

Invited Clinical Commentary

A Multi-Systems Approach to Human Movement after ACL Reconstruction: The Nervous System

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Postoperative rehabilitation of anterior cruciate ligament (ACL) reconstruction mainly focuses on the restoration of strength and range of motion with a long-term goal to return athletes to their prior level of activity. Of those wanting to return to sport, many are either unable and/or experience protracted recovery despite extensive rehabilitation. To holistically care for patients recovering from ACL reconstructions, reframing rehabilitation to consider a comprehensive systems approach (including musculoskeletal, cardiovascular, endocrine, and neurologic systems) may help improve treatment outcomes. The American Physical Therapy Association has adopted a vision statement that embraces the concept of a 'movement system,' but validation of the movement system has been challenging. Application of a multi-physiologic systems approach may provide a unique perspective to better understand the nervous system and its interactions after ACL reconstruction. The purpose is to focus on the nervous system contributions to a multi-physiologic system approach to rehabilitation from ACL reconstruction.

Level of Evidence

5

INTRODUCTION

Following anterior cruciate ligament reconstruction (ACLR), many athletes experience suboptimal outcomes including low rates of returning to sports, high rates of reinjury (graft and contralateral ACL ruptures), and early onset post-traumatic osteoarthritis.^{1,2} Traditionally, rehabilitation from ACLR focuses on restoring the musculoskeletal system to its pre-injured state³ (i.e., normalize strength, range of motion, biomechanics, etc.) with little targeted recovery of the neurophysiologic consequences of both the peripheral (PNS) and central nervous systems (CNS), coupled with the psychological contributions to physical recovery.

ACL injuries most commonly occur in strategy sports^{4, 5} (i.e., soccer, basketball), that require high-velocity cutting, pivoting and deceleration.⁶ These high-speed sports require not only physical quickness, but also quick sensory integration and cognitive processing of the environment (i.e., sports balls, opponents, teammates) likely resulting in movement prediction errors. Feedforward (anticipatory/prediction) and feedback (reactive) loops of the nervous system allow an athlete to navigate and demonstrate success within these highly chaotic environments.^{7,8} For movement, the nervous system makes predictions based on previous experiences, then uses feedback (and error) from the movements to update future movement plans.⁹ The nervous system is a highly sophisticated and a crucial con-

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tributor to goal oriented, efficient movement during athletic activities.

As an effort by the American Physical Therapy Association (APTA) to establish the profession's identity, the adoption of a new vision statement in 2013 called for physical therapists to 'transform society by optimizing movement to improve the human experience.'¹⁰ From this, the human movement system was promoted as an effort to further establish professional identity. The movement system has been described by the APTA as being comprised of a collection of body systems including the nervous, musculoskeletal, endocrine, cardiopulmonary, and integumentary systems.¹¹ In many ways, the integration of the body systems described in the movement system approach¹¹ to rehabilitation integrates similar elements of a common theoretical model in motor learning, the dynamical systems theory.¹² The dynamical systems theory is a well adopted framework pertaining to movement development, motor control, and skill acquisition which aims to explain variability in human goal-directed movement.¹² Dynamical systems theory is a conceptual framework that builds understanding of a complex system (human movement) through individual component parts.¹² The interaction and collaboration of component systems is what drives the success of the entire system, which is similarly described in the APTA movement system framework. This commentary provides a perspective where each physiologic system can be thought of as a component system necessary to efficiently optimize human movement. The purpose of this commentary is to focus on the nervous system contributions to a multi-physiologic system approach to rehabilitation from ACLR.

NERVOUS SYSTEM CONSEQUENCES ASSOCIATED WITH ACL INJURY AND RECONSTRUCTION

Models describing the neurophysiologic consequences to the sensorimotor system after ACL injury have previously been developed.^{13,14} In short, these models provide a framework outlining the impact of ACL rupture (i.e., mechanoreceptor instability, joint instability, and pain) on central nervous system (CNS) reorganization. CNS reorganization due to an afferent disruption (ligament rupture) leads to changes in efferent output to muscles, impacts reflexes, and involves voluntary and involuntary movement strategies.^{13,14} Common clinical manifestations of altered sensorimotor processing include altered knee mechanics during squatting, running, jumping, and hopping.¹⁵ Previous authors have aimed to better understand the cortical contributions to altered sensorimotor processing, potentially predisposing individuals to ACL injury risk¹⁶ as well as protracted recovery following ACLR.^{17,18} Research tools such as neuroimaging (functional magnetic resonance imaging [fMRI]) and transcranial magnetic stimulation (TMS) are commonly used to determine whole brain and motor cortex alterations respectively, after ACLR. Changes within the spinal cord are commonly measured using the Hoffmann Reflex (H-Reflex) which assesses the integrity of Ia afferent synaptic transmission contributing to the alpha

motor neuron pool of the quadriceps within the anterior horn of the spinal cord.^{19,20}

THE WHOLE-BRAIN & COGNITION

On two occasions, Diekfuss et al.^{16,21} have demonstrated prospectively that athletes who sustain ACL injuries have altered cortical connectivity via fMRI between regions responsible for sensorimotor processing and error correction compared to healthy athletes. This literature begins to suggest that a neural biomarker may exist for those at risk for sustaining an ACL injury.^{16,21} After ACLR, fMRI analyses revealed that individuals demonstrate greater levels of neural activity in regions responsible for cognition, visual-spatial sensory integration, and motor and somatosensory areas.^{17,18,22} Furthermore, metrics of corticospinal tract contributions to quadriceps function have been evaluated with TMS and demonstrate lingering alterations bilaterally after ACLR.^{19,20} Thus, despite rehabilitation efforts, both whole brain and efferent drive to the quadriceps may be altered.

More recently, researchers have aimed to evaluate if neurocognitive processing (i.e., reaction time, processing speed, and visual-spatial memory) during computerized assessments is related to lower extremity injury risk and injury risk biomechanics. Healthy individuals with lower neurocognitive performance have been shown to demonstrate injury-risk biomechanics in jumping and cutting tasks.^{23,24} Additionally, lower baseline neurocognitive performance has been retrospectively associated with increased risk of ACL injury occurrence.²⁵ Although continued evidence is needed to understand the relationships between various neurocognitive processes and lower extremity injury risk, the available evidence warrants consideration for integration of neurocognitive interventions to rehabilitation from lower extremity musculoskeletal injury.²⁶

Although computerized assessments of neurocognitive function demonstrate merit in identifying injury-risk, they might not be readily available in all clinical settings. Instead, dual-task paradigms (the simultaneous completion of two tasks) are commonly used to assess attentional resource allocation during cognitive-motor tasks²⁷ and have been examined in those with ACL deficiency and after ACLR.^{28,29} Attentional resource allocation during cognitive-motor task selection is important, as task difficulty and novelty seem to elicit performance deficits during dual-task assessments according to age³⁰ and may present during more challenging³¹ compared to easier³² tasks in those following ACLR. Motor tasks involving various metrics of postural control and gait overlaid with cognitive tasks (auditory or working memory) are the most used metrics for evaluating dual-task performance in individuals with ACLR and ACL-deficiency.³¹⁻³⁴ More recently, sport-specific motor tasks that are clinician-friendly, such as the tuck jump assessment, have shown deteriorating movement quality with the addition of a cognitive task in healthy individuals.³⁵ Thus, dual-task paradigms may offer a potential future direction for clinically evaluating efficiency of cognitive-motor interplay after ACLR.^{36,37} Interventions leveraging cognitive-motor dual-task challenges may im-

prove ecological utility of rehabilitation interventions and may provide a potential avenue of future research in ACL injury prevention.³⁸

THE SPINAL CORD & PERIPHERAL NERVOUS SYSTEM

The spinal cord contributes to the recovery of quadriceps muscle activation, especially in the early phases after ACLR.¹⁹ Greater deficits in quadriceps H-reflex are seen acutely post operatively, but as time from surgery increases, deficits in spinal reflex excitability decrease relative to healthy individuals.³⁹ In fact, evidence supports that at late timeframes (>24months) post-reconstruction spinal reflex excitability is potentially increased.²⁰ Therefore, the literature suggests that prolonged quadriceps activation deficits are mediated by the supraspinal level (corticospinal tract excitability) in the chronic stages of injury recovery.^{19,20} Ia afferent contributions to quadriceps activation deficits are difficult to quantify clinically, as they require expensive equipment (recording and stimulating electrodes, stimulator), time, and expertise to complete and interpret.⁴⁰ The spinal cord with integration from cortical/subcortical regions is also critical for proprioception, pain (at rest), and vibration pain thresholds which continue to be impaired years after ACLR.⁴¹ Future research is required to understand the neurophysiologic contributions of each sub-system to overall recovery from ACLR and develop targeted interventions.

After ACL injury, alterations within the PNS secondary to afferent disruption manifests as diminished proprioceptive and balance control.⁴²⁻⁴⁴ Whenever sensory input is disrupted, spinal reflexes (e.g. H-reflex),³⁹ vestibular responses (e.g. balance, proprioception),⁴⁵ and motor responses (e.g. strength, speed, and power),⁴⁶ are altered due to impaired/inhibitory afferent input. Originally the pathophysiology of poor dynamic control of the knee with diminished single-leg balance were attributed to the loss of ACL proprioceptive feedback, capsular disruption after surgery, and edema.⁴⁵ However, Krogsgaard et al.⁴⁷ found that the reconstructed ACL graft required higher sensory stimulation than the native posterior cruciate ligament to elicit an inhibitory (afferent) muscular reflex response eight or more months after the ACLR, identifying that the ACL graft does not fully reinnervate after reconstruction.⁴⁷ Furthermore, Bonfim et al.⁴⁵ found individuals after ACLR had increased anterior-posterior and medial-lateral sway that improved with heightened sensory input (light touch to a bar), as compared to the healthy cohort.⁴⁵ Thus, the somatosensory deficit that occurs from ACL disruption appear to have negative consequences to both proprioception and balance long after ACLR surgery. Rehabilitation should aim to *up-weight the somatosensory system* to promote restoration of afferent function. Over time, feedback loops like the H-reflex⁴⁸ and some metrics of single-leg static balance improve.^{49,50} However, there continue to be alterations in afferent feedback and nervous system responses that cause poor biomechanical control during dynamic tasks such as jumping or cutting.³⁹

In addition to ACL mechanoreceptor disruption from the ligament rupture, skin sensory organs are also impaired

secondary to surgical reconstruction. Pacinian corpuscles and Ruffini endings within the skin are thought to contribute to proprioception⁵¹ and pain responses. It has been assumed these sensory afferents from Pacinian corpuscles and Ruffini endings associated with light touch normalize within a month^{52,53} following reconstruction. However, if superficial skin sensation, pain, and sense of position are impaired long-term, they will likely alter somatosensory (afferent) input and influence CNS, interneuron, and pain-response pathways.

PSYCHOSOCIAL CONSIDERATIONS AND PAIN

While the biomechanical and biological factors for consideration after ACLR are of utmost importance, the psychosocial factors cannot be overlooked. The biopsychosocial model has continued to grow in acceptance among health care providers through the years since its introduction by Dr. George Engel.⁵⁴⁻⁵⁷ As understanding of the interplay between the biological, psychological, and social mechanisms continues to evolve, it is undeniable that each of these factors plays a significant role in recovery from ACLR. The biomedical deficit of a torn ACL and subsequent reconstruction are universal in all patients that present to rehabilitation after ACLR, however, the psychosocial aspects of each individual's recovery are diverse. The literature surrounding the psychosocial factors impacting recovery from ACLR is growing.^{58,59} A large body of evidence in other populations, such as those with whiplash syndrome or chronic low back pain, exists that may help inform clinicians in understanding the psychosocial aspects of injury recovery.⁶⁰⁻⁶⁵ Wiese-Bjornstal's biopsychosocial sport injury risk profile serves as a framework representing the various internal (biological and psychological) and external (physical and sociocultural) factors contributing to injury recovery.⁶⁵ Utilizing the sport injury risk profile promotes consideration for the sociocultural influences (i.e., coach/team RTS time expectations), mixed psychological states (i.e., fear of reinjury), and acknowledgement of shifted athlete goals throughout the recovery process. Biologically, an athlete's musculoskeletal, cardiopulmonary, integumentary and nervous system have been altered. The athlete must also process the confounding neurocognitive and environmental components of RTS (i.e., weather, fan/opponent reactions, altered decision making in sport). It is well established that neurocognition and emotions can influence adherence to rehabilitation programs.⁶⁶ Adherence is a crucial component to successful recovery. With that in mind, clinicians should consider the multitude of psychosocial factors the athlete with ACLR must navigate during the rehabilitation process in order to maximize rehabilitation outcomes.

The current understanding of pain has advanced significantly in the last couple of decades, which has led to changes in pain assessment methodology.⁶⁷ Historically, pain rating scales have been used clinically as a measure of intensity, but are also viewed by some clinicians to be associated with the amount of tissue damage. It is now understood that pain rating scores are poor indicators of tissue health, especially as pain persists.⁶⁷⁻⁶⁹ However, uti-

lization of pain rating scores,⁷⁰ such as the numeric rating scale (0=no pain, 10=worst imaginable pain), still hold clinical value. Pain rating scores allow patients to express their pain and for the clinician to demonstrate compassion for the patient and their pain experience. During the rehab process, pain rating scores can provide a marker to acknowledge that some pain increase is normal and safe and a means to develop a patient-centered agreement on an acceptable pain experience.

Newer scales, such as the PROMIS Pain Interference Scale,⁷¹ may have utility with patients who are experiencing pain that is interfering with daily and functional activities.⁷² This scale provides a self-reported measure of the consequences of pain on relevant aspects of the patient's life. The Pain Interference Scale comes in a computer adapted testing format or short-form versions with four, six, and eight Likert questions. Because of the normative data collected, a representative T-score can be calculated to provide a standardized score with a mean of 50 and a standard deviation of 10. Other measures to assess catastrophizing (Pain Catastrophizing Score),⁷³ kinesiophobia (Tampa Scale for Kinesiophobia)⁷⁴ or sensitization (Central Sensitization Inventory),⁷⁵ may be beneficial for patients experiencing ongoing pain and poor recovery to assess more complex constructs of the patient's pain experience. Each self-reported outcome measure is best if chosen individually based upon a specific patient's presentation and not applied universally to all patients.

MULTI-PHYSIOLOGIC SYSTEM INTERVENTIONS FOR THE NERVOUS SYSTEM AFTER ACLR

A major challenge clinicians face in clinical practice is concurrently addressing alternations in the nervous system after ACLR while simultaneously addressing deficits in the musculoskeletal, cardiopulmonary, and other systems. Thus, the purpose of this section is to provide explanations, interventions and rationale for integrating targeted nervous system interventions into rehabilitation post-ACLR within the context of a multi-physiologic systems approach to human movement.

NERVOUS SYSTEM INTEGRATION WITH THE MUSCULOSKELETAL SYSTEM

Immediate priorities in rehabilitation from ACLR consist of limiting knee joint effusion, pain and restoring full extension range of motion and quadriceps muscle function. A cascade effect exists where joint injury and effusion results in quadriceps arthrogenic muscle inhibition,⁷⁶ making it difficult to achieve and maintain active end-range knee extension motor control.⁷⁷ Therefore, it is standard of care to provide neuromuscular electrical stimulation (NMES) for at least six-weeks after ACLR to optimize recovery of quadriceps function.³ Other modalities such as sensory transcutaneous electrical nerve stimulation (TENS) and focal knee joint cooling promote improved quadriceps function for a therapeutic window of targeted intervention.^{78,79} More recently, improving quadriceps muscle strength utilizing

cross-training⁸⁰ and eccentric exercise⁸¹ has also demonstrated effectiveness.

Motor control dysfunctions after ACLR are likely present immediately post-operatively but become more apparent in the intermediate stages of recovery, manifesting as a biomechanical tendency toward limb stiffness with decreased hip and knee flexion on the involved limb upon landing during single-limb hopping tasks.⁸² Additionally, trunk lean, hip drop, and dynamic valgus are biomechanically faulty positions that place the ACL in a position of excessive torque (force), load, and tension.^{83,84} As a result, rehabilitation interventions focus to restore biomechanical symmetry and often excessively raise the patient's self-awareness of their lower limb position for all tasks (i.e., internal focus of attention). Growing evidence in motor learning indicates that for learning a goal-oriented skill, an internal focus of attention may be less optimal than an external focus of attention, in which the patient's attention is directed toward the environment and actionable goal.^{15,85} For strategy sports, which comprise the majority of ACL injuries, promoting an external focus of attention in rehabilitation more closely mimics both the sport environment and associated neurocognitive demands. An external focus of attention and neurocognitive challenges can easily be implemented throughout the rehabilitation continuum.^{86,87} Neurocognitive interventions aim to challenge cognitive processes such as working memory, decision making, and response inhibition, which are a common requirement of team-based sports. In the early phases of rehabilitation through late stages and return to sport, incorporating interventions that challenge neurocognitive processing is attainable with little added time and resources (Table 1).^{88,89} Table 1 presents examples of internal and external intervention classes as well as clinical intervention examples with progression of both the motor and cognitive skills. The internal class consists of interventions that aim to manipulate the patient's attentional focus and neurocognitive processing, whereas the external class are examples to manipulate the task or environment. Although motor learning, cognitive-motor, and visual-motor intervention categories are often displayed independently, it is essential to note the overlap in utility between them.

Acutely after ACLR, regaining standing balance control is one of the first interventions implemented to restore postural control and is the basis for progressing to more dynamic tasks such as walking, stair climbing and squatting. Balance requires sensory integration from multiple systems, the most pertinent being the somatosensory, vestibular, and visual systems.⁹⁰ Multi-system integration for balance allows the nervous system to *reweight* or change the level of dependence between systems depending on the given context.⁹⁰ After ACL injury, the use of the somatosensory system is decreased due to the disruption of ligamentous afferent receptors and a shift to visual dependence to maintain stability is noted.⁹¹ To appropriately restore balance, a clinician should aim to *upweight the somatosensory system* and decrease compensatory reweighting to the visual system.^{15,92,93} This can be accomplished by using visual disturbances (i.e., eyes closed, flash-

Table 1. Classes of Interventions and Examples

Class of Intervention	Intervention Example	Progression Ideas	
<i>Internal</i>		Motor Task	Cognitive/Skill Task
Focus of Attention	External Focus of Attention "Keep your knee pointed at the cone as you lunge forward."	Forward lunge → Multidirectional lunge	"Perform a lunge in the direction where I am pointing."
Single Cognitive-Motor Challenge	Arithmetic "As you perform straight leg raises, count backwards from 100 by 7s."	Straight leg raises → Straight leg raise hold/oscillate	"As you perform your straight leg raises, tell me the answer of the math problems on the flashcards I show you"
	Working Memory "As you perform your double leg squats, I want you to name all the professional basketball teams." (or something patient-centered)	Double leg squat → Split squat	"As you perform your double leg squats, I want you to try to name the professional basketball teams in alphabetical order."
	Auditory "Perform a 45° lunge when you hear the command 'ball'" (simulating a basketball pass to an open teammate)	45° lunge → Drop step lunge	"Perform a 45° lunge if you hear the command 'ball' (simulating a basketball pass), and a drop step lunge if you hear the command 'match up' (simulating defensive shuffle)."
Cognitive-Motor Dual Task with Decision Making	Single-Step "When I flash the number 3, perform a forward lunge, when I flash the number 1 perform a curtsy lunge."	Increase difficulty in motor task accordingly	Use more challenging methods of arithmetic
	Double-Step "When the math problem sums to an even number jump left. When the math problem sums to an odd number jump right."		
<i>External</i>		Motor Task	Cognitive/Skill Task
Manual (object manipulation)	Ball Toss "As you perform continuous single leg squatting, we will toss this ball back and forth."	Forward toss → Lateral toss	"As you perform continuous single leg squatting, I want you to catch the yellow ball with your left hand and the red ball with your right hand."
	Ball Dribble "Dribble the ball in place as you perform a single leg squat and hold."	Single leg squat → Alternating sides single leg squat	"Dribble the ball using a front-back dribbling direction as you perform a single leg squat and hold."
Perturbation (external force)	During any exercise, a quick manual perturbation to the patient is given.	Providing perturbations toward the center of mass (trunk) versus extremities	Moving from anticipated to unanticipated perturbations.
Environment	Clinic Environment Interventions might start in quiet treatment room and progress to busy weight area.	Interventions in a clinic environment progressing to on-field/court	
	Vision Interventions using eyes open versus closed	Transition to a dimly lit area or use visual disturbance training systems/glasses; Visual tracking with numbers written on a ball – "tell me the number written on this tennis ball before you catch it."	

Class of Intervention	Intervention Example	Progression Ideas	
	Distraction/Attention Gradually introduce relevant distractors according to sport	Moving from anticipated to unanticipated distractors (sound, play calling, simulated game situations, etc.); Progress from stationary to moving objects (chair v. coach); Incorporate teammates into return to sport drills	
Object/ Opponent Navigation or Avoidance	"While performing this squatting exercise, don't let the tennis ball contact you after it's thrown. You may need to duck or shift your weight."	"While performing this side-stepping exercise, don't let the tennis ball contact you after it's thrown. You may need to duck or shift your weight."	Therapist is positioned (hidden) behind an object and uses a foam roll to serve as the "opponent." As the athlete moves toward the barrier, the therapist quickly positions the foam roll on either side of the barrier – requiring the athlete to move in the opposite direction.

ing glasses, etc.), virtual reality (i.e., smartphone or headset), and integrating neurocognitive challenges (Table 1) while simultaneously training balance and dynamic tasks. Clinicians should aim to increase somatosensory input using dynamically challenging positions such as squatting/lunging, and by adding unanticipated reactions such as squatting to an adjustable plinth and varying the plinth height between repetitions. When using movement-related interventions within the context of a multi-physiologic systems approach, it is paramount to consider the interaction between the musculoskeletal and nervous systems to optimize a patient's recovery.

NERVOUS SYSTEM INTEGRATION WITH THE INTEGUMENTARY SYSTEM

Elements of the PNS should be evaluated and integrated into the treatment plan post ACLR and can be directed cohesively while performing neurocognitive challenges as previously discussed. This can include range-of-motion exercises and early exercises such as quadriceps sets, long arc knee extensions, and standing pre-gait exercises (i.e., weight shifts, squats, calf raises, etc).⁹² Additionally, interventions to normalize sensation should start early with scar mobility and addressing areas of decreased or altered sensation. Sensation can be addressed through TENS for pain relief during provocative activities that cause pain.⁹⁴ Such activities can be progressed through different textures (from a mat table to a floor) or intensity (kneeling weight in quadruped transitioning to tall kneeling). The afferent input from the integumentary system, including tactile sensation from the skin and incision healing, provides constant feedback that is integrated with the rest of the neurological input of the body.

The integumentary system is best treated by first keeping the incision site clean and hydrated⁹⁵ and second, maximizing healing and normalization of sensation. If the wound becomes infected, an uptake in inflammatory cytokines will increase the inflammatory state. The increased inflammatory state can lead to increased PNS sensitivity, leading to inflammatory and neuropathic pain. Antibiotics can help decrease inflammation and the residual inflammation and neuropathic pain should be addressed.⁹⁶ Creams and wraps can help the hypertrophy, but a scar revision surgery may be warranted if they are not successful.⁹⁶ An-

other side-effect found with alteration of the integumentary system is the development of numbness along the saphenous nerve.⁹⁷ Damage to the saphenous nerve after surgery is common, and appropriate retraining of the somatosensory system during the peripheral nerve regeneration process is needed. In the context of a multi-physiologic systems approach, interventions dual-targeting the integumentary system and nervous system impairments are warranted.

NERVOUS SYSTEM INTEGRATION WITH THE CARDIOPULMONARY SYSTEM

The PNS and CNS are extremely metabolically active tissues. The human nervous system accounts for two to three percent of an individual's total body mass, yet 20-25 percent of the available oxygen circulating in the bloodstream is consumed by the nervous system.⁹⁸ Aerobic exercise has been shown to have multiple effects on the brain and neurocognition. Evidence supports the link between aerobic activity and improved cognition in older populations with⁹⁹ and without cognitive impairment.¹⁰⁰ Even in younger populations (ages 20-67) without cognitive impairment, improved executive function and increased cortical thickness were found after participating in a six-month, four times per week aerobic training regimen.¹⁰¹ Acute bouts of moderate intensity exercise also appear to promote improved cognitive processing speed.¹⁰² Therefore as an athlete recovers from ACLR, the importance of cardiovascular exercise for overall health, returning to prior level of function, and impact on cognitive function should be appreciated.

Integrating neurocognitive training and cardiopulmonary conditioning can begin as soon as the wound is healed, and range of motion is adequate for the task (such as aquatic therapy, swimming, and stationary biking).⁵² When implementing neurocognitive training with cardiopulmonary tasks, one consideration is not just the physical retraining of the cardiopulmonary system but the psychological aspects of being able to break through mental/emotional barriers.

As the athlete progresses to RTS tasks, biomechanics, neurocognitive training, psychological readiness, and cardiopulmonary conditioning all converge.¹⁰³ If any of these factors have not been addressed prior to RTS tasks, they will likely hinder an athlete's ability to return to full activity

safely.¹⁰⁴ Repetitive tasks such as walking, biking, and jogging should be seen as opportunities for neuromuscular retraining and neurocognitive training. As running, jumping, and cutting tasks are added, psychological readiness and neurocognitive training should progress to more complex neurocognitive problem-solving and increased speed and power once strength, form, and psychological readiness goals have been met.⁹² Prior to RTS, cardiopulmonary conditioning should be assessed, using speed and endurance tests, as well as resting heart rate and VO₂max recovery to evaluate cardiopulmonary recovery prior to progressions.¹⁰⁴ The interplay between the cardiopulmonary and nervous systems are strong contributors to physical function after ACLR.

PAIN & PSYCHOSOCIAL CONSIDERATIONS

A comprehensive approach to rehabilitation after ACLR demonstrates a critical need for clinician mindfulness to treat each patient as a whole, including acknowledging psychosocial factors such as patient's changing their "sense of self" or athletic identity. Some patients may no longer view themselves as an "indestructible high performing athlete," but as someone who can get injured and may not return to the same level of performance. When an individual has doubts and suffers loss, fear and anxiety are natural psychological responses.^{105,106} Rebuilding a sense of safety and security is vital within the rehabilitation process to overcome those fears. Evidence demonstrates that lower levels of fear and higher self-efficacy scores are associated

with better resolution of knee impairments.¹⁰⁷ Discussions over normal psychological states of fear and worry need to occur within the context of using psychological informed practices throughout recovery. The use of graded exposure with exercise and activities has been shown to help reduce fear and improve functional gains.¹⁰⁸⁻¹¹⁰

CONCLUSION

In alignment with a multi-physiologic systems approach to human movement, clinicians should aim to comprehensively treat patients through a multi-system lens. The nervous system is vastly integrated with the other system components essential for promoting optimal patient function after ACLR. Incorporating intervention strategies that target the nervous system, address the psychosocial aspects of rehabilitation, and incorporate an integrated systems approach are needed throughout the continuum of recovery.

FINANCIAL DISCLOSURES

The authors have declared no conflict of interest.

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REFERENCES

1. Sepúlveda F, Sánchez L, Amy E, Micheo W. Anterior cruciate ligament injury: return to play, function and long-term considerations. *Curr Sports Med Rep*. 2017;16(3):172-178. [doi:10.1249/jsr.0000000000000356](https://doi.org/10.1249/jsr.0000000000000356)
2. Webster KE, Hewett TE. What is the evidence for and validity of return-to-sport testing after anterior cruciate ligament reconstruction surgery? A systematic review and meta-analysis. *Sports Med*. 2019;49(6):917-929. [doi:10.1007/s40279-019-01093-x](https://doi.org/10.1007/s40279-019-01093-x)
3. Logerstedt DS, Scalzitti D, Risberg MA, et al. Knee stability and movement coordination impairments: knee ligament sprain revision 2017. *J Orthop Sports Phys Ther*. 2017;47(11):A1-A47. [doi:10.2519/jospt.2017.0303](https://doi.org/10.2519/jospt.2017.0303)
4. Fajen BR, Riley MA, Turvey MT. Information, affordances, and the control of action in sport. *Int J Sport Psych*. 2009;40:79-107.
5. Meng FW, Yao ZF, Chang EC, Chen YL. Team sport expertise shows superior stimulus-driven visual attention and motor inhibition. *PLoS One*. 2019;14(5):e0217056.
6. Montalvo AM, Schneider DK, Webster KE, et al. Anterior cruciate ligament injury risk in sport: a systematic review and meta-analysis of injury incidence by sex and sport classification. *J Athl Train*. 2019;54(5):472-482. [doi:10.4085/1062-6050-407-16](https://doi.org/10.4085/1062-6050-407-16)
7. Taberner M, Allen T, Cohen DD. Progressing rehabilitation after injury: consider the 'control-chaos continuum.' *Br J Sports Med*. 2019;53(18):1132-1136. [doi:10.1136/bjsports-2018-100157](https://doi.org/10.1136/bjsports-2018-100157)
8. Kandel ER, Schwartz JH, Jessell TM, Siegelbaum SA, Hudspeth AJ. *Principles of Neural Science*. 5th ed. McGraw-Hill; 2013.
9. Kilner JM, Friston KJ, Frith CD. Predictive coding: an account of the mirror neuron system. *Cogn Process*. 2007;8(3):159-166. [doi:10.1007/s10339-007-0170-2](https://doi.org/10.1007/s10339-007-0170-2)
10. Mission, Vision, and Strategic Plan. American Physical Therapy Association Website. Accessed June 17, 2021. <https://www.apta.org/apta-and-you/leadership-and-governance/vision-mission-and-strategic-plan>
11. American Physical Therapy Association. An American Physical Therapy Association white paper. Physical therapist practice and the human movement system. Published online 2015:1-4.
12. Davids K, Glazier P, Araújo D, Bartlett R. Movement systems as dynamical systems. *Sports Medicine*. 2003;33(4):245-260. [doi:10.2165/00007256-200333040-00001](https://doi.org/10.2165/00007256-200333040-00001)
13. Ward S, Pearce AJ, Pietrosimone B, Bennell K, Clark R, Bryant AL. Neuromuscular deficits after peripheral joint injury: a neurophysiological hypothesis. *Muscle Nerve*. 2015;51(3):327-332. [doi:10.1002/mus.24463](https://doi.org/10.1002/mus.24463)
14. Kapreli E, Athanasopoulos S. The anterior cruciate ligament deficiency as a model of brain plasticity. *Med Hypotheses*. 2006;67(3):645-650. [doi:10.1016/j.mehy.2006.01.063](https://doi.org/10.1016/j.mehy.2006.01.063)
15. Gokeler A, Neuhaus D, Benjaminse A, Grooms DR, Baumeister J. Principles of motor learning to support neuroplasticity after ACL injury: implications for optimizing performance and reducing risk of second ACL injury. *Sports Med*. 2019;49(6):853-865. [doi:10.1007/s40279-019-01058-0](https://doi.org/10.1007/s40279-019-01058-0)
16. Diekfuss JA, Grooms DR, Nissen KS, et al. Alterations in knee sensorimotor brain functional connectivity contributes to ACL injury in male high-school football players: a prospective neuroimaging analysis. *Braz J Phys Ther*. 2020;24(5):415-423. [doi:10.1016/j.bjpt.2019.07.004](https://doi.org/10.1016/j.bjpt.2019.07.004)
17. Criss CR, Melton MS, Ulloa SA, et al. Rupture, reconstruction, and rehabilitation: A multi-disciplinary review of mechanisms for central nervous system adaptations following anterior cruciate ligament injury. *Knee*. 2021;30:78-89. [doi:10.1016/j.knee.2021.03.009](https://doi.org/10.1016/j.knee.2021.03.009)
18. Neto T, Sayer T, Theisen D, Mierau A. Functional brain plasticity associated with ACL injury: a scoping review of current evidence. *Neural Plast*. 2019;2019:3480512. [doi:10.1155/2019/3480512](https://doi.org/10.1155/2019/3480512)
19. Rodriguez KM, Palmieri-Smith RM, Krishnan C. How does anterior cruciate ligament reconstruction affect the functioning of the brain and spinal cord? A systematic review with meta-analysis. *J Sport Health Sci*. 2021;10(2):172-181. [doi:10.1016/j.jshs.2020.07.005](https://doi.org/10.1016/j.jshs.2020.07.005)

20. Rush JL, Glaviano NR, Norte GE. Assessment of quadriceps corticomotor and spinal-reflexive excitability in individuals with a history of anterior cruciate ligament reconstruction: a systematic review and meta-analysis. *Sports Med.* 2021;51(5):961-990. [doi:10.1007/s40279-020-01403-8](https://doi.org/10.1007/s40279-020-01403-8)
21. Diekfuss JA, Grooms DR, Yuan W, et al. Does brain functional connectivity contribute to musculoskeletal injury? A preliminary prospective analysis of a neural biomarker of ACL injury risk. *J Sci Med Sport.* 2019;22(2):169-174. [doi:10.1016/j.jsams.2018.07.004](https://doi.org/10.1016/j.jsams.2018.07.004)
22. Lepley AS, Grooms DR, Burland JP, Davi SM, Kinsella-Shaw JM, Lepley LK. Quadriceps muscle function following anterior cruciate ligament reconstruction: systemic differences in neural and morphological characteristics. *Exp Brain Res.* 2019;237(5):1267-1278. [doi:10.1007/s00221-019-05499-x](https://doi.org/10.1007/s00221-019-05499-x)
23. Herman DC, Barth JT. Drop-jump landing varies with baseline neurocognition: implications for anterior cruciate ligament injury risk and prevention. *Am J Sports Med.* 2016;44(9):2347-2353. [doi:10.1177/0363546516657338](https://doi.org/10.1177/0363546516657338)
24. Monfort SM, Pradarelli JJ, Grooms DR, Hutchison KA, Onate JA, Chaudhari AMW. Visual-spatial memory deficits are related to increased knee valgus angle during a sport-specific sidestep cut. *Am J Sports Med.* 2019;47(6):1488-1495. [doi:10.1177/0363546519834544](https://doi.org/10.1177/0363546519834544)
25. Swanik CB, Covassin T, Stearne DJ, Schatz P. The relationship between neurocognitive function and noncontact anterior cruciate ligament injuries. *Am J Sports Med.* 2007;35(6):943-948. [doi:10.1177/0363546507299532](https://doi.org/10.1177/0363546507299532)
26. Avedesian JM, Forbes W, Covassin T, Dufek JS. Influence of cognitive performance on musculoskeletal injury risk: a systematic review. *Am J Sports Med.* Published online 2021:363546521998081. [doi:10.1177/0363546521998081](https://doi.org/10.1177/0363546521998081)
27. McIsaac TL, Lamberg EM, Muratori LM. Building a framework for a dual task taxonomy. *Biomed Res Int.* Published online 2015:591475. [doi:10.1155/2015/591475](https://doi.org/10.1155/2015/591475)
28. Miko SC, Simon JE, Monfort SM, Yom JP, Ulloa S, Grooms DR. Postural stability during visual-based cognitive and motor dual-tasks after ACLR. *J Sci Med Sport.* Published online 2020. [doi:10.1016/j.jsams.2020.07.008](https://doi.org/10.1016/j.jsams.2020.07.008)
29. Negahban H, Hadian MR, Salavati M, et al. The effects of dual-tasking on postural control in people with unilateral anterior cruciate ligament injury. *Gait Posture.* 2009;30(4):477-481. [doi:10.1016/j.gaitpost.2009.07.112](https://doi.org/10.1016/j.gaitpost.2009.07.112)
30. Huxhold O, Li SC, Schmiedek F, Lindenberger U. Dual-tasking postural control: aging and the effects of cognitive demand in conjunction with focus of attention. *Brain Res Bull.* 2006;69(3):294-305. [doi:10.1016/j.brainresbull.2006.01.002](https://doi.org/10.1016/j.brainresbull.2006.01.002)
31. Negahban H, Ahmadi P, Salehi R, Mehravar M, Goharpey S. Attentional demands of postural control during single leg stance in patients with anterior cruciate ligament reconstruction. *Neurosci Lett.* 2013;556:118-123. [doi:10.1016/j.neulet.2013.10.022](https://doi.org/10.1016/j.neulet.2013.10.022)
32. Lion A, Gette P, Meyer C, Seil R, Theisen D. Effect of cognitive challenge on the postural control of patients with ACL reconstruction under visual and surface perturbations. *Gait Posture.* 2018;60:251-257. [doi:10.1016/j.gaitpost.2017.12.013](https://doi.org/10.1016/j.gaitpost.2017.12.013)
33. Mohammadi-Rad S, Salavati M, Ebrahimi-Takamjani I, et al. Dual-tasking effects on dynamic postural stability in athletes with and without anterior cruciate ligament reconstruction. *J Sport Rehabil.* 2016;25(4):324-329. [doi:10.1123/jsr.2015-0012](https://doi.org/10.1123/jsr.2015-0012)
34. Nazary-Moghadam S, Salavati M, Esteki A, Akhbari B, Zeinalzadeh A. Effect of dual-tasking on variability of spatiotemporal parameters in subjects with and without anterior cruciate ligament deficiency using linear dynamics. *Phys Treat.* 2015;4:213-220.
35. Schnittjer A, Simon JE, Yom J, Grooms DR. The effects of a cognitive dual task on jump-landing movement quality. *Int J Sports Med.* Published online 2020. [doi:10.1055/a-1195-2700](https://doi.org/10.1055/a-1195-2700)
36. Ness BM, Zimney K, Kernozek T, Schweinle WE, Schweinle A. Incorporating a dual-task assessment protocol with functional hop testing. *Int J Sports Phys Ther.* 2020;15(3):407-420. [doi:10.26603/ijsp.20200407](https://doi.org/10.26603/ijsp.20200407)
37. Simon JE, Millikan N, Yom J, Grooms DR. Neurocognitive challenged hops reduced functional performance relative to traditional hop testing. *Phys Ther Sport.* 2020;41:97-102. [doi:10.1016/j.ptsp.2019.12.002](https://doi.org/10.1016/j.ptsp.2019.12.002)
38. Burcal CJ, Needle AR, Custer L, Rosen AB. The effects of cognitive loading on motor behavior in injured individuals: a systematic review. *Sports Med.* 2019;49(8):1233-1253. [doi:10.1007/s40279-019-01116-7](https://doi.org/10.1007/s40279-019-01116-7)

39. Lepley AS, Gribble PA, Thomas AC, Tevald MA, Sohn DH, Pietrosimone BG. Quadriceps neural alterations in anterior cruciate ligament reconstructed patients: a 6-month longitudinal investigation. *Scand J Med Sci Sports*. Published online 2015. [doi:10.1111/sms.12435](https://doi.org/10.1111/sms.12435)
40. Palmieri RM, Ingersoll CD, Hoffman MA. The hoffmann reflex: methodologic considerations and applications for use in sports medicine and athletic training research. *J Athl Train*. 2004;39(3):268-277.
41. Courtney CA, Atre P, Foucher KC, Alsouhibani AM. Hypoesthesia after anterior cruciate ligament reconstruction: the relationship between proprioception and vibration perception deficits in individuals greater than one year post-surgery. *Knee*. 2019;26(1):194-200. [doi:10.1016/j.knee.2018.10.014](https://doi.org/10.1016/j.knee.2018.10.014)
42. Niederer D, Giesche F, Janko M, et al. Unanticipated jump-landing quality in patients with anterior cruciate ligament reconstruction: How long after the surgery and return to sport does the re-injury risk factor persist? *Clin Biomech*. 2020;72:195-201. [doi:10.1016/j.clinbiomech.2019.12.021](https://doi.org/10.1016/j.clinbiomech.2019.12.021)
43. Paterno MV, Schmitt LC, Ford KR, et al. Biomechanical measures during landing and postural stability predict second anterior cruciate ligament injury after anterior cruciate ligament reconstruction and return to sport. *Am J Sports Med*. 2010;38(10):1968-1978. [doi:10.1177/0363546510376053](https://doi.org/10.1177/0363546510376053)
44. Weir G, van Emmerik R, Jewell C, Hamill J. Coordination and variability during anticipated and unanticipated sidestepping. *Gait Posture*. 2019;67:1-8. [doi:10.1016/j.gaitpost.2018.09.007](https://doi.org/10.1016/j.gaitpost.2018.09.007)
45. Bonfim TR, Grossi DB, Paccola CA, Barela JA. Additional sensory information reduces body sway of individuals with anterior cruciate ligament injury. *Neurosci Lett*. 2008;441(3):257-260. [doi:10.1016/j.neulet.2008.06.039](https://doi.org/10.1016/j.neulet.2008.06.039)
46. Lepley AS, Ericksen HM, Sohn DH, Pietrosimone BG. Contributions of neural excitability and voluntary activation to quadriceps muscle strength following anterior cruciate ligament reconstruction. *Knee*. 2014;21(3):736-742. [doi:10.1016/j.knee.2014.02.008](https://doi.org/10.1016/j.knee.2014.02.008)
47. Krogsgaard MR, Fischer-Rasmussen T, Dyhre-Poulsen P. Absence of sensory function in the reconstructed anterior cruciate ligament. *J Electromyogr Kinesiol*. 2011;21(1):82-86. [doi:10.1016/j.jelekin.2010.09.012](https://doi.org/10.1016/j.jelekin.2010.09.012)
48. Hoffman M, Kocaja DM. Hoffmann reflex profiles and strength ratios in postoperative anterior cruciate ligament reconstruction patients. *Int J Neurosci*. 2000;104(1-4):17-27. [doi:10.3109/00207450009035006](https://doi.org/10.3109/00207450009035006)
49. Howells BE, Ardern CL, Webster KE. Is postural control restored following anterior cruciate ligament reconstruction? A systematic review. *Knee Surg Sports Traumatol Arthrosc*. 2011;19(7):1168-1177. [doi:10.1007/s00167-011-1444-x](https://doi.org/10.1007/s00167-011-1444-x)
50. Lehmann T, Paschen L, Baumeister J. Single-leg assessment of postural stability after anterior cruciate ligament injury: a systematic review and meta-analysis. *Sports Med Open*. 2017;3(1):32. [doi:10.1186/s40798-017-0100-5](https://doi.org/10.1186/s40798-017-0100-5)
51. Johansson H, Sjölander P, Sojka P. Receptors in the knee joint ligaments and their role in the biomechanics of the joint. *Crit Rev Biomed Eng*. 1991;18(5):341-368.
52. van Grinsven S, van Cingel RE, Holla CJ, van Loon CJ. Evidence-based rehabilitation following anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc*. 2010;18(8):1128-1144. [doi:10.1007/s00167-009-1027-2](https://doi.org/10.1007/s00167-009-1027-2)
53. Wright RW, Haas AK, Anderson J, et al. Anterior cruciate ligament reconstruction rehabilitation: MOON guidelines. *Sports Health*. 2015;7(3):239-243. [doi:10.1177/1941738113517855](https://doi.org/10.1177/1941738113517855)
54. Engel GL. The need for a new medical model: a challenge for biomedicine. *Science*. 1977;196(4286):129-136. [doi:10.1126/science.847460](https://doi.org/10.1126/science.847460)
55. Engel GL. From biomedical to biopsychosocial. Being scientific in the human domain. *Psychosomatics*. 1997;38(6):521-528. [doi:10.1016/s0033-3182\(97\)71396-3](https://doi.org/10.1016/s0033-3182(97)71396-3)
56. Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC. The biopsychosocial approach to chronic pain: scientific advances and future directions. *Psychol Bull*. 2007;133(4):581-624. [doi:10.1037/0033-2909.133.4.581](https://doi.org/10.1037/0033-2909.133.4.581)
57. Holopainen R, Simpson P, Piirainen A, et al. Physiotherapists' perceptions of learning and implementing a biopsychosocial intervention to treat musculoskeletal pain conditions: a systematic review and metasynthesis of qualitative studies. *Pain*. 2020;161(6):1150-1168. [doi:10.1097/j.pain.0000000000001809](https://doi.org/10.1097/j.pain.0000000000001809)
58. Baez SE, Hoch JM, Cramer RJ. Social cognitive theory and the fear-avoidance model: an explanation of poor health outcomes after ACL reconstruction. *Athl Train Sport Health Care*. 2018;11(4):168-173.

59. te Wierike SC, van der Sluis A, van den Akker-Scheek I, Elferink-Gemser MT, Visscher C. Psychosocial factors influencing the recovery of athletes with anterior cruciate ligament injury: a systematic review. *Scand J Med Sci Sports*. 2013;23(5):527-540. [doi:10.1111/sms.12010](https://doi.org/10.1111/sms.12010)
60. Ferrari R, Schrader H. The late whiplash syndrome: a biopsychosocial approach. *J Neurol Neurosurg Psychiatry*. 2001;70(6):722-726. [doi:10.1136/jnnp.70.6.722](https://doi.org/10.1136/jnnp.70.6.722)
61. Nelson S, Conroy C, Logan D. The biopsychosocial model of pain in the context of pediatric burn injuries. *Eur J Pain*. 2019;23(3):421-434. [doi:10.1002/ejp.1319](https://doi.org/10.1002/ejp.1319)
62. Samoborec S, Ruseckaite R, Ayton D, Evans S. Biopsychosocial factors associated with non-recovery after a minor transport-related injury: a systematic review. *PLoS One*. 2018;13(6):e0198352. [doi:10.1371/journal.pone.0198352](https://doi.org/10.1371/journal.pone.0198352)
63. Schemitsch C, Nauth A. Psychological factors and recovery from trauma. *Injury*. 2020;51 Suppl 2:S64-s66. [doi:10.1016/j.injury.2019.10.081](https://doi.org/10.1016/j.injury.2019.10.081)
64. Truchon M. Determinants of chronic disability related to low back pain: towards an integrative biopsychosocial model. *Disabil Rehabil*. 2001;23(17):758-767. [doi:10.1080/09638280110061744](https://doi.org/10.1080/09638280110061744)
65. Wiese-Bjornstal DM. Psychology and socioculture affect injury risk, response, and recovery in high-intensity athletes: a consensus statement. *Scand J Med Sci Sports*. 2010;20 Suppl 2:103-111. [doi:10.1111/j.1600-0838.2010.01195.x](https://doi.org/10.1111/j.1600-0838.2010.01195.x)
66. Pizzari T, McBurney H, Taylor NF, Feller JA. Adherence to anterior cruciate ligament rehabilitation: a qualitative analysis. *J Sport Rehabil*. 2002;11(2):90-102. [doi:10.1123/jsr.11.2.90](https://doi.org/10.1123/jsr.11.2.90)
67. Moseley GL. Reconceptualising pain according to modern pain science. *Phy Ther Reviews*. 2007;12(3):169-178. [doi:10.1179/108331907X223010](https://doi.org/10.1179/108331907X223010)
68. Baliki MN, Geha PY, Apkarian AV, Chialvo DR. Beyond feeling: chronic pain hurts the brain, disrupting the default-mode network dynamics. *J Neurosci*. 2008;28(6):1398-1403. [doi:10.1523/jneurosci.4123-07.2008](https://doi.org/10.1523/jneurosci.4123-07.2008)
69. Woolf CJ. What is this thing called pain? *J Clin Invest*. 2010;120(11):3742-3744. [doi:10.1172/jci45178](https://doi.org/10.1172/jci45178)
70. Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). *Arthritis Care Res*. 2011;63 Suppl 11:S240-252. [doi:10.1002/acr.20543](https://doi.org/10.1002/acr.20543)
71. Amtmann D, Cook KF, Jensen MP, et al. Development of a PROMIS item bank to measure pain interference. *Pain*. 2010;150(1):173-182. [doi:10.1016/j.pain.2010.04.025](https://doi.org/10.1016/j.pain.2010.04.025)
72. Bernstein DN, Kelly M, Houck JR, et al. PROMIS Pain Interference is superior vs Numeric Pain Rating Scale for pain assessment in foot and ankle patients. *Foot Ankle Int*. 2019;40(2):139-144. [doi:10.1177/1071100718803314](https://doi.org/10.1177/1071100718803314)
73. Sullivan MJL, Bishop SR, Pivik J. The Pain Catastrophizing Scale: development and validation. *Psychol Assess*. 1995;7(4):524-532. [doi:10.1037/1040-3590.7.4.524](https://doi.org/10.1037/1040-3590.7.4.524)
74. Lundberg MKE, Styf J, Carlsson SG. A psychometric evaluation of the Tampa Scale for Kinesiophobia — from a physiotherapeutic perspective. *Physiother Theory Pract*. 2004;20(2):121-133. [doi:10.1080/09593980490453002](https://doi.org/10.1080/09593980490453002)
75. Neblett R, Cohen H, Choi Y, et al. The Central Sensitization Inventory (CSI): establishing clinically significant values for identifying central sensitivity syndromes in an outpatient chronic pain sample. *J Pain*. 2013;14(5):438-445. [doi:10.1016/j.jpain.2012.11.012](https://doi.org/10.1016/j.jpain.2012.11.012)
76. Rice DA, McNair PJ. Quadriceps arthrogenic muscle inhibition: neural mechanisms and treatment perspectives. *Semin Arthritis Rheum*. 2010;40(3):250-266. [doi:10.1016/j.semarthrit.2009.10.001](https://doi.org/10.1016/j.semarthrit.2009.10.001)
77. Grapar Žargi T, Drobníč M, Vauhnik R, Koder J, Kacin A. Factors predicting quadriceps femoris muscle atrophy during the first 12 weeks following anterior cruciate ligament reconstruction. *Knee*. 2017;24(2):319-328. [doi:10.1016/j.knee.2016.11.003](https://doi.org/10.1016/j.knee.2016.11.003)
78. Pietrosimone BG, Ingersoll CD. Focal knee joint cooling increases the quadriceps central activation ratio. *J Sports Sci*. 2009;27(8):873-879. [doi:10.1080/02640410902929374](https://doi.org/10.1080/02640410902929374)

79. Pietrosimone BG, Hart JM, Saliba SA, Hertel J, Ingersoll CD. Immediate effects of transcutaneous electrical nerve stimulation and focal knee joint cooling on quadriceps activation. *Med Sci Sports Exerc.* 2009;41(6):1175-1181. [doi:10.1249/MSS.0b013e3181982557](https://doi.org/10.1249/MSS.0b013e3181982557)
80. Harput G, Ulusoy B, Yildiz TI, et al. Cross-education improves quadriceps strength recovery after ACL reconstruction: a randomized controlled trial. *Knee Surg Sports Traumatol Arthrosc.* 2019;27(1):68-75. [doi:10.1007/s00167-018-5040-1](https://doi.org/10.1007/s00167-018-5040-1)
81. Lepley LK, Wojtys EM, Palmieri-Smith RM. Combination of eccentric exercise and neuromuscular electrical stimulation to improve quadriceps function post-ACL reconstruction. *Knee.* 2015;22(3):270-277. [doi:10.1016/j.knee.2014.11.013](https://doi.org/10.1016/j.knee.2014.11.013)
82. Kotsifaki A, Korakakis V, Whiteley R, Van Rossom S, Jonkers I. Measuring only hop distance during single leg hop testing is insufficient to detect deficits in knee function after ACL reconstruction: a systematic review and meta-analysis. *Br J Sports Med.* 2020;54(3):139-153. [doi:10.1136/bjsports-2018-099918](https://doi.org/10.1136/bjsports-2018-099918)
83. Bates NA, Schilaty ND, Nagelli CV, Krych AJ, Hewett TE. Multiplanar loading of the knee and its influence on anterior cruciate ligament and medial collateral ligament strain during simulated landings and noncontact tears. *Am J Sports Med.* 2019;47(8):1844-1853. [doi:10.1177/0363546519850165](https://doi.org/10.1177/0363546519850165)
84. Hewett TE, Myer GD. The mechanistic connection between the trunk, hip, knee, and anterior cruciate ligament injury. *Exerc Sport Sci Rev.* 2011;39(4):161-166. [doi:10.1097/JES.0b013e3182297439](https://doi.org/10.1097/JES.0b013e3182297439)
85. Lohse KR, Sherwood DE, Healy AF. How changing the focus of attention affects performance, kinematics, and electromyography in dart throwing. *Hum Mov Sci.* 2010;29(4):542-555. [doi:10.1016/j.humov.2010.05.001](https://doi.org/10.1016/j.humov.2010.05.001)
86. Faltus J, Criss CR, Grooms DR. Shifting focus: a clinician's guide to understanding neuroplasticity for anterior cruciate ligament rehabilitation. *Curr Sports Med Rep.* 2020;19(2):76-83. [doi:10.1249/JSR.0000000000000688](https://doi.org/10.1249/JSR.0000000000000688)
87. Benjaminse A, Gokeler A, Dowling AV, et al. Optimization of the anterior cruciate ligament injury prevention paradigm: novel feedback techniques to enhance motor learning and reduce injury risk. *J Orthop Sports Phys Ther.* 2015;45(3):170-182. [doi:10.2519/jospt.2015.4986](https://doi.org/10.2519/jospt.2015.4986)
88. Walker JM, Brunst CL, Chaput M, Wohl TR, Grooms DR. Integrating neurocognitive challenges into injury prevention training: a clinical commentary. *Phys Ther Sport.* 2021;51:8-16. [doi:10.1016/j.ptsp.2021.05.005](https://doi.org/10.1016/j.ptsp.2021.05.005)
89. Wohl TR, Criss CR, Grooms DR. Visual perturbation to enhance return to sport rehabilitation after anterior cruciate ligament injury: a clinical commentary. *Int J Sports Phys Ther.* 2021;16(2):552-564. [doi:10.26603/001c.21251](https://doi.org/10.26603/001c.21251)
90. Peterka RJ. Chapter 2 - Sensory integration for human balance control. In: Day BL, Lord SR, eds. *Handbook of Clinical Neurology.* Vol 159. Elsevier; 2018:27-42.
91. Chaput M, Onate JA, Simon JE, et al. Visual cognition associated with knee proprioception, time to stability, and sensory integration neural activity after ACL reconstruction. *J Orthop Res.* Published online 2021. [doi:10.1002/jor.25014](https://doi.org/10.1002/jor.25014)
92. Grooms D, Appelbaum G, Onate J. Neuroplasticity following anterior cruciate ligament injury: a framework for visual-motor training approaches in rehabilitation. *J Orthop Sports Phys Ther.* 2015;45(5):381-393. [doi:10.2519/jospt.2015.5549](https://doi.org/10.2519/jospt.2015.5549)
93. Grooms DR, Page SJ, Nichols-Larsen DS, Chaudhari AM, White SE, Onate JA. Neuroplasticity associated with anterior cruciate ligament reconstruction. *J Orthop Sports Phys Ther.* 2017;47(3):180-189. [doi:10.2519/jospt.2017.7003](https://doi.org/10.2519/jospt.2017.7003)
94. Vergne-Salle P. Management of neuropathic pain after knee surgery. *Joint Bone Spine.* 2016;83(6):657-663. [doi:10.1016/j.jbspin.2016.06.001](https://doi.org/10.1016/j.jbspin.2016.06.001)
95. Jourdan M, Madfes DC, Lima E, Tian Y, Seit  S. Skin care management for medical and aesthetic procedures to prevent scarring. *Clin Cosmet Investig Dermatol.* 2019;12:799-804. [doi:10.2147/ccid.S218134](https://doi.org/10.2147/ccid.S218134)
96. Judd D, Bottoni C, Kim D, Burke M, Hooker S. Infections following arthroscopic anterior cruciate ligament reconstruction. *Arthroscopy.* 2006;22(4):375-384. [doi:10.1016/j.arthro.2005.12.002](https://doi.org/10.1016/j.arthro.2005.12.002)
97. Mousavi H, Mohammadi M, Aghdam HA. Injury to the infrapatellar branch of the saphenous nerve during ACL reconstruction with hamstring tendon autograft: a comparison between oblique and vertical incisions. *Arch Bone Jt Surg.* 2018;6(1):52-56.
98. Dommissie GF. The blood supply of the spinal cord and the consequences of failure. In: Boyling J, Palastanga N, eds. *Grieve's Modern Manual Therapy.* 2nd ed. Churchill Livingstone; 1994.

99. Song D, Yu DSF. Effects of a moderate-intensity aerobic exercise programme on the cognitive function and quality of life of community-dwelling elderly people with mild cognitive impairment: A randomised controlled trial. *Int J Nur Stud*. 2019;93:97-105. [doi:10.1016/j.ijnurstu.2019.02.019](https://doi.org/10.1016/j.ijnurstu.2019.02.019)
100. Angevaren M, Aufdemkampe G, Verhaar HJ, Aleman A, Vanhees L. Physical activity and enhanced fitness to improve cognitive function in older people without known cognitive impairment. *Cochrane Database Syst Rev*. 2008;(3):Cd005381. [doi:10.1002/14651858.CD005381.pub3](https://doi.org/10.1002/14651858.CD005381.pub3)
101. Stern Y, MacKay-Brandt A, Lee S, et al. Effect of aerobic exercise on cognition in younger adults: A randomized clinical trial. *Neurology*. 2019;92(9):e905-e916. [doi:10.1212/wnl.00000000000007003](https://doi.org/10.1212/wnl.00000000000007003)
102. McMorris T, Hale BJ. Is there an acute exercise-induced physiological/biochemical threshold which triggers increased speed of cognitive functioning? A meta-analytic investigation. *J Sport Health Sci*. 2015;4(1):4-13. [doi:10.1016/j.jshs.2014.08.003](https://doi.org/10.1016/j.jshs.2014.08.003)
103. Cheney S, Chiaia TA, de Mille P, Boyle C, Ling D. Readiness to return to sport after ACL reconstruction: a combination of physical and psychological factors. *Sports Med Arthrosc Rev*. 2020;28(2):66-70. [doi:10.1097/jsa.0000000000000263](https://doi.org/10.1097/jsa.0000000000000263)
104. Myer GD, Paterno MV, Ford KR, Quatman CE, Hewett TE. Rehabilitation after anterior cruciate ligament reconstruction: criteria-based progression through the return-to-sport phase. *J Orthop Sports Phys Ther*. 2006;36(6):385-402. [doi:10.2519/jospt.2006.2222](https://doi.org/10.2519/jospt.2006.2222)
105. Hsu CJ, Meierbachtol A, George SZ, Chmielewski TL. Fear of reinjury in athletes: implications for rehabilitation. *Sports Health*. 2017;9(2):162-167. [doi:10.1177/1941738116666813](https://doi.org/10.1177/1941738116666813)
106. Papadopoulos S, Tishukov M, Stamou K, Totlis T, Natsis K. Fear of re-injury following ACL reconstruction: an overview. *J Res Pract Musculoskelet Syst*. 2018;2(4):124-130.
107. Chmielewski TL, George SZ. Fear avoidance and self-efficacy at 4 weeks after ACL reconstruction are associated with early impairment resolution and readiness for advanced rehabilitation. *Knee Surg Sports Traumatol Arthrosc*. 2019;27(2):397-404. [doi:10.1007/s00167-018-5048-6](https://doi.org/10.1007/s00167-018-5048-6)
108. López-de-Uralde-Villanueva I, Muñoz-García D, Gil-Martínez A, et al. A systematic review and meta-analysis on the effectiveness of graded activity and graded exposure for chronic nonspecific low back pain. *Pain Med*. 2016;17(1):172-188. [doi:10.1111/pme.12882](https://doi.org/10.1111/pme.12882)
109. Macedo LG, Smeets RJ, Maher CG, Latimer J, McAuley JH. Graded activity and graded exposure for persistent nonspecific low back pain: a systematic review. *Phys Ther*. 2010;90(6):860-879. [doi:10.2522/ptj.20090303](https://doi.org/10.2522/ptj.20090303)
110. McCrone P, Sharpe M, Chalder T, et al. Adaptive pacing, cognitive behaviour therapy, graded exercise, and specialist medical care for chronic fatigue syndrome: a cost-effectiveness analysis. *PLoS One*. 2012;7(8):e40808. [doi:10.1371/journal.pone.0040808](https://doi.org/10.1371/journal.pone.0040808)