) that includes scores of physical functioning, role physical, bodily pain, and general health, as well as a mental health component score (MCS) that includes scores of vitality, social functioning, role emotional, and mental health.

Approximately 6 months later, a second questionnaire focusing on memory and issues related to MCI was sent to a subset of 1754 retirees. The subset was comprised of all respondents from the original health questionnaire who were ages 50 and older. The same instrument was also sent to an informant (spouse or close relative) to collect collateral data on any cognitive problems exhibited by the retiree but not personally reported on the retiree's instrument. From the MCI questionnaire, we captured data relative to sadness and feelings of depression, which were cross-tabulated with the results from the original general health questionnaire. Before completing both questionnaires, it was explained that participants would not be identified and that research records would be kept confidential. By completing and submitting the survey, participants were acknowledging and consenting that they agreed to take part in this research study, which was approved by the biomedical internal review board at the University of North Carolina at Chapel Hill.

Previous concussion was based on the player's retrospective recall of injury events and was defined on the questionnaire as an injury resulting from a blow to the head that caused an alteration in mental status and one or more of the following symptoms: headache, nausea, vomiting, dizziness/balance problems, fatigue, trouble sleeping, drowsiness, sensitivity to light or noise, blurred vision, difficulty remembering, and difficulty concentrating.

Chi-square analyses were conducted to identify associations and trends between diagnoses of depression and concussion history. The groups were stratified by concussion history (none, 1–2 previous, 3+ previous). Prevalence ratios were calculated using a binary regression model (log link, binary residual). We used the model to control for the following potential confounding factors: age, years since retirement, number of years played (in quartiles), physical component score on the SF-36, and diagnosed comorbidities including osteoarthritis, coronary heart disease, stroke, cancer, and diabetes. Level of significance for all analyses was set *a priori* at $P < 0.05$.

RESULTS

Of the original 3683 general health surveys sent to retired players, 2552 were returned, for a 69.3% response rate. Age of respondents averaged 53.8 (± 13.4) yr, with an average professional football-playing career of 6.6 (± 3.6) yr. Respondents reported having played organized football (junior high, high school, college, armed service, and professional) for an average of 15.1 (± 4.3) yr, with an average of 24.7

(± 13.7) yr since having last played. In response to the questions on concussion history, 1513 (60.7%) of the retired players reported having sustained at least one concussion during their professional playing career, 884 (36.3%; 95% CI: 34.4, 38.2) reported one or two previous concussions, and 595 (24.4%; 95% CI: 22.7, 26.1) reported three or more concussions. Of those retired players who had sustained concussions, more than half reported experiencing loss of consciousness (817; 54.0%; 95% CI: 51.5, 56.5) or memory loss (787; 52.0%; 95% CI: 49.5, 54.5) from at least one of their concussive episodes. We asked players whether they considered their concussive injuries to have impacted their cognitions later in life. Of the retirees who had sustained one or two previous concussions, 102 (11.5%; 95% CI: 9.4, 13.6) reported that the injuries have had a permanent effect on their thinking and memory skills as they had gotten older. The number and prevalence increased to 185 (31.1%; 95% CI: 27.4, 34.8) in those with three or more previous concussions, suggesting a positive association between a higher number of concussions and the perception that those concussions now negatively affect cognitive functioning ($\chi^2 = 226.71$, $df = 4$, $P < 0.001$). Although these data reflect players' perceptions rather than clinical testing, the relatively high proportion who thought their cognition had been affected is of concern.

Analysis of responses to questions regarding clinical depression revealed that 269 (11.1%; 95% CI: 9.9, 12.3) of the 2434 respondents with complete data reported having been diagnosed previously with clinical depression. The group of retirees diagnosed with depression had lower (worse) mental component scores and physical component scores on the SF-36 compared with retirees not diagnosed with clinical depression (Table 1). There was an association between recurrent concussion and diagnosis of depression ($\chi^2 = 71.21$, $df = 2$, $P < 0.005$), with a significant test for linear trend ($\chi^2 = 63.76$, $df = 1$, $P < 0.005$) suggesting that the prevalence increases in a linear fashion with increasing concussion history. Thus, retired players reporting a history of three or more previous concussions were three times more likely (prevalence ratio of 3.06; 95% CI: 2.29, 4.08) to be diagnosed with depression, and those with a history of one or two previous concussions were 1.5 times more likely (prevalence ratio of 1.48; 95% CI: 1.08, 2.02) to have been diagnosed with depression, relative to retirees with no concussion history (Fig. 1).

Because we were concerned this association could be confounded by other factors, we conducted a multivariate

TABLE 1. Short Form 36 mental component scale score and physical component scale score stratified by diagnosis of clinical depression.

	No Depression Diagnosis (N = 1999)	Depression Diagnosis (N = 254)	
Mental component scale	54.27 (7.96)	39.28 (12.96)	$F = 673.25$, df 1, 2251; $P < 0.001$
Physical component scale	46.11 (10.31)	42.09 (12.54)	$F = 32.56$, df 1, 2251; $P < 0.001$

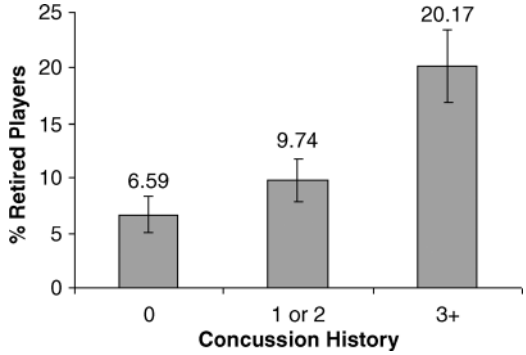

FIGURE 1—Percentage (± 95% CI) of retired players with known diagnoses of clinical depression (N = 269), stratified by number of previous concussions (none; one or two; or three or more). Test for linear trend: $\chi^2 = 63.76$, $df = 1$, $P < 0.005$.

binary regression analysis in which we controlled for the following factors: age, number of years since retirement, number of years played (in quartiles), physical component score on the SF-36, and diagnosed comorbidities including osteoarthritis, coronary heart disease, stroke, cancer, and diabetes. We observed only a small reduction in the prevalence ratios (2.58; 95% CI: 1.90, 3.55 and 1.39; 95% CI: 1.03, 1.96, respectively) after controlling for these factors, suggesting that the significant association we found between concussion history and diagnosis of depression was not attributable to confounding by these factors.

We were also concerned that the observed association between depression and concussion could be confounded by MCI. Thus, for the subset of subjects who completed the MCI follow-up questionnaire, we conducted additional analyses, controlling for diagnosis of MCI. The prevalence ratios for a history of three or more previous concussions (3.42; 95% CI: 2.12, 5.52) and for one or two previous concussions (1.79; 95% CI: 1.08, 2.94) were essentially unchanged relative to the larger group. Thus, prevalence of MCI did not confound the association between concussion history and diagnosed clinical depression.

Of those reporting any history of depression, 234 (87%; 95% CI: 83.0, 91.0) reported still suffering from the condition, and 124 (46.1%; 95% CI: 40.1, 52.1) were currently being treated with antidepressant medications. Of those 234 retirees with current symptoms of depression, 180 (76.9%; 95% CI: 71.5, 82.3) reported that the condition limits their activities of daily living to some degree. Retired players with depression were more likely to feel as though they should cut down their weekly alcohol consumption compared with those without depression (30.3% compared with 18.0%, respectively) and were more likely to be separated or divorced (14.0% compared with 8.9%, respectively).

In addition to capturing data from the general health questionnaire, follow-up MCI questionnaires were sent to all retired players over the age of 50 yr; 965 of the 1754 surveys were returned, for a 55% response rate (average age = 62.4 yr). We also obtained questionnaires from 797 retired players' spouses or close relatives. Our findings

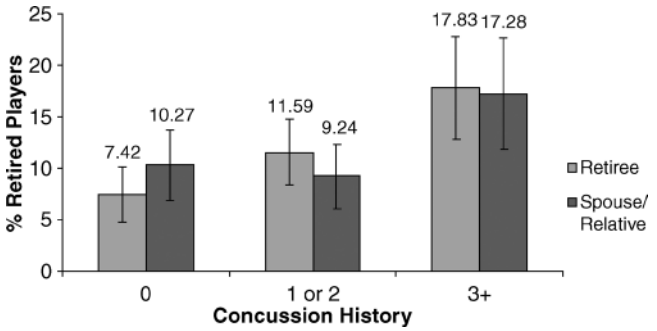

FIGURE 2—Percentage (± 95% CI) of retired players and spouses responding that the retiree has "a lot of the time or always" been unusually sad, nervous, or under a lot of stress. Data are stratified by number of previous concussions (none; one or two; or three or more). Test for linear trend: $\chi^2 = 32.96$, $df = 1$, $P < 0.005$.

revealed that a combined 111 (11.5%) of the respondents 50 yr or older reported being unusually sad, nervous, or under a lot of stress "a lot of the time" or "always." This finding was corroborated with responses by the spouse/close relative (92; 11.5%) when asked the same question, suggesting high consistency (ICC, $R = 0.84$) in the players' responses to depression diagnosis and their responses to these additional questions regarding sadness, nervousness, and stress. Further analyses of the retired players' data identified an association between recurrent concussion and the degree to which the retiree responded being "recently unusually sad, nervous or under a lot of stress" ($\chi^2 = 35.39$, $df = 4$, $P < 0.005$), with a significant test for trend ($\chi^2 = 32.96$, $df = 1$, $P < 0.005$) suggesting that the response severity increases in a linear fashion with increasing concussion history (Fig. 2). After controlling for the aforementioned factors, the association remained unchanged.

Finally, in the absence of the retired players' medical records, we wanted to better understand the validity of self-reported concussions. We asked a sample of 83 retired players to complete the identical general health questionnaire a second time between 36 and 48 months after completing the original questionnaire. Intraclass correlation analysis showed high consistency (ICC, $R = 0.90$) when concussion history questions were compared between the two questionnaires. This led us to believe that the self-reported concussion history was likely accurate.

DISCUSSION

The findings from our study of retired professional football players support the notion that lifetime prevalence of depression and feelings commonly associated with a depressed state increases as a function of previous head injury exposure. Our questionnaire return rate of nearly 70% was unusually high, providing a strong argument to support the validity of the findings. Eleven percent ($N = 269$) of the respondents reported having at least one episode of depression, a finding generally consistent with the lifetime prevalence in the general U.S. population. Our observed threefold prevalence ratio for retired players with three or more concussions is daunting, given that depression is typically characterized by sadness, loss of interest in activities, decreased energy, and loss of confidence and self-esteem. These findings call into question how effectively retired professional football players with a history of three or more concussions are able to meet the mental and physical demands of life after playing professional football. Furthermore, our findings suggest that a single concussion does not provide the risk for subsequent depression, and they provide an extension to the findings on the cumulative risk of repeat concussion demonstrated in collegiate football players (14). In combination, these studies suggest that football players with three or more concussions are at a threefold risk for sustaining future concussions, with a subsequent threefold risk of being diagnosed with clinical depression compared with those with limited or no prior history.

Depression is common after TBI of all severities (21,33), especially in those involving more severe TBI (1,12,16,20). Our sample included a unique group, retired professional football players, who, for the most part, experienced mild TBI combined with a number of subconcussive impacts, which also may have contributed to an increased likelihood for neurologic decline. In considering our findings, it is important to recognize that individuals suffering from chronic pain are at an increased risk for experiencing depressive states (3,7). This creates a potential confounder when studying professional football players who often experience significant postcareer pain resulting from the many musculoskeletal injuries sustained during their playing days. Because our analysis controlled for these factors, we believe that the identified associations between depression and past concussions are not spurious.

Our findings also suggest that, in general, retired professional football players who have a history of concussion and depressive episodes report greater physical limitations that interfere with their ability to perform daily physical activities compared with those without depression. The SF-36 results for mental and physical functioning reveal that those with a history of depression are more likely to be restricted by muscle and joint pain, feel helpless, have difficulty sleeping, and, in general, feel as though their health is declining. Individuals with a history of depression also reported more alcohol-related problems and were more likely to be separated or divorced.

One of the challenges in studying the association between prior head trauma and depression is that both may be accompanied by cognitive complaints. Furthermore, the cooccurrence of perceived cognitive problems and symptoms of depression has been cited repeatedly in the literature (2,5,30), with one study identifying neuropsychiatric symptoms to be present in 43% of MCI patients within the past month, and depression occurring in 20% of those individuals (23). The perceived cognitive problems reported by patients with depression have been illustrated more

objectively through neuropsychological studies (4,17,40). However, no studies have differentiated between cognitive deficits resulting from mild TBI and depression.

Moreover, researchers have suggested that postconcussion syndrome results from a combination of factors, including biological effects, psychological factors, psychosocial factors (broadly defined), and chronic pain (15,19,24). Many of the specific depressive symptoms are similar to the postconcussion syndrome, making it difficult to distinguish between depression that is secondary to the head trauma and symptomatology consistent with persistent postconcussion syndrome (18). The diagnosis criteria for major depression include the following symptoms: a) diminished ability to think or concentrate, b) indecisiveness, c) fatigue or loss of energy, d) sleep problems, and e) irritability, excessive worry over one's health, and persistent headaches (2). Common lifestyle changes and psychosocial problems, many of which were described by subjects in our study, include strained social relationships, marital and family distress, occupational problems, academic problems, and substance abuse (2).

Despite the challenges of differentiating between these interacting factors, we are confident that our controlled analyses (controlling for MCI and other physical comorbidities) suggest a real association between prior concussions and diagnosis of depression. The next intriguing question becomes, why are prior mild TBI linked to clinical depression?

Explanation for the association between TBI and depression is not fully understood, although several causes have been postulated. These include neurobiological factors such as direct neuroanatomic and neurochemical effects of TBI on mood. Recent studies have found correlations between major depression and structural changes in the brain. Specifically, individuals diagnosed with major depression have smaller hippocampal and amygdala volumes (34,35), structural and morphological changes in the prefrontal and orbitofrontal cortex (22), and basal ganglia structures (6). These structures are all intensively interconnected and are believed to compose a neuroanatomical circuit (26) that plays a key role in mood regulation. The vast majority of head injuries described in our study were mild in nature.

Several psychosocial correlates between TBI and depression have been identified. The most common correlate is the disruption of social relationships. This occurs with family members who bear the burden of long-term care for the TBI patient, and it also occurs among friends and coworkers of the TBI patient (25). Old friendships are often disrupted, and it is often difficult for the TBI patient to form new friendships. Many TBI patients may delay their return to work or never work again, which can negatively influence any relationships with coworkers. The depressed TBI patient most likely does not engage in activities that were once enjoyable; this can cause social isolation and lowered self-image. It is also important to note that any TBI patient with a history of preexisting depression is likely to suffer from bouts of depression after a head injury (12).

Our study is influenced by the limitations of any retrospective self-report study. The study is limited by the uncertainty of how well the retired players recalled the concussions sustained during their careers, and by the accuracy of reporting memory problems and diagnosis of MCI. Recent literature has reported selective preservation of older information in subjects with Alzheimer disease–related dementia, suggesting that recollection of events involving prior injuries is likely in these retired athletes (32). The purpose of the spouse/close-relative questionnaire was to confirm the retired players' memory status and any physician-diagnosed MCI. In cases where there was disagreement in the responses of the retiree and the spouse/relative, phone calls and medical records were used when possible to confirm the diagnosis. When the difference in responses could not be reconciled, the case was eliminated from the analyses. Furthermore, there are several obvious methodological limitations to studying the association between TBI and depression. These limitations include, but are not limited to, the facts that 1) varying diagnostic criteria for TBI, and severity of TBI, exist; 2) cases involving single episodes of depression are often collapsed with cases involving recurrent episodes of depression; and 3) a wide variety of depression-grading scales have been used in the literature. Although much of the literature reports that depressive symptoms are associated with specific subgroups of TBI that are probably linked to injury severity and recovery status at 6 months after injury, there is some indication that cases of mild TBI may result in a higher prevalence of depression. Alexander (1) has revealed that a *mild* TBI group (LOC < 15 min) experienced a significantly higher proportion of cases involving depression than a *severe* TBI group.

CONCLUSIONS

Our findings have implications for understanding the relationship of TBI to lifetime history of depression. TBI can result in diffuse lesions in the brain, depending on the mechanism of injury. These lesions result in biochemical changes, including an increase in excitatory neurotransmitters, which has been implicated in neuronal loss and cell death (38). A potential mechanism for lifelong depression could be this initial loss of neurons, which could be compounded by additional concussions, eventually leading to the structural changes seen with major depression. The structural changes could put the individuals at greater risk of depressive episodes, creating a positive-feedback cycle predicated on the original injury.

Depression can affect one's ability to function in multiple realms, including interpersonal relationships, productivity at work, and self-care. In older adults, depression is associated with significantly higher health care costs (37) and significant risk of functional decline (27). Our findings suggest that professional football players with a history of three or more concussions are at a significantly greater risk for

having depressive episodes later in life compared with those players with no history of concussion. The mechanism of interaction between the pathophysiology of concussion or mild TBI in these players and the lifetime risk of depression is unclear, and it warrants further investigation. Future prospective studies will be necessary to determine whether there is a causal relationship and whether such structural and biochemical changes take place after multiple concussive episodes in professional football players.

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