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Menstrual cycle changes among female athletes post a traumatic brain injury: A systematic review

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Abstract

Introduction: Traumatic brain injury (TBI) commonly affects athletes and can lead to menstrual cycle changes in female athletes. This review highlights the existing literature on menstrual cycle changes post-TBI. TBI disrupts the hormonal regulation of the menstrual cycle, causing irregular or absent periods, hormonal imbalances, and related symptoms. These changes impact the physical and psychological well-being of athletes during recovery. However, research in this

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area is limited, necessitating further investigation into the mechanisms and implications of menstrual cycle changes in female athletes post-TBI. Healthcare providers and sports medicine professionals must be aware of these effects and provide appropriate care and support. Prioritizing overall health and well-being, including menstrual health, is crucial for female athletes post-TBI. This involves nutrition, stress management, and adjustments to training and competition schedules as necessary. Raising awareness and educating athletes, coaches, and stakeholders is vital for proper care and support. Additional research on menstrual cycle changes in female athletes post-TBI will inform clinical practice and enhance the health and performance outcomes of female athletes.

Methods: A comprehensive literature search was conducted using databases including PubMed, Embase, Scopus, Web of Science, and SPORTDiscus. The search strategy employed relevant keywords and MeSH terms to identify observational and experimental studies published from the inception of each database until the present day. Inclusion criteria encompassed studies involving female athletes diagnosed with a concussion, assessing the physiological or pathological changes during the menstrual cycle, and reporting data on hormone fluctuations, symptomatology, cognitive function, mood, neuroimaging, or biomarkers. Independent reviewers screened articles, extracted data, and resolved disagreements through consensus.

Results: The initial search yielded 500 articles, and after applying inclusion criteria, 108 studies were included. Menstrual cycle disruptions were assessed through self-reporting and hormonal analysis. Findings indicated potential links between sports-related concussions and irregularities in cycle length, alterations in hormone levels, and changes in menstrual symptoms. However, heterogeneity among the studies and lack of standardized methodologies limited definitive conclusions.

Conclusion: This systematic review underscores the need for further research to elucidate the relationship between sports-related concussions and menstrual cycle disturbances in female soccer players. Future studies should employ standardized methodologies, including objective measures and larger sample sizes. Understanding the impact of concussions on the menstrual cycle is vital for holistic care and optimal performance of female athletes in contact sports. Identifying underlying mechanisms will facilitate the development of targeted interventions and preventive strategies to ensure long-term reproductive health and overall well-being after head injuries in female soccer players.

Keywords: Traumatic Brain Injury; Athletes; Menstrual Cycle Changes; Female Athletes; Sports Medicine; Concussion.

1. Introduction

The menstrual cycle is regulated by the hypothalamic-pituitary-gonadal axis, involving a complex interplay of hormones, including gonadotropin-releasing hormone (GnRH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), estrogen, and progesterone. Regular menstrual cycles are important markers of reproductive health and hormonal balance in females, with the average length of a menstrual cycle ranging from 21 to 35 days [1]. Traumatic brain injuries, such as concussions, are common in sports and can result from direct or indirect head trauma. TBIs can cause a wide range of physical, cognitive, and emotional symptoms, and may also disrupt the normal functioning of the hypothalamic-pituitary-gonadal axis. The physiological and hormonal changes associated with TBIs, such as inflammation, oxidative stress, and alterations in neurotransmitter levels, could potentially disrupt the normal hormonal regulation of the menstrual cycle [2]. It has been suggested that female athletes who have sustained TBIs may be at risk of experiencing alterations in their menstrual cycle. Several studies have reported menstrual irregularities, such as amenorrhea (absence of menstruation) or oligomenorrhea (infrequent or irregular menstruation), in female athletes following a TBI [3, 4]. However, the existing literature on this topic is limited and lacks comprehensive synthesis.

A systematic review of the available literature on menstrual cycle changes among female athletes post-TBI can provide a comprehensive overview of the existing evidence and help identify potential patterns, mechanisms, and implications of menstrual cycle changes in this population. This review may also inform clinical practice, injury prevention strategies, and future research directions in this field. By understanding the potential effects of TBIs on menstrual function in female athletes, clinicians, coaches, and athletes themselves can be better equipped to manage and optimize menstrual health in this population.

2. Literature Review

2.1. Traumatic Brain Injury (TBI)

Concussion, also known as mild traumatic brain injury (MTBI), is a pathophysiological condition that affects the brain and is caused by direct or indirect biomechanical pressures [5]. Every year, around 1.6 million people in the United States suffer from traumatic brain injury, with 800,000 receiving emergency room treatment and 270,000 requiring hospitalization . About 52,000 people die as a result of TBI, and 80,000 have lifelong neurological abnormalities [6]. The signs and symptoms of concussion are headache, cognitive issues such as mental fogginess or memory alterations, balance and coordination problems, behavioral changes such as irritation, and reduced reaction time. Although transient loss of consciousness is not common with concussions, it may occur . Concussions can occur in any sport then there is trauma to the head, neck, or body that transmits the force to the head. Neurocognitive difficulties such as clouding of consciousness or memory abnormalities are possible indicators of concussion [7]. Any evidence of loss of consciousness (LOC) during a concussion should be interpreted as indicating a potentially serious traumatic brain injury [8]. According to research, axonal injury is a common aspect of all traumatic brain injuries, and the quantity and distribution of injured axons increase with the degree of the trauma, which can be mild, moderate, or severe [9].

TBI is the outcome of a variety of mechanisms. Blunt trauma, penetrating force, or blast overpressure can all cause it mechanically. Penetrating injuries have a strong link to a poor prognosis. For the other types of mechanisms, however, there is no particular prognosis [10]. TBI can also occur as a result of mechanical forces being transmitted to the skull through contact and acceleration/deceleration. Shock waves are created instantly in contact injuries and then propagate across the hemispheres, putting extra pressure on the tissues [11]. The maJordanity of brain injuries, such as hematomas, contusions, and fractures, are caused by this pressure.

2.2. Gender differences and the incidence of concussions among collegiate athletes

Many factors play a role in increasing the risk of traumatic brain injury, such as age, where the older the athlete is, the more susceptible to traumatic brain injuries, on the other hand, young athletes and adolescents have a slower rate of recovery post-traumatic brain injury . Another factor is impact sports, where in the last few years numerous young athletes below the age of 18 were at increased risk of developing concussions, this mainly occurs in soccer, ice hockey, and lacrosse, especially during the game itself rather than practice [5]. Gender was also suggested, as the rate of concussion was higher in female athletes in sports such as basketball and soccer since the cervical spine region is an area of high risk and vulnerability to injuries because of its proximity to the head and lack of protection relative to other regions. A cohort study which was conducted over 3 years suggested that female athletes sustained 3.6% of concussions during practices and 9.5% during games, while male athletes sustained 5.2% during practices and 6.4% during games [12]. An opposing theory suggested that estrogen and progesterone in females play a role in neuroprotective functions such as reducing intracranial pressure as well as improving cerebrocranial pressure and neurological score, however, this theory is still controversial and needs further research [13].

On the other hand, it has be hypothesized that females are more prone to traumatic brain injuries due to the lower head-to-neck ratio [14], meaning they have thinner necks with the same-sized heads as males. Which makes males less susceptible to injury in addition to a decrease in anthropometric measures in comparison to females leading to an increase in head impact kinematics during soccer heading [15]. Lastly, preexisting conditions in athletes such as migraines, attention deficit disorder, and learning disabilities were associated with increasing the risk of traumatic brain injury but there is not enough evidence to support that aspect [5].

Although traumatic brain injuries are very common among athletes and may lead to misdiagnosis. Diagnosis of traumatic brain injury depends on the method used which could either be neurological or pathological. The neurological aspect of the diagnosis is based on conducting a complete neurological exam which evaluates thinking, motor function, sensory function and coordination, eye movement, and reflexes [5]. While the diagnostic value of computed tomography (CT) and magnetic resonance imaging (MRI) in identifying certain conditions may not be extensively utilized from a pathological perspective, there are specific indications where their application proves beneficial. For instance, these imaging techniques can effectively assess the presence of associated injuries, including intracranial bleeding, cerebellar edema, diffuse axonal injury, and skull fractures. Moreover, they can also aid in evaluating the severity of signs and symptoms, such as memory loss, thereby providing valuable scientific insights into the underlying pathology. Some additional tests that help in diagnosis include neuropsychological testing Biomarkers like S100 proteins are still under trial because they are still inclusive for identifying individuals with concussions [5, 16]. The return to play decision should be individualized and not based on a rigid timeline where ultimately it is concluded by the team physician. there is no same-day return to play decision for concussed athletes and they are only allowed to return when they are asymptomatic and return to baseline symptoms of rest with them no longer taking medications to mask the concussion symptoms [5].

The only way to prevent head injuries is through communication between the coach and athletes to promote a safe playing environment as well as changing the culture of intentional acts of unsportsmanlike conduct [5].

2.3. Head Injuries in Female Athletes: How Common? Which Sports? Underreporting of Concussion

Sports-related concussion (SRC) is a type of traumatic brain injury that is defined as a complex pathophysiological process that affects the brain and is triggered by biomechanical stressors. It has various characteristics that assist in identifying its nature. The existing diagnostic criteria for SRCs are clinically oriented, and there is no gold standard to examine their diagnostic qualities, according to the limitations identified. By establishing strong predictive positive/negative values, a future, the more reliable definition of SRC would better detect concussed players [17]. In sex-comparable sports, female athletes had a 1.9 times higher chance of suffering SRCs than male athletes, with higher risks in basketball, soccer, and baseball/softball. In lacrosse, male athletes had a higher clinical incidence than female athletes, but they were not more likely to have an SRC. However, due to contact and equipment variations between male and female lacrosse, lacrosse is not truly a sex-comparable sport [18]

Athletes under-report concussions at a rate of 50-75 percent of total injury occurrence, which continues to be a source of worry for clinicians and athletic training personnel [19]. Underreporting of concussions among players appears to be common, and it's linked to misconceptions about injury risk, as well as a culture that both perpetuates and encourages it, with parents' and coaches' tacit or overt cooperation [20]. In addition, players' desire to win, group membership dynamics such as a player's role as the team's "enforcer," and coaches' desire to win to advance their opportunities in the sport play a role in under-reporting concussions. Moreover, parents' financial interests or alternative agenda in terms of time commitments and their child's future career prospects are all factors that contribute to underreporting of concussions [20]. The assumption that the hit to the head was not substantial enough is the most common reason for underreporting a suspected concussion [21, 22]. Underreporting is at least partly motivated by a desire to keep playing, and computerized or onsite testing metrics are frequently used to supplement the diagnosis of sports-related concussions [23]. These metrics consider objective measures like cognition testing, but they also rely on athletes' self-reported symptoms for psychological and somatic issues. As a result, clinician judgment about return-to-play decisions may be skewed toward symptoms measured objectively by neurological and cognitive examinations [23]. The subject of sex-based differences in SRC has sparked a lot of debate due to the limited studies on female athletes compared to male athletes. Nevertheless, SRC is more common among female athletes than in male athletes who participate in similar activities, but the reason for this is unknown. Disparities in regulations or way of play, neuroanatomic differences in neck strength and head mass, cerebral blood flow, or more frequent injury reporting among females are all hypothesized to contribute to sex-based differences in concussions [24]. These factors could influence males' and females' post-injury experiences, as well as the apparent differences in reporting injury and symptoms, and care-seeking behaviors [25]. For instance, female soccer players have a lower head-neck segment mass, which results in greater angular acceleration of the head, lower neck strength, and neck girth, and a larger ball-to-head size ratio, all of which have been postulated as possible causes for their higher concussion risk. Female athletes also have a higher number of symptoms in the acute phase and took longer to recover from injury, In addition, females have a higher cerebral blood flow rate and a higher basal rate of glucose metabolism, which may interact with an elevated neurometabolic demand after a concussion, exacerbating the severity of post-concussive symptoms [26].

Hormonal variables, such as circulating estrogens, may also cause females to have a different pain response than males. Recently, alterations in hormone levels, notably in the lowering of progesterone concentration after mild TBI, have been demonstrated to have an impact on recovery outcomes in females, leading to a withdrawal of its claimed neuroprotective characteristics [27]. Estrogen has also been demonstrated to aggravate females' post-injury energy metabolism deficits [25].

2.4. Pathological Findings in The Management of Sports-Related Concussions

In situations where a confirmed diagnosis of concussion is lacking, the utilization of diffusion imaging to examine structural connectivity and magnetic resonance spectroscopy to evaluate brain metabolite composition enables differentiation between contact-sport athletes and non-contact-sport players. These techniques provide valuable insights into the intricate neural connections and chemical composition of the brain, allowing for a clearer and more understandable distinction between individuals engaged in different types of sports. White matter in the brains of contact-sport athletes has higher fractional anisotropy, a lower mean diffusivity (signifying more constrained water diffusion), a lower N-acetylaspartate/creatine ratio, and bigger abnormalities in athletes with a history of concussion.

The impact of playing collision sports may be sufficient to change the functional, structural, and chemical properties of brain tissue even in the absence of clinically diagnosable concussive symptoms [28, 29]. MicroRNAs, which are small, non-coding RNAs with 20-23 nucleotides showed a possible use as biomarkers for concussion. For instance, In Collegiate football, microRNAs predicted spatial memory deficits over the course of a season without a concussion and have above-average diagnostic accuracy for mild to severe traumatic brain damage [28, 30].

Studies on concussions that use arterial spin labeling typically reported reductions in local cerebral blood flow soon after injury, which coincide with cognitive decline and the intensity of acute symptoms. Previous research found a relationship between cerebral blood flow and lower levels of symptom severity, cognitive function, and stress and anxiety [31]. Several studies indicated chronic reductions in cerebral blood flow up to many months after an injury as recovery times increased, whereas others found that cerebral blood flow returned to normal within a month [31]. While several studies also noted an increase in either global or local cerebral blood flow, it seems to be mostly related to those who were exhibiting symptoms [32, 33]. Because most of the research only featured male athletes [31], it is unknown whether sex differences or hormonal influences on cerebral blood flow exist [28].

Typically, during the acute phase, there is an increase in connectivity in the default-mode network, which is an active network at rest (24 hours). After a week of injury, there is less connectivity within the default-mode network, although there are reports of both hyper- and hypo-connectivity throughout the entire brain, and the degree of connectivity is correlated with verbal and visual memory losses [28, 34, 35]. One month after the injury, default-mode network connectivity is still anomalous but is getting closer to baseline levels [36]. About six months after the damage, the brain's executive function-related regions are hyperconnected [37]. When an athlete deviates from the typical recovery trajectory, connectivity varies dynamically. This information can be used to identify the deviation [28].

Measurements of tissue iron content and venous oxygen saturation can be made using quantitative susceptibility mapping, a quantitative extension of susceptibility-weighted imaging [28, 38]. Quantitative susceptibility mapping has just recently been applied to concussions. There was no change in susceptibility among high school football players after an injury or after a season, according to two studies [39, 40]. Nonetheless, in the most recent publication, which included a larger cohort of collegiate and high school football players followed longitudinally, there was a significant increase in white matter susceptibility that persisted after clinical symptom resolution and was correlated with the length of time spent returning to play [28, 41].

In a study done in Sweden on twelve athletes (6 males and 6 females) with repeated sports-related concussions (rSRC) and post-concussion symptoms lasting six months or more, diagnosed as having post-concussion syndrome (PCS) with another group of six patients (4 males and 2 females) with a moderate to severe TBI. Both the repeated sports-related concussions (rSRC) and TBI groups had lower Repeated Battery Assessment of Neurological Status (RBANS) scores, which are used to assess cognitive function. In TBI but not in rSRC, neurofilament-light (NF-L) levels were elevated in plasma and cerebrospinal fluid, and serum tau levels were decreased. PET imaging in rSRC athletes revealed increased neuroinflammation in the hippocampus and tau accumulation in the corpus callosum. Tau aggregations were seen in the thalami, temporal white matter, and midbrain of TBI patients, and there was widespread neuroinflammation across the brain, including the temporal white matter, the hippocampus, and the corpus callosum. Increased tau aggregation and neuroinflammation were seen with PET imaging at around 6 months after injury in mixed-sex cohorts of young adult athletes with persisting post-concussion symptoms and in TBI patients [42].

2.5. The Effects of Menstrual Cycle Phases on Clinical Measures of Concussion in Healthy College-Aged Females

Clinicians have been investigating potential disparities in neurocognitive function, postural stability, and self-reported symptoms during different phases of the menstrual cycle. Additionally, they have examined performance variations between females with regular menstrual cycles (eumenorrheic) and those with irregular or absent menstruation (non-eumenorrheic) [43]. By exploring these factors, researchers aim to shed light on potential influences of hormonal fluctuations on various aspects of female physiology and cognition, ultimately contributing to a better understanding of the interplay between the menstrual cycle and these physiological parameters [43].

Females with premenstrual syndrome have been found to have more postural sway during the mid-luteal phase than during the early follicular or ovulatory phases, according to a prior study [44]. Also, females excelled in verbal and fine motor abilities during the mid-luteal phase compared to the menstrual phase [45]. Previous studies have found that the menstrual cycle phase has little effect on verbal sequential and visuospatial cognitive tests [46]. These parameters have almost not been studied in the context of a sports-related concussion model [43].

In a study, 36 healthy college females participated and were classified into two groups (OCP users and eumenorrheic), data were collected and investigated by using ImPACT [43]. The Immediate Post Concussion Assessment and Cognitive Test, attention, memory, response time, and information processing speed are among the characteristics of cognitive functioning measured by this computer-administered neuropsychological test battery, which consists of seven distinct test modules [47], including Post Concussion Symptom Scale (PCSS) which is a tool that assesses the presence and severity of 22 symptoms that are typically linked with a concussion [43].

For the following neuropsychological test outcome measures: verbal memory, visual memory, visual motor processing speed, and response time, no significant interaction effects between the menstrual cycle phase and OCP use were identified [43], and these results are supported by a previous paper [48].

The findings suggest that the quantity and severity of symptoms remain consistent throughout different phases of the menstrual cycle in young, healthy females attending college. However, it was observed that these symptoms tend to be more pronounced in individuals with regular menstrual cycles (eumenorrheic females). These insights highlight the potential influence of menstrual regularity on the manifestation of symptoms in this specific population group. [43]. This contradicts prior research that found females reported more PMS symptoms during the follicular phase of menstruation than during the late luteal phase [49]. When compared to OCP users, eumenorrheic females have more mood-related symptoms and depression ratings [50].

The mean severity score for eumenorrheic females showed a twofold to threefold increase in symptom severity in comparison to OCP users. Both the usage of OCP and the menstrual cycle phase appear to not affect postural stability; any deficit in postinjury postural stability test measurements may be attributed to the suspected concussion rather than the menstrual cycle phase [43]. Postural stability abnormalities in concussed athletes have been documented in published research papers lasting for 3-5 days after injury [51].

In conclusion, menstrual cycle phases have no differences in clinical measures of concussion, while eumenorrheic females experience more acute symptoms, and no abnormalities in cognition or balance had been predicted, at this time it is unable to eliminate variations in balance, cognition, and symptom severity between females with and without PMS [43].

2.6. Hormones Influence The Specificities of Female Physiology

Estrogen may improve endurance performance through modifying carbohydrate, lipid, and protein metabolism, whereas progesterone appears to have an opposing relationship [52]. Estrogen enhances glucose availability and absorption into type I muscle fibers, making it the preferred fuel during short-duration exercise; this activity is reduced by progesterone. In comparison to the low estrogen environment of the early follicular phase, a high estrogen content in the luteal phase increases muscle glycogen storage capacity [52].

Resting blood pressure in young females is lower than in males. When females reach menopause, their sympathetic nerve activity increases, and their chance of developing systemic hypertension rises dramatically. In females, reproductive hormones, such as estradiol, appear to enhance vasodilation and heat dissipation, which affects vascular responses to thermal stress, including cutaneous vasodilation and vasoconstriction [53]. Estrogen tends to encourage lower body temperatures by enhancing heat dissipation reactions; however, progesterone promotes higher body temperatures. Recent research reveals that estrogen has particular effects on central autonomic nuclei that regulate cutaneous blood flow and sweating. Estrogen also increases vasodilation by affecting peripheral blood vessels directly [54].

In a study done on the role of 17-Beta Estradiol on exercise metabolism [55], it was found that during endurance exercise, females oxidize higher lipids while consuming less glucose and protein, oxidizing less leucine than males. Females also had lower rates of glucose appearance and disappearance than males, with no alteration in basal muscle glycogen and modest indications of muscle glycogen sparing during endurance activity [55]. The fact that acute 17-estradiol delivery to males moves fuel selection toward increased fat oxidation, indicates that fiber type isn't the primary reason for the sex metabolic difference, and giving males 17-estradiol lowered their basal muscle glycogen content by a small but considerable amount [56]. One study on exercising females used pharmacological inhibition of intrinsic sex hormone secretion as well as selective replacement of 17-estradiol with and without progesterone; the study discovered that 17-estradiol lowered CHO oxidation by lowering both glucose Ra (entry rate) and estimated muscle glycogen use [55]. At least part of the sex difference can be attributed to females' greater levels of 17-estradiol; as 17-estradiol injection to males causes decreased amino acid and CHO (and higher fat) oxidation during endurance exercises [55].

The results mentioned above correlate with another study that finds females at either follicular or luteal phase had a larger pre-translational abundance of fat oxidation genes and a higher transcriptional capacity for sarcolemmal, cytosolic, and mitochondrial fatty acid transport, IMCL synthesis, and fatty acid oxidation at rest and during exercise, in comparison to males [57]. In response to endurance exercise and at rest, the menstrual cycle affects the profile of mRNA implicated in lipid and CHO metabolism and E2 appears to be a predictor of steady-state mRNA levels for genes engaged predominantly in skeletal muscle fat metabolism [57].

According to a study [58], when female sex hormones (17-estradiol and progesterone) concentrations were highest, salivary IL-6 levels were lowest (luteal phase). The menstrual cycle had a substantial effect on salivary IL-6 concentrations, but had no effect on plasma IL-6 concentrations in young healthy females at rest however, the study observed no significant associations between saliva and circulatory IL-6 (and IL-8) concentrations in recreationally active healthy females at rest [58]. In another study, it was found that only during the menstrual phase was a positive connection between exercise-induced alterations in plasma IL-6 as well as calprotectin concentration observed [59]. Although ventilatory threshold intensity exercise is not a strenuous exercise, it was discovered that plasma IL-6 and calprotectin levels continue to rise during the menstrual cycle following exercise [60].

2.7. Could sports affect menstrual bleeding?

Menstruation is a determinant of a female's performance, which can be influenced by a variety of factors including exercise [61]. Although the gender gap in exercise participation is narrowing, females continue to be underrepresented in sport and exercise medicine research [62].

Some studies suggest more significant premenstrual symptoms among females who are inactive physically [63, 64]. While other studies suggest that females who participate in sports that require fitness and leanness are more prone to eating disorders. So, secondary amenorrhea in these groups can be as high as 69% [65]. This is explained by low leptin resulting from a decrease in fat mass. Because leptin stimulates gonadotropin-releasing hormone secretion and modulates gonadotropin release, its lack contributes to menstrual irregularities [65, 66]. Although heavy exercisers or females with low BMI are linked to hypothalamic-pituitary-adrenal axis (HPA) dysregulation, as a consequence of heavy exercise which causes energy expenditure and low leptin. It reduces insulin and free androgen levels in overweight and obese females (with or without PCOS), resulting in the restoration of HPA control of ovulation [67].

In addition, stretching exercises help females with primary dysmenorrhea to reduce pain severity, duration, and the amount of analgesics pills they take during their menstrual cycle [68]. Another study supports this finding and suggests that athletes do have lower rates of dysmenorrhea, but they have considerably greater rates of irregular periods and heavy menstrual flow [69]. Meanwhile, a delay in the onset of menarche is greater in athletes than in non-athletes [70].

In summary, the paucity of communication between the obstetrics and gynecology section and sports dietitians remains an issue, so cooperation between the two departments should be established [71].

2.8. Concussion and its relation to the development of abnormal menstrual bleeding

Traumatic brain injuries have been linked to the development of irregular menstruation cycles. In a retrospective study of 104 females who had suffered a TBI between the ages of 5 and 12 years, with the results compared to that of matched controls, 46 percent of the 104 females with TBI (W-TBI) had amenorrhea that lasted up to 60 months. Following the injury, 68% of W-TBI's cycles were irregular. These results differed significantly from those of the controls [72]. Mechanisms by which mild forms of TBI such as brain concussion can affect menstruation through alteration of gonadotropin secretion were proposed to be related to transient ischemic injury to the hypothalamus, infundibulum, and/or pituitary gland [73, 74].

The exact cause behind pituitary dysfunction following head injury is hypothesized to be related to multiple mechanisms including neuroinflammation, autoimmunity, vascular insufficiency, and direct damage to the gland within the sella turcica [75, 76, 77]. Multiple studies demonstrated that one of the most commonly reported hormonal insufficiencies post-TBI was in sex hormones regulating gonadotropins like LH and FSH [78, 79], which can partly explain the menstrual irregularities reported in some female athletes post-concussion [80]. Depression and anxiety are two emotional responses that have been linked to concussions increasing psychological stress response [81].

A study conducted on 532 German female elite athletes in which concussion history was taken into consideration, showed that 22.2% of them reported irregularity in their menstrual cycle however it is not fairly known whether these irregularities are related directly to their concussion history or other factors [82].

In a recent study on 97 female athletes aged 11-20 years old, the incidence of menstrual irregularity following sport-related concussion was found to be 26.8%, and although not statistically significant but 84.6% of them reported prolonged recovery time post-concussion compared to other females [83].

2.9. The effects of the menstrual cycle phase on elite athlete performance

Various sports performance-related measures are influenced by the menstrual cycle in elite athletes, but the parameters themselves, as well as the size and direction of the impacts, are yet unknown. To enable suggestions and training individualization in female top athletes, more longitudinal and prospective studies to systematically assess on-field performance metrics are critically needed [84].

Many studies have found that performance is unaffected by menstrual cycle phases. There were variations in findings in the studies that did identify a menstrual cycle influence on performance, however, strength and aerobic performance were more commonly reported to be affected during the late luteal phase, and anaerobic performance was most commonly reduced in the late follicular phase [85].

The evidence regarding the cyclic impacts of the regular or normal menstrual cycle on performance is examined in a review that looks at the effects of the menstrual cycle on athletic performance, psychological and perceptual factors, maximum oxygen uptake, endurance, time to fatigue, temperature, sweating, body weight, respiratory drive, blood lactate, carbohydrate and lipid metabolism, and cardiovascular parameters, as well as surveyed evidence [86]. The findings of this comprehensive review and meta-analysis suggest that exercise performance during the early follicular phase of the menstrual cycle may be somewhat impaired when compared to all other phases because of the small effect size [87]. The menstrual cycle has some significant effects on elite athletes' performance, according to the real-world performance data examined in 2020. These differences are most likely explained by a complex set of mechanisms, including the influence of ovarian hormones and heat regulation, that together contribute to the menses phase's superior performance over the proliferative and secretory phases. However, because of heightened impulsivity, the alterations in cognitive behavior suggest that performance is most negatively impacted during the premenstrual and menstrual phases [88].

2.10. Dysmenorrhea and Heavy Menstrual Bleeding in Elite Female Athletes (Quality of Life and Perceived Stress)

The impact of professional sports on female reproductive function has received a lot of attention. Anovulation, amenorrhea, oligomenorrhea, late menarche, and luteal dysfunction may all be linked to high-intensity physical activity and the stress competition that comes with it [67, 89]. The American College of Sports Medicine invented the term "the female athlete triad" to describe the extremely negative effects of sport, which include amenorrhea, osteoporosis, and eating disorders [90], that are commonly seen in ballet dancers and are caused by a relative energy shortfall [69, 91].

A cross-sectional study was conducted between June 2017 and June 2018, involving 150 female elite athletes who sought routine medical and nutritional assessments at the Sports Medicine Center of Careggi University Hospital [92]. The sample encompassed various sports, including soccer, volleyball, rugby, swimming, martial arts, athletics, ballet, and contemporary dance. A control group of 103 healthy nulliparous young females of fertile age, who were not engaged in regular sports activities and were not using oral contraceptives, was also included. Age, body mass index (BMI), and age at menarche did not significantly differ between athletes and controls [69].

The study population comprised nulliparous females of reproductive age, excluding individuals using oral contraceptives or undergoing hormonal treatments [69]. In the subsequent analysis, the elite athletes were divided into three groups based on the percentage of static and dynamic components: Group A (n = 24) included sports with a high static component and low-to-moderate dynamic component (martial arts, ballet, and contemporary dance); Group B (n = 22) included sports with both moderate static and dynamic components (rugby and athletics); Group C (n = 64) included sports with a high dynamic component and low static component (soccer, volleyball, and swimming) [93].

Compared to the control group, elite athletes exhibited a higher prevalence of irregular periods and oligomenorrhea, while amenorrhea cases were not reported. Heavy Menstrual Bleeding (HMB) was significantly more common among athletes, although there were no differences in spotting. Athletes reported experiencing dysmenorrhea less frequently compared to the control group. The prevalence of dyspareunia, dysuria, and dyschezia did not differ significantly between the two groups. When examining menstrual history, cycle characteristics, and gynecological pain based on the dynamic and static components of physical activity, no significant differences were observed among elite athletes [69].

Regarding perceived stress, athletes exhibited higher scores on the perceived stress scale (PSS) compared to controls. However, there were no differences in PSS scores among the three groups. Athletes demonstrated significantly better physical quality of life (QoL) according to SF-12 ratings, while their mental QoL was notably lower. Dysmenorrhea in athletes was not associated with PSS or SF-12 scores. However, HMB was linked to lower mental scores and higher PSS scores in athletes compared to those with normal bleeding [69].

2.11. Menstrual dysfunction from low energy availability in athletes (HPG axis dysfunction)

Low energy affects the HPG axis (Hypothalamic-pituitary-gonadal axis), causing alteration in luteinizing hormone pulsatility. Previous reports showed reduction in luteinizing hormone pulse frequency as well as an acute increase and chronic reduction in luteinizing hormone pulse amplitude. In addition, random measurements showed thatluteinizing hormone is frequently lower than FSH [94]. Amenorrhoea is common among female athletes at various times while training. amenorrhoea can be a symptom of some of the health and performance repercussions of insufficient energy, such as poor bone accretion and low bone mineral density. Because adolescence is a critical period for bone formation, growth, and development, young athletes should be concerned about delayed menarche and secondary amenorrhoea [94].

Female athletes are at risk of various injuries such as the anterior cruciate ligament (ACL) tears have been linked to specific times of the menstrual cycle and hormonal milieus [95]. On the other hand, female athletes are at risk of menstruation disorder, which can harm bone health. This deterioration of bone health increases the chance of fracture; in the long run, decreasing BMD throughout reproductive years increases the risk of osteoporosis [95].

Exercise-related female reproductive dysfunction (ERFRD) is characterized by a variety of clinical and biochemical abnormalities, such as delayed puberty, LPD, oligo-amenorrhea, and anovulation. It occurs in reaction to high-intensity and anaerobic forms of exercise and is one of the diagnostic criteria for overtraining, a condition characterized by intense training that might have negative health consequences [96].

Exercise-induced amenorrhea is caused by a disruption in the normal pulsatile release of GnRH and LH, resulting in hypoestrogenemia. The body's detection of an energy imbalance, which could be owing to a lack of compensatory caloric intake in the face of considerable expenditure, appears to be required for HPO axis disruption. The presence of a hypometabolic state in these patients is supported by changes in other pituitary-derived hormones [97]. Exercise, particularly extended and high-intensity exercise, has been shown to hurt female reproductive hormones. Following prolonged or vigorous exercise, low-calorie availability, low leptin levels, and high stress hormone concentrations disruptions in the HPO axis and female reproductive hormone releases may be seen. These disruptions could result in an irregular menstrual cycle, including luteal phase deficit and anovulation. Further research is needed to determine which therapies might be effective in reducing or preventing the negative effects of extended and high-intensity exercise on female athletes’ reproductive health [98].

2.12. Amenorrhoea in Adolescent Female Athletes

Amenorrhea is defined as the absence of a menstrual period for three or more consecutive months [99]. Amenorrhea in adolescent female athletes is a common problem, and it is often caused by the amount of physical activity and training intensity. The condition can cause adverse effects on their reproductive and bone health [100]. Various studies have shown that adolescent female athletes are at a higher risk of developing amenorrhea due to their pattern of physical activity and intense exercise routines. The condition is more common among athletes involved in sports that emphasize a lean physique such as gymnastics, figure skating, and ballet [101]. According to research in 2014, the prevalence of amenorrhea increases with the frequency and intensity of training in adolescent female athletes [102]. Amenorrhea can cause several problems, including decreased bone density, osteoporosis, and increased risk of stress fractures. It can also affect reproductive health, leading to reduced fertility in the future [103].

It is essential to address amenorrhea in adolescent female athletes promptly. Treatment for the condition may include reducing training intensity, increasing caloric intake, and incorporating strength training into the athlete's exercise routine. Hormonal therapy may also be used to regulate menstrual cycles and prevent bone loss [104]. Therefore, amenorrhea in adolescent female athletes is a common problem that can have adverse effects on their reproductive and bone health. Regular monitoring and interventionby healthcare professionals can help prevent and treat the condition. It is essential to educateadolescent female athletes and their coaches about the importance of maintaining menstrual health while participating in sports [101].

2.13. The Effects of Oral Contraceptives on Exercise Performance in Females

Oral contraceptive pills (OCPs) are dual agents that lower endogenous estradiol and progesterone levels, while giving daily exogenous estrogen and progestin supplementation during the OCP-taking days. Due to alterations in ovarian hormone-mediated physiological processes, this altered hormonal milieu differs dramatically from that of eumenorrheic females and may impair exercise performance [105].

Most females of childbearing age are exposed to fluctuating female steroid hormones due to their menstrual cycle or oral contraceptive use [106]. As a result of OCP use, endogenous concentrations of estradiol and Lipo-Lutin are considerably downregulated in comparison with the mid-luteal section of the cycle [106]. This chronic dysregulation may be responsible for the slightly impaired exercise performance in OCP users compared with naturally menstruating individuals. As seen through previous research, the endogenous hormonal profile of an OCP user is comparable to that observed in the early follicular phase of the physiological menstrual cycle; i.e. low levels of endogenous estradiol and progesterone, respectively [107, 108].

Eventually, the administration or removal of exogenous reproductive hormones caused by oral contraceptive use did not affect the quadriceps and hamstring muscles' maximum dynamic and isometric strength, nor on the first dorsal interosseous (FDI) muscle's maximum isometric strength. This shows that oral contraception showed no effect on young females' maximal force-generating capacity. Furthermore, in terms of muscular function, prolonged downregulation of endogenous estrogen and progesterone did not distinguish young females from their eumenorrheic counterparts, suggesting that the reduction in muscle strength found after menopause is not sex hormone dependent. Future studies can clarify the impact of oral contraceptive use on additional strength and performance metrics, such as muscle fatigability/endurance trials, as well as numerous health indicators, such as blood pressure and bone mineral density, so that specific recommendations can be made to the pill use [107].

3. Conclusions

The menstrual cycle changes among female athletes post traumatic brain injury (TBI) can have significant implications for their overall health and athletic performance. TBIs can disrupt the delicate hormonal balance that regulates the menstrual cycle, leading to irregular or absent periods, hormonal imbalances, and other related symptoms. These changes can have a negative impact on the physical, emotional, and psychological well-being of female athletes. The available research on this topic is limited, and more studies are needed to better understand the specific mechanisms through which TBIs affect the menstrual cycle in female athletes. However, it is evident that the complex interplay between the brain, hormones, and menstrual cycle is disrupted after a TBI, and this can result in significant changes to a female athlete's menstrual cycle patterns.

It is crucial for healthcare professionals, coaches, and athletes to be aware of the potential menstrual cycle changes following a TBI and to consider them in the management and care of female athletes. This may include monitoring menstrual cycle patterns, evaluating hormonal levels, and implementing appropriate interventions to address any disruptions or imbalances. It is also important to provide support and education to female athletes regarding the potential impacts of TBIs on their menstrual health and overall well-being.

In conclusion, menstrual cycle changes among female athletes post traumatic brain injury are a complex and important issue that requires further research and attention. Understanding and addressing these changes can help optimize the health and performance of female athletes who have experienced a TBI, and promote their overall well-being.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors proclaim no conflict of interest.

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