

MORE THE NUMBER OF SPORT-RELATED CONCUSSIONS,WORSE THE OUTCOME; FACT OR FALLACY: A SYSTEMATIC REVIEW

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ABSTRACT

Background: Sport-related concussion (SRC) is a highly ubiquitous injury afflicting millions of sport-persons. Regarding underlying pathophysiology and long-term neurologic repercussions of SRC, literature encompasses a broad range of conclusions. The number of SRCs sustained and associated symptomology have been subject to conflict with mixed results. Thereby, the objective of this systematic review was to fill lacunae on implications of SRCs and determine whether concussion count has considerable adverse effects. **Methods:** Electronic literature search was developed utilizing a Peer Review of Electronic Search Strategies Checklist. Reporting conforms to Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist. Google-scholar, PubMed, Medline were systematically searched to identify articles with limits to English, published between January 2001-July 2021. Review articles, editorials, and gray literature were excluded. Articles were critically appraised using Structured Effectiveness for Quality Evaluation of Study scoring and risk of bias assessment using Downs & Black checklist. **Results:** 1679 articles were identified. 40 met inclusion criteria. They were reviewed and data were extracted. **Conclusions:** Given the dearth of available data, this systematic review includes parameters for SRC prognosis and highlights novel domains and future perspectives for SRC research. It was observed multiple self-reported SRCs have non-significant impacts in long term. Symptom reporting was related to psychiatric history, career duration, playing position, substance abuse, and lastly the number of concussions. Varying implications are attributable to premorbid cognitive-reserve, injury type, genes, concussion timing, or as-yet-unidentified factors. Concussion count doesn't impact treatment interventions response. Utilizing advanced imaging and biomarkers may provide additional understanding of by identifying changes in brain physiology.

Keywords: Sport-Related Concussion, Traumatic Brain Injury, Neuropsychological Testing

1. INTRODUCTION

Sports-related concussion is a mild head trauma subgroup where the propagated biomechanical stresses cause physiological and neurological abnormalities and initiate a complicated chain of processes. Concussions, particularly in the field of sports, are vital serious public health problems that risk millions of athletes of all ages confront.[1]The incidence rates vary across age, sex, sport, and level of competition and are increasing attributable to higher symptom reporting, awareness and regulations. It affects 300,000 young American adults annually. These are common especially in rugby with 3 incidents per 1000 exposures.[2] Pathogenesis of sports injury mediated is still widely debated and remains unclear. The absence of effective and consistent neuroimaging techniques is a challenging issue to resolve as it's driven by functional rather than a structural injury and anatomical locus is not always cortical. Amnesia, loss of consciousness, headache, dizziness, impaired vision, impaired cognition, and nausea are among the acute manifestations that have been prospectively validated in published studies.[3] Proclivity for repeated injuries is a distinguishing feature of sports-related concussions. Biomechanical stresses impart deficits in absence of overt macrostructural damage and a complicated cascade of events. Microstructural alterations determined using advanced neuroimaging have failed to produce consistent evidence of injury severity gradient.[1]It's thus difficult to pinpoint its exact cause. There is no consensus on the classification of individuals who have suffered from concussions in literature and in clinical practice unless for an unconscious athlete or someone who is significantly impaired. The criteria for assessing and managing concussion are not universal for return to athletic participation despite substantial breakthroughs. Clinical practice defies the conventional notion of head injury as a linear plot from mild to severe with neuropathological accompaniments.[4] Medical problems concerning concussion are evidently multifaceted implying a multidisciplinary approach to evaluation and management. Prospect for long-term cumulative impairments over an athlete's career is a mounting problem. Multiple sports-related concussions raise concerns about the likelihood of neurocognitive impairments and what factors raise or lessen the risk of concussion should be fully understood. What diagnostic methods and parameters are used that detect long-term early deficits and neurologic catastrophe. What factors are affected, and how long will it take for them to recover to their previous state.[5]

The rationale to carry out this systematic review was that due to methodological differences and limits in different studies, literature on this topic is quite fragmented. The sample size is typically a limiting factor so we can coalesce multiple results. Scientific literature encompasses a broad range of conclusions, with some studies suggesting no long-term effects and others alleging widespread neurodegeneration as a result of a single concussive blow to the head emphasizing multimodal assessment. Concussion has been linked to a slew of cognitive issues like reaction inhibition, working memory but the extent to which these cognitive symptoms are widespread has been the subject of conflict. Thereby, the objective was to have an imperative look over the latest research on the effects of recurrent concussions, recovery from subsequent injuries, what parameters are altered both in neurophysiological testing and computerized testing, and does the count of concussions sustained really has a significant effect on sports performance.

2. METHODOLOGY

2.1 Search Strategy

A literature search was developed by the primary author. An electronic literature search of studies published between January 2021 and July, 2021 was completed. Studies published

before 2000 were not included in this search to maintain recency. Keywords used were “neuropsychological testing”, “mild traumatic brain injury”, “sport-related concussion”, “multiple concussions”, “neuropsychological testing”. Bibliographies of full texts were surveyed for additional pertinent studies through a manual search of the citations. This was done to minimize the possibility of overlooking any studies missed in the computerized database searches. A repeat search was done in June 2021 to assess any changes. Limits were applied to the English language and dates.

This systematic review conformed to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.[6]

2.2 Eligibility criteria

2.2.1 Inclusion criteria

(1) published between January 2001 and January 2021; (2) human subjects; (3) the use of primary, original data; (4) being available in English; (5) including a population or sub-population of participants who sustained a sport-related concussion or mild traumatic brain injury (mTBI); (6) Due to the paucity of tools and guidelines that address the specific needs of a pediatric population, only studies with participants that were the equivalent of at least 6 human years old were included. (7) have the outcome of interest.

2.2.2 Exclusion criteria-

Reviews, case series, editorials, grey literature publications were excluded. Gray literature was excluded because it does not often include the necessary level of detail that allows for a thorough examination of methodological and reporting qualities.

2.3 Information sources

The searched databases included PubMed, Google Scholar, and Medline. An electronic literature search was developed utilizing the Peer Review of Electronic Search Strategies (PRESS) Checklist.[7]. This checklist helps to improve electronic search and minimize errors.

2.4 Selection process

Once studies were identified, 2 independent reviewers examined each article’s title and abstract to determine whether the article met the inclusion criteria. If the reviewers disagreed, a third reviewer made the determination and then was confirmed for eligibility and relevance. At least 1 reviewer examined reference lists of accepted articles to identify any studies that were not retrieved through the literature search.

2.5 Data collection process

One reviewer worked independently and extracted data on a uniform abstraction template and was cross-checked by another reviewer independently, any discrepancies were sought using a third reviewer. Microsoft Excel (Student 2019) was used to extract data from the selected studies

2.6 Data items

Extracted data included author name, year of publication, population characteristics, study type and name and short summary. No assumptions were made for unclear information and were marked undetermined.

2.7 Study selection and characteristics

All the studies meeting the criteria were considered for qualitative syntheses only. 40 studies met the inclusion criteria.

2.8 Critical appraisal tools

The quality of studies was evaluated using Structured Effectiveness for Quality Evaluation of Study (SEQES) and risk of bias assessed using Downs and Black (DB) checklist

similar to one of previously published systematic-review. [8] The SEQES is a 24-item tool to evaluate methodological characteristics and rate its quality. Every question can be scored as 0,1,2, the maximum score is 48. A score between 33-48, 17-32, below 16 is considered high, moderate, and low quality respectively. A graphical representation of the quality of studies is in Figure 1. The obtained values in this systematic review, the mean score is 27.12, the median being 27, and mode 26, indicating moderate to the high quality of studies.

Original DB consists of 27-items addressing reporting, external validity, internal validity (bias, confounding), and power, all scored 0 or 1 except item 5 which can be scored 2, maximum score reaching 28. For this systematic review, it was modified to 21 applicable questions as done previously in a published systematic review. [9] The maximum score attainable was 22. Strong and moderate-quality indicated a low risk of bias. strong quality (≥ 16) represented the top 75%, moderate quality (scored 11-15) represented 50% to 74%, limited quality (6-10) represented 25% to 49%, and poor quality (0-5) represented less than 25%. 2 independent reviewers appraised studies and were blinded to each. Any discrepancies were discussed. If consensus couldn't be reached, a third reviewer arbitrated. The DB scoring of all included is graphically represented in Figure 2. The obtained values in this systematic review, the mean score is 14.62, the median being 15 and mode 15, indicating moderate to the high quality of studies and henceforth low risk of bias. The PRISMA flow diagram for the above-obtained studies is represented in Figure 3.



Figure 1: SEQES scoring for quality of studies

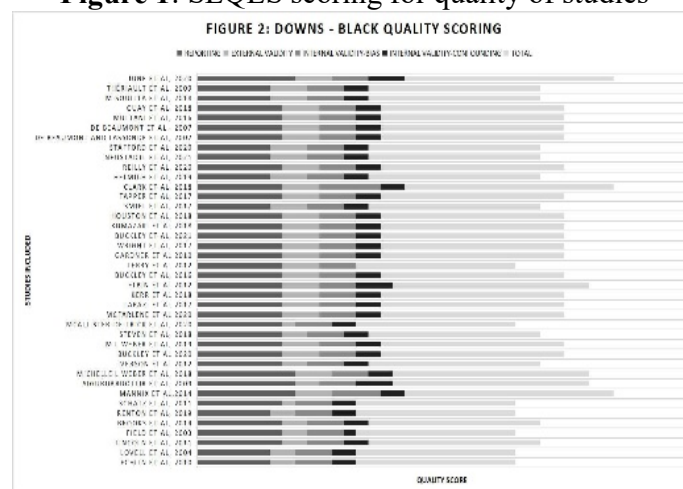


Figure 2: Downs and Black scoring for quality of studies

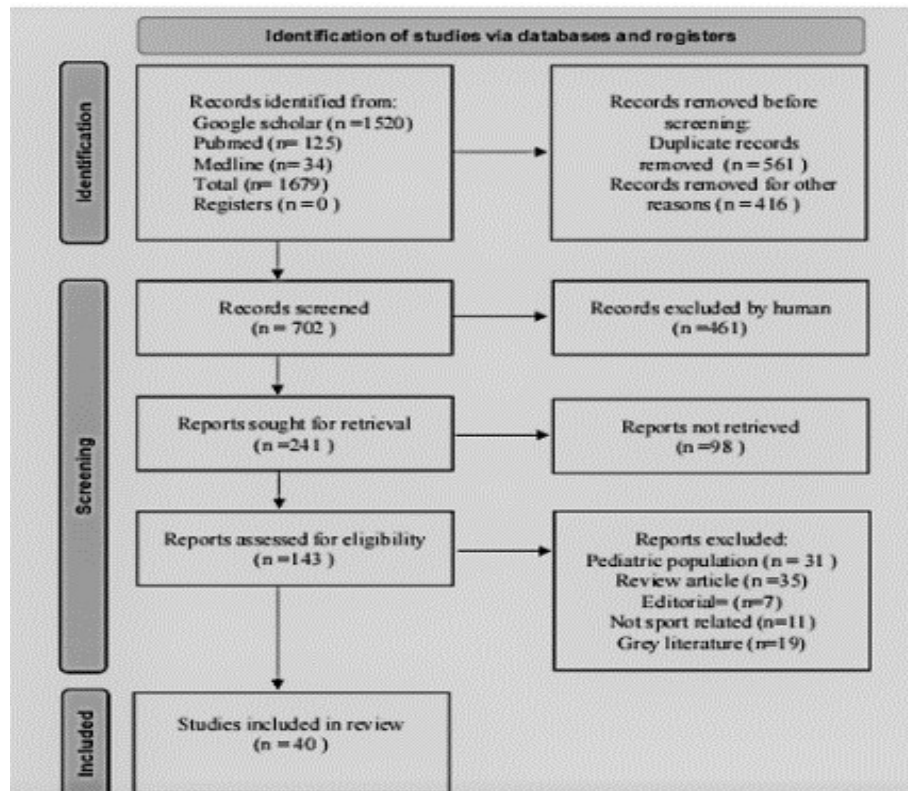


Figure 3: PRISMA CHECKLIST

3. RESULTS

1679 articles were identified. 40 met inclusion criteria.

4. DISCUSSION

4.1 Epidemiology

Contact sports, such as ice hockey, American Football, and rugby are thought to have a particularly high concussion risk.[10] There may be higher rates of concussion in high school athletes compared to adult athletes.[11] Concussions are substantially increasing globally in sports. Soccer and basketball are most dangerous for females. Females have roughly twice the rate of concussion as males in comparable sports (soccer, basketball, softball, baseball).[12] Repeat TBI rates range from 5.6 percent to 36 percent of the overall TBI population, and are likely greater in contact/collision sports.[13] No evidence of sex differences in cognitive or symptoms in adolescent athletes who have had prior concussions with no changes in neurocognition [14]. At least one diagnosed concussion is reported by around 22% of all athletes, 21.7 percent of females, and 21.8 percent of males. Recurrent concussion history is unrelated to gender. [15] These show that further studies with wide and diverse subgroups must be undertaken to reflect the extrapolation of the findings. These prospective studies should cover other sports involving contact and non-contact games along with those during training sessions with integrating sex, age, ethnicity, experience, and skill levels. Identification of incidence rates is also important to identify the population at high risk and thus helps to design strategies to combat these.

4.2 Sport-related concussion implications in high school and college athletes

A prospective cohort study by Field et al in 2003 was first to suggest that concussions have a cumulative effect in high school athletes with ≥ 3 concussions, being more likely to

experience on-field positive loss of consciousness, anterograde amnesia, and confusion after a subsequent cerebral concussion, emphasizing the need for more long-term outcome studies. In comparison to concussed college athletes, high school athletes demonstrated prolonged memory loss. Despite more severe in-season concussions, college athletes performed similarly to matched control participants by day three post-concussion, suggesting high school athletes may take longer to recover from concussions.[13] These findings were partially supported by another study where youth athletes who sustained multiple concussions experienced a variety of subtle effects, which may be possible precursors of the future onset of concussion-related difficulties. [16]In another retrospective investigation, 6075 student-athletes were recruited. Consistent association of increased concussion with composite measures for baseline neurocognitive testing was hypothesized basically indicating towards dose-response relationship. However, the association was found to be neither inconsistent nor strong, rather was associated with various demographic and clinical factors.[17]In a prospective study, 115 people were administered questionnaires like The Rivermead Post Concussion Symptoms Questionnaire (RPQ) and Hospital Anxiety and Depression Scale (HADS) to assess post-concussion symptoms and predictors. 27.8% of TBI cases developed post-concussion syndrome at 3 months and 23.6 percent at 12 months post-injury however no variations in presence of symptoms one year after injury across TBI groups were observed thus implying a resolution of symptoms irrespective of the degree of concussion.[18] Thus, findings were mixed with some showing the significant impact of concussion in both the short and long term. Concussion Assessment, Research, and Education (CARE) Consortium included 8652 collegiate student-athletes in a cross-sectional study. Baseline assessments, Standardized Assessment of Concussion, Balance Error Scoring System, psychological state assessment, Immediate Post-concussion Assessment, and Cognitive Test were all completed, revealing that individuals with a protracted history of concussions are more prone to depression and somatization and may have higher symptom score and severity at outset of the study. [19]Thus, psychiatric symptoms came into the picture but with inconsistent findings. An archival database was utilized to compare 786 male athletes, 26 with multiple-concussion and 26 with no concussion history in a case-control study. Amongst dependent variables, only verbal memory composite had a tangible effect. [20] In yet another longitudinal evaluation of performance through clinical milestones of cumulative recovery and return-to-play (RTP), a reliable change index was computed and found persistent deficiencies in postural control indicating continuous neurophysiological deficiencies despite clinical restoration.[21]Another study assessed Health-Related Quality of Life in concussed and non-concussed athletes. A mixed Analysis of variance (ANOVA) model in groups with and without concussion history was carried out. Physical (PCS) and mental(MCS) component scores were looked for amongst many parameters. Subscores returned to baseline 6 months after an injury. At no time did MCS-12 subscores differ. Scores deteriorated 24–48 hours after injury but improved gradually. [22]While modest and transient decreases are recorded, they are clinically insignificant. Evaluation of the impact of concussion by individual student-athletes may differ between individuals in the context of various other aspects.

4.3 Psychiatric symptoms post multiple SRCs

Attention-Deficit-Hyperactivity-Disorder with concussion increases anxiety and depression and scores were considerably higher in the concussion group compared to other groups.[23]Another study investigated the impact of documented sleep problems on concussion symptoms, cognition, and balance at baseline. The sleep disturbance group scored higher on the Balance Error scoring system, Brief Symptom Inventory-18, Post-Concussion Symptom Scale

while no variations in ImPACT performance between groups. [24] Rugby union players with multiple concussions have slower processing speeds and revealed distant concussion history has negligible long-term neurocognitive depreciation. [25] A pilot study was conducted to assess the effect of SRC and reported a negative effect on the ability to form cognitive maps, despite no significant differences in average response time between groups and no correlation between participants' performance as measured by SCAT5. [26]

4.4 Multiple SRCs sequelae in long term / retired

Motor function in multiply concussed former professional soccer players was assessed and there was noted considerable memory, executive, and behavioral complaints, however, the neuropsychological assessment revealed no substantial difference.[27] In a 15-year follow-up from NCAA Study on Concussion(1999-2001), associations were discovered among ≥ 3 multiply-concussed former college soccer players and adverse health outcomes. [28]

4.5 SRCs and their multi-domain ramifications

Concussion may result in altered kinematics and gait postural control, this Buckley et al assessed conservative gait strategy with concussions history. Various gait characteristics like the center of velocity, step length, and width were analyzed. Amongst these, the only center-of-velocity parameter was altered with a number of concussions, the rest all remaining being clinically incognizant changed. [29]In another study, gait initiation performance in concussed and non-concussed athletes in a cohort study was evaluated. Step kinematics and center of pressure (COP) were investigated. Acute Concussion participants performed worse than the control group for COP but with limited statistical relevance indicating minor neurophysiological abnormalities, and more research across the lifetime is needed.[30] These indicate there might be subtle deficits in gait characteristics but their effect on game performance should be further evaluated. Houston et al investigated the relationship between athlete's gender and the number of concussions and musculoskeletal injury history.468 student-athletes were recruited. Females with concussion history were more likely to report an ankle sprain or knee injury (Odds ratio = 1.88–2.54; p 0.020). No differences were observed between single or several concussions implying that there is no absolute elevated musculoskeletal risk with increased frequency of concussions. [31] Tapper et al explored deficits of executive functions like multitasking and memory in athletes. When completed alone, no differences were seen; in dual-task condition, performed significantly worse on tone discrimination task. This may be attributed to the disruption of cognitive sources. Thus executive function and divided attention tests appear to be useful for prognosis. [32] Brooks et al. uncovered athletes with preceding concussions have revealed more symptoms, but neurocognition does not differ.[14]

4.6 Neuropsychological and physiological implications of SRCs

Elbin et al evaluated brain activation patterns in a paired case-control study. The Blood-oxygen-level-dependent (BOLD) fluctuation was investigated in all respondents during the N-back working memory task. After complete resolution of symptoms hasn't any significant changes in regional brain activation are observed. For a brief period post-concussion, there may persist changes in compensatory activation, but later they resolve.[33] In order to throw light on the ubiquity of cognitive symptoms, Terry et al studied 21 athletes till 6 months post-concussion. They reported SRC lacks long-term fMRI differences. In the concussion group only at the generous quantitative threshold, the attention index score for the Repeatable Battery for the Evaluation of Neuropsychological Status (RBANS) had been less. No group differences observed in reaction time, neural activation during neurobehavioral tasks were seen. [34]

No significant association between self-reported concussion history assessed through a computer or traditional neuropsychological tests and cognitive performance was found.[25]Wright et al. investigated blood pressure and cerebral blood velocity utilizing photoplethysmography and doppler. They found numerous concussions don't confer long-term impairments to dynamic cerebral autoregulation indicating the buffering capacity of the cerebral vasculature. [35]Clark et al discovered significant subgroup differences in white matter integrity using fractional anisotropy and working memory-related functional neural activation patterns using blood oxygen level-dependent (BOLD) percent signal change in a cohort study, Athlete's exposure history, career duration career longevity, and playing position were linked to structural and functional MRI results and act as modifiers. [36] A similar investigation, the effects of multiple concussions on cognitive function and dynamic cerebral autoregulation were assessed and found no significant differences in the groups except short-term working memory thus changes at the cellular level are not in linearity with cognitive functions. [37]In a similar study, it was observed that the ability of cerebrovasculature to maintain nutrition delivery in cortical areas according to Smirl et al, is unaffected by the history of recurrent concussions. This is a significant discovery because, despite long-term neurocognitive impairment associated, transcranial Doppler evaluation of neurovascular coupling appears to be unaffected. [38]Brooks et al. uncovered athletes with preceding concussions have revealed more symptoms, but neurocognition does not differ.[14]Ingo et al examined nonverbal movements of hands in three matched groups using the Elan analysis system for Neuropsychological Gesture (NEUROGES). Duration of irregular Structure units was longer in symptomatic compared to asymptomatic athletes. Thus, neuropsychological analysis can be used as a future diagnostic parameter.[39]Reilly et al predicted concussion history may predispose lower static stability. For 30seconds under 4 conditions for variable position and number of tasks, 54 healthy adults were tracked for Center-of-Pressure. No significant variations were observed in CoP displacement or elliptical area between groups during single tasks while aggravated under dual tasks, implying diminished capability to allocate proper attention resources to multiple concurrent objectives.[40] These findings are similar to those found by Tapper et al.Neustadtl and colleagues evaluated performance following concussion to assess previously undetected subclinical abnormalities in ice hockey players. Goals, assists, points, plus-minus, time on ice, and hits were assessed and only time on ice differed insignificantly and there was a modest decline from pre to post-injury.[41] In a large cohort study, on 11 of 12 cognitive tests used, Stafford et al found no differences between post-concussion and non-concussed participants unique to the task's incongruent circumstances in the standard Stroop paradigm indicating no long-term differences in terms of cognition.[42]

In group studies, Iverson et al reported athletes recover from past concussions in terms of experienced symptoms and neuropsychological test performance in 2–28 days, with the majority of evidence indicating that recovery takes 5–10 days. De Beaumont et colleagues evaluated motor cortex in athletes using four distinct transcranial protocols for magnetic stimulation, excitation, and inhibition processes. The first dorsal interosseous muscle was employed to obtain motor-evoked potentials. When compared to normal control subjects, the duration of the cortical silent period was longer in athletes who had repeated concussions, although the difference was not significant.[43]In a similar investigation, De Beaumont et al investigated long-term electrophysiological changes using the oddball paradigm revealing the link between concussion number and P3 amplitude attenuation was weak, implying that other factors influence the size of

the P3 component in multi-concussion athletes. [44] Thus these changes may be attributable to changes in brain metabolism and neural activity post-concussion.

In a case-control study, how compromised tracts correspond to neuropsychological competence post-concussion was studied. Repetitive concussions in former professional football players were linked to localized white-matter tract abnormalities attributable to increased axial diffusivity, according to Multani et al, explaining neuropsychiatric symptoms and cognitive deficiencies these athletes have. [45] Guay et al examined alpha activity using time-frequency methods. Multiply-concussed athletes showed considerably less event-related perturbations time-locked to stimulus presentation as compared to non-concussed athletes Concussions sustained were strongly linked to changes in Alpha activity reflecting low-level neurophysiological differences[46]Misquitta et al. examined explored connection between brain atrophy and cognitive-behavioral symptoms in retired Canadian football players. Age had a higher impact on hippocampus volume and amygdalae. Multiple concussions may result in early localized atrophy, according to these findings, albeit longitudinal research is needed to fully understand this association.[47] Multiple concussed athletes showed considerable ERN amplitude reduction prompted by error generation, according to Debeaumont et al. Two different experimental paradigms designed to probe concussion-sensitive cognitive functions like attention and short-term memory demonstrated these cumulative effects of concussions on ERN amplitude. [48]According to Mcfarlane et al, findings provided evidence that SRC may affect the ability to familiarise with a spatial environment which is consistent with the integrity of extended neural networks required for effective spatial orientation and navigation. [26]Individuals with a history of concussion had substantially lower postural stability during dual-task conditions, as reflected by increases in average displacements and elliptical area of postural sway, as well as a reduction in CoP sample entropy, according to a study by Reiley et al.[40]Participants with previous concussions exhibited more brain atrophy in temporal lobe white matter and hippocampus according to June et al, which remained constant during follow-up visits. In terms of neuropsychological performance, there were no significant differences between groups.[49] Thus, long-term and accumulated repercussions of sport-induced concussions on activity in the brain can be determined by event-related potentials.

5. CONCLUSION

The effect of multiple concussions is an emerging research area with inconsistent findings and has garnered attention as findings remain unconcluded. The Association between frequency of concussions and neurocognitive testing was not found to be significant. Traumatic stress can act as an arbitrator between concussions and post-concussive symptom severity. The pervasiveness of symptoms is controversial with minimal differences which points to relative plasticity following concussion. Association of cognitive health and concussion history is evolving in retired athletes but there are lacunae and a lack of clarity in the context of Cause-and-effect. An insignificant number of reinjuries are observed, indicating a lack of clarity on whether the period of vulnerability exists. Whether neuroimaging changes are associated with changes in cognitive function in high school and collegiate football players has not been determined. Lack of classification for identification of sustenance of concussion warrants multifaceted assessment battery. Several factors are significantly related to symptom reporting along with concussion history. In descending order of magnitude, baseline symptom reporting was related to mental health history, headache/migraine history, gender, developmental and/or learning problems, and a number of prior concussions. Career duration, playing position, concussions occurring during practice sessions, medical and psychiatric history, substance abuse,

developmental and/or learning problems, and a number of prior concussions all contribute to sequelae. Athletes with a history of trait anxiety, depression, sleep disorders, ADHD, migraines, and substance abuse may report elevated symptom scoring and severity at baseline. Pronounced concussion history may be associated with greater depression and somatization. There's a dearth of perceptible equations between concussion history and baseline cognitive performance. No prospective exploration with adequate controls has demonstrated these declines are present outside of a highly selective sample. We should extend research and safety measures during practice sessions too as significant concussions are sustained out of a competitive environment too. Cognitive changes could be counterpoised by repeated assessment ascribable to learning effect signifying eclectic effects of concussion. Not all individuals experience some kind of prognosis attributable to various factors owing to their unique characteristics. Additionally, concussion-like symptoms aren't very specific too. The cognitive loading used in tests might be submaximal to elicit the response indicating effects of concussion are heterogeneous. Henceforth, other evaluative measures might be taken into consideration.

6. FUTURE DIRECTIONS

Potentially deleterious effects of repeated concussion warrant further study to develop scientifically valid management protocols for return-to-play. What factors impact concussive injuries and their sequelae like moderator variables. Track structural, cognitive, and behavioral progression over time can provide additional insight and study cognitive health outcomes in diverse athlete samples to delineate the long-term effects of sports participation on cognitive functioning. Incorporation of rigorous study designs inclusive of diverse ages, socioeconomic status, and racial/ethnic groups to improve behavioral outcomes around concussion prevention, reporting, and management. Use of normative data and reference tables stratified by sex and pre-existing health conditions to interpret symptoms in concussed athletes. Additional cognitive tests like N-back should be explored by researchers. A multimodal approach to concussion assessment that encompasses the assessment of multitudinous functions is consigned. More culturally appropriate concussion initiatives are needed globally to ensure that athletes around the world can identify concussive injuries and understand the dangers of continued sports participation while concussed.

7. LIMITATIONS

While these findings are persuasive, there are some limitations to this study. There's a probability of language bias. In studies of risk, prognosis, and long-term repercussions, information bias would be prevalent, explaining the heterogeneity of findings. Because respondents in all groups are subject to recall bias, memory errors may influence an individual's beliefs about his or her aptitudes, which may, in turn, influences motivation on testing time since injury isn't reported in the retrieved studies, also self-reported concussion history may affect the findings of this review. Retrospective investigations were carried out in various testing conditions that could have impacted cognitive performance. Impact test scores could be compromised by poor test taker performance, resulting in inaccurate baseline ratings. Due to a lack of literature, high-level research such as RCTs is not included. Neurophysiological evaluation measures have been used in studies, however more sensitive measures such as diffusion tensor imaging, functional magnetic resonance imaging, and magnetic resonance spectroscopy may assist uncover more useful information

ETHICAL APPROVAL

As this systematic review was compiled of already ethically approved studies, no ethical clearance was needed, moreover, it is just qualitative synthesis, not involving any human or animal subjects.

ACKNOWLEDGEMENTS

Primarily I would like to thank all the authors and participants of all studies included in this review. I would also like to thank Sudeshna Das for serving as the third reviewer. Last but not least I would like to thank our friends and family for their constant support.

CONFLICTS OF INTEREST

There is no potential conflict of interest that could have hampered the final version of this manuscript.

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