THE ASSOCIATIONS AMONG SPORT-RELATED CONCUSSION, HEAD IMPACT BIOMECHANICS, AND EMOTION DYSREGULATION IN HIGH SCHOOL ATHLETES

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ABSTRACT

Melissa Ann Fraser: The Associations Among Sport-Related Concussion, Head Impact Biomechanics, and Emotion Dysregulation in High School Athletes
(Under the direction of Kevin M. Guskiewicz)

Background: Current recommendations advise athletic trainers to develop and implement plans for athletes' with psychological concerns.[1] Associations between head impact severity (impact frequency, location, and magnitude) and sport-related concussion (SRC) have been identified in football players. However, it is unknown if the inclusion of emotion dysregulation measures may improve clinicians' ability to identify at-risk players at baseline with respect to head impact biomechanics and incident SRC. **Objectives**: This prospective longitudinal study included four objectives: 1) To assess the associations between concussion history and preseason emotion dysregulation measures in high school student-athletes, 2) to assess the associations among preseason baseline emotion dysregulation scores, competition Impact Severity Profiles (ISP), and in-season incident concussion in high school football players, 3) To determine the associations among in-season incident SRC, full season ISPs and emotion dysregulation change-scores in high school football players, and 4) To determine the association of in-season incident SRC and full season emotion dysregulation change-scores (postseason-preseason) in high school student-athletes over one season. **Methods**: 1,053 student-athletes (age = 15.59 ± 1.21) from three high schools completed preseason and postseason concussion history and emotion dysregulation questionnaires during the 2013/14–2015/16 academic years. Of these individuals, 182 football players were chosen to have their helmets instrumented with Head Impact Telemetry System (HITS) accelerometers. Data from these sensors were used to formulate Impact Severity Profiles (ISP) (normal, moderate, poor).

Our emotion dysregulation measures included depression (PHQ-9), anxiety (GAD-7), impulsivity (BIS-11), and aggression (BPAQ), and perceived stress (PSS4, covariate only). Linear regressions were utilized for all analyses. **Results:** Our data only supported our first hypothesis. Concussion history was associated with significantly higher depression (p=0.004) and impulsivity (p=0.014, p=0.002). Preseason scores were associated with age, sex, concussion history and sport. **Conclusions**: The emotion dysregulation scores were not significantly associated with the competition or full season ISPs, or in-season incident concussion. Our emotion dysregulation data supported preseason sex-related findings as well as novel associations that had not previously been reported. These findings indicate that the current protocol still requires further investigation before it could be utilized as an effective prediction method for at-risk athletes.

To my mother, mentor, best friend, confidante, and advisor, Cindy Moegenburg. My path has not always been smooth and often much longer and more difficult than necessary probably. But through it all I could always count on you to be there to give me guidance, support, the truth, a smile, a thoughtful card, and most importantly your love and prayers. Never in my wildest dreams did I think that I would be getting my doctorate, but here I am and I owe a great deal of this accomplishment to you. Even though the miles between us the last 15 years have been great (certainly not by your choosing), you have been my rock and my inspiration. Your path to personal, professional, and spiritual success was also not straight and was fraught with several challenges. Yet through it all your determination and beautiful soul helped elevate you past the difficult tasks and decisions. I am so proud of all that you have accomplished and never miss the chance to tell people all about you. Everyone who meets you is forever changed for the better. I hope to one day be as strong and faithful of a Good Samaritan as you have been your entire life. God blessed me with you. I hope one day you are as proud of me as I am of you.

Love always,

-Missy

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Lastly, to Kevin Church, thank you for all your patience, understanding, grace and support. It meant the world to me.

PREFACE

A PhD was never in my plans, yet here I am. Several factors let me to this place including the guidance of those mentioned above. What has not been mentioned are all the current and former athletes I have encountered and how their experiences, along with my own, have shaped who I am and why I have chosen this path. As a former athlete myself, I thought I was invincible and did not flinch when risks were placed in my way. I overcame injuries that doctors said would make it difficult, if not impossible to return fully to competition. I have seen this same strength and dedication in so many others, but I have also seen many who have sustained injuries, including SRCs, from which full recovery was not possible. I thought I knew what SRCs were and how they affected my athletes in all facets of life. I was wrong. That fateful day at Tarleton State changed my life in more ways than I ever thought possible. I didn't know it at the time, but my life would move down a new path from that moment on. While I wish I hadn't gotten hit by that baseball, I also wouldn't change how it has opened up an entirely new world for me that will hopefully allow me to help others. My research agenda is in large part due the emotional rollercoasters I have personally witnessed my athletes' and myself endure. I have spoken to many more athletes and their loved-ones who have reported similar experiences. SRCs and emotion dysregulation are united in that they are invisible to the outside world. There are no crutches, or slings, or boots to signify an injury has occurred. It is not uncommon for individuals to have extreme difficulty describing or even recognizing what they are feeling. The athletic culture teaches athletes to bury their emotional issues, but I hope that my research can help bring to light how honestly reporting psychological states can improve short-term and long-term quality of life and maybe, just maybe prevent someone from ever experiencing an SRC.

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LIST OF ABBREVIATIONS

ACC	Anterior Cingulate Cortex
AD	Alzheimer's Disease
ADD/ADHD	Attention Deficit Disorder/Attention Deficit Hyperactivity Disorder
AT	Athletic Trainer
BDI-II	Beck Depression Inventory - II
BPAQ	Buss Perry Aggression Questionnaire
BIS	Barratt Impulsivity Scale
CG	Center of Gravity
CSF	Cerebrospinal fluid
CTE	Chronic Traumatic Encephalopathy
dlPFC	Dorsolateral PreFrontal Cortex
DSM	Diagnostic Statistical Manual of Mental Health Disorders
FB	Football
IL	Interleukin
fMRI	Functional Magnetic Resonance Imaging
GAD	Generalized Anxiety Disorder
GAD-7	Generalized Anxiety Disorder 7-Item Scale
GCS	Glasgow Coma Scale
GSI	Gadd Severity Index
HIC	Head Injury Criterion
HITS	Head Impact Telemetry System
HITsp	Head Impact Telemetry severity profile
HS	High School
ICC	Intraclass Correlation Coefficient
ICD	International Classification of Diseases

IED	Intermittent Explosive Disorder
ISP	Injury Severity Profile
LOC	Loss of Consciousness
LHA	Lifetime History of Aggression
MCI	Mild Cognitive Impairment
MDD	Major Depressive Disorder
mOFC	Medial Orbitofrontal Cortex
MRI	Magnetic Resonance Imaging
mTBI	Mild Traumatic Brain Injury
NA	Negative Affect
NFL	National Football League
OFC	Orbitofrontal Cortex
PA	Positive Affect
PAG	Periaqueductal Gray
PCC	Posterior Cingulate Cortex
PCS	Postconcussive Syndrome
PD	Parkinson’s Disease
PFC	Prefrontal Cortex
PHQ-9	Patient Health Questionnaire 9-Item
Pre	Preseason
Post	Postseason
PI#1	Post Injury #1
PIRTP	Post-Injury Return to Play
PTSD	Posttraumatic Stress Disorder
RHI	Repeated Head Impacts
SRC	Sport-related concussion

STAI	State-Trait Anxiety Inventory for Adults
TBI	Traumatic Brain Injury
TNF-α	Tumor Necrosis Factor –α
UNC-CH	The University of North Carolina at Chapel Hill

CHAPTER 1: INTRODUCTION

An estimated 1.6 million sport-related concussions (SRC) occur annually in the United States.[2] At least 5.3 million Americans are currently suffering from long-term effects of concussion equating to $60 billion lost in medical benefits and productivity.[2] Non-athletic moderate-severe traumatic brain injury (TBI) typically results in a greater number of significant short- and long-term repercussions compared to SRCs. However, the risk of sustained deficits has been shown to increase as the number of SRCs reaches and then surpasses three.[3-5] TBIs are associated with structural,[6-8] functional,[9-27] and neurometabolic[28] brain changes, emotion dysregulation[29-51] (personality and affect), cognitive,[37, 52-60] vestibular,[21, 53, 61, 62] and physiological alterations,[63-70] as well as increased risk and earlier incidence of developing neurodegenerative diseases.[71] There is a plethora of research evaluating the relationship between SRCs and structural,[72, 73] functional[72, 74-88] and neurometabolic[89] brain activity, cognition,[3, 90-99] balance,[92, 95, 100-117] mild cognitive impairment (MCI),[3] and impact biomechanics,[106, 108, 110, 118-143] but data evaluating potential emotion dysregulation consequences are lacking. [77, 83, 144-147]

1.1. Head impact biomechanics

Several SRC assessment tools have been evaluated and employed effectively over the last several decades addressing symptomology, cognition, balance, and vision. Head impact biomechanics have also been studied at both the high school and collegiate levels adding depth to our understanding of concussion mechanisms, how impact biomechanics correlate with clinical measures, improvements to protective

equipment, and rule changes to increase safety. Sport-related head impact biomechanics studies have demonstrated a direct relationship between head impact location, frequency, and magnitude with athletes who are at risk for head and neck trauma during participation.[5, 106, 134, 135, 137, 148-151]

American football has been the most widely analyzed sport with the Head Impact Telemetry System (HITS) (Riddell, Elyria, OH) being the most commonly utilized head impact biomechanics assessment tool in literature.[5, 106, 125-127, 152] This triaxial accelerometer system contains six single-axis accelerometers, a wireless telemetry unit, a removable battery, and an onboard data storage unit arranged in a horseshoe pattern (Appendix 1). The system is triggered when an athlete sustains a linear impact ≥10g, recording the subject ID, date, time, magnitude, and location of the impact. High school football players sustain an average of 520-652 impacts per season, while the range of impacts sustained by collegiate football players per season varies far more (258-1400).[127] The average linear (93.3g and 118.4g) and rotational (6505.2 rad/sec^2 and 5311.6 rad/sec^2) acceleration for concussive impacts in high school football and collegiate football players was reported in a 2012 meta-analysis of football concussion biomechanics. Of note, only 0.02% (98) of the 560,000 collisions analyzed resulted in SRCs.[153]

Studies involving head impact biomechanics analyses of football and ice hockey athletes (including youth, high school, college, and professional) have provided several important observations. First, impacts occur more frequently and at higher linear and rotational accelerations in games than in practices.[106, 110, 125, 126, 128, 134, 149] Secondly, these impact frequencies and magnitudes have been correlated with player positions.[106, 121, 123, 125, 126, 128, 134, 149, 154] Linemen traditionally sustain a higher frequency of impacts, but at a lower magnitude compared to other players. Conversely, linebackers, defensive backs, and running backs, incur a moderate number of impacts, but at a much higher

magnitude compared to linemen. Thirdly, impact biomechanics are not correlated with any of the current clinical measures for SRC[106, 123] and therefore cannot be used as a diagnostic tool or to predict concussion outcomes.

Prolonged alterations in symptoms, cognition, and balance after SRC have been reported in a multitude of studies. [95, 100, 104, 105, 155-158] However, there is a lack of evidence evaluating changes that may occur over time due to repeated head impacts (RHI),[152] or if an association exists between head impact biomechanics and clinical measures of SRC in humans. [108] Broglio, et al. did not observe a correlation between symptoms, neurocognitive change scores, and their head impact biomechanics data (peak linear and rotational acceleration, HIT severity profile (HITsp) in a four-year high school football study that included 20 reported concussions.[123] They also did not observe significant relationships between the neurocognitive change-scores and impact frequency, cumulative linear or rotational acceleration, or the cumulative HITsp from all impacts leading up to a concussive injury. These findings gave support to a similar study evaluating the relationship between the acute effects of concussion and impact biomechanics in collegiate football players.[106] The authors of both studies concluded that football impact biomechanics are not useful predictors of injury severity in concussed athletes.

It is important to note that while these studies have compared impact biomechanics measurements to baseline symptom, cognition, and balance scores, they have left out an important piece of the puzzle, the emotion dysregulation aspect of sport. This key factor is a common omission in SRC research, but one that has been included in a large number of moderate-severe TBI studies.

1.2. Emotion Dysregulation

Neuropsychiatry is the study and treatment of cognitive, emotional, and behavioral problems caused by neurologic disorders. This field is unique from both neurology and psychiatry due to its belief that the two fields are in fact intertwined and that all patients should be treated as such. The general position of neuropsychiatrists is that mental states are brain states and that any neurological illness or injury will lead to alternations in cognition, emotion, and behavior.[159] As mentioned above, SRC research has been investigating the cognitive and balance effects of SRC for decades. However inadvertently, researchers have consistently omitted emotion dysregulation measures (i.e., the negative psychological consequences of injury) as outcome variables in their SRC studies. The same cannot be said of studies involving moderate and severe TBI.

Investigators of non-athletic moderate-severe TBIs have been exploring the emotion dysregulation consequences of head injuries for more than 50 years. Moderate-severe TBI studies with non-athletic,[39, 160-164] military,[41, 165, 166] and animal[167, 168] populations have correlated heightened depression, anxiety, aggression, and impulsivity with poor long-term health outcomes (violence, loss of job/relationships, neurodegenerative disease, etc.).[41, 169] Similar emotion dysregulation consequences have also been found in adolescents who have sustained a moderate-severe TBI.[170-175] Previous research has shown two negative affect disorders, depression and anxiety, are significantly correlated in injured[29, 31, 36, 44, 46, 49, 163, 176] and non-injured[177-179] populations. To a limited degree, depression and anxiety have been investigated in athletes with and without concussion,[4, 85, 99, 180] but none of these studies have prospectively assessed changes over time. Elevation of these affect disorders are common following TBI and SRC in the short-[32] and long-term.[4, 36, 37, 99, 181, 182] Alterations in personality, specifically aggression and impulsivity, have been strongly correlated with depression.[183-187] These

personality disorders are also strongly correlated with one another in all populations, including moderate-severe TBI.[33, 42, 160, 186, 188-191]

More importantly, no studies currently exist evaluating the associations between sport exposure, SRC, impact biomechanics, and emotion dysregulation measures. If the clinical goal is to treat the entire person and ensure optimal outcomes, this line of research appears to be the next logical step (**Figure 1.1**). To fully understand the relationships among sport, head impact biomechanics, and SRCs (history and incidence) on short- and long-term emotion dysregulation alterations, it is necessary to expand this science to include a variety of sports, including football, in a longitudinal prospective analysis.

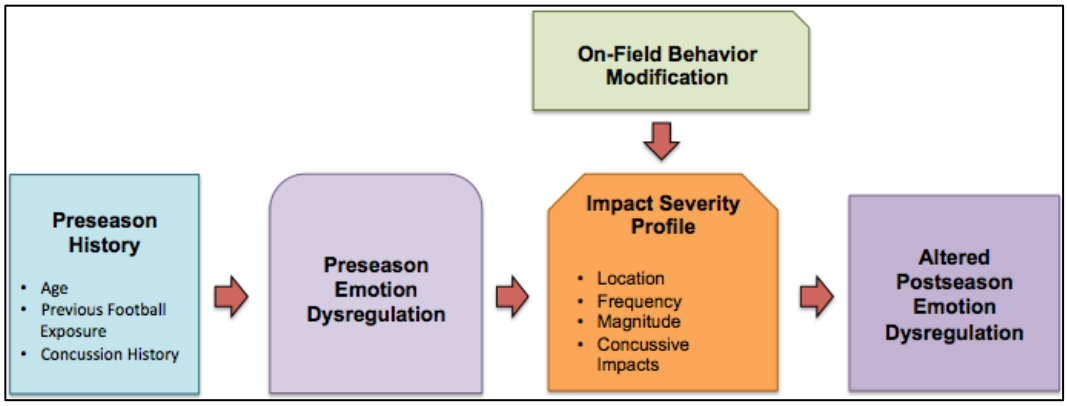

Figure 1.1: Procedural Progression

1.3 Statement of the Problem

Understanding the association of SRC, history of contact versus non-contact participation, head impact biomechanics, and emotion dysregulation measures could allow for early, cost-effective annual athlete evaluations with additional interventions to assess changes after each season and/or SRC. It would then be possible to prospectively track the incidence and potential increases in emotion dysregulation, resulting in treatment for individuals at symptom onset rather than delaying care until after significant life alterations have already occurred. The end goal is to delay or prevent

the progression of symptoms associated with significant neurodegenerative diseases through early detection and interventions (behavior modification, counseling, etc.). Our current study will be a first-step in evaluating the associations that exist between history of sport participation, SRC history and incidence, head impact biomechanics, and emotion dysregulation measures in high school athletes (**Figure 1.2**).

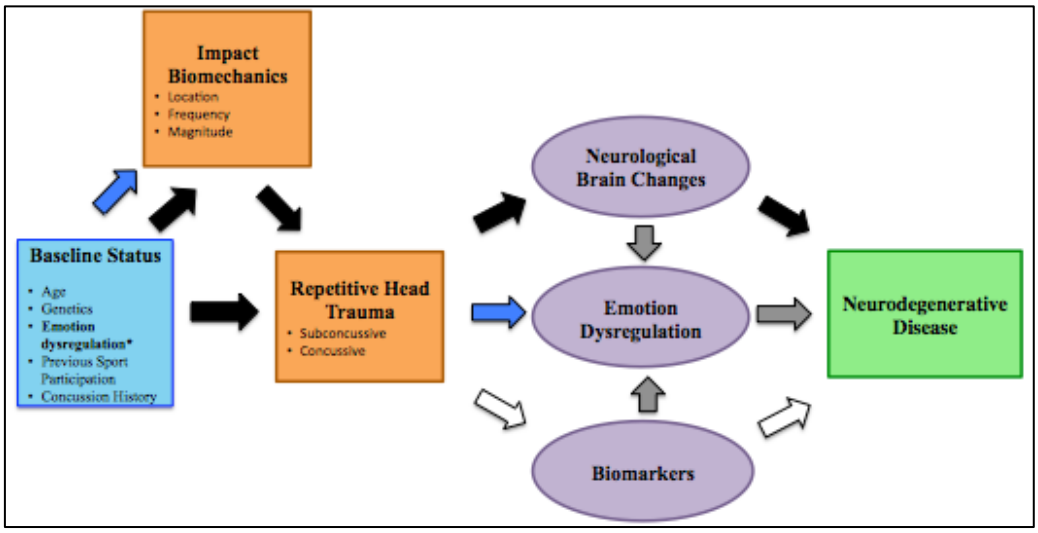

Figure 1.2. Theoretical progression from pre-competition status to neurodegenerative disease in athletes. Black arrows represent what we currently know. Grey arrows are based on non-sport related TBI and limited sport-related concussion data. White arrows have yet to be determined. Blue arrows represent our research questions.

1.4 Research Variables

*The use of these as independent or dependent variables is listed in Tables 3.3 and 3.4.

1. *Group*
    a. *Participant (P): Full-time student-athletes who were on the active varsity or junior varsity roster for their respective sport at one of the three schools at the start of the study.*

i. *Football player (FB): Full-time student-athletes who were on the active varsity or junior varsity football roster at one of the three respective schools at the start of the study.*

ii. *Teammate Control (Control): Full-time student-athletes on the active team roster at one of the three respective schools at the start of the season that were matched to the Age, position, play*

2. *Age: Age was evaluated as a continuous variable from 13-19 years of age.*
3. *Time*
    a. *Preseason:* Preseason Concussion History and Emotion Dysregulation Questionnaire (all) were gathered in the first few weeks of preseason participation for all participants.
    b. *Postseason*: Postseason Concussion History and Emotion Dysregulation Questionnaire were collected within 4 weeks of the last game/practice for each participant.
    c. *Post-concussion – initial injury*: Post-Injury #1 Concussion History and Emotion Dysregulation Questionnaire were collected within 72 hours of the student-athlete reporting the SRC, from the injured student-athlete, a matched teammate and a non-contact sport control.
    d. *Post-concussion – return to play (RTP):* After completion of a school-based return to play protocol the Full Return to Play Concussion History and Emotion Dysregulation Questionnaire were completed by the concussed athlete, a matched teammate, and a non-contact sport control.
4. *Contact Level*
    a. *No-contact:* cross country, swimming, tennis, track
    b. *Low-contact:* baseball, basketball, diving, pole vault, softball, volleyball
    c. *High-contact:* field hockey, football, lacrosse, soccer, wrestling

5. *Sport Type*
    a. *Individual:* cross country, diving, pole vault, swimming, tennis, track, and wrestling
    b. *Team:* baseball, basketball, field hockey, football, lacrosse, soccer, softball, and volleyball
6. *Emotion Dysregulation measures:* The following emotion dysregulation measures were collected via the four Concussion History and Emotion Dysregulation Questionnaires.
    a. *Affective measures:*
        i. *Depression: Patient Health Questionnaire 9-item (PHQ-9)*
        ii. *Anxiety: Generalized Anxiety Disorder 7-item Scale (GAD-7)*
    b. *Personality measures:*
        i. *Impulsivity: Barrett Impulsivity Scale – 11 (BIS-11)*
        ii. *Aggression: Buss Perry Aggression Questionnaire (BPAQ)*
    c. *Stress measure:*
        i. *Perceived Stress Scale – 4 (PSS-4).* The PSS-4 was included only as a covariate. It was not analyzed as a primary outcome variable.
7. *Impact Biomechanical measures (Football only)*
    a. *Impact frequency: The number of impacts sustained by a football player ≥10g.*
    b. *Impact magnitude: The severity of an impact to the body or head.*
        i. *Linear acceleration (g): The rate of change in velocity along a straight line. All impacts ≥ 10g were recorded.*
        ii. *Rotational acceleration (rad/s^2): The rate of change in angular/rotational velocity per second squared.*

c. *Impact location: The HITS system data were used to determine the location of the impact to the head. It was divided into the following four categories*[134]

   i. *Front: Any impact within 45 degrees from either side of the anterior mid-sagittal plane (Includes impacts to the facemask)*

   ii. *Top: Any impact at an angle >60 degrees in elevation*

   iii. *Side: Any anterior or posterior impact within 45 degrees of the mid-sagittal plane. This is further defined as occurring to the right or left of the helmet.*

   iv. *Back: Any impact within 45 degrees from either side of the posterior mid-sagittal plane*

8. *Impact Severity Profile (ISP) (football only):* At the completion of the season the following criteria were used to determine each player's profile status: Player sustained 1) more than 20% of their impacts were to the crown of their head, or 2) more than 7% of impacts exceeded 2 standard deviations above the mean peak linear acceleration (≥60 g linear acceleration). All impact data were gathered via the HITS accelerometers.

   a. Poor: Players who met two of the criteria denoted above.

   b. *Moderate: Players who met one of the criteria noted above.*

   c. *Normal:* Any football player who did not meet any of the above criteria.

1.5. Research Questions (Figure 1.3)

Research Question 1: What is the association between concussion history and preseason emotion dysregulation measures in high school student-athletes?

Hypothesis 1: SRC history will be associated with worse (higher) emotion dysregulation scores at preseason in high school student-athletes.

Research Question 2: What are the associations among preseason emotion dysregulation, competition ISPs, and in-season incident concussion in high school football players wearing instrumented helmets?

Hypothesis 2: A worse emotion dysregulation profile at preseason will be associated with a worse competition ISP and/or an increased likelihood for in-season incident SRC over the course of one season.

Research Question 3: What are the associations among in-season incident SRC, full season ISP, and emotion dysregulation change-scores in high school football players wearing instrumented helmets over one season?

Hypothesis 3: In football players, incident SRC and a worse full season ISP (top of head impacts and/or more severe impacts) during one season will be associated with worse emotion dysregulation profiles at postseason, relative to the preseason emotion dysregulation profiles in the same individuals.

1.6. Exploratory Research Question

Exploratory Research Question: What is the association between in-season incident concussions on emotion dysregulation change-scores (postseason-preseason) in high school student-athletes over one season?

Exploratory Hypothesis: Student-athletes sustaining an in-season incident concussion will present with worse (higher) emotion dysregulation change-scores compared to age, position, and playing time matched teammate controls over one season.

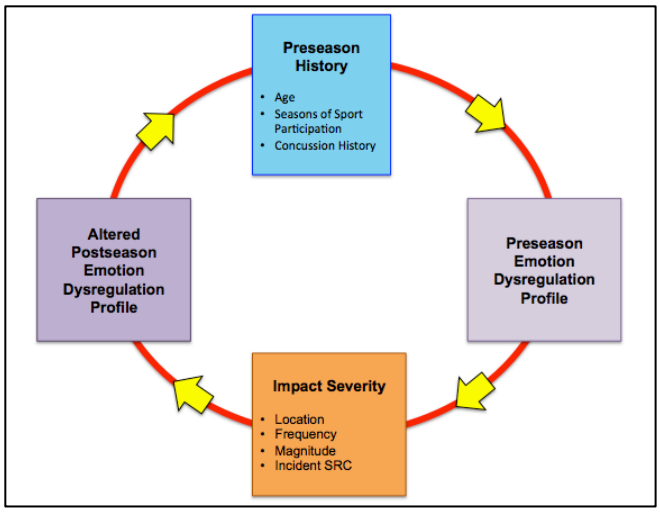

Figure 1.3. Conceptual model of the cyclical relationship between Emotion Dysregulation Profile and Impact Severity Profiles (ISP) over sequential seasons.

1.7. Operational Definitions

Concussion: A complex pathophysiological process affecting the brain, induced by biomechanical forces.[192]

Emotion Dysregulation Profile: The emotion dysregulation measures (PHQ-9, GAD-7, BIS-11, and BPAQ) were evaluated independently to determine *individual* profiles and together to determine *full* profiles (analyses contained both affective and personality measures). A higher score on these measures indicated a worse emotion dysregulation profile and a lower score indicated a healthier Emotion Dysregulation Profile.

Repeated head impacts (RHI): All impacts (concussive and subconcussive) to the football players' bodies or heads that result in ≥10g of linear acceleration were time and date stamped by the Head Impact Telemetry System (HITS). We attempted to record and remove all impacts that occurred outside of team activities and impacts that occur when the helmet is not being worn (e.g., a thrown or kicked helmet).

*Seasons of sport participation: At preseason, t*he participants were asked to sum all years of organized participation for their respective sport. This count included organized youth teams and partial seasons that ended early due to injury, illness, etc. At postseason they were instructed to include the season they had just finished in their count.

Sport-related concussion (SRC): Any concussion that occurred during sports participation that was diagnosed by a medical provider.

Traumatic Brain Injury (TBI): While SRC falls under the broader definition of TBI, for the purposes of this study TBI referred to all non-sport-related head injuries. It encompassed a range from mild to severe in nature. These injuries commonly result in the following reductions in the patient's Glasgow Coma Scale scores: mild TBI (mTBI): 13-15, moderate TBI: 9-12 severe TBI: <8.

1.8. Assumptions

1. All football helmets were fit correctly, and the football players had their helmets properly secured to their heads for all impacts.
2. The high school football players enrolled in this study were representative of all football players of similar age and level.
3. The amount of contact within each sport among the schools was homogeneous.
4. All participants were able to accurately recall all past SRCs.
5. All participants honestly answered the emotion dysregulation measure items at all time points.

6. There was homogeneity between the participants and within the respective high school groups (football players vs. non-contact controls, males vs. females, contact vs. low-contact vs. no-contact) at baseline.
7. Contact with the parent/guardian(s) and athletic trainers concerning elevated emotion dysregulation scores did not affect the study outcomes.

1.9. Delimitations

1. Data were collected from public high schools and not private because public schools were the most accessible schools with football teams for our researchers.

1.10. Limitations

1. One of the high school football teams had worn accelerometers during the 2012/13-2014/15 academic years, but the 2015/16 academic year was the first year for the other two high school football teams. Their comfort level wearing the accelerometers could have affected enrollment and data collection.
2. Additionally, it is possible that the emotion dysregulation scores for the student-athletes at the two new schools could have differed from the returning school, due to a novelty affect for these athletes.
3. Emotion dysregulation measures were collected via a self-report Internet based program, Qualtrics.com, instead of using a licensed neuropsychologist. However, the measures have been well validated and have been utilized in this manner by our group in previous studies.
4. This study was part of a larger study (BEMOD) evaluating an on- and off-field behavior modification intervention for high-risk football players at 2 of the 3 high schools involved in this study. The third school was the control for the BEMOD

study. Exposure to the intervention could have lead to heterogeneity between the intervention and control schools.

1.11. Significance of the Proposed Study

The National Football League (NFL) has agreed to pay $765 million with a $5 million per person cap to 2,400 retired players who report long-term emotion regulation and neurological alterations after sustaining SRCs in the NFL.[193] The retired NFL players have reported developing conditions including chronic headaches,[194] depression,[4, 99, 144, 182] Alzheimer's disease (AD),[194] mild cognitive impairment (MCI),[4, 99, 144, 182, 194] dementia[4, 144, 194] and chronic traumatic encephalopathy (CTE).[194] Researchers have found retired NFL players with 3+ SRCs are more likely to experience neurological problems and depression than players with 0-2 SRCs.[3, 4, 182] The average recovery from a SRC is 7-10 days[195] with a significant increase in recurrent SRCs as the history increases from 0-3.[5]

Non-athletic moderate-severe TBIs are commonly an isolated incident associated with structural damage and lengthy recovery periods, if full recovery is attained. TBIs have been correlated with increased emotional arousal, specifically depression,[4, 36, 44, 163, 196, 197] anxiety,[29, 32, 36, 56, 176, 198] impulsivity,[38, 52, 199, 200] aggression[38, 43, 44, 164, 197] resulting in diminished short and long-term quality of life.

To date, only depression has been analyzed as a psychiatric outcome following repeated head impacts (RHI) and SRC, leaving a significant gap in the literature concerning their effects on other affective emotions. The contribution of the proposed research is expected to determine the association of SRC history and incidence, sport participation, head impact biomechanics, and emotion dysregulation measures in high school student-athletes compared to controls throughout a 3-year prospective study. The contribution will be significant because it will uncover new markers for short- and long-

term outcomes of RHI and SRC, and will have implications on accelerated diagnosis and treatment of at-risk athletes. The ability to identify an association between SRC, head impact biomechanics, and self-reported emotional regulation changes will help us ascertain a more efficient method to identify early onset of neurological dementia, including CTE. These findings will allow at-risk athletes to receive improved treatment for psychological conditions and potentially prevent catastrophic outcomes due to self/other directed violent acts.

CHAPTER 2: LITERATURE REVIEW

Introduction

Traumatic brain injury (TBI) is “an alteration in brain function, or other evidence of brain pathology, caused by an external force”.[201] Under this definition, an “alteration in brain function” necessitates the presence of at least one of the following: decreased or loss of consciousness (LOC), any memory loss (amnesia), neurological deficits, or an altered mental state. The literature describes TBI as continuum spanning from mild to severe, with sport-related concussion (SRC) situated to the far left, below mild TBIs (mTBI). Most studies involving TBI research are conducted in emergency departments, in- or out-patient rehabilitation centers, or a mixture of these. The majority of participants recruited for these studies experience at least one of the following: diminished Glasgow Coma Scale (GCS) scores, confirmed structural damage via imaging, LOC, and/or amnesia. It is not uncommon for these individuals to exhibit prolonged deficits for weeks to years.

Unlike individuals who are affected by TBI, the estimated 1.6 million Americans affected annually by SRC[2] typically recover fully within 7-10 days without long-term physical or cognitive impairment.[195] Therefore, they are not included in the majority of TBI studies. However, some SRCs result in lingering effects long after the concussive incident. It is believed approximately 15% of these individuals go on to suffer from post-concussive syndrome (PCS)[202] even after very “mild” head injuries. The effects of PCS are not well defined, again due to the extreme variability in symptoms that may be exhibited, but most definitions require the presence of post-concussive symptoms for at least 3 months after injury.[203] The general areas most often affected include: vision,

balance, sleep, fatigue, cognition (memory, executive control), and psychological disturbances (including depression, aggression, and anxiety).

One important distinction that has been overlooked by TBI researchers is the frequency in which athletes sustain concussive and subconcussive repeated head impacts (RHI) compared to those who suffer a mild-severe TBI. Most individuals may sustain 1-2 TBIs in their lifetime, whereas some contact sport athletes have been shown to sustain more than 1000 subconcussive RHI in one season[5] and report multiple SRCs throughout the duration of their athletic career.[3, 4, 99] The accumulation of RHI and multiple SRCs some athletes sustain over the course of their athletic career may in fact increase the overall severity of these head injuries and shift SRCs to the right on the TBI continuum. This lateral shift may help explain why some athletes later in life have been shown to display cognitive deficits and emotional dysregulation similar to those described in the TBI literature.[3, 4, 99]

2.1. Head Impact Biomechanics

Naunheim et al. published the first sport-related head impact biomechanical study using triaxial accelerometers in 2000.[204] This study was the jumping point for all subsequent studies, with the first on-field application of this technology occurring in 2003.[205] Since then, a multitude of researchers have investigated the relationships between sport-related head impact biomechanics and level (adolescent, middle school, high school, college, professional), event (practice vs. game), position, play type, sex, infractions, anticipation level, neck strength, and incidence of SRC.

Head impact biomechanical analyses allow researchers to evaluate not only the frequency of impacts, but also the magnitude, location, and duration. Head impact frequency increases with level of play as does impact severity.[130] Athletic-exposures are also positively correlated with impact frequency.[128] An athletic-exposure is defined as “1

student-athlete participating in 1 practice or competition in which he or she was exposed to the possibility of athletic injury, regardless of the time associated with that participation".[206]

Head impact biomechanics studies have consistently found several important football-related factors indicating elevated injury risk. Across all impact biomechanical studies impact frequency and magnitude are greater in games compared to practices.[106, 121, 126-129, 134, 137, 142] Several studies have found correlations between player position and impact magnitude in high school and collegiate football players[106, 121, 126-128, 134, 142] suggesting a potential injury risk escalation for certain field positions (e.g., linemen, running backs, linebackers). Linemen consistently sustain the greatest number of impacts over the course of a season, but these impacts are typically lower in magnitude than the specialty players. In 2009, Broglio et al. reported high school football players average 15.87 ± 17.87 impacts per session, with impacts occurring 1.04, 1.69, and 1.98 times more frequently for defensive line players than offensive line, offensive skill, and defensive skill respectively.[126] However, others have reported a slightly differing distribution of player position impact frequency for both high school and collegiate football players.[106, 122, 128] In a college sample, event (practice, game) impacts ranged from 11.5 (defensive linemen) to 3.2 (quarterbacks) in practices and from 29.8 (defensive linemen) to 7.3 (wide receivers) in games, with impacts occurring 2.4 times more often in games than in practices for all positions.[128] Youth football studies have found similar impact ratios for games versus practices.[207] Impact frequency has not been correlated with cognitive or balance changes over the course of one football season[122, 152] and a study of retired NFL players indicated that SRC history outweighs impact frequency for long-term cognitive and functional changes (unpublished UNC study – Eleanna Varangis). An earlier NFL study also found no correlation between football exposure (impact frequency) and anatomical MRI findings.[77]

A great deal of research has investigated the frequency, magnitude and subsequent effects of impact location. Impacts occur most often to the front of the helmet (facemask) followed by the back, side, and top,[106, 121, 126-129, 134] with one middle school study finding back impacts to slightly surpass front.[130] Crisco et al. reported that offensive linemen experience the greatest percentage of front impacts, whereas quarterbacks experience the opposite (back>front).[128] Additionally, linemen, defensive backs, and linebackers all had a greater frequency of front impacts compared to back. Importantly, regardless of playing level, top of the head impacts result in the highest linear magnitude in football and ice hockey athletes.[106, 121, 126-129, 134, 137, 142] This finding is concerning due to the increased risk of head and neck injuries with top of the head impacts. However, our 2014 pilot data indicated that the number and magnitude of top impacts provided by the HITS data may be exaggerated and should be investigated further. Additionally, top of head impacts also result in more SRCs compared to other head impact locations.[152]

Ommaya and Gennarelli discovered that rotational accelerations were far more critical in determining concussion outcomes compared to translational forces using a head acceleration device able to isolate linear and rotational acceleration forces.[208] They found concussion incidence was more common with moving rhesus monkey heads as opposed to fixed heads receiving blows with similar forces. Football athletes are often taught to contract their neck musculature (bull their neck, “hulk up”) prior to impacts and look straight ahead to couple the head and neck thus reducing rotational forces. While this approach may be effective on the field for reducing neck injures, human studies using player neck strength, neck circumference, height, and body mass have not unanimously supported Ommaya and Gennarelli’s theory of reduced linear and rotational acceleration or concussion incidence.[138, 209, 210] A soccer study comparing males and females found females experience significantly greater head acceleration putting them at

greater risk for head injury.[210] Of note, two football studies indicated individuals with stronger musculature might actually be a greater risk for higher magnitude impacts.[138, 209] All such studies recommend further investigation with improved methodology to determine the practicality of Ommaya and Gennarelli's theory in sports.

A youth ice hockey biomechanical study found head impacts related to infractions result in significantly greater linear magnitudes compared to impacts without associated infractions.[136] Interestingly, Mihalik et al. did not find any significant differences in impact magnitude between striking and struck ice hockey players indicating both players are at an increased risk for injury.[136] Additionally, increased closing distance[135, 139] (e.g. open field/ice impacts) and unanticipated impacts[135] result in increased linear acceleration. Together these studies indicate an on- and off-field behavior modification intervention to improve technique and field awareness may result in reduced impact severity, top of the head impacts, and overall risk of injury. Finally, It is important to note that studies investigating the influence of head impact biomechanics on emotion dysregulation in the short- and long-term are lacking.

2.1.1 Head Impact Telemetry System (HITS)

The majority of sport-related head impact biomechanics research has utilized the Head Impact Telemetry System (HITS) (Riddell, Elyria, OH) in football populations. This triaxial accelerometer system contains six single-axis accelerometers, a wireless telemetry unit, a removable batter, and an onboard data storage unit arranged in a horseshoe pattern (Appendix 1). HITS accelerometers are only compatible with Riddell L-XL VSR-4, or M-XL Revolution and Revolution Speed helmets. Each accelerometer is spring-mounted to ensure constant contact between the head and each accelerometer. This design is crucial for measuring head acceleration and not just helmet movement. This 5-degree of freedom system estimates rotational acceleration about the antero-

posterior and mediolateral axes.[211] All linear measures are calculated using the center of the head as the center of gravity (CG) and a novel algorithm developed by Simbex.[212] The algorithm is oriented with the x-axis in the positive direction posteriorly, the y-axis positive moving away from the right side of the head, and the z-axis is positive in the superior direction, with the CG at (0,0,0).[205] The linear acceleration vector is combined with the assumed rotation point 10cm inferior to the CG to estimate rotational acceleration.[211] Error has been estimated at 10% in magnitude and 10 degrees for impact location with these algorithms. The azimuth and elevation are used to determine the impact location. Azimuth is the angle between the point of interest and the reference vector on the reference plane (sagittal, coronal, transverse). The HITS azimuth angle is the angle between the impact direction vector as it passes through the CG and a horizontal plane that also passes through the CG.[205]. The HIT system has been validated in the field[205, 212] and in the laboratory.[213] Using a Riddell VSR-4 helmet, Duma et al. reported the estimated impact location and magnitude for each location were replicated within ± 0.41 cm and the average impact location error for both the azimuth and elevation was limited to ±1.20 cm.[205]

The system is triggered when an athlete sustains a linear impact ≥10g to their head or body. Data is recorded for 40 ms (8 ms prior to the impact and 32 ms afterwards) at 1000 Hz and then wirelessly transmitted via radio frequency (903-927 MHz) to the sideline computer in real-time.[126] The encoders have a range of at least 150 yards and are able to store up to 100 impacts in the on-board storage unit if they move out of range from the sideline device. Subject ID, date, time, magnitude (e.g., severity), and impact location are all recorded for every triggered event. The HIT System is able to simultaneously monitor up to 64 players with a single sideline system. The data is stored in the onboard data storage unit until transmitted via wireless FM waves to a sideline laptop where it is stored until uploaded to a secure cloud. Once the data is uploaded to

the cloud, the system removes all data points deemed to be artifact and stores the remaining impacts on their system, which is then available for download and analysis by the research team.

The HITS impact data can be used to calculate head impact severity measures that are commonly used and have been validated, including Head Injury Criterion (HIC) and Gadd Severity Index (GSI),[205] as well as a Head Impact Telemetry severity profile (HITsp).[214] HIC is the likelihood of an injury arising from an impact. Duma et al. defined it as the maximum value of the integral of acceleration over a 36 second pulse, but may also be calculated using smaller time intervals (e.g., 15 ms).[205] HITS data is reported in relation to this shorter time interval as HIC15 in several studies.[75, 119, 120, 213, 214] The average injury threshold is determined through the GSI calculation. GSI calculates a value for pulses with various durations using the integral of acceleration with respect to time.[205] Finally, HITsp is a predictive measure used to determine the risk of concussion. It uses the peak linear and rotational accelerations, impact duration and location to determine a weighted composite score.[214] SRC incidence in high school and collegiate football players has been correlated with HITsp.[214] It was also found to be more predictive of injury than HIC and GSI. All three of these composite scores have been described in detail previously and are computed by the HITS software.[205, 214]

Football studies have shown biomechanical data (impact magnitude and location) correlate well with concussion incidence, but that the sensitivity of these variables is still quite low.[3, 125, 214] Using the model described previously, Ommaya developed an injury risk curve using rhesus monkeys and isolated linear and rotational accelerations, suggesting greater magnitudes are more deleterious.[215] His injury risk model indicated a rotational acceleration of 4500 rad/sec^2 threshold when the rotational velocity is under 30 rad/sec in the sagittal plane. Ommaya was able to measure magnitudes related to pure rotational forces, thus a limitation of his model is the practical

application of his methods with humans is nearly impossible. Human studies and real-life impacts never occur in this manner. Linear and rotational acceleration has been noted with every impact recorded and these impacts typically involve some form of rotation in all three planes.

Efforts have been made to improve the clinical utility of HITS data by determining a more practical injury risk curve. Rowson et al. were able to determine a risk injury curve utilizing HITS data collected over 3 seasons from 335 Division I collegiate football players.[211] In that time, they captured nearly 287,000 impacts, including 57 concussive head impacts. Subconcussive and concussive impacts to the front and back together constituted 67.5% and 57.9% of the total impacts, followed by side (17.3%, 12.3%) and top (15.2%, 29.8%) impacts. As expected, the rotational acceleration for concussive impacts was greater than subconcussive. The researchers were quick to point out that rotational acceleration is only a piece of the puzzle and rotational velocity has equal importance. Ommaya et al. found velocity and duration were instrumental in their whiplash findings.[216] This finding was significant since many football impacts involve some form of whiplash that produces the rotational and linear accelerations seen using the HIT Systems.

Head impact biomechanics measures over the last 15 years have improved immensely. Algorithms have been altered to improve impact magnitude accuracy (e.g., HITS). Technological advances have resulted in miniaturized accelerometers that can be worn by helmetless athletes (e.g., X2 XPatch and Mouthguard [X2 Biosystems, Seattle, WA]). The validity and reliability for these measures have yet to be determined, but the advent of these systems now gives researchers the ability assess the head impact biomechanics of non-helmeted sports (soccer, basketball, field hockey) as well as helmeted sports other than football and ice hockey (lacrosse). Even with these technological advances and a multitude of studies investigating the relationship between

head impact biomechanics and concussion incidence and outcome, there is a gap in current literature investigating it's association with the emotion dysregulation seen in TBI literature and reported by retired professional athletes. Thus, a prospective longitudinal study investigating this relationship is the next step to improving the safety and care of our current and future athletes.

2.2: The Neurometabolic Cascade of Concussion

Giza and Hovda have amassed the results of several head impact biomechanical and physiological studies to describe the "Neurometabolic Cascade of Concussion".[217, 218] The presence of a neurometabolic cascade following head injury has been established, during which the affected cells experience a rapid increase in calcium and sodium and a decrease in potassium.[219, 220] This ionic flux triggers hyperglycolysis to alleviate the increased demand for adenosine triphosphate and increased adenosine diphosphate. The resulting glycolytic hyper-drive occurs when most of the surrounding vessels are vasoconstricted, thus causing a mismatch in nutrient supply and demand. The mitochondria attempt to correct the issue by increasing uptake of the calcium. However, this is only effective for a short time before the calcium influx results in mitochondrial dysfunction, consequently aggravating the oxidative metabolism failure and sending the system further into an energy crisis. Additionally, the injured cells are releasing free radicals, which only potentiate the issue. A state of decreased metabolic functioning follows shortly thereafter, lasting for up to 7 to 10 days.[217, 218] Not surprisingly, most individuals who sustain SRCs experience symptoms for approximately the same length of time. The duration of these effects seems to be related to age, concussion history, and injury severity.[5, 106, 149] To fully understand the effects of sport, head impact biomechanics, and SRCs on short- and long-term alterations, it is necessary to expand this science to include all sports.

2.3. Emotion Dysregulation and TBI

A history of mild-severe TBI has been shown to lead to psychological long-term decline.[39, 47, 48, 51, 177] Victims of TBI suffer cognitively, physiologically, physically, and have reported difficulties with emotion regulation. Researchers have begun to evaluate emotion dysregulation after non-athletic TBI and SRC utilizing multiple measures including self-report measures.[8, 163, 221-224] Moderate-severe TBI research has shown up to 75%[38, 43, 44, 164] of these individuals experience increased depression, anxiety, aggression, and/or impulsivity resulting in diminished short and long-term quality of life. Additionally, these four affective behaviors are highly correlated in TBI populations.[42, 43, 49, 160, 169, 181, 191, 225-227] In a 12-month study comparing TBI patients to trauma patients without neurological consequences, 33% (30 out of 91) of the TBI patients developed major depressive disorder (MDD).[44] Of those who developed MDD, 76.7% and 56.7% also developed anxiety and aggressive behaviors respectively. It is widely believed that depression and anxiety result from difficulties in emotion regulation and that those with less effective management techniques are more likely to experience more severe symptoms and for longer durations eventually cascading into clinical levels of depression and anxiety.

The most frequently reported emotional alterations are depression and anxiety after head injuries. These two affective emotions/behaviors are highly correlated in all populations.[228] Elevations in depression and anxiety have been noted in both sport-related and non-sport related groups[4, 85, 99, 180, 228, 229] as well as after single[85, 97, 229] and repetitive concussions.[4, 97, 99] There is also evidence of metabolic changes correlating with elevated depression despite negative neuroimaging findings.[229] Other affective behaviors have been reported after non-sport related head injuries including impulsivity,[42] & aggression.[38, 39, 41, 42] There has been very little research done in the short-term to show how these affective behaviors are altered in both sport-related and

non-sport related populations. Some of the TBI studies were not conducted until several decades after the head injuries occurred so it is difficult to determine how much and at what point these changes occurred.[58] Most of the SRC-related work has involved long-term emotion regulatory complications.[4, 99] It is possible that these changes started early in their sporting careers and continued to progress with continued sport participation. Continued football participation necessitates continued exposure to head impacts. While a few may result in SRCs, the greater majority of these impacts are typically subconcussive. To date, no published research indicates how subconcussive impacts may affect emotion regulation in athletes (male or female, contact or non-contact sports).

It has been argued by some TBI researchers that a large number of individuals who suffered moderate-severe TBIs were already experiencing (un)diagnosed emotion regulation conditions (e.g., depression, anger, anxiety, disinhibition) prior to their injury.[42, 44] Alternately, it is possible that these individuals actually do experience significant personality and affective changes after their TBIs. In a study of severe TBI patients with no previous history of emotion dysregulation, Ciurli et al. found increased age to be significantly correlated with dysphoria/depression and nighttime disturbances, and individuals with focal lesions had 4 times greater risk of developing anxiety compared to healthy controls at a minimum of 30 days post-injury.[230] Overall, their participants reported a high number of emotion dysregulation symptoms, apathy (42%), irritability (37%), dysphoria/depressed mood (29%), disinhibition (28%), eating disturbances (27%), and agitation (24%). Anxiety, depression, aggression, and fatigue were significantly correlated with psychosocial function (Sydney Psychosocial Reintegration Scale) and with one another in a 10-year follow-up study of mild to severe TBI patients.[36]

TBI neuroimaging and physiological biomarker studies further support the relationship between head injuries and emotion dysregulation. Several studies have

found associations between depression, structurally altered brain regions (gray matter, white matter, ventricles, cerebrospinal fluid [CSF]), regional and network activation abnormalities, and physiological biomarkers in those with and without TBI patients.[83, 99, 177, 231-249] These studies accentuate the importance of evaluating and treating the entire person after a head injury, which cannot be attained with current SRC evaluation and treatment protocols that omit emotion dysregulation measures.

2.3.1. Differences in SRC and TBI Mechanisms and Outcomes

There is a great disparity in the frequency of impacts sustained when comparing TBI and SRC populations. Most TBI victims experience one traumatic event resulting in both focal and gross damage. In 2010, the Centers for the Study of Disease Control and Prevention released a report detailing the epidemiology of TBI in the United States from 2002-2006.[250] The most common mechanisms for TBI-related hospitalizations and deaths in the United States were motor vehicle accidents (20.7%, 31%), falls (22.7%, 18.9%), and assaults (5.6%, 11.3%), with male hospitalization and deaths (61.9%, 73.7%) exceeding females' (38.1%, 26.3%) respectively. TBI mechanisms are typically at a much higher velocity and are more commonly associated with additional injuries including skull and cervical spine fractures, intracranial hemorrhage, and extended recovery compared to SRC.

Conversely, athletes may sustain thousands of recurrent head impacts[106, 132] and more than one SRC [4, 5, 90, 251] throughout the course of their athletic career with a typical recovery of 7-14 days in adults.[5, 112, 252, 253] Recurrent head trauma denotes two very different connotations in athletics. The first refers to multiple diagnosed SRCs and the second pertains to the repetitive, subconcussive impacts many athletes experience throughout their athletic careers. Subconcussive impacts are primarily a product of contact sport participation, but may also occur in non-contact sports as well. Fortunately,

the greater majority of these impacts do not result in concussions.[106] As stated previously, SRCs have been correlated with increased risk for long-term health consequences, however the subconcussive impacts have not yet been shown to predict late-life outcomes. Nevertheless, the cumulative magnitude and/or frequency of subconcussive and concussive head impacts may result in many of the same emotion dysregulation changes noted in TBI literature. For instance, a group of retired NFL players suspected to have developed chronic traumatic encephalopathy (CTE) after recurrent RHIs and SRCs were believed to have increased emotion dysregulation possibly causing them to commit murder and/or suicide.[146, 194] However, these decreases in emotion regulation are speculative as CTE can only be diagnosed post-mortem and the players were not evaluated for emotion dysregulation prior to their death.

Finally, structural and functional changes have been noted in TBI and SRC populations. Interestingly, differences have been noted in structural changes with respect TBI history. Typically, total brain, gray, and white matter volumes are diminished compared to healthy controls and the ventricles are enlarged in moderate-severe TBI patients without increased emotion dysregulation.[32, 254] Specifically, the somatosensory, temporal, cerebellar, parietal, and parahippocampal gray matter regions in those with multiple mild TBIs were significantly smaller compared to those with a history of only one SRC and healthy controls.[255] Those with a history of only one mild TBI showed significant atrophy compared to healthy controls in the ventrolateral prefrontal regions external capsule, cerebellum, temporal lobes, and parahippocampal gyri. Studies have also indicated, white matter may also be affected after mild TBI with atrophy in the right internal capsule and right ventrolateral prefrontal regions.[255] These findings suggest that anatomical changes may occur even after one mild TBI and indicate the need for further diagnostic and prognostic evaluation. It is important to point out that these individuals

were not experiencing increased emotion dysregulation, but imaging detected significant changes compared to healthy controls. Therefore, it is probable that since the seat of emotion regulation responses lies within the brain, that the increased emotion dysregulation associated with TBI must at least be driven in part by some form of structural or functional modification.

2.3.2. Emotion Dysregulation and Postconcussive Syndrome (PCS)

It is believed approximately 15% of the estimated 1.6 million SRCs that occur annually go on to suffer from post-concussive syndrome (PCS).[202] PCS occurs even after very “mild” traumatic brain injuries (mTBI). Mild TBIs are typically defined as having LOC less than 30min and a Glasgow Coma Scale (GCS) of 13-15, with the majority of SRCs falling within this definition. Most PCS definitions require the presence of post-concussive symptoms for at least 3 months after injury.[203] However, the symptom incidence and severity can be extremely variable. The general areas most often affected include: vision, balance, sleep, fatigue, cognition (memory, executive control), and increased emotion dysregulation (depression, anxiety, aggression, and impulsivity). LOC, amnesia,[256] and initial symptom severity[256] are strongly correlated with PCS. Additionally, a history of three or more (3+) concussions is another sound indicator for these sustained deficits.[4, 5, 257, 258]

Individuals who develop Postconcussion Syndrome (PCS) are at a much greater risk of developing depression and anxiety disorders (posttraumatic stress disorder [PTSD]) compared to those who do not develop PCS.[259] Moreover, those meeting PTSD criteria are 3.1 times more likely to develop PCS at 3 months post-injury than those who do not. SRC, and TBI studies indicate that individuals with greater social support, lower self-reported depression symptoms, high socioeconomic status, greater

cognitive abilities, who are younger, and are male, are less likely to develop PCS.[97, 170, 181, 260]

One of the issues in diagnosing PCS is that increased emotion dysregulation complications are sometimes present in the absence of cognitive deficits.[59] Most field clinicians, particularly certified athletic trainers and team physicians, are not clinical psychologists and do not have the objective psychological measures available, or the training to interpret them. Commonly, this gap in concussion care results in undiagnosed emotion dysregulation sequelae that may lead to physical and/or psychological complication for the athletes in the short and/or long term. Linking this gap in research with previous findings indicating long-term emotion dysregulation as well as structural and functional brain changes after non-athletic TBIs, have led us to question if these same long-term consequences are also present after SRC.

2.3.3. Depression

In 2008, The World Health Organization declared major depressive disorder (MDD) as the leading neuropsychiatric disorder worldwide.[261] One's inability to regulate their emotions may result in depression.[262-266]. Harder, Cutler, and Rockart suggested that shame may be another route to depression.[267] This seems particularly applicable in all levels of sport. If an athlete performs either extremely poorly in one competition, or consistently below their own or others' expectations, they may feel shame concerning their athletic abilities. These athletes may feel that they let themselves, their team, coaches, parents, fans, classmates, and even the community down with a suboptimal performance. If this were to become a more consistent occurrence, it is possible that these athletes could develop depression-like symptoms.

Clark et al. found dysphoric individuals report increased loss of social resources after negative interpersonal events.[268] Due to the same events, dysphoria was also

associated with loss of personal goal attainment. Sociotropic individuals are more likely to report depressive symptoms from a strained interpersonal relationship, whereas unattained personal goals are more likely to cause depression in those with more autonomy. These findings may give us insight as to why not all athletes develop depression when held from participation due to an injury. If they are more sociotropic in nature, but still allowed to attend team activities, they may not experience depressive symptoms even though they are not allowed to participate. However, an autonomous athlete would be more likely to report elevated levels of depression with similar involvement due to their lack of athletic participation, and thus diminishing their ability to attain personal goals and assist the team in athletic achievements. Thus each individual's interpretation and reaction to the social, educational, and athletic stressors imposed upon or by them will be determined by their underlying personality.

Studies have indicated that depression is correlated with total symptom reporting and cognition in student-athletes. In a preseason baseline study of healthy high school and collegiate student-athletes Covassin et al. found significant group differences for depression in total reported symptoms, somatic/migraine symptoms, emotional symptoms, sleep and cognition (visual memory).[269] The severe depression group was significantly higher in all symptom categories and had a significantly lower verbal memory score compared to the minimal depression group. They also reported significantly more total and migraine-related symptoms compared to the moderate group. The mild depression group reported significantly fewer cognitive symptoms compared to the severe group. Finally, the moderate and mild groups reported significantly more emotional symptoms compared to minimal group.

Depression symptoms have also been correlated with decreased activation of the nucleus accumbens, bilateral dorsal caudate, and left posterior putamen via neuroimaging studies suggesting less positive affect and arousal to stimuli.[270] Studies

have also been conducted to support positive neurological alterations due to treatment for depression.[271-274] Functional neuronal alterations seem to be dependent on the previous and current medications.[275] Patients with decreased symptoms also show increased activity in Brodmann area 10 and the right dorsolateral prefrontal cortex (dlPFC).[245] Treatments to increase positive affect in depressed patients have resulted in increases in sustained nucleus accumbens and fronto-straital connectivity.[271] These findings all support altered neuronal function exists in those with depression, but that with the correct treatment, abnormal functions may be diminished or resolved. For the current project, these findings suggest that elevated depression over the course of a competitive season, or following a concussion may be attenuated with treatment. More importantly, if participants are currently taking medications to moderate pre-existing depression, their depression scores may not be affected by time or SRC to the same degree as participants not taking these medications. Additionally, if a participant seeks medical attention for depression after completing their baseline assessment, and begins taking medication for depression, their post-injury or pre- to postseason change scores may not accurately reflect their depression level if they were to complete an emotion dysregulation assessment without medication. However, the likelihood of a large number of participants initiating this care during our study is low.

Not surprisingly, depression is one of the most commonly reported and studied postconcussion symptoms. However, there have been mixed results regarding the correlation of depression with single and recurrent head trauma in both non-athletic[57, 59, 181, 196, 197, 276] and athletic[4, 83, 99, 144] populations. These changes may be caused by a myriad of events including: functional and structural brain changes, altered biochemical markers, stress, and emotional response to physical and cognitive impairments. A review of TBI literature in 1998 reported that even with limited studies at that time, depression should still be considered a significant consequence of TBI.[276] Importantly,

individuals who present with depression/anxiety post-TBI are significantly more likely to report more symptoms with greater severity, view their injury/neurological condition as being worse and, view their cognitive abilities as being significantly worse than those without depression/anxiety.[277]

Failiia et al. found TBI patients with a pre-morbid history of mood disorders (depression, anxiety) were 2.15 and 2.02 times more likely to experience risk for posttraumatic depression at 6 and 12 months post-injury compared to those with no history of mood disorder.[241] Hart et al. also found an increased risk for depression following TBI in those with pre-existing mood disorders as well as substance abuse.[196] Importantly, Tessa Hart's group found women to be more at risk for depression following TBI. This finding is supported by a great deal of literature suggesting females are more likely to report symptoms after an injury than males. Sex differences for depression incidence are not isolated to TBI. Significantly more females are consistently reported to experience depressive symptoms than males for numerous reasons including, social power, victimization, chronic stress, hormonal fluctuations, and coping abilities.[278] However, a large study of collegiate and high school athletes found no sex or age differences for total symptom score on the Beck Depression Inventory-II (BDI-II).[269] This inconsistency may be related to the measure utilized in the athlete study. The BDI-II may not be a sensitive enough measure to capture depressive symptoms in this population. Other possibilities for the non-significant findings may be a reflection of the test administration mode, regional differences, or that athletes have been found to have more optimistic and positive attitudes than the general population.[279] This study will investigate these differences with an alternate depression instrument in an effort to determine answers some of these questions.

In a study of 666 TBI patients, 27% met the Diagnostic Statistical Manual of Mental Health Disorders – IV (DSM-IV) criteria for MDD.[197] The three symptoms that

separated the depressed from the nondepressed patients were feeling hopeless, worthless, and difficulty enjoying activities. The most commonly reported symptoms in the depressed group were fatigue (29%), anger/irritability (28%), distractibility (28%), and rumination (25%). Those who were impoverished and unemployed were among the most likely to meet the MDD criteria. Surprisingly, injury severity was not significantly correlated with reported depression symptoms.[196, 197] MDD at 1-year post-TBI was associated with higher odds of depression one year later[181] suggesting possible emotional dysregulation issues. Those who are not depressed one year after a TBI, but become dependent on illicit substances, have lower cognitive scores and increased overall disability are correlated with symptom worsening. Depression is a common symptom of both Alzheimer's disease (AD) and mild cognitive impairment (MCI)[99] and has been tied to chronic traumatic encephalopathy (CTE),[146, 194, 280, 281] all of which have negative ties to quality and longevity of life.

Additionally, several studies have identified physiological changes correlated with depression-related TBI. The primary TBI depression-related biomarkers mentioned in the literature include cerebral spinal fluid surface markers, inflammatory biomarkers (interleukins, TNF-α), brain-derived neurotrophic factor, and S100B in human and animal models.[64, 162, 282-284] Little work has been done in this area with SRC populations and should be considered as the next step in SRC emotion regulation research.

Compared to TBI literature, there has been very little emphasis put on determining the relationship between SRC and depression. 75 high school and collegiate athletes, who sustained a SRC in the course of one year, reported significantly higher levels of depression through 14 days post-SRC compared to their preseason baseline measures.[97] Interestingly, the collegiate student-athletes scored significantly worse on the Beck Depression Inventory-II (BDI-II) compared to high school student-athletes at day 14. Interestingly, they did not find any sex differences at any of the time

points, which is a deviation from the general populace. Nonsignificant sex differences in athletes are not unusual and may be associated with their overall elevated optimism levels. Female (n=147) and male (n=385) athletes currently in training, ranging in age from 16-30 years, exhibit lower pessimism than their non-athlete cohorts (n=262, n=435).[279] BDI-II depression symptom scores also correlated with cognitive abilities (memory, reaction time) through day 14. Specifically, they found somatic depression was related to slower reaction times at 7 days post-injury and lower visual memory at 14 days post-injury. Neural responses in depression-related brain regions have been correlated with symptom severity after SRC in adult males.[85] A neuroimaging study involving 45 retired NFL players with a history of SRC found one third of the players reported symptoms of depression (mild to marked) on the BDI-II and nine players met the criteria for major depression or other depression on the patient health questionnaire (PHQ).[77] Carson et al. did not find any associations between depression and the neuroimaging measures, but the neuroimaging alterations were related to alcohol usage.

Chen et al. found male contact sport athletes (recreational, amateur, professional) complaining of mild and moderate depression post-SRC had significantly greater PCS scores than the controls and those without depression post-SRC.[85] This finding is consistent with both TBI and SRC literature. Depressed individuals are more likely to complain of a greater number and severity of symptoms. The concussed athletes exhibiting depression symptoms tended to be less accurate and slower during memory and control tasks compared to the controls, but the differences were not significant. This finding indicates a potential correlate between psychiatric symptoms and cognition, which again is supported by literature. This is particularly important in athletics due to the speed and quick thinking that is required to remain not only competitive, but also safe during participation. They also found diminished grey matter in several areas related to depression in those with a concussion compared to the controls. Those with

mild depression presented with atrophy in several brain regions. Of interest, they found differences in grey matter in the left and right insula in the group with no depression symptoms compared to the healthy control group. The insula are important in emotion and homeostatic functions of the body, including self-awareness, cognition, and motor control. Functional imaging revealed few differences in activation between the healthy control and concussed athletes without depression symptoms. While they did find that the activation of several brain regions (dlPFC, dorsal ACC, insular cortex, striatum, and thalamus) decreased with increased depression symptoms and other regions increased (right ACC, posterior cingulate cortex [PCC], mOFC, and parahippocampal gyrus bilaterally) in the mild and moderately depressed groups, there was inconsistency in those reporting elevated PCS scores and BDI-II scores. This is an interesting finding indicating SRC-related depression is associated with both structural and functional brain changes. Brain activity was positively correlated between the BDI-II scores and the right ACC, mOFC, posterior cingulate, and bilateral parahippocampal gyri, and negatively correlated in the left insula, left striatum, and bilateral dlPFC, which are all areas correlated with emotion. Athletes who scored higher on the Postconcussion Symptom Scale typically scored higher on the BID-II. The authors did find a subgroup (N=6) that had elevated PCS scores and normal BDI-II scores. The concussed athletes without depression did exhibit diminished right dlPFC activation compared to the controls during task-related activities, similar to the depressed groups. However, the activation of their right ACC and mOFC were not significantly different from the controls, as opposed to the mild and moderate groups who had significantly reduced activation in these areas, suggesting mechanisms other than SRC and PSC may be related to depression incidence in this population. The findings of this study were important in several ways. First, it supported earlier findings that not all concussed athletes experience the same number or severity of symptoms. Secondly, it established the functional and structural

regions of interest in athletes experiencing depression symptoms post SRC. Thirdly, it demonstrated a relationship between emotion dysregulation measures and structural and functional changes post SRC. Fourth, the functional findings were similar to several previous mild TBI studies.

2.3.4. Anxiety in TBI

Anxiety is also a common psychological complication after TBI, occurring in 47-63% of the affected population.[198, 285] The most common anxiety-related disorders reported after TBI include, posttraumatic stress disorder, generalized anxiety disorder (GAD), obsessive-compulsive disorder, and panic disorder. Diagnosis of one of more of these is often problematic because they are often co-morbidities of each other and/or with depression. Similar to depression, females are twice as likely to report symptoms of anxiety compared to males for many of the same reasons listed above.[286, 287] Many of these anxiety-related disorders have been positively correlated with mild to moderate military TBIs.[59] PTSD, characterized by nightmares and intrusive thoughts, is more common after mild-moderate TBI than severe TBI, especially if the patient suffered a bout of amnesia.[288] PTSD is primarily associated with experiencing various forms of trauma (physical & psychological), much like what an athlete would experience when they sustain a SRC. LOC and amnesia after a TBI may function as a protective mechanism resulting in inability fully remember the traumatic episode. PTSD is far less common in both military and civilians who experience these symptoms.

GAD is defined as excessive worry and/or distress about a wide variety of activities that cannot be attributed to other anxiety disorders that has been present for at least 6 months.[203] Individuals who are diagnosed with GAD experience difficulty controlling their worry. It also must be accompanied by at least three somatic symptoms including muscle tension, sleep disturbances, fatigue, irritability, and difficulty

concentrating. It is considered the most common TBI-related anxiety disorder.[289] The lifetime incidence of TBI-related GAD (10.2%)[288] is twice that of the general population (5.1%),[290] but studies have found it as high as 24%.[277] Alternately, GAD has also been found to be one of the least common anxiety disorders associated with TBI.[291] The discrepancy between these studies may be related to sample size, history of education, measures utilized, and delay between injury and testing. Hibbard et al. tested 100 well-educated TBI outpatients an average of 7.6 years after their injury. Fann et al. enrolled 50 TBI outpatients with an average education of 13 years 2.7 years after their injury. Additionally, the measures use to characterize symptoms and anxiety did not have the ability to diagnose the same disorders.

Schoenbuer et al. were not able to identify a significantly elevated risk for anxiety in athletes between 5 and 17 months post-SRC compared to matched controls using the STAI-Y.[163] However, in their second study of 103 concussed patients who were tested using brain-stem auditory evoked responses within 48 hours of injury and again one year post-injury, 26% did have symptoms of anxiety at both time points.[292] It is possible that these findings are conflicting due simply to the nature of the studies. The first study measured the patients' conscious recognition of these symptoms and the second recorded brainwaves in responses to emotive questions to evaluate subconscious alterations in their subjects. This brings to light a very important point; concussions may cause brain alterations (either functional or structural) that linger at the subconscious level for months or years going undetected due to insufficient diagnostic evaluations (i.e., questionnaires, neurocognitive testing, training, etc.).

Animal models have suggested TBI is associated with subsequent anxiety-like behavior and have proposed mechanisms causing these changes. Ajao et al. found correlations between TBI in juvenile mice, anxiety-like behavior, and brain volume and immunohistochemistry alterations.[32] These results indicate juvenile TBI can result in

long-term white matter tract changes, delayed behavioral development and sustained behavioral alterations that mimic clinical and longitudinal TBI findings. Another study found the incidence of emotion dysregulation and functional brain changes in adult male mice were related to impact magnitude.[167] As the impact magnitude increased (0-20, 25-40, 50-60 psi), anxiety, depression, fear, and prepulse inhibition became more evident. While immunolabeling was negative for microglial reaction, axonal degeneration in several brain regions was noted only in the mice receiving the most severe impacts (50-60 psi). Importantly, the blast impact was centered on left parieto-temporal region of the head, but the axonal damage was noted in other major fiber tracts including bilateral deficits in the basolateral amygdala. Involvement of this structure has been implicated as a major mediator for fear. Thus, the authors determined that damage to this structure could contribute to the increased anxiety, fear, and impulsivity seen after impacts that are more significant.

Conversely, our unpublished 2013 high school football pilot study did not find an increase in anxiety in non-concussed high school football players. However, if emotion dysregulation is positively correlated with impact severity, it is possible that the individual and cumulative magnitudes were not great enough to induce anxiety-like changes. A shortcoming of this study was the lack of a true control. While we did not find significant within subject changes from pre- to postseason, this does not exclude the fact that these athletes may have experienced significant changes compared to age, sex matched non-contact sport athletes, or non-athlete classmates. The 2013 pilot study was used as a building block for the current study involving male and female contact and non-contact sport high school student-athletes.

Over the past several years, researchers have utilized multiple measures to evaluate behavioral alterations after TBI.[8, 163, 221-224, 292] The State-Trait Anxiety Inventory for Adults (STAI Forms Y-1 and Y-2) is used widely as a validated measure of anxiety in

all adult populations (injured, personality disorders, and general populace).[293] However, it is lengthy and expensive. Several other measures have been utilized to measure anxiety, but many of these are also long and some are quite costly.

In 2006, the Generalized Anxiety Disorder Seven Item Scale (GAD-7) was found to be a valid and reliable measure for GAD, but in a much shorter format than previously available.[294] While GAD does not fully encompass all anxiety disorders, it is highly prevalent in the U.S. and is one the most common anxiety disorders across all age groups.[290, 295] The GAD-7 was initially designed with 9 questions that reflected the DSM-IV symptom criteria for GAD with 4 additional items they selected from existing anxiety measures.[294] The measure inquires about the patients' symptoms over the past 2 weeks and is scored on a Likert-like scale ranging from 0 ("not at all") to 3 ("nearly every day"). The validity of the measure was compared to two other anxiety measures (12-item anxiety scale from the Symptom Checklist-90 and Beck Anxiety Inventory) in two separate phases of their study. The final analysis showed seven items from the 13-item scale had the highest correlation, and the highest rank correlations in the developmental group as well as the two replication studies. These items were retained, while the other 6 were dropped from the measure. The GAD-7 is scored from 0 to 21 with a higher score indicating greater generalized anxiety. The internal consistency (Cronbach = .92) and test-retest reliability (ICC = 0.83), and validity (ICC = 0.83) are good to excellent. Patients with GAD (n=73) scored a mean value of 14.4 ± 4.7 on the GAD-7, while those without GAD scored 4.9 ± 4.8. Spitzer et al. found a greater percentage of females (9%) had been diagnosed with GAD compared to the males (4%).[294] The mean scores for the females and males were 6.1 and 4.6 respectively.

Unlike the PHQ-9, the GAD-7 can only be used as a tool to indicate GAD diagnosis probability and should be followed by a more in depth evaluation for diagnosis.[294] Comparisons of primary care patients' scores with and without GAD were

assessed for sensitivity and reliability. 89% of the patients with GAD had scores ≥10 and 82% of those without GAD had scores <10. The GAD-7 cut point for identifying GAD was set at 10 or greater with a sensitivity and specificity of 0.80 or better for both males and females. Overall, 23% of the patients scored above 10. Similar to the severity-related cut off values on the PHQ-9, scores of 5, 10, and 15 are used to identify mild, moderate, and severe GAD, but again these are only predictors. Individuals with scores ≥ 10 should be referred for a confirmatory diagnosis.

2.3.5. Impulsivity and TBI

As discussed above, anxiety is highly correlated with impulsivity, which is considered a multifactorial construct.[296] However, the exact definition and even the terminology utilized are inconsistent. Ernest S. Barratt devised the Barratt Impulsiveness Scale (BIS) in 1959.[297] During subsequent studies he and his colleagues worked to define impulsivity, arriving at the decision that impulsivity encompassed three divisions: motor, cognition, and nonplanning.[298] The motor component was defined as an action without thought. Quick decision making and having a “present orientation” (not thinking about the future) described the cognitive and nonplanning domains. Several researchers have utilized impulsivity definition and measures designed by Barratt’s group to investigate differences between varying populations, including TBI.[42, 299-302] While other researchers have chosen to form their own definitions,[200, 303-305] all of them use many of the same constructs as Barratt’s group. In 1985 Barratt Dickman described one important and insightful alteration to the theories surrounding impulsivity, a separation between advantageous and disadvantageous impulsivity.[305] Aeschleman and Imes and Votruba et al. found direct observation to be a key element in determining impulsivity.[303, 304]

Additional complexities for defining impulsivity include the variable nature of the

disorder and its connection with other disorders including those that are attention based. Attention deficit hyperactivity disorder (ADHD) is divided into 3 subtypes: predominately hyperactive-impulsive (AHDH-H/I), predominantly inattentive (ADHD-I), combined hyperactive-impulsive and inattentive (ADHD-C). The latter is the most common form in children and adolescents. ADHD-C is diagnosed when individual experiences at least 6 symptoms of both ADHD-H/I and ADHD-I. Most children have both according to the National Institute of Mental Health. They also list a multitude of disorders that may accompany ADHD (learning disability, oppositional defiant disorder, conduct disorder, anxiety, depression, bipolar disorder, and Tourette syndrome) that may increase the individual's inability to adapt socially and likelihood of developing aggressive behaviors. Finally impulsivity, particularly after TBI, is associated with physical aggression, temper outburst, inappropriate sexual behavior, and stealing. For the purposes of this paper, Barratt's definition will be used, as it is the most accepted to date.

In the last 15 years, neuroimaging studies have worked to correlate impulsivity with structural brain changes. Through these studies, BIS scores have been correlated with several neuroimaging findings. Total OFC gray matter volume and the individual right and left halves have been significantly and positively correlated with BIS scores.[33] While this finding is counter-intuitive, the authors note that it is an important distinction from aggression-related imaging associations. Additional analyses revealed the presence or absence of an affective disorder (aggression) determined the OFC relationship. Individuals who only scored highly on aggressive measures (Buss Perry Aggression Questionnaire [BPAQ] and Lifetime History of Aggression [LHA]) showed a significant association with OFC asymmetry. A group of patients having ADHD, alcoholism, and antisocial personality disorder (non-affect disorders) exhibited significant associations between total OFC volume and motor and non-planning scores on the BIS and no aggressive association further suggesting that these disorders are in fact

separate disorders and should be evaluated and treated as such.

Impulsivity has been tested using the shortened version of the BIS, the Barrett Impulsiveness Scale -11 (BIS-11),[306] which is highly utilized and validated across a wide range of individuals.[307] The incidence of TBI-related impulsivity has been mentioned in the literature for over three decades.[308] Unfortunately, an impulsivity measure has not been specifically designed for TBI populations. To date, the most common measure for TBI populations has been the BIS and BIS-11.

To our knowledge, no published works have investigated the relationship between repeated head impacts (subconcussive and concussive) and impulsivity. In addition, studies correlating head impact biomechanics and impulsivity are also lacking. The 2013 pilot study for this project suggested a trend toward increased impulsivity from pre- to postseason in high school football players. However, this increase was not significant, possibly due to the small sample size and lack of a control. The findings from the TBI literature and our pilot study indicate a need for a prospective cohort study investigating the associations between RHI, head impact biomechanics, and impulsivity.

2.3.6. Aggression and TBI

Imaging and physiological studies have correlated aggression with several brain regions and biomarkers.[33, 147, 183, 184, 309-315] OFC asymmetry (right half greater than left) is strongly, positively associated with Buss Perry Aggression Questionnaire (BPAQ) and Lifetime History of Aggression (LHA) scores.[33] Robert James Blair made the argument that impulsive aggression is related to increased risk of frustration instead of sensitivity to threat.[309] He supported this claim with fMRI studies indicating the importance of the amygdala-hypothalamus-periaqueductal gray (PAG) in regulating response to threat and that these areas are controlled by several areas within the OFC, medial frontal cortex, and the ventrolateral frontal cortex. Those with psychopathy respond with decreased

amygdala-hypothalamus-PAG activity to threat, whereas individuals with impulsivity disorders respond with increased activity.

Aggression has been found to be significantly higher in contact[316] and power sport[317] athletes, with sport participation leading to an enhancement of aggression outside of sport over time. In a recent cross-sectional study of men 30-74 years old, behavioral differences and structural and functional brain alterations related to increased aggression and impulsivity were observed in retired professional football players with histories of multiple concussions compared to controls.[318] This study was retrospective in nature and lacked a control group of retired football players without a history of concussion, so it is impossible to determine if these group differences were caused by their exposure to football, subconcussive RHIs, SRC, TBIs, or other unknown factors. It is possible that these differences were pre-existing and were in fact what led these individuals to suffer multiple concussions. Thus, we believe a prospective study determining pre-participation emotion dysregulation profiles and subsequent change scores over one or more seasons of sport participation would add significantly to this area of research.

Heightened aggression[39, 59, 160, 164] and abnormal neural connectivity patterns have been reported in non-athletic and military concussion populations, leading to poor long-term health outcomes (violence, loss of job/relationships, neurodegenerative disease, etc.)[41, 169] and decreased quality of life.[38, 43, 164] Research in the non-athletic concussion population has shown up to 75%[38, 43, 44, 164] of these individuals experience increased aggression. Of these individuals 25-39% are classified as high average-very high on anger, and 35-38% are classified as high average-very high on verbal aggression.[38] Of note, no differences were found by Dyer et al. comparing TBI patients to spinal cord injured patients and normal controls in physical aggression, but they did find higher levels of impulsivity in the TBI group compared to the other groups. Around

60% of those reporting increased aggression are diagnosed with a mild concussion.[319] Depression,[4, 182] AD,[320] and CTE[280, 281, 321-323] are associated with increased aggression, and are believed to be linked to sport-related concussions.[320] Increased aggression has been positively correlated with non-sport-related concussions[36, 38-40, 160] in both the short and long-term scenarios, but no published studies have evaluated these relationships in athletic populations to date.

Another complication in diagnosing aggression in athletes is the positive implication it holds in athletics. Aggression is a coveted ability in athletic arenas. Athletes who are aggressive are typically successful and have increased longevity in their sport. Most individuals entrenched in the athletic world would not consider increased aggression to be a hindrance, but instead a benefit. In support of this idea, the data from our 2013 pilot study suggested aggression increases in high school football players throughout one season. Due to the study design we were not able to determine causality. It is possible that 1) there were outside mitigating factors leading to the increased aggression, or 2) some aspect of football itself instigated the increased aggression. These studies indicate a need for a more in depth investigation concerning the association between SRC, football participation, RHI, and aggressive behaviors.

2.3.7. Emotion Dysregulation and Neurodegenerative Diseases

Neurodegenerative diseases are not evaluated, and subsequently treated until symptoms have already appeared. Thus, the majority of neurodegenerative studies (i.e., AD, PD, CTE) are retrospective in nature. The unfortunate consequence of designing retrospective studies is the investigators rarely have access to pre-injury emotion dysregulation measurements for their participants. All post-injury data must therefore be compared to normative scores for these individuals. Some studies have attempted to determine the pre-injury personality and affective status of their participants through self-

and close-other interviews as well questionnaires.[42] However, there is a significant probability that recall bias may skew their recollection of past behaviors, thus we can only estimate the actual psychological effects of TBI.

TBI has also been associated with early development of several neurodegenerative disorders including MCI,[324] AD,[29, 325-328] PD,[329] and dementia;[328, 330, 331] all of which are associated with some of the emotion dysregulation consequences TBI patients report. SRC researchers have also found correlations with earlier incidence of MCI[3, 99, 332] and AD[3] in retired NFL players. Guskiewicz et al. found a dose relationship between concussion frequency and MCI prevalence.[3] They also reported an earlier incidence of AD in retired NFL players compared to the general male population, which was not correlated with concussion history. This study did not investigate the estimated number of repeated head impacts using the Head Impact Exposure Estimate, which has been describe in other studies.[132] Unfortunately, a group of retired NFL players suspected to have developed CTE after recurrent RHIs and SRCs were believed to have decreased emotion regulation capabilities possibly causing them to commit murder and/or suicide.[146, 194] However, the increased emotion dysregulation is speculative as CTE can only be diagnosed post-mortem and the players were not evaluated just prior to their death.

It is possible that the prevalence and earlier incidence of these neurodegenerative diseases could be triggered by an increased impact frequency and severity compared to the athletes who do not develop these diseases, as well as those in the general public. Another possibility is that these players took a higher number of impacts at a greater magnitude to certain location(s) on the head that are considered more vulnerable resulting in greater acute and chronic emotion dysregulation and physiological changes.

In a 2010 met-analysis, Swardfager et al. reported both IL-6 and TNF-α were significantly elevated in Alzheimer's patients, again supporting the theory that neurodegenerative diseases are accompanied by prolonged inflammatory responses. The incidence of AD was found to occur earlier in retired NFL players than the general populace[3] regardless of SRC history, suggesting the mediating factor is RHI. These RHIs may lead to brain, behavioral, and physiological alterations over time. Therefore, it is important to investigate the incidence of these behavioral changes in a younger population.

2.4 Age related differences

Adolescents have a greater risk of sustaining a concussion and experiencing more severe effects due to their developing neural pathways. Annually, an estimated 1.1 million high school students and 100,000 post-high school athletes play football in the United States.[333] Overall, approximately 4.2 million individuals are playing football every year in the US.[333] SRC represent approximately 8.9% of all high school and 5.8% of all collegiate injuries.[251] More importantly to this project, several studies have found football players sustain the greatest number of SRC compared to all other sports in high school and college.[251, 334, 335] While rarely fatal,[333] they may have prolonged consequences, particularly in younger athletes due to increased brain vulnerability. Pediatric and adolescent athletes often take longer to recover from SRC. While the exact cause is unknown, there is evidence to suggest increased sensitivity to excitatory neurotransmitters in the developing brain.[336] This has been supported by neuroimaging literature indicating altered brain and cerebrospinal fluid volumes in children after all levels of TBI, with greater and more severe changes occurring in those with severe TBI.[34] The authors concluded that TBI, particularly severe, may cause diffuse pathological changes that disrupt brain regions from developing normally.

Cognition, symptoms, and balance all take longer to return to baseline in high school athletes compared to collegiate.[94] Adolescents are also the only group at risk for second impact syndrome, which is a rapid vascular response to injury causing diffuse cerebral swelling and death in approximately 50% of those affected.[337] As described previously, Kantos et al. found high school and collegiate athletes experience significant increases in depression after SRC.[97] However, evidence supporting dysregulation of other emotions/behaviors in relations to SRC or RHI is absent. It is highly probable that these changes noted in retired NFL players are initiated at the youth level.

The ability to associate SRC history and self-reported emotion dysregulation measures with physiological changes would help contribute to the development of more efficient and cost-effective diagnostic tools as well as development of treatments targeting early signs of emotion regulation impairments leading to improved long-term outcomes. To date, the current treatment for SRC-related emotion regulation changes rarely occurs. Most athletes are proud and unwilling to admit weakness in any form. They will hide or deny altered behaviors until they are undeniable. Unfortunately, not all cases are caught in time; resulting in the premature, tragic deaths of those afflicted and/or their loved ones, as has been reported in a few retired athletes diagnosed post-mortem with CTE.[146, 194] An association of SRC, head impact biomechanics, and increased emotion dysregulation could lead to testing with simple and cost-effective paper and pencil measures throughout athletic careers and after retirement. We could then track individual and group RHI and SRC-related emotion regulation alterations over time, resulting in predictive models for those at-risk. The over-arching goal is to delay or prevent these at-risk athletes from experiencing significant neurodegenerative changes that may lead to AD and CTE.

While TBI research has demonstrated several long-term consequences, prospective studies investigating the relationships between emotion dysregulation with

respect to head impact biomechanics and SRC are lacking. Football players may sustain several thousand RHI and repeated SRCs over several years of participation as opposed to a one-time traumatic event in the TBI population. Our *rationale* in studying the relationship between head impact biomechanics, SRC, and emotion regulation is to advance our understanding of the long-term emotion dysregulation consequences of SRC, resulting in earlier identification of SRC adaptations, and appropriate, cost-effective and timely healthcare for these at-risk individuals. The current study is innovative because it is the first project to *evaluate how RHI and SRC affect emotion regulation over time.* The proposed research is significant because it will undoubtedly expand our understanding of how SRC history modifies behavioral long-term outcomes potentially linked to AD and CTE. Ultimately, such knowledge could allow us to empirically relate self-reported emotion dysregulation measures, SRC incidence and history, and RHI history to determine more appropriate, cost-effective, and timely healthcare for these at-risk individuals.

CHAPTER 3: METHODOLOGY

During recruitment, participants (and their guardians when applicable) were asked to sign a UNC approved consent form, given a brief explanation about the study, and inclusion and exclusion criteria were discussed. See **Table 3.1** for the Procedures Schedule. Football participants were eligible to have their helmets instrumented with Head Impact Telemetry System (HITS) sensors.[106] Clinical experience suggested that our dependent measures could have been affected by increased season of football participation, repeated head impacts (RHI), and SRCs. Therefore, we recruited all grades to increase our ability to capture an adequate sample of freshmen and seniors. The recruitment and consent of all participants occurred between July 2013 and February 2016. Preseason testing (*preseason*) was conducted within 3 weeks of each participant starting practice with any team. Postseason testing (*postseason*) was conducted within 4 weeks of the last competition for each team. For athletes who sustained an in-season SRC, Two additional questionnaires were completed in the event of a reported SRC. *Post-injury #1* testing was completed within 72 hours of a concussed athlete reporting their injury by the injured player and at least one age, position, and playing time-matched teammate. After the concussed athlete completed their return-to-play (RTP) criteria, the injured and control participants were asked to complete an additional questionnaire (*full RTP*). The purpose of these additional measures for those diagnosed with a SRC was to determine the emotion dysregulation short-term effects related to SRC. The matched teammate(s) served as the control for the effects of RHI and sport exposure, emotion regulation maturation, and seasonal alterations. See **Figure 3.1** for a pictorial representation of the participant groupings. The post-injury

questionnaires were not used to answer any questions for this study and will not be discussed further. We had ≥ 25 participants in each cell (sex, team, SRC) giving us adequate power compared to similar head impact biomechanical.[106, 122, 126] See **Table 3.2** For the Project Timeline and **Appendix 2** for the Master Protocol.

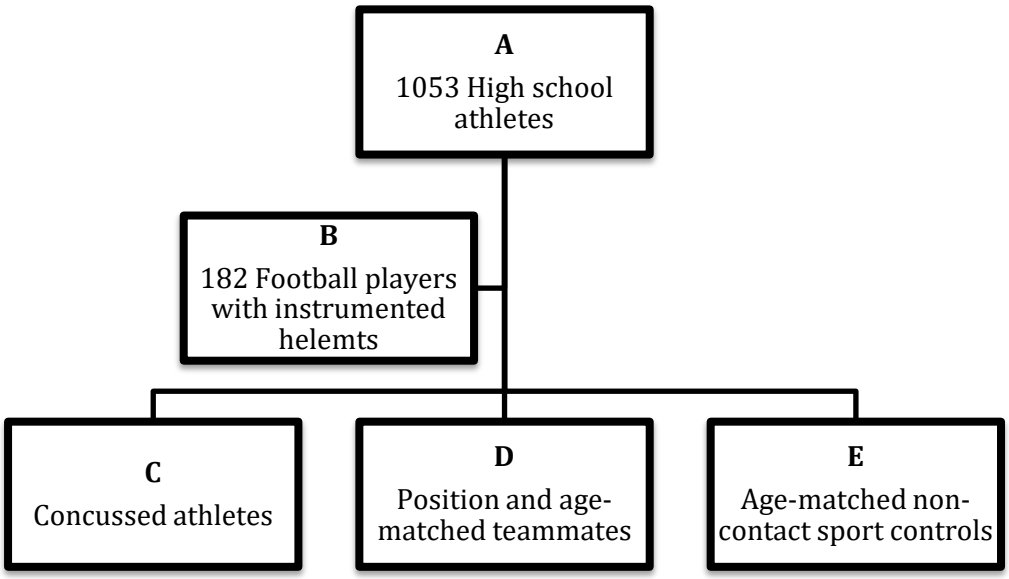

Figure 3.1. Participant Groupings

Table 3.1. Schedule of Procedures

	Preseason	Postseason	Post-Injury #1	Full RTP
Measures	Preseason	Within 4 weeks of last game	Within 72 hours of the injury being reported	After completion of RTP protocol
Recruitment and Consent	A			
Concussion History and Emotion Dysregulation Questionnaires	A	A	CDE	CDE
HITS sensors*	B			

Participants = (A) 1053 high school athletes; (B) a subset of 182 football players with instrumented helmets; When an athlete was diagnosed with a concussion during their respective season the following individuals were tested (C) the concussed athlete, (D) a position and age-matched teammate, and (E) an age-matched non-contact sport control.
Personality Questionnaires: Patient Health Questionnaire (PHQ-9), General Anxiety Disorder 7-item scale (GAD-7), Buss-Perry Aggression Questionnaire (BPAQ), Barrett Impulsiveness Scale 11 (BIS-11), Perceived Stress Scale – 4 (PSS4).
*Helmets of all consented football players were eligible for instrumentation with Head Impact Telemetry System (HITS) sensors at the beginning of their participation.

Table 3.2. Project Time Line

	July 2013- September 2016				
Task	July-Aug	Sept-Oct	Nov	Dec-Jan	Feb-Sept
Subject Recruitment			#	#	#
Football Helmet Instrumentation - (HITS) Accelerometers					
Preseason Baseline Testing			#	#	#
Postseason Testing			#	#	#
Post-Concussion Testing (Post-injury #1 and Full RTP)					#
Emotion Dysregulation Analyses					#
Biomechanical Analyses					
Abstract (A) & Manuscript (M) Preparation			A*		M*

2014/15 – 2015/16 only
* 2015/16 only

3.1. Recruitment

3.1.1. Participant Recruitment

The researchers contacted the Chapel Hill-Carrboro and Chatham County School District Administration to gain permission to recruit participants from three of the high schools under their jurisdiction. The researchers also met with the athletic directors and head coaches for all of the teams recruited for this study. Once granted permission, the researchers attended the first available coach-parent and coach-athlete meetings. At the meetings, the purposes of the study and the requirements of each participant were explained followed by a distribution of a parental letter (**Appendix 7**), a 1-page study explanation (**Appendix 8**), and assent/consent forms. Parents of high school participants wishing to enroll in the study were instructed to review the parent letter and parental informed consent document. The student-athletes and their parents/guardians were then given an opportunity to discuss their participation as a possible study participant with the research team members at the conclusion of the presentation. Athletes and parents were allowed to review the informed consent documents individually. Athletes and parents could discuss any questions or concerns

that they had in a private room with a member of the research team after their respective meeting, or were encouraged to contact the research team for additional information via phone or email. All parental consent and student-athlete assent forms were to be submitted concurrently. All announcements and follow-up reminder emails were done as mass emailing's to the entire team and/or their parents/guardians. Athletes were not included in the study if they or their parent/guardians (minors only) did not consent to participate. The researchers contacted parents who did not attend these meetings through mass emailing's and arranged to provide them with the study materials and an opportunity to meet with the research team to discuss the study and answer any questions. Written participant assent/consent and parental consent were collected prior to the preseason testing. During the recruitment process all participants were informed that they could withdrawal from the study at any time. Parent/Guardian consent forms had an option to indicate that they were not interested in having their child participate.

Email addresses and cell phone numbers were requested on the student-athlete's assent/consent form to improve confidentiality, distribution of the concussion history and emotion dysregulation questionnaire, and any study or SRC-related communications. In addition, the parent/guardian's email address and cell phone number were requested to allow for improved communication between the research group and the parents/guardians concerning study updates, and increased emotion dysregulation scores indicating possible clinical concerns.

3.2. Participants

Over a three-year period (72 team-seasons), one thousand seven hundred and forty six junior varsity and varsity athletes between the ages of 13 and 18-years-old were recruited to participate in this study from three different schools. One thousand one

hundred and ninety participants were enrolled (68.2%). The mean age was 15.59 ± 1.21 with 5.82 ± 3.51 seasons of sport participation.

Three hundred and thirty four of the 1,746 high school student-athletes recruited for this study were football players (5 team-seasons). All interested football players and their parents/guardians gave written assent/consent prior to their enrollment in the study (n=275, 82.3%). The helmets of a subset of football players (n=182, 66.2%) were instrumented with HITS accelerometers at the start of the season.

3.2.1. Inclusion

Participants were included if they were a full-time student at one of the respective schools. All participants were required to be active players on their respective rosters at the start of the study.

3.2.2. Exclusion

Participants were excluded by the following criteria: 1) not fluent in English, 2) not a current participant on a junior varsity or varsity sport at one of the three schools in our study, 3) were still experiencing any deficits/alterations from their last concussion during recruitment, 4) parental permission was not granted (applied only to minors), 5) visual impairments that could not be rectified with corrective lenses, 6) a history of psychoses beyond general psychological disorders (e.g., depression, anxiety).

3.3. Instrumentation

3.3.1. Head Impact Telemetry System (HITS)

The Head Impact Telemetry System (HITS) is a device used to measure the incidence and severity of head impacts. The HIT System was developed by SIMBEX (Lebanon, NH) in 2001. Each waterproof HITS sensor contains six single-axis

accelerometers, a wireless telemetry unit, a removable batter, and an onboard data storage unit arranged in a horseshoe pattern (Appendix 1). The accelerometers communicate via radio frequency with a sideline unit that captures the impact data (location, magnitude [measured in g's and radians/s^2], and duration) from the helmet. Each impact is individually time and date stamped with the subject ID. When the sensors are out of range from the computer, the onboard data storage unit is able to record up to 100 impacts. This data is automatically downloaded to the computer once the sensor is back in range.

All participating football players were eligible to be given Riddell helmets, which were fit with 6 small (approximately the size of a dime) single axis accelerometers at the start of their football season that was worn for all practices and games. Riddell (Elyria, OH) is the only certified American football helmet manufacturer who currently produces helmets (Revolution and Speed) that are compatible with the HITS sensors. The addition of the HITS sensors to the helmets does not change their function or look compared to non-HITS helmets and has been approved by the National Operating Committee on Standards for Athletic Equipment. This system allows clinicians to track impacts in real time during practices and game. The HITS was the first clinical tool produced to measure impact biomechanics and has been used in a multitude of high school,[121-124, 126, 149] collegiate[5, 72, 75, 82, 106, 108, 149] football studies. Recently, there has been an influx of studies utilizing the HITS with adolescent football players as well.[129, 130, 143] The HITS system has been validated against the Hybrid III anthropometric headform for impact location and magnitude.[213]

Implementation of the Head Impact Telemetry System (HITS)

After IRB approved assent and consent were collected from the perspective student-athletes and parent/guardian(s), 29-46 enrolled varsity and junior varsity football

players at each school were randomly selected each year to have their helmets instrumented with the HITS accelerometers (n=182 over 5 team-seasons). Each helmet was instrumented with a HITS accelerometer at the start of the season. Selected participants wore these devices for all practices, scrimmages, and games. The batteries were maintained by the research team and changed at least once a week for the duration of the season. A designated person referred to as the site HITS technician (i.e., research assistant, athletic trainer, or student athletic trainer), set up the HITS sideline controller for all team activities that might have involved head impacts. The data were uploaded to the Simbex cloud 1-2 times a week for filtering and processing. All data needed the following day was uploaded prior to midnight EST, as this is when the Simbex data cleaning process begins. All data uploaded to the Simbex cloud after midnight was not processed until the following day (24 hours later). Researchers downloaded the sensor data from the Simbex cloud at least once a week and saved it on password-protected files in the Matthew Gfeller Center. Three players (2%) requested to have their accelerometers removed from their helmet throughout the study.

We kept a Daily Log (**Appendix 6**) at each school including: the date, site HITS technician, participation level, battery, and sensor status, when the HITS sideline system was turned on, start and end time of the event, event (practice, game, scrimmage, off), and type (helmets only, half shell, full contact, conditioning/lifting only, indoor practice), and the at each session. The start and stop times for the warm-up and practices were recorded on these forms to help clarify any inconsistencies with the data recorded by the HITS. This also assisted with data cleaning by eliminating impacts recorded outside of football sessions.

If at any time a sensor did not activate at the beginning of a session, the site HITS technician first sought out the helmet and 1) attempted to impose an impact to the crown of the helmet, and/or 2) placed their hand inside the helmet near the crown for at

least 20 seconds. Either of these two actions should activate the sensor. If the sensor did not activate (per the sideline controller), the battery was be replaced. Careful notes detailing the times of these events and the location of the impact, if appropriate, were recorded on the Daily Log. If a sensor did not activate after the battery had been changed, the site HITS technician notified the lead researcher for further analysis of the situation. In the event that all troubleshooting failed, Simbex was contacted. Damaged or problematic sensors were replaced as needed throughout each football season.

3.4. Concussion History and Emotion Dysregulation Questionnaires (PHQ-9, GAD-7, BIS-11, BPAQ, PSS4)

The purpose of the concussion history and emotion dysregulation measures was to assess changes in negative affect and personality traits related to age, sex, contact level, SRC history and incidence, and head impact biomechanics. These emotion dysregulation measures were administered via four separate Qualtrics.com (Provo, Utah) Concussion History and Emotion Dysregulation Questionnaires in past pilot studies conducted by the UNC-CH research team. Qualtrics.com is a secure internet-based data collection format that allows for increased ease of completion by the participants compared to paper versions. This method of data collection was chosen to improve the comfort of the participants and the validity of their answers. Lind et al. found that people are more truthful about reporting sensitive information when taking an online assessment compared to personal interviews.[338] They found people react to the presence of a human face by reducing their disclosure of information.

We began collecting this data during the 2013/14 high school football season at Chapel Hill High School where several of the football players' helmets were instrumented with HITS accelerometers. Twenty-five football players completed pre- and postseason emotion dysregulation measures, with 18 of them also wearing instrumented

helmets. The 2013/14 pilot data showed significant elevations ($p<0.048$) in aggression in high school football players from pre- to postseason. Impulsivity scores were unaffected ($p=0.329$). A small cohort (n=3) was asked to complete an additional questionnaire 1 month after the season ended. While their 1-month postseason scores regressed back toward the mean, they were still higher (worse) than their preseason scores. One non-instrumented athlete was concussed and completed a post-injury #1 questionnaire. However, they did not complete the preseason questionnaire. A limitation of this study was the lack of a non-contact sport group to control for maturation and school-related stressors (exams, holidays, etc.).

The questionnaires were modified to include measures of depression (PHQ-9), anxiety (GAD-7), and affect (Positive and Negative Affect Scale) and were administered at pre- and postseason to 19 high school sports, including football, for the 2014/15 academic year at the same high school. Questions concerning reduced class load related to sustaining a SRC were added to address academic deficits. The protocol at the end of the 2014/15 academic year was modified per UNC IRB Board recommendations to include an action plan for elevated emotion dysregulation scores as described below. This protocol was put in place at the request of the UNC IRB Board for a similar study involving male and female soccer athletes.

The cutoff points for depression and anxiety were set at ≥10 per recommendations by the authors of each measure. Researchers sent an email to the parents/guardians and school athletic trainer(s) when elevated depression and anxiety scores ($\geq$10) were noted (**Appendix 5**). These individuals were reminded that the emotion dysregulation measures are not diagnostic tools and should only be used as an indication for further diagnostic testing by a neuropsychologist. The student-athletes were informed of this during the recruitment process. All student-athletes who were over 18 years of age had the option to request that we not share this information with their

parents/guardians on their adult consent forms (n=0 requested we not share their information with their parents). Regardless, the student-athlete's AT were alerted when elevated scores were identified so they could include this information in the student-athlete's medical records. The purpose of sharing this information was to give these medical professionals a deeper insight to the psychological health of these student-athletes; thus improving their ability to provide immediate psychological and physical care and rehabilitation to their athletes.

The previous pilot behavior modification project yielded a 96% participation rate and a 100% compliance rate once enrolled. The emotion dysregulation pilot study yielded a 98% participation rate with 100% and 34% compliance rates once enrolled for the pre- and postseason testing respectively.

3.4.1. Implementation of the Concussion History and Emotion Dysregulation Measures

A link to the Preseason Concussion History and Emotion Dysregulation Questionnaire (**Appendix 3**) was emailed via Qualtrics.com to each student-athlete with a request that they complete the questionnaire prior to their school's preseason baseline concussion testing session. Automated group reminders were sent out to those student-athletes who had not completed the questionnaire prior to the testing date. Student-athletes who had not completed the questionnaire prior to their preseason concussion baseline testing session had the opportunity to complete it at that time. The Postseason Concussion History and Emotion Dysregulation Questionnaire (**Appendix 4)** link was emailed to the participants after their last practice or game. Up to four automated reminders were sent to those student-athletes who had not completed the postseason questionnaire for up to 4 weeks following their last practice/game. Each questionnaire required <15 minutes to complete on average. Therefore, the required time commitment was <30 minutes for most participants.

The concussion history portion of the questionnaires changed with each time point. The preseason questionnaire (**Appendix 3**) gathered limited demographic and sport exposure information and helped the authors determine the participant's past SRC and non-sport related concussion history. The postseason questionnaire (**Appendix 4)** inquired about the total incidence of diagnosed and undiagnosed concussions (sport and non-sport related) the student-athlete experienced that season, and if they missed practice or playing time as a result of these concussions.

The five emotion dysregulation measures that were included in each of the Concussion History and Emotion Dysregulation Questionnaires were the: Patient Health Questionnaire (PHQ-9), Generalized Anxiety Disorder 7-item scale (GAD-7), Barrett Impulsiveness Scale -11 (BIS-11), Buss-Perry Aggression Questionnaire (BPAQ), Perceived Stress Scale – 4 item (PSS4). These measures are not time dependent allowing all participants to take as much time as they required to read and honestly answer each item.

3.4.2. Patient Health Questionnaire (PHQ-9)

The Patient Health Questionnaire (PHQ-9)[339] is a highly utilized and validated diagnostic depression measure.[339] This measure has good agreement with mental health professional depression diagnoses (sensitivity = 75% and specificity = 90%) and as compared to the Primary Care Evaluation of Mental Disorders for 1 or more PHQ diagnoses. The PHQ diagnoses have been previously detailed by Spitzer et al.[339] Administration of the PHQ-9 was significantly faster than the previously utilized Primary Care Evaluation of Mental Disorders. The PHQ-9 is a 9 item 4-point Likert scale with answers ranging from "not difficult at all" to extremely difficult". The questions reflect the individual's feelings over the past 2 weeks with scores ranging from 0-27. The PHQ-9 can either be used as a possible predictive tool for major depressive disorder (MDD), or

with cut points at 5, 10, 15, and 20 to represent mild, moderate, moderately severe, and severe depression. MDD should be considered if a patient endorses 5 of more of the 9 symptoms as present 'more than half the days", if one of the first 2 symptoms (depressed mood or loss of interest) or the last symptom (suicidality) are endorsed. It is a well-validated study with good reliability across sex, age, and ethnicity and has been validated in TBI populations.[181, 339-344] The PHQ-9 has also been used in non-sport related concussion research[241] and with adolescents.[344] Computerized administration of this measure has also been validated.[342]

The PHQ-9 may be used to detect various levels of depression. It may be used as a diagnostic tool for depression, but referral for further evaluation should be considered in the presence of elevated scores (≥10). For the purposes of this study, emails were send to the respective parents/guardians (high school participants) and the school AT(s) for all PHQ-9 scores that met the MDD criteria and/or were ≥10.[345]

3.4.3. Generalized Anxiety Disorder 7-item Scale (GAD-7)

The Generalized Anxiety Disorder 7-item scale (GAD-7) is one of the most popular and utilized anxiety measures.[294] This measure has been validated in multiple populations in its ability to detect generalized anxiety, panic, social anxiety, and PTSD.[346] This behavioral measure assesses the person's anxiety levels over the past 2 weeks using 7 validated and highly correlated items.[294] Answers range from "not at all" to "nearly every day" on a 4-point Likert scale (0-3). Total scores may range from 0-21 with higher scores indicating greater anxiety. The accepted cut point for identifying GAD is 10. Further cut points are 0-4 (minimal), 5-9 (mild), 10-14 (moderate), and 15-21 (severe).

The GAD-7 may be used as a clinical indicator for panic, social anxiety, PTSD, and GAD. For the purposes of this study, we notified the parents/guardians of minors in

our study and their ATs for all scores on this measure that fell into the moderate-severe ranges (10-21).[345]

3.4.4. Barrett Impulsiveness Scale –11 (BIS-11)

Impulsivity has been tested using the Barrett Impulsiveness Scale (BIS-11),[306] which is highly utilized and validated across a wide range of individuals.[307] The incidence of TBI-related impulsivity has been mentioned in the literature for over three decades.[308] Unfortunately, an impulsivity measure has not been specifically designed for TBI populations. To date, the most common measure for TBI populations has been the BIS and BIS-11.

In addition to Barratt's definition for impulsivity being one of the most widely accepted, the BIS[347] and its subsequent revisions have become the most utilized measures of impulsivity worldwide in all age groups (12-89 years).[302, 348] This impulsivity measure was revised several times before arriving at the current versions, the BIS-11.[306]

The BIS-11 is a 30 item 4-point Likert scale ranging from "Rarely/Never" to "Almost Always/Always" used to assess trait impulsivity.[302] This particular measure can be broken down into six first order oblique factors and three second order factors. The Attentional 2nd Order Factor is associated with Attention (5 items) and Cognitive Instability (3 items); Motor is associated with Motor (7 items) and Perseverance (4 items), and Nonplanning is associated with Self Control (6 items) and Cognitive Complexity (5 items). It is important to note that several of the items (1, 7, 8, 9, 10, 12, 13, 15, 20, 29, 30) are reverse scored, meaning lower scores are reflective of higher impulsivity rather than lower.

While other studies have found this measure to work well as written in this population, we discovered in during the 2014/15 academic year the meaning of several

questions contained in this measure did not transfer well to high school student-athletes. Researchers frequently were required to give additional information about questions for our participants to accurately provide answers. “I save regularly” was one question that often required explanation. The addition of “money” into the question improved their understanding and allowed all participants to answer the question. Overall 5 of the questions were modified in a similar fashion to improve understanding, accessibility, and consistency for our participants. The modified questions were numbers: 7, 10, 13, 16, and 21 (**Appendix 9**). The modified version was pilot tested by two age appropriate individuals. They confirmed that they were able to complete the measure without difficulty and that the modifications increased their ability to comprehend the questions.

As noted in Chapter 2, this measure is not a tool use to diagnose impulse control disorders (DSM-IV and ICD) and no set cut points have been identified in the literature. Scores on this measure were not reported to participants, their parents/guardians, or their ATs.

3.4.5. Buss-Perry Aggression Questionnaire (BPAQ)

The Buss-Perry Aggression Questionnaire (BPAQ) was originally written as 52 question measures including 6 subcomponents of aggression: physical aggression, verbal aggression, anger, indirection aggression, resentment, and suspicion.[221] A correlational matrix revealed 4 principle factors, physical aggression, verbal aggression, anger, and resentment and suspicion were combined to form hostility. The other two factors were dropped from the measure. The model was replicated to determine reliability and resulted in slight variations, but the variation was also replicable. Additionally, there were slight variations in factor loading between males and females, but the again the variations were repeatable. Three variations of the model were run against a separate sample to assess goodness of fit. The authors determined the best

fitting model was one that assumes the four factors are similarly related to form a common, higher order aggression factor. Anger is highly correlated with all three factors. Hostility is only moderately correlated with physical and verbal aggression, but the latter two are strong correlated. Internal consistency for the measure is high over all (.89), with moderate to high consistency for the individual components (Physical aggression = .85, Verbal aggression = .72, anger = .83, and Hostility = .77). Sex differences have been noted. Males score significantly higher than females on all factors, except anger. The Cohen alpha for physical aggression was large, moderate for verbal aggression, and small for hostility, with no differences in anger. The overall effect size is .57 (medium). A study of elderly individuals in Spain showed men and women reported significantly higher physical aggression and anger respectively.[349] The physical aggression effect size (.306) found by Morales-Vives et al. was smaller than reported by Buss and Perry in 1992. The Cohen d for anger was .47, which may be reflective of this nationality, age group, lack of education, or other socioeconomic covariates.

The long (BPAQ) and short (BAAQ) versions have been found to be valid across a multitude of populations as a measure of aggressiveness overall.[221] The longer version was utilized in this study. It contains 29 items that are scored on a 5-point Likert scale (1-5) ranging from “extremely uncharacteristic” to “extremely characteristic” with a high score of 145.[221] As mentioned previously, it is capable of breaking aggressive behavior into 4 subscales, physical aggression (9 items), verbal aggression (5 items), anger (7 items), and hostility (8 items).

The DSM-IV and V do not recognize aggression as its own disorder. This measure is not utilized as a diagnostic tool and no cutoff values have been identified to suggest possible clinical concern. Similar to the BIS-11 scores, this measure is purely experimental at this point. Our pilot data using the BPAQ has found increased aggression over the course of a sport season. Scores on this measure were not reported

to participants, their parents/guardians, or their ATs.

3.4.6. Perceived Stress Scale – 4 item (PSS4)

Academic performance and pressure to succeed academically are two of the top three concerns for undergraduate collegiate students.[350] These same concerns exist for high school students as well. As described above, stress has been associated with both depression and anxiety, thus we found it necessary to include a measure of stress in our study as a covariate for these measures. Our inclusion of non-contact sport athletes allowed us to rule out season and maturational alterations, as well as the effects of academic stressors through the use of the Perceived Stress Scale – 4 item (PSS4).

The PSS4 is a well-validated and highly utilized 4 item measure of one's perception of stressful events occurring in the last month. [351] This version is a shorter variation of the PSS, which is the most widely utilized measures of perceived stress.[352] Scoring for the PSS4 includes reverse scoring of items 1 and 4 and positive scoring for items 2 and 3 on a 5-point-Likert scale (0 = never to 4 = very often) with a range from 0-16. Higher scores indicate higher levels of perceived stress. The educational requirement for this assessment is at least a junior high school education, making this appropriate for high school participants.

3.5. Potential Problems and Alternative Strategies

The HITS sensors do not pose an additional time burden on the football participants. The only potential burden was during the initial acclimation period at the beginning of 2-a-days during which they became accustomed to the feel of the sensors in their helmets.

In an effort to reduce participant burden, we collected the participant's email addresses and cell phone numbers at the time of consent so we could email each

participant the link to the online concussion and personality questionnaires. This allowed them to complete the questionnaires at any time prior to or during their testing sessions. Each questionnaire took approximately 15 minutes to complete regardless of the time point resulting in a time commitment of 30-60 minutes per player for the entire study.

Although neurodegenerative diseases like CTE have been primarily reported in retired professional athletes, there have been cases indicating neurodegeneration in younger athletes as well.[353] Because of this we chose to study high school athletes to address these long-term emotion dysregulation questions by evaluating: 1) an age group with much greater participation numbers and global generalizability and 2) the cause and effect relationship between RHI and SRC and emotion dysregulation changes, which cannot be addressed in most retired players.

Lastly, all emotion dysregulation data were reviewed within 14 days after baseline testing. While the PHQ-9 and GAD-7 are able to indicate mood disorders, the BIS-11, BPAQ, and PSS4 are not. In the event an athlete presented with abnormal ($\geq$10) PHQ-9 and GAD-7 scores indicating clinical concerns at any of the time point, their athletic trainer and parent/guardian (when applicable) were contacted.

We removed all identifiable data and stored it with de-identifiable codes. These data were only used for research purposes and was used in the diagnosis, treatment, or return to play criteria for any injured athlete. The linkage file was stored separately in an alternate password-protected file in the Matthew Gfeller Center. Accelerometer data were downloaded and reviewed weekly. Accelerometer data were de-identified and thus cannot be linked to a specific player without gaining access to our linkage file that will be stored in a separate password protected file in the Matthew Gfeller Center.

3.6. Statistical Analysis

3.6.1. General Information

The covariates for this study included age, *sport, team (football only)*, general position (line, back, skill, and special teams), player group (offense, defense, both) and the Perceived Stress Scale 4-item (PSS4). Concussion history (yes/no) was an independent variable. Impact biomechanical measures (*frequency, magnitude, impact location*) were used to calculate Injury Severity Profiles (ISP). The competition ISPs were analyzed as dependent variables and the full season ISPs were analyzed as independent variables. The Emotion dysregulation measures (*PHQ-9, GAD-7, BIS-11, BPAQ*) were analyzed in this study as both independent (preseason) and dependent (change-scores) variables. Participant's self-reported responses to the emotion dysregulation questionnaires were scored individually at all four time points on a continuous scale. Full emotion dysregulation profile analyses included all emotion dysregulation measures, while individual emotion dysregulation profiles were conducted for each individual emotion dysregulation score or change-score. Between and within group scores were assessed across all testing sessions (preseason and postseason-preseason).

Data were collected from 25 sports over 72 team-seasons. Ten sports out of 25 had ≤ 25 active student-athletes complete the preseason questionnaire (**Manuscript 1 Table 4.1.1**). In an effort to increase generalizability and applicability of our results we chose to merge these sports. Sports were merged if at least one of the sports had ≤ 25 student-athletes complete the preseason questionnaire and they met at least two of the following criteria: 1) same sex, 2) closely-related sport, but different seasons (i.e., cross country, indoor and outdoor track and field), 3) the sports were categorized as the same *contact level* (high, low, no). Softball (n=24) was not merged with another sport because

no female divers completed the preseason questionnaire and we did not want to merge sex-comparable sports differently (i.e., baseball was merged with boys diving).

3.6.2. Football Specific Information

HITS usage has been well documented by our group and was used to collect our head impact biomechanics variables.[106, 134, 135, 137] SRC history was recorded via self-report and physician diagnoses throughout the study.[4, 5, 354] SRC history, biomechanical, and emotion dysregulation cumulative data were analyzed in a linear fashion. Maximum linear and rotational accelerations were grouped as *low* (<25 g), *moderate* (25-59.99 g), or *high* ($\geq$60 g). We chose to use lower cut points compared to previous literature.[106, 108, 134] Based on our data these changes were more representative of high school concussive impact risk. 25 g represented the 62nd percentile for all impacts in our study, while 60 g represented the 95th percentile. Our group had utilized these cut points previously. Nearly all high school and collegiate concussive impacts have been recorded at or above 60 g in past studies[107, 123] supporting our decision to use 60 g as our cut point for the high group. Additional support for lowering impact magnitude cut points comes from a study involving 3 collegiate football teams.[355] Crisco et al. found the 50th and 95th percentiles for competition impacts to be 20.2 g and 49.6 g respectively. Additionally, they found the 50th and 95th percentiles for all impacts to be 20.3 g and 62.2 g respectively. Further support of our cut points comes from an early head impact biomechanics study conducted by Rowson et al. who reported similar percentages for comparable cut points for collegiate football players; 60% occur above 20 g and 3% of impacts occur above 60 g.[356]

Several past studies have suggested that using a multimodal head impact biomechanics approach to determine SRC risk would be advantageous over the individual variables.[119, 148, 153] Importantly, most of these studies have found impact

location and linear acceleration/peak linear acceleration to be positively associated with incident SRC, but rotational acceleration has not proven to be as effective of a predictor.[119, 120, 148]

This study was conducted simultaneously with a larger study (BEMOD) investigating the effects of an on- and off-field behavior modification program for football players with elevated risk of head and neck injury during the 2015/16 academic year. The BEMOD project utilized the same inclusion criteria for Impact Severity Profiles (ISP) outlined in Section 1.4.6 (Research Variables). The inclusion criteria to be enrolled in the intervention sessions were as follows: Player sustains 1) more than 20% of their impacts were to the crown of their head, 2) more than 7% of impacts exceeded 2 standard deviations above the mean peak linear acceleration (60 g), or 3) an incident concussion during football related activities. A player was required to satisfy only one of the three criteria to be included in the BEMOD intervention sessions. The cut points were determine from previous pilot data with all criteria equally weighted in importance. The same three football teams enrolled in the BEMOD study were also enrolled this study during the 2015/16 academic year. Team 1 and Team 2 were intervention schools and Team 3 acted as the control school.

For the purposes of this study, we only used the top of head and impact severity data to calculate the ISPs. The participants were placed into ordinal-like groups based on the number of criteria met throughout the football season. This approach is based off previous studies suggesting a combination of several biomechanical inputs is more predictive of SRC than a single biomechanical measure[214] and that several neuropsychological tests can effectively diagnose and determine safe return to play compared to only using one test.[148]

3.6.3. Covariates

Team 3 sustained significantly more incident concussions compared to Team 1 ($p=0.008$). While age was not a significant predictor of the emotional dysregulation measures, age and years of sport participation did significantly predict head impact biomechanics. Age and years of sport participation were moderately correlated, $r(155) = 0.36$, $p<0.0001$. We felt years of sport participation was a more appropriate predictor for our analyses since it has a higher likelihood of reflecting our participants' skill, knowledge, and comfort levels with the sport of football; thus, we chose to include team and years of sport participation as covariates in all RQ2 models.

Additional covariates were utilized in our analyses to replicate previous high school impact biomechanics studies and improve generalizability including: general position and player group.[122, 126] Player position (primary and secondary position) was used to formulate each football participant's general position. Primary and secondary positions were grouped into the following categories: defensive back (DB), linebacker (LB) running back (RB), defensive line (DL), wide receiver (WR), tight end (TE), quarterback (QB), offensive line (OL), special teams (ST), kicker (K), and punter (P). Researchers alternated assigning participants who played offense and defense approximately equal amounts of time in competitions to either a primary or secondary position. For example, if Participants A and B and played OL and DL equally they were assigned to OL and DL for their primary position and DL and OL for their secondary position respectively. General position determined by the each player's primary position and was categorized as: Back (LB, RB, QB), Line (OL, DL, TE), Skill (DB, WR), and Special Teams (K, P, ST). This grouping is very similar to previous studies.[122] However we chose to group tight ends with the linemen instead of the skill players as the participating offenses used their tight ends for blocking more than as a downfield

receiver. Finally player group was determined by estimating the amount of time the players participated in offensive and defensive plays during competitions. If a participant played more than 30% of the time in offensive and defensive plays they were categorized as “Both”, otherwise they were categorized as either “Offense” or “Defense”. All statistical analyses were performed using SAS 9.4 (SAS Institute Inc. Cary, NC). See **Table 3.3** for the statistical analyses.

Table 3.3. Research Questions Statistical Analyses

Hypothesis	Description	Data Source	Comparison	Method
1	Association between SRC history and preseason emotion dysregulation (n=1,053)	SRC history and emotion dysregulation measures	**IV:** SRC history **DV:** PHQ-9, GAD-7, BIS-11, BPAQ	General Linear Mixed model. Covariates: Age, Sport
2	Associations among preseason emotion dysregulation, competition head Impact Severity Profiles, and incident SRC (HS n=155)	Emotion dysregulation measures, SRC incidence, and competition impact biomechanical measures	**IV:** PHQ-9, GAD-7, BIS-11, BPAQ **DV:** Incidence of SRC; Head Impact Severity Profile (poor, moderate, normal) = Impact frequency, magnitude, and location	Log-binomial regression and Proportional odds model. Covariates: PSS4, General Position, Player Group, Team, Seasons of sport participation
3	Associations among full season head Impact Severity Profiles, incident SRC, and emotion dysregulation change-scores (n=105)	SRC incidence, impact biomechanics, and Emotion Dysregulation measures	**IV:** Head Impact Severity Profile (poor, moderate, normal) = Impact frequency, magnitude, and location; Incident SRC **DV:** PHQ-9, GAD-7, BIS-11, BPAQ change-score (Postseason-Preseason)	General Linear Mixed model. Considerations: multiple assessments per person Covariates: PSS4, General Position, Player Group, Team, Seasons of sport participation
Exploratory RQ	Association between SRC incidence and emotion dysregulation change-scores (postseason-preseason) (n=46)	SRC incidence and Emotion Dysregulation measures	**IV:** SRC incidence **DV:** PHQ-9, GAD-7, BIS-11, BPAQ change-score (Postseason-Preseason)	General Linear Mixed model. Covariates: Sex, Sport

3.7. Power Analysis

Assuming a two-sided type I error of .05 the study had 80% power to detect a moderate to large effect size (ES = 0.5) with 142 participants (n=71 male and female). We collected preseason data for 1,053 participants (females = 446).

CHAPTER 4: MANUSCRIPTS

Manuscript 1: Associations between Sport-Related Concussion and Emotion Dysregulation in High School Student-Athletes

OBJECTIVE: To examine 1) the cross-sectional associations at preseason between concussion history and emotion dysregulation and 2) the longitudinal association between in-season incident sport-related concussion and change in emotion dysregulation from preseason to postseason among high school student-athletes.

DESIGN, SETTING, AND PARTICIPANTS: A total of 1,053 high school student-athletes (age = 15.59 ± 1.21) representing 22 sports were enrolled during the 2013/14-2015/16 academic years.

MAIN OUTCOME and MEASURES: At preseason and postseason, four measures of emotion dysregulation were assessed including depression (The Patient Health Questionnaire [PHQ-9]), anxiety (The Generalized Anxiety Disorder 7-item scale [GAD-7]), impulsivity (Barrett Impulsiveness Scale [BIS-11]), and aggression (The Buss-Perry Aggression Questionnaire [BPAQ]). Our primary predictor variables were concussion history at preseason and incident concussion in-season (yes/no). We controlled for age, sex, sport.

RESULTS: Cross-sectional associations at preseason: concussion history was associated with preseason depression scores in high school student-athletes (p=0.004) when controlling for age and sport. Concussion history was associated with preseason impulsivity scores in high school student-athletes with (p=0.015) and without (p=0.002) covariates. Longitudinal associations across one season: The mean anxiety change-score over one season for concussed athletes was 2.69 points lower (better) than that of age and position matched healthy teammate controls (p=0.011, 95% CI: -4.75,-0.64). Concussion status (concussed vs. not) was not associated with

changes in depression (p=0.264), impulsivity (p=0.934), or aggression (p=0.295) over one season.

CONCLUSIONS AND RELEVANCE: Our preseason data support findings from previous literature that concussion history results in higher (worse) emotion dysregulation scores**.** Emotion dysregulation over one season was not associated with incident concussion in an adverse manner.

Key words: Sport-related concussion, depression, anxiety, impulsivity, aggression, sex, contact level

INTRODUCTION

Investigators of non-athletic moderate-severe traumatic brain injury (TBI) have explored the emotion dysregulation consequences of head injuries and have consistently reported persistent emotion dysregulation. Moderate-severe TBI studies with non-athletic,[1-3] military,[4-6] and animal[7, 8] populations have correlated heightened depression, anxiety, aggression, and impulsivity with poor long-term health outcomes (violence, loss of job/relationships, neurodegenerative disease, etc.).[4, 9] Similar emotion dysregulation consequences have also been found in adolescents who have sustained moderate-severe TBIs.[10-13] Previous research has also shown two negative affect disorders (e.g., depression and anxiety) are significantly correlated in injured[14-18] and non-injured[19-21] populations. To a limited degree, depression, anxiety, impulsivity, and aggression have been investigated in athletes with and without sport-related concussion (SRC),[22-26] but none of these studies have prospectively assessed changes over time following concussive injury. Long-term elevation of these affect disorders have been reported following TBI and SRC.[24, 27]

Studies have indicated an association between TBI with several neurodegenerative diseases including Alzheimer's disease (AD),[28] and Parkinson's.[29] Similarly, SRC has been associated with mild cognitive impairment (MCI),[30] AD,[30] and chronic traumatic encephalopathy

(CTE).[31] Each of these neurodegenerative diseases has been reported to be associated with increased depression,[32-34] anxiety,[34, 35] impulsivity,[34, 36] and aggression.[34, 36] In addition, stress has been shown to increase short- and long-term depression and anxiety,[37, 38] but this has not been investigated specifically in SRC research. Therefore, emotion dysregulation may be a key component to injury evaluations, referrals, and return to play decisions and may possibly help researchers and clinicians answer the long sought after question of "how many concussions are too many?"

Importantly, no studies currently exist evaluating the associations between SRC and emotion dysregulation measures at preseason or postseason. This study was a first-step in evaluating potential associations between these factors in high school student-athletes. The objectives for this longitudinal study were two-fold. The first objective was to assess the cross-sectional preseason association between concussion history and emotion dysregulation measures in high school student-athletes. The hypothesis for objective 1 was that a history of SRC measured at preseason would be associated with higher (worse) emotion dysregulation scores at preseason. The second objective was to determine the association of in-season incident concussions and emotion dysregulation change-scores (postseason-preseason) in high school student-athletes over one season. The hypothesis for objective 2 was that student-athletes sustaining an in-season incident concussion would present with worse (higher) emotion dysregulation scores at postseason relative to preseason.

METHODS

Participants

One thousand seven hundred and forty sixe student-athletes were recruited for our study from three high schools during the 2013/14 to 2015/16 academic years. All interested student-athletes (n=1,190) and their parents/guardians gave written assent/consent prior to their enrollment in the study. Exclusion criteria included individuals who: were not fluent in English,

had visual impairments that could not be rectified with corrective lenses, were not on the active roster at the start of the season due to injury, had an unresolved SRC at the start of their season, and had history or psychoses beyond anxiety or depression.

Concussion History and Emotion Dysregulation Questionnaires

The purpose of the concussion history and emotion dysregulation measures was to assess changes in negative affect and personality traits related to SRC history and incidence. All enrolled participants were asked to complete a preseason and postseason Concussion History and Emotion Dysregulation Questionnaire lasting approximately 15 minutes each. The questionnaires were completed via an online survey platform (Qualtrics.com). The participants were asked to complete the preseason Concussion History and Emotion Dysregulation Questionnaire at the start of their athletic season and the postseason questionnaire within 4 weeks of their season ending. Up to four follow-up email reminders were sent to participants to encourage them to complete either of the respective questionnaires.

Concussion was defined as a complex pathophysiological process affecting the brain, induced by biomechanical forces.[39] *Sport-related concussion (SRC)* was defined as any concussion that occurs during sports participation that is diagnosed by a medical provider. The participants were asked several demographic questions concerning their concussion history and seasons of sport participation on the preseason questionnaire. Concussion history was analyzed as a binary variable (yes/no). Participants were given the following statement to assist them in determining if they had ever sustained a concussion, “A concussion is a blow to the head followed by a variety of symptoms that may include any of the following: headache, dizziness, loss of balance, blurred vision, "seeing stars", getting "dinged", feeling in a fog or slowed down, memory problems, poor concentration, nausea, or throwing-up. Getting "knocked out" or being unconscious does NOT always occur with a concussion.” All *incident concussion*s included in our analyses occurred in-season and were confirmed by a certified athletic trainer

and/or physician. On the postseason questionnaire the athletes were asked if they believed they had sustained a concussion during their season. Incident concussion was analyzed as a continuous (2 athletes sustained 2 SRCs in one season) and binary variable (yes/no).

For objective 2 the school athletic trainer assisted in identifying potential non-concussed teammate controls that most closely resembled the concussed athlete in age, position and playing time when the concussion was reported. The athletes were matched in this way to control for these factors during the preseason to postseason change-score analyses.

Depression. The Patient Health Questionnaire (PHQ-9)[40] is a highly utilized and validated diagnostic depression measure.[40] This measure has good agreement with mental health professional depression diagnoses (sensitivity = 75% and specificity = 90%) and as compared to the Primary Care Evaluation of Mental Disorders for 1 or more PHQ diagnoses. The PHQ-9 is a 9 item 4-point Likert scale with answers ranging from "not difficult at all" to extremely difficult". The questions reflect the individual's feelings over the past 2 weeks with scores ranging from 0-27. The PHQ-9 can either be used as a possible predictive tool for major depressive disorder (MDD), or with cut points at 5, 10, 15, and 20 to represent mild, moderate, moderately severe, and severe depression. MDD should be considered if a patient endorses 5 or more of the 9 symptoms as present "more than half the days", if one of the first 2 symptoms is endorsed (depressed mood or loss of interest), or they report any score above 0 on the last question (suicidality). The PHQ-9 may be used as a diagnostic tool for depression, but referral for further evaluation should be considered in the presence of elevated scores (≥10).

*Anxiety***.** The Generalized Anxiety Disorder 7-item scale (GAD-7) is one of the most popular and utilized anxiety measures.[41] This measure has been validated in multiple populations in its ability to detect generalized anxiety, panic, social anxiety, and post-traumatic stress disorder.[42] This behavioral measure assesses the person's anxiety levels over the past 2 weeks using 7 validated and highly correlated items.[41] Answers range from "not at all" to "nearly every day" on a 4-point Likert scale (0-3). Total scores may range from 0-21 with higher

scores indicating greater anxiety. Similar to the PHQ-9, the accepted cut point for identifying GAD is 10. Further cut points are 0-4 (minimal), 5-9 (mild), 10-14 (moderate), and 15-21 (severe).

Impulsivity. Impulsivity has been tested using the Barrett Impulsiveness Scale (BIS-11),[43] which is highly utilized and validated across a wide range of individuals.[44] The incidence of TBI-related impulsivity has been mentioned in the literature for over three decades.[45] The BIS-11 is a 30 item 4-point Likert scale ranging from “Rarely/Never” to “Almost Always/Always” used to assess trait impulsivity.[46] It is important to note that several of the items (1, 7, 8, 9, 10, 12, 13, 15, 20, 29, 30) are reverse scored.

While other studies have found this measure to work well as written in this population, throughout the course of our study it became evident that the meaning of several questions contained in this measure did not transfer well to high school student-athletes. The participants frequently asked the researchers to provide additional information about questions so they could accurately provide answers. “I save regularly” was one question that often required explanation. The addition of “money” into the question improved their understanding and allowed all participants to answer the question. Overall, 5 questions were modified (7, 10, 13, 16, and 21) in a similar fashion to improve understanding, accessibility, and consistency for our participants. The modified version was pilot tested by two age appropriate individuals. They confirmed that they were able to complete the measure without difficulty and that the modifications increased their ability to comprehend the questions.

Aggression. The Buss-Perry Aggression Questionnaire (BPAQ) has been found to be valid across a multitude of populations as a measure of aggressiveness.[47] The BPAQ has 29 items, graded on a 5-point Likert scale (1-5) ranging from “extremely uncharacteristic” to “extremely characteristic”.[47] This measure can be broken down into 4 subscales, physical aggression (9 items), verbal aggression (5 items), anger (7 items), and hostility (8 items). The DSM-IV and V do not recognize aggression as its own disorder. This measure is not utilized as

a diagnostic tool and no cutoff values have been identified to suggest possible clinical concern.

Stress. Academic performance and pressure to succeed academically are two of the top three concerns for undergraduate collegiate students.[48] These same concerns exist for high school students. Stress has been associated with depression and anxiety, thus it was prudent to include a measure of stress as a covariate for the emotion dysregulation measures.

The Perceived Stress Scale 4-item (PSS4) is a well-validated and highly utilized 4-item measure of one's perception of stressful events occurring in the last month.[49] Scoring for the PSS4 includes reverse scoring of items 1 and 4 and positive scoring for items 2 and 3 on a 5-point-Likert scale (0 = never to 4 = very often) with a range from 0-16. Higher scores indicate higher levels of perceived stress. The PSS4 was included as a potential covariate but was not a primary emotion dysregulation outcome measure.

A score of $\geq$10 on the PHQ-9 (major depressive disorder [MDD]) and GAD-7 (panic, social anxiety, PTSD, and GAD) may be used as clinical indicators for several psychological disorders.[50] For the purposes of this study, emails were sent to each participant's respective parent/guardian and the school AT for all PHQ-9 and GAD-7 scores $\geq$10. These individuals were reminded that the emotion dysregulation measures are not diagnostic tools and should only be used as an indication for further diagnostic testing by a neuropsychologist. The BIS-11 and BPAQ are not tools use to diagnose impulse control, or aggressive disorders (DSM-IV and ICD) and no set cut points have been identified in the literature. Scores on these measures were not reported to participants, their parents/guardians, or their ATs.

Adjusted Emotion Dysregulation Scores

Missing values occurred for some questionnaire items. To minimize the potential impact of attrition over time and/or loss of scores due to a limited number of missing values for a measure, missing values were replaced using a standardized approach. If an individual did not answer at least 75% of the items for a particular measure the total score for that measure was

considered missing (e.g., completion of only six of the nine PHQ-9 items). The BPAQ is a summation of its 4 subscales (physical aggression, verbal aggression, anger, hostility). The individual subscales were also required to have at least 75% item completion to be calculated. If one of the subscales was considered missing (<75% completion), the BPAQ Total score was also missing. All emotion dysregulation measures were summed per their respective method. The score for each measure that had less than 100% but ≥75% of its respective items completed was then adjusted as follows:

$$\text{Adjusted Score} = \frac{\text{Total score} \times \text{Total number of items}}{\text{\# of items completed}}$$

Current *age* and *sport* were collected via the questionnaires from 25 sports (female sports = 11) (**Tables 4.1.1 and 4.1.2**). Ten sports had ≤ 25 active student-athletes complete the preseason questionnaire. In an effort to increase generalizability and applicability of our results we chose to merge these sports. Sports were merged if at least one of the sports had ≤ 25 student-athletes complete the preseason questionnaire and they met at least two of the following criteria: 1) same sex, 2) closely-related sport, but different seasons (i.e., cross country, indoor and outdoor track and field), 3) the sports were categorized as the same *contact level* (high, low, no). Softball (n=24) was not merged with another sport because no female divers completed the preseason questionnaire and we did not want to merge sex-comparable sports differently (i.e., baseball was merged with boys diving).

Data Analysis

The preseason emotion dysregulation scores (objective 1) were analyzed as continuous variables. These scores were evaluated independently to evaluate the associations between emotion dysregulation scores and concussion history (binary variable). Emotion dysregulation change-scores (objective 2) were calculated by subtracting the participant's preseason score from their postseason score for each of the four outcome measures and the PSS4. The change-

scores were then analyzed as continuous variables. The change-scores were evaluated independently to determine the associations between changes over one season for each emotion dysregulation measure and incident SRC (binary variable). A higher score for each of the emotion dysregulation measures indicated a worse score and a lower score indicated a healthier score.

Linear regression was used to determine if concussion history could predict preseason emotion dysregulation scores. Linear regression was also used to determine the association between incident concussion and the individual emotion dysregulation change-scores (postseason-preseason). Age and sport were used as covariates in adjusted analyses involving preseason emotion dysregulation, because both were associated with the preseason emotion dysregulation scores. Sex and sport were both associated with the emotion dysregulation change-scores, thus were used as covariates for the associated adjusted analyses. Alpha at 0.01 was used to determine statistical significance. All analyses were performed in SAS (version 9.4; SAS Institute Inc. Cary, NC).

RESULTS

A total of 1,190 (68.16%) of the recruited student-athletes (age 15.59 ± 1.21) at three high schools during the 2013/14-2015/16 academic years were enrolled representing 72 team-seasons. Football was the best-represented sport in this study comprising nearly 21% of the sample followed by men's lacrosse (7.60%), women's soccer (7.50%), field hockey (7.22%), and women's lacrosse (6.55%) (**Table 4.1.1**). As a result football was used as the reference for all sport-related analyses. There were thirteen 13-year-olds and one 19-year-old enrolled, who were merged into the 14 and 18-year-old groups, respectively.

Two hundred and forty three (23.08%) student-athletes had at least 1 previous concussion (Males = 176, Football = 69) (**Table 4.1.2**). A history of concussion was not associated with diagnosed (p=0.071), or non-diagnosed (p=0.667) concussions at preseason.

The student-athletes' previous history of diagnosed (1.02 ± 0.80) and non-diagnosed (0.44 ± 1.03) concussions ranged from 0-5 and 0-9, respectively. Mean preseason emotion dysregulation scores by concussion history can be found on **Table 4.1.3**.

Concussion history was associated with significantly higher preseason depression (p=0.004) in the adjusted model and impulsivity in the adjusted (p=0.015) and the unadjusted (p=0.002) models (**Table 4.1.4**). Concussion history was not significantly associated with any of the other preseason emotion dysregulation scores p≥0.023).

Sex ($p \geq 0.162$) and age ($p \geq 0.143$) were not associated with any of the full season emotion dysregulation change-scores. Sport was not associated with any of the full season emotion dysregulation change-scores for the concussed athletes ($p \geq 0.165$), but it was a significant predictor for anxiety change-scores for all student-athletes included in the longitudinal analyses (p=0.013). Stress was not an overall predictor of any of the full season emotion dysregulation change-scores ($p \geq 0.320$), nor was it a predictor for the concussed athletes ($p \geq 0.161$), or their teammate controls ($p \geq 0.360$). Female teammate controls reported higher stress full season change-scores compared to the male teammate controls (p=0.012). Sport was a significant predictor for higher (worse) anxiety full season change-scores for the teammate controls (p=0.011). Finally, Due to these associations, sex and sport were used as covariates for all full season change-score analyses.

Preseason and postseason data was captured for 46 concussions (Males = 37, Football = 22, High contact = 41) (**Table 4.1.5**)**.** Data for 30 (65.22%) concussions were captured during the 2015/16 academic year. This was the only year student-athletes from three schools were enrolled. Information for 16 concussions was captured during the 2013/14 (n=2) and 2014/15 (n=14) academic years. We collected data from one football team during the 2013/14 academic year and one school (17 sports teams) for the 2014/15 academic year, hence the lower numbers during those years.

Anxiety was the only emotion dysregulation measure with a significantly different full season change-score between the concussion groups (p=0.011). The mean anxiety full season change-score for concussed athletes was 2.69 points lower (better) compared to their non-concussed teammate controls (B= -2.693 95% CI: -4.745,-0.640). Concussion status was not associated with depression (p=0.264), impulsivity (p=0.934), or aggression (p=0.295).

DISCUSSION

The most important findings of the current study were preseason concussion history was significantly associated higher (worse) depression (adjusted model) and impulsivity (adjusted and unadjusted model) and that incident concussion was not associated with worse full season emotion dysregulation change-scores (postseason – preseason) compared to age, position, and playing time matched, non-concussed teammates. It should be noted that our mean preseason aggression score (58.51±17.23) was nearly 10 points lower than the mean aggression score (67.2±16.4) reported by Santisteban and Alvarado for their sample of 2,208 14-18 year-old male and female adolescents.[51] This may be an effect of general sampling differences in urban North Carolina. It is also possible that our preseason scores and postseason change-scores varied from other studies as a result of response biases associated with social desirability.[52] Our best indicator that social desirability may have been a factor was the men's runners reported higher (worse) preseason aggression compared to the football team. While this difference was not statistically insignificant it was unexpected.

The concussion history results (**Table 4.1.4**) did support previous studies finding elevated depression (p=0.004) after TBI[10, 53] and SRC,[24] but not for increased anxiety ($p \geq 0.335$) in the adjusted model.[54, 55] The purpose of the adjusted models were to evaluate the effect of age and sport type on the association between concussion history and emotion dysregulation. The interpretation of this is that when the ages of the student-athletes and the sports they participate in are considered equal, individuals with a history of concussion reported

higher preseason depression scores compared to those without a concussion history. However, when the varying ages and sports were not equalized (unadjusted model) there was no difference between the concussion history groups' preseason depression scores. These findings suggest that concussion history is associated with elevated preseason depression in high school student-athletes regardless of age or sport, which is an important clinical finding for athletic trainers. Elevated depression has been noted in retired NFL athletes with a history of 3+ SRC,[24, 25] but many of our athletes only had one SRC. If high school student-athletes demonstrate elevated depression with only one SRC, then clinicians would be remiss to not take depression scores into consideration when evaluating, rehabilitating, and considering return to play for athletes with 1+ SRCs.

Concussion history predicted higher preseason impulsivity scores in the adjusted ($p=0.015$) and unadjusted models ($p=0.002$), but was not associated with aggression in either model ($p \geq 0.034$). These findings indicate two separate associations are present between concussion history and impulsivity. The adjusted model (covariates) suggests that regardless of age or sport concussion history is associated with higher (worse) preseason impulsivity scores. The interpretation of unadjusted finding (no covariates) is that age and sport also have a significant effect on preseason impulsivity scores for the concussion history groups. Together these suggest that athletes with a SRC history are more likely to report higher (worse) preseason impulsivity scores and that those who participate in certain sports and/or are at certain ages are more likely to report increased preseason impulsivity scores compared to other sports/ages. Furthermore, the moderating effect of sport and/or age may have a greater association with preseason impulsivity than concussion history itself, or these two factors could have a compounding effect. In support of this data, some of our previous work found that high contact sports reported greater preseason impulsivity compared to no contact sports.[56] In addition, Goswami, et al. found 19 retired professional football players (mean age = 50 ± 12yrs) with a history of concussion scored worse on impulsivity and aggression measures in addition to

exhibiting maladaptive structural and functional brain changes compared to 17 healthy, age matched controls.[26] These studies indicate long-term emotion dysregulation related to SRC and possibly contact level (high, low, no), which lends more support to incorporating these measures into current SRC protocols.

Admittedly the scores between all groups are relatively close in our study. It is unlikely that differences as small as these would be clinically relevant. However, if these athletes were tracked overtime, previous studies associating SRC with MCI, AD, and CTE suggest the scores of the student-athletes with a concussion history would increase at a greater rate compared to those with no concussion history. Furthermore, as concussion history increases, particularly in high contact sports, so would emotion dysregulation. This is exemplified by Goswami, et al. who found retired players had scores that exceeded their controls by >5 point for impulsivity and >10 points for aggression and mania. Implementation of emotion dysregulation measures at the onset of sport participation would allow clinicians, parents, and athletes to track changes over time and more objectively assess if an athlete has returned to baseline in more aspects of life than just cognition and balance. Anecdotally, the authors have personally witnessed athletes who had returned to baseline on their clinical tests, but were still exhibiting elevated negative emotions and behaviors. Neuroimaging and blood biomarker tests are cost-prohibitive and timely. Yet future investigations of the associations among neuroimaging, other biomarkers, and emotion dysregulation assessed both by self-reports and through novel behavioral markers may reveal whether athletes with SCR (history, incident) differ from sport-matched control athletes. The results of such investigations may point to cost effective ways to identify at-risk athletes.

It is possible that athletes do not follow the general emotion dysregulation trends reported for general or clinical populations due to their highly competitive, physical environments and possibly due to genetic or environmental pre-participation influences. It is also possible that athletes have different normative values and ranges compared to their non-athletic classmates. If athletes do have different normative values compared to the national

averages, it is important that large-scale studies are conducted at all age levels to gather this information so sex, age, and sport-appropriate normative values can be calculated. This is particularly important for athletes who sustain SRCs. Our study found that athletes who had at least 1 previous concussion scored higher in both depression and impulsivity. Elevated scores for both depression and impulsivity have been associated with AD,[32] Parkinson's,[57] TBI,[10, 53, 58] and may be linked with CTE.[31] Furthermore, depression has been associated with SRC.[24] In addition, TBI has been associated with increased risk of AD[28] and Parkinsonism.[29]

Our data support sport-related differences, to some degree, for all four of the emotion dysregulation measures, which indicates that some sports, and therefore large groups of athletes, already have a higher propensity for issues with emotion dysregulation, which could then be exacerbated by SRC in the short- and long-term. Additionally, these measures are not currently included in SRC care protocols. If athletes are exhibiting increased depression and impulsivity post-SRC incorporating these measures into current protocols may allow clinicians to better understand and interpret emotion dysregulation changes and improve their ability to safely return athletes after injury. Several studies have shown that cognition and balance typically return to baseline within 7-10 days after an SRC. While, none of the athletes enrolled in this study had sustained a SRC for at least one month prior to completing their preseason questionnaire and were all asymptomatic based on the traditional measures, those with a concussion history reported significantly higher depression and impulsivity compared to those with no concussion history. This indicates that athletes are exhibiting increased preseason emotion dysregulation issues compared to their cohorts. It is important to point out that athletes who sustain SRCs may have had elevated scores prior to their injury, which then predisposed them to an SRC instead of the SRC causing the elevated scores.

Incident concussion was hypothesized to be associated with worse (higher) postseason emotion dysregulation scores compared to the preseason scores. Only males who were concussed reported an increase in anxiety over the course of one season, which then resulted

in the overall anxiety score to also be higher since they represented the majority of concussed athletes (80.43%) (**Table 4.1.5**). Surprisingly, these changes in anxiety scores over one season were actually significantly lower than their non-concussed teammate's scores. The lack of significant findings may be related to our small age range (13-18 years-old). Kontos et al. found collegiate student-athletes reported significantly higher depression scores compared high school student-athletes at 14 days post-SRC.[59] Inclusion of a more diverse age range is recommended for future studies to determine the association of age with SRC and emotion dysregulation.

As suggested previously, it is possible that the concussed athletes reported increased emotion dysregulation scores at baseline, therefore resulting in a ceiling effect for their scores at postseason and potentially a propensity to sustaining an incident concussion. Athletes who are injured, or held out of participation for any period of time often experience increased emotion dysregulation and clinicians have been advised to devise and implement protocols to evaluate and refer athletes that exhibit subclinical and clinical changes.[60] It is possible that the concussed athletes experienced heightened emotion dysregulation at the onset of their injury and during their recovery, but once they had fully recovered and had returned to sport their emotion dysregulation issues seemed to be far less significant compared to when they were injured so they under-reported any symptoms that they were experiencing at postseason.

All three schools enrolled in this study employed full time athletic trainers who set aside time daily to speak to and evaluate each concussed athlete. Strong social support has been negatively associated with global burnout and emotional/physical exhaustion and trait optimism has been positively associated with well-being across a competitive season,[61] suggesting individuals with strong social support and elevated euthymic mood are more likely to be resilient against negative life stressors. We believe that the athletic trainers' concern and support for their athletes safe return to play may have improved (lowered) the concussed athletes' postseason scores.

It is also possible that a percentage of the athletes who were concussed had elevated preinjury resilience and euthymic mood (a reasonably positive mood), thus protecting them from significant alterations in their emotion dysregulation scores. Resilience generally refers to one's ability to maintain a stable psychological equilibrium in the face of adversity.[62] Individuals with high resilience are exposed to the same transient perturbations as everyone else, but are able to exhibit a more stable trajectory and long-term outcome compared to individuals with lower resilience. Euthymic mood has been associated with a decrease in inflammatory biomarkers and depression in adolescents[63] suggesting euthymic mood may be protective against emotion dysregulation and biomedical complications. It is also possible that incident concussion has no effect on emotion dysregulation change-scores. It is our recommendation that future studies investigate emotion dysregulation associations with preseason scores, recovery, social support, resilience, and euthymic mood to determine if these associations exist. If so, they could help inform clinicians about best practices for evaluation and treatment for athletes who sustain both SRC and orthopaedic injuries.

Our results provide intriguing insight into the potential associations between SRC history and emotion dysregulation. The data presented demonstrate the utility of these measures and support further investigative studies as mentioned above. Longitudinal studies that start with early primary school-aged children are necessary to determine many of these relationships and to control for unknown/forgotten past medical history, maturation, and exposure to various sports. Additionally, longitudinal studies would allow researchers to develop more generalizable normative values that follow the growth and maturation curves compared to cross-sectional studies. If our goal is to improve the long-term outcomes of current and future athletes, our finding indicate the importance of involving emotion dysregulation measures in our studies. Our data do support the inclusion of emotion dysregulation measures in clinical baseline, but not post-injury testing at this time. However, our data suggest that with further investigation

researchers may determine whether these measures are beneficial as predictive tools for at risk athletes as well as in return to play decisions.

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Table 4.1.1. Sex, Sport Type, and Contact Level by Sport

Team	Sex		Sport Type		Contact Level			Merged Sports	
	Male n (%)	Female n (%)	Individual	Team	No	Low	High	Male	Female
Baseball	60 (5.70)			X		X		A	
Basketball	54 (5.13)	60 (5.70)		X		X			
Cross-Country	8 (0.76)	15 (1.42)	X		X			B	C
Diving	2 (0.19)		X			X		A	
Field Hockey		76 (7.22)		X			X		
Football	219 (20.80)			X			X		
Golf	3 (0.28)		X		X			D	
Lacrosse	80 (7.60)	69 (6.55)		X			X		
Soccer	54 (5.13)	79 (7.50)		X			X		
Softball		24 (2.28)		X		X			
Swimming	20 (1.90)	17 (1.61)	X		X			D	E
Tennis	23 (2.18)	26 (2.47)	X		X			D	E
Track and Field	15 (1.42)	21 (1.99)	X		X			B	C
Volleyball		56 (5.32)		X		X			
Wrestling	59 (5.60)		X				X		

Track and Field includes both indoor and outdoor seasons
Merged Sports: Matching letters denote sports that were merged to make "new sports" for analysis purposes

Table 4.1.2. Demographics at Preseason

Concussion History	N	Age (yrs)$	Seasons of sport participation (yrs)$	Diagnosed concussion	Non-diagnosed concussion
		Mean ± SD	Mean ± SD (n)	Mean ± SD (n)	Mean ± SD (n)
Yes	243	15.92 ± 1.19	6.45 ± 3.54 (237)	1.03 ± 0.80 (234)	0.45 ± 1.04 (241)
No	810	15.50 ± 2.00	5.62 ± 3.48 (744)		
Total	1053	15.58 ± 1.23	5.83 ± 3.51	1.02 ± 0.80 (236)	0.45 ± 1.03 (242)

If a student-athlete noted that they had a concussion history they were asked to provide the number of diagnosed and non-diagnosed concussions, hence the reduced numbers.
$ Concussion History was a significant predictor ($p \leq 0.002$).
Significant at p=0.01.

Table 4.1.3. Preseason Emotion Dysregulation Scores by Concussion History

		Depression (PHQ-9)^	Anxiety (GAD-7)^	Impulsivity (BIS-11)	Aggression (BPAQ)^	Stress (PSS4)
		X ± SD (n)	X ± SD (n)	X ± SD (n)	X ± SD (n)	X ± SD (n)
Concussion History	Yes (n=243)	3.22 ± 3.66 (228)	3.00 ± 3.91 (228)	61.59 ± 9.13 (238)	60.60 ± 18.25 (235)	7.16 ± 2.45 (128)
	No (n=810)	2.65 ± 3.23 (766)	3.29 ± 3.92 (768)	59.38 ± 9.59 (798)	57.89 ± 16.89 (796)	7.50 ± 2.27 (401)
Overall (1053)		2.78 ± 3.34 (994)	3.22 ± 2.92 (996)	59.89 ± 9.52 (1036)	58.51 ± 17.23 (1031)	7.42 ± 2.31 (529)

Behavioral Measures: Depression = Patient Health Questionnaire – 9 (PHQ-9), Anxiety = Generalized Anxiety Disorder 7-item scale (GAD-7), Aggression = Buss Perry Aggression Questionnaire (BPAQ), Impulsivity = Barrett Impulsiveness Scale – 11 (BIS-11), Stress = Perceived Stress Scale 4-item (PSS4).
Age is significant ($p \leq 0.013$).
^ Sport is significant ($p \leq 0.0003$).
Significant at p=0.01

Table 4.1.4. Mean Difference (95% CI and p-value) Preseason Concussion History and Individual Emotion Dysregulation Models

	Model	Group	Depression (PHQ9) (n=994)	Anxiety (GAD7) (n=996)	Impulsivity (BIS-11) (n=1036)	Aggression (BPAQ) (n=1031)	Perceived Stress (PSS4) (n=529)
Concussion History	U		0.5712 (0.0776,1.0649) 0.023	-0.2852 (-0.8655,0.2952) 0.335	2.2086 (0.8333,3.5838) 0.002	2.7171 (0.2108,5.2235) 0.034	-0.2450 (-0.8046,0.1146) 0.141
	A		0.7178 (0.2273,1.2282) 0.004	0.0925 (-0.4734,0.6584) 0.749	1.7547 (0.3475,3.1618) 0.0146	1.4242 (-1.1069,3.9553) 0.270	-0.2387 (-0.7024,0.2249) 0.312

U: Unadjusted Model (No covariates).
A: Adjusted Model (Covaried for age and sport [reference = football]).

Table 4.1.5. Demographic Data and Emotion Dysregulation Change-Scores for Concussed Athletes

	Group (n)	Age (yrs)	Depression (PHQ-9)	Anxiety (GAD-7)#%	Impulsivity (BIS-11)	Aggression (BPAQ)^	Stress (PSS4)$
		X ± SD	X ± SD (n)	X ± SD (n)	X ± SD (n)	X ± SD (n)	X ± SD (n)
Concussed Athletes	Males (37)	15.62 ± 1.40	-1.09 ± 5.07 (35)	0.97 ± 4.63 (35)	-2.56 ± 10.65 (37)	-8.01 ± 23.41 (37)	-1.21 ± 3.28 (24)
	Females (9)	16.33 ± 1.22	-0.33 ± 4.42 (9)	-0.56 ± 5.41 (9)	-3.22 ± 11.45 (9)	-1.78 ± 17.22 (9)	-3.75 ± 4.57 (4)
	Overall (46)	15.76 ± 1.39	-0.93 ± 4.91 (44)	0.66 ± 4.77 (44)	-2.69 ± 10.68 (46)	-6.79 ± 22.30 (46)	-1.57 ± 3.51 (28)
Teammate Controls	Males (37)	15.32 ± 1.20	0.00 ± 3.20 (36)	1.78 ± 5.12 (36)	-3.30 ± 10.95 (3)	-2.85 ± 16.45 (37)	-0.14 ± 2.73 (21)
	Females (12)	15.42 ± 1.31	-1.50 ± 3.41 (12)	6.08 ± 6.10 (12)	0 09 ± 15.73 (12)	-6.42 ± 30.16 (12)	3.60 ± 2.97 (5)
	Overall (49)	15.35 ± 1.22	-0.37 ± 3.29 (48)	2.85 ± 5.63 (48)	-2.46 ± 12.22 (48)	-3.72 ± 20.34 (49)	0.58 ± 3.10 (26)
All Athletes (95)		15.55 ± 1.31	-0.64 ± 4.13 (92)	1.80 ± 5.33 (92)	-2.07 ± 11.44 (94)	-5.21 ± 21.25 (95)	-0.54 ± 3.46 (54)

Sport was significant overall (p=0.013).
^ Sport was significant for the teammate controls (p=0.019).
# Sport was significant for the teammate controls (p=0.011).
% Sex was significant for the teammate controls (p=0.020).
$ Sex was significant for the teammate controls (p=0.012).
Significant at p=0.01

Manuscript 2: Emotion Dysregulation Measures and Impact Severity Profiles in High School Football Players

BACKGROUND: Current recommendations advise athletic trainers to develop and implement plans for athletes' with psychological concerns.[1] Associations between head impact severity (impact frequency, location, and magnitude) and sport-related concussion (SRC) are still elusive in football players. It is unknown if the inclusion of emotion dysregulation measures may improve clinicians' ability to identify at-risk players.

PURPOSE: This longitudinal study was two-fold. Our objectives were to examine 1) the association between preseason baseline emotion dysregulation scores and competition Impact Severity Profiles (ISP) (competition impact frequency, location, and linear magnitude) and incident SRC over one season and 2) the association between full season ISPs (all impact frequency, location, and linear magnitude data collected over one season), incident SRC, and emotion dysregulation change-scores (postseason – preseason) in high school football players wearing instrumented helmets over one season.

STUDY DESIGN: Prospective longitudinal study; Level of evidence 2

METHODS: 275 football players from 3 schools (5 separate team-seasons) were enrolled during the 2013/14 to 2015/16 academic years. Preseason (n=204, 74.2%) and postseason (n=154, 56.0%) concussion history, key demographics, and self-reported scores on four emotion dysregulation measures were collected via Qualtrics.com. The emotion dysregulation measures included depression (PHQ-9), anxiety (GAD-7), impulsivity (BIS-11), and aggression (BPAQ). Individual (models containing only one emotion dysregulation measure) and Full (models containing all four emotion dysregulation measures) Emotion Dysregulation Profiles were utilized to evaluate the associations between ISP and the general (individual) and pure (full) emotion dysregulation scores. 182 of the participants were selected to wear helmets instrumented with Head Impact Telemetry (HIT) System sensors for all games and practices. The HIT System data were used to formulate ISPs that were categorized as normal, moderate,

or high. Linear regressions were conducted to examine the associations between the preseason emotion dysregulation measures and the competition ISPs. Additional linear regressions were conducted to examine the associations between the full season ISPs and the emotion dysregulation profile change-scores over one season. Seasons of sport participation, team, perceived stress (PSS4), general position (line, back, skill, special teams), and player group (offense, defense, and both) were used as covariates.

RESULTS: ISP was not associated with any of the emotion dysregulation preseason ($p \geq 0.055$) or post-preseason change-scores ($p \geq 0.092$). However, the moderate ISP group had significantly lower (better) depression change-scores compared to the normal group ($p=0.012$).

CONCLUSIONS: The emotion dysregulation scores were not significantly associated with the competition or full season ISPs. These findings indicate that the current protocol still requires further investigation before it could be utilized as an effective prediction method for at-risk athletes.

Keywords: depression, anxiety, impulsivity, aggression, sport-related concussion, head impact biomechanics

INTRODUCTION

Traumatic brain injury (TBI) is “an alteration in brain function, or other evidence of brain pathology, caused by an external force”.[2] Under this definition, an “alteration in brain function” necessitates the presence of at least one of the following: decreased or loss of consciousness (LOC), any memory loss (amnesia), neurological deficits, or an altered mental state. The literature describes TBI as a continuum spanning from mild to severe, with sport-related concussion (SRC) situated to the far left, below mild TBIs.

Unlike individuals who are affected by TBI, adults who sustain a SRC typically recover fully within 7-10 days without long-term physical or cognitive impairment.[3-5] Importantly, some adolescents have been shown to require a more lengthy recovery period than their older

counterparts (22+days),[6-8] but some SRCs result in lingering sequelae for several months to years. Recent literature suggests approximately 15% of these individuals go on to suffer from post-concussive syndrome (PCS).[9] The effects of PCS are not well defined, but the general areas most often affected include: visual, vestibular, sleep, fatigue, cognition (memory, executive control), and psychological disturbances (including depression, aggression, and anxiety).[10] Stress is another factor that has been associated with depression and anxiety.[11, 12] However, these associations have not been investigated with respect to head impact biomechanics or SRC.

Psychological disturbances (emotion dysregulation) have been noted as a potential consequence of SRC,[13-16] but current recommendations for SRC baseline, post-injury testing, and return to play decisions do not specify how to evaluate or treat emotional dysregulation.[17, 18] The 2012 Consensus Statement on Concussion in Sport did mention that mental health issues (e.g., depression) may be a consideration for return to play and that functional magnetic resonance may display pathophysiological alterations after SRC.[18] However, their recommendation was that the identification of emotion dysregulation be left up to the treating physician, who in the authors' clinical experience is often a physician in an emergency room, or acute care facility. These physicians do not know their patients well enough to determine if their patients are experiencing SRC-related emotion dysregulation. Even when athletes are seen by their personal physician, who is often a pediatrician for individuals who are ≤18, they are only treated for cognitive and balance deficits. Additionally, functional magnetic resonance scans are considered an elective diagnostic tool and would typically not be covered by insurance. These images are extremely costly and generally only available in select areas. Importantly, the National Collegiate Athletic Association has put forth a position statement recommending the recognition and referral of student-athletes with psychological concerns, but it does not pertain specifically to athletes who have sustained a SRC.[19]

Furthermore, athletes may sustain thousands of recurrent head impacts[20, 21] and more

than one SRC [4, 6, 22] throughout the course of their athletic career. Recurrent head trauma refers to 1) multiple diagnosed SRCs or 2) repetitive, subconcussive impacts. Fortunately, the greater majority of impacts do not result in concussions.[20] Football players have been shown to sustain more than 1000 subconcussive head impacts in one season[4] and report multiple SRCs throughout the duration of their athletic career.[22-24] Athletes who sustain multiple subconcussive and concussive head impacts may experience increased likelihood of developing depression,[22] and mild cognitive impairment,[23] earlier onset of Alzheimer's Disease,[23] or may develop chronic traumatic encephalopathy (CTE) later in life.[25] The accumulation of subconcussive impacts and multiple SRCs over the course of an athletic career may increase the overall severity (e.g., increased emotional dysregulation, cognitive decline) of these head injuries and shift SRCs to the right on the TBI continuum (**Figure 4.2.1**). This lateral shift may help explain why later in life some athletes have displayed cognitive deficits and emotional dysregulation similar to those described in the TBI literature.[22-24]

Studies involving head impact biomechanics at the high school and collegiate levels have provided several important observations. First, impacts occur more frequently and at higher linear and rotational accelerations in games than in practices.[20, 26, 27] Secondly, these impact frequencies and magnitudes have been correlated with player positions.[20, 26-28] Thirdly, impact biomechanics are not correlated with any of the current clinical measures for concussion[20, 28] and therefore cannot be used as a diagnostic tool, or to predict concussion outcomes. It is important to note that while studies have compared impact biomechanics measurements to symptom,[20, 28] cognition,[20, 28] and balance[20] change-scores (postinjury-preseason), they have left out an important piece of the puzzle, emotion dysregulation. Although several position statements recognize that emotion dysregulation is a concern for athletes with and without SRC, scientific studies investigating the associations between head impact biomechanics, SRC, and emotion dysregulation are lacking. To fully understand the relationships among head impact biomechanics, SRCs, and short- and long-term emotion

dysregulation alterations and to ensure optimal short and long term outcomes, expanding research methodologies to include emotion dysregulation may be warranted (**Figure 4.2.1**).

This study was a first step in evaluating the associations that exist between SRC incidence, head impact severity, and emotion dysregulation measures in high school athletes (**Figure 4.2.2**). The objective of this longitudinal study was two-fold. Our first objective was to assess the association between preseason baseline emotion dysregulation scores, competition ISPs, and incident concussion in high school football players wearing instrumented helmets. Our hypothesis for objective 1 was that instrumented football players with a worse (higher) emotion dysregulation score at preseason would be associated with a poor (worse) competition ISP (top of head impacts and/or more severe impacts) and/or an increased likelihood of sustaining an incident SRC over the course of one season. Our second objective was to determine the association between incident SRC, ISPs, and emotion dysregulation change-scores (postseason-preseason) in high school football players wearing instrumented helmets over one season. Our hypothesis for objective 2 was that instrumented football players with an incident SRC and/or a poor (worse) *ISP* during the season would be associated with worse (higher) emotion dysregulation scores at postseason, relative to the pre-season emotion dysregulation scores in the same individuals. Team, seasons of sport participation, perceived stress (PSS4), general position (line, back, skill, special teams), and player group (offense, defense, and both) were used as covariates for our analyses.

METHODS

Participants

All active football players (n=334) from three high schools during the 2013/14 to 2015/16 academic years were invited to participate in our study. Participating football players and their parents/guardians gave written assent/consent prior to their enrollment in the study (n=275, 82.3%). Exclusion criteria included: females, those who were not fluent in English, individuals

with visual impairments that could not be rectified with corrective lenses, participants who were not on the active roster at the start of the season due to injury, individuals with an unresolved SRC at the start of their season, and history or psychoses beyond anxiety, or depression.

Concussion History and Emotion Dysregulation Questionnaires

The purpose of the concussion history and emotion dysregulation measures was to assess changes in negative affect and personality traits related to SRC history and incidence, and head impact severity. All enrolled participants were asked to complete a preseason and postseason Concussion History and Emotion Dysregulation Questionnaire lasting approximately 15 minutes each. The questionnaires were completed via Qualtrics.com. The participants were asked to complete the preseason Concussion History and Emotion Dysregulation Questionnaire at the start of their football season and the postseason Concussion History and Emotion Dysregulation Questionnaire within four weeks of their season ending (mean =10.48 ± 9.27 days). Up to four follow-up email reminders were sent to participants to encourage them to complete either of the respective questionnaires.

Concussion was defined as a complex pathophysiological process affecting the brain, induced by biomechanical forces.[18] *Sport-related concussion (SRC)* was defined as any concussion that occurs during sports participation that was diagnosed by a medical provider. Only *Incident concussion*s that occurred during the season and were confirmed by a certified athletic trainer and/or physician were included in our analyses. Incident concussion was analyzed as a continuous variable because two players during the 2015/16 academic year sustained two SRCs in one season. This allowed us to determine if the preseason emotion dysregulation scores were able to predict the number of incident concussions sustained in one season and to determine if the number of incident concussions was associated with emotion dysregulation change-scores (postseason-preseason). Incident concussion was also analyzed as a binary variable, which allowed us to investigate the association of any incident SRC with

the preseason and postseason-preseason emotion dysregulation change-scores.

Depression. The Patient Health Questionnaire (PHQ-9)[29] is a highly utilized and validated diagnostic depression measure.[29] This measure has good agreement with mental health professional depression diagnoses (sensitivity = 75% and specificity = 90%) and as compared to the Primary Care Evaluation of Mental Disorders for 1 or more PHQ diagnoses. The PHQ-9 is a 4-point Likert scale containing 9 items with answers ranging from "not difficult at all" to extremely difficult". The questions reflect the individual's feelings over the past 2 weeks (range 0-27). The PHQ-9 can be used as a possible predictive tool for major depressive disorder (MDD). Cut point scores at 5, 10, 15, and 20 can also be used to represent mild, moderate, moderately severe, and severe depression. MDD should be considered if a patient endorses 5 or more of the 9 symptoms as present "more than half the days" and if one of the first 2 symptoms (depressed mood or loss of interest) of the last symptom (suicidality) are endorsed Referral for further evaluation should be considered in the presence of elevated scores (≥10).

*Anxiety***.** The Generalized Anxiety Disorder 7-item scale (GAD-7) is one of the most utilized anxiety measures.[30] This measure has been validated in multiple populations in its ability identify various anxiety disorders.[31] The GAD-7 assesses a person's anxiety levels over the past 2 weeks using 7 validated and highly correlated items.[30] Answers range from "not at all" to "nearly every day" on a 4-point Likert scale (0-3). Higher scores indicate greater anxiety (range 0-21). The accepted cut point for identifying GAD is 10, with additional cut points at 0-4 (minimal), 5-9 (mild), 10-14 (moderate), and 15-21 (severe). Referral for further evaluation should be considered for scores ≥10.

Impulsivity. The Barrett Impulsiveness Scale (BIS-11) is a common impulsivity assessment.[32] It is highly utilized and validated across a wide range of individuals.[33] TBI-related impulsivity has been investigated for over three decades.[34] The BIS-11 is a 30 item 4-point Likert scale ranging from "Rarely/Never" to "Almost Always/Always" (range: 30-120).[35] It is

important to note that items 1, 7, 8, 9, 10, 12, 13, 15, 20, 29, 30 are reverse scored.

The meaning of several questions contained in this measure may not transfer well to high school student-athletes. The researchers were frequently asked to provide additional information about questions so the participants could accurately provide answers. “I save regularly” was one question that most often required further explanation. When the participants were told to add “money” into the statement, it improved their understanding and allowed all participants to answer the question. Overall, 5 questions were modified (7, 10, 13, 16, and 21) to improve understanding, accessibility, and consistency. The modified version was pilot tested by two age appropriate individuals, who confirmed that the modifications increased their ability to comprehend the statements.

Aggression. The Buss-Perry Aggression Questionnaire (BPAQ) has been validated across a multitude of populations as a measure of aggressiveness.[36] It is a 29 item assessment (range 29-145), graded on a 5-point Likert scale (1-5) ranging from “extremely uncharacteristic” to “extremely characteristic”.[36] This measure contains 4 subscales, physical aggression (9 items), verbal aggression (5 items), anger (7 items), and hostility (8 items). Aggression is not recognized as a disorder by the DSM-IV or V. The BPAQ is not utilized as a diagnostic tool, nor have any cutoff values been identified to suggest possible clinical concern.

Stress. Stress has been associated with depression and anxiety, thus it was prudent to include a measure of stress as a covariate for the emotion dysregulation measures. The Perceived Stress Scale 4-item (PSS4) is a valid and highly utilized 4-item measure of one’s perception of stressful events occurring in the last month.[37] Scoring for the PSS4 (range 0-16) includes positive scoring for items 2 and 3 and reverse scoring of items 1 and 4 on a 5-point-Likert scale (0 = never to 4 = very often). Higher scores indicate higher levels of perceived stress. The PSS4 is a measure of generalized stress, which seemed most appropriate for this study since we were attempting to control for a variety of stresses that may have affected our

participants. This measure was only used as a covariate for our analyses, not an outcome variable of interest.

A score of ≥10 on the PHQ-9 (MDD) and GAD-7 (panic, social anxiety, PTSD, and GAD) may be used as clinical indicators for several psychological disorders.[38] The researchers worked closely with a neuropsychologist and the University and secondary school district IRB departments to formulate the notification letter sent to the parents. For the purposes of this study, emails were sent to the respective parents/guardians (high school participants) and the school AT(s) for all PHQ-9 (n=10) and GAD-7 (n=6) scores ≥10 during the 2015/16 academic year (preseason n=12, postseason n=4). These individuals were reminded that the emotion dysregulation measures are not diagnostic tools and should only be used as an indication for further diagnostic testing by a neuropsychologist. Two football players reported a score of ≥10 on both measures at preseason and one football player reported a depression (PHQ-9) score ≥10 at preseason and postseason).

Missing values occurred for some questionnaire items. To minimize the potential impact of attrition over time and/or loss of scores due to a limited number of missing values for a measure, missing values were replaced using a standardized approach. If a participant failed to answer at least 75% of the items for a particular measure their total score for that measure was not calculated. For instance, the PHQ-9 has 9 items, thus participants had to complete at least seven items for their PHQ-9 score to be included in our analyses. If a participant only completed eight of the nine PHQ-9 items we used the algorithm below to calculate the value for the missing item resulting in an adjusted score.

The BPAQ is a summation of its 4 subscales (physical aggression, verbal aggression, anger, hostility), which were each calculated individually. If one of the subscales was considered missing (less than 75% of the items had been completed), the BPAQ Total score was also missing because the total score requires completion of all four subscales. All emotion dysregulation measures were summed per their respective method. The adjusted score for each

measure that had less than 100% but ≥75% of its respective items completed was then calculated as follows:

$$\text{Adjusted Score} = \frac{\text{Total score x Total number of items}}{\text{\# of items completed}}$$

Emotion Dysregulation Data Reduction

The four preseason emotion dysregulation measures of interest (PHQ-9, GAD-7, BIS-11, and BPAQ) and the PSS4 (covariate) were analyzed as continuous variables for our first objective. The preseason emotion dysregulation scores were evaluated independently to determine the associations between each emotion dysregulation score (*individual)* and the competition ISPs. These analyses allowed us to determine the association between the general emotion dysregulation for each measure and the competition ISPs. Additional analyses were performed that included all four emotion dysregulation measures in the same model (*full model*). The purpose of the full model was to determine if an association existed between each of the purified emotion dysregulation measures and the competition ISPs. A higher score for each emotion dysregulation measure indicated a worse emotion dysregulation profile and a lower score indicated a healthier emotion dysregulation profile.

The emotion dysregulation change-scores (postseason-preseason) were formed by subtracting the participant's preseason score from their postseason score for each measure (PHQ-9, GAD-7, BIS-11, BPAQ, and PSS4). The change-scores were then analyzed as a continuous variable. Similar to the preseason emotion dysregulation scores, the change-scores were evaluated independently (individual) to determine the associations between the change-scores for each emotion dysregulation measure and the full season ISPs. These analyses allowed us to determine the association between the general emotion dysregulation measure change-scores and the full season ISPs.

Impact Severity Profiles

The helmets of 182 players were instrumented with Head Impact Telemetry (HIT) System accelerometers (Riddell, Elyria, OH) at the start of the season. The instrumentation procedures and data collection have been previously described.[20] If a football player was chosen for the impact severity portion of this study, his helmet was instrumented with HIT System accelerometers for the duration of his time playing football at his respective school, unless he asked for the accelerometer to be removed, he withdrew from the study, or sustained a season ending injury.

Previous studies have found associations between HIT System outcome variables and player positions.[39-41] To control for this association the players were grouped into *player group* and *general position*. The head football coaches, athletic trainers, and the on-site research coordinators collectively determined the following groupings. Player group was divided into three categories: offense, defense, and both. It is not uncommon for high school football players to play nearly equal time/number of plays on both offense and defense during practices and games. The percentage of time spent playing these positions is often dependent on the skill of the opposing team and thus typically changes week-to-week over one season. If a participant spent at least 30% of their overall time in both offensive and defensive plays during games and practice drills they were assigned to “both”, otherwise they were assigned to either “offense” or “defense”. As expected several players qualified for “both” with offensive-defensive line, defensive back/safety-wide receiver, and linebacker-running back being the most commonly shared positions. These players were randomly assigned to one of their specified positions (e.g., offensive or defensive line) to avoid placing all players in the same primary position category. General position was determined by the participant’s primary playing position and was divided into four categories: line (offensive and defensive linemen, tight ends), backs (quarterbacks, running backs, full backs, and linebackers), skill (wide receivers, defensive backs, safety), and special teams (kickers, punters, and players who only played special

teams). Player group and general position were both used as covariates. None of the positional variables were included as outcome variables.

Head impact biomechanics studies have suggested that head impact frequency, impact location, and linear acceleration are associated with incident SRC.[20, 42-44] As a result these measures were chosen to form the Impact Severity Profiles (ISP). This study was in concert with a study investigating the effects of an on- and off-field behavior modification intervention (BEMOD) on head impact severity measures. The predetermined cut points for intervention enrollment were 1) greater than 20% of impacts to the top of the head, 2) greater than 7% of impacts $\geq$ 60 g, and 3) a player sustained an incident concussion during football participation. 60 g was chosen as the cut point for high magnitude impacts since most concussions occur at or above 60 g at all levels of football. For simplicity, the same top of head and impact severity cut points were utilized for our ISPs. Each player's total number of top of head impacts and impacts $\geq$ 60 g were summed. We then divided the total number of top of head impacts and impacts $\geq$ 60 g by the total impact frequency and multiplied by 100. Players were assigned a "1" if they met the BEMOD criteria for either top of head or impacts $\geq$ 60 g. Their scores were then added together to form 3 ISP groups (normal, moderate, poor). Players who scored a 2 formed the poor group. The moderate group was comprised of players who scored a 1, and the normal group scored a 0.

The data from all competition impacts in one season were used to formulate the competition ISPs for our first objective. We limited our data to only competitions for objective 1 because we felt that the players were more likely to demonstrate their normal hitting techniques during a game vs. a practice since many of the practices did not involve hitting or full-speed hitting. The full season ISPs (objective 2) are reflective of all impacts recorded over one full football season. We included all impacts that occurred over one season in the objective 2 analyses because we believed that all impacts were important in determining emotion dysregulation change-scores (postseason-preseason).

The following variables were used as covariates or to determine the most appropriate covariates for our analyses due to their associations with the emotion dysregulation scores and competition and full season ISPs. Current *age* was collected via the preseason questionnaire and postseason questionnaires. Of the individuals included in our analyses, only one 13-year-old and six 18-year-old participants completed the preseason questionnaire. Seven 18-year-old participants and one 19-year-old completed the postseason questionnaire. To improve the power and generalizability of our findings we merged the 13-year-old participant with the 14-year-olds and the 18 and 19-year-old participants with the 17-year-olds. Age was analyzed as a continuous variable.

To determine *seasons of sport participation for our first objective,* at preseason the participants were asked to sum all years of organized participation for their respective sport. This count included organized youth teams and partial seasons that ended early due to injury, illness, etc., excluding the current season. At postseason the participants were asked to include the season that they had just completed in their count. Seasons of sport participation was analyzed as a continuous variable.

Team was confirmed through 3 mechanisms 1) a team identifier was part of each participant's study ID, 2) participants identified their respective team on all questionnaires, 3) each team had a unique HIT System ID that was included in the head impact severity output. Age (15.83 ± 1.10 yrs) and seasons of sport participation (5.92 ± 3.12 yrs) were moderately correlated ($r = 0.36$, $n=155$, $p<0.0001$) at preseason and postseason ($r = 0.41$, $n=105$, $p<0.0001$). Team was associated with age ($p=0.001$, $p=0.002$), but not seasons of sport participation ($p=0.025$, $p=0.022$) at preseason or postseason, respectively. To correct for team and seasons of sport participation variations both variables were included as covariates for all analyses.

Data Analysis

It is important for us to note that some players participated in more than one season. Each season of participation was analyzed as a separate exposure. We chose to do this because some players changed primary and/or secondary positions yearly, which also affected their general position and player group. In addition, this age group can experience significant cognitive, behavioral, and physical changes from year to year.

The linear magnitude HIT System data was transformed using a natural logarithmic function to meet the assumptions of normality for the subsequent analyses. These data were then analyzed as continuous and categorical variables. The categorical groupings were as follows (0-24.99 g = low, 25-59.99 g = moderate, ≥60 g = high). The categorical groupings were used to determine how many impacts were ≥60 g, which was important for assigning ISP group membership.

For our first objective, linear regressions were used to determine if the preseason emotion dysregulation scores could predict the ISPs for competition impacts. Linear regressions were used again for our second objective to determine if the full season ISPs were able to predict the individual emotion dysregulation change-scores. Seasons of sport participation, team, stress (PSS4), general position, and player group were used as covariates for our analyses. To account for possible Type II error due to the number of impacts included in our study and the number of analyses p=0.01 was used to determine statistical significance. All analyses were performed in SAS (version 9.4; SAS Institute Inc. Cary, NC).

RESULTS

Two hundred and seventy-five football players attending three different high schools (5 team-seasons) were enrolled in our study during the 2013/14 to 2015/16 academic years. One hundred and eighty-two (66.2%) of those players wore helmets instrumented with HIT System sensors. Thirty-eight (20.9%) of the 182 participants did not finish the season with instrumented helmets for various reasons. Importantly, only 8% of the sensor attrition was due to discomfort.

The other 35-instrumented participants who did not finish the season were primarily due to injuries/illnesses (n=31, 81.6%). Our overall attrition due to injury/illness is similar to previous studies.[44] One hundred and fifty five (85.2%) of the instrumented participants completed the preseason questionnaire. One hundred and five of the 155 (67.7%) who completed the preseason questionnaire also completed the postseason questionnaire. Across all four outcome measures (depression, anxiety, impulsivity, aggression) and the stress covariate (PSS4) we adjusted 12 (1.8%) preseason (impulsivity n=7, aggression n=5) and 16 (2.7%) postseason scores (impulsivity n=7, aggression n=9).

The means and standard deviations for the preseason emotion dysregulation scores by ISP group can be found in **Table 4.2.1.** Of the 155 players with instrumented helmets who also completed the preseason questionnaire, 26 (16.77%) sustained an incident SRC during their season. The means and standard deviations for the head impact severity variables and incident SRCs for objective 1 (actual scores) can be found on **Tables 4.2.2.** ISP was not associated with incident SRC (p=0.408). None of the preseason individual ($p \geq 0.080$) (**Table 4.2.3**) or full ($p \geq 0.055$) **(Table 4.2.4**) emotion dysregulation models were able to predict competition ISP.

The means and standard deviations for the full season emotion dysregulation change-scores by ISP group can be found in **Table 4.2.5**. Two participants included in the full season (1.90%) analyses sustained 2 incident SRCs. The means and standard deviations for the full season head impact severity variables and incident SRCs can be found on **Table 4.2.6**. Over the course of one full season, two participants (1.90%) did not sustain any top of head impacts and three participants (2.86%) did not sustain any impacts ≥ 60 g. Of the 105 players include in the full season analyses, 20 (19.05%) sustained an incident SRC. Two of these participants (10%) sustained 2 incident SRCs. Full season ISP was not significantly associated with incident SRC (p=0.517).

ISP (p=0.140) was not a significant predictor for full season depression change-scores (**Table 4.2.5**). However, the moderate ISP group trended toward significantly lower full season

depression change-scores compared to the normal ISP group when controlling only for team and seasons of sport participation (p=0.022), and when adding stress (p=0.029), general position (p=0.022), and player group (p=0.024) as separate covariates to the model. None of the other full season emotion dysregulation change-scores were significantly associated with ISP ($p \geq 0.032$), or the individual ISP group differences ($p \geq 0.047$) (**Table 4.2.5**). None of the ISP models were able to predict any of the individual emotion dysregulation change-scores ($p \geq 0.020$) (**Table 4.2.7**).

DISCUSSION

The most important finding of the current study was that overall there was no association between the emotion dysregulation scores (preseason and change-scores) and the ISPs. While the depression scores did not change over one season, the anxiety and impulsivity mean scores increased over one season for all players. Anxiety was an especially surprising finding since previous research has shown physical exercise decreases anxiety and depression.[46, 47] However, exercise for quality of life compared to playing competitive football is arguably two very different types of exercise. The specific effects of football participation on any emotion dysregulation measure over one season had not been investigated prior to this study. It is possible that participation in football does increase anxiety. It is also possible that some of the players' scores were elevated at the end of the season because their football careers were ending (seniors), they were preparing for finals, or moving on to another sport and were anxious because they had missed the preseason workouts for the subsequent sport. An important consideration is that most of the exercise studies included an exercise and control group. It may be that anxiety increased over one season in our study, but the increase may have been small compared to a non-athletic sample. This should be investigated further.

Additionally, impulsivity has not been a focus in SRC studies to date, so our impulsivity findings are novel and support TBI studies showing impulsivity increases after head-injuries.[48-

[50] It should be noted that the mean change-scores for the normal and moderate ISP groups were not clinically meaningful. The poor group change-score (mean = 8.0) may have been clinically meaningful however. This is an area that needs further investigation to determine exactly what change-score is necessary to be clinically meaningful. Nineteen percent (n=20) of the athletes included in the objective 2 analyses sustained an incident SRC over one season (n=2 sustained 2 SRC over one season). Post-hoc analyses determined that participants who sustained an incident concussion did not have significantly different change-scores compared to those who did not sustain an incident SRC over one season (p=0.053). It is possible that by all participants experiencing multiple subconcussive impacts (range 10-1874) they may have experienced physiological and neuronal brain changes that manifested in increased anxiety and impulsivity. Since generalized anxiety has a tendency to decrease from childhood to early adulthood[51] and impulsivity remains constant,[52, 53] or decreases,[35] it is not likely that these changes were maturational in nature.

Finally, aggression scores decreased over one season. Again, the aggression change-scores were surprising based on our 2013-2014 pilot data, which showed a significant increase in aggression over one season. Studies also support an increase in aggression after TBI.[48] Our 2013-2014 findings may have captured elevated postseason aggression scores compared to other high school football teams and/or seasons of football. It is also possible that enrollment in the BEMOD study altered the players' aggression over the course of one season by exposing them to safer heads up playing techniques. Future studies should investigate the relationships between emotion dysregulation, athletes vs. non-athlete controls, incident SRC, and football environments.

The means for all four emotion dysregulation measures were on the low end of the normative ranges with relatively small standard deviations (**Tables 4.2.1 and 4.2.5**). Very few of our football participant's self-reported scores were $\geq$10 for depression (n=10) or anxiety (n=6), the standard cut points for referral on these measures. Richardson et al. reported 12% of their

sample screened positive for depression-like symptoms (≥10).[54] This may have been due to their inclusion of females (60%). Females from the age of 13 are at a greater risk for reporting higher depression compared to males until mid-late adulthood (55-65 years).[55]

The ranges for the impulsivity and aggression scores were fairly large, but as for depression and anxiety, the means for these measures were within expected values (impulsivity= 64.2±10.7,[35] aggression = 73.1±16.6[56]). It is interesting that the preseason impulsivity (62.09±7.60) and aggression (63.40±17.02) mean scores were lower than the normative mean values. The baseline scores were collected at the end of the summer (beginning of preseason workouts), which may have lowered their preseason emotion dysregulation scores. Additionally, the 2014/15 team and two of the three teams enrolled during the 2015/16 season had highly successful seasons, which could have also lowered their postseason scores. This is an important consideration that should be investigated in future research. The lower impulsivity and aggression scores could also be a result of sampling bias due to the three enrolled schools being different from the general population, or a result of regional attitudes/behaviors that differ from the general population. Future studies should investigate if these findings are a result of the (seasonal) timing of the data collection, a sampling bias in our study, or if high school male football players have slightly lower mean scores compared to the age-matched controls from a non-athletic population.

The number of incident concussions in our study (26/155 and 20/105) was higher than previous reported percentages for high school football teams.[6] This may be due to several football-related environmental factors including age, seasons of sport participation, and level of play (JV vs. Varsity). During the 2015/16 academic year 2 players sustained 2 incident concussions in the same season. Past studies have shown that once a player sustains one concussion in a season they are at a greater risk to experience more in the same season.[57] It is important to acknowledge that this study was conducted in unison with another study (BEMOD) that implemented an on- and off-field behavior modification program for all participants who met

predetermined enrollment criteria. Nine players were enrolled in the intervention during the 2015/16 academic year. The research team did not attempt to conceal which players were enrolled in the behavior modification intervention from the coaches or the unselected participants. Concealment would have been difficult to accomplish since the coaches were instructed to devise specific head up practice drills for the enrolled players to improve their collision technique. The researchers observed the coaches providing additional reinforcement of head up techniques with the enrolled athletes during practices. Importantly, the coaches included unselected participants in the new practice drills to improve safe collision habits. Future studies should attempt to enroll teams who are either not involved in behavior modification programs, or investigate the differences between those in a behavior modification program and those who are not.

Incident concussion was not predictive of ISP (p=0.517). Several previous studies have found that higher magnitude impacts and top of head impacts result in a greater number of incident SRC.[26, 43] ISP integrates these two factors that are believed to elevate concussion risk, with opposite findings. This difference could be because our sample is significantly different from the other teams utilized in similar studies. Another possibility is that most/all of the other studies only report these measures independently and not as a unified variable. What is particularly interesting is that the two athletes who sustained 2 incident SRCs during one season were categorized in the normal ISP group (**Table 4.2.2**). This finding was extremely surprising and further supports that incident SRC may not be related to a player's impact biomechanics. Unfortunately, football players do sustain unanticipated impacts during play. Unanticipated impacts have been found to result in a higher impact magnitude,[58, 59] but the association between impact anticipation and SRC incidence is lacking in football.

Preseason Emotion Dysregulation and Competition ISPs

The hypothesis for objective 1 was that worse emotion dysregulation measures would be associated with worse competition ISPs. This hypothesis was not supported. The finding was unexpected that no associations emerged between the preseason emotion dysregulation scores and competition ISP with or without additional covariates indicating that general stress, general position, and player group do not have an effect on these relationships (**Tables 4.2.3 and 4.2.4**). The timing of the preseason data collection, environmental team-related differences, and the teams' simultaneous involvement in the BEMOD study may have been large factors in our non-significant findings between preseason emotion dysregulation measures and competition ISP. Pre-morbid impulsivity and aggression have been associated with TBI incidence.[48] SRC research investigating the role of premorbid emotion dysregulation in post-injury behavioral changes is lacking. This study attempted to address this dearth of information and found no association with competition ISP.

Emotion Dysregulation Change-Scores (Postseason-Preseason) and Full Season ISPs

The hypothesis for objective 2 was that worse full season ISPs would be associated with higher (worse) emotion dysregulation change-scores (postseason-preseason). This hypothesis also received no empirical support. A plethora of TBI studies have reported an association with increased levels of depression, anxiety, impulsivity, and aggression post-injury.[48, 60, 61] SRC studies have only evaluated depression and anxiety post-injury.[14, 15, 62] Of interest, the TBI studies have shown that pre-morbid emotion dysregulation is strongly associated with post-injury exacerbation and prolonged recovery. It may be that we did not find significant differences between the full season ISP groups because very few athletes experience prolonged recovery. This could be explained by SRC and TBI studies that indicate individuals with greater social support, lower self-reported depression symptoms, who are younger, and are male, are less likely to develop PCS.[62-65] All participants were 18 years or younger and male with a mean

baseline depression score of 1.92 ± 2.34, which is below the national average. All three schools had full-time athletic trainers who provided physical and social support and care for the injured participants from the time they reported their injury until they were cleared for participation.

The fact that the moderate group was associated with significantly lower (improved) depression change-scores compared to the normal group for full season ISP (p=0.012) may be explained by **Table 4.2.6**. The normal full season ISP group had the lowest means for all four of the head impact severity variables compared to the other two full season ISP groups. This suggests that the players in the normal group were either 1) more skilled players who did not make contact with their head as often as the moderate and poor groups, or 2) they were less skilled players who did not see the field as often and thus sustained fewer impacts throughout all the head impact b severity variables. Additional seasons of sport participation typically reflect an athlete's increased knowledge and ability in a sport. Since seasons of sport participation was not significantly associated with full season ISP, but it was positively associated with all of the head impact severity variables, option #2 is more likely.

General Comments

While our emotion dysregulation ranges were somewhat large (due to outliers), the means and standard deviations were fairly small. The outliers were not excluded from the analyses because doing so would have decreased the generalizability of our findings. It is possible that statistical significance was affected by the overall homogeneity of our sample. The sample selected for this study has been raised in an environment that is highly aware of SRC protocols, symptoms, and safe impact techniques due to their proximity to our University. Many of the players had taken baseline neurocognitive and balance tests and had concussion policies in place with their youth programs before most states mandated these procedures for school-affiliated programs. Recruitment of a larger sample from a more diverse cultural, socioeconomic, and environmental background may not only improve the generalizability of

these findings, but also may result in a wider array of emotion dysregulation scores at preseason and postseason.

It is important to acknowledge that the emotion dysregulation measures chosen for this study may not be the best measures for athletic populations since they are written to address general emotion dysregulation issues. Utilization of measures that are more specific to sport may be more appropriate and/or associated with the head impact severity measures. However, the carry-over of sport into general activities of daily living is an important consideration to continue investigating due to some of the quality of life issues associated with repeated SRCs.[14, 24, 66] This study contained a cross-sectional component (preseason emotion dysregulation scores) and a brief (5 month) longitudinal component. A longitudinal study following athletes over multiple seasons of sport participation may be of greater benefit for devising the best ISPs and also selecting the most appropriate emotion dysregulation measures.

As mentioned above, individuals who sustain TBI commonly report elevated pre-injury emotion dysregulation scores. Utilization of raw postseason scores controlling for preseason scores may have been a superior method to investigate the effects of ISP on postseason emotion dysregulation. This method would allow researchers to determine if those with poor ISPs report higher (worse) postseason scores compared to the moderate and normal groups, which would be far more telling than change-scores. This methodology should be utilized in subsequent studies.

The coaching styles may have significantly affected our outcomes. While team-related differences were controlled for in our models, these statistical differences were fairly small from a clinical perspective. This was probably driven by two factors 1) preexisting coaching techniques and beliefs about contact in practice, and 2) involvement in a SRC study that was promoting heads-up tackling. If the coaches in our study have always taught their players to use a heads up technique and limit contact during practices, the BEMOD study would not have that

big of an effect on their players' collision technique. This was true for at least 1 team (3 team-seasons), and the other 2 teams moved toward this model throughout the 2015/16 season. While this coaching style may common for schools around our University, it may not be the most common coaching style for most/all high school football programs. It would be interesting to enroll a more diverse group of teams with dissimilar coaching, playing, and contact styles. It is possible that the involvement of a wider array of teams would again not only improve the generalizability of the findings, but also allow the researchers to investigate the associations of these football-related environmental factors.

Finally, the ISP algorithms may have grouped the head impact severity scores too much, making these scores also overly homogenous. It is also possible that the addition of rotational acceleration may have assisted in the predictability of ISP. While animal studies have shown associations between rotational magnitude and head impact severity/incident concussions,[67] human studies have not been as conclusive[26, 42, 43] with several reporting rotational acceleration may not be the best predictor of impact severity and incident SRC. As suggested previously, removing impact frequency as the denominator and instead adding it directly to the equation may be a more efficacious method, especially since impact frequency has been found to be a critical factor on days of SRC diagnosis. It is important to acknowledge that devising a specific ISP may in fact not be the best method. Recent SRC literature has investigated the association of SRC with each of the head impact severity measures in isolation. Future studies should investigate the relationship between emotion dysregulation and the individual head impact severity measures. Continued investigations into the utility of ISPs in predicting at risk-players for SRC are strongly encouraged.

Conclusions

While TBI research has produced a plethora of studies associating varying degrees of brain injury with emotion dysregulation, SRC studies investigating these associations are

lacking. SRC has been associated with elevated anxiety and depression following SRC, but again studies associating pre-morbid emotion dysregulation with SRC and post-injury emotion dysregulation are lacking. Head impact biomechanical research has shown associations with head impact frequency, impact location, and impact magnitude with incident SRC. However, a Head Impact Severity Profile to help clinicians predict at-risk athletes has been elusive.

If future research were to reveal an association of SRC, sport exposure, head impact severity, and emotion dysregulation measures this could inform clinicians about the utility of early, cost-effective annual athlete evaluations with additional interventions to assess changes after each season and/or SRC. Researchers and clinicians could then prospectively track the incidence and potential increases in emotion dysregulation, resulting in treatment for individuals at symptom onset rather than delaying care until after significant life alterations have already occurred. The end goal is to delay or prevent the progression of symptoms associated with significant neurodegenerative diseases through early detection and interventions (behavior modification, counseling, etc.). However, until more investigations can be conducted to improve understanding of these relationships and the additional covariates mentioned above (e.g., pre-morbid emotion dysregulation status, football-related environmental factors, player position, etc.), emotion dysregulation measures should remain as research tools. Our hope is that this study will spur on other researchers to join in our investigation of these associations not only with football, but also with other contact sports.

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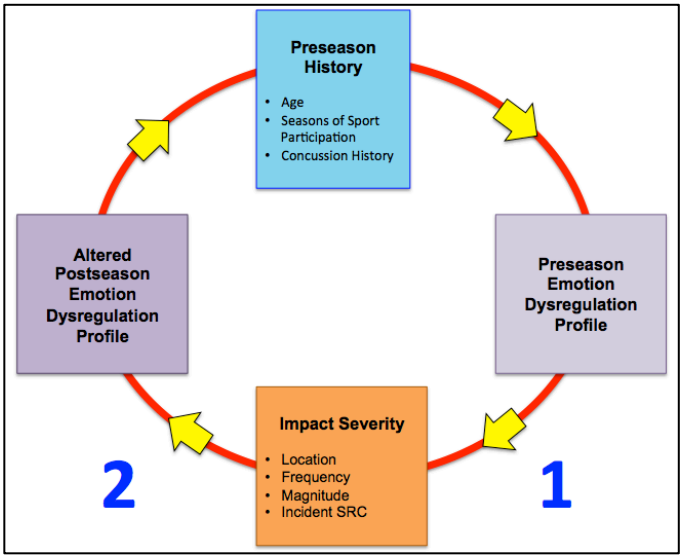
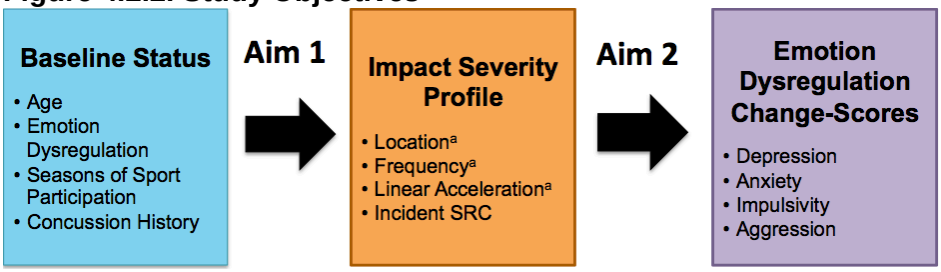
Figure 4.2.1. Theoretical Model: The Cyclical Relationship Between Emotion Dysregulation Profiles and Impact Severity Profiles Over Sequential Seasons



The numbers represent the associations (objectives) that were investigated by this study.

Figure 4.2.2. Study Objectives



Objective **1:** To determine the association between a worse Emotion Dysregulation Profile at pre-season, Impact Severity Profiles (ISP), and SRC incidence in football players wearing instrumented helmets
Objective **2:** To determine the association between incident SRC, ISPs, and emotion dysregulation measure change-scores in high school football players wearing instrumented helmets
[a] Measures comprising the Impact Severity Profiles (ISP)

Table 4.2.1. Preseason Emotion Dysregulation Scores for Instrumented Football Players: Competitions Only

		Depression (PHQ9)		Anxiety (GAD-7)		Impulsivity (BIS-11)		Aggression (BPAQ)		Stress (PSS4)	
		X ± SD (n)	Range	X ± SD (n)	Range	X ± SD (n)	Range	X ± SD (n)	Range	X ± SD (n)	Range
ISP	Normal	1.79 ± 2.39 (86)	0-12	1.64 ± 2.36 (86)	0-11	62.69 ± 7.93 (101)	40-86	64.62 ± 17.43 (100)	36-114	6.53 ± 2.68 (67)	0-11
	Moderate	2.19 ± 2.16 (37)	0-8	1.56 ± 2.15 (37)	0-10	61.84 ± 5.97 (44)	49-77	61.19 ± 15.84 (43)	37-110	6.71 ± 2.53 (21)	0-10
	Poor	2.00 ± 2.83 (9)	0-8	3.00 ± 5.41 (9)	0-15	56.53 ± 9.36 (9)	45-71	60.33 ± 18.28 (9)	37-89	4.50 ± 6.36 (2)	0-9
All Players		1.92 ± 2.34 (132)	0-12	1.71 ± 2.61 (132)	0-15	62.09 ± 7.60 (154)	40-86	63.40 ± 17.02 (152)	36-114	6.53 ± 2.71 (90)	0-11

Impact Severity Profile (ISP)

Table 4.2.2 Cumulative Competition Impact Severity Variables for Instrumented Football Players

	N (%)	Total Impacts^#&		Top of Head Impacts^#&		# of Impacts ≥ 60 g^#&		Incident SRC	
		X ± SD	Range	X ± SD	Range	X ± SD	Range	X ± SD (n)	Range
ISP	Normal (101)	184.12 ± 194.56	2-955	18.91 ± 21.69	0-109	7.61 ± 10.48	0-60	0.19 ± 0.44	0-2
	Moderate (45)	287.27 ± 241.57	11-805	42.31 ± 39.08	2-137	28.58 ± 30.21	0-138	0.13 ± 0.34	0-1
	Poor (9)	86.00 ± 169.22	3-522	22.44 ± 37.46	2-109	7.11 ± 12.15	1-37	0.33 ± 0.50	0-1
All players	155	208.37 ± 214.43	2-955	25.91 ± 30.43	0-137	13.67 ± 20.77	0-138	0.18 ± 0.42	0-2

Team was significant.
^Age was significant.
Seasons of sport participation was significant.
& Impact Severity Profile (ISP) was significant.
Significant at p=0.01.

Table 4.2.3. Prediction of Competition Impact Severity Profiles (ISP) Using Individual Preseason Emotion Dysregulation Measure Models Controlling for Team and Seasons of Sport Participation: B (95% CI) p-value

	Model	Depression (PHQ-9) (n=132)	Anxiety (GAD-7) (n=132)	Impulsivity (BIS-11) (n=154)	Aggression (BPAQ) (n=152)
ISP	A	0.0154 (-0.0304,0.0611) 0.508	0.0166 (-0.0252,0.0584) 0.433	-0.0114 (-0.0239,0.0012) 0.075	-0.0037 (-0.0094,0.0020) 0.198
	B^	0.0106 (-0.0334,0.0546) 0.633	-0.0010 (-0.0488,0.468) 0.697	-0.0186 (-0.0158,0.0121) 0.792	-0.0001 (-0.0056,0.0064) 0.972
	C	0.0142 (-0.0319,0.0604) 0.542	0.0159 (-0.0262,0.0580) 0.457	-0.0114 (-0.0241,0.0014) 0.080	-0.0036 (-0.0094,0.0021) 0.215
	D	0.0162 (-0.0296,0.0620) 0.586	0.0165 (-0.0257,0.0587) 0.440	-0.0103 (-0.0229,0.0024) 0.111	-0.0035 (-0.0092,0.0022) 0.220

Models: Four separate prediction models were conducted for competition ISPs with the four individuals emotion dysregulation measures (depression, anxiety, impulsivity, aggression) All models include one emotion dysregulation measure,ISP, team, and seasons of sport participation, with the following additional covariates:
A) None (df =4),
B) Perceived stress (PSS4) (df =5),
C) General position (line, back, skill [reference], special teams) (df = 7),
D) Player group (offense [reference], defense, both) (df =6).
^ Depression, anxiety, impulsivity n=90, and aggression n=88.
Significant at p=0.01.

Table 4.2.4. Prediction of Competition Impact Severity Profile (ISP) Using Full Preseason Emotion Dysregulation Measure Models Controlling for Team and Seasons of Sport Participation: B (95% CI) p-value

Head impact Severity	Model	Depression	Anxiety	Impulsivity	Aggression
ISP	A	0.0072 (-0.0475,0.0620) 0.794	0.0272 (-0.0242,0.0787) 0.297	-0.0161 (-0.0327,0.0004) 0.055	-0.0009 (-0.0085,0.0068) 0.820
	B^	0.0112 (-0.0441,0.0665) 0.687	-0.0070 (-0.0664,0.0525) 0.816	-0.0026 (-0.0189,0.0136) 0.747	0.0003 (-0.0075,0.0080) 0.947
	C	0.0070 (-0.0484,0.0624) 0.803	0.0264 (-0.0255,0.0783) 0.316	-0.0159 (-0.0327,0.0008) 0.062	-0.0008 (-0.0085,0.0069) 0.840
	D	0.0080 (-0.0477,0.0637) 0.775	0.0261 (-0.0265,0.0786) 0.328	-0.0156 (-0.0322,0.0010) 0.066	-0.0007 (-0.0084,0.0070) 0.849

Models: Five separate prediction models were conducted for the competition ISPs with the four emotion dysregulation measures (depression, anxiety, impulsivity, aggression) All models include all four emotion dysregulation measures, ISP, team, and seasons of sport participation, with the following additional covariates:
A) None (df =7),
B) Perceived stress (PSS4) (df =8),
C) General position (line, back, skill [reference], special teams) (df = 10),
D) Player group (offense [reference], defense, both) (df =9).
N=130 for ISP models except model B^ where n=88.
Significant at p=0.01.

Table 4.2.5. Emotion Dysregulation Change-scores (Postseason – Preseason) for Instrumented Football Players: Full Season

	Group (total possible)	Depression (PHQ-9)!		Anxiety (GAD-7)		Impulsivity (BIS-11)		Aggression (BPAQ)		Stress (PSS4)	
		X ± SD (n)	Range	X ± SD (n)	Range	X ± SD (n)	Range	X ± SD (n)	Range	X ± SD (n)	Range
ISP	Normal (83)	0.78 ± 2.73 (69)	-5 to 10	1.23 ± 3.75 (69)	-8 to 13	0.86 ± 7.23 (83)	-17 to 24	-1.08 ± 15.43 (82)	-39 to 56	-0.42 ± 3.00 (59)	-7 to 7
	Moderate (20)	-1.07 ± 1.69 (16)	-4 to 2	1.06 ± 5.20 (16)	-4 to 17	0.63 ± 6.57 (20)	-17 to 10.31	1.18 ± 15.81 (19)	-20.33 to 47	-0.15 ± 4.14 (13)	-9 to 6
	Poor(2)	3.00 ± 4.24 (2)	0 to 6	2.50 ± 6.36 (2)	0 to 6	8.00 ± 21.21 (2)	-7 to 23	5.00 ± 9.90 (2)	-2 to 12	0.00 (0)	0.00
All Players		0 ± 2.22 (87)	-4 to 4	1.23 ± 4.04 (87)	-8 to 17	0.95 ± 7.37 (105)	-17 to 24	-0.54 ± 15.34 (103)	-39 to 56	-0.38 ± 3.20 (72)	-9 to 7

All change-scores were calculated as postseason-preseason.
Significant at p=0.01.
! Impact Severity Profile (ISP) was significant.

Table 4.2.6. Cumulative Impact Severity Variables for Instrumented Football Players: Full Season

		N (%)	Total Impacts		Top of Head Impacts!		# of Impacts > 60 g!		Incident SRC	
			X ± SD	Range	X ± SD	Range	X ± SD	Range	X ± SD	Range
ISP	Normal	83 (79.05)	462.94 ± 374.73	52-1794	51.57 ± 49.41	3-212	17.41 ± 20.10	0-88	0.19 ± 0.43	0-2
	Moderate	20 (19.05)	618.20 ± 436.80	74-1874	105.70 ± 83.14	12-336	50.45 ± 44.24	3-160	0.30 ± 0.57	0-2
	Poor	2 (1.90)	641.00 ± 892.37	10-1272	146.50 ± 202.94	3-290	54.5 ± 74.25	2-107	0.00	0.00
All Players		105	495.90 ± 396.71	10-1874	63.69 ± 64.60	3-336	24.41 ± 30.26	0-160	0.21 ± 0.45	0-2

Significant at p=0.01.
! Impact Severity Profile (ISP) was significant.

Table 4.2.7. Prediction of Individual Emotion Dysregulation Change-Scores Using Full Season Impact Severity Profile (ISP) Models Controlling for Team and Seasons of Sport Participation: B (95% CI) p-value

Head impact Severity	Model	Group	Depression (PHQ-9) (n=87)	Anxiety (GAD-7) (n=87)	Impulsivity (BIS-11) (n=105)	Aggression (BPAQ) (n=103)
ISP	A	Normal	-2.1344 (-5.9426,1.6739) 0.268	-0.1024 (-5.7664,5.5615) 0.971	-7.2867 (-17.7065,3.1331) 0.168	-4.9188 (-26.6443,16.8066) 0.654
		Moderate	-3.8939 (-7.9060,0.1182) 0.057	0.2384 (-5.7288,6.2055) 0.937	-7.5589 (-18.4065,3.2888) 0.170	-3.1709 (-25.8262,19.4843) 0.782
	B^#	Normal	2.0185 (0.3293,3.7077) 0.020	1.1601 (-0.4792,2.7995) 0.162	1.7059 (-2.6757,6.0876) 0.440	#3.8776 (-4.6066,12.3619) 0.365
	C	Normal	-2.0137 (-5.9043,1.9768) 0.306	-0.1598 (-5.8914,5.5758) 0.956	-6.6568 (-16.7625,3.4689) 0.195	-5.0626 (-27.1316,17.0065) 0.650
		Moderate	-3.7972 (-7.8895,0.2951) 0.069	0.1640 (-5.8647,6.1928) 0.957	-6.9279 (-17.4547,3.5989) 0.195	-3.4325 (-26.4456,19.5806) 0.768
	D	Normal	-2.3747 (-6.2380,1.4885) 0.225	-0.2810 (-6.0362,5.4742) 0.923	-7.6096 (-18.2302,3.0111) 0.158	-6.6237 (-28.5804,15.3331) 0.551
		Moderate	-4.1180 (-8.1748,-0.0612) 0.047	0.1068 (-5.9367,6.1504) 0.9720	-7.8405 (-18.8636,3.1827) 0.161	-4.6582 (-27.4992,18.1829) 0.687

Models: Four separate prediction models were conducted for the full season ISPs with all four individual emotion dysregulation measures (PHQ-9, GAD-7, BIS-11, BPAQ) All models include one emotion dysregulation measure, ISP, team, and seasons of sport participation, with the following additional covariates:
A) None (df =5).
B) Perceived stress (PSS4) (df =6).
C) General position (line, back, skill [reference], special teams) (df = 8).
D) Player group (offense [reference], defense, both) (df =7).
All analyses were performed using the poor ISP group as the reference.
^ depression, anxiety, impulsivity n = 72, aggression n=70.
# Reference = moderate ISP (no poor group available).
Significant at p=0.01.

CHAPTER 5: SUMMARY OF FINDINGS AND ADDITIONAL DATA ANALYSES AND TABLES

5.1. Overall Summary of Findings

Our data only supported hypothesis 1, “A SRC history measured at preseason will be associated with worse emotion dysregulation scores at preseason.” Concussion history was associated with significantly higher depression (p=0.004, p=0.023) and impulsivity (p=0.015, p=0.002) in the adjusted and unadjusted models respectively. It was surprising that concussion history was not associated with anxiety based on the findings of several TBI studies.[289, 357] As expected, aggression was not significantly associated with concussion history in any of our analyses. Concussion history ranged from 1-5 with the majority of our participants reporting only 1 SRC at preseason (81.01%). SRC studies have only found long-term depression changes in athletes with 3+ concussions,[4, 99] thus it would have been concerning to find aggression changes with less than 3 concussions. Regardless, the authors find it concerning that even though the clinical significance is lacking between groups’ emotion dysregulation scores, they are still present in adolescents with less than 20% reporting 2 or more concussions. If these student-athletes continue to participate in sports and sustain additional SRCs it is possible that these subclinical differences may become clinically relevant. This is particularly concerning since several of our athletes who reported 1+ concussions were 14-15 years of age.

Our ISP models did not support either of our hypotheses. Hypothesis #2 was “A worse emotion dysregulation profile at preseason will be associated with a worse competition ISP and/or an increased likelihood for in-season incident SRC over the course of one season.” Hypothesis #3 was “In football players, incident SRC and worse full season ISPs (top of head impacts and/or more severe impacts) during one season will be associated with worse emotion

dysregulation profiles at postseason, relative to the preseason emotion dysregulation profiles in the same individuals." It is likely that our null findings were in large part based on how the ISP were formed. Initially this seemed to be the most informative method. However, our data indicate that either our algorithm was amiss or it is better to utilize the parts instead of the whole for these measures. We ran some additional analyses that support this idea (**Table 5.1-5**). The primary take home point from these additional analyses is that player position (broken further down into primary and secondary positions), general position (line, back, skill, special teams), and player group (offense, defense, both) are all critical components to these analyses and should be included in future algorithms (Section 5.2).

As discussed in the manuscripts, the null findings for research questions 2, 3, and the exploratory questions are related to several factors. Our data suggest that the student-athletes' premorbid emotion dysregulation levels (levels prior to and during the early years of sport participation) are driving factors in what sports they choose to participate in and thus the level of concussion risk they incur. As mentioned previously, it is possible that participation in specific sports may further enhance emotion dysregulation scores as well over time. The type of sport an athlete chooses can be broken down into individual and team, both of which bring about their own inherent stressors and support systems. While some individuals revel in the spotlight and are highly successful in high stress situations, others fair very poorly in the same environment. If the latter person is in an individual sport they will not be successful and will either most likely quit, or our data suggests their anxiety and depression will increase. Conversely, team sports allow all personalities to thrive if the rest of the environment is suitable (e.g., coaches, teammates, competition, media, parents). The sport-related environments that athletes are exposed to for multiple hours each week for months on end is a large factor in what emotion dysregulation variables are exacerbated and which are not. These are all factors that have not been thorough investigated, especially with regards to SRC.

In order for researchers to determine if these emotion dysregulation measures are suitable for clinical application and how they may best be used, these studies must be conducted. It would also be useful to conduct longitudinal studies involving youth prior to, or within 1 year of them initiating sport participation. To determine the chicken-or-the-egg question of environment vs. genetics, and elevated emotion dysregulation vs. SRC we must collect data on individuals before they are already vested in athletics. While our results were inconclusive, we still believe that emotion dysregulation measures could be one of those missing pieces to the SRC puzzle and with further research we will be able to assist clinicians and athletes by improving acute care, return to play decisions, and long-term quality of life.

5.2. Additional Head Impact Severity Analysis Results, Interpretations, and Tables

5.2.1. Additional Results: Cumulative Head Impacts and Emotion Dysregulation

For every 1-point increase in depression (PHQ-9) scores athletes sustained 26.0 more competition impacts over the season when anxiety (GAD-7), impulsivity (BIS-11), and aggression (BPAQ) were held constant (p=0.007) (**Table 5.1**). Similarly for every 1-point increase in depression scores athletes sustained 29.4, 22.5, 23.5, and 25.0 more competition impacts over one season when the other 3 emotion dysregulation measures, stress (p=0.010), player position (0.013), general position (0.008), and player group (0.009) were held constant respectively. Conversely, for every 1-point increase in anxiety scores athletes sustained 22.3 fewer competition impacts over one season when anxiety, impulsivity, and aggression were held constant (p=0.012). In addition, for every 1-point increase in anxiety scores athletes sustained 22.2, and 21.4 fewer competition impacts over one season when the other 3 emotion dysregulation measures, general position (0.008), and player group (0.010) were held constant respectively. No other models were significant for total competition impacts.

5.2.1.1. Cumulative Head Impact Severity and Full Emotion Dysregulation Models at Preseason

For every 1-point increase in depression scores athletes sustained 4.0 additional competition top of head impacts over one season when anxiety, impulsivity, and aggression were held constant (p=0.004) (**Table 5.1**). Therefore, players who scored a zero on the baseline PHQ-9 were more likely to have poor impact profiles such as sustaining 25 top of head competition impacts, equating to 73 top of head competition impact for a player who scored a 12 on the PHQ-9 at baseline. Similarly, for every 1-point increase in depression scores athletes sustained 4.1, 4.1, 3.7, 4.0 more competition top of head impacts over one season when the other 3 emotion dysregulation measures, stress (p=0.013), player position (0.002), general position (0.005), and player group (0.011) were held constant respectively.

For every 1-point increase in depression scores athletes sustained 2.4 additional competition impacts that were ≥ 60 g when anxiety, impulsivity, and aggression were held constant (p=0.011) (**Table 5.1**). Similarly, for every 1-point increase in depression scores athletes sustained 2.2, and 2.4 more competition impacts that were ≥ 60 g over one season when the other 3 emotion dysregulation measures, *general position* (0.015), and player group (0.013) were held constant respectively. The head impact severity measures were not associated with any of the other full emotion dysregulation models (p≥0.02).

5.2.1.2. Head Impact Severity and Individual Emotion Dysregulation Models at Preseason

For every 1-point increase in depression scores, cumulative competition top of head impacts increased by 3.0 over one season when holding constant player position (p=0.005). When controlling for player position, players with higher (worse) anxiety scores were 29% more likely to sustain an incident SRC than those with normal anxiety (OR = 1.286, p=0.012, 95% CI: 1.0575,1.5635). None of the other individual depression (p≧0.028), anxiety (p≧0.039), impulsivity (p≧0.134), or aggression (p≧0.038) models were significant predictors for the cumulative competition head severity variables or incident concussion (**Table 5.2**).

5.2.1.3. Individual Competition Head Impact Severity Measures and Full Emotion Dysregulation Scores

Over three seasons 31,492 competition impacts were recorded. The players sustained 3,879 (12.32%) impacts to the top of their heads. Players with higher anxiety scores were 6% less likely to hit with the top of their head compared to those with lower anxiety scores when the other three emotion dysregulation measures are held constant (OR=0.938, p= 0.011, 95% CI: 0.893,0.985) (**Table 5.3**). Additionally, when depression, impulsivity, and aggression were held constant, players with higher anxiety scores were 6% less likely to hit with the top of their head when controlling for general position (OR= 0.935, p= 0.008, 95% CI: 0.889, 0.982) compared to those with lower anxiety scores. None of the other emotion dysregulation measure models were significant for prediction of any of the other individual head impact severity measures.

5.2.1.4. Competition Head Impact Severity and Individual Emotion Dysregulation Scores

As anxiety scores increased the number of competition top of head impacts also increased for models A, C, D, and E ($p \leq 0.011$) (**Table 5.4**). See **Table 5.5** for the associated mean accelerations and 95% confidence intervals for the 5th and 95th percentiles for these analyses.

5.2.2. Additional Interpretations: Cumulative Head Impacts and Emotion Dysregulation

5.2.2.1. Cumulative Head Impact Severity and Full Emotion Dysregulation Models at Preseason

Depression and Anxiety

Higher (worse) depression and lower anxiety were significant predictors of total competition and top of head impacts. Higher depression was also a significant predictor for increased number of impacts ≥ 60 g, while higher anxiety was a significant predictor of incident concussion (**Table 5.1**). A 1-point increase in a depression scores was associated with an increase in total competition impacts ranging from 22.5-29.4. To put this in terms of how these statistically significant differences apply clinically, our participants' depression scores ranged

from 0-12. If a player with a depression score of zero sustained 200 total impacts over one season, a player with a depression score of 12 would sustain 470-553 impacts over one season, indicating higher depression scores are more likely to have poor impact profiles such as sustaining a higher number of competition impacts over the course of one season. For every 1-point increase in depression scores athletes sustain 4.0 additional competition top of head impacts over one season when anxiety, impulsivity, and aggression were held constant (p=0.004). An example of this would be if a player who scored a zero on the baseline PHQ-9 sustained 25 top of head competition impacts over one season, a player who scored a 12 on the baseline PHQ-9 may sustain 73 top of head competition impacts during one season. For every 1-point increase in depression scores athletes sustained 2.4 additional competition impacts that were ≥ 60 g when anxiety, impulsivity, and aggression were held constant (p=0.011). Again, if a player scored a zero on the baseline PHQ-9 sustained 4 competition impacts that were ≥ 60 g, a player who scored a 12 would be projected to sustain 37 competition impacts that were ≥ 60 g. These finding partially support TBI associations between depression, anxiety and increased concussion risk.[289] Higher depression and anxiety have been associated with increased risk for TBI. Football players who sustain higher magnitude impacts, and impacts to the top of their head are at a greater risk for SRC.[106, 123, 125, 149]

It is interesting that decreased anxiety was a predictor for increased cumulative number of competition impacts overall. The range of anxiety scores (GAD-7) at baseline was 0-15. When the other three emotion dysregulation measures were held constant, a 1-point decrease in an anxiety score was associated with a 22.3 increase in total competition impacts. Again, using the example from above, a player who scored 15 on the GAD-7 might sustain 200 competition impacts over one season, but a player who scored a 0 would sustain 535 competition impacts over one season. This finding suggests higher anxiety scores on the GAD-7 are associated with a lower frequency of competition impacts and are more likely to be protective. Notably, the association between anxiety and incident concussion is in the opposite

direction of the head impact biomechanics measures. Individuals with higher baseline GAD-7 scores have 29% greater odds of sustaining an incident concussion than those with lower baseline GAD-7 scores. Together with our previous findings these data indicate that players with higher anxiety may not play as often, (lower frequency) or play as high risk/collision positions (fewer linear and rotational magnitude impacts) as those with lower anxiety, but may play with worse technique leading them to greater risk of incident concussion over one season. These associations have not been investigated previously to our knowledge and should be further investigated using video confirmation to confirm their body position at impact.

Impulsivity and Aggression

The lack of significant findings for impulsivity and aggression (**Table 5.1**) seem counter-intuitive and do not support our hypotheses or TBI literature reporting elevated risk of TBI for individuals with pre-existing impulsivity and aggression.[42] The non-significant differences for baseline impulsivity ($p \geq 0.187$) and aggression ($p > 0.090$) scores with all HITS models indicate that they are not important predictors for these outcome variables. However, these findings may be reflective of our sample and not generalizable to all high school football players. It is also possible that our measures were not sensitive enough measure for this population. The Barrett Impulsiveness Scale-11 (BIS-11) has been shown to be sensitive and reliable in a multitude of populations,[297, 298, 302, 306, 358] however it has not been used in an athletic population to predict injury risk to our knowledge. The Buss Perry Aggression Questionnaire (BPAQ) assesses general aggression through a composite of 4 sub-component scores: physical aggression, verbal aggression, anger, and hostility. It is possible that these generalized impulsivity and aggressive behaviors may not reflect sport-specific impulsivity and aggression closely. Future research should determine if more sport-specific measures produce different results.

Seasons of Sport Participation

Seasons of sport participation was positively associated with all four HITS outcome variables over one season in each of the 5 models with the four emotion dysregulation measures held constant. While not statistically significant, as seasons of sport participation increased so did all four HITS outcome variables ($p \leq 0.034$). Again, this is to be expected and supports what clinicians see in the field. Players who are older typically have greater experience playing a particular sport resulting in larger, faster, stronger players who are more skilled and knowledgeable about the sport and compared to younger players with fewer years of experience. This confounder could be an important factor for our findings. Players who have more experience should have a better understanding of the rules, regulations, and techniques associated with a particular sport compared to players who have recently begun participation. Improved sport knowledge, skill, and exposure with a football environment may lead to decreased anxiety on the competition field. Clinically older players often exhibit these behaviors by confidently completing the warm-up drills and adjusting to audible plays more easily during competitions compared to the younger players. However, it could also be argued that older players with more years of participation also feel a greater responsibility for team/personal success due to their elevated years of participation on a football team compared to younger players with few years of experience. Older players are usually associated with harder impacts and sport specific aggression. Seasons of sport participation was not associated with incident concussion over one season ($p \geq 0.482$).

Position

It is important to point out that player position, general position, and player group also were important factors in these models. The significant findings for Models C-E (**Table 5.1**) suggest that specific positions on the field are more likely to have poor HITS profiles, thus elevating risk for incident concussion. We did not investigate this finding further, but we

recommend that future studies investigate the associations between player position, general position, and player group with head impact biomechanics measures and emotion dysregulation.

5.2.2.2. Head Impact Severity and Individual Emotion Dysregulation Models

Our results suggest depression and anxiety are the strongest two individual emotion dysregulation predictors of worse cumulative competition head impact biomechanics and incident concussion (**Table 5.2**). Anxiety was inversely associated with cumulative competition impacts for one year, supporting our earlier findings with the full model emotion dysregulation analyses. This finding again suggests that higher anxiety scores are less likely to have poor impact profiles by reducing the risk of increased cumulative competition impacts over one season and are thus somewhat protective. Top of head impacts were positively associated with depression scores (PHQ-9). These findings also support the full model findings, indicating higher depression scores are more likely to have poor impact profiles with an increased risk of top of head competition impacts over one season

5.2.2.3. Competition Head Impact Severity and Full Emotion Dysregulation Scores

Elevated anxiety may be a protective mechanism for football players. When the other 3 emotion dysregulation measures were held constant, football players with elevated anxiety were less likely to use the top of their heads during competitions (**Table 5.3**). This indicates that pure anxiety (i.e., anxiety by itself) was an indicator of safe play. Athletes who were more anxious tended to not use the top of their heads as often as players with lower anxiety scores. This could also be a consequence of playing time and level. Further investigations should determine the associations among age, playing level (JV, Varsity, college), playing time (either number of plays or number of minutes played in competitions), top of head impacts and baseline anxiety scores.

Importance of Player Position

Our findings support the notion that an improved predictive model would include general position and/or player group due the number of significant models including them as covariates. Future research should also investigate the associations between the emotion dysregulation measures and primary and secondary player positions. Studies have shown head impact severity measures are significantly associated with player position. Personal clinical experience suggests that emotion dysregulation scores will also be associated with player position. Much like our preseason emotion dysregulation scores that were associated with team, clinical experience indicates that each individual has a genetic predisposition to varying degrees of our emotion dysregulation variables of interest and are thus attracted to certain sports and positions within those sports. Our preseason data suggested both males and females with elevated aggression were more likely to participate in high contact sports, while those with high anxiety scores were more likely to participate in no contact sports. Our analyses did not include positional differences in all sports, or the different football positions. Anecdotally, clinical experience suggests that the more aggressive players either self-select or are coach-selected to participate in the higher risk positions (i.e., linebackers, running backs, etc.).

Elevated emotion dysregulation scores (i.e., aggression) are not always detrimental to an individual. In athletics, aggression is often one of the behavioral traits that separate the mediocre from the highly successful. All sports require a certain amount of innate aggression, but when the measures reach unhealthy levels, or when an individual is not able to control their aggression on and off the competitive field is when steps need to be made to intervene, especially if these changes were a result of a SRC.

Table 5.1. Prediction of Cumulative Competition Head Impact Severity Using Full Preseason Emotion Dysregulation Measure Models, Controlling for Team, and Seasons of Sport Participation: B (95% CI) p-value

Head impact Severity	Model	Depression	Anxiety	Impulsivity	Aggression
Total Impacts	A	25.9671 (7.4053,44.5290) 0.007*	-22.3483 (-39.7852,-4.9115) 0.012*	-0.5519 (-6.1376,5.0437) 0.846	-1.2606 (-3.8546,1.3333) 0.338
	B^	29.4193 (7.1200,51.7186) 0.010*	-25.3105 (-49.2851,-1.3360) 0.039*	-1.3578 (-7.9284,5.2128) 0.682	-1.5178 (-4.6289,1.6133) 0.339
	C	22.5426 (4.7728,40.3123) 0.013*	-18.6993 (-34.9916,-2.4070) 0.025*	1.4502 (-3.9395,6.8399) 0.5949	-1.5293 (-3.9450,0.8864) 0.212
	D	23.5154 (6.1567,40.8742) 0.008*	-22.1943 (-38.4672,-5.9214) 0.008*	0.4714 (-4.7822,5.7251) 0.8593	-1.3325 (-3.7516,1.0865) 0.2776
	E	25.0455 (6.1237,43.9673) 0.009*	-21.3622 (-39.2196,-3.5047) 0.010*	-0.5047 (-6.1500,5.1407) 0.860	-1.2507 (-3.8636,1.3622) 0.345
Top of Head Impacts	A	4.0389 (13440,6,7338) 0.004*	-1.5956 (-4.1372,0.9360) 0.215	-0.2330 (-1.0454,0.5794) 0.571	-0.1622 (-0.5387,0.2144) 0.396
	B^	4.1588 (0.9152,7.4024) 0.013*	-2.5609 (-6.0482,0.9263) 0.1478	-0.1312 (-1.0870,0.8245) 0.785	-0.2057 (-0.6597,0.2482) 0.370
	C	4.0567 (1.5519.6.5615) 0.002*	-1.3132 (-3.6097,0.9834) 0.260	0.1648 (-0.5949,0.0246) 0.668	-0.2365 (-0.5770,0.1040) 0.171
	D	3.7352 (1.1664,6.3042) 0.005*	-1.5570 (-3.9652,0.8512) 0.2030	-0.1066 (-0.8840,0.6709) - .7865	-0.1713 (-0.5293,0.1867) 0.3454
	E	3.9952 (1.2521,6.7384) 0.005*	-1.5616 (-4.1504,1.0272) 0.235	-0.2092 (-1.0276,0.6092) 0.614	-0.1563 (-0.5351,0.2225) 0.416
Linear Impacts >60 g	A	2.3768 (0.5478,4.2059) 0.011*	-1.8108 (-3.5289,-0.0926) 0.039*	0.0944 (-0.4570,0.6458) 0.735	-0.1167 (-0.3723,0.1389) 0.368
	B^	1.7613 (-0.0472,3.5697) 0.056	-1.6263 (-3.5706,0.3180) 0.100	0.1341 (-0.3988,0.6669) 0.618	-0.1232 (-0.3764,0.1299) 0.335
	C	1.9605 (0.3140,3.6070) 0.020*	-1.2637 (-2.7733,0.2459) 0.100	0.2822 (-0.2171, 0.7816) 0.265	-0.1786 (-0.4024,0.0453) 0.117
	D	2.2338 (0.4389,4.0288) 0.015*	-1.7985 (-3.4812,-0.1159) 0.036*	0.1526 (-0.3907,0.6958) 0.579	-0.1225 (-0.3726,0.1276) 0.334
	E	2.3741 (0.5062,4.2420) 0.013*	-1.8078 (-3.5706,-0.0450) 0.045*	0.0944 (-0.4628,0.6517) 0.738	-0.1167 (-0.3746,0.1413) 0.372
Rotational Impacts >4085 rad/s^2	A	1.7083 (0.0147,3.4020) 0.048*	-1.8277 (-3.4187,-0.2368) 0.025*	0.1537 (-0.3569,0.6642) 0.552	-0.1314 (-0.3681,0.1053) 0.274
	B^	1.3980 (-0.2893,3.0853) 0.103	-1.3717 (-3.1857,0.4424) 0.136	0.1316 (-0.3656,0.6288) 0.600	-0.1045 (-0.3406,0.1317) 0.381
	C	1.2222 (-0.3685,2.8129) 0.131	-1.2431 (-2.7015,0.2153) 0.094	0.2642 (-0.2183,0.7466) 0.280	-0.17112755 (-0.3874,0.0451) 0.120
	D	1.5897 (-0.0840, 3.2635) 0.063	-1.8217 (-3.3908,-0.2527) 0.023*	0.2018 (-0.3047,0.7084) 0.432	-0.1364 (-0.3696,0.0969) 0.249
	E	1.6409 (-0.0844,3.3661) 0.062	-1.7475 (-3.3757, -0.1192) 0.036*	0.1435 (-0.3712,0.6582) 0.582	-0.1341 (-0.3724,0.1041) 0.267

Head impact Severity	Model	Depression	Anxiety	Impulsivity	Aggression
Incident Concussion	A	0.8737 (0.6786,1.1249) 0.295	1.2578 (1.0189,1.5528) 0.033*	1.0456 (0.9729,1.1237) 0.225	0.9830 (0.9510,1.0160) 0.308
	B^	1.0264 (0.7643,1.3783) 0.863	1.1832 (0.8967,1.5613) 0.234	1.0402 (0.9549,1.1332) 0.367	0.9634 (0.9228,1.0058) 0.090
	C$				
	D	0.8698 (0.6787,1.1147) 0.271	1.2509 (1.0166,1.5392) 0.034*	1.0491 (0.9770,1.1265) 0.187	0.9838 (0.9519,1.0168) 0.332
	E	0.5892 (0.6670,1.1067) 0.240	1.2881 (1.0333,1.6058) 0.024*	1.0466 (0.9711,1.1278) 0.234	0.9815 (0.9496,1.0144) 0.267

Models: Five separate prediction models were ran for the Cumulative Competition Head Impact Severity variables with the four emotion dysregulation measures (Depression, Anxiety, Impulsivity, Aggression) All models include all four emotion dysregulation measures, team, and seasons of sport participation, with the following additional covariates:
A) None (df =7),
B) Perceived Stress (PSS4) (df =9),
C) The two Player Position groupings (primary, secondary [wide receiver = reference]) (df =22),
D) General Position (Line, Back, Skill [reference], Special Teams) (df = 10),
E) Player Group (Offense [reference], Defense, Both) (df =9).
N=130 for Head impact biomechanics models except model B^ where n=88.
N=151 for the Incident Concussion Models, except for model B# where n=107.
$ The data did not fit the model, thus it did not converge.
NOTE: If a player only had a primary position listed, the same position was used for their secondary position.
Incident concussion was analyzed as a binary variable. SRC totals were yes = 25 and no = 105 for all models except B^ where SRC yes = 18 and no = 70.
*Significant at p=0.01.

Table 5.2. Prediction of Cumulative Competition Head impact Severity Using Preseason Individual Emotion Dysregulation Measure Models: B (95% CI) p-value

Head impact Severity	Model	Depression (n=132)	Anxiety (n=132)	Impulsivity (n=154)	Aggression (n=152)
Total Impacts	A	8.8490 (-6.8817,24.5796) 0.395	-13.1805 (-27.4539,1.0929) 0.070	-2.4913 (-6.8653,1.8826) 0.262	-1.3517 (-3.3284,0.6249) 0.179
	B^	11.6190 (-6.7073,29.9453) 0.211	-11.3439 (-31.2744,8.5867) 0.261	-2.7059 (-8.5445,3.1327) 0.359	-1.4639 (-4.2225,1.2947) 0.294
	C	9.0536 (-5.8153,23.9224) 0.230	-10.4140 (-23.5297,2.7018) 0.119	-0.8272 (-5.0057,3.3513) 0.696	-1.7523 (-3.5994,0.0949) 0.063
	D	7.3358 (-7.3796,22.0511) 0.326	-13.6118 (-26.8897,-0.3339) 0.045*	-1.5146 (-5.6787,2.6495) 0.473	-1.5488 (-3.4080,0.3104) 0.102
	E	8.3216 (-7.4576,24.1007) 0.299	-12.1176 (-26.5547,2.3194) 0.971	-2.2585 (-6.6338,2.1168) 0.309	-1.3449 (-3.3086,0.6188) 0.178
Top of Head Impacts	A	2.5102 (0.2773,4.7431) 0.028*	-0.1846 (-2.2664,1.8971) 0.861	-0.2706 (-0.8898,0.3485) 0.389	-0.0830 (-0.3641,0.1982) 0.561
	B^	2.2295 (-0.3805,4.8396) 0.093	-0.5086 (-3.3881,2.3710) 0.726	-0.2455 (-1.0858,0.5949) 0.563	-0.1527 (-0.5511,0.2457) 0.448
	C	2.9861 (0.9065,5.0657) 0.005*	0.1967 (-1.7110,2.10440) 0.839	-0.0432 (-0.6370,0.5506) 0.886	-0.1311 (-0.3923,0.1301) 0.323
	D	2.3312 (0.2110,4.4514) 0.031*	-0.2223 (-2.1955,1.7509) 0.824	-0.1416 (-0.7390,0.4558) 0.6402	-0.1067 (-0.3753,0.1619) 0.434
	E	2.4852 (0.2418,4.7286) 0.030*	-0.0710 (-2.1764,2.0345) 0.947	-0.2208 (-0.8435,0.4019) 0.485	-0.0779 (-0.3584,0.2027) 0.584
Linear Impacts >60 g	A	1.0702 (-0.4517,2.5921) 0.167	-0.8489 (-2.2437,0.5459) 0.231	-0.0803 (-0.5114,0.3507) 0.713	-0.0918 (-0.2871,0.1034) 0.354
	B^	0.7685 (-0.6829,2.2199) 0.295	-0.6685 (-2.2478,0.9108) 0.402	0.0151 (-0.4483,0.4785) 0.949	-0.0757 (-0.2952,0.1437) 0.494
	C	1.2439 (-0.2281,2.7159) 0.097	-0.5489 (-1.8653,0.7676) 0.411	0.0463 (-0.3759,0.4686) 0.829	-0.1471 (-0.3219,0.0278) 0.099
	D	0.9871 (-0.5074,2.4816) 0.194	-0.8768 (-2.2427,0.4891) 0.206	-0.0224 (-0.4488,0.4039) 0.917	-0.1065 (-0.2977,0.0846) 0.272
	E	1.0498 (-0.4855,2.5851) 0.178	-0.8113 (-2.2284,0.6057) 0.259	-0.0626 (-0.4977,0.3725) 0.776	-0.0911 (-0.2868,0.1045) 0.359
Rotational Impacts >4085 rad/s^2	A	0.3975 (-1.0190,1.8139) 0.580	-1.1857 (-2.4662,0.0948) 0.917	-0.0968 (-0.5132,0.3195) 0.547	-0.1301 (-0.3180,0.0579) 0.174
	B^	0.5650 (-0.7811,1.9111) 0.406	-0.6002 (-2.0618,0.8613) 0.416	0.0240 (-0.4047,0.4528) 0.912	-0.0637 (-0.2672,0.1397) 0.535
	C	0.4661 (-0.9238,1.8561) 0.508	-0.8800 (-2.1030,0.3429) 0.157	-0.0010 (-0.4169,0.4150) 0.996	-0.1855 (-0.3616,-0.0095) 0.039*
	D	0.3271 (-1.0744,1.7286) 0.645	-1.2127 (-2.4759,0.0506) 0.060	-0.0517 (-0.4663,0.3629) 0.806	-0.1434 (-0.3286,0.0418) 0.128
	E	0.3545 (-1.0689,1.7779) 0.623	-1.1294 (-2.4264,0.1675) 0.087	-0.0925 (-0.5112,.3263) 0.663	-0.1320 (-0.3196,0.0557) 0.167

Head impact Severity	Model	Depression (n=132)	Anxiety (n=132)	Impulsivity (n=154)	Aggression (n=152)
Incident Concussion	A	1.0059 (0.8321,1.2159) 0.951	1.0024 (1.0040,1.3599) 0.044*	1.0424 (0.9837,1.1045) 0.160	0.9994 (0.9739,1.0256) 0.967
	B#	1.0707 (0.8639,1.3271) 0.533	1.1538 (0.9311,1.4300) 0.191	1.0126 (0.9435,1.0867) 0.730	0.9813 (0.9483,1.0154) 0.278
	C	1.0467 (0.8490,1.2902) 0.670	1.2858 (1.0575,1.5635) 0.012*	1.0514 (0.9829,1.1246) 0.145	1.0039 (0.9673,1.0338) 0.794
	D	0.9972 (0.8256,1.2047) 0.977	1.1650 (1.0009,1.3560) 0.049*	1.0453 (0.9865,1.1077) 0.134	0.9997 (0.9742,1.0259) 0.982
	E	1.0028 (0.8306,1.2107) 0.977	1.1759 (1.0082,1.3716) 0.039*	1.0420 (0.9828,1.1048) 0.169	0.9992 (0.9738,1.0254) 0.954

Models: Five separate prediction models were ran for the Cumulative Competition Head Impact Severity variables for each of the emotion dysregulation measures. All models include the individual emotion dysregulation measure, Team, and Years of sport participation, with the following additional covariates:
A) None,
B) Perceived Stress (PSS4) as the covariate,
C) The two Player Position groupings (primary, secondary [wide receiver = reference]) as the covariates,
D) General Position (Line, Back, Skill [reference], Special Teams) as the covariate,
E) Player Group (Offense [reference], Defense, Both) as the covariate.
^Depression, Anxiety, Impulsivity n = 90, Aggression = 88
NOTE: If a player only had a primary position listed, the same position was used for their secondary position. Incident concussion was analyzed as a binary variable.
SRC totals were yes = 26 and no = 126 for all BPAQ models except B^ where SRC yes = 18 and no = 70.
SRC totals were yes = 26 and no = 128 for all BIS models except B^ where SRC yes = 18 and no = 72.
SRC totals were yes = 25 and no = 107 for all PHQ9 and GAD models except B^ where SRC yes = 18 and no = 72.
Incident concussion (reference = yes)
*Significant at p=0.01.

Table 5.3. Prediction of Individual Competition Head impact Severity for Individual Impacts Using Full Season Emotion Dysregulation Measure Models: B (95% CI) p-value

Head impact Severity	Model	Depression (PHQ9)	Anxiety (GAD7)	Impulsivity (BIS-11)	Aggression (BPAQ)
Top of Head	A	0.0105 (-0.0426,0.0636)	-0.0644 (-0.1137,-0.0151)*	0.0010 (-0.0155,0.0173)	0.0054 (-0.0020,0.0127)
	B	0.0045 (-0.0591,0.0681)	-0.0401 (-0.1086,0.0285)	-0.0072 (-0.0263,0.0120)	0.0049 (0-0.0041,0.0138)
	C	0.0060 (-0.0501,0.0620)	-0.0591 (-0.1102,-0.0081)*	-0.0036 (-0.0209,0.0137)	0.0050 (-0.0027,0.0127)
	D	0.0149 (-0.0387,0.0685)	-0.0676 (-0.1172,-0.0179)*	0.0012 (-0.0153,0.0177)	0.0050 (-0.0024,0.0124)
	E	0.0040 (-0.0459,0.0579)	-0.0584 (-0.1086,-0.0082)*	0.0004 (-0.0162,0.0170)	0.0053 (-0.0021,0.0127)
Log Linear Acceleration (g)	A	0.0082 (-0.0032,0.0196) 0.155	0.0035 (-0.0072,0.0142)	-0.0010 (-0.0045,0.0025)	-0.0011 (-0.0027,0.0004)
	B	0.0086 (-0.0036,0.0207)	-0.0038 (-0.0169,0.0094) 0.523	-0.0009 (-0.0045, 0.0028) 0.562	-0.0006 (-0.0041,0.0155) 0.147
	C	0.0119 (0.0001,0.0237) *	0.0017 (-0.0092,0.0125)	-0.0003 (-0.0039,0.0034)	-0.0009 (-0.0025,0.0007)
	D	0.0085 (-0.0028,0.0197)	0.0027 (-0.0079,0.0133)	-0.0007 (-0.0042,0.0028)	-0.0012 (-0.0028,0.0003)
	E	0.0074 (-0.0042,0.0189)	0.0046 (-0.0063,0.0155)	-0.0013 (-0.0048.0.0023)	-0.0013 (-0.0027,0.0005)
Log Rotational Acceleration (rad/s^2)	A	0.0154 (-0.0013,-0.0321)	-0.0141 (-0.0298,0.0015)	0.00001 (-0.0051,0.0051)	-0.0024 (-0.0047,-0.0001)*
	B	0.0126 (-0.0055,00308)	-0.0133 (-0.0328,0.0063)	-0.0010 (-0.0065,0.0044)	-0.0012 (-0.0038,0.0013)
	C	0.0187 (0.0013,0.0362)*	-0.0158 (-0.0318,0.0003)*	0.0001 (-0.0053,0.0054)	-0.0023 (-0.0047,0.0001)
	D	0.0169 (0.0005,0.0333)*	-0.0158 (-0.0312,-0.0004)*	0.0002 (-0.0048,0.0053)	-0.0026 (-0.0048,-0.0003)*
	E	0.0124 (-0.0043,0.0291)	-0.0108 (-0.0266,0.0050)	0.0004 (-0.0055,0.0048)	-0.0024 (-0.0047,-0.0001)*

Models: Five separate prediction models were ran for the log Head Impact Severity variables. Covariates for all models included School and Years of sport participation. All models include the individual emotion dysregulation measure with the following additional covariates:
A) None. (df = 124).
B) Perceived Stress (PSS4) (df = 82),
C) The two Player Position groupings (primary, secondary) (df = 111),
D) General Position (Line, Back, Skill, Special Teams),
E) Player Group (Offense, Defense, Both).
NOTE: If a player only had a primary position listed, the same position was used for their secondary position.
Top of Head (reference = not top)
*Significant at p=0.01.

Table 5.4. Prediction of Competition Head Impact Severity for Individual Impacts Using Preseason Individual Emotion Dysregulation Models: B (95% CI) p-value

Head impact Severity	Model	Depression (PHQ-9) (n=131, obs = 27409)	Anxiety (GAD-7) (n=131, obs = 27409)	Impulsivity (BIS-11) (n=139, obs = 31420)	Aggression (BPAQ) (n=137, obs =30848)
Top of Head	A	1.021 (0.975,1.068) 0.375	1.057 (1.015,1.100) 0.007*	#	0.998 (0.993,1.003) 0.440
	B@	1.018 (0.968,1.071) 0.483	1.051 (0.995,1.110) 0.074	1.005 (0.989,1.022) 0.535	0.998 (0.989,1.007) 0.637
	C	1.023 (0.975,1.074) 0.347	1.053 (1.012,1.096) 0.011*	0.998 (0.985,1.011) 0.769	0.998 (0.992,1.004) 0.473
	D	1.023 (0.975,1.074) 0.347	1.057 (1.016,1.101) 0.007*	0.996 (0.983,1.009) 0.550	0.998 (0.993,1.003) 0.433
	E	1.024 (0.979,1.071) 0.298	1.053 (1.012,1.096) 0.011*	0.997 (0.984,1.009) 0.604	0.998 (0.993,1.003) 0.436
Log Linear Acceleration (g)	A	0.011 (-0.0004, 0.021) 0.059	0.0003 (-0.010, 0.011) 0.954	-0.0001 (-0.004, 0.003) 0.947	-0.001 (-0.003, 0.0001) 0.074
	B	0.011 (-0.001,0.022) 0.062	-0.004 (-0.016, 0.009) 0.549	-0.0002 (-0.004,0.003) 0.894	-0.0005 (-0.002,0.001) 0.570
	C	0.014 (0.002,0.025) 0.020*	-0.002 (-0.012,0.009) 0.822	0.0007 (-0.003,0.004) 0.684	-0.001 (-0.003,0.0004) 0.151
	D	0.010 (-0.0004,0.021) 0.060	0.00005 (-0.010,0.010) 0.992	0.00008 (-0.003,0.003) 0.961	-0.001 (-0.003,0.0001) 0.068
	E	0.010 (-0.001,0.021) 0.087	0.001 (-0.009.0012) 0.812	-0.0002 (-0.004,0.003) .0889	-0.001 (-0.003,0.0001) 0.073
Log Rotational Acceleration (rad/s^2)	A	0.018 (-0.001,0.035) 0.033*	-0.018 (-0.034,-0.002) 0.024*	0.001 (-0.004,0.006) 0.680	-0.003 (-0.005,-0.0004) 0.023*
	B	0.015 (-0.003,0.033) 0.100	-0.014 (-0.034,0.005) 0.149	-0,0002 (-0.006,0.005) 0.939	-0.001 (-0.004,0.001) 0.336
	C	0.021 (0.003,0.038) 0.021*	-0.019 (-0.035,-0.002) 0.025*	0.0008 (-0.005,0.006) 0.763	-0.002 (-0.005, 0.0008) 0.058
	D	0.019 (0.003,0.035) 0.024*	-0.019 (-0.034,-0.003) 0.018*	0.001 (-0.004,0.006) 0.698	-0.003 (-0.005,-0.0005) 0.018*
	E	0.015 (-0.002,0.0232) 0.075	-0.015 (-0.031,0.0008) 0.063	0.0008 (-0.004,0.006) 0.758	-0.003(-0.005,-0.0005) 0.019*

Models: Five separate prediction models were ran for the log Head Impact Severity variables for each of the emotion dysregulation measures. All models include the individual emotion dysregulation measure, team, and seasons of sport participation, with the following additional covariates:
A) None (df = 126).
B) Perceived Stress (PSS4) (df = 84),
C) The two Player Position groupings (primary, secondary; ref = WR) [df = PHQ-9 112, GAD-7:119, BIS-11 (), BPAQ ()],
D) General Position (Line, Back, Skill, Special Teams) [df = PHQ-9 (), GAD-7 (123), BIS-11 () , BPAQ ()],
E) Player Group (Offense, Defense, Both) [df = PHQ-9 (), GAD-7(119), BIS-11 (134), BPAQ(134)]
@ Number of participants/observations used for PHQ-9, GAD-7, and BIS-11 = 90/18845, BPAQ =88/18273.
# Data did not support the model.
NOTE: If a player only had a primary position listed, the same position was used for their secondary position.
Top of Head (reference = top)
*Significant at p=0.01.

Table 5.5. Comparison of 5th (score) and 95th (score) Percentiles for Individual Competition Impacts Using Full Preseason Emotion Dysregulation Measure Models: Mean Acceleration (95% CI)

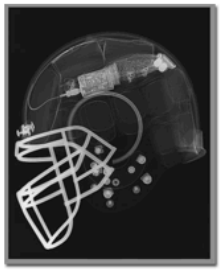
Head impact Severity	Model	Depression		Anxiety		Impulsivity		Aggression	
		5% (0)	95% (7)	5% (0)	95% (6)	5% (51)	95% (75)	5% (37)	95% (94)
Linear Acceleration (g)	A	22.101 (18.080,27.015)	23.788 (19.312,29.303)	22.101 (18.080, 27.015)	22.134 (17.729,27.649)	21.971 (19.967,24.170)	21.911 (19.360, 24.801)	20.987 (17.012,25.891)	19.381 (15.093,24.886)
	B	19.432 (15.604,24.199)	20.945 (16.587,26.449)	19.432 (15.604,24.199)	18.999 (14.939,24.163)	19.200 (16.883,21.835)	19.093 (16.374,22.262)	19.096 (15.241,23.929)	18.593 (14.288,24.196)
	C^								
	D	21.503 (17.484,26.446)	23.141 (18.640,28.726)	21.503 (17.484,26.446)	21.510 (17.131,27.007)	21.596 (19.517,23.896)	21.641 (19.070,24.557)	20.399 (16.443,25.307)	18.808 (14.585,24.254)
	E	22.334 (18.236,27.355)	23.896 (19.362,29.491)	22.334 (18.236,27.355)	22.506 (17.977,28.177)	22.061 (20.037,24.286)	21.931 (19.362,24.841)	21.200 (17.152,26.204)	19.562 (15.206,25.169)
Rotational Acceleration (rad/s^2)	A	1,333.284 (983.679, 1807.500)	1,512.62 (1102.792, 2074.758)	1,333.284 (983.679, 1807.139)	1195.257 (853.888, 1673.546)	1408.809 (1219.261, 1627.662)	1183.581 (1197.870, 1744.634)	1205.802 (877.345, 1657.391)	1032.873 (707.120, 1508.845)
	B	1224.515 (863.074, 1737.496)	1361.306 (937.672, 1976.139)	1227.826 (863.074, 1737.496)	1122.822 (765.631, 1646.653)	1211.119 (987.326, 1485.490)	1204.838 (943.787, 1538.095)	1168.411 (815.254, 1674.383)	1086.808 (716.229, 1655.072)
	C^								
	D	1327.828 (973.210, 1811.662)	1516.560 (1095.756, 2098.966)	1327.828 (973.210, 1811.662)	1184.765 (841.764, 1667.365)	1398.003 (1200.988, 1627.337)	1432.247 (1184.528, 1731.944)	1197.750 (866.533, 1665.735)	1021.881 (697.429, 1497.422)
	E	1365.260 (1008.985, 1847.151)	1516.712 (1108.098, 2076.004)	1365.260 (1008.985, 1847.151)	1247.628 (892.387, 1744.459)	1422.114 (1232.007, 1641.556)	1449.828 (1203.754, 1746.205)	1232.377 (898.476, 1690.365)	1052.580 (722.849, 1532.874)

Models: Five separate prediction models were ran for the log Head Impact Severity variables for each of the emotion dysregulation measures. All models include the individual emotion dysregulation measure, team, and Seasons of sport participation with the following additional covariates:
A) None (n=129, df = 121).
B) Perceived Stress (PSS4) (n=88, df = 79),
C) The two Player Position groupings (primary, secondary; ref = WR) (n=129, df = 108),
D) General Position (Line, Back, Skill, Special Teams) (n=129, df = 118),
E) Player Group (Offense, Defense, Both) (n=129, df = 119)
^These models did not converge.
NOTE: If a player only had a primary position listed, the same position was used for their secondary position.
*Significant at p=0.01.

APPENDIX 1: HIT System

Basic Description:
(Information below, directly taken from- http://www.simbex.com/BRP/research.html)

The HIT System™



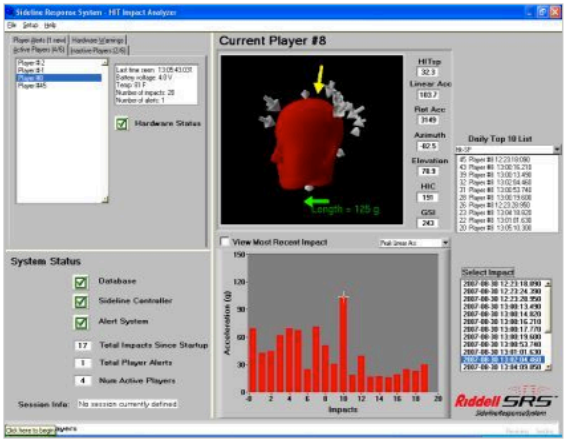
Sports provide an Ideal Environment for Monitoring Head Impacts

Real-time monitoring and recording of all significant head impacts using the Head Impact Telemetry (HIT) System™. HIT System™ computes head acceleration, impact duration and impact location for multiple athletes simulatiously to alert team physicians and athletic trainers to potentially injurious impacts.

The Head Impact Telemetry (HIT) System™ monitors, records and processes head impacts in real-time during all practices and competitions. The HIT System™ measures *impact magnitude, location and duration.*

The HIT System™ is the first and only commercially available system that can measure head accelerations (impacts) in real-time during games and practices. The HIT System™ sensor/encoder package contains impact sensors, a processor, and a transmitter. (A commercial version of this product for football use will be available from Riddell this fall.)

The HIT System™ transforms a helmet or headgear into a head-impact monitor. A microprocessor-based data collector receives impact data continuously from encoders that can be hundreds of meters away. The HIT System™ can monitor dozens of athletes or soldiers



The data collector stores all of the key signatures of each impact — peak linear acceleration, rotational acceleration, impact duration and location, etc. — with a time stamp for future analysis. The data can be accessed to compute commonly used head-impact severity measures (HIC, GSI, etc.).

Impacts are immediately transmitted (via radio frequence) to a Sideline Controller which records, processes and stores the data.

The HIT System™ reflects more than a decade of research (supported in part by the National Center for Medical Rehabilitation Research at the National Institutes of Health).

HITS has been tested in the crucible of NFL, college and high school football stadiums and practice fields since 2004. Using the HIT System, we have recorded over two million impacts and corresponding data on head injuries.

APPENDIX 2: MASTER PROTOCOL

1. Obtaining approval from the Chapel Hill-Carrboro School District and the University of North Carolina – Chapel Hill (UNC-CH) for student-athlete participation, and UNC-CH IRB approval,
2. Hold an informational and recruitment meeting at all participating high schools and UNC-CH for potential participants (parent/guardians when applicable) and the school's athletic trainer(s).
3. Collect consent forms and keep them in a locked file in the Matthew Gfeller Center at UNC-CH.
4. All testing and data collection will be conducted at each of the respective schools outside of regular class time.
5. Keep all data either in either locked (consent forms) or password encrypted files (Behavioral measures, and accelerometer data) in the Matthew Gfeller Center.
    a. De-identify all data prior to analysis. Store the file matching their data to identifiable information in an alternate password encrypted file.
6. Preseason testing (Pre):
    a. All Participants
        i. Complete the Preseason Concussion History and Personality Questionnaire (PHQ-9, GAD-7, BIS-11, BPAQ), lasting approximately 15min.
7. Accelerometer Installation (Football players only):
    a. Instrument the helmets of interested participants with Head Impact Telemetry System accelerometers.
    b. Charge and connect HITS batteries prior to the first practice. Link the time stamps between the accelerometer system and the video cameras.
    c. On the first day of practice (prior to the start of practice):
        i. Set up the HITS
        ii. Selected participants will wear these devices for all games and practices.
    d. The HITS:
        i. Charge and change batteries at least weekly.
        ii. Download sensor data after every 1-2 consecutive practices or games.
        iii. Download data from the HITS program regularly throughout the season and save on password-protected files in the Matthew Gfeller Center (UNC-CH).
8. Athletes who are diagnosed with a concussion and their 2 matched controls (by age, position, concussion history):
    a. Within 48 hours of reporting a concussive injury (PI#1):
        i. All Participants:
            1. Complete the Post-Injury #1 Concussion History and Personality Questionnaire lasting approximately 15 minutes.
    b. After completion of return to play progression (PIRP):
        i. Complete the Post-Injury Full Return Concussion History and Personality Questionnaire lasting approximately 15 minutes.
    c. Conduct additional testing sessions per the direction of the participant's attending physicians when directed.
9. Postseason (Post): Within 21 days following the last game of the football season collect the following measures:
    a. All Participants:
        i. Postseason Concussion History and Personality Questionnaire, including a short questionnaire about their football season, lasting approximately 15 minutes
10. Athletes or guardians who decline to participate at the beginning or during the study:
    a. Remove their data from analyses and recover all equipment they may have been given (e.g., HITS sensors from helmet).
11. Report all unanticipated problems or breaches of confidentiality immediately to the UNC-CH IRB.
12. Perform data analyses throughout the duration of the study and at the end of the season per the direction of Stephen Marshall (Professor in Epidemiology and Director of the Injury Prevention Research Center at UNC-CH).
13. Interpretation of data analyses by the research team in preparation dissemination of findings through publications and presentations.

APPENDIX 3: PRESEAON CONCUSSION HISTORY AND EMOTION DYSREGULATION QUESITONNAIRE

1. Introduction and Consent

Hello and thank you for taking the following questionnaire. Please complete the following questions to the best of your ability. If you do not wish to respond to a particular question(s), you have the right to leave it (them) blank.

Your participation in this research study is voluntary, and will help us to learn more about potential short and long term medical risks of playing sports. No participant names will be identified in any report or publication. All research records will be kept confidential.

2. Personal Information

Which of the following schools do you attend?

- ○ Carrboro
- ○ Chapel Hill
- ○ Northwood

Today's Date: It must be typed exactly as follows including back-slashes (mm/dd/yyyy)

For example, if today is August 7th, 2015 it must be typed, 08/07/2015

Date of Birth: It must be typed exactly as follows including back-slashes (mm/dd/yyyy)

For example, if your date of birth is April 9th, 2000 it must be typed, 04/09/2000.

Current Age:

5. Which of the following sports or activities will you be starting in the next few days to weeks?

APPENDIX 4: POSTSEASON CONCUSSION HISTORY AND EMOTION DYSREGULATION QUESTIONNAIRE

1. Introduction and Consent

Hello and thank you for taking the following post-season questionnaire!

Please complete the following questions to the best of your ability. If you do not wish to respond to a particular question(s), you have the right to leave it (them) blank.

Your participation in this research study is voluntary, and will help us to learn more about potential short and long term medical risks of playing sports. No participant names will be identified in any report or publication. All research records will be kept confidential.

2. Personal Information

Which of the following schools do you attend?

- ○ Carrboro
- ○ Chapel Hill
- ○ Northwood

Today's Date: It must be typed **exactly** as follows including back-slashes (mm/dd/yyyy).

For example, if today is August 7th, 2015 it must be typed, 08/07/2015

Date of Birth: It must be typed **exactly** as follows including back-slashes (mm/dd/yyyy).

For example, if your date of birth is April 9th, 2000 it must be typed, 04/09/2000

Current Age:

Which of the following school-related sports / activities did you just finish?

APPENDIX 5: PARENT/GUARDIAN LETTER FOR ELEVATED DEPRESSION AND ANXIETY SCORES

Dear Mr/Ms. _____,

As you are aware, your son/daughter is a participant in a concussion and behavior study being conducted by our research team at the University of North Carolina at Chapel Hill. The project involves high school athletes at three local schools. As part of the baseline screenings, which you and your son/daughter consented to conducting, we agreed to provide you with any information that may be useful to you and your son/daughter.

This email is to inform you that your son/daughter reported levels of anxiety/depression above the expected values for their age and sex on the questionnaire they recently completed. The Generalized Anxiety Disorder Scale (GAD-7) and the Patient Health Questionnaire (PHQ-9) are not diagnostic tools, but are used by clinicians as screening tools to determine if further testing may be warranted. There are various reasons as to why a person can score outside the expected range so it is not appropriate for us to speculate as to the nature of the results. Rather, we wanted to inform you of this situation and offer some resources that may be helpful in the event that you wanted additional insight into the test results. For the purpose of this study, scores at or above 10 on both measures suggest further assessment may be warranted.

If you choose to take your son/daughter for a more thorough evaluation, we recommend that you start by scheduling an appointment with his/her primary health care provider (i.e., general medical doctor, or pediatrician).

If he/she does not have a primary care physician, we recommend you contact your insurance provider to locate an adolescent health specialist.

If he/she does not have insurance you may contact your local community mental health center. These centers are organized by county and can be found on the following website: http://www.ncdhhs.gov/providers/lme-mco-directory.

Sincerely,
Missy Fraser and Kevin Guskiewicz
Gfeller Center, UNC-Chapel Hill

APPENDIX 6: FOOTBALL DAILY LOG

DATE			Tech			
ID	Jersey	Participating	Battery OK	Battery Changed	Sensor OK	Issues/Notes (Type of practice/scrim/game/etc)
TOTAL						
Varsity Event		JV Practice Event		Data Dump (MISSY)		1st Half Cameras on @	
Varsity Session		JV Session		HITS computer on @		2nd Half Cameras on @	

VARSITY INFORMATION ONLY

Warm-Up	Start	
	End	
Practice	Start	
	End	
1st Half	Start	
	End	
2nd Half	Start	
	End	
	Opponent	
OT	Start	
	End	

GAMES ONLY INFO

JV INFORMATION ONY

Warm-Up	Start	
	End	
Practice	Start	
	End	
1st Half	Start	
	End	
2nd Half	Start	
	End	
	Opponent	

APPENDIX 7: ALL SPORTS PARENT LETTER

Dear Parent or Legal Custodian:

Your child's school is conducting a study regarding the head impacts sustained by athletes participating in high school sports. If you agree to allow your child to participate in this study, and your child wishes to participate, then they will receive an on-line concussion history and neurobehavior questionnaire. In the event that your child is diagnosed with a concussion they will be asked to complete a questionnaire containing information about their concussion and several behavioral measures within 48 hours of reporting the injury and again after they have returned to full participation. Your child may also be asked to be a control for a concussed teammate. This means they will be asked to complete both post-injury measures even though they are not concussed.

We are writing to ask your permission to use your child's information as part of this ongoing research. The study is voluntary and your child does not have to participate.

If you agree to allow us to use your child's data as part of this research project, please complete the following forms. **Each form contains several places that require initials and/or signatures**.

1) **If your child is 18 or older**, have him/her review and sign the **YELLOW** adult high school athlete consent form in the packet provided.

2) **If your child is 15-17 years old**, have him/her review and sign the **PINK** adolescent assent form included in the in the packet **AND** their parent/guardian needs to review and sign the **BLUE** parental consent from.

3) **If your child is 14 years old or younger**, have him/her review the **GREEN** adolescent assent form included in the in the packet **AND** their parent/guardian needs to review and sign the **BLUE** parental consent from.

If both you and your child agree to participate, please return these forms at the informational forum held prior to the beginning of the sport season. If you have questions or concerns, feel free to call us at (919)962-0409, or ask them at the informational forum. Thank you for your time and consideration. Please let us know if you have any questions or concerns.

Sincerely,

Kevin M. Guskiewicz, PhD, ATC
Principle Investigator
Kenan Distinguished Professor and
Senior Associate Dean for Natural Sciences

Missy Fraser, MS, ATC
Study Coordinator, Co-Investigator
Phone: (919) 962-0409
Email: mafraser@live.unc.edu

APPENDIX 8: 1-PAGE EXPLANATION FOR PARENTS

Explanation for IRB 14-1109: Prospective Investigation of Sport-Related Concussion: Relationship Between Biomechanical, Clinical, and Behavioral Factors

Our Goals:

- To determine the association between concussion history and the previous number of football seasons played and four neurobehavioral measures at preseason.
- To determine if preseason neurobehavioral scores are associated with head impact biomechanics during the season.
- To determine head impact biomechanics are associated with changes from pre- to postseason in the neurobehavioral measures.

What is being asked of your children:

1. **Preseason** (approximately 15 minutes)
    a. Completion of the online Preseason Concussion History and Neurobehavior Questionnaire (Qualtrics)

2. **If an athlete sustains a concussion** (approximately 15minutes each)
    a. Completion of the online Post-Injury #1 Concussion History and Neurobehavior Questionnaire within 72 hours of reporting the injury*
    b. Completion of the online Post-Injury Return-to-Play Concussion History and Neurobehavior Questionnaire after they have completed all return to play criteria under the direction of their school athletic trainer*

* A teammate who is the same age and playing position and an age matched non-contact sport athlete will be asked to complete these 2 questionnaires to serve as the injured athlete's comparisons.

3. **Postseason** (approximately 15 minutes)
    a. We would like to test all athletes within 3 weeks of their sport ending
    b. Completion of the online Postseason Concussion History and Neurobehavior Questionnaire (Qualtrics)

In the event that your son scores above the expected values for the neurobehavioral measures, we will contact you via email to discuss his scores.

APPENDIX 9: BIS-11: ITEM MODIFICATIONS

7. I plan trips (outings with my friends and family) well ahead of time.
10. I save money regularly.
13. I make plans about the best way to keep my position on sports teams.
16. I change my mind about what I want to do after graduation often.
21. I change where I hang out often.

REFERENCES

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