3. SIGNIFICANCE

3.a Injury incidence in adolescent soccer due to player collisions

Epidemiological studies point to the occurrence of more than 3.75 million youth injuries in sport each year[1], with on-field collisions accounting for over 50% of contact sport injuries.[2–5] Collisions are, thus, expected to be the cause of approximately 1.75 million athletes suffering musculoskeletal injuries annually. This highlights the significant health impact of collision-based injuries, and research shows that soccer injury rates are higher, overall, compared to other contact and collision sports.[19] Collisions account for 57% of all soccer injuries[4], and 40% of knee ligament injuries.[20] Female soccer athletes, specifically, are twice as likely to suffer a collision-based anterior cruciate ligament (ACL) tear compared to males.[8] Perhaps most salient, while high-school soccer players experience significantly fewer collision impacts per hour of exposure compared to football lineman or hockey athletes, each soccer collision is associated with higher impact *g-forces*: 20% of all soccer impacts were over 75*g* compared to only 5% over 75*g* in the other two cohorts.[21] While the relation between impact force and musculoskeletal injury is not well understood, collisions greater than 8.1*g* are significantly associated with greater and more protracted skeletal muscle damage.[16] Thus, it is likely that both collision frequency and impact forces are associated with increased frequency and severity of musculoskeletal injury—with unanticipated collisions a multiplier (compared to anticipated) for musculoskeletal injury.

The significant health impact of collision-induced musculoskeletal injury has motivated calls for training interventions to reduce unanticipated collisions on the field of play.[4,5] Yet, effective interventions for collision prevention or impact force mitigation are lacking. Solving this problem requires a concerted effort to determine the underlying mechanisms that lead to unanticipated collisions. Our previous experience with a related issue supports this claim. Two decades ago, the sports medicine community faced a similar problem with non-contact ACL injury prevention. To meet this challenge, our team utilized a federally funded approach to *first* identify the mechanisms of non-contact ACL injuries in athletes (R01 AR056259-01). Identifying these mechanisms drove the development of targeted neuromuscular training (NMT) interventions to recategorize athletes from high to low risk (R01 AR05563-02).[22–24] Today, the related advancements in NMT reduce the risk of non-contact ACL-injury by 46% in female athletes[25], and the field has progressed to optimizing NMT programs for high-efficiency prevention—an effort reflected in the parent clinical trial (U01 AR067997-01A1) to this ancillary proposal. In light of this success, we will develop a line of research to identify mechanisms underlying unanticipated collisions and the mitigation of associated impact forces. The rationale is that until this knowledge is obtained, the development of targeted interventions to successfully decrease injuries from unanticipated collisions will not be possible.

3.b Multimodal mechanisms underlying collision anticipation and impact force mitigation

The mechanisms for collision avoidance have been extensively examined in pedestrian locomotion[26–28] and driving;[29–32] however, little attention has been given to these mechanisms in sport. Two American football studies have focused on factors related to the mitigation of head impact forces, with results that converge with our own preliminary data.[13,33] Specifically, higher impact forces were associated with low performance on a battery of visual tasks (i.e., perception span, go/no go and target capture), indicating a key role of visual performance in impact force mitigation.[13] Attentional performance (i.e., near-far attentional focus) also plays a role in mitigating head impact forces.[33] Both results support a perceptual-motor approach to impact mitigation, but by implicating both visual and attentional performance they also indicate a more fundamental process related to collisions: the rudimentary eye (i.e., oculomotor) behaviors that underlie both attention and visual behavior is likely the more central mechanism at play. Oculomotor actions such as saccade and fixation behaviors play an important role in competitive sport performance.[34–36] They provide the foundation for more overt perceptual-motor control—i.e., the perception of action possibilities, and the subsequent selection and execution of the most effective action.[12] Vision plays a preparatory role in collision mitigation and avoidance, allowing for the prospective control of avoidance maneuvers.[12] Further, collision detection is likely dependent on attention to stimuli in the central visual field and rapid, efficient switching between various opponents and objects to quickly process the visual scene. Oculomotor behaviors drive the successful acquisition and processing of this visual information[37], and are, thus, foundational to these perceptual-motor processes.[38]

The identification of oculomotor behaviors that support efficient perceptual-motor control provide a means for understanding visual and attentional performance in the context of collisions; however, a singular focus on these mechanisms ignores the important interrelation between perceptual-motor and neuromechanical mechanisms—with the latter also a significant aspect of athletic performance (i.e., fitness).[6,17,18,39,40] From the pedestrian and driving literature it is understood that collision avoidance and impact mitigation behavior is driven by interacting, multimodal mechanisms that map perceptual (e.g., visual) information to neuromechanical variables to generate adaptive movements.[41] This is also true in sport[12,42], and has been demonstrated in athletic contexts.[43,44] A framework to understand these behaviors must account for the tight coupling between perceptual-motor and neuromechanical control.[12] Failure to do so risks marginalizing potentially important variables that promote complex, injury-resistant on-field behaviors. Thus, understanding the association between these mechanisms and unanticipated collisions is key to determining whether particular training programs can potentially improve the anticipation of collisions and the mitigation of associated impact forces.

3.c Phenotypic Plasticity

Phenotypic plasticity (PP) is a principle from evolutionary biology that originated in the 20th century, but was recently given primacy in the field.[15] PP is defined as an environmentally-based change in an organism's phenotype[45], or observable properties.[14] Traditionally, it was believed that environmentally affected phenotypes were less important for understanding biological behavior given the lack of genetic basis; however, phenotypic plasticity has a genetic basis and is adaptive to environmental contexts.[15,46] For present purposes, reduced plasticity reflects a deficiency in mechanisms that guarantee fitness or adaptability of biological organisms to their environment. However, differences in fitness between two organisms are not intrinsically determined; they tend to be detectable only within a particular set of environments, or during rapid environmental transitions. The implication for sports medicine is that establishing an athlete's risk of injury (due to collision or not) requires attention to mechanisms that support an athlete's ability to modify behavior in response to dynamic conditions on the field (i.e., environment). Our approach exploits the well-established link between PP and adaptive behavior to identify multimodal mechanisms related to unanticipated collisions in sports contexts.

PP is a modifiable characteristic of an organism contingent on a number of organism-specific factors including, but not exclusively, neural plasticity, behavior plasticity, epigenetic plasticity and physical activity that, in combination, promote adaptability to environmental challenges, or stressors.[14] These factors are consistent across organisms, regardless of taxonomy[14]; therefore, PP can similarly capture how adaptable an athlete may be in a variety of on-field environments. In the context of sport collisions, the first step is to identify mechanisms (i.e., perceptual-motor; neuromechanical) that define an athlete's fitness with regard to collision mitigation and avoidance on the field of play. Next, sets of variables that capture the status of these mechanisms are selected, measured at multiple time points, and used to create a series of fitness scores based on one or more of the identified variables. PP is then quantified not based on one isolated score, but based on the longitudinal fitness curve created by plotting a time series of fitness scores. PP is obtained by computing the area under the longitudinal fitness curve (Figure 1). Importantly, PP can be computed from a series of fitness scores created by either repeated measures of one variable or, as we propose to innovate here, by the linear combination of a set of variables. Thus, PP provides a comprehensive approach to investigate the athlete's adaptability to heterogeneous sport environments. The PP approach contrasts sharply with approaches from previous work that utilized isolated measures of behavior to predict number and magnitude of unanticipated collisions.[13,33] The PP approach recognizes the dynamic nature of adaptive processes and, therefore, is expected to be more sensitive in detecting changes in athletes' behaviors that explain failures to successfully anticipate collisions and mitigate their impact forces.

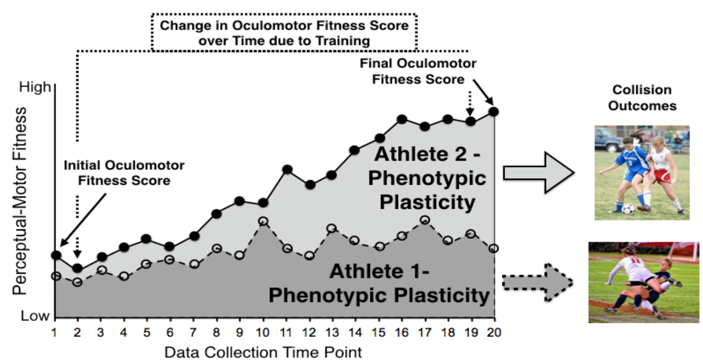


Figure 1. A representative plot of perceptual-motor based Phenotypic Plasticity (PP) for two athletes. Each circle data point is a composite fitness score from three oculomotor (saccade) variables (self-paced positional error variability, self-paced velocity variability, and prosaccade velocity variability) collected at successive time points. The perceptual-motor PP dimension for each athlete is represented by the dark (athlete 1) and combined light and dark (athlete 2) areas under the composite fitness curve. Athlete 1 is exhibiting lower PP (due to no training), leading to poor collision outcomes on the field of play. Athlete 2 is exhibiting higher PP (due to training) and, thus, has improved collision outcomes.

3.c.1 Preliminary Data

Identifying specific variables to compute fitness scores and the resultant curves is key in leveraging the PP approach. Our strong preliminary data provide the necessary empirical basis for selecting a group of oculomotor and neuromechanical fitness variables reflective of perceptual-motor and neuromechanical mechanisms, respectively. Using these pilot data to drive our hypotheses, the proposed PP approach allows us to account for the interactions between multimodal mechanisms associated with collisions and impact forces.

3.c.1.a Indexing Perceptual-Motor Fitness: Oculomotor dynamics

Our preliminary study examined the pre-season perceptual-motor fitness of high school female soccer athletes: the association of oculomotor variables to collisions and impact forces during the competitive season was examined. We computed perceptual-motor fitness scores from each oculomotor variable collected during the athletes' performance on a series of self-paced and prosaccade tasks (Figure 2). Saccade performance was

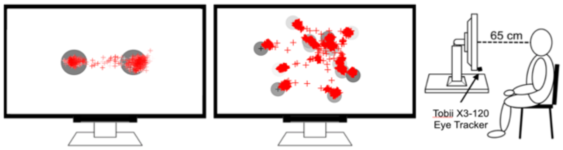


Figure 2. Representation of the self-paced saccade (A) and prosaccade (B) target displays and the tracked eye gaze position (small crosshairs), which were used to establish speed and accuracy of saccadic movements. The eye-tracking assessment set-up (C) was desktop based.

assessed because efficient saccadic movements—brief, simultaneous movements of the eyes that occur between periods of fixation—allow athletes to quickly and selectively discriminate between objects of interest in the visual field.[47] The self-paced saccade task required the athletes to direct their gaze back and forth between cross-hairs in the middle of two targets as quickly and accurately as possible. The prosaccade task required the athletes to track a discrete, randomly placed target that appeared within a randomly determined magnitude (between 4˚ and 10˚ in any direction from the center of the PC laptop screen) and time (between 1 and 2 s). The athletes were instructed to focus their eyes on the center of the cross-hairs in the target and to quickly move their gaze to the next target when it appeared. The three oculomotor fitness scores included initial saccade position error variability (self-paced) and saccade velocity variability (self-paced and prosaccade), and quantified the athletes' adaptive responsiveness to our custom developed targets.[48] Eye gaze was measured at 120 Hz using a Tobii X3-120 Eye Tracker (Tobii Pro, Stockholm, Sweden).

Collision data were indexed using xPatch accelerometers (X2 Biosystems, Seattle, WA) worn behind the ear affixed to the skin. Only accelerations greater than 20g recorded during gameplay were aggregated from each athlete's data. To control for false collisions (i.e., headers and other spurious accelerations due to non-player collisions), we recorded all game activities via standard 2D video. A single rater, blinded to the oculomotor measures, coded game videos to identify anticipated vs. unanticipated collisions and to disqualify all non-player collisions. Our rating methods were based on our previous research that established the consistency of accelerometer data in collegiate lacrosse[49], and collision anticipation was rated using a soccer-specific modified version of the ice-hockey checklist developed previously.[10]

Collision data. Over the season there were a total of 52 anticipated and 75 unanticipated collisions, with no significant difference between the average number of collisions per athlete (anticipated vs. unanticipated; $p>.05$). Our percentage of unanticipated collisions (59%) is similar to previous data from lacrosse (56%)[50] and greater than that of hockey (15%).[10] There was a trend ($p=.11$) toward unanticipated collisions resulting in greater impact forces per collision compared to anticipated (unanticipated M=39.01±3.33*g* vs. anticipated M=33.66±2.84*g*). Thus, our preliminary data support previous work[10], and we expect our hypotheses to hold with the larger sample size (N=108) in the current proposal. Further, the observed mean difference in our preliminary data is clinically meaningful given impact forces as low as 8.1*g* lead to greater risk of skeletal muscle damage.[16] Importantly, the collisions tracked in our pilot study included slide tackles and other collisions with primary impact points in the lower kinetic chain. Thus, head mounted accelerometers are sensitive to impacts at other areas of the body and, combined with 2D video analysis, demonstrate reliability among a variety of collision locations.

Unanticipated Collisions. The self-paced saccade fitness score based on the variability of initial saccade positional error, was positively correlated with the total number of unanticipated collisions, $r_s(31) = .36$, $p = .05$. Likewise, two self-paced fitness scores based on the initial saccade positional error and variability of saccade velocity, were both associated with greater impact forces, overall, throughout the season; $r_s(31) = .44$, $p = .02$ and $r_s(31) = .39$, $p = .03$, respectively. A prosaccade fitness score based on the variability of saccade velocity was positively associated with greater impact forces/collision, $r_s(31) = .40$, $p = .03$, and mildly associated with total impact forces experienced, $r_s(31) = .31$, $p = .09$. Thus, the more variable the speed at which the athletes responded to the appearance of a discrete stimulus, the greater the impact forces for a given unanticipated collision on the field of play. Combined, a lack of consistent saccade performance, whether proactive or reactive, led to a greater number of unanticipated collisions and greater associated impact forces (both a proxy for musculoskeletal injury) on the field of play.

3.c.1.b Indexing Neuromechanical Fitness: Center of Pressure Dynamics and Power

In a second study, we examined the association of neuromechanical fitness with in-game collisions and impact forces. Neuromechanical fitness was indexed by two variables: center of pressure (CoP) dynamics and vertical ground reaction force (vGRF) power. These variables were assessed in varsity high school male ice hockey athletes during performance of cutting and jumping maneuvers. The athletes stood on dual force plates (AMTI, Watertown, MA) in a ready position, with knees bent, while they focused their attention on a computer monitor in front of them. After a period of time randomized between 5 and 7 s, a stimulus arrow appeared on the screen and pointed to the left, up, or to the right and signaled a 45˚ cut forward and to the left, a vertical jump, or a 45˚ cut forward and to the right, respectively (Figure 3). Each athlete responded to the arrow as quickly as possible with the appropriate action. The athletes' CoP velocity dynamics (collected at 50Hz), taken prior to the stimulus onset, along with peak vGRF power normalized to body weight after stimulus onset were used to

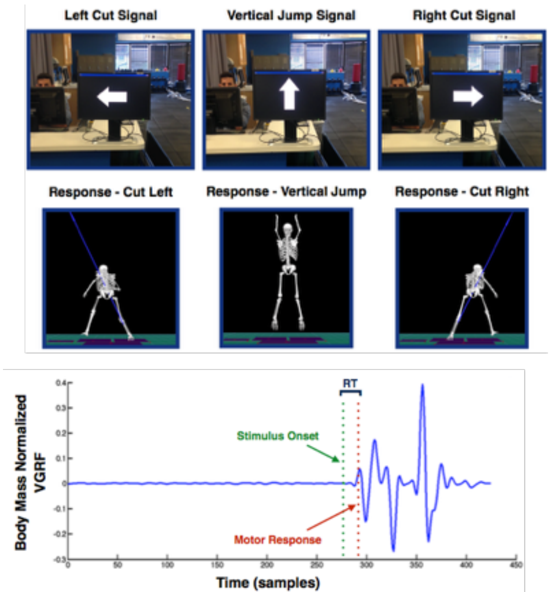


Figure 3. The stimulus arrow for each of the three directions (top), the participants response with associated ground reaction force vector (middle), and a visual representation of the computation of response time (bottom).

separately index neuromechanical response fitness, or adaptability. Reaction times (RT) were computed by subtracting the stimulus onset time from the time each athlete exhibited a body mass normalized change in vGRF, equal to 20 N with no body mass present, after stimulus onset.

Collision data were collected via GForceTracker triaxial accelerometers (Calgary, Canada) secured in the back of each hockey helmet in the same location and orientation. All athletes wore standardized headgear (Bauer RE-AKT). In-game accelerations > 20*g* were aggregated from each athlete's data.

Total Collisions. We examined the overall impact forces experienced and the impact forces per collision in the subsequent analyses. The data demonstrated that the fitness score based on CoP dynamics was strongly correlated with greater impact forces per collision, $r(10)=.75$, $p=.02$, while RT was not related to any of the collision variables ($p>.05$). CoP dynamics in this case was indexed by the nonlinear variable, percent laminarity (See Research Strategy 5.a.4.b). In a previous study, we have demonstrated that this variable is associated with greater adaptability in adolescent female athletes.[17] Thus, our preliminary data suggest that the less adaptive the athletes' neuromechanics, the more extreme the impact forces were for each collision. Peak vGRF power, while not significant, did show a moderate inverse relation to impact forces per collision, $r(10)=-.44$. Similar to the CoP velocity dynamics data, these data provide evidence that greater neuromechanical fitness (as indexed via greater explosive power) is related to the mitigation of collision forces as well. These two fitness variables provide a more complete profile of neuromechanics as related to collision impact mitigation, with both fitness scores more sensitive indicators of adaptability for mitigation than RT data.

3.c.1.c Summary of Preliminary Data

Taken together, our combined perceptual-motor and neuromechanical data provide strong support for the current proposal, demonstrating effects in the targeted population, as well as generalizability across different contact sports. They also support prior evidence that laboratory training of similar mechanisms enhances on-field performance.[51,52] Specifically, our data indicate that greater perceptual-motor fitness is associated with fewer unanticipated collisions and associated impact forces, and that greater neuromechanical fitness is associated with reduced impact forces, overall. These findings directly support the current proposal, serving as the impetus for our central hypothesis: greater PP (quantified via perceptual-motor and neuromechanical fitness scores) will lead to fewer unanticipated collisions and greater mitigation of impact forces on the field of play.

3.d aNMT intervention for collision prevention and mitigation

The NIH-funded parent project to this ancillary proposal, "Real-time Sensorimotor Feedback for Injury Prevention Assessed in Virtual Reality" is designed to determine the efficacy of a real-time, augmented neuromuscular training (aNMT; pronounced "animate") biofeedback intervention to improve high-risk landing and cutting mechanics associated with non-contact ACL injury risk. aNMT is premised on two fundamental principles of sensorimotor control: (1) complex neuromechanical actions can be accomplished by moving to achieve a perceptual outcome representing a desired movement (i.e., perceptual feedback)[53–57], and (2) perceptual-motor learning is enhanced when the athletes focus attention on the external consequences of their actions instead of focusing attention internally on limbs, segments or joints.[58–64] Both principles emerge from the natural linkage between neuromechanical actions and their perceptual outcomes. The relation between the two is not arbitrary, as a given movement reliably produces a specific perceptual outcome, and aNMT leverages this interaction by manipulating both the neuromechanics and the perceptual information with a feedback display. The result is a biofeedback intervention that capitalizes on well-established visual feedback strategies[65,66] to promote efficient and robust neuromechanical processes. Importantly, aNMT was designed to correct deficits in movement patterns previously identified by members of our team as risk factors for ACL-injury.[67–80]

The principles of aNMT, while useful for non-contact ACL injury prevention, also hold potential for promoting collision mitigation, anticipation and, ultimately, prevention of collision-based injury in contact sports. For example, in our preliminary aNMT intervention study, female high school athletes performed a single session of aNMT to targeted body-weight squat movement patterns. After only 40 body-weight squats performed with biofeedback, the athletes showed a positive 8.6±6.3% (p = .002) change in relative knee extensor moment and a 3.2±3.5% (p=.02) increase in knee flexion from pre-aNMT during a drop vertical jump (DVJ) transfer test. These adaptive results to aNMT reflect an acute response of increased posterior chain recruitment to enhance safe biomechanics simultaneous with performance improvements. Similar adaptive net joint moments are significant contributors to vertical jump performance in adolescent girls, and are frequently targeted to enhance power in athletic actions.[81] Our previously published research has also shown that standard NMT leads to improved skill performance in female adolescents, including: single-leg hop distance, vertical jump height, and sprint speed.[18] Our preliminary data indicate that such athletic performance improvements would likely be magnified for multiple aNMT sessions relative to athletes who participate in our sham biofeedback training group in the parent clinical trial. The aspects of skilled performance that aNMT addresses relate to the neuromechanical mechanisms (i.e., the neuromechanical PP dimension) that support collision impact mitigation and avoidance. In particular, the ability to produce greater speed and power allow for a greater range of possible responses to unanticipated situations (i.e., greater PP) across a variety of scenarios. In other words, aNMT enhances neuromechanical fitness that promotes responsiveness to an upcoming collision by: (a) reducing the contact force via movements that promote a glancing blow rather than a full-on collision, (b) bracing for impact prior to collision onset to promote a position that better absorbs and dissipates the transfer of impact forces, or (c) promoting more adaptive, injury resistant biomechanics during balance and fall recovery, if the resultant collision is unavoidable.

Although athletic skill performance has been improved with standard NMT, it has an important limiting factor. Feedback is explicit, typically through verbal instructions about how to correct movements. For instance, there are a number of ACL injury prevention programs using explicit instructions regarding desired landing positions to emphasize proper alignment of the hip, knee, and ankle.[18,82–86] This feedback simply requires athletes to think too much—to think analytically about how they are controlling their body movements. The undesirable consequence is that standard NMT might improve neuromechanical responses at the cost of attentional resources that should be directed to the visual scene. The result of enhanced internal focus of attention in the field is that an upcoming collision might not be perceived in time to drive effective collision avoidance behavior. In sum, NMT might improve the neuromechanical dimension of PP while reducing perceptual-motor PP.

In contrast, aNMT is designed to help athletes learn biomechanically robust responses without explicit instructions about joint and limb movements. Athletes simply interact with a real-time visual display that is coupled to, and informative of, their movement patterns. The only instruction is to move to create a simple goal shape (e.g., a rectangle or square); if the shape is achieved, so is the robust movement pattern. To train proper neuromechanical responses, athletes need no explicit knowledge of the particular mapping between their movements and the visual display. aNMT effectively trades perception and action coupling for complex cognition; that is, it promotes *implicit* control of body movements through the use of visual information about such movements available in the visual scene. The desirable consequence is that aNMT enhances neuromechanical responses while allowing attention to be directed externally, to the task environment. Thus, aNMT holds potential to affect perceptual-motor fitness. For example, if an athlete maintains an external focus of attention in the field, she likely to perceive changes in contextual conditions and organize her behavior accordingly. Given the evidence that anticipation of collisions results in less impact forces,[87] aNMT can be expected to promote the necessary coupling between neuromechanical and perceptual-motor mechanisms underlying optimal collision anticipation, avoidance and impact force mitigation. Thus, we expect that aNMT will affect both neuromechanical and perceptual-motor PP and, consequently, athletes undergoing aNMT training will experience fewer unanticipated collisions, and less intense impact forces, than athletes undergoing sham training.

3.e Synergy with Parent Project and Impact

Dr. Adam Kiefer (ancillary proposal PI; parent project Co-I) and Dr. Gregory Myer (parent project PI; ancillary proposal Co-I) make up two-thirds of the synergistic team working on both the parent project and the ancillary proposal. The third member of the team, Dr. Paula Silva (ancillary proposal Co-I), is heavily involved with the parent project in a voluntary role. The formalization of this partnership through the present proposal will serve to expand the time all three investigators will have dedicated to the two studies, thus <u>maintaining the integrity of the parent project while ensuring successful completion of the ancillary study</u>. To further ensure synergy between the two projects, Dr. Jane Khoury (lead biostatistician on the parent project) will act as a biostatistics liaison, in collaboration with Drs. Altaye (lead biostatistician on ancillary project) and Kiefer, for the life of the ancillary study.

The parent project provides the ideal cohort—adolescent female soccer athletes—for investigating mechanisms of unanticipated collisions during competitive sport, and for the examination of the aNMT program for the remediation of risk factors related to on field collisions. Female soccer athletes provide a high-exposure sample of contact sport athletes who are known to experience almost 60% of injuries due to on-field collisions. The parent project also provides a perfect data collection schedule that aligns with the current proposal, including: pre-season screening, pre-season training/post-training screening, and post-season screening. Thus, the parent project provides a captive athlete population for all activities and testing. In conjunction, the ancillary proposal is also synergistic with the parent project in that it enhances the injury surveillance through impact force and video based surveillance. The timeliness of the current proposal cannot be overstated. With a proposed start date of May 1, 2018, the ancillary project aligns well with the majority of the soccer data collection of the parent project (See Timeline), and once this deadline passes, the opportunity will be lost. The parent project has successfully piloted the integration of the proposed ancillary methods (see Section 5.a.1). Thus, the opportunity to capitalize on existing NIH investment in the parent project, and the timely and cost-effective addition of the ancillary proposal, are highlighted by the proposed project's complimentary and additive aims.

The impact of the current approach for prevention of unanticipated collision and associated musculoskeletal injuries is high. Player-to-player collisions have been implicated in over 50% of all musculoskeletal injuries in a variety of contact sports.[2–5] These injuries can lead to serious long-term negative health consequences including physical inactivity and obesity due to chronic joint pain and osteoarthritis.[9] While research has been conducted on modifiable risk factors for prevention of non-contact musculoskeletal injury,[17,18] modifiable risk factors for collision-based injury have been largely ignored. There are currently no identified mechanisms for collision injury risk on the field of play, despite repeated calls for training interventions to reduce unanticipated collisions during competition.[4,5] After the completion of the proposed objectives, we will have: (a) identified the mechanisms that underlie unanticipated collision risk and (b) determined the effectiveness of aNMT as a complete (i.e., non-contact and contact) injury prevention intervention. In the event that aNMT is successful in modifying PP, we will have, for the first time, identified an effective training program for the reduction and mitigation of collision risk on the field of play, and we will be poised to implement such training to improve injury prevention strategies in female contact sports. Alternatively, if aNMT does not fully (or effectively) modify the mechanisms underlying PP, our data will break ground for informing and facilitating the advancement of basic and epidemiological-based training interventions for the reduction of unanticipated collision and mitigation—an urgent need in the field.

If the results of the present proposal support the expectation that aNMT will affect both neuromechanical and perceptual-motor PP, then the application of aNMT will be expanded to the prevention of collision-based injuries. This expansion is significant in that one of the great barriers to translating effective prevention strategies from the laboratory to the field is convincing athletes, coaches and other sports staff that the financial and time investment is worthwhile. Demonstrating that aNMT is a general strategy for injury prevention (not just prevention of non-contact ligament injury) is fundamental to enhancing its impact. Conversely, if aNMT does not enhance perceptual-motor PP to the same extent as neuromechanical PP, modifications can be identified and proposed to more specifically address oculomotor fitness (e.g. training scenarios that require the tracking of moving stimuli while the athlete performs a specific biomechanical movement). The modified protocol can be used to specifically target athletes with high collision risk due to low perceptual-motor fitness, guaranteeing efficient use of training resources and time. In sum, the new mechanistic insights regarding prevention of unanticipated collision can be expected to amplify the scientific content and value of the parent project by either (a) expanding its application and, consequently, enhancing its impact, or (b) providing a clear direction for modifications in the aNMT protocol leading to its expansion (i.e., provide a risk profile to identify athletes most benefited from a modified protocol).

4. INNOVATION

The proposed line of research is highly innovative for multiple reasons. First, it directly targets, for the first time, multimodal mechanisms—perceptual-motor and neuromechanical—that directly contribute to collision mitigation and avoidance on the field. Our PP approach recognizes the interrelation between these mechanisms and is likely more sensitive in detecting changes in athletes' behaviors relative to collision anticipation.

Second, PP holds several important benefits over traditional approaches to the identification of injury risk, and specifically collisions. A primary advantage is that PP accounts for fluctuations in fitness for each athlete across sessions, reflecting athletes' overall adaptability (and training-based improvements) of perceptual-motor and neuromechanical based fitness. Thus, PP is a true reflection of the kinds of adaptive processes expected to support resilient behavior on the field, and is more likely to be a sensitive and robust predictor of the frequency and magnitude of unanticipated collisions compared to isolated measures of fitness, or other traditional variables.

The oculomotor-based eye tracking measurement approach that underlies the perceptual-motor PP dimension is also novel. While visual and attentional variables have been examined in past studies[13,33], an eye gaze tracking approach enables the study of foundational aspects of movement control that, in turn, have been linked specifically to perceptual variables that modulate collision risk in locomotion across non-sport contexts.[26–28] Thus, it has a direct theoretical and functional link to the visual information for collision avoidance strategies.[88]

Lastly, by measuring PP at each training session, we will be able to determine how many training sessions are necessary for athletes to improve their PP, and also, whether an aNMT-based pre-season intervention leads to better sustained fitness over the course of a competitive season. Taken together, these innovations will lead to much needed interventions to remediate collision-based injury risk and will promote long-term sports participation while reducing the persistent negative sequelae associated with these musculoskeletal injuries.

5. RESEARCH STRATEGY

5.a Overview of proposed research

Specific Aim 1: **Evaluate if prospective PP measures predict frequency and magnitude of unanticipated collisions on the field of play.** PP measures will be derived from mechanism-specific neuromechanical (center of pressure dynamics and cutting/jumping power) and perceptual-motor (oculomotor eye gaze tracking) models, and individual association with outcomes will be examined then optimized via integrated, multivariate models.

Hypothesis 1.1: Neuromechanics-based measures of PP will predict the frequency and magnitude of unanticipated collisions on the field of play during the competitive sports season.
Hypothesis 1.2: Perceptual-motor measures of PP will predict the frequency and magnitude of unanticipated collisions on the field of play during the competitive sports season.
Hypothesis 1.3: The integration of both the perceptual-motor and neuromechanical mechanisms into an additive, multivariate model will provide the strongest prediction of frequency and magnitude of competition based unanticipated collisions during competition.

Specific Aim 2: Determine the effect of a pre-season aNMT intervention on the measures of PP and the underlying fitness scores. PP will be measured using time-series of fitness scores obtained during aNMT training. Fitness scores obtained at post-training and post-season will also be compared to identify changes in and sustainability of perceptual-motor and neuromechanical adaptations following aNMT.

Hypothesis 2.1: The athletes that participate in aNMT will exhibit enhanced neuromechanics-based PP at the conclusion of training, and greater fitness at the conclusion of the soccer season, compared to the sham group.
Hypothesis 2.2: The athletes that participate in aNMT will exhibit enhanced perceptual-motor PP at the conclusion of training, and greater fitness at the conclusion of the soccer season, compared to the sham group.

5.a.1 Fitness Scores and Phenotypic Plasticity Assessment (Aims 1 & 2)

Female high school soccer athletes (n=108; ages 12-18), who will already be enrolled in the parent clinical trial, will be enrolled in the current proposal. The aNMT clinical trial requires athletes to participate in a pre-training biomechanical assessment, six weeks (three sessions/week) of either an aNMT (n=54) or sham (n=54) training intervention (as randomly assigned based on the parent project's stratified randomization scheme, prior to recruitment), and both a post-training and post-season biomechanical assessment. The current proposal leverages this data collection and training schedule with concomitant assessments of neuromechanical and oculomotor fitness at the aforementioned pre-training, post-training and post-season assessment time points. These same fitness assessments will also be conducted during each training session (i.e., three times per week), resulting in a total of 21 fitness scores for each variable of interest (1 pre-training, 18 during training, 1 post-training, and 1 post-season). We have previously piloted the integration of both tasks into pre-/post-testing and aNMT training. The combined length of the oculomotor and neuromechanical testing is less than 5 min per athlete. This minor time burden is further reduced once athletes are comfortable with test instructions. Our pilot testing has confirmed that these tests are of inconsequential burden to the athletes and seamlessly integrate into all sessions. Moreover, both tasks have been designed with random components integrated into the presentation (e.g., randomized target position, randomized time to target appearance). This, along with the randomized control trial design, mitigates potential for confounding learning effects, and test-retest reliability over 50 days has demonstrated to be strong for these types of measures, even when accounting for learning-based effects.[89] At the completion of data collection, PP will be computed from the area under the curve (AUC) that connects data points 1 to 20 for each athlete (i.e., from pre-training through post-training; Figure 4).

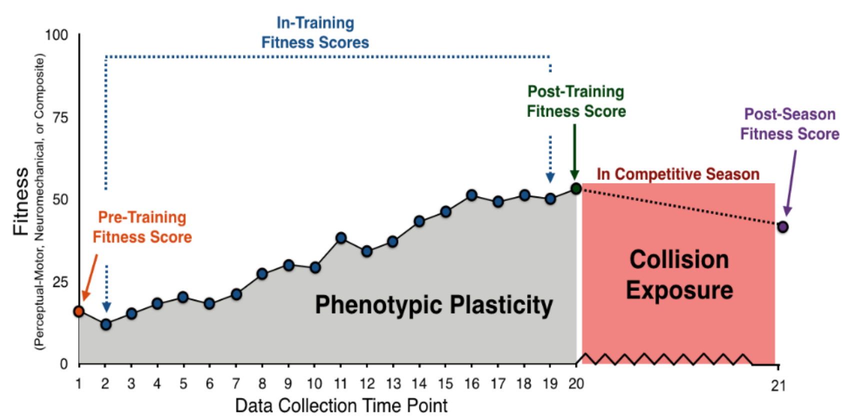


Figure 4. A schematic of the proposed data collection. Individual fitness scores will be computed from specific perceptual-motor or neuromechanical variables, or a combination of the two, based on data collections at 21 time points (1 pre-training, 18 in-training, 1 post-training, and 1 post-season). Phenotypic plasticity (PP) will be computed based on the area under the curve of the resultant fitness score time series. Collision and impact force exposure will be collected in-season, and the association between PP and both collisions and impact forces will be examined. Finally, the influence of the biofeedback intervention will be assessed via the computed PP for each of two groups: aNMT vs sham biofeedback, and the effect of biofeedback on the change from post-training to post-season fitness will be evaluated.

5.a.2 On-field Collision Assessment (Aim 1)

The in-season collision surveillance will be identical to our preliminary soccer study. That is, the number of collisions and associated impact forces will be collected via xPatch accelerometers worn behind the athlete's ear at every game. Standard 2D video will be recorded for every game to allow for rater coding of unanticipated collisions along with additional information for collision categorization (see Appendix 1). As stated previously, our method is nearly identical to our team's previous research on accelerometer data verification with 2D video[49], and the collision coding procedure will be identical to our preliminary soccer study. We will utilize Cohen's kappa (κ) to quantify interrater reliability with an agreement cutoff of κ>.4.[10] Given previously identified muscular injury data for collisions greater than 8.1*g*, we will include collisions with impact forces greater than 10*g*. We have elected to focus on in-game collisions only, as previous literature identified collisions to be 4-6 times greater with significantly greater injury risk, compared to practice.[3] In addition, practice environments (e.g., structures of drills, simulated positioning of athletes, differing performance goals) artificially increase the variability of outcome variables. Thus, it is difficult and potentially invalid to quantify their relation to targeted PP mechanisms. We will, however, monitor practice collisions to control for their potential confounding effects on our primary outcomes.

5.a.3 Description of aNMT and Sham intervention groups (Aim 2)

As part of the parent project, both aNMT and sham biofeedback groups will undergo identical pre-season NMT adapted from our prior published protocols,[69,72,75,90,91] and will perform the same volume and progressions of each exercise. The primary training difference will involve the mapping of each athlete's movements to the stimulus. The aNMT stimulus will map the values of key variables, computed continuously in real-time, to the shape of a stimulus that athletes will view through a head-mounted display. The sham biofeedback, viewed through the same display will consist of a graded, inconsistent mapping between the athletes' movements and the stimulus. Thus, while the sham biofeedback stimulus will promote external-focus and the same phenomenological experience, the it will not promote learning of safe biomechanical movement strategies, and also will diminish attentional "rewards" for external focus as an effective attentional strategy.

5.a.4 Description of the Fitness assessments for Phenotypic Plasticity (Aims 1 & 2)

PP computation is a three-step process. First, a series of fitness scores are computed from a composite set of variables indexing a particular adaptation mechanism (i.e., perceptual-motor or neuromechanical). Second, fitness scores are plotted over time to capture the change of the related mechanisms over time due to either the aNMT or sham training intervention. Third, the AUC for the longitudinal fitness curve is calculated. The result is a PP measure reflecting the mechanism indexed by the fitness scores. In the current proposal, we are examining three fitness-based PP models that target two potential mechanisms of collision anticipation and mitigation: (1) perceptual-motor, (2) neuromechanical, and (3) an additive multivariate PP model that integrates both the perceptual-motor and neuromechanical mechanisms as separate model terms, and examines the association with unanticipated collisions. The variables used for each modality are based on our preliminary data.

5.a.4.a Oculomotor Fitness Dimensions for Phenotypic Plasticity

Oculomotor testing will replicate the procedure used in our soccer preliminary study. It will consist of a 3 min eye gaze tracking session to assess oculomotor performance on a series of self-paced saccade and prosaccade blocks using our custom developed method.[48] The self-paced saccade task consists of two 30 s trials. Two targets will be displayed vertically at 50% of the height of a 15 in PC laptop monitor and horizontally equidistant from the center of the monitor, 8˚ apart. The prosaccade task will consist of two 30 s blocks of approximately 20 trials of discrete target presentation in a randomly determined magnitude (between 4˚ and 10˚ in any direction from the center of the screen) and time (between 1 to 2 s). An important advantage of our method is that it is automated from calibration through collection, and successful and reliable data collection does not require intervention from the experimenter. Automated calibration checks are in place and, if the athlete fails the initial calibration, their eye gaze is automatically recalibrated. Calibration checks are also in place prior to the outset of each trial (or block of trials). If the athlete has adjusted in her seat or moved her head between trials (or blocks) that increases gaze error ≥ .5 cm, her eye gaze will automatically recalibrate before moving on to the next trial (or block) collection. Eye gaze data will be collected at 120 Hz using a Tobii X3-120 desktop eye tracker.

All eye gaze data post-processing will be performed using custom Matlab scripts (Matlab, Natick, MA, USA). For all tasks, the gaze data from both eyes will be converted into one data set by averaging the two-dimensional position of the gaze point of each eye relative to the screen. Gaze data will be smoothed using a symmetrical moving average filter with an averaging window of 83 ms (10 samples), with samples before and after each data point used to produce an average position.[48,88,92] Following smoothing, the x- and y-coordinate positions of both the stimulus target(s) and gaze data will be converted to absolute measures of displacement (cm) relative to the center of the monitor. Gaze velocity will be calculated via the angular displacement of gaze position over subsequent samples, N – 1, where N is the total number of gaze data samples recorded. Saccades will be

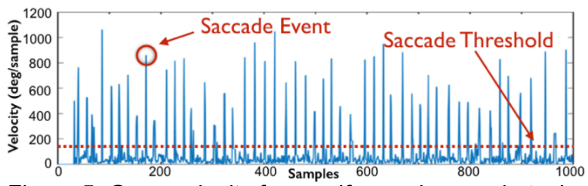


Figure 5. Gaze velocity for a self-paced saccade task. The dotted line indicates the threshold (30˚ * s^{-1}), with velocity values above the line categorized as saccadic events.

identified via a standard gaze velocity threshold of 30˚*s^{-1} (Figure 5). The saccade beginning will be identified when the gaze velocity surpasses this threshold, with the saccade end designated at the subsequent point when the velocity falls below this threshold.[48] Prosaccade latency will be computed by subtracting the beginning of the saccade from the time at which the change in target position occurred, and positional error will be computed as the absolute difference between the final position of the saccade and the center of the cross-hairs in each target. The perceptual-motor PP will be made up of self-paced saccade (i.e., positional error and variability of velocity) and prosaccade (i.e., variability of velocity) fitness measures.

5.a.4.b Neuromechanic Fitness Dimensions for Phenotypic Plasticity

Neuromechanics testing will utilize the same RT task as the preliminary hockey study. The task will require athletes to stand on dual force platforms in an athletic "ready" position (i.e., knees bent, arms at their side) with their visual attention focused on a black projector screen. After a period of time, randomized between 5 and 7 s, an arrow will appear on the screen. The arrow will point: (a) to the left, indicating a 45˚ cut forward and to the left, (b) to the right, indicating a 45˚ cut forward and to the right, or (c) vertically, indicating a vertical jump. Each athlete will be instructed to respond to the arrow with the appropriate action as quickly as possible. The task will consist of six randomized trials (two trials each of the three stimulus arrows). Each trial takes approximately 10 s to complete, so the overall task duration is approximately 90-120 s per athlete.

For the time duration prior to the onset of the visual stimulus, athletes' CoP will be measured at 50 Hz. From this data, the CoP velocity will be determined by computing the positional displacement of the combined x- and y-coordinates over subsequent samples, N – 1, where N is the total samples recorded. The subsequent CoP dynamics will be indexed using recurrence quantification analysis (RQA)[93,94], a nonlinear time series analysis that indexes the presence or absence and nature of recurrent patterns (i.e., repeating segments) within a single time series (*x*). RQA is a multistep process (described in Figure 6) that culminates with a recurrence plot (RP) that visually illustrates the patterns of recurrence in *x*. Once the RP is generated, several RQA output variables can be computed, with each one capturing the extent to which a particular pattern of recurrence is present. The current proposal will focus on percent laminarity—the percentage of darkened pixels that fall along vertical lines (in temporal succession) in the RP. Vertical lines mark time intervals in which a state does not change, or changes very slowly.[94] Thus, high laminarity equates to a movement system that is inflexible, and does not readily adapt to change.[17] RQA also requires the selection of several parameters for optimizing the analysis. Our team has extensive experience with RQA (and parameterization) in a variety of neuromechanical-based sports injury and performance contexts. We will utilize similar parameterization methods to our previous work.[17,95–97]

Peak vGRF, calculated from the vGRF time series trimmed to contain only data from stimulus onset through the athlete's body mass normalized change in vGRF (equivalent to 20 N with no body mass present) will also be computed. The peak vGRF is a measure of *power*, or the explosive force at which an athlete can execute a ballistic, full-body movement trajectory. We will compute power similarly to our published method.[98]

Neuromechanic PP will consist of CoP velocity dynamics (i.e., percent laminarity) and power (i.e., peak vGRF). Trial to trial CoP measures, and CoP velocity dynamics in particular, demonstrate reliablility[99], and power is reliable across laboratory contexts.[100,101]

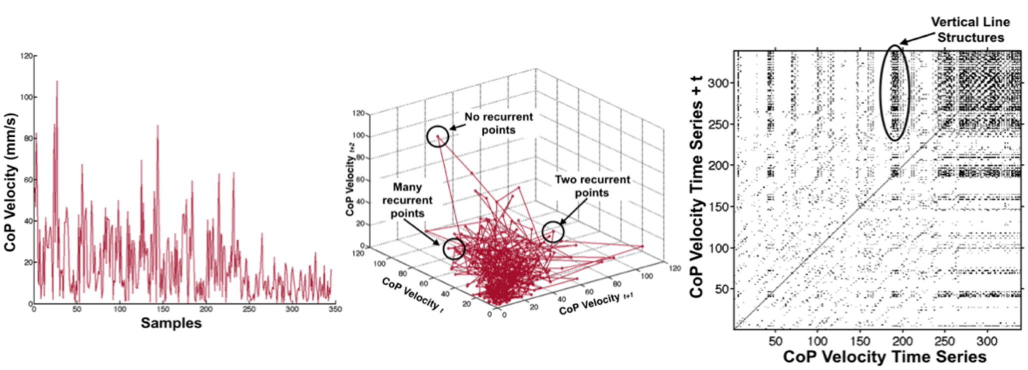


Figure 6. A schematic of the RQA multi-step process. Step 1: The original time-series (left) is embedded in multi-dimensional phase space (center). Dimensions of the space are the time-series and its delayed copies. Step 2: The distance of each data point (x_i) to every other data point (x_j) is measured. If the distance between any pair (x_i, x_j) is smaller than a pre-determined radius, the two points count as recurrent. Step 3: Create an RP – a two dimensional plot of time points of x_i vs. time points of x_j in which a darkened pixel is added at each (x_i,x_j) coordinate where a recurrence was identified (right). Step 4: Relevant measures are computed. Percent Laminarity (our target measure) is defined as the percentage of two or more consecutive darkened pixels that fall on vertical lines within one half of the RP.

5.a.5 Computing Perceptual-Motor, Neuromechanical and Combined Phenotypic Plasticity (Aims 1 & 2)

PP scores are traditionally computed from fitness scores based on a single outcome variable.[14] However, in our approach we will develop fitness scores from three variables to quantify perceptual-motor PP, and from two variables to quantify neuromechanical PP. Thus, for the computation of perceptual-motor PP, a longitudinal curve of composite perceptual-motor fitness scores will be created, based on a combination of self-paced initial positional error variability, self-paced velocity variability, and prosaccade velocity variability collected at multiple time points. The computation of neuromechanical PP will be based on a longitudinal curve of composite neuromechanical fitness scores based on CoP percent laminarity and vGRF power, also collected at multiple time points. The AUC will quantify the two PP modalities. The building of a composite PP fitness score for each modality is an innovation of the PP approach, and will be completed with an exploratory factor analysis for both PP dimensions. Specifically, a perceptual-motor composite score will be estimated based on a linear combination of self-paced initial positional error variability, self-paced velocity variability and prosaccade velocity variability. Similarly, a neuromechanical composite score will be derived based on a linear combination of CoP percent laminarity and vGRF power. Hence, we will model fitness scores as linear combinations of potential factors (with error terms). This approach will utilize the information gained from the interdependencies between our fitness variables in order to potentially reduce the set of variables in our data set, thereby allowing us to provide the most explanatory composite fitness scores for the creation of multimodal PP.

5.b. Analytic Plan to Address Aims 1 & 2

All statistical analyses will be performed using the SAS statistical package (Cary, NC) in a Microsoft Windows (Redmond, WA) environment. First, univariate descriptive statistics (e.g., means, medians, frequencies and percentages) will be examined for each variable at each data collection time point to examine the data distribution, identify outliers and/or erroneous values and the variability of the measures. We will also examine the continuous variables for deviations from normality, and transform data where appropriate.

For Aim 1, a bivariate analysis will examine the association among demographic variables and other potential confounders or covariates with outcome measures (i.e., frequency and magnitude of unanticipated collisions). We will use Chi-square, two sample *t*-test or Wilcoxon rank sum tests, as appropriate, to examine these associations. The PP measures obtained during training sessions (2 to 20 in Figure 4) will be summarized using an AUC measurement to reflect the aggregate over time. This will be done separately for the neuromechanical and perceptual-motor dimensions of PP. Next, the frequency and magnitude of collisions at post-season will be modeled as a function of the summary AUC measure of neuromechanical PP (Hypothesis 1.1) and perceptual-motor PP (Hypothesis 1.2), while accounting for potential confounders and covariates (if significant at $p<.1$ in bivariate analysis, liberally to allow inclusion of variables in the multivariate analysis). Intervention group membership will also be included as a covariate, regardless of statistically significance. Collision frequency will be modeled using Poisson regression, while collision magnitude will be modeled using a general linear model (GLM). For Hypothesis 1.3 we will fit the model using both neuromechanical and perceptual-motor fitness scores at the same time, assuming additivity to predict the outcome. This allows for the estimate of the additive effect of both measures on the prediction of the outcome, and enables measurement of the relative strength of association between each fitness score and the outcome in the presence of the other fitness scores in the model. Similar to H1.1 and H1.2, we will use Poisson regression with collision frequency measured as a function of the two PP measures (nueromechnical and perceptual-motor), while accounting for potential confounders and covariates. GLM will be used to fit collision magnitude as a function of both PP measures. As an exploratory analysis, the potential interaction effect of the two PP measures will be investigated by modeling each collision outcome (frequency and magnitude) as a function of neuromechanical, perceptual-motor and their interaction, while controlling for potential confounders. For example, $\text{Outcome}=\beta_1\text{NM}+\beta_2\text{PM}+\beta_3\text{NM}*\text{PM}+\beta_4\text{covariates}$ (with NM equal to the neuromuscular and PM equal to the perceptual-motor fitness variables). As a secondary outcome, we will model outcome as a function of all five components of the PP measures (two neuromechanical, three perceptual motor). This will allow for the evaluation of the influence of individual mechanisms for prediction of the collision-based outcomes. The goodness of fit of each model will be evaluated via goodness of fit statistics, AIC or BIC criteria, as well as the residual plot.

For Aim 2, we will compare the neuromechanical PP (Hypothesis 2.1) and perceptual-motor PP (Hypothesis 2.2), among the intervention and control group at the end of the training session using the summary AUC measures via a two-sample *t*-test for each PP dimension. We will also compare the two groups on the fitness score obtained both at the end of training and end of season using a mixed effect model (fitness score at both time points will be modeled as a function of group, time, and group × time interaction). In this model, subject ID will be included as a random effect, with group and time treated as a fixed effect. Although subject randomization will assure that covariates will be distributed equally among the two groups, imbalance in covariate distribution between the groups may still occur. Thus, we will conduct a bivariate analysis where the distribution of demographic variables and other potential confounders and covariates among the groups can be examined using Chi-square, *t*-test or Wilcoxon rank sum tests, as appropriate. Those variables found to be differentially distributed among the groups will be included in a regression model. We will use a GLM where the PP measures will be modeled as a function of group membership (aNMT or sham). A similar analysis will be conducted for comparing the post-season fitness score between the groups. As a secondary analysis, we will compare the individual components of the PP measures (two neuromechanical and three perceptual-motor) among the intervention and control groups. We will examine the goodness of fit of each model using AIC or BIC criteria, and will create a combined score using multivariate techniques such as factor analysis as well as a simple average of the AUC value obtained for each PP dimension. Importantly, both MacPherson and Harrison (data collection personnel) will be blinded to intervention group membership for all subjects, as it pertains to Aim 2.

Missing Data. While every effort will be made to minimize data loss, missing data may occur. In that case, we will examine the missing pattern to determine if missing data occurs systematically and differentially for each group. Assuming that missing data occur at random, we will use a multiple imputation technique to generate multiple datasets and systematically combine the estimates obtained from each dataset, along with the associated variability. If missing data are not at random, a sensitivity analysis recommended for clinical studies with non-monotone missing data will be utilized.[102] This method includes the use of pattern mixture modeling and shared parameter models. Suspected biases will be taken into account in the interpretation of results.

5.b.1 Power analyses for testing hypotheses 1.1, 1.2 and 1.3

The sample size for our current proposal is restricted by the number of athletes enrolled in the parent clinical trial. We anticipate, after accounting for expected attrition, 108 subjects will be available for our study. Power justification is based on our preliminary data obtained from hockey and soccer players that examined the relationship between PP and collision. For H1.1, we obtained data from male hockey players (N=10) and looked at the correlation of percent laminarity and peak power with impact force per collision to be 0.74 and -0.44, respectively. In order to detect such a correlation using 80% power at 5% significant level and adjusting for a potential 15% variation between other confounders and outcomes, the required sample size is 11 and 42 respectively. While we do not have preliminary data relating PP and frequency of unanticipated collisions, the proposed sample size is adequate and will allow us to detect correlations as small as 0.26.

For H1.2, we assessed female soccer players (N=31) and estimated the correlation between saccade dimension (based on the variability of initial saccade positional error) and number of collision to be 0.36 requiring a sample size of 65 following the specification for power, significance level and covariate adjustment as in H1.1. Similarly, we estimated the correlation of fitness score (based on the initial saccade positional error and variability of saccade velocity) with impact force to be 0.44 and 0.39, respectively. Using the same specification as above, the required sample size to detect such effects are 42 and 55.

For H1.3, we expect the additive effect of PP based on perceptual-motor and neuromechanical mechanisms will increase the correlation with collision beyond that which each of the individual PP measures will produce individually. Thus, the sample size needed to detect a higher correlation value should be less than proposed for the individual PP measures. For Aim 1, the required sample size based on our preliminary data range from 11 to 55 athletes. The proposed sample size of 108 will, therefore, provide adequate power to test all of the hypotheses of Aim 1 even after adjusting for potential multiple testing issues induced by multiple outcomes.

5.b.2 Power analyses for testing hypotheses 2.1, 2.2 and 2.3

For H2.1 and H2.2 our power justification is based on data obtained from 11 female volleyball athletes, using knee extensor moment as a proxy for a power-based fitness score and PP. In this pilot intervention study, the athletes performed a single session of aNMT. The mean and standard deviation of the baseline knee moment was -120.65±23.4 Nm. Based on a two sample t-test, 80% power and 5% significance level, for the proposed sample size of 108 (54 per intervention arm), we should be able to detect an 11% reduction in the outcome in the intervention group. Note that the anticipated number of available subjects of 54 per group for this study, as proposed by the parent clinical trial factors in an expected drop-out of 24 athletes over the life of the study.

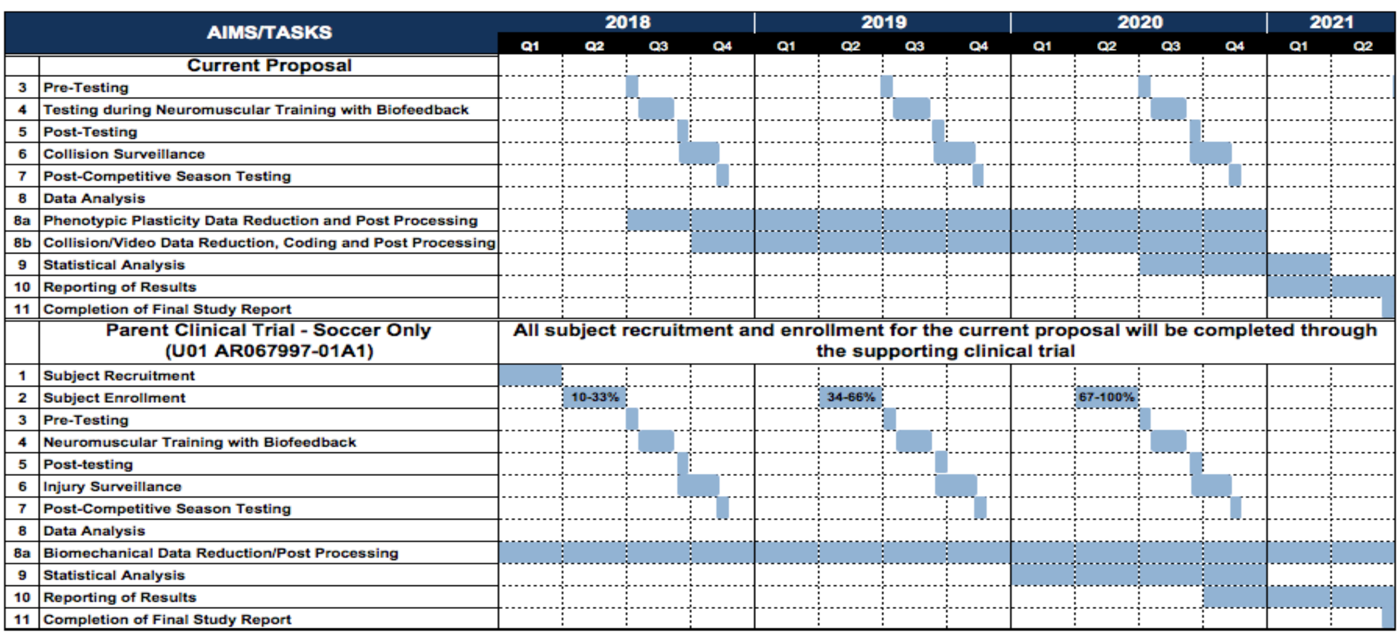
6. Expected Outcomes

Aim 1 will evaluate whether three prospective PP measures—perceptual-motor, neuromechanical, or both neuromechanical and perceptual-motor—predict the frequency and magnitude of unanticipated collisions on the field of play. We expect that the associative relationships identified in this Aim will provide insights into mechanisms that lead to unanticipated collisions, increased impact forces, and the resultant musculoskeletal injuries. The obtained mechanistic insights will enhance the value of the parent project through the accomplishment of the following expected outcomes. First, we expect to identify a highly sensitive fitness-based, risk profile for injuries related to unanticipated collisions. This profile will be based on the results of Aim 1 and will guide the selection of athletes for participation in prevention programs. Second, by completing Aim 2, we will determine aspects of the identified risk profile that can be modified by aNMT. The results of Aim 2 will reveal the specific effects of a pre-season aNMT intervention on both mechanisms. While aNMT was designed to prevent non-contact ACL injury, neuromechanical adaptations promoted by aNMT likely enable additional preventative benefits to collision-based injury. The principles of aNMT prompt athletes to utilize an external focus of attention to the environment and away from joint-specific movement positions. Thus, aNMT is expected to promote the coupling between neuromechanical and perceptual-motor control supportive for prevention of unanticipated collisions and related injuries. If so, aNMT will be expanded to the prevention of collision-based injuries and with a significantly enhanced impact. If aNMT does not fully (or effectively) modify the mechanisms underlying PP, we expect the results to provide a strong empirical basis for modifying the aNMT protocol, or advancing new epidemiological-based training interventions for the unanticipated collisionreduction and mitigation.

7. Potential Problems and Alternative Approaches

Given the synergy between this ancillary proposal and the parent project, we will rely on previously addressed strategies from the parent project for dealing with potential problems of participant drop-out and/or non-adherence. Athletes will be directly bussed to and from our facility to overcome transportation limitations, and the training interventions will provide the same phenomenological experience so as to maintain engagement, regardless of group membership. The parent grant will also utilize stratified randomization within team and school to provide optimal comparisons, which we will also leverage in the ancillary proposal. One potential problem that is unique to the ancillary proposal is whether the AUC measure that defines PP will effectively capture a sensitive and specific measure to determine the association between PP and collision-based outcomes. We are pioneering the PP approach for use in sports medicine and, thus, it is very possible that there will be unforeseen limitations. Should such issues come to pass, we will propose modelling techniques (linear or nonlinear) that utilize data from all time points to further increase sensitivity of our PP outcome measures. For example, assuming linearity, we can fit PP using the equation, PP=B0+B1time+B2group+B3time*group+b4*covariates, and fit a linear mixed effect model, to evaluate the hypothesized group differences in Aim 2. A similar modelling strategy (without the group terms) will be used to evaluate the hypotheses in Aim 1. Thus, we are confident that our analytic approach will be successful, even in the face of unexpected limitations.

8. Proposed Timeline



9. Additional Opportunities

The 2D video will provide a number of outcome variables beyond identification and validation of unanticipated collisions. Specifically, injury surveillance (in combination with the parent grant), field zone, athletic action and positioning at the time of collision will all be coded and available for further analysis. While these variables are not central to the Aims and objectives of the current proposal, they provide an additional opportunity to evaluate the role PP plays in on-field activities known to relate to injury.[4,8] In addition, these data will provide additional opportunities for the parent clinical trial to gain important pilot data relative to the effect of aNMT on injury prevention beyond biomechanical risk factors.