Association between History of Concussion and Substance Use Is Mediated by Mood Disorders

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Abstract

Understanding the impact of concussion history on mental health—mood disorders and substance use—is an essential step in characterizing the psychological and behavioral consequences of concussion and in developing effective treatments. The objective of this study was to examine the association between the history of concussion and substance abuse by investigating both its direct and indirect association via mood disorder. A secondary objective was to determine whether gender moderates the association. A comprehensive survey was administered to 4849 college-age adults that assessed history of concussion; depression, anxiety, and panic disorders using the Patient Health Questionnaire (PHQ); and substance use using the Alcohol Use Disorders Identification Test (AUDIT) (alcohol) and Cannabis Use Disorders Identification Test-Revised (CUDIT) (cannabis). Regression models were used to examine the association between concussion history and substance use. Mood disorders were entered into the model as mediators and gender as a moderator variable. Those with a history of concussion had higher panic, AUDIT, and CUDIT scores than those with no history of concussion, and AUDIT and CUDIT scores showed an interaction between concussion history and gender. The regression models revealed significant direct and indirect (via depression and panic disorder) effects of concussion history on alcohol and cannabis use, which was moderated by gender. Concussion can have long-term psychological consequences and appears to affect both mood and substance use. The results presented demonstrate that the relationship between concussion and substance use is complex with mood disorder mediating the effect.

Keywords: alcohol; anxiety; cannabis; concussion; depression; panic disorder

Introduction

IN THE UNITED STATES, approximately 1.25 million people sustain a mild traumatic brain injury (mTBI) or concussion each year.¹ Although concussion rarely results in focal brain damage, the ventromedial prefrontal cortex (vmPFC) has been found to be susceptible to damage by a concussive event.^{2,3} This damage to vmPFC has been linked to increased impulsivity and aggression that is often reported in concussed patients.⁴ Additionally, concussion has been associated with a change in baseline physiological arousal (i.e., electrodermal activation levels).^{5,6} Trauma-induced disruptions to vmPFC processing and the suppression of arousal is thought to impact the ability to anticipate negative outcomes in unpredictable/risky situations,⁷ which can trigger an increase in impulsive, aggressive, or risk-taking behavior. One such behavior is an increase in substance use that has been reported in individuals with a history of concussion.⁸

The majority of studies examining the link between substance abuse and a history of concussion have focused on alcohol use and have examined athletes or former athletes. In one such study, it was

found that 50% of individuals refrain from using alcohol after a traumatic brain injury (TBI); however, 43% of the study participants were found to be moderate or heavy drinkers.⁹ Therefore, although the majority refrained from drinking after a TBI, a large percentage did use alcohol in excess. Additionally, Alcock and colleagues¹⁰ reported that there were no differences in alcohol consumption levels between athletes and non-athletes when both groups were free of concussion history. However, individuals with a history of concussion, regardless of athletic status, drank more per outing than those without a history of concussion, suggesting a relationship between concussion and drinking behavior independent of whether the participant is an athlete. Using an innovative protocol, Martin and associates¹¹ examined bar patrons in a college town. They obtained hazardous drinking scores, performed breathalyzer exams, and obtained concussion history from people at a local bar. The study found that hazardous drinking predicted concussion history, reiterating a strong connection between substance abuse, in this case alcohol, and concussion.

Although concussive injury-related changes in risk-taking behavior and arousal may be responsible for increased substance use,

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emerging evidence begins to underpin the possibility of an indirect influence of mood disorders. Several studies have found that concussion is related to an increase in mood disorders (depression and anxiety; see article by Hutchison and co-workers¹² for a review). Briefly, a significant link between depression and history of concussion has been observed in studies that examined clinical depression,^{13,14} studies using standardized questionnaires that quantify depressive symptoms,^{15–20} and the relationship between depression and concussion remained after accounting for familial history of depression and alcohol dependency.¹⁷ Individuals with mood disorders are also at risk for developing substance abuse, both alcohol and cannabis.^{21–25} However, the three-way relationship among a history of concussion, substance abuse, and mood disorders remains unclear.

The objective of this study was to examine the direct impact of history of concussion on substance abuse (alcohol and cannabis) as well as a potential indirect effect mediated by mood disorders. We also examined whether gender moderates these relationships, because women are suggested to have increased risks of being diagnosed with mood disorders,^{26,27} having more severe consequences from substance use disorders,^{28,29} and sustaining concussion,³⁰ as well as having a prolonged recovery duration from concussion.^{31–32}

Methods

Participants

College-age adults ($n=4849$) completed a series of survey questionnaires, as part of an introductory psychology course at Indiana University. The study was conducted in a span of 2 years (2015–2017). Inclusion criterion included being enrolled in the introductory psychology course. Conditional exclusion criterion for the final analysis was reporting a non-binary gender identification. The research protocol was approved by Indiana University's Institutional Review Board for the protection of human subjects.

Measures

A survey with questions regarding concussion history, current physical and mental health, and sociodemographic characteristics was administered. Concussion included head trauma, TBI, or concussion. The measure was dichotomous with “1” denoting a history of concussion and “2” denoting no history of concussion. The following mental health scales were included.

Patient Health Questionnaire (PHQ): Depression, Anxiety, and Panic disorder. The PHQ was employed for the assessment of panic disorder, other anxiety disorders, and depressive disorders.^{31–35} Depression was assessed using the depression module of the PHQ (PHQ-9).³⁶ Each of the nine PHQ-9 depression items describes one symptom corresponding to one of the nine diagnostics in the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (DSM-4). Anxiety disorder was assessed using the anxiety module of the PHQ (GAD-7).³⁶ Panic disorder was assessed using the panic disorder module of the PHQ.³⁶

Alcohol Use Disorders Identification Test (AUDIT). The AUDIT³⁷ is a 10-item screening tool developed by the World Health Organization (WHO) to assess alcohol consumption, drinking behaviors, and alcohol-related problems.

Cannabis Use Disorders Identification Test-Revised (CUDIT). The CUDIT is a brief, eight-item screening measure.³⁸ It is a valid measure for the identification of likely cases of DSM-5 cannabis use disorder and is a screening tool to identify problematic cannabis use.

Statistical analysis

An analysis of variance (ANOVA) with concussion history and gender as factors was performed on the measures of mood and substance use using SAS version 9.4. Statistical regression models predicting AUDIT and CUDIT scores with concussion history as the predictor, mood measures (depression and panic) as a mediator, and gender as a moderator were calculated. Analyses were performed using Process,³⁹ model 7, implemented in SPSS version 24.

Results

Nine participants were removed from the analysis because they had a non-binary gender identification and an additional seven participants failed to report their history of concussion. As a result, data from 4833 subjects were used in the final analyses. Demographic information is presented in Table 1.

Group differences

A two-factor ANOVA with concussion history (a binary yes/no) and gender (women vs. men) as factors was performed on the measures (see Table 2 and Fig. 1 for results). As shown, whereas depression and anxiety failed to show main effects of concussion, panic disorder had a significant main effect of history of concussion. All mood disorder scales showed a significant effect of gender with women having higher scores than men. Both the AUDIT and CUDIT revealed significant effects of both concussion and gender as well as an interaction between the two. Individuals who have a history of concussion have higher scores on both measures and men have higher scores than women.

Depression models. Regression models were used to characterize the relationship between alcohol and cannabis (outcome measures) use with a history of concussion (predictor) and depression symptoms (mediator). Gender was also entered into the model as a factor that may moderate the effect of concussion history.

When examining CUDIT, the results show that concussion history and gender have a small but significant effect on depression ($F[3,4829]=4.64$, $p=0.0031$, $R^2=0.0029$) (see Fig. 2); however, the betas were not significant and neither was the interaction between concussion history and gender. Additionally, concussion history and depression have a significant effect on CUDIT ($F[2,4830]=46.95$, $p\leq 0.0001$, $R^2=0.019$). Percentile bootstrap 95% confidence intervals were computed using 5000 iterations to test the indirect effect of concussion history, mediated by depression, and the moderated (by gender) mediated effect on CUDIT. The results revealed a significant indirect effect (effect = -0.5597 ; 95% interval: -0.8594 to -0.2599) as well as a moderated, mediated effect (effect = 0.0066 ; 95% interval: -0.0757 to 0.0864). Similar results were observed for AUDIT. Concussion history and gender have a small but significant effect on depression ($F[3,4820]=4.55$, $p=0.0035$, $R^2=0.0028$) (see Fig. 2); however, the betas were not significant and neither was the interaction between concussion history and gender. Additionally, concussion history and depression showed a significant effect on AUDIT ($F[2,4821]=32.22$, $p\leq 0.0001$,

TABLE 1. DEMOGRAPHIC CHARACTERISTICS

	Women	Men
<i>N</i>	3305	1528
Age (years)	19.0 ± 1.7	19.3 ± 1.6
% who had at least one concussion	21.2% (702)	30.5% (466)

TABLE 2. ANOVA RESULTS

	<i>F</i> (<i>p</i> -value)		
	<i>Concussion</i>	<i>Gender</i>	<i>Interaction</i>
Depression	1.93 (0.16)	10.43 (0.0012)	0.03 (0.87)
Anxiety	1.42 (0.23)	20.61 (<0.0001)	0.21 (0.65)
Panic	11.63 (0.0007)	50.46 (<0.0001)	1.17 (0.28)
AUDIT	47.6 (<0.0001)	25.93 (<0.0001)	9.95 (0.0016)
CUDIT	11.76 (0.0006)	82.49 (<0.0001)	6.02 (0.0142)

ANOVA, analysis of variance; AUDIT, Alcohol Use Disorders Identification Test; CUDIT, Cannabis Use Disorders Identification Test-Revised.

$R^2=0.013$). The indirect effect of concussion history, mediated by depression, on AUDIT was significant (effect= -1.1255 ; 95% interval: -1.4572 to -0.7938) as well as the moderated, mediated effect (effect= 0.0023 ; 95% interval: -0.0454 to 0.0477).

Panic models. Regression models were explored to characterize the relationship between alcohol and cannabis use (outcome measures) with history of concussion (predictor) and panic disorder symptoms (mediator). Gender was also entered into the model as a factor that may moderate the effect of concussion history.

The model testing CUDIT revealed that concussion history and gender had a significant effect on panic score ($F[3,4829]=22.01$, $p\leq 0.0001$, $R^2=0.014$); as shown in Figure 3, the betas were also significant, whereas the interaction between concussion history and gender was not. Additionally, concussion history and depression had a significant effect on CUDIT ($F[2,4830]=23.97$, $p\leq 0.0001$, $R^2=0.01$). The indirect effect of concussion history, mediated by depression, on AUDIT was significant (effect= -0.5425 ; 95% interval: -0.8438 to -0.2411) as well as the moderated, mediated effect (effect= 0.0286 ; 95% interval: -0.0232 to 0.0834). Similar results were observed for AUDIT. Concussion history and gender have a significant effect on panic score ($F[3,4820]=21.84$, $p\leq 0.0001$,

$R^2=0.0134$) (see Fig. 2); unlike with depression, the betas were also significant but the interaction between concussion history and gender was not. Additionally, concussion history and panic disorder have a significant effect on AUDIT ($F[2,4821]=26.61$, $p\leq 0.0001$, $R^2=0.011$). The indirect effect of concussion history, mediated by depression, on AUDIT was significant (effect= -1.1164 ; 95% interval: -1.4487 to -0.7840) as well as the moderated, mediated effect (effect= 0.0149 ; 95% interval: -0.0142 to 0.05018).

Discussion

The goal of the study was to examine the relationship between a history of concussion, mood disorders, and drug use (alcohol and cannabis). Previous studies have suggested that a history of concussion may lead to depression and anxiety¹² as well as an increase in substance use.¹⁰ In the current study, a regression model was used to examine the relationship between these three factors and determine whether gender moderated their relationship. The results show that history of concussion has both a direct and indirect (via depression and panic symptoms) association with both alcohol and cannabis use. Our analysis further indicated that gender was a significant moderating factor to the relationship such that the relationship between mood disorder and concussion is stronger for females than males as well as the relationship between mood disorder and substance use. These results replicate previous studies by showing an effect of concussion history on mood disorders and substance use. It also extends previous research by showing that at least part of the effect of concussion on substance use is mediated by mood disorders that may result from concussion.

There is a rather extensive literature that reports a relationship between concussion history and depression.^{13,40} For example, a retrospective cohort study conducted by Chrisman and Richardson⁴⁰ indicated that history of concussion was associated with a 3.3-fold greater risk for depression diagnosis in adolescents, after controlling for age, sex, parental mental health, and socioeconomic status. Similarly, Kerr and colleagues using longitudinal data found

FIG. 1. Bar graph depicting the depression, panic disorder, alcohol use, and cannabis use measures.

FIG. 2. Regression models with depression as the mediator and alcohol use (AUDIT) and cannabis use (CUDIT) as outcome measures. AUDIT, Alcohol Use Disorders Identification Test; CUDIT, Cannabis Use Disorders Identification Test-Revised.

a robust relationship between concussion history and a 9-year risk of depression diagnosis. Further, the relationship between concussion history and depression is dose dependent such that multiple concussions are more likely to lead to greater depressive symptoms, which were correlated with an increased axonal diffusivity in frontal lobe white matter (i.e., superior longitudinal fasciculus, uncinate fasciculus; see article by Strain and associates⁴¹). In the current study, con-

cussion history was inquired in a binary form rather than the number of previous concussions, hence we were unable to investigate the possible dose-dependent association among concussion history, substance abuse, and mood disorder. In contrast to previous studies, our sample is a more diverse cohort representing the general population.

Although anxiety often presents similar clinical symptoms as depression, a more severe form of anxiety, panic disorder, showed a

FIG. 3. Regression models with panic disorder as the mediator and alcohol use (AUDIT) and cannabis use (CUDIT) as outcome measures. AUDIT, Alcohol Use Disorders Identification Test; CUDIT, Cannabis Use Disorders Identification Test-Revised.

stronger relationship with history of concussion than that of depression. There are only a few studies that have explored the relationship between concussion and anxiety.^{15,20} Kerr¹⁷ found that anxiety (16.3%) was reported at a greater rate than depression (10.4%) by former professional football players. College athletes had a similar pattern as professional football players, where a history of concussion was able to predict anxiety, depression, and problems with alcohol use.¹⁵ However, evidence regarding the relationship between panic disorder and concussion history is scarce and limited to a case report on a patient with moderate TBI, suggesting that brain injury may increase one's susceptibility in developing panic-related symptoms.⁴² Our data confirmed such a relationship by demonstrating a strong association between concussion history and panic disorder score and that gender moderates their relationship.

There is a larger literature examining the relationship between concussion history and mood disorders than a literature examining its relationship with drug use. That said, there are previous studies that do examine alcohol use after concussion.^{11,43} When focusing on the chronic stage (months to years after concussion), studies suggest that there is an increase in hazardous drinking.⁴³ Like in the studies that have focused on mood disorders, these studies tend to focus on athletes. For example, Martin and Chaney⁴³ found that individuals who had a sports concussion had significantly higher concussion frequency scores and hazardous drinking scores than those who have had a concussion that was not sport-related. Therefore, it is unclear whether the relationship between hazardous drinking and concussion is related to having multiple concussions or participating in a contact sport that exposes the athlete to multiple sub-concussive events in addition to concussive events.

In the current study both direct and indirect effects of concussion history on alcohol use disorder scores were found, which supports previous studies showing a link between concussion and drinking behavior. It should be noted that cannabis use shows a similar pattern as alcohol use. There are few studies examining the relationship between concussion and cannabis use. Recently, there has been interest in using cannabis to treat chronic pain in high impact sport athletes.⁴⁴ Although cannabis has been found to be an effective anesthetic, there is insufficient research examining how it impacts the concussed brain. Additionally, there is significant evidence linking mood disorders and cannabis use with cannabis use contributing to depressive symptoms.^{45,46} The current results do show that concussion history impacts cannabis use via at least two routes, with one being via mood disorders.

Limitations

The first limitation of our study is that the concussion history measure may be prone to measurement and recall bias.¹⁴ Second, we do not have the number of concussions; therefore, we were unable to examine the impact of dose. A third limitation is that we failed to obtain information about history of impact-sport participation. These limitations should be addressed in future studies.

Implications

Concussion can have long-term psychological consequences and appears to affect both mood and substance use. The results presented demonstrate that the relationship between concussion and substance use is complex with mood disorder potentially mediating the effect. Previous research has shown that substance use, particularly cannabis use, can contribute to the development of mood disorders as well as be used to self-medicate in hopes of alleviating the symptoms of mood disorder. This potentially complicated under-researched effect makes it important for future research to

focus on characterizing these relationships, especially with the increasing use of cannabis to treat pain in concussed patients.

Gender differences have been found in many of these measures. The incidence, severity, and recovery time for concussion has been found to vary with gender.³² The incidence of mood disorders²⁶ and substance use⁴⁷ also vary with gender. In fact, the current results are in line with these gender effects. The mechanisms that underlie these gender effects are unknown, but they do appear to moderate the impact of concussion and demonstrate the need for studies that are designed to explicate these effects of gender.

Again, the primary goal of this study was to examine the relationship between concussion history and substance use. Two explanations have been provided for the increased drug use in individuals with a concussion history: 1) increased risk-taking due to damage to the vmPFC and 2) changes in baseline arousal. The results presented here provide another explanation—mood disorders. These results suggest the importance of monitoring patients after a concussion for mood disorders closely to potentially mediate the development of substance use disorders.

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