

PAIN CATASTROPHIZING IN INDIVIDUALS WITH ANTERIOR CRUCIATE LIGAMENT
RECONSTRUCTION

By

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ABSTRACT

Individuals who sustain an anterior cruciate ligament (ACL) injury and undergo subsequent ACL reconstruction (ACLR) frequently experience psychological responses to their injury. Increased injury-related fear post-ACLR has been found to be associated with neuroplastic adaptations and injury-related outcomes including perceptual-motor coordination (P-MC) and landing biomechanics. However, limited evidence has explored the impact of pain-related psychological responses, such as pain catastrophizing, on neural function and injury-related outcomes in individuals with ACLR. Understanding the association between pain catastrophizing and neural mechanisms that may contribute to functional and injury-related outcomes after ACLR could allow for identification of modifiable factors that, if addressed throughout rehabilitation, may positively influence clinical outcomes and secondary injury risk among individuals with ACLR. Therefore, the purposes of this three-study dissertation were to: 1) examine the influence of pain catastrophizing on lower extremity perceptual-motor coordination (P-MC) after ACLR, 2) explore the relationship between pain catastrophizing and neural activity in individuals with ACLR, and 3) examine the influence of pain catastrophizing on changes in P-MC and jump-landing biomechanics in a setting with distractions that mimic a sport environment in individuals with ACLR.

In the first cross-sectional study assessing the influence of pain catastrophizing on lower extremity P-MC, 45 individuals with ACLR completed the Pain Catastrophizing Scale (PCS) and a lower extremity P-MC task with the ACLR limb and contralateral limb using a series of wireless light discs. Separate multiple regression analyses identified that pain catastrophizing was not associated with ACLR limb P-MC ($\beta=0.002$, $p=0.247$) or contralateral limb P-MC ($\beta=0.001$, $p=0.410$) in individuals with ACLR. These findings indicate that pain catastrophizing may not contribute to lower extremity perceptual-motor function after ACLR.

In the second study exploring the relationship between pain catastrophizing and neural activity, 15 individuals with ACLR completed the PCS and underwent full brain functional

magnetic resonance imaging while engaging in a picture imagination task (PIT) that included images depicting activities of daily living (ADL) and physical activity. A whole-brain exploratory analysis revealed pain catastrophizing to be correlated with neural activity in brain regions associated with aspects of emotional perception and processing, anticipation of pain, memory, attention, and visuospatial function when imagining completing ADLs and physical activity. The findings of this study suggest that individuals with ACLR who exhibit greater pain catastrophizing may experience altered brain activity when engaging in ADLs and physical activity, however these results should be interpreted with caution given there were no significant correlations present after correcting for multiple comparisons ($p>0.10$).

In the third study examining the influence of pain catastrophizing on changes in P-MC and jump-landing biomechanics in a setting with distractions that mimic a sport environment, 23 individuals with ACLR completed the PCS, a lower extremity P-MC task, and a jump-landing task in the presence of sport-specific visual and auditory stimuli (distraction condition) and without the sport-specific visual and auditory stimuli (control condition). Differences in lower extremity P-MC and peak vertical ground reaction force (vGRF) symmetry between the distraction and control condition were calculated and separate multiple linear regression analyses indicated that PCS scores were not significantly associated with the change in ACLR limb P-MC ($\beta=0.001$, $p=0.477$), contralateral limb P-MC ($\beta=0.001$, $p=0.438$), or peak vGRF symmetry ($\beta=-0.117$, $p=0.855$) between conditions. These study findings suggest that pain catastrophizing may not be a critical psychological factor impacting perceptual-motor or biomechanical injury-related outcomes in sport-like settings in individuals with ACLR.

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CHAPTER 1: INTRODUCTION

STATEMENT OF THE PROBLEM

Anterior cruciate ligament (ACL) tears are a common sport and physical activity-related injury with over 200,000 tears occurring annually.¹ Individuals who sustain an ACL injury frequently pursue surgical intervention to repair the integrity of the ACL, restore knee function, and return to previous levels of activity.^{2,3} However, 30% of individuals who return to high levels of physical activity after ACL reconstruction (ACLR) will sustain a second ACL injury within 24-months of return to sport (RTS).⁴ Previous research has identified common psychological responses to injury, specifically injury-related fear, to be associated with neuroplastic adaptations that may contribute to errors in motor coordination after ACLR,⁵ and injury-related outcomes including lower extremity biomechanics and perceptual-motor coordination (P-MC).^{6,7} However, the association of pain-related psychological responses experienced after ACLR, such as pain catastrophizing, with these critical outcomes has yet to be explored among individuals with a history of ACLR.

Pain catastrophizing is a cognitive-affective response to anticipated or actual pain and is characterized by rumination (i.e., difficulty in shifting attention away from pain), magnification (i.e., perceiving pain as unusually more intense), and helplessness (i.e., feeling helplessness in controlling pain).⁸ Pain catastrophizing is considered a natural psychological response after ACL injury and has been identified among individuals at pre-surgical timepoints,^{9,10} immediately post-ACLR,^{10,11} throughout the rehabilitation process,^{10,12-14} and approximately one to two-years post-ACLR.^{15,16} Unfortunately, increased pain catastrophizing post-ACLR negatively influences pertinent clinical and injury-related outcomes such as pain severity and self-reported knee function throughout the rehabilitation process.^{10,17} Furthermore, among healthy individuals, those who report higher levels of pain catastrophizing exhibit greater attentional interference during task completion when anticipating pain.^{18,19} Individuals with ACLR and increased pain catastrophizing may

consequently experience difficulty in diverting attention away from anticipated or actual pain during sport-specific tasks and activities of daily living.

Sport performance and the execution of complex motor skills requires an athlete to simultaneously attend to relevant information while excluding irrelevant information and distracting stimuli.²⁰⁻²³ However, individuals who experience pain catastrophizing and a heightened anticipation of pain are more likely to shift their attentional resources to the expected threat.^{24,25} This may adversely affect the ability to respond to the surrounding environment and consequently impact injury-related outcomes during sport. Both P-MC, the ability to interpret and use sensory information to execute motor tasks,²⁶ and jump-landing biomechanics are critical components of sport participation and are predictive of lower extremity injury.²⁷⁻³⁰ Therefore, determining which factors may influence jump-landing biomechanics and P-MC after ACLR is critical to reduce secondary injury risk upon RTS after ACLR.

Individuals with history of ACL injury and reconstruction also exhibit a variety of neuroplastic alterations that may negatively influence clinical outcomes such as neuromuscular control.³¹ The neuroplastic alterations examined in this population may occur as a result of the damage to the native ligament and subsequent disrupted sensory feedback to the brain.³² Increased activation of brain regions associated with emotional regulation, and alterations in regions associated with motor, visual, cognitive, and pain processing have been observed.³³⁻³⁵ Due to the connection between pain catastrophizing and brain regions associated with pain perception,³⁶ it is possible that increased activation of pain-related areas among individuals with ACLR may result from psychological processes that can influence an individual's pain experience, such as pain catastrophizing, thus warranting further investigation of this outcome in this population.

When considering that individuals with history of primary ACLR have an increased risk of secondary ACL injury and experience varying degrees of pain catastrophizing after their injury

and subsequent reconstruction, there is a critical need to identify whether pain catastrophizing is associated with neural function after ACLR and to characterize the role of pain catastrophizing on injury-related outcomes in this population.

STATEMENT OF PURPOSE

Individuals with ACLR commonly exhibit psychological responses to their injury that are associated with neuroplastic adaptations and that may negatively influence functional outcomes, RTS, and risk of secondary ACL injury.³⁷⁻³⁹ However, limited evidence has explored pain-related psychological responses experienced after ACLR, like pain catastrophizing. As a result, it is unclear whether pain catastrophizing is associated with neural mechanisms that may impact injury-related outcomes for individuals with a history of ACLR. In the absence of such knowledge, individuals with ACLR may continue to demonstrate poor outcomes and increased risk of secondary injury upon RTS. Therefore, the purposes of this dissertation are threefold: 1) to examine the influence of pain catastrophizing on lower extremity P-MC after ACLR, 2) to explore the relationship between pain catastrophizing and neural activity in individuals with ACLR, and 3) to examine the influence of pain catastrophizing on changes in lower extremity P-MC and jump-landing biomechanics in a setting with distractions that mimic a sport environment.

RESEARCH QUESTIONS AND EXPERIMENTAL HYPOTHESES

Manuscript 1 Research Question and Experimental Hypothesis

Primary Purpose 1.1

The primary purpose of this study was to examine the influence of pain catastrophizing on lower extremity P-MC in individuals 4-months to 5-years post-ACLR.

Hypothesis 1.1

The primary hypothesis is that individuals with ACLR who exhibit higher levels of pain catastrophizing will demonstrate worse lower extremity P-MC.

Manuscript 2 Research Question and Experimental Hypothesis

Primary Purpose 2.1

The primary purpose of this study was to examine the association between pain catastrophizing and neural activity during a picture imagination task (PIT) among individuals 4-months to 5-years post-ACLR.

Hypothesis 2.1

The primary hypothesis is that individuals with ACLR who exhibit higher levels of pain catastrophizing will demonstrate increased blood oxygen level dependent (BOLD) percent signal changes in brain regions associated with pain perception and/or emotional regulation during a PIT.

Manuscript 3 Research Question and Experimental Hypothesis

Primary Purpose 3.1

The primary purpose of this study was to examine the influence of pain catastrophizing on changes in lower extremity P-MC and peak vertical ground reaction (vGRF) symmetry in the presence of sport-specific visual and auditory stimuli in individuals 1- to 5-years post-ACLR.

Hypothesis 3.1

The primary hypothesis is that individuals with ACLR and greater pain catastrophizing will exhibit larger changes in P-MC and vGRF symmetry in the presence of sport-specific distraction.

SIGNIFICANCE OF THE STUDY

Psychological response to injury is a critical factor in recovery after ACLR and may affect injury-related outcomes including P-MC and lower extremity landing mechanics. However, little is known about the association of pain catastrophizing with central and peripheral neural mechanisms that may influence functional and injury-related outcomes among individuals with a history of ACLR. Better understanding of these mechanisms will allow for identification of

modifiable outcomes that, if addressed throughout ACLR rehabilitation and recovery, may positively influence clinical outcomes, and reduce the risk of secondary injury among individuals with ACLR.

CHAPTER 2: REVIEW OF LITERATURE

INTRODUCTION

This literature review will begin by exploring the epidemiology of anterior cruciate ligament (ACL) injury and reconstruction with brief discussion of risk factors for primary and secondary ACL injury. Next, this review will discuss rehabilitation practices after ACL reconstruction (ACLR) and pertinent outcomes after ACLR including pain catastrophizing, neurocognitive function, landing kinetics, neural activity, and associated outcome measurement techniques. Finally, this review will summarize psychosocial factors and perceptual changes that may occur during stressful situations and the connection to injury risk.

EPIDEMIOLOGY OF ACL INJURY AND ACLR

ACL Anatomy

The knee joint is responsible for providing both motion and stability during static and dynamic activity.⁴⁰ The combination of motion and stability is provided by the interaction of bony structures, ligaments, menisci, and surrounding musculature.⁴⁰ The tibiofemoral joint, comprised of the femur, tibia, and patella, is a synovial hinge joint that allows movement in flexion and extension, as well as minimal internal and external rotation.⁴¹ Primary stabilization of the knee is provided via ligaments which are fibrous bands of tissue that connect bone to bone.⁴¹ The primary stabilizing ligaments of the knee include the transverse, arcuate, popliteal, oblique popliteal, popliteofibular, medial collateral, lateral collateral, posterior cruciate and anterior cruciate ligaments.⁴¹

The ACL is considered the main stabilizer of the knee and prevents anterior displacement of the tibia on the femur.⁴¹ From its origin on the medial aspect of the lateral femoral condyle, the ACL passes anteriorly, distally and medially to the tibia where it attaches in the anterior aspect of the intercondylar fossa.⁴² The ACL can be further separated into two bundles: the posterolateral bundle which bears most of the load when the knee is in full

extension or at 15% of flexion and the anteromedial bundle which bears the majority of load when the knee is past 30% of flexion.⁴³

In addition to providing mechanical stability, the ACL plays a critical role in proprioceptive function and contains various mechanoreceptors including Ruffini corpuscles, Paccinian corpuscles, Golgi Tendon-type organs, and free nerve endings which contribute to functional stability of the knee joint.^{44,45} Together, the Paccinian, Ruffini, and Golgi Tendon-type organs detect changes in tension, speed, acceleration, and direction of movement while also allowing an individual to determine the position of their knee joint in space.⁴⁶⁻⁴⁹ When the ACL is injured, it is hypothesized that damage to the mechanoreceptors alters neuromuscular function of the knee due to reduced processing of somatosensory information.^{45,50}

Primary ACL Injury Epidemiology

Over 200,000 ACL injuries occur on an annual basis and are frequently the result of sport participation.^{1,51} The ACL may be injured as a result of a contact (e.g., player-player contact, player-playing surface contact, player-playing apparatus contact) or non-contact mechanism (e.g., landing, plant-and-cut maneuvers).^{52,53} Previous research has identified that approximately 72% of ACL injuries result from non-contact mechanisms that involve changes in velocity or increases in multidirectional forces through the knee joint during weight bearing which may include activities such as landing, cutting, or sudden deceleration.⁵³⁻⁵⁵ Consequently, ACL injuries occur commonly in sports that involve these types of movements, with the highest incidence of ACL injuries occurring in alpine skiing, soccer, basketball, and football.^{56,57} When controlling for athletic exposure and population size, female athletes have a higher incidence of ACL injury in an athletic season, regardless of participation level,⁵⁸ and are at greater risk of ACL injury during contact sport participation when compared to male athletes.⁵⁹ When taking into account participation level, the difference in ACL injury incidence rate between females and males is reported to be highest for amateur athletes.⁵⁸ Incidence of ACL injury between males and females may also differ by age. It is estimated that 50% of individuals who sustain an ACL

injury are between the ages of 15 and 25.⁵⁷ However, for males the incidence rate is higher between the ages of 19-25 whereas for females the incidence rate is higher between the ages of 14 and 18.⁶⁰

Risk Factors Associated with Primary ACL Injury

A variety of non-modifiable and modifiable factors have been linked to ACL injury risk. Non-modifiable factors, which cannot be altered, include factors such as biologic sex while modifiable factors, which may be addressed through intervention, include factors such as muscular strength and function, neurocognitive function, and lower extremity biomechanics.

Increased risk of ACL injury among females has been previously attributed to anatomical, biomechanical, and neuromuscular differences that commonly arise after puberty.⁶¹⁻
⁶³ Specifically, females exhibit differences in bony knee geometry, have smaller ACLs with decreased stiffness, and greater laxity of the ACL when compared to males which may contribute to ACL injury risk in this population.⁶⁴⁻⁶⁷ Additionally, female athletes demonstrate unique movement patterns with greater landing forces and force loading rates.⁶⁸ Differences in muscle activation patterns including increased dependence on activation of the quadriceps muscles when compared to the hamstring muscles, decreased gluteus maximus activity, and smaller medial-to-lateral activation ratio of the quadriceps and hamstrings have also been demonstrated by females.^{69,70} Furthermore, although certain neuromuscular training programs have been shown to address ACL injury risk factors among female athletes,⁷¹⁻⁷³ young female athletes are frequently not offered the same strength and conditioning-specific training opportunities when compared to their male counterparts.⁷⁴ This lack of access to strength and conditioning programs shown to optimize performance and mitigate injury risk may also contribute to the increased risk of ACL injury among females.

Modifiable outcomes, including muscular strength and neuromuscular function, also impact the risk of sustaining an ACL injury. Strength deficits of the hip abductors, external rotators, and the hamstrings may be considered predisposing risk factors for non-contact ACL

injury.^{75,76} Furthermore, decreased resistance to fatigue of the hamstring group, strength imbalances between the hamstrings and quadriceps muscle groups, and deficits in neuromuscular control of the trunk may also contribute to ACL injury.^{77,78} In addition to adequate neuromuscular function, sport performance requires adequate higher level neurocognitive functioning (e.g., working memory, inhibition control, and cognitive flexibility), and lower order cognitive functioning (e.g., visual attention, processing speed, and dual tasking) to successfully adapt to changing environmental cues during sport.⁷⁹⁻⁸¹ Previous research has identified neurocognitive function as a predictor of non-contact ACL injuries among athletes.²⁸ Specifically, when measured at baseline, athletes who went on to sustain a non-contact ACL injury exhibited slower reaction time and processing speed, in addition to lower visual and verbal memory scores when compared to uninjured athletes.²⁸

Individuals at risk of sustaining an ACL injury also commonly exhibit aberrant lower extremity movement patterns including increased knee abduction angle/moment and decreased knee flexion angles.^{82,83} Additionally, injury risk may be increased by faulty movement patterns at other locations of the kinetic chain, including the hip and foot. Lateral displacement of the trunk during perturbation and increased heel to flat-foot loading mechanisms during landing have been associated with ACL injury.^{78,84} Stiff landings, often identified through alterations in kinematics (e.g., decreased knee flexion angle) and kinetics (e.g., higher ground reaction forces (GRFs) upon landing), also contribute to knee instability and have been linked to ACL injury.^{29,85,86} Previous research has identified 20% larger peak vertical GRFs (vGRF) during landing among individuals who go on to injure their ACL compared to those who do not experience an ACL tear.³⁰

ACL Reconstruction

Upon injury to the ACL, individuals may pursue a non-surgical treatment approach through structured rehabilitation or pursue surgical intervention in which the ACL is reconstructed (ACLR). Of the 200,000 ACL injuries that occur annually, more than half will

undergo surgical reconstruction at an estimated annual cost of \$4 billion.^{87,88} The primary goal of ACLR is restore the function of the ACL and improve knee joint stability.⁴² The ACL is reconstructed with a graft that attempts to mimic both the anatomical and biomechanical properties of the native ACL.⁸⁹ This allows for adequate fixation and biological integration of the graft subsequently improving recovery time.⁸⁹ Given these parameters, a variety of autografts or allografts may be used for the reconstruction. Popular autografts, or tissues taken from the patient's body, include the bone-patellar-bone tendon graft, hamstring tendon graft, or quadriceps tendon graft.⁸⁹ Allograft choices, which come from a cadaver, commonly include the achilles tendon, tibialis posterior tendon, tibialis anterior tendon, bone-patellar-bone tendon (BPTB), or peroneus longus tendon.⁸⁹ Graft choice is frequently dependent on factors such as age, functional demands, pre-existing anterior knee pain, and surgeon preference.⁹⁰ However, graft type may influence numerous patient outcomes post-ACLR such as self-reported symptoms, knee function and strength, and pain.⁹¹⁻⁹³ These variables should therefore be taken into consideration prior to ACLR.

The BPTB graft has historically been a popular graft choice due to its equivalent strength and stiffness to the native ACL.⁹⁴ Furthermore, patients who receive a BPTB graft exhibit a high rate of return to pre-injury levels of physical activity.⁹⁵ However, use of this graft has also been linked to higher incidence of complications including quadriceps weakness,^{96,97} development of patellar tendonitis,^{96,97} loss of knee extension,⁹⁸ and anterior knee pain which occurs in 5 to 55% of cases.⁹⁰ Similar to the BPTB graft, the hamstring graft demonstrates good tensile strength and increased rate of return to pre-surgical conditions, but also allows patients to maintain adequate extension range of motion and has a high patient satisfaction rate.^{99,100} Despite these benefits, patients who use a hamstring graft may experience a longer healing process and demonstrate short-term deficits in peak hamstring muscle torque.^{90,101} In 2010, only 2.5% of ACL reconstructions used the quadriceps tendon graft,¹⁰² however this graft choice has since become more popular due to evidence demonstrating similarities in stability outcomes,

functional outcomes, range of motion, patient satisfaction, and complications when compared to other graft options.¹⁰³

REHABILITATION AFTER ACLR

Current Practices

The main goals of ACLR rehabilitation are to prevent deficits in range of motion and to restore muscular strength while protecting the graft.^{104,105} The rehabilitation process traditionally includes four post-operative phases: phase 1 (0-2 weeks post-surgery), phase 2 (2-6 weeks post-surgery), phase 3 (6-14 weeks post-surgery), phase 4 (14-22 weeks post-surgery), and phase 5 (22 weeks post-surgery and onward).¹⁰⁶ Early post-operative phases prioritize gaining full knee extension, decreasing edema, and the initial development of quadriceps strength. Throughout subsequent phases, neuromuscular training should be integrated into rehabilitation and therapeutic exercises should progress in difficulty to maximize strength and meet the demands of daily activity. The late phase of rehabilitation should prepare patients to meet the demands of their individual sport activity and may include plyometric and agility activities.¹⁰⁶ However, rehabilitation protocols have recently begun shifting towards a more individualized approach, considering patient-specific needs, and using clinical milestones to determine progression as opposed to timepoints which has demonstrated improvements in patient function and earlier return to sport.¹⁰⁵ Upon completion of the rehabilitation program, a variety of criteria including strength, physical performance-based criteria, and patient-reported criteria, are commonly used to determine a patient's readiness to return to sport.¹⁰⁷ However, recent literature have highlighted the importance of using a holistic rehabilitative approach by examining psychological variables that may influence recovery and return to sport following ACLR to maximize patient outcomes.^{105,108-110}

Psychological factors, such as fear of reinjury and lack of confidence, are commonly experienced after ACLR recovery and have been cited as barriers for RTS and physical activity.¹¹¹ Furthermore, psychological responses exhibited among this population have been

linked to critical clinical outcomes including quadriceps weakness and self-reported knee function which may negatively influence recovery.¹¹¹ Therefore, implementation of psychologically informed practice in the clinical setting and measurement of psychological factors that are likely to affect an individual's recovery is imperative to improve short- and long-term outcomes for patients who demonstrate psychological deficits post-ACLR. This examination and treatment approach integrates psychoeducation, cognitive behavioral, and acceptance and commitment techniques with traditional musculoskeletal rehabilitation to address psychological factors that could affect outcomes after injury.¹¹² Common intervention strategies used in clinical practice to improve psychological response to injury may include patient education, imagery, goal setting, relaxation, self-talk, and graded exposure.¹¹³

Limitations in Current Practice

Rehabilitation programs and the progression of activity post-ACLR most commonly occurs in a controlled environment such as a physical therapy clinic or athletic training facility. Although functional assessments may be used to mimic the physical demands of sport participation and determine readiness to RTS,¹¹⁴ individuals post-ACLR may have limited exposure to settings that include common distractions and stressors experienced during sport. This is concerning as stressful events may increase risk of injury by causing decreased vigilance which is the ability to sustain attention and remain alert over extended periods of time.^{115,116} In sport settings, auditory and visual changes that occur in the surrounding environment may shift attention away from skill performance and increase injury risk.¹¹⁷⁻¹¹⁹ Without the ability to maintain attention or filter irrelevant information during a task, individuals are less likely to simultaneously execute complex motor skills,^{17,18} which may increase risk of injury during sport. Furthermore, the Stress and Injury Model proposes that psychological factors may influence injury outcomes through changes in an individual's stress response (Figure 2.1).¹²⁰ The central hypothesis of this model is that when experiencing a stressful athletic situation, individuals with a history of stressors, certain personality characteristics, and

limited coping resources will appraise the situation as more stressful and consequently experience an altered stress response.¹²⁰ This stress response, marked by negative physiological and attentional changes, may then lead to increased risk of injury.¹²⁰

Since the proposal of the Stress and Injury Model, research has identified psychosocial factors and perceptual changes, specifically negative life events and peripheral narrowing, to be predictive of injury occurrence.¹²¹ Furthermore, previous research has identified visual and auditory peripheral narrowing in stressful conditions during completion of a task.¹²²⁻¹²⁴ In a study examining recreational athletes, those with increased occurrence of major life events within the previous year reported higher state anxiety and exhibited greater peripheral vision narrowing in a high stress condition (e.g., performance of a cognitive task in the presence of auditory distraction) when compared to athletes who had experienced fewer major life events.¹²⁵

Given that pain catastrophizing is traditionally viewed as a maladaptive coping strategy,¹²⁶ history of an ACL rupture combined with pain catastrophizing may negatively influence an athlete's cognitive appraisal of a stressful athletic situation and consequently alter their stress response. The resulting physiological and attentional adaptations may lead to loss of coordination when performing sport-related skills and affect injury-related outcomes, such as lower extremity landing mechanics and P-MC and increase risk of secondary ACL injury. Therefore, there is a critical need to identify the impact of pain catastrophizing on injury-related outcomes in a setting with attentional demands and stressors that mimic a sport-environment to identify interventions that may assist in reducing risk of secondary ACL injury.

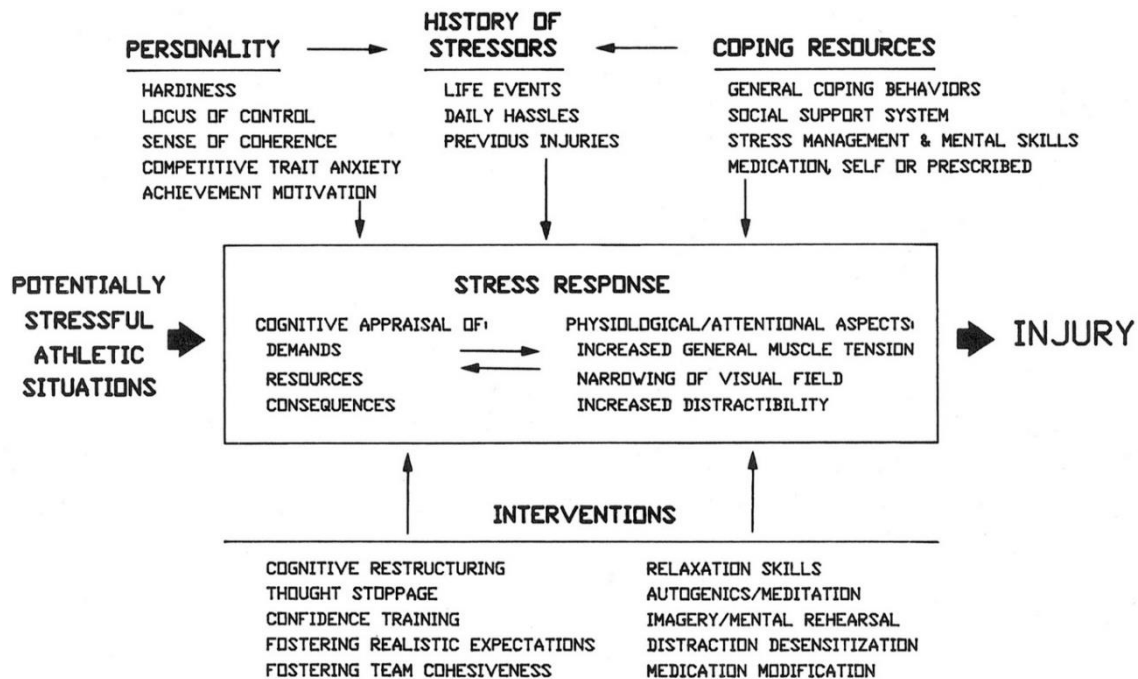


Figure 1.1: The theoretical model of stress and athletic injury which serves as a framework for the prediction and prevention of stress-related injuries.

RISK FACTORS FOR SECONDARY ACL INJURY: A BRIEF OVERVIEW

Of the patients who undergo ACLR to improve functional stability of the knee joint, up to 28% will experience a secondary ACL injury.^{127,128} This increased risk of secondary injury has been linked to a variety of factors such as age, activity level, biologic sex, lower extremity biomechanics, neuroplastic alterations, and psychological responses associated with ACLR.

Younger individuals (<25 years) and those who return to high levels of activity have a secondary ACL injury prevalence of 23%, an ipsilateral reinjury prevalence of 10%, and a contralateral reinjury prevalence of 12%.¹²⁹ Furthermore, young females with ACLR are more likely to sustain a second ACL injury within the first 2 years following primary ACLR when compared to males with ACLR.⁴ After primary ACLR, females also consistently exhibit poorer clinical outcomes than males including worse neuromuscular function and decreased self-reported knee function which are associated with secondary ACL injury risk.^{130-132,6}

After primary ACLR, individuals also exhibit changes in lower extremity biomechanics and neuromuscular function. In a study exploring biomechanical differences between athletes with history of ACLR who returned to sport, it was found that individuals who sustained a secondary ACL injury exhibited alterations in landing with transverse plane hip kinetics, frontal plane kinematics, sagittal plane kinetics, and postural stability when compared to athletes with primary ACLR that did not sustain a secondary injury.¹³³ Greater knee kinetic asymmetry during jump-landing among individuals returning to sport and physical activity post-ACR is also associated with increased risk of secondary ACL injury.¹³³

The altered movement control exhibited by individuals with ACLR may be a result of central nervous system (CNS) adaptations that occur after ligamentous injury. It has been proposed that the peripheral joint injury and subsequent pain, inflammation, peripheral deafferentation, and laxity cause a disruption in sensory feedback to the CNS which consequently leads to altered motor output and a negative cycle of altered feedback and output.³² This ultimately causes the functional reorganization of the somatosensory and motor cortices of the brain frequently exhibited by individuals with ligamentous injury and may contribute to the functional deficits that increase risk of injury after ACLR.^{32,35} This theory has been further supported by findings that an individual with ACLR exhibited increased activation of brain regions responsible for motor-planning, sensory-processing, and visual-motor control approximately 26 days prior to experiencing a contralateral ACL injury.¹³⁴

Psychological variables associated with ACL injury and reconstruction have also been linked to secondary injury risk after ACLR. Previous research has identified that individuals with scores of 19 or greater on the Tampa Scale of Kinesiophobia-11 (TSK-11), which assesses fear of movement/reinjury, at the time of RTS are 13 times more likely to suffer an ipsilateral, but not contralateral, second ACL injury within 24 months of RTS.³⁷ Younger patients with lower psychological readiness, which is assessed via emotions, confidence, and risk appraisal for sport (i.e., the perception that sport participation is associated with risk of injury), similarly

demonstrate increased risk of second ACL injury upon RTS.³⁸ Interestingly, literature has also identified higher risk of secondary ACL injury among female athletes who report better psychological readiness.¹³⁵ These results were postulated to be due to athletes perceiving their risk of secondary injury as low and having minimal concern about experiencing surgery and rehabilitation a second time.¹³⁵ These beliefs could therefore result in an overconfidence in their sport-related ability and early RTS which may consequently increase injury risk.¹³⁵ Likewise, individuals with higher self-reported knee confidence have been identified to be two times more likely to suffer a second ACL injury when compared to those with lower confidence.¹³⁶

The following sections will provide theoretical support for the exploration of pain catastrophizing after ACLR, as well as a more in-depth discussion of outcomes associated with pertinent secondary ACL injury risk factors (i.e., perceptual-motor coordination, landing kinetics and kinematics, and neuroplasticity after ACLR) and related measurement techniques.

PAIN CATASTROPHIZING AFTER ACLR

Pain catastrophizing is defined as an “exaggerated negative mental set brought to bear during actual or anticipated painful experience” and is considered a key cognitive factor in emotional dysregulation.^{126,137} This cognitive-affective response to actual or anticipated pain is characterized by three primary components: magnification (e.g., perceiving pain as unusually more intense), helplessness (e.g., feeling helpless in controlling pain), and rumination (e.g., difficulty in shifting attention away from pain).⁸ Due to these factors, pain catastrophizing may interfere with the capacity to inhibit thoughts and switch focus of attention, which are important aspects of executive function.^{137,138} Pain catastrophizing is also considered one of the most reliable predictors of an individual’s pain experience and is strongly associated with a variety of clinical pain-related outcomes in both pain-free and chronic pain populations.^{126,139-141} Specifically, associations have been observed between pain catastrophizing and clinical pain severity, pain-related activity interference, disability, exaggerated negative mood and depression, emotional distress, and alterations in social support networks.^{126,139,142} Furthermore,

in surgical populations, increased pre-surgery pain catastrophizing has been linked to differences in post-surgical pain ratings, narcotic usage, depression, pain-related activity interference and disability levels.¹⁴³⁻¹⁵⁰

Among individuals with ACLR, pain catastrophizing has been investigated in a small number of studies and has been identified through use of the Pain Catastrophizing Scale (PCS) in this population at pre-surgical timepoints, throughout rehabilitation, and up to approximately two-years post-ACLR.⁹⁻¹⁶ Although pain catastrophizing may be considered a natural psychological response after ACL injury,¹⁰ it can negatively influence critical clinical outcomes for individuals with ACLR. Previous research has identified high levels of pain catastrophizing immediately following initial ACL injury and reconstruction to be associated with increased knee pain post-ACLR which may negatively affect rehabilitation outcomes.¹⁰ Specifically, individuals who exhibit higher levels of catastrophic thinking report worse knee function during the post-operative phase, as well as at the conclusion of a subsequent rehabilitation program.¹² Furthermore, higher pain catastrophizing scores are associated with depressive symptoms 2-weeks after ACLR which may consequently increase symptom severity and negatively impact participation in rehabilitation.^{13,151} Although patients commonly report high levels of pain catastrophizing after initial ACL injury and in the immediate post-operative phase, it has been found that PCS scores may steadily decline throughout the ACLR rehabilitation process.^{10,12}

Theoretical Perspectives

Various theoretical models have been used to explain the role of pain catastrophizing on an individual's multidimensional pain experience.^{126,152-158} Most recently, the Neuromatrix Theory of Pain and Transactional Model of Stress and Coping have been used to improve understanding of the development and effects of pain catastrophizing specifically among individuals with ACLR.¹⁵⁹ Integration of the proposed ideas that follow may better explain how individual appraisal-specific factors (e.g., values, beliefs, and expectations) could interact with

predetermined genetic components or neural changes and how these factors may influence appraisal of pain and coping in individuals with ACLR.¹⁵⁹

Traditionally, pain has been depicted as a sensation produced solely by injury, inflammation, or tissue pathology.¹⁶⁰ Pain was thought to be detected by nociceptors that cause pain signals to be sent to the CNS where they would be received and registered.¹⁶⁰ Later, the Gate Control Theory of Pain was developed which advanced our understanding of pain processing by introducing the spinal cord and brain as critical and active components in pain processing as opposed to passive transmission stations.¹⁶¹ However, a recently proposed pain model, the Neuromatrix Theory of Pain, has shown that fear and anxiety may influence the experience of pain.^{162,163} The Neuromatrix Theory of Pain portrays pain as a multidimensional *experience* generated by various influences, such as cognitive and affective events.¹⁶²

To better depict the Neuromatrix Theory of Pain, four components of a novel conceptual nervous system were proposed which includes the body-self neuromatrix, production of a neurosignature pattern, the conversion of neurosignatures into awareness, and stimulation of the action neuromatrix.¹⁶² The basis of this theory starts in the body-self neuromatrix, which is a large neural network throughout the brain that is responsible for the generation of neural patterns and the processing of sensory, cognitive, and motivational information that dictates perception and action.¹⁶² Due to the interdependent perceptual relationships between cells, tissues, body, self, and society these factors may also influence common psychosocial responses examined after injury.¹⁶⁴ Furthermore, it is proposed that the neuromatrix is comprised of genetically programmed neurons that leave a specific mark on all nerve impulse patterns that pass through it which produces a unique “neurosignature” pattern.¹⁶² This neurosignature is left on all neural impulses that travel through the neuromatrix but may be modified and marked with subsignatures created from sensory input.¹⁶² The continuous flow of the neurosignature from the body-self neuromatrix is sent to areas of the brain that transform the signal to a changing sense of awareness. It is theorized that the change of the

neurosignature to awareness leads to stimulation of an action-oriented neuromatrix which in turn activates neurons within the spinal cord to produce muscle movement and ultimately action.¹⁶²

A unique component of the Neuromatrix Theory of Pain when compared to traditional models of pain is that it includes multiple determinants of pain.¹⁶² Although the theory proposes that the neurosignature for pain experience is genetically determined and influenced by sensory input, it is also proposed that this neurosignature pattern may be impacted by cognitive and affective factors, such as psychological stress.¹⁶² This is further supported by the concept of phantom limb pain and the experience of pain in the absence of a limb or after destruction of its sensory roots.¹⁶⁵ The stress experience may also negatively affect systems that aid in regulating stress and may ultimately lead to an increase in pain sensitivity, the development of pain conditions, and resistance to many common treatment methods that attempt to treat sensory-based pain.¹⁶² Therefore, psychological impairments, such as pain catastrophizing, may have the ability to impact an individual's neurosignature pattern and exacerbate the pain experience.

Pain catastrophizing may influence the neurosignature of individuals with ACLR and alter their pain experience despite adequate physiological and structural healing after surgery. Previous research has found increased levels of pain catastrophizing to be strongly associated with higher levels of knee pain during activity after ACLR.¹² As proposed in the Neuromatrix Theory of Pain, it is possible that pain catastrophizing negatively affects regulatory systems which results in the increased sensitivity to pain observed in this population during physical activity.

Higher levels of pain catastrophizing have also been associated with a heightened perception of pain.¹⁶⁶ Functional magnetic resonance imaging (fMRI) of the brain in individuals with a history of ACLR showed increased activation of the secondary somatosensory cortex during completion of a knee flexion-extension task.³³ The posterior region of the secondary somatosensory cortex is responsible for processing of painful stimuli,¹⁶⁷ however, the study

participants did not report experiencing any physical pain while completing the movement task. This observed brain activity in the absence of a painful stimulus exemplifies the ability of potential cognitive and affective factors to influence an individual's neurosignature and alter their pain experience. Additional fMRI studies have found that individuals with ACLR were unable to suppress the default mode network (DMN) during a picture imagination task.¹⁶⁸ The DMN is a brain network that is most active at rest and is strongly associated with rumination,¹⁶⁹ a primary component of pain catastrophizing. It was proposed that although patients with a history of ACLR are structurally healed, they may be continuously processing, or ruminating, over the memory of their painful ACL injury.¹⁶⁸ These ideas and evidence further support the Neuromatrix Theory of Pain and the notion that psychological stress and affective factors experienced after ACLR, such as pain catastrophizing, may play a prominent role in pain perception and processing in the absence of a painful sensory stimulus.

In addition to psychological impairments influencing neurosignature patterns, the damage that occurs to the mechanoreceptors in the ACL at the time of initial injury may also affect the neurosignature. The altered somatosensory feedback that occurs because of ACL injury may change the signal being sent from the neurosignature to the brain and ultimately modify perceptions of the body,¹⁷⁰ and even behavioral patterns for individuals with ACLR. Furthermore, given the ability for neurosignature patterns and resulting actions to continue without ongoing sensory input,¹⁷¹ altered neurosignature patterns may linger despite physiological healing after ACLR. Long-term modifications to these patterns, which influence awareness and action, may contribute to behavioral changes examined in individuals with ACLR. This may include decreased knee function,¹⁷² reduced levels of physical activity,¹⁷³ or the development of psychological impairments such as pain catastrophizing which may lead to disuse or disability.¹⁶³

The Transactional Theory of Stress and Coping is based on the appraisal of transactions (e.g., events) between an individual and their environment.¹⁵² Incorporated in this theory are the

individual's values and beliefs as well as environmental factors, such as demands being placed on the individual and the available resources to respond to these demands.¹⁵² Cognitive appraisal is the subjective interpretation of an individual's situation and may be further categorized into primary and secondary appraisal. Primary appraisal identifies how significant an individual/environmental transaction is on the individual's well-being and may be defined as benign-positive, irrelevant, or stressful.¹⁵² Benign-positive transactions result in a positive effect on well-being while irrelevant transactions have no significance on an individual's well-being.¹⁵² However, it is suggested that a stressful transaction may result in the appraisal of substantial harm and/or loss, threatened harm and/or loss, or challenge which may elicit negative emotions.¹⁷⁴ In the event of a stressful transaction, secondary appraisal occurs during which the individual assesses situational factors and coping resources before initiating coping strategies.¹⁵² From this process, an individual can establish what they can do to manage the initial stressor and subsequent distress.

Coping is considered a process-oriented task that requires purposeful actions.^{152,175} Two primary forms of coping incorporated in this theory include problem-focused coping and emotion-focused coping. Problem-focused coping strategies try to directly manage the stressor whereas emotion-focused coping strategies aim to regulate emotions resultant of the stressful situation.¹⁵² Once coping strategies are initiated and new environmental information is present, cognitive reappraisal occurs. Through reappraisal, an individual is able to reevaluate and identify whether the coping strategy employed was successful or if the transaction has become irrelevant or benign-positive instead of stressful.¹⁵² If the utilized coping strategy is considered sufficient, positive emotions will be produced; however, if the coping strategy is considered insufficient, the individual will be in distress which will lead to consideration of other coping strategies.¹⁵²

The rumination and magnification associated with pain catastrophizing may negatively influence an individual's primary appraisal of pain and consequently cause an individual who

experiences pain catastrophizing to interpret the painful stimulus as threatening.¹⁷⁶ This catastrophic thinking and threatening interpretation of pain may then lead to a maladaptive recovery process consisting of fear of movement/reinjury, avoidance behaviors, and ultimately disuse or disability.¹⁷⁷ Individuals with a history of ACLR spend less time engaging in moderate to vigorous physical activity when compared to their peers.¹⁷³ It is possible that the presence of pain catastrophizing and consequent increased sensitivity to pain may worsen avoidance behaviors in this population and lead to this lifestyle modification after ACLR.

Additionally, the helplessness component of pain catastrophizing may affect an individual's secondary appraisal and lead to an inability to cope with pain.¹⁷⁶ Helplessness is the sense of being unable to act or react to a negative situation. It has been hypothesized that the pain, swelling, and loss of mechanoreception that occurs after ACL injury and ACLR leads to changes in neural activity.¹⁷⁸ These physiological changes may subsequently initiate feelings of uncontrollability and thus lead to learned helplessness when patients are unable to complete specific tasks.¹⁷⁸ Poor psychological responses, such as pain catastrophizing, may further worsen neural responses and create a negative cyclical pattern that decreases post-surgical outcomes and quality of life in this population.¹⁷⁸ Therefore, there is a critical need to assess psychological responses, particularly pain catastrophizing after ACLR, to reduce secondary ACL injury risk.

Measurement of Pain Catastrophizing

Pain catastrophizing is most effectively assessed with the PCS, a patient-reported outcome designed to measure an individual's perceptions of their pain experience.⁸ The 13-item questionnaire includes three subscales which examine the primary components of pain catastrophizing: rumination, helplessness, and magnification. The questionnaire asks users to reflect on past painful experiences and to identify the degree to which they experienced each of 13 feelings or thoughts when experiencing pain on a 5-point Likert scales with end points of 0 (not at all) and 4 (all the time).⁸ The PCS total score is computed by summing responses to all

13 questions and may range from 0-52. The Rumination subscale score ranges from 0-12 and is computed by summing the responses to items 8, 9, 10 and 11. The Magnification subscale score ranges from 0-9 and is computed by summing the responses to items 6, 7, and 13. The Helplessness subscale score ranges from 0-24 and is computed by summing the responses to items 1, 2, 3, 4, 5, and 12. Higher PCS total and subscale scores indicate greater pain catastrophizing. Individuals whose total score falls between the 50th and 75th percentiles are considered at moderate risk for the development of chronic pain and individuals who score above the 75th percentile are considered at high risk for the development of chronic pain.⁸ The PCS may be found in the Appendix.

When considering the psychometric properties of the PCS and its subscales, it has been shown to have adequate to excellent internal consistency (Cronbach α : total PCS=.87, rumination=.87, magnification=.66, helplessness=.78),⁸ and good to excellent test-retest reliability (ICC=0.99-.90) and adequate validity (0.40-0.42).¹⁷⁹ The PCS is also significantly correlated with measures such as fear of pain, pain intensity, and negative affectivity.⁸ In summary, the PCS provides a short, valid, and reliable method of evaluating pain catastrophizing across a variety of clinical populations.

Considerations and Gaps in the Current Literature

Despite previous reports of pain catastrophizing decreasing throughout ACLR rehabilitation, recent literature has identified that college-aged individuals approximately two-years post-ACLR exhibit significantly higher levels of pain catastrophizing when compared to healthy counterparts.¹⁶ This is concerning as 30% of individuals who return to high levels of activity after ACLR will sustain a second ACL injury within 24 months.⁴ Previous research has found other psychological impairments experienced after ACLR, such as self-reported fear, to be predictive of secondary ACL injury.³⁷ However, it remains unclear how pain catastrophizing may influence critical injury-related outcomes for individuals with history of ACLR.

NEUROCOGNITIVE FUNCTION AFTER ACLR

Neurocognitive function includes six domains: language, executive function, complex attention, social cognition, learning and memory, and perceptual-motor function.¹⁸⁰ Higher level cognitive function, or executive function, is the ability to coordinate cognitive, emotional, and motor processes in response to changing environmental cues, and is essential when completing tasks that require concentration, coordination, and control to overcome internal or external stimuli.^{80,181} Higher level cognitive function can be divided into the components working memory, inhibitory control, and cognitive flexibility, whereas lower order cognitive functions, which are necessary for successful complex functioning, include mechanisms such as visual attention, processing speed, and dual tasking.⁸⁰ Assessment of neurocognitive function therefore commonly includes tasks that measure aspects of inhibitory control, working memory (visual and verbal), and cognitive flexibility.⁸⁰

Interestingly, previous research has identified that individuals with ACLR exhibit comparable cognitive performance when completing upper extremity tasks that require visual attention when compared to healthy controls.¹⁸² It was postulated that successful completion of tasks that require visual attention may be due to neuroplastic adaptations exhibited in brain regions responsible for visual processing among individuals with ACLR.^{33,182} When faced with increased cognitive load and performing a dual-task, individuals with ACLR exhibit similar working memory to healthy controls, but with resultant deficits in postural control.¹⁸³ However, in the presence of a more attentionally demanding dual-task, individuals with ACLR exhibited worse reaction time when compared to healthy adults.¹⁸⁴ This decline in performance in a dual-task condition may occur when there is an exchange of attentional resources and priority is given to one task instead of the other.¹⁸⁴ Neurocognitive performance may also be mediated by psychological factors. Previous research exhibits that individuals with history of ACLR and increased injury-related fear demonstrate slower lower extremity visuomotor reaction time.^{7,185}

Perceptual-Motor Function and Coordination

Perceptual-motor function is the efficient integration of the central and peripheral nervous system to process a stimulus in the surrounding environment and respond through movement.^{186,187} Therefore, perceptual-motor function may be considered a critical cognitive function during sport performance as a combination of motor and perceptual-cognitive skill is required to identify and process information in the surrounding environment.⁸¹ Perceptual-motor function may be further categorized into visual perception, visuoconstructional reasoning, and P-MC.¹⁸⁰ Visual perception represents an individual's overarching ability to receive, interpret, and execute an action in correspondence to a visual stimulus, visuoconstructional reasoning represents the brain's ability to organize and use spatial information, and perceptual-motor coordination represents the brain's ability to interpret and use sensory information to execute physical activities.²⁶ For athletes, P-MC may be a critical factor for sport performance as it represents the ability to process and respond to varying environmental stimuli that may be experienced during sport.¹⁸⁸

Measurement of Perceptual-Motor Coordination

Perceptual-motor coordination is most frequently determined by measuring the time it takes to process and respond to visual stimuli such as light or moving objects.²⁶ P-MC may be evaluated as a component of neurocognitive function through a variety of computerized neurocognitive assessments such as the Automated Neuropsychological Assessment Metric, the Axon Sports Computerized Neurocognitive Assessment, Defense Automated Neurobehavioral Assessment, and Immediate Post-Concussion Assessment and Cognitive Testing.¹⁸⁹ However, a lower extremity task that combines response to visual stimuli and lower extremity reaching has also been developed to assess P-MC in patient populations that have experienced lower extremity injury.¹⁹⁰ For the task, individuals are placed at the center of a 180° semicircle with five light discs (FitLight Sports Corp, Aurora, Ontario, Canada), secured to the ground in increments of 45° (Figure 2.2). For testing, a random sequence of visual stimuli is

generated amongst the five light discs and individuals are instructed to deactivate the randomly illuminated lights by tapping the disc with a designated foot as quickly as possible. This task has demonstrated excellent right limb reliability ($ICC=.86$) and good left limb reliability ($ICC=.80$).¹⁹⁰



Figure 1.2: Set-up and completion of the lower extremity perceptual-motor coordination task with the left limb as the active limb and the right limb as the stabilizing limb. Participants were instructed to deactivate the randomly illuminated lights by tapping the disc with their foot as quickly as possible.

LANDING KINETICS AFTER ACLR

Landing is a critical component of many sport activities and involves varying degrees of ground reaction force (GRF).⁸⁵ GRF is a kinetic parameter that is greatest during the landing phase of a jump, specifically when the knee is between 0 and 25 degrees of flexion as this is when the knee must withstand the greatest change in kinetic energy.⁸⁶ Asymmetries in vertical GRF (vGRF), or total limb loading, between the ACLR limb and contralateral limb have been examined among individuals up to 2-years post-ACLR both while walking and during jump-landing tasks.^{191,192} These exhibited asymmetries may be due to compensation strategies individuals with ACLR commonly employ when performing lower extremity movements leading to offloading of the ACLR limb and overloading of the contralateral limb.¹⁹³⁻¹⁹⁷ Factors including greater drop height,⁶⁹ decreased quadriceps to hamstrings activation ratio,^{198,199} decreased

neuromuscular control,³⁰ maturity,^{62,200} and increased joint stiffness may also produce larger vGRFs.^{201,202} Lower extremity kinetics post-ACLR may also be influenced by a variety of factors, including fear of reinjury,⁶ biologic sex,²⁰³ quadriceps neuromuscular function,²⁰⁴ attentional focus,²⁰⁵ knee symptoms, and time since surgery.²⁰⁶

Measurement of Vertical Ground Reaction Force

To obtain kinetic measures associated with ACL injury risk such as vGRF asymmetry, individuals typically perform a drop-vertical jump (DVJ) task onto two adjacent force platforms embedded in the ground in a laboratory setting.²⁰⁷ For this task, individuals drop from a 30-cm box onto a standardized landing area $\frac{1}{2}$ of the individual's height away and immediately jump upward with maximal effort (Figure 2.3). Throughout this task, vGRF may be measured during the initial drop landing and during the second landing that follows the maximal vertical jump.²⁹ Collected force data is commonly sampled at 800 to 2500 Hz and vGRFs should be normalized to body weight to reduce variance when comparing forces between individuals.²⁰⁸ Use of force platforms that are able to individually examine limb GRFs are deemed the gold standard for assessment of vGRF and report an average margin of error < 5 N.¹⁹¹ However, rehabilitation specialists are frequently limited in their ability to analyze knee kinetics within the clinical setting due to the cost, time, and expertise required for collection and processing of data with this type of technology.

Recently, more clinically translatable and implementable technology, including wireless insertable insole devices, have been identified as a valid and reliable alternative for vGRF measurement during walking and jump-landing tasks among individuals with and without knee injury.²⁰⁹⁻²¹¹ Loadsol® (Loadsol, Novel Electronics, St. Paul, MN) is a force-measuring insole that may be placed directly into an individual's personal shoe which allows for portable measurement of vGRF outside of the laboratory setting.²¹⁰ Furthermore, this technology can be easily calibrated for each user and is able to capture a large volume of data when compared to traditional laboratory devices.^{209,210}

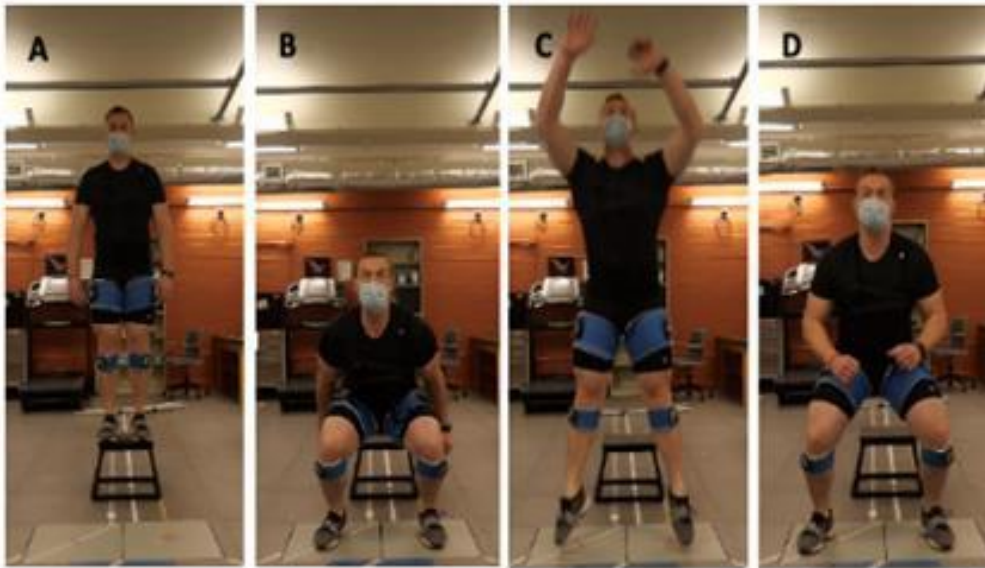


Figure 1.3: (A) Participant stands on 30-cm box. (B) Participant then drops from the box to the landing area (initial contact and peak flexion). (C) Participant then jumps upward to attain maximal height (vertical jump). (D) Participant then lands safely in the same landing area (second landing).

NEURAL ACTIVITY AFTER ACLR

A disturbance in function anywhere along the neural chain may cause deficits in vestibular, visual, motor, or cognitive function.²¹² For example, when the mechanoreceptors of the ACL are damaged, altered afferent input is sent from the peripheral nervous system to the CNS.⁴⁸ In response, modified efferent output is relayed from the CNS and may include altered spinal and cortical excitability as well as reflexive adaptations in the lower extremity.^{33,213,214} These adaptations may ultimately cause the functional reorganization of the somatosensory and motor cortices of the brain commonly exhibited by individuals with ligamentous injury, such as an ACL tear.³²

Alterations in Brain Regions Associated with Visual, Motor, and Sensory Processing

Functional magnetic resonance imaging, a non-invasive imaging technique used to measure neural activity,²¹⁵ has identified that patients with history of ACL injury exhibit altered activation of brain regions involved in somatosensory, motor, and cognitive and visual

processing during a basic knee flexion/extension movement.³³⁻³⁵ Furthermore, when completing a more complex multi-joint movement involving the hip, individuals with ACLR demonstrate increased activity and connectivity in regions involved in visual-spatial cognition and orientation, and in areas responsible for attention for motor control of the hip and knee when compared to healthy individuals.²¹⁶ The results of these studies suggest that individuals with ACLR may require greater neural activation for sensory and motor planning and may rely more on visual-motor processing when engaging in lower extremity movement with their involved limb.^{33,216}

In addition to these neuroplastic adaptations, individuals with ACLR have exhibited increased activation of regions associated with pain processing, specifically the secondary somatosensory area and frontal lobe areas including the frontal gyri, inferior frontal pole, and paracingulate gyrus.^{33,34} In a study by Grooms et al.,³³ individuals with ACLR demonstrated greater activity in the ipsilateral secondary somatosensory area, a region responsible for the processing of painful stimuli,^{167,217} during a knee flexion/extension task compared to controls, but reported not experiencing acute pain during task performance.³³ Similarly, in a study conducted by Lepley et al.,³⁴ individuals with ACLR exhibited increased activation among pain processing regions of the frontal lobe while performing a knee movement task. Increased activation of these areas was positively correlated with self-reported knee pain and symptoms among this sample.³⁴

Alterations in Brain Regions Associated with Emotional Processing

Kinesiophobia, the fear of movement/reinjury, is a common psychological response experienced after ACL injury that has also been linked to neural activation among individuals with ACLR during an action-observation motor imagery task of a DVJ.⁵ Notably, individuals who reported higher scores on the TSK-11, a questionnaire that measures fear of movement/reinjury, exhibited greater neural activity in the left cerebellum crus I and crus II, the right cerebellum lobule IX, amygdala, middle temporal gyrus, and temporal pole.⁵ Given the involvement of these regions in cognitive processing, lower extremity movement, and the

processing of fearful or potentially-pain inducing events, it was concluded that the increased neural activation examined in these areas may signify a DVJ as a fearful or adverse event among individuals with ACLR and elevated kinesiophobia.⁵

In another recent study using fMRI, it was found that females with ACLR exhibited increased activation of the mediodorsal thalamus, inferior parietal lobule, and cerebellar lobule IX during a picture imagination task (PIT) of sport-specific images and activities of daily living images when compared to uninjured individuals.¹⁶⁸ The inferior parietal lobule contributes to the perception of emotions in facial stimuli and body images,²¹⁸ while the mediodorsal thalamus plays a role in a variety of cognitive functions including attention, planning, abstract thinking, working memory, and emotion through its connection to the prefrontal cortex.²¹⁹⁻²²¹ Furthermore, the mediodorsal thalamus has been linked to mediation of emotional responses connected to pain-inducing stimuli.²²² It was postulated that individuals with ACLR may have experienced an emotional response during the PIT due to memories associated with their ACL injury.¹⁶⁸ The ACLR group also exhibited an inability to suppress the DMN, a system where regions are commonly more active at rest and deactivated during cognitive tasks,²²³ during the PIT when compared to healthy controls. Being unable to suppress the DMN during performance of tasks has been connected to psychopathological conditions and the development of chronic pain.²²⁴⁻²²⁷ However, it was proposed that for individuals with history of ACLR, continuous processing of the memory and painful event may occur.¹⁶⁸

Measurement of Neural Activation Using Functional Magnetic Resonance Imaging

Functional magnetic resonance imaging is a noninvasive neuroimaging tool that can be used to study cognition in the brain.²²⁸ This technique uses a magnetic resonance contrast mechanism to visualize changes in brain tissue caused by a hemodynamic process. When neuronal activity occurs, it changes relative levels of oxygenated and deoxygenated blood which leads to changes in the magnetic resonance signal being recorded.²²⁹ This change in signal

within the brain tissue characterizes the blood oxygenation-level dependent (BOLD) response that is measured in fMRI and used to identify areas of neural activity within the brain.²³⁰

In fMRI research, neural activity can be assessed through the performance of tasks that engage cognitive processes or can occur spontaneously while at rest.²²⁸ These two types of assessment techniques are referred to as task-based design or resting-state design. Task-based designs utilize a cognitive task to alter neuronal activity and compare time series data.²²⁸ Task-based fMRI study designs can be further categorized as Block designs, Event-Related designs,²³¹⁻²³⁵ or Mixed Block/Event-Related designs.²³⁶⁻²³⁸ Block designs divide the scan into timed blocks that are associated with conditions in order to identify differences between the conditions.²²⁹ This approach typically uses a sensory stimulus (e.g., visual, auditory, etc.) to cue a cognitive change while BOLD contrast images are obtained during a set amount of time.²²⁸ For event-related designs, stimuli are presented in a random order instead of in an alternating fashion.²²⁹ Mixed block/event-related designs combine both the block design and event-related design to allow for identification of activity related to trial and block transitions and sustained activity connected to task-level processing.²³⁸ Block designs are considered the best design-type for detecting an activation, whereas event-related designs are most efficient in distinguishing the time course of the activation.²³⁹ Mixed designs may provide a more thorough interpretation of how brain regions function over various time scales.²³⁸

In contrast to task-based designs that involve cognitive manipulation, resting-state designs record consistent low frequency changes in BOLD signals while an individual is at rest to examine the connection between brain regions that are functionally, but not anatomically linked.^{229,240} Functional connectivity refers to comparing changes in BOLD signal that occur over time between two regions of interest.²⁴¹ In contrast to task-based fMRI, resting-state fMRI can be completed without a specific task or input, requires fewer trials, and gathers more information on overall brain function when compared to task-based fMRI.²⁴²

The primary objective of fMRI analysis is to identify voxels that display signal changes in the brain across sequential images.²⁴³ However, before higher level analyses can be performed, a set of procedures commonly referred to as the “preprocessing pipeline” are performed to remove non-neural variations that may have occurred during the scan, such as subject movement and physiological cycles.²²⁸ Preprocessing steps frequently include quality assurance testing, slice timing correction, head motion correction, distortion correction, temporal filtering, spatial smoothing, physiological noise correction, functional-structural co-registration, and spatial normalization.²²⁸ Use of these procedures limits the risk of structured noise negatively affecting the neural function-related results and increases the functional signal to noise ratio.²²⁸ However, preprocessing parameters may be dictated by the study design being employed.²²⁹

For task-based studies, brain regions associated with the stimulus may be identified through examination of each brain voxel’s alignment in time and with the task sequence.²²⁸ Common statistical approaches used in single subject analysis of task studies include the t test, correlation analyses, general linear model analyses, multivariate pattern analyses, correction for multiple comparisons, and inter-subject analyses. For task-based studies with event or block designs, a general linear model with one dependent variable is a common analysis method.^{244,245} To make inferences regarding task activation across multiple individuals, inter-subject analyses including a fixed-effect or random-effect analysis may be used.²⁴⁶ A fixed-effect analysis combines all subject timepoints into one time series prior to implementing a single-subject analysis. In a random-effect analysis, each subject’s summary statistics from the task activation is independently analyzed before testing the significance of the distribution of summary statistics.²²⁸ When assessing resting state functional connectivity, a seed-based analysis is commonly used which involves correlating average BOLD signals within a region of interest with BOLD signals from every other voxel in the brain.²⁴⁷⁻²⁵⁰ This method allows for detailed examination of the connectivity between brain areas of particular interest.^{251,252}

Considerations and Gaps in the Current Literature

Individuals with ACLR exhibit neuroplastic alterations in areas responsible for processing of emotions and pain. Due to the connection between pain catastrophizing and brain regions associated with pain perception,³⁶ it is possible that increased activation of pain-related areas during basic movement among individuals with ACLR may result from psychological processes that can influence an individual's pain experience, such as pain catastrophizing. Investigation of neural factors associated with pain catastrophizing among individuals with ACLR may allow for the identification of intervention strategies to address pain catastrophizing after ACLR.

CONCLUSION

Individuals with history of ACLR exhibit varying degrees of pain catastrophizing and have an increased risk of secondary injury when compared to uninjured individuals. The risk of secondary ACL injury has been previously linked to psychological impairments, neuroplastic adaptations, and changes in lower extremity biomechanics exhibited after ACL injury and reconstruction. However, there is a vital gap in the literature investigating the association of pain catastrophizing with central and peripheral neural mechanisms that may influence injury-related outcomes post-ACLR and how these outcomes may be further affected in the presence of sport-specific distraction. Therefore, the purpose of the following studies is to investigate the role of pain catastrophizing on neural and injury-related outcomes among individuals with a history of ACLR. Completion of these studies will provide greater understanding of the presentation of pain catastrophizing after ACLR, identify modifiable outcomes that may reduce the risk of secondary ACL injury, and assist in intervention development to improve injury-related outcomes post-ACLR.

CHAPTER 3: THE INFLUENCE OF PAIN CATASTROPHIZING ON LOWER EXTREMITY PERCEPTUAL-MOTOR COORDINATION IN INDIVIDUALS WITH ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION

ABSTRACT

Context: Psychological impairments experienced after anterior cruciate ligament reconstruction (ACLR) may negatively influence components of perceptual-motor function, such as perceptual-motor coordination (P-MC). Slower P-MC, the time it takes to interpret sensory information and execute a movement, is associated with increased risk of lower extremity musculoskeletal injury and may influence risk of secondary injury in patients with ACLR. Pain catastrophizing, a psychological response experienced after ACLR, is a cognitive–affective response associated with greater pain intensity, poor rehabilitative outcomes, and decreased quality of life in individuals with ACLR. However, the association of pain catastrophizing on injury-related outcomes such as P-MC, is unknown. Therefore, the purpose of this study was to examine the influence of pain catastrophizing on lower extremity P-MC in individuals with ACLR.

Methods: A total of 45 participants (age=19 [4] years) with history of primary unilateral ACLR (time since ACLR=9.23 [17.85] months) were included in this study. Participants completed the Pain Catastrophizing Scale (PCS) and a lower extremity P-MC task using a series of wireless light discs with both the ACLR limb and contralateral limb. Separate multiple linear regression models were used to examine whether PCS scores are associated with ACLR limb and contralateral limb P-MC in individuals with ACLR. Age and sex were controlled for in each regression model due to their potential influence on P-MC. Alpha was set *a priori* $p < .05$.

Results: Descriptive statistics (median [interquartile range]) for our primary outcome measures were as follows: PCS=4 [14], ACLR Limb P-MC=.511 [.106] sec, Contralateral Limb P-MC=.532 [.094] sec. The results of the separate multiple linear regression analyses indicated that PCS scores were not significantly associated with ACLR limb P-MC ($\beta=0.002$, $p=0.247$) or contralateral limb P-MC ($\beta=0.001$, $p=0.410$) when controlling for sex and age.

Conclusion: Pain catastrophizing was not associated with lower extremity P-MC in individuals with ACLR. These findings suggest that although individuals with ACLR experience pain catastrophizing, this type of pain-related psychological response may not be a critical factor contributing to lower extremity P-MC in this population. Future research should explore longitudinal changes in pain catastrophizing, lower extremity P-MC, and their association throughout ACLR rehabilitation, as well as after return to activity, to better understand pain-related psychological and perceptual-motor adaptations that may occur over time in this population.

INTRODUCTION

Anterior cruciate ligament (ACL) tears are sports-related injuries that affect knee stability and often result in ACL reconstruction (ACLR).²⁵³ Although many individuals are able to regain adequate objective knee function post-ACLR, approximately 30% of individuals will experience a secondary ACL injury to the contralateral or ipsilateral limb within 24 months of return to sport and physical activity.⁴ Increased risk of secondary ACL injury has been attributed to psychological impairments commonly experienced after ACLR, such as increased injury-related fear.³⁷ In addition to injury-related fear, individuals post-ACLR may exhibit other psychological responses such as pain catastrophizing.²⁵⁴ Pain catastrophizing is a cognitive–affective response to anticipated or actual pain and has three primary components: rumination, magnification, and helplessness.^{8,126} Although pain catastrophizing may be considered a natural psychological response after ACL injury,¹⁰ it can negatively influence significant clinical outcomes for patients after ACLR, such as pain intensity and self-reported knee function.^{10,12} Furthermore, pain catastrophizing may interfere with an individual's ability to inhibit thoughts and switch focus of attention which are important aspects of neurocognitive function.^{137,138}

Perceptual-motor coordination (P-MC), a component of neurocognitive function, is the time it takes to interpret sensory information and execute a movement.²⁶ Furthermore, P-MC may be considered a critical factor for sport performance as it represents an athlete's ability to process and respond to varying environmental conditions during sport.¹⁸⁸ Previous research has found deficits in P-MC to be associated with increased risk of lower extremity musculoskeletal injury, including knee sprain, in collegiate athletes.²⁵⁵ Furthermore, among individuals with ACLR, deficits in lower extremity P-MC are associated with psychological responses experienced after ACLR, specifically increased injury-related fear.⁷ However, the association between pain-specific psychological responses experienced after ACLR and P-MC is unknown.

Individuals who experience pain catastrophizing and a heightened anticipation of pain may allocate their attentional resources to the expected location of the threat.^{24,25} For individuals

engaging in sport, negative attentional changes may adversely affect their ability to respond to their environment and consequently affect injury-related outcomes,¹²⁰ such as P-MC. Pain catastrophizing is a modifiable outcome that, if addressed appropriately throughout ACLR rehabilitation and recovery, may positively influence P-MC, and reduce the risk of secondary injury among individuals with ACLR. Therefore, the purpose of this study was to examine the influence of pain catastrophizing on lower extremity P-MC in individuals with ACLR. We hypothesized that individuals with higher levels of pain catastrophizing would demonstrate worse lower extremity P-MC. Understanding the association between these variables may provide the impetus to further investigate effective intervention strategies to address psychological and perceptual-motor impairments in individuals with ACLR.

METHODS

A cross-sectional study design was used to examine the influence of pain catastrophizing on lower extremity P-MC in individuals with ACLR. The independent variable for this study was pain catastrophizing, measured by the Pain Catastrophizing Scale (PCS). The dependent variables for this study were ACLR limb and contralateral limb P-MC measured using the FitLight Trainer™ (FitLight Sports Corp, Aurora, Ontario, Canada). Study procedures were approved by the Michigan State University Institutional Review board and informed consent for those over 18 years, or parental consent and child assent, was obtained from all participants prior to study enrollment.

Participants

Individuals with a history of ACLR were recruited for this study from a local University, sports medicine clinic, and the surrounding community. Individuals were eligible to participate in the study if they met the following inclusion criteria: (1) were between the ages 14-35 years, (2) were between 4-months and 5-years post-ACLR, and (3) injured their ACL participating in sport or physical activity. Individuals were excluded from the study if they had a history of bilateral ACLR, had a history of secondary ACL injury or reconstruction to the ipsilateral limb, sustained

an injury to the medial collateral ligament, lateral collateral ligament, or posterior collateral ligament at the same time as their index ACL injury, were currently injured at the time of study participation, sustained a lower extremity injury within the three months prior to study participation, sustained a concussion within the three months prior to study participation, or had any neurological conditions that would affect the central or peripheral nervous system (e.g., epilepsy).

Procedures

Participants reported to the Athletic Injury and Rehabilitation Laboratory at Michigan State University for a single testing session. Participants completed a demographics questionnaire which collected information on age, height, weight, sex, race, physical activity level, orthopedic history, and ACL surgical and rehabilitation history. Participants then completed the PCS and lower extremity P-MC task.

Pain Catastrophizing Scale

The PCS is a 13-item questionnaire constructed to measure an individual's perceptions of their pain experience and includes three subscales which examine the primary components of pain catastrophizing: magnification (e.g., "I become afraid the pain will get worse"), helplessness (e.g., "It's terrible, and I think it's never going to get better"), and rumination (e.g., "I keep thinking about how much it hurts").⁸ Questionnaire items are scored on a Likert scale from 0 (not at all) to 4 (all the time) with the total PCS score ranging from 0-52. Higher PCS scores indicate greater pain catastrophizing. The PCS has adequate to excellent internal consistency (Cronbach α : total PCS=.87, rumination=.87, magnification=.66, helplessness=.78),⁸ good to excellent test-retest reliability (ICC=0.99-.90), and adequate concurrent validity ($r= 0.42$) when compared to a related measure of negative thoughts in response to pain.¹⁷⁹ The PCS may be found in the Appendix.

Lower Extremity Perceptual-Motor Coordination

Lower extremity P-MC was measured using a reliable task via the FitLight Trainer™ (FitLight Sports Corp, Aurora, Ontario, Canada), a series of wireless light discs.¹⁹⁰ Participants were placed at the center of a 180° semicircle with five light discs secured to the ground in increments of 45° (Figure 2.1). The distance of each light disc was normalized to the length of the participant's shank, except for the light lateral to the stance limb, which was placed at half the distance of the participant's shank. For testing, the system generated a random sequence of visual stimuli amongst the five light discs. Participants were instructed to deactivate the randomly illuminated lights by tapping the disc with their foot as quickly as possible. Each limb was tested independently and the test limb (moving limb deactivating the lights) order was counterbalanced between participants. Participants completed three 30-second familiarization trials followed by one 60-second test trial with their ACLR limb as the stance limb (Contralateral Limb P-MC) and with their ACLR limb as the moving limb extinguishing the lights (ACLR Limb P-MC). Lower extremity P-MC was measured as the average time (seconds) between deactivating the lights during the 1-minute trial. Higher times are indicative of slower lower extremity P-MC. This task has demonstrated excellent right limb reliability (ICC=.86) and good left limb reliability (ICC=.80).²⁵⁶

Statistical Analysis

The data were inspected for normality using the Shapiro-Wilk test and descriptive statistics were calculated for all pertinent demographic variables, total PCS score, and lower extremity P-MC. Separate multiple linear regression analyses were conducted to examine the association between PCS scores (independent variable), ACLR limb P-MC (dependent variable), and contralateral limb P-MC (dependent variable) in individuals with ACLR. When performing linear regression analyses, a minimum of 10 participants should be included per predictor variable.^{257,258} Therefore, no more than 4 predictor variables were to be included in the final regression models. Univariate analyses were completed to identify potential demographic confounders, and age and sex were controlled for in each regression model due to their

potential influence on P-MC.^{259,260} Covariates were entered into each regression model first, followed by PCS scores. The assumptions of independence of residuals, normality, homoscedasticity, and linearity were verified for each regression model and the models were examined for outliers using the standardized residuals from the regression model. The overall percent of the explained variance (R^2) for each regression analysis was identified and the regression coefficient (β), constant, p values, confidence intervals, and individual predictive power of each variable are reported. Alpha was set *a priori* $p < .05$. All statistical analyses were conducted using STATA statistical software (StataCorp LLC, College Station, TX).

RESULTS

A total of 45 participants (age= 19[4] years) with history of unilateral ACLR (time since ACLR= 9.23[17.85] months) were enrolled in this study. Descriptive statistics for participant characteristics and main outcome measures are presented in Table 3.1. One individual was characterized as an outlier in each regression model due to the standardized residuals of their lower extremity P-MC data being >3 . However, the outlier was retained in the dataset as the inclusion of their data points did not affect the results of the analysis or violate any other assumptions. When controlling for age and sex, total PCS scores were not significantly associated with ACLR limb P-MC ($\beta=0.002$; $p=0.247$) or contralateral limb P-MC ($\beta=0.001$; $p=0.410$). Results of the separate multiple linear regression analyses are presented in Table 3.2.

Table 3.1: Descriptive Statistics of Participant Characteristics and Primary Outcome Measures

Sex	
Females	32 (71.1%)
Males	13 (28.9%)
Age, years	19 [4]
Height, cm	168.88 (8.69)
Weight, kg	65.77 [10.43]
Time Since ACLR, months	9.23 [17.85]
PCS	4 [14]
ACLR Limb P-MC, sec	.511 [.106]
Contralateral Limb P-MC, sec	.532 [.094]

Data are reported as frequency (%), median [interquartile range], or mean (standard deviation). Abbreviations: Anterior Cruciate Ligament Reconstruction (ACLR), Pain Catastrophizing Scale (PCS), Perceptual-Motor Coordination (P-MC)

Table 3.2: Multiple Linear Regression Results for Lower Extremity Perceptual-Motor Coordination

Predictor Variables	ACLR Limb P-MC			Contralateral Limb P-MC		
	β (95% CI)	<i>p</i> value	R^2	β (95% CI)	<i>p</i> value	R^2
Overall Model		0.221	0.101		0.187	0.109
Constant	0.560 (0.417, 0.704)	0.000		0.601 (0.470, 0.731)	0.000	
Sex	0.045 (-0.011, 0.101)	0.112		0.038 (-0.011, 0.089)	0.136	
Age	-0.003 (-0.010, 0.004)	0.333		-0.005 (-0.011, 0.001)	0.120	
PCS	0.002 (-0.001, 0.004)	0.247		0.001 (-0.001, 0.003)	0.410	

Abbreviations: Anterior Cruciate Ligament Reconstruction (ACLR), Perceptual-Motor Coordination (P-MC), Pain Catastrophizing Scale (PCS)

DISCUSSION

The purpose of this study was to examine the influence of pain catastrophizing on lower extremity P-MC in individuals with ACLR. We hypothesized that individuals who exhibited higher levels of pain catastrophizing would demonstrate worse lower extremity P-MC. Contrary to our hypothesis, we did not find PCS scores to be significantly associated with ACLR limb P-MC or contralateral limb P-MC in our sample. We interpret these findings to suggest that pain catastrophizing strategies may not be a critical factor contributing to lower extremity P-MC performance among individuals with ACLR.

Our previous work identified a positive relationship between fear-avoidance, a component of injury-related fear, and lower extremity P-MC after ACLR,⁷ but to our knowledge, this is the first study to examine the association between pain catastrophizing and lower extremity P-MC in this population. It is possible that differences in the psychological constructs of fear-avoidance and pain catastrophizing may have contributed to the current study findings. Pain catastrophizing is a cognitive and emotional response to pain, whereas fear-avoidance beliefs are a combination of emotional and information-based fears of pain and (re)injury.²⁶¹ Although both pain catastrophizing and fear-avoidance beliefs involve aspects of pain, beliefs shape human behavior and directly influence decisions to perform or avoid activities that may be associated with pain/(re)injury and subsequently contribute to resultant levels of ability or disability.²⁶¹ Given the influence of fear-avoidance beliefs on behavior, this type of psychological response may be more likely to impact aspects of behavioral performance, such as P-MC, when compared to pain catastrophizing. Additionally, the Fear-Avoidance Beliefs Questionnaire Physical Activity and Sport subscales previously used to examine the relationship between injury-related fear and lower extremity P-MC in individuals with ACLR were adapted for a physically active population with knee pathologies.⁷ The adapted questionnaire includes items such as “my pain was caused by my physical activity” and “my sport might harm my knee.”²⁶² These types of questions may be more relevant for individuals with ACLR who are engaged in

physical activity and sport when compared to the PCS which only includes general questions about pain that are unrelated to knee pathologies and physical activity (e.g., I become afraid that the pain will get worse). Given that ACL injuries are a common result of sport participation,⁵¹ development and use of a new questionnaire to assess pain catastrophizing strategies in a high functioning, physically active population with ACLR may be warranted to better understand how pain-related responses may influence sport-related task performance.

Interestingly, the cohort of individuals in this study that was approximately 9 months post-ACLR demonstrated slightly faster lower extremity P-MC scores (ACLR Limb= 0.51 [.11]; Contralateral Limb= 0.53 [.10]) to those we previously found to be associated with greater injury-related fear in a cohort of individuals approximately 7 years post-ACLR (ACLR Limb= 0.55 [0.07]; Contralateral Limb= 0.57 [0.08]).⁷ Thus, it is possible that psychological responses to injury that are unresolved throughout rehabilitation may lead to diminished perceptual-motor outcomes at later timepoints post-ACLR via lifestyle modifications such as decreased physical activity engagement. However, the interaction between psychological responses to injury and P-MC may also be due to changes in psychological responses throughout ACLR rehabilitation and after return to physical activity/sport. Jochimsen et al.,¹⁰ previously found pain catastrophizing to gradually decrease throughout the ACLR rehabilitation process with individuals reporting an average PCS score of 0.8 (range= 0-11) at 6-months post-ACLR. However, our sample of individuals approximately 9 months post-ACLR exhibited slightly higher and more variable PCS scores (median [interquartile range]: 4 [14]; range= 0-33) than those reported by Jochimsen et al.¹⁰ These findings suggest that PCS scores may increase and become more variable at later post-surgical timepoints. Possible increases in pain catastrophizing after ACLR may be better explained by the fear-avoidance model of musculoskeletal pain. This framework proposes that when an individual interprets their pain as threatening, they may experience catastrophic thoughts about pain, go on to develop pain-related fear and anxiety, and avoid activities that could potentially increase their pain.²⁶³ These actions may consequently lead to the

development of disability, disuse, and depression.²⁶³ If pain catastrophizing is present and goes unaddressed throughout the rehabilitation process, individuals may then find themselves in a negative cycle of pain and dysfunction which could contribute to greater levels of pain catastrophizing at later timepoints post-ACLR. This idea is further supported by previous findings of individuals 1-year-post-ACLR exhibiting an average PCS score of 12 (range= 0-36),¹⁵ as well as individuals approximately 22 months post-ACLR exhibiting a median PCS score of 14.²⁶⁴ Future research may benefit from exploring longitudinal changes in pain catastrophizing, lower extremity P-MC, and their association throughout ACLR rehabilitation, and after return to unrestricted activity, to better understand pain-related psychological and perceptual-motor adaptations that may occur over time in this population.

The lack of association between pain catastrophizing and lower extremity P-MC in our study may also be due to the relatively low PCS scores reported by our cohort when compared to other populations. Sullivan et al.⁸ previously identified clinical levels of catastrophizing as scores > 30, with scores higher than this cutoff indicating scoring over the 75th percentile of persons with chronic pain. Based on these cutoff scores, only two participants in our sample exhibited clinical levels of pain catastrophizing. Therefore, although high pain catastrophizers have been shown to engage their attention toward pain-related information and exhibit changes in spatial attention when anticipating pain,^{25,265} the levels of pain catastrophizing exhibited in our sample may not have been high enough to compete for attentional resources and alter performance of the lower extremity P-MC task used in this study.

Individual factors, such as positive adaptations to pain and executive functioning abilities, may have also contributed to our study findings. Pain resilience, the ability to maintain goal-oriented motivation despite pain, is a behavioral adaptation that has been found to promote task persistence and performance.²⁶⁶ Furthermore, when combined with low pain catastrophizing, high pain resilience is associated with better task performance when experiencing pain and it is theorized that this type of positive psychological influence promotes

flexibility in the allocation of attentional resources.^{266,267} Additionally, previous research has found aspects of executive function, including greater selective attention, to positively influence the attentional modulation of pain experiences.²⁶⁸ Such positive psychological influences and executive functioning abilities could have allowed individuals in our sample to maintain adequate attention during completion of the lower extremity P-MC task despite the presence of pain catastrophizing. Future studies should investigate the influence of positive pain-related behavioral adaptations and selective attention on pain catastrophizing and the performance of functional tasks in individuals with ACLR.

There are limitations to our study that should be considered to better inform future research. First, although the PCS has been used in ACLR literature, it has yet to be validated for the ACLR population and future research is needed to identify clinical levels of catastrophizing among individuals with ACLR. Furthermore, use or development of other outcome measures examining psychological aspects of sport or activity-related pain may be more useful in understanding how these factors might influence sport-related functions such as P-MC. Second, although we had an appropriate sample size for the number of predictor variables included in our regression model, there may be other confounding variables (e.g., physical activity level, sport type, time since ACLR) that were not accounted for that could influence the relationship between pain catastrophizing and lower extremity P-MC post-ACLR. Future research with larger sample sizes should explore other potentially confounding variables to better understand the interaction of these outcomes in this population.

CONCLUSION

Pain catastrophizing was not significantly associated with lower extremity P-MC in individuals with ACLR and may not be a critical factor contributing to aspects of perceptual-motor function and possible secondary injury risk in this population. However, assessment of pain catastrophizing and P-MC throughout ACLR rehabilitation and after return to activity may be warranted to better understand longitudinal changes in these outcomes and to identify

individuals who may benefit from interventions to address perceptual-motor and pain-related responses after ACLR. Future research should explore additional psychological factors that may influence lower extremity P-MC in individuals with ACLR and whether pain catastrophizing is associated with performance of tasks at later timepoints post-surgery.

CHAPTER 4: THE RELATIONSHIP BETWEEN PAIN CATASTROPHIZING AND NEURAL ACTIVITY IN INDIVIDUALS WITH ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION DURING A PICTURE IMAGINATION TASK: AN EXPLORATORY FUNCTIONAL MAGNETIC RESONANCE IMAGING STUDY

ABSTRACT

Context: Individuals with anterior cruciate ligament reconstruction (ACLR) exhibit neuroplastic alterations in brain regions associated with fear and emotional regulation. However, this population commonly experiences other psychological responses with affective components, such as pain catastrophizing, which is linked to decreased self-reported knee function and increased pain sensitivity after ACLR. Characterizing central neural mechanisms associated with pain catastrophizing may help to improve clinical and functional outcomes for individuals with ACLR. Therefore, the purpose of this study was to examine the relationship between pain catastrophizing and neural activity in individuals with ACLR during a picture imagination task (PIT).

Methods: A total of 15 participants (age= 22.80 ± 4.71 years) with history of primary unilateral ACLR (time since ACLR= 23.09 ± 14.18 months) were included in this study. Participants underwent full brain functional magnetic resonance imaging while completing a PIT that included two image conditions: 1) activities of daily living (ADL), and 2) physical activity, and then completed the Pain Catastrophizing Scale (PCS). A whole-brain exploratory analysis was conducted to examine the relationship between brain activity and pain catastrophizing.

Results: At the uncorrected voxel-level ($p < 0.02$), PCS scores were correlated with neural activity in the mid orbital gyrus, paracentral lobule, middle cingulate cortex, posterior cingulate cortex, cerebellum cortex, inferior frontal gyrus, inferior temporal gyrus, middle frontal gyrus, and superior parietal lobule during imagination of ADLs. During imagination of physical activities, PCS scores were correlated with neural activity in the mid orbital gyrus, paracentral lobule, superior parietal lobule, middle occipital gyrus, and superior occipital gyrus. No

significant clusters remained after correcting for multiple comparisons at the cluster level with a significance of $p < 0.05$.

Conclusion: Individuals with ACLR and greater pain catastrophizing may experience alterations in brain activity when engaging in ADLs and physical activity. However, these findings should be interpreted with caution given the lack of statistical significance examined after correcting for multiple comparisons at the cluster level. Future research should explore differences in neural activity between high and low pain catastrophizers with ACLR during a PIT to better understand the impact of pain catastrophizing on central neural mechanisms in this population.

INTRODUCTION

Injury to the anterior cruciate ligament (ACL), the primary stabilizing ligament within the knee joint,⁴¹ may result from participation in sports that require activities such as landing, cutting, or sudden deceleration.^{53,55} ACL reconstruction (ACLR) is frequently performed to improve stability of the knee joint and to allow individuals to return to sport and physical activity.^{42,269} Despite this, up to 28% of patients who undergo ACLR will experience a secondary ACL injury.^{127,128} Increased risk of secondary injury has previously been linked to factors such as younger age and increased activity level after surgical reconstruction.¹²⁹ However, neuroplastic adaptations have also been demonstrated after ACL injury which may negatively influence recovery and pertinent clinical outcomes linked to secondary injury risk after ACLR.^{31,35,270}

Neuroplasticity, the brain's ability to reorganize and adapt to extrinsic or intrinsic factors,²⁷¹ may lead to changes in cognitive strategies, recruitment of different neural circuits, or changes in activation and connection among certain brain areas.²⁷² Neuroplasticity can occur after ligamentous injury in response to disrupted sensory feedback from the damaged mechanoreceptors of the injured ligament to the brain.³² Individuals with a history of ACL injury and reconstruction exhibit a variety of neuroplastic alterations, such as sensory and visual-motor processing compensations, which have been identified through functional magnetic resonance imaging (fMRI).¹⁷⁰ Specifically, patients with ACLR demonstrate increased activation in brain regions responsible for sensory, motor, sensory-visual-spatial, and cerebellar processing, and attention during lower extremity movement tasks when compared to healthy individuals.^{170,216} These neuroplastic alterations are suggested to contribute to motor control deficits that may be exhibited during knee and hip movement after ACLR.^{170,216} Psychological responses commonly experienced after ACLR, such as kinesiophobia, have also been linked to increased activation of brain regions involved in cognition and emotion during a visual and kinesthetic movement imagery task.⁵ However, it is unknown how other psychological

responses with affective components, like pain catastrophizing, may be associated with central neural mechanisms among individuals with ACLR.

Pain catastrophizing, a cognitive–affective response to anticipated or actual pain, has been exhibited by individuals following ACLR.^{10,12} Pain catastrophizing is considered one of the most reliable predictors of an individual's pain experience and is strongly associated with a variety of clinical pain-related outcomes in healthy individuals, as well as in individuals with chronic pain conditions including fibromyalgia, arthritis, and other rheumatic diseases.^{126,139-141} Among individuals with ACLR, previous research has identified high levels of pre-surgery pain catastrophizing to be associated with increased knee pain immediately following ACLR which may negatively affect rehabilitation outcomes.⁹ Individuals with ACLR who exhibit greater pain catastrophizing in the early post-operative period have also reported worse knee pain and function at both the start and conclusion of a subsequent rehabilitation program,¹² exemplifying the potential impact of pain catastrophizing on clinical outcomes after ACLR. Interestingly, even in the absence of pain, individuals with ACLR have also exhibited increased activation of brain regions responsible for the processing of painful stimuli when completing a knee flexion/extension motion.³³ It is possible that the increased activation of pain-related brain areas during basic movement among individuals with ACLR may be explained by the connection between pain catastrophizing and brain regions associated with pain perception.³⁶ Therefore, further investigation of psychological processes that can influence an individual's pain experience after ACLR is warranted.

To explore affective dimensions of pain in fMRI studies, use of a picture imagination task (PIT) has been proposed to better understand how individuals process information about specific actions that may cause pain- and/or movement-related anxiety and fear.^{224,273} During a PIT, individuals are instructed to imagine how they would feel both mentally and physically completing the task being shown in the image. Among individuals with chronic musculoskeletal pain, this approach has demonstrated increased activation in numerous regions associated with

pain processing and memory.²²⁴ Furthermore, among individuals with ACLR, a previous fMRI study using a PIT paradigm with images of activities of daily living and sport-specific images found increased activation in brain regions involved in emotional regulation when compared to individuals without ACLR.¹⁶⁸ It was proposed that individuals with ACLR may thus be more susceptible to processing fear, anxiety, and/or pain for sport-specific activities and activities of daily living when compared to individuals without ACLR,¹⁶⁸ however the underlying mechanisms of pain-specific psychological responses, such as pain catastrophizing, has yet to be explored in individuals with ACLR. Use of a PIT will assist in identifying actions associated with pain catastrophizing among individuals with ACLR.

Examination of the relationship between pain catastrophizing and neural activity during a PIT in individuals with a history of ACLR may allow for characterization of central neural mechanisms associated with clinical outcomes after ACLR and identification of intervention strategies to improve clinical outcomes in this population. Therefore, the purpose of this exploratory study was to examine the relationship between pain catastrophizing and brain activity among individuals with ACLR during a PIT. We hypothesized that individuals who reported higher levels of pain catastrophizing would demonstrate increased blood oxygen level dependent (BOLD) percent signal changes in brain regions associated with pain perception and/or emotional regulation, indicating increased neural activity, during the PIT.

METHODS

A cross-sectional study design was used to examine the association between pain catastrophizing and neural activity in individuals with ACLR during a PIT. The independent variable for this study was pain catastrophizing, measured by the Pain Catastrophizing Scale (PCS). The dependent variable for this study was BOLD percent signal change demonstrated during the PIT. Study procedures were approved by the Michigan State University Institutional Review board and informed consent, or parental informed consent and child assent, was obtained from all participants prior to study enrollment.

Participants

All participants met the following inclusion criteria: (1) were between the ages of 14 and 35 years old, (2) sustained their ACL injury participating in sport, (3) underwent unilateral ACLR, (4) were between 4-months and 5-years post-surgery, and (5) were magnetic resonance imaging (MRI) compliant. Individuals were not eligible for study participation if they had history of bilateral ACLR, had a history of secondary ACL injury or reconstruction to the ipsilateral limb, sustained an injury to the medial collateral ligament, lateral collateral ligament, or posterior collateral ligament at the same time as their index ACL injury, were currently injured or had injured their lower extremity within the 3 months prior to testing, or if they had experienced a concussion within the 3 months prior to testing. Informed consent or informed assent was obtained from all participants prior to study participation.

Procedures

Individuals reported to the Department of Radiology at Michigan State University to complete all assessments. Participants completed a demographics questionnaire which collected information including age, sex, race, height, weight, physical activity level, orthopedic history, and ACL surgical and rehabilitation history. Participants then underwent an fMRI scan. Upon completion of the fMRI scan, participants completed the PCS.

Neuroimaging Data Collection

Images were acquired on a GE Signa HDX 3T scanner (GE Healthcare, Waukesha, WI) with an 8-channel head coil. Functional data were acquired with echo-planar imaging (EPI) (TR= 2.5s; TE= 22 ms; flip angle= 80; 44 slices; matrix= 64x64; FOV= 22x22 cm; slice thickness= 3 mm) and 132 EPI volumes were collected in each run. High-resolution anatomical data were acquired with a T1 magnetization prepared and rapid-acquisition gradient echo sequence (MPRAGE, FOV= 256 mm, matrix= 256x256, slice thickness= 1.0 mm, 184 slices).

The fMRI paradigm for this experiment included 96 digitized black-and-white images. Specifically, 48 active images depicting individuals engaging in physical activity (e.g., jumping,

running, hopping) and 48 resting images depicting individuals engaging in activities of daily living (e.g., sitting, reading, listening to music) were used one time each throughout the paradigm. All images were cropped to the same size and are of the same resolution. Images selected for the task were chosen from the International Affective Picture System (IAPS) and Google Images. The IAPS consists of a set of images of normative emotional stimuli for investigations on personality traits of reactivity and emotional states.²⁷⁴ A total of 19 active images and 32 resting images were selected from the IAPS catalog. Active images were selected if the description included physical activity (e.g., weightlifting, football, rower, etc.). Additional images were selected from Google Images to ensure that the PIT had enough power to identify neural changes. Active and resting images were selected from Google Images if they exhibited similar, but not identical, activities to those demonstrated in the IAPS catalog. Images from the IAPS and Google Images were combined and randomly distributed throughout the fMRI scan. A projection screen (1024×768, 60 Hz) located in the scanner bore displayed the images with the use of a Digital Light Processing projector. Participants viewed the image from an angled mirror attached to the head coil while in the supine testing position.

The paradigm was controlled via MatLab software (MATLAB 2015b, The MathWorks, Inc., Natick, Massachusetts, United States). The stimulus presentation followed a block design with image blocks (Active v. Resting) presented in a random order and distributed once each across three fMRI runs, lasting five minutes and 40 seconds each (Figure 4.1). Specifically, each run began with a 20-second fixation cross followed by a random image block (Active or Resting) consisting of four images. Each image in the block was presented for five seconds. Each image block was followed by a fixation cross presented for 20 seconds to allow activation to return to baseline measures. Based on a previously established protocol by Taylor et al.,²²⁴ participants were given standardized instructions to imagine themselves physically and mentally completing the tasks demonstrated in the picture while each image was displayed.

Statistical Analysis

Descriptive statistics were calculated for participant demographics and PCS scores using STATA statistical software (StataCorp LLC, College Station, TX).

fMRI Data Analysis

fMRI data were analyzed using Analysis of Functional NeuroImages (AFNI) software.²⁷⁵ The initial 4 volumes were discarded for each participant for the T1 magnetization effect to reach steady state and for the adaptation of the participant. The remaining images were slice-timing corrected to the beginning of each volume. Next, anatomical and functional data were aligned via an automated algorithm implemented in AFNI and the datasets were aligned to the MNI space. Finally, a brain mask was generated for each participant to remove non-brain voxels and each voxel time series was scaled to have a mean of 100.

First-level analysis consisted of the preprocessed time series in each voxel being fit with a multiple linear regression model and using the AFNI 3dDeconvolve function. Two regressors were used to model the timing of the Active and Resting stimuli, respectively. The regressors were constructed by convolving a box car function corresponding to the stimulation block and a canonical hemodynamic response function. Beta weights for each regressor were obtained using the AFNI 3dbucket function, and the AFNI 3DTcorr1D function was used to compute Pearson's correlation coefficients between the beta weights of each PIT condition and PCS scores. To visualize the results, the voxel-wise p-value was set to 0.02, the cluster threshold to 30 voxels, and the NM level to 2.

RESULTS

A total of 15 individuals with a history of ACLR were included in this study. Descriptive statistics of participant characteristics are presented in Table 4.1. The median PCS score of our sample was 3 with an interquartile range of 8. At the uncorrected voxel-level, we identified seven small left-lateralized clusters of activation and one right-lateralized cluster of activation that were positively correlated with PCS scores during imagination of ADLs. This included the

mid orbital gyrus (126 voxels; $r=0.820$), middle cingulate cortex (92 voxels; $r=0.804$), paracentral lobule (92 voxels; $r=0.785$), posterior cingulate cortex (83 voxels; $r=0.811$), cerebellum cortex (78 voxels; $r=0.790$), inferior frontal gyrus (57 voxels; $r=0.839$), inferior temporal gyrus (38 voxels; $r=0.884$), and middle frontal gyrus (31 voxels; $r=0.709$). We also identified one small right lateralized cluster that was negatively correlated with PCS scores during imagination of ADLs in the superior parietal lobule (47 voxels; $r=-0.722$). Areas of brain activity correlated with PCS scores during imagination of ADLs are presented in Table 4.2 and Figure 4.2. During imagination of physical activity, we identified two small left-lateralized clusters of activation that were positively correlated with PCS scores in the mid orbital gyrus (48 voxels; $r=0.819$) and the paracentral lobule (36 voxels; $r=0.868$), as well as three small right-lateralized clusters of activation that were negatively correlated with PCS scores in the superior parietal lobule (44 voxels; $r=-0.772$), middle occipital gyrus (34 voxels; $r=-0.830$), and superior occipital gyrus (31 voxels; $r=0.833$). Areas of brain activity correlated with PCS scores during imagination of physical activity are presented in Table 4.3 and Figure 4.3. Despite the examined activation and corresponding correlations at the voxel threshold of $p < 0.02$, no significant clusters remained after correcting for multiple comparisons at the cluster level with a significance level of $p < 0.05$.

Table 4.1: Descriptive Statistics of Participant Characteristics and Pain Catastrophizing Scale Scores

Sex	
Females	10 (66.7%)
Males	5 (33.3%)
Height (cm)	168.14 (8.20)
Weight (kg)	69.34 (9.16)
Age (years)	22.8 (4.71)
Time Since ACLR (months)	23.09 (14.18)
PCS	3 [8]

Data are reported as frequency (%), mean (standard deviation), or median [interquartile range]. Abbreviations: Anterior Cruciate Ligament Reconstruction (ACLR), Pain Catastrophizing Scale (PCS)

Table 4.2: Areas of Brain Activity Correlated with Pain Catastrophizing Scale Scores During Imagination of Activities of Daily Living

Brain Area	Voxels	MNI Coordinates			<i>r</i>	<i>p</i> _{cluster_corrected}
		<i>x</i>	<i>y</i>	<i>z</i>		
Positive Correlations						
Mid Orbital Gyrus L	126	-8	61	-2	0.820	>0.10
Middle Cingulate Cortex L	92	-8	-47	37	0.804	>0.10
Paracentral Lobule L	92	-2	-35	55	0.785	>0.10
Posterior Cingulate Cortex L	83	-5	-41	7	0.811	>0.10
Cerebellum Cortex L	78	-5	-44	-17	0.790	>0.10
Inferior Frontal Gyrus L	57	-32	28	16	0.839	>0.10
Inferior Temporal Gyrus L	38	-53	-59	-11	0.884	>0.10
Middle Frontal Gyrus R	31	37	55	4	0.709	>0.01
Negative Correlations						
Superior Parietal Lobule R	47	19	-59	66	-0.722	>0.10

Abbreviations: Montreal Neurological Institute (MNI), Left (L), Right (R). Notes: Coordinates represent the maximum peak coordinates for clusters of activation with intensity exceeding a cluster threshold ≥ 30 at a voxel threshold of $p < 0.02$, uncorrected for multiple comparisons across the whole brain volume. The corresponding neuroanatomical areas are described as derived from the N27-MNI atlas. Correlation coefficients and corresponding cluster corrected *p*-values are also provided.

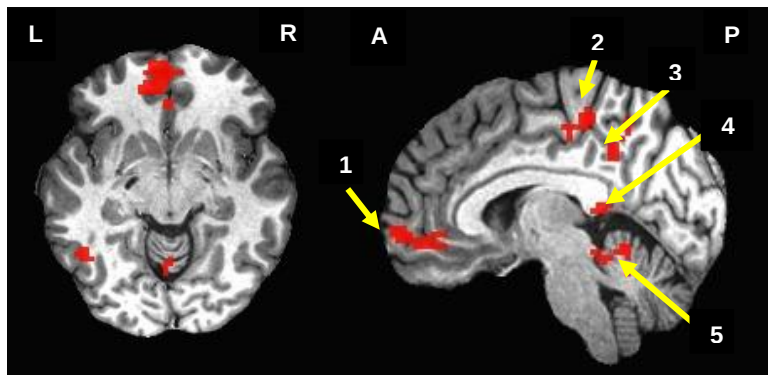


Figure 4.2: Combined functional magnetic resonance images of brain areas showing activation positively correlated with Pain Catastrophizing Scale scores during imagination of activities of daily living at a statistical threshold of $P < 0.02$ (uncorrected) at the voxel level. 1= mid orbital gyrus, 2= paracentral lobule, 3= middle cingulate cortex, 4= posterior cingulate cortex, 5= cerebellum cortex.

Table 4.3: Areas of Brain Activity Correlated with Pain Catastrophizing Scale Scores During Imagination of Physical Activity

Brain Area	Voxels	MNI Coordinates			<i>r</i>	<i>p</i> _{cluster_corrected}
		<i>x</i>	<i>y</i>	<i>z</i>		
Positive Correlations						
Mid Orbital Gyrus L	48	-5	52	-8	0.819	>0.10
Paracentral Lobule L	36	-2	-23	55	0.868	>0.10
Negative Correlations						
Superior Parietal Lobule R	44	22	-56	52	-0.772	>0.10
Middle Occipital Gyrus R	34	46	-77	1	-0.830	>0.10
Superior Occipital Gyrus L	31	-23	-87	33	-0.833	>0.10

Abbreviations: Montreal Neurological Institute (MNI), Left (L), Right (R). Notes: Coordinates represent the maximum peak coordinates for clusters of activation with intensity exceeding a cluster threshold ≥ 30 at a voxel threshold of $p < 0.02$, uncorrected for multiple comparisons across the whole brain volume. The corresponding neuroanatomical areas are described as derived from the N27-MNI atlas. Correlation coefficients and corresponding cluster corrected *p*-values are also provided.

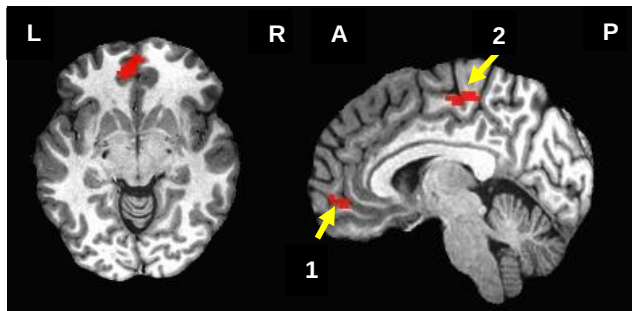


Figure 4.3: Combined functional magnetic resonance images of brain areas showing activation positively correlated with Pain Catastrophizing Scale scores during imagination of activities of daily living at a statistical threshold of $P < 0.02$ (uncorrected) at the voxel level. 1= mid orbital gyrus, 2= paracentral lobule.

DISCUSSION

To our knowledge, this is the first study to explore the relationship between pain catastrophizing and brain activity during a PIT in individuals with ACLR. At the uncorrected voxel-level, our exploratory analyses revealed correlations between pain catastrophizing and neural activity in the mid orbital gyrus, paracentral lobule, middle cingulate cortex, posterior cingulate cortex, cerebellum, inferior frontal gyrus, inferior temporal gyrus, and superior parietal lobule during imagination of ADLs. We also identified correlations between pain catastrophizing and neural activity in the mid orbital gyrus, paracentral lobule, superior occipital gyrus, superior parietal lobule, and middle occipital gyrus when imagining physical activity. These results suggest that pain catastrophizing may impact neural activity in a variety of pain and emotion-related brain regions among individuals with ACLR. However, these findings should be interpreted with caution as the identified correlations were no longer significant after correcting for multiple comparisons at the cluster level.

The area of greatest activation associated with pain catastrophizing during both the imagination of ADLs and physical activity occurred in the mid orbital gyrus. This area of the brain plays a role in emotional perception and specifically recognizes unpleasant emotions including fear and anxiety,^{276,277} which are commonly associated with pain and pain catastrophizing.^{137,278} Increased activation in this area has been identified among individuals with greater fear of pain when experiencing a painful stimulus compared to a non-painful stimulus.²⁷⁹ Although participants in our study were not exposed to a painful stimulus during the fMRI scan, the presence of pain catastrophizing combined with pain-related fear or anxiety during the PIT could have resulted in increased activation in this area. Furthermore, patients with chronic pain who experience unpleasant emotions and increased activity in the orbitofrontal region during mild pain are more likely to exhibit pain-related catastrophic thinking.²⁷⁷ It is then also possible that individuals with ACLR who experience unpleasant emotions, such as fear or anxiety, may be more likely to engage in pain catastrophizing strategies during tasks that could

evoke pain. Given that injury-related fear is a common psychological response exhibited after ACL injury and reconstruction,¹⁰⁸ future research should explore the connection between fear responses and pain catastrophizing post-ACLR to better understand how these psychological constructs may interact to influence central neural mechanisms in this population.

During the imagination of ADLs, greater pain catastrophizing was also associated with increased activation in the posterior cingulate cortex and inferior frontal gyrus which are regions involved in emotional processing and memory.²⁸⁰⁻²⁸³ It is possible that the positive correlation between pain catastrophizing and neural activity in these areas during the imagination of ADLs may be the result of negative pain-related emotions and memories associated with the tasks shown in the ADL images during the PIT task. This idea is supported by previous findings from Kelly et al.,²⁸⁴ which demonstrated that memories associated with pain-related words led to increased activation in the left anterior cingulate cortex and left inferior frontal gyrus. Similarly, Maddock et al.,²⁸¹ found that listening to emotionally unpleasant words resulted in increased activation of the posterior cingulate cortex when compared to listening to words that were considered emotionally neutral and suggested that the posterior cingulate cortex may play a mediating role in emotional and memory-related processes. Additionally, ACLR is associated with moderate to severe pain during the early post-operative and rehabilitation periods.²⁸⁵⁻²⁸⁷ Early stage rehabilitation is also a time when patients start to engage in physical tasks of daily life such as sitting, standing, walking, and ascending or descending stairs.²⁸⁷ Although individuals in our study were not instructed to generate personal pain-related memories or emotions corresponding to the images shown during the PIT, it is possible that individuals with greater pain catastrophizing associated the ADL images with memories of previous painful episodes during early phases of rehabilitation or negative pain-related emotions which could have resulted in the observed increased activation of the left inferior temporal gyrus and posterior cingulate cortex.

Pain catastrophizing was also positively correlated with activation in brain areas associated with the anticipation of pain, specifically the middle cingulate cortex and cerebellum,^{288,289} as well as in the paracentral lobule, a sensorimotor brain area, when imagining both ADL's and physical activity. The positive correlation identified in the cerebellum is consistent with previous research demonstrating increased activation in this area when high catastrophizers with fibromyalgia were anticipating a painful pressure stimulus.²⁹⁰ Individuals with chronic musculoskeletal pain and greater catastrophizing have also exhibited increased activation in the cerebellum, but when completing a PIT of ADLs, similar to the task used in this study, and in the absence of a painful stimulus.²²⁴ Additionally, Kokonyei et al.²⁹¹ identified that healthy individuals who exhibit greater rumination, a primary component of pain catastrophizing, demonstrate increased activation in the paracentral lobule when anticipating a painful stimulus. Therefore, it is possible that the positive correlation between pain catastrophizing and activation in these regions may be due to individuals anticipating feeling pain or ruminating on pain-related thoughts when imagining themselves physically completing different types of ADLs and physical activity. This is concerning as the anticipation of pain has been found to modulate spatial attention among high pain catastrophizers.²⁵ If individuals with ACLR who experience greater pain catastrophizing anticipate pain in situations that require adequate attentional functioning, such as sport, they may be less likely to attend to other relevant environmental stimuli which could increase risk of secondary injury. However, future research is needed to better understand the influence of pain catastrophizing on aspects of attention in sport-like settings among individuals with ACLR.

In our sample of individuals with ACLR, PCS scores were negatively correlated with brain activity in only two right-lateralized areas: the superior parietal lobule and the middle occipital gyrus. Furthermore, greater pain catastrophizing scores were associated with decreased activation in the superior parietal lobule during the imagination of both ADLs and physical activity. The superior parietal lobule is involved in a variety of functions including

visuospatial perception and aspects of attention.²⁹² The middle occipital gyrus also plays a role in visuospatial function which is an individual's ability to process the visual orientation or location of objects in space.²⁹³ Thus, it is possible that decreased activation in this area during the PIT among individuals with greater pain catastrophizing may be partly due to the attentional biases associated with pain catastrophizing. Pain catastrophizing involves heightened attention to pain-related stimuli and potential pain-related threats.²⁹⁴ Despite participants in this study not receiving a painful stimulus during the scan, if the actions shown in the PIT were perceived as potentially threatening for evoking pain when imagining physically completing them, individuals with greater pain catastrophizing may have had less attentional resources available to process non-pain related visuospatial information during the PIT which could have resulted in the decreased activation observed in the superior parietal lobule and middle occipital gyrus. Decreased activation in the superior parietal lobule in individuals with greater pain catastrophizing also reflects neuroplastic changes associated with chronic pain.²⁹⁵ Among patients with fibromyalgia, PCS scores were negatively correlated with activity in the superior parietal lobule when anticipating a painful stimulus.²⁹⁵ These findings suggest that it may have been possible for participants in our study to be anticipating experiencing pain when imagining the performance of ADLs and physical activity. This idea is further supported by the increased activation in the cerebellum and posterior cingulate cortex as previously discussed.

Interestingly, PCS scores were correlated with greater neural activity in more brain areas during the imagination of ADLs than during the imagination of physical activity in our sample of individuals with ACLR. Although we did not statistically compare differences in the correlation of PCS scores and brain activity between picture categories, these findings suggest that individuals with ACLR may be more likely to engage in pain catastrophizing strategies when completing daily tasks than when participating in physical activity and sport despite ACL injuries commonly resulting from sport participation.⁵¹ These findings may be partly due to the connection between pain, pain catastrophizing, and ADLs exhibited among individuals with

ACLR. Tichonova et al.¹² identified higher levels of pain catastrophizing to be strongly associated with greater knee pain and decreased knee-related function during ADLs within approximately one month of ACLR, as well as at the conclusion of a 12-week rehabilitation program. Jochimsen et al.¹⁰ also found pain catastrophizing to be significantly associated with pain, and more strongly associated with knee-related function for ADLs than sport and recreation at 6 months post-ACLR. These findings suggest that the presence of pain and pain catastrophizing at earlier timepoints post-ACLR may be more likely to contribute to an individual's perceived ability to engage in ADLs which may help to explain the greater number of correlations between brain activity and pain catastrophizing found among our sample during the imagination of ADLs. These findings may also be partly due to the salience or emotional importance of the images included in the PIT paradigm. The ADL images included in the PIT showed individuals engaging in tasks that would be common in daily life, such as talking on the phone, listening to music, or reading a book whereas the physical activity images showed individuals participating in various forms of physical activity and sport, such as running, jumping, skiing, football, gymnastics etc. Although general forms of physical activity that were shown, such as running, may have been relevant for all participants, the specific sport-related activities shown may not have been perceived as salient if participants did not commonly engage in that activity or the corresponding movements of that activity. Given that the ADL images displayed actions that participants would be more likely to perform regularly, it is possible that these tasks were perceived as more salient by our sample of participants when compared to the physical activity images that were included in the PIT paradigm.

This idea is supported by the increased activation of the middle cingulate cortex exhibited during the imagination of activities of daily living as this region commonly shows increased activity when stimuli are considered personally salient.²⁹⁶ Even though individuals in our cohort demonstrated various levels of pain catastrophizing, brain activity associated with pain catastrophizing strategies may be dependent on the personal salience of the activity.

Previous research utilizing a PIT paradigm to investigate neural responses in patients with chronic musculoskeletal pain asked participants to identify types of activities that were most troublesome for them to perform and then determined what activity pictures would be included in the PIT based on participant responses to ensure salience of the pictures.²²⁴ Similarly, a study examining pain-related fear in patients with chronic low back pain used a visualization task that showed someone carrying something in a crouched position which would be likely to elicit low back pain.²⁷³ As a result, individuals with chronic low back pain exhibited increased activation in brain areas associated with pain and emotion when compared to healthy controls.²⁷³ Identifying emotionally salient activities associated with pain among individuals with ACLR and using these images in a PIT may be warranted in future research to better understand the link between pain catastrophizing and neural activity in this population.

The lack of correlations identified between PCS scores and neural activity during the imagination of physically active tasks may also be partly due to the composition of the PCS. The PCS is designed to measure an individual's level of pain-related catastrophic thinking, but not in regard to specific situations or activities. The questionnaire instructs users to reflect on past painful experiences and then to indicate the degree to which they experience certain catastrophizing-related thoughts or feelings when experiencing pain. The 13 thoughts and feelings listed in the questionnaire are related to the primary components of pain catastrophizing and thus assess aspects of magnification (e.g., "I become afraid the pain will get worse"), helplessness (e.g., "It's terrible, and I think it's never going to get better"), and rumination (e.g., "I keep thinking about how much it hurts"). However, given that the questions on the PCS assess general pain-related thoughts as opposed to pain-related thoughts specific to sport or physical activity, participants may have found the questions to be more relevant to daily activities when compared to physical activity. Additionally, although the PCS instructs individuals to reflect on thoughts and feelings about previous pain experiences, participants in our study may have reflected on pain experiences unrelated to their ACL injury and

reconstruction which could have also contributed to more correlations being present during the imagination of ADLs. However, given that ACL injuries are a common result of sport and physical activity,⁵¹ use of a questionnaire that instructs users to specifically reflect on their ACLR- or knee-related pain experiences may allow for better understanding of the connection between pain-related thoughts and brain activity when imagining physical activity.

A number of limitations should be noted for this study. First, although our sample was similar in size to those previously used to investigate neural correlates of brain activity and psychological outcomes in individuals with ACLR,²⁹⁷ we may have been underpowered to identify significant correlations between neural activity and pain catastrophizing. Second, despite previous use of the PCS in ACLR literature, it has yet to be validated for the ACLR population. Furthermore, many participants in our sample scored at, or near, the lowest possible PCS value, which could have caused a floor effect making meaningful relationships more difficult to detect. Future research may benefit from using a median split to explore differences in brain activity during a PIT between individuals with high and low pain catastrophizing to better understand how pain catastrophizing strategies may impact neural activity in individuals with ACLR. Third, we did not measure whether participants were actively experiencing pain while completing the PIT which could have led to some of the correlations examined in this study. Finally, although use of a PIT with images depicting engagement in ADLs has been previously used to identify neural correlates of pain catastrophizing,²²⁴ future research using images identified as being personally salient to individuals with ACLR may help to better understand the relationship between pain catastrophizing and brain activity in this population.

CONCLUSION

Among individuals with ACLR, pain catastrophizing was correlated with brain activity in regions associated with aspects of emotional perception and processing, anticipation of pain, memory, attention, and visuospatial function during imagination of ADLs and physical activity. However, these findings should be interpreted with caution given the small sample size, lack of

variability in pain catastrophizing scale scores among our sample, and absence of statistical significance after correcting for multiple comparisons. Future research should explore differences in neural activity between high and low pain catastrophizers with ACLR during a PIT of salient activities to better understand the impact of pain catastrophizing on central neural mechanisms in this population.

CHAPTER 5: THE INFLUENCE OF PAIN CATASTROPHIZING ON CHANGE IN LOWER EXTREMITY PERCEPTUAL-MOTOR COORDINATION AND LANDING KINETICS IN THE PRESENCE OF SPORT-SPECIFIC DISTRACTION IN INDIVIDUALS WITH ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION

ABSTRACT

Context: Approximately 30% of patients will sustain a secondary anterior cruciate ligament (ACL) injury upon return to sport (RTS). In sport settings, auditory and visual changes that occur in the surrounding environment may shift attention away from skill performance and increase injury risk. Attention may also be negatively affected by pain catastrophizing, a cognitive-affective response to anticipated or actual pain that is frequently exhibited after ACLR.

Attentional changes that occur because of pain catastrophizing, as well as distractions that commonly occur during sport, may consequently impact perceptual and landing-specific injury-related outcomes for individuals with a history of ACLR. However, the influence of pain catastrophizing on such injury-related outcomes has yet to be explored in this population.

Therefore, the primary purpose of this study was to examine the influence of pain catastrophizing on changes in lower extremity perceptual-motor coordination (P-MC) and peak vertical ground reaction force (vGRF) symmetry in the presence of sport-specific visual and auditory stimuli in individuals with ACLR.

Methods: A total of 23 participants (age= 20.43 ± 2.99 years) with history of primary unilateral ACLR (time since ACLR= 28.61 ± 13.00 months) were included in this study. Participants completed the Pain Catastrophizing Scale (PCS), a lower extremity P-MC task, and a jump-landing task in a 360° immersive visualization room under two conditions: 1) distraction: sport-specific visual and auditory stimuli playing during testing, and 2) control: no sport-specific visual or auditory stimuli playing during testing. Differences in lower extremity P-MC and peak vGRF symmetry between the control and distraction condition were calculated to determine the change score for each outcome measure. Separate linear regression models were then used to

examine the association between PCS scores, P-MC change scores, and the peak vGRF symmetry change score. Alpha was set *a priori* $p < .05$.

Results: The multiple linear regression analyses indicated that PCS scores were not significantly associated with change in ACLR limb P-MC ($\beta = 0.001$, $p = 0.477$) or change in contralateral limb P-MC ($\beta = 0.001$, $p = 0.438$) between the control and distraction condition when controlling for age. Similarly, PCS scores were not significantly associated with change in peak vGRF symmetry ($\beta = -0.117$, $p = 0.855$) between the control and distraction condition.

Conclusion: Pain catastrophizing was not associated with changes in lower extremity P-MC or peak vGRF symmetry among individuals with ACLR in the presence of sport-specific visual and auditory stimuli. Future research should explore the influence of pain catastrophizing on the performance of different sport-related tasks and in the presence of different types of stimuli to better understand how this pain-related psychological response may impact individuals with ACLR upon RTS.

INTRODUCTION

Injury to the anterior cruciate ligament (ACL) is common among physically active individuals and may occur from activities that require change of direction, cutting, and/or jumping.⁵¹ The primary purpose of ACL reconstruction (ACLR) is to repair the integrity of the ACL and allow patients to return to previous levels of physical activity or sport.²⁹⁸ However, 30% of individuals who return to high levels of activity will sustain a second ACL injury within 24-months of return to sport (RTS).⁴ Increased risk of secondary ACL injury has previously been linked to a variety of modifiable factors including impaired lower extremity biomechanics (e.g., greater kinetic asymmetry during jump-landing),¹³³ and psychological responses commonly exhibited after ACLR, such as increased injury-related fear.³⁷ However, secondary injury risk may also be partly due to changes in distraction and attention that can occur during sport.^{299,300}

Selective attention, the ability to attend to relevant information while excluding irrelevant information and distracting stimuli, is required for effective sport performance.²⁰⁻²³ However, auditory and visual changes that commonly occur in the surrounding environment during sport may shift attention away from skill performance and consequently increase injury risk.^{117,299,300} External visual and auditory stimuli have been shown to negatively affect aspects of neurocognitive function including reaction time, among healthy individuals.³⁰¹⁻³⁰³ This is concerning for individuals with ACLR who have an increased risk of secondary ACL injury as deficits in components of neurocognitive function, such as perceptual-motor coordination (P-MC) or the time it takes to interpret sensory information and execute a movement,²⁶ have been linked to increased injury risk during sport.²⁵⁵ Visual distraction has also been shown to cause changes in jump-landing biomechanics among healthy individuals.³⁰⁴ Given that individuals with ACLR commonly demonstrate changes in landing biomechanics, including asymmetries in vertical ground reaction force (vGRF),¹⁹² visual distractions that occur in the surrounding environment during sport may further contribute to

biomechanical impairments and injury risk in this population upon RTS. However, individuals who RTS after ACLR may also experience attentional changes due to psychosocial factors.

The Stress and Injury Model proposes that psychosocial factors, including history of stressors (e.g., previous injury), personality (e.g., locus of control), and coping resources (e.g., general coping behaviors) may cause negative attentional changes during stressful athletic situations.¹²⁰ Pain catastrophizing, a cognitive–affective response to anticipated or actual pain,¹²⁶ is considered a maladaptive coping strategy that may be experienced after ACLR and may further influence aspects of attention. Furthermore, rumination, a component of pain catastrophizing characterized by repetitive focus on discomforting emotions or stimuli, may interfere with an individual's ability to inhibit thoughts and switch focus of attention.¹³⁷ Specifically, previous research has identified that individuals with greater pain catastrophizing experience changes in spatial attention when anticipating pain.²⁵ A heightened attention to anticipated pain also increases the difficulty of directing attention to other environmental stimuli.²⁵ For individuals with ACLR who experience pain catastrophizing, attentional fixation due to anticipation of pain may thus negatively influence sport performance, consequently affecting injury-related outcomes, such as P-MC and vGRF, and increase risk of secondary ACL injury.

Given the consequences of visual and auditory distractions examined among healthy individuals and the attentional changes that may occur as a result of pain catastrophizing, there is a need to examine the influence of pain catastrophizing on biomechanical and perceptual-motor outcomes in individuals with ACLR in settings that mimic the distraction experienced during sport. Exploration of this relationship may highlight the need to address psychological impairments that impact attention after ACLR. Therefore, the primary purpose of this study was to examine the influence of pain catastrophizing on changes in lower extremity P-MC and vGRF symmetry in the presence of sport-specific visual and auditory stimuli in individuals 1- to 5-years

post-ACLR. We hypothesized that individuals with greater pain catastrophizing would exhibit larger changes in P-MC and vGRF in the presence of sport-specific distraction when compared to a controlled setting without distraction.

METHODS

A cross-sectional study design was used to examine the influence of pain catastrophizing on lower extremity P-MC and jump-landing biomechanics in individuals with ACLR. The independent variable for this study was Pain Catastrophizing Scale (PCS) scores. The dependent variables for this study were (1) change in lower extremity P-MC measured using the FitLight Trainer™ (FitLight Sports Corp, Aurora, Ontario, Canada), and (2) change in vGRF limb symmetry (%) which was measured with force-measuring insoles (Loadsol, Novel Electronics, St. Paul, MN). Study procedures were approved by the Michigan State University Institutional Review board and informed consent or parental informed consent and child assent, was obtained from all participants prior to study enrollment.

Participants

Individuals were eligible for study participation if they had a history of unilateral ACLR, if they sustained their knee injury during sports participation, if they were between 1 and 5 years post-ACLR, and if they had been cleared for RTS by their physician. Individuals were excluded from the study if they had a history of secondary ACL injury, history of ACL injury or reconstruction to the ipsilateral limb, sustained an injury to the medial collateral ligament, lateral collateral ligament, or posterior collateral ligament in the same knee at the same time as their index ACL injury, injured their lower extremity within the 3 months prior to testing, experienced a concussion in the 3 months prior to testing, were taking medications that affected the CNS, had any neurological conditions that affected their cognitive status, experienced severe motion sickness, or if they participated in a sport that falls out of the scope of the sports-specific videos that were accessible by the research team.

Procedures

Individuals reported to the Digital Scholarship Laboratory at Michigan State University to complete all assessments. All participants completed a demographics questionnaire which inquired about pertinent health history and previous rehabilitation activities. Next, participants completed the PCS. Upon completion of questionnaires, participants completed the lower extremity P-MC task and the jump-landing task in an immersive condition with sport-specific visual and auditory distraction and in a non-immersive condition without distraction. Testing condition and order of task completion were counterbalanced between participants.

Pain Catastrophizing Scale

The PCS is a 13-item questionnaire designed to measure an individual's perceptions of their pain experience and includes three subscales which examine the primary components of pain catastrophizing: magnification (e.g., "I become afraid the pain will get worse"), helplessness (e.g., "It's terrible, and I think it's never going to get better"), and rumination (e.g., "I keep thinking about how much it hurts").⁸ Questionnaire items are scored on a Likert scale from 0 (not at all) to 4 (all the time) with the total PCS score ranging from 0-52. Higher PCS scores indicate greater pain catastrophizing. The PCS has adequate to excellent internal consistency (Cronbach α : total PCS=.87, rumination=.87, magnification=.66, helplessness=.78),⁸ as well as good to excellent test-retest reliability (ICC=0.99-.90) and adequate validity (0.40-0.42).¹⁷⁹ The PCS may be found in the Appendix.

Condition

Distraction condition testing was conducted in an Igloo Vision 360° immersive visualization room (Igloo Vision Ltd., New York, NY). The immersive visualization room is a cylinder 20-feet in diameter with 10 ft. walls and a projector system that creates a 360° floor to ceiling visual display (Figure 5.1). During distraction condition testing, a sport-specific video was shown on the walls with the accompanying audio playing through the surround-sound system. The selected video displayed individuals actively engaging in the sport that the participant was

playing at the time of ACL injury. Control condition testing was conducted in the same room, but without the use of visual display and audio.

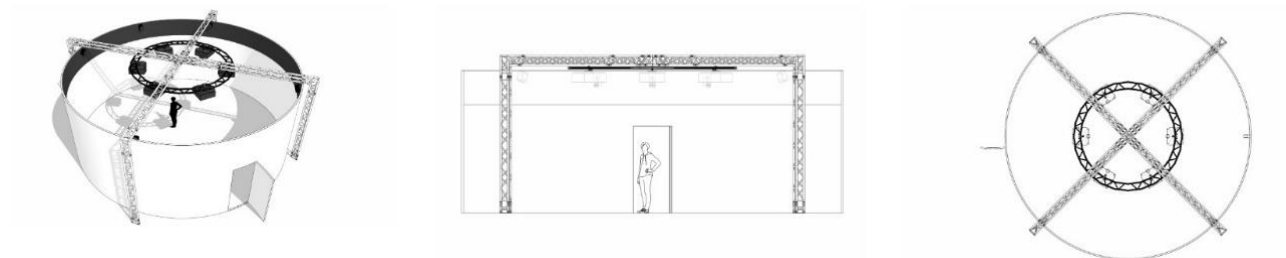


Figure 5.1: A model of the Igloo Vision immersive visualization cylinder that was used to provide sport-specific distraction in the form of floor-to-ceiling visual display and surround sound audio during distraction condition testing.

Lower Extremity Perceptual-Motor Coordination

Lower extremity P-MC was measured using a reliable task via the FitLight Trainer™ (FitLight Sports Corp, Aurora, Ontario, Canada), a series of wireless light disks.¹⁹⁰ Participants were placed at the center of a 180° semicircle with five light discs secured to the ground in increments of 45° (Figure 2.1). The distance of each light disc was normalized to the length of the participant's shank, except for the light closest to the stance limb, which was placed at half the distance of the participant's shank. For testing, the "Hand/Eye Coordination" mode of the system was used to generate a random sequence of visual stimuli amongst the five light discs. Participants were instructed to respond and deactivate the randomly illuminated lights by tapping the disc with their foot as quickly as possible. The assessment was completed bilaterally and test limb (moving limb deactivating the lights) order was counterbalanced between participants. Participants completed three 30-second familiarization trials followed by one 60-second test trial with their ACLR limb as the stance limb (Contralateral Limb P-MC) and with their ACLR limb as the moving limb deactivating the lights (ACLR Limb P-MC). Lower extremity P-MC was calculated as the average time (seconds) between light hits. Higher lower extremity

P-MC scores are indicative of slower lower extremity P-MC. This task has demonstrated excellent right limb reliability (ICC=.86) and good left limb reliability (ICC=.80).²⁵⁶

Vertical Ground Reaction Force

All participants were fitted with a pair of force-measuring insoles (Loadsol, Novel Electronics, St. Paul, MN) while wearing their personal athletic shoes. The Loadsol® has a single force sensor along the length of the insole to collect vGRF without the need for traditional forceplates.²¹⁰ The following procedures have been used with the Loadsol® that has been shown to be reliable and valid when assessing jump-landing biomechanics.²⁰⁹ The Loadsol-s mobile application on a 10.5" iPad (Apple Inc., Cupertino, CA) was used to calibrate and collect the biomechanics data via Bluetooth. We followed manufacturer calibration recommendations and tested the calibration during single limb stance trials to confirm the insoles measured $\pm 5\%$ of the participant's body weight. Participants were then asked to complete a drop-vertical jump task in which they dropped from a 30-cm box onto a standardized landing area and immediately jumped upward with maximal effort (Figure 2.2).²¹⁰ The box was positioned at $\frac{1}{2}$ the participant's height away from the designated landing area. Participants completed one practice trial and three test trials and data was simultaneously collected from the Loadsol® (100 Hz) during each test trial. Loadsol® data was exported to text files and analyzed using the Load Analysis Program (<https://github.com/GranataLab/LAP>) in Matlab (Mathworks, Natick, MA). Peak vGRF symmetry was computed for each trial and an average symmetry index across three successful trials ($\text{Limb Symmetry [\%]} = \frac{\text{Healthy Limb} - \text{ACLR Limb}}{\frac{1}{2}(\text{Healthy Limb} + \text{ACLR Limb})}$) was calculated.³⁰⁵

Statistical Analysis

Descriptive statistics were calculated for PCS scores, ACLR limb P-MC (seconds), contralateral limb P-MC (seconds), and peak vGRF symmetry (%) in the distraction condition and control condition. Change scores were then calculated to determine changes in each variable between conditions and paired t-tests were conducted to identify potential differences in P-MC

and peak vGRF symmetry between conditions. Separate multiple linear regression models were used to examine the association between PCS scores (independent variable), change in ACLR limb P-MC (dependent variable), change in contralateral limb P-MC (dependent variable), and change in peak vGRF symmetry (dependent variable). When performing linear regression analyses, a minimum of 10 participants should be included per predictor variable.^{257,258} Because of this, no more than 2 predictor variables were included in the final regression models. Univariate analyses were completed to identify potential demographic confounders. Age was most strongly associated with lower extremity P-MC in our sample and therefore was included as a covariate in the regression models including P-MC outcomes. Covariates were entered into the regression model first, followed by PCS scores. The assumptions of normality, homoscedasticity, and linearity were verified for each regression model and the models were examined for outliers using the standardized residuals from the regression model. The overall percent of the explained variance (R^2) for the regression analysis was identified and the regression coefficient (β), constant, p values, confidence intervals, and individual predictive power of each variable was reported. Alpha was set *a priori* $p < .05$. All statistical analyses were conducted using STATA statistical software (StataCorp LLC, College Station, TX).

RESULTS

A total of 23 participants with history of primary unilateral ACLR were included in this study. Participant characteristics are presented in Table 5.1. Descriptive statistics of lower extremity P-MC and peak vGRF symmetry in each condition, as well as the change in each variable between conditions, are presented in Table 5.2. Results of the separate multiple regression analyses indicated that PCS scores were not significantly associated with change in ACLR or contralateral limb P-MC between the control and distraction condition when controlling for age (ACLR Limb P-MC Change: $R^2=0.073$, $\beta=0.001$, $p=0.477$; Contralateral Limb P-MC Change: $R^2=0.080$, $\beta=0.001$, $p=0.438$; Table 5.3). Four participants were excluded from the regression analysis exploring the association between PCS scores and change in peak vGRF

symmetry due to data errors and unsuccessful task completion. Results of the multiple linear regression identified that PCS scores were not significantly associated with change in peak vGRF symmetry between the control and distraction condition ($R^2=0.002$, $\beta=-0.117$, $p=0.855$; Table 5.4).

Table 5.1: Participant Characteristics

Sex	
Females	17 (73.91%)
Males	6 (26.08%)
Age, years	20.43 (2.99)
Height, cm	168.26 (8.20)
Weight, kg	69.55 (9.64)
Time Since ACLR, months	28.61 (13.00)
PCS	5 [11.5]
Sport Type	
Soccer	7 (30.43%)
Volleyball	2 (8.70%)
Basketball	6 (26.09%)
Softball	1 (4.35%)
Cheer	2 (8.70%)
Football	1 (4.35%)
Handball	1 (4.35%)
Gymnastics	1 (4.35%)
Dance	1 (4.35%)

Data are reported as frequency (%), mean (standard deviation), or median [interquartile range]. Abbreviations: Anterior Cruciate Ligament Reconstruction (ACLR), Pain Catastrophizing Scale (PCS)

Table 5.2: Descriptive Statistics of Lower Extremity Perceptual-Motor Coordination and Peak Vertical Ground Reaction Force Symmetry Across Conditions and the Change Between Conditions

Variable	Condition		Change	p-value
	Distraction	Control		
ACLR Limb P-MC (sec)	0.487 [0.061]	0.491 [0.059]	-0.007 [0.034]	0.077
Contralateral Limb P-MC (sec)	0.479 [0.061]	0.488 [0.061]	-0.009 [0.031]	0.314
Peak vGRF Symmetry (%)	91.77 (15.53)	93.73 (14.81)	1.96 (20.35)	0.680

Data are presented as median [interquartile range] or mean (sd). Abbreviations: Anterior Cruciate Ligament Reconstruction (ACLR), Perceptual-Motor Coordination (P-MC), Vertical Ground Reaction Force (vGRF)

Table 5.3: Multiple Linear Regression Results for Change in Lower Extremity Perceptual-Motor Coordination Between the Control and Distraction Condition (N=23)

Predictor Variables	ACLR Limb P-MC Change			Contralateral Limb P-MC Change		
	β (95% CI)	<i>p</i> value	R^2	β (95% CI)	<i>p</i> value	R^2
Overall Model		0.471	0.073		0.436	0.080
Constant	-0.077 (-0.187, 0.033)	0.158		-0.091 (-0.234, 0.053)	0.202	
Age	0.002 (-0.002, 0.008)	0.254		0.004 (-0.003, 0.010)	0.284	
PCS	0.001 (-0.002, 0.002)	0.620		0.001 (-0.002, 0.004)	0.438	

Abbreviations: Anterior Cruciate Ligament Reconstruction (ACLR), Perceptual-Motor Coordination (P-MC), Pain Catastrophizing Scale (PCS)

Table 5.4: Multiple Linear Regression Results for Change in Peak Vertical Ground Reaction Force Symmetry Between the Control and Distraction Condition (N=19)

Predictor Variables	β (95% CI)	<i>p</i> value	R^2
Overall Model		0.855	0.002
Constant	2.859 (-11.568, 17.286)	0.681	
PCS	-0.117 (-1.445, 1.212)	0.855	

Abbreviations: Pain Catastrophizing Scale (PCS)

DISCUSSION

The aim of the present study was to examine the influence of pain catastrophizing on change in lower extremity P-MC and vGRF symmetry in the presence of sport-specific visual and auditory stimuli in individuals with ACLR. It was hypothesized that individuals with greater pain catastrophizing would exhibit larger changes in P-MC and vGRF when in a setting with distractions compared to a control setting. However, our results did not support our hypothesis as pain catastrophizing was not significantly associated with change in lower extremity P-MC or vGRF symmetry among individuals with ACLR when immersed in sport-specific visual and auditory stimuli.

Despite previous research demonstrating that individuals who interpret pain as threatening and who catastrophize on the possible consequences of a pain experience exhibit increased disruptions in attention,³⁰⁶⁻³⁰⁹ we were unable to link pain catastrophizing with changes in task performance in the presence of sport-specific distraction in our sample of individuals with ACLR. These findings may be partly due to the lack of meaningful change in task performance between the distraction and control condition. In this study, we used visual and auditory stimuli specific to the sport each participant was engaged in at the time of their ACLR injury in an attempt to increase the relevance of the stimuli for each participant and to replicate sport-specific distractions that they may experience when engaged in sport post-ACLR. However, we identified a small and non-significant change in P-MC and peak vGRF symmetry between the distraction and control condition. This may have been impacted by the perceived salience or importance of the external stimuli used in the distraction condition as an individual's ability to selectively attend to something is influenced by the salience of the stimulus.³¹⁰ The stimulus salience may have also contributed to the lack of association between pain catastrophizing and change in task performance as previous research exploring the effects of pain and pain catastrophizing on task completion and distraction has commonly used nociceptive sensory stimuli, such as an electrocutaneous stimulus,^{25,311,312} heat stimulus,²⁶⁸ or a

mechanical pressure stimulus,²⁶⁷ as the competing sensory stimulus while performing a task. Given that pain is considered highly salient,³¹³ a nociceptive sensory stimulus combined with pain catastrophizing strategies may be more effective in influencing attention or aspects of behavioral performance (i.e., reaction time) during task completion when compared to sport-specific visual and auditory stimuli.

Similarly, the perceived salience of the tasks being performed when compared to the external stimuli or catastrophic thoughts about pain may have also contributed to our study findings. While engaging in movement, the brain directs the most attentional capacity toward more salient signals in order to complete the movement successfully.³¹⁴ If a competing stimulus is perceived as irrelevant, the brain may inhibit activity of neurons that would otherwise respond to the irrelevant stimuli.³¹⁵ When irrelevant stimuli are dismissed, individuals are able to allocate more attention to task-relevant information and are less likely to have distractors negatively influence their performance.³¹⁶ The movement-based lower extremity P-MC task and DVJ task used in this study were focused attention tasks in which the added visual and auditory stimuli were irrelevant to the completion of the tasks. These types of tasks allow for a greater attentional load, or amount of attention that can be invested in a task, which decreases the ability of stimuli that are irrelevant to the task to capture attention.³¹⁷ Therefore, it is possible that participants in our study deemed the external stimuli irrelevant to the tasks and were subsequently able to direct more attentional capacity toward task-relevant stimuli while completing the movements required for the P-MC and DVJ tasks despite experiencing pain catastrophizing. Additionally, the lower extremity P-MC task used in this study prompted participants to keep their gaze focused downward which could have further minimized the ability of the sport-specific visual stimuli to influence aspects of attention during task completion. Given that athletes commonly experience cognitive loading in the form of decision making and divided attention,³¹⁸ use of a dual-task condition in which individuals are required to simultaneously perform a motor task and a cognitive task may be warranted to better replicate common

attentional demands of sport and improve understanding of how pain catastrophizing may influence injury-related outcomes upon RTS post-ACLR.

Additionally, although previous research by Van Damme et al.²⁵ found greater pain catastrophizing to modulate spatial attention when anticipating pain, the PCS scores in our sample were significantly lower than those previously used to identify 'high catastrophizers'. In the Van Damme et al.²⁵ study, changes in spatial attention when anticipating pain were demonstrated in individuals with a median PCS score >18. However, our cohort of individuals with a history of ACLR had a median PCS score of 5. Thus, it is possible that the level of pain-related catastrophic thinking demonstrated by our sample was too low to compete for attentional resources and consequently influence performance of the P-MC and DVJ tasks despite the competing visual and auditory stimuli in the distraction condition. Furthermore, the P-MC and DVJ tasks used in this study may not have been perceived as threatening or elicited any sort of salient pain-related stimulus given that our cohort was approximately 2 years post-surgery and had received medical clearance for return to sport. At this timepoint post-surgery, many individuals have returned to regular sport and physical activity participation and may have had significant previous exposure to the movements required for the tasks used in this study which could decrease potential perceptions of a pain-related threats associated with the tasks. If individuals were not experiencing or anticipating pain during the P-MC and DVJ task, there may have then been less competition for attentional resources subsequently allowing for a greater amount attention to be dedicated to the task-relevant stimuli despite the presence of the visual and auditory distraction. Future research may benefit from having individuals with ACLR and greater pain catastrophizing perform injury-related tasks perceived as threatening or salient in the presence of distraction to better understand the potential impact of this pain-related psychological response on injury-related outcomes after ACLR.

Prior literature that has examined pain catastrophizing in collegiate athletes identified a median PCS score of 5 among previously injured athletes which is similar to the score of our

sample of current and former athletes with history of ACLR.³¹⁹ However, despite our findings supporting that pain catastrophizing may be present in previously injured athletic populations, the lack of association between pain catastrophizing and change in performance in the presence of sport-specific distraction in this study may be the result of differences in aspects of attention between athletes and non-athletes. Research has shown that athletes are better able to distribute and quickly switch their attention across multiple locations when compared to non-athletes.³²⁰ Furthermore, athletes trained in visually dynamic team sport environments (i.e., soccer, volleyball) demonstrate better visual focused attention in the presence of auditory distraction when compared to athletes trained in static visual environments common in individual sports (i.e., track and field, gymnastics).³²¹ Interestingly, 22 out of the 23 participants in our sample participated in visually dynamic team sports which could have positively influenced their ability to effectively attend to the P-MC and DVJ tasks despite any catastrophic thoughts about pain and the presence of the sport-specific visual and auditory stimuli in the distraction condition. Exploring the influence of individual factors that may contribute to the performance of sport-related tasks in the presence of external stimuli (e.g., attentional control, sport type) among individuals with pain catastrophizing and ACLR may be warranted.

This study is not without limitations. First, the small sample size of this study allowed us to control for only one variable in the regression analyses with P-MC outcomes and did not allow us to control for any confounding variables in the regression analysis examining change in peak vGRF symmetry. Future research should aim to enroll larger samples to allow for the inclusion of other potentially confounding variables of perceptual-motor and biomechanical outcomes (e.g., time since ACLR, age, sex, physical activity level). Second, the PCS used in this study has not been validated for the ACLR population and additional research is needed to identify clinical levels of catastrophizing in this patient population. Third, the low PCS scores reported by our sample could have caused a floor effect and did not allow for the conduction of any secondary analyses using the PCS subscales. Future research should explore the potential

influence of pain-related rumination, magnification, and helplessness on change in perceptual-motor and biomechanical performance in sport-like settings among high catastrophizers with ACLR.

CONCLUSION

Pain catastrophizing was not associated with changes in lower extremity P-MC or peak vGRF symmetry when in the presence of sport-specific visual and auditory stimuli in individuals 1- to 5-years post-ACLR. These findings suggest that pain catastrophizing may not be a critical factor contributing to perceptual-motor or biomechanical injury-related outcomes in sport-like settings among individuals with ACLR. However, future research may benefit from exploring the influence of pain catastrophizing and its individual components on the performance of tasks perceived as salient, as well as in the presence of salient stimuli, to better understand how pain catastrophizing may impact aspects of attention after ACLR.

CHAPTER 6: SUMMARY

PURPOSES AND HYPOTHESES

The overarching goal of this dissertation was to better understand whether pain catastrophizing is associated with central and peripheral neural mechanisms after ACLR and to characterize the role of pain catastrophizing on injury-related outcomes in individuals with ACLR. To do this, three studies were conducted with the following purposes and hypotheses:

1. To examine the influence of pain catastrophizing on lower extremity perceptual-motor coordination (P-MC) in individuals 4-months to 5-years post-ACLR.

Hypothesis: Individuals with ACLR who exhibit higher levels of pain catastrophizing will demonstrate worse lower extremity P-MC.

2. To examine the association between pain catastrophizing and neural activity during a picture imagination task (PIT) among individuals 4-months to 5-years post-ACLR.

Hypothesis: Individuals with ACLR who exhibit higher levels of pain catastrophizing will demonstrate increased blood oxygen level dependent (BOLD) percent signal changes in brain regions associated with pain perception and/or emotional regulation during a PIT.

3. To examine the influence of pain catastrophizing on the change in lower extremity P-MC and peak vertical ground reaction (vGRF) symmetry in the presence of sport-specific visual and auditory stimuli in individuals 1- to 5-years post-ACLR.

Hypothesis: Individuals with ACLR and greater pain catastrophizing will exhibit larger changes in P-MC and peak vGRF symmetry in the presence of sport-specific distraction.

FINDINGS

The findings for each study and corresponding purpose include:

1. To examine the influence of pain catastrophizing on lower extremity P-MC in

individuals 4-months to 5-years post-ACLR.

Findings: The hypothesis was not supported. Pain catastrophizing was not associated with lower extremity P-MC in individuals with ACLR.

2. To examine the association between pain catastrophizing and neural activity during a PIT among individuals 4-months to 5-years post-ACLR.

Findings: The hypothesis was supported, but our findings that pain catastrophizing was correlated with brain activity in regions associated with aspects of emotional perception and processing, anticipation of pain, memory, attention, and visuospatial function during imagination of ADLs and physical activity should be interpreted with caution due to the absence of statistical significance after correcting for multiple comparisons.

3. To examine the influence of pain catastrophizing on the change in lower extremity P-MC and peak vGRF symmetry in the presence of sport-specific visual and auditory stimuli in individuals 1- to 5-years post-ACLR.

Findings: The hypothesis was not supported. Pain catastrophizing was not associated with changes in lower extremity P-MC or peak vGRF symmetry among individuals with ACLR in the presence of sport-specific visual and auditory stimuli.

CONCLUSIONS

Individuals with ACLR experience varying degrees of pain catastrophizing after injury and reconstruction.^{10,12,15,16} Our results indicate that pain catastrophizing in this population may correspond with altered brain activity in areas associated with emotional perception and processing, anticipation of pain, memory, attention, and visuospatial function. However, pain catastrophizing does not appear to influence perceptual-motor or biomechanical outcomes in individuals with ACLR. Future research should explore longitudinal changes in pain catastrophizing and its potential influence on injury-related outcomes at various timepoints

throughout the ACLR rehabilitation process, as well as after return to activity, and among individuals with high and low catastrophizing to better understand how this pain-related psychological response may impact aspects of recovery and secondary injury risk among individuals with ACLR.

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APPENDIX

Pain Catastrophizing Scale (PCS)

When I'm in pain...

1. I worry all the time about whether the pain will end
 2. I feel I can't go on
 3. It's terrible and I think it's never going to get any better
 4. It's awful and I feel that it overwhelms me
 5. I feel I can't stand it anymore
 6. I become afraid that the pain will get worse
 7. I keep thinking of other painful events
 8. I anxiously want the pain to go away
 9. I can't seem to keep it out of my mind
 10. I keep thinking about how much it hurts
 11. I keep thinking about how badly I want the pain to stop
 12. There's nothing I can do to reduce the intensity of the pain
 13. I wonder whether something serious may happen
-

Each item is scored on a 4-point scale from 'Not at all' to 'All the time'