The role of neurological pathways in non – contact anterior cruciate ligament injury and rehabilitation

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Abstract
Rupture of ACL is a common musculoskeletal injury.Rehablitation after ACL injury is long and should be criteria based when progressing through specific rehabilitaiton phases. Beside mechanic role, ACL also has neurophysiologic role, as it provides barage of afferent inputs into the CNS. That is why ACL injury is more complex than just simple mechanic deficit. Researchers have in the past years discovered how ACL injury affects the processeing of CNS and the effects it has on neuromuscular function. They have also discovered the neurological risk factors for ACL injury, which are considered as neurological biomarkers. Neuroplastic changes of the CNS after the ACL injury can negatively impact the neuromuscular functions like the ability to contract quadriceps muscle. There is also change in processing of somatosensory and visual information which affects the planning and execution of motor programs. ACL injury also impacts the capacity of the neurocognitive system. ACL injured individuals showed increased demand of focused attention during simple motor tasks. All of this points out to numerous neurophysiological changes after the ACL injury which affects the motor control and risk for second ACL injury. Based on neurological changes after ACL injury we are able to battle with these neuroplastic changes using principles of motor learning. Beside this visual training and training using virtual reality enable us to target changed visual – sensory – motor procesing after ACL injury. Key words: ACL injury, neuromuscular changes after ACL injury, sensorimotor changes after Acl injury, neuroplastic changes after ACL injury.

Vloga živčnih poti pri nekontaktnih poškodbah in rehabilitaciji sprednje križne vezi

Povzetek
Ruptura sprednje križne vezi je pogosta mišično-skeletna poškodba. Rehabilitacija po poškodbi SKV je dolgotrajna in temelji na doseganju kriterijev za napredovanje v določene faze rehabilitacije. Poleg mehanske vloge ima SKV tudi nevrofiziološko funkcijo, saj s svojimi številnimi mehanoreceptorji omogoča bogat aferentni dovod informacij v CŽS. Prav zaradi tega je poškodba SKV kompleksnejši pojav od izključno mehanske poškodbe. Raziskovalci so v zadnjih letih začeli odkrivati, kako poškodba in rekonstrukcija SKV vplivata na delovanje živčnega sistema in živčno-mišične funkcije. Poleg tega so začeli odkrivati nevrofiziološke dejavnike tveganja za poškodbo SKV, ki tako predstavljajo nevrološki biomarker za poškodbo SKV. Nevroplastične spremembe v živčnih poteh in mrežah živčnega sistema lahko negativno vplivajo na živčno-mišične funkcije, kot je denimo aktivacija sprednjih stegenskih mišic. Poleg tega se spremeni procesiranje vidnih in somatosenzornih informacij, kar vpliva na motorično planiranje in oblikovanje motoričnih programov. Poškodba SKV prav tako vpliva na kapaciteto nevrokognitivnega sistema, in sicer posamezniki po poškodbi SKV kažejo večjo potrebo po fokusirani pozornosti med enostavno motorično nalogo v primerjavi s kontrolno skupino. Vse to kaže na številne nevroplastične procese, ki se odvijajo po poškodbi SKV in vplivajo na posameznikovo motorično kontrolo in tveganje za ponovno poškodbo SKV. Glede na nevrološke spremembe lahko s pomočjo principov motoričnega učenja vplivamo na nevroplastične spremembe v CŽS. Poleg tega vidni trening in trening s pomočjo virtualne resničnosti omogočata najnovejši pristop, s katerim vplivamo na spremenjeno vidno-senzomotorično procesiranje po poškodbi SKV. Ključne besede: živčno – mišične spremembepo poškodbi sprednje križne vezi, nevroplastične spremembe po poškodbi sprednje križne vezi.

INTRODUCTION

Injury to the anterior cruciate ligament (ACL) is an extremely common musculoskeletal injury. The highest frequency of this injury is among individuals aged between 15 and 40 who are actively engaged in sports involving directional changes, pivoting, jumping and landing (Prodromos et al., 2007). The incidence rate of ACL injuries is 68 per 100 000 people in the general population, while the incidence rate among atheltes is 3.5% for women and 2% for men, with an incidence rate of 1.5 and 0.9 injuries per 10.000 exposures (Montalvo et al., 2019), (Sanders et al. 2016). After an ACL injury, the rate of return to professional sport is often lower than many athletes expect. The results show that the rate of return to any sports activity after ACL injury is 81%, the rate of return to same sport activity is 65%, and the rate of return to porfessional sports is only 55% (Ardern et al., 2014). Athletes with shorter interval between the injury and ACL reconstruction have a higher rate of returning to professional sports (Lai et al., 2018), and the rate of return to sport activity is also higher for males compared to females (Ardern et al., 2014). After the ACL reconstruction, the risk of re-injuring is 30 to 40 timed higher than for uninjured athlete (Wiggins et al., 2016). Additionally, the risk of ACL injury on the uninjured limb increases (Sward et al., 2020). There are many reasons for this and increasingly recognised are the changes in CNS function in terms of sensorimotor, neuromuscular and higher neurologic functions (D. Grooms et al., 2015). As much as 60-80% of ACL injuries occur in non – contact situations, meaning without contact or collision with another player (Krosshaug et al., 2007). This suggest the possibility that the motor control error exceeds the CNS's reaction abilities and this depends on the pre – mediated mechanisms such as planning, decision making, dual task performance and other neurocognitive functions (D. Grooms et al., 2015). There is new evidence about neurological risk factors such as impaired visual fusion, altered functional neurological connection between certain brain regions, poor cortical inhibition control as well as other neurocognitive factors (Gokeler et al., 2024), (Chen et al., 2022). These neurological risk factors also raises likehood of characteristic biomechanical patterns for non – contact ACL injury (C. B. Swanik et al., 2007), (Bertozzi et al., 2023). In addition to neurophysiological risk factors, scientists have identified numerous neurophysiological consequences after injury, reconstrunction, rehabilitation and even after returning to sports activity (D. Grooms et al., 2015). Due to these facts, an ACL injury can be defined as neurophysiological dysfunction and not merely a mechanical joint injury (Dingenen et al., 2016). Because of the disruption of afferent sensory pathways that occur due to injury of ligament mechanoreceptors, numerous neuroplastic changes begin to occur in the CNS, negatively affecting neuromuscular function as well as neurocognitive and visual – sensory – motor functions (Palmieri et al., 2005). New knowledge in the field of motor learning allows us to improve these neuroplastic changes and optimize the transfer of skills to a sport specific environment through rehabilitation (Gokeler et al., 2016). Strategies such as visuo – motor training, application of dynamic system theory in rehabilitation, neurocognitive testing and training, can improve rehabilition outcomes and potentially reduce the rate of reinjury (Gokeler et al., 2016), (Chaput et al., 2022). New evidence shows that applying neurocognitive challanged hop tests can determine athelte's neurocognitive overreliance during movement and improve rehabilitaiton outcomes (D. R. Grooms et al., 2023). The aim of our research was to review the literature about neurological alternations before and after ACL injury. Our aim was also to deterimne if there is evidence that can help physiotherapists assess and treat neurological alternations after ACL injury and design return to sport phase of rehabilitation that can prepare ahtletes for inherently dynamic and unpredictable sport environment.

METHODOLOGY

Our work is based on the literature review. For the review, we used PubMed database. The inclusion criteria for our final work encompass the studies whose topic is the change in nervous system function as a cause and consequence of ACL injury. We included clinical studies, randomized controlled trials, meta – analyses, systematic reviewes and peer – reviewed articles in English, published between 1980 and 2024. For selection and synthesis of articles we used PRISMA protocol for systematic reviews and meta-analyses (Page et al., 2021). A search on PubMed was conducted using the following queries:

»ACL injury«, »neuromuscular changes after ACL injury«, »sensorimotor changes after ACL injury«, »neuroplastic changes after ACL injury«

RESULTS

The search strategy resulted in 392 articles. After examining titles and abstract we excluded 326 articles. Remaining 66 articles were further accessed and analysed for eligibility. Based on inclusion criteria and relevance of the subject matter of the text we excluded another 48 articles. Articels were finally included in this review.

Tabel 1: Characteristics of the studies included

Author, Year	*Study objective*	*Results*
Valeriani et al. 1996	*The aim of the study was to examine impact of the loss of affetent signals on the CNS using SEPs (somatosensory evoked potentials)*	*Central somato – sensory neural pathways are altered after an ACL injury, which authors indicated by abnormal SEPs.*
Rodriguez, Palmieri . Smith and Krishnan, 2021	*Aim of the study was to review the literature on changes in excitability of spinal reflexes and corticospinal pathways following ACL injury, and to examine the degree of weakness and inability to activate the quadricapes muscles.*	*Authors found reduced bilateral excitability of corticospinal pathways and increased excitability of spinal reflex pathways. They also observed a bilateral decrease in strenght and the ability to activate the quadriceps muscles in injured individuals.*
Rice and McNair, 2010	*Aim of the study was to review literature about arthrogenic muscle inhibition (AMI) after ACL injury, with emhasis on neurological mechanisms.*	*They found that AMI is important barrier in rehabilitation of patient after ACL rehabilitation. It contributes to the atrophy of the quadriceps and it prevent its full activation .*
Neto et al. 2019	*Aim of the study was to review literature about changes in brain activation after ACL injury.*	*Literature shows evidence of functional neuroplastic changes after ACL injury in sensory as well as motor areas of the brain.*
Diekfuss et al. 2019	*Purpose of the study was to examine if there exist neurological factors before ACL injuries.*	*Results show that there are changes in nurological pathways before ACL injury and present potential neurological biomarker for ACL injury.*

Author, Year	*Study objective*	*Results*
Needle, Lepley and Grooms, 2017	*Purpose was to review literature about neuroplastic changes of brain after ACL injury.*	*ACL injury has dramatic impact on brain and it causes neuroplastic changes in various brain regions.*
Lepley et al. 2020	*Purpose was to quantify hemispheric neuroplastic changes as well as changes in corticospinal motor pathways.*	*Injured patients showed decreased volume of corticospinal path which is related with decreased excitability of this pathway*
Grooms et al. 2017	*Aim of the study was to compare brain activation during knee motion between control and patients who injured their ACL.*	*They found alterd brain activation in patient group, which shows presence of neuroplastic changes after ACL injury.*
Konishi, Konishi in Fukubayshi, 2003	*Aim of the study was to examine if the gamma motor neuron loop dysfunction was also present on the uninjured limb after ACL injury*	*They found neurophysiological abnormality in gamma motor neuron loop on both sides which indicates more general neuroplastic changes that affect motor control on both sides. These findings have important implicaitons for the rehabilitation after ACL injury.*
Konishi, Konishi and Fukubayashi, 2003	*Aim of the study was to identify if loss of afferent signals after ACL injury lead to dysfunction of the gamma motor neuron loop and quadriceps inhibition.*	*Deafferentiation after ACL injury disrupts normal function of gamma motor neuron loop which causes quadriceps inhibition and weakness.*
Kapreli et al. 2009	*Aim of the study was to identify brain activation pattern after ACL injury.*	*ACL injury and deafferation causes reorganisation of CNS and altered activation of certain brain regions.*
Grooms, Appelbaum and Onate, 2015	*Aim of the study was to review and present neuroplastic adaptation of CNS after ACL injury and possible neuromodulatory interventions that can improve these changes.*	*Review emphasises the integration of visual – motor training into rehabilitation after ACL injury. In this way physiotherapists can add neurocognitive approach to treatment after ACL injury.*

Author, Year	*Objective*	*Results*
Gokeler et al. 2016	*Aim of the study was to asses the impact of virtual reality immersion after ACL injury as new neurocognitive approach to rehabilitation after ACL injury.*	*Application of virtual reality glasses during rehabilitation after ACL injury, caused altered movement patterns which are more comparable to uninjured individuals.*
Diekfuss et al. 2020	*Aim of the study was to assess if there are alternations in central nervous system functional connection between various brain regions.*	*Authors identified altered functional connections between knee specific sensory – motor brain areas, before ACL injury.*
Weiss, 2008	*Aim of the study was to check if ACL injury influence CNS information processing during sensory – motor task.*	*Authors found altered CNS processing during movement task. This showed as altered brain waves in frontal and parietal networks.*
Gokeler et al. 2019	*Aim of the study was to present clinically integrated principles of motor learning which can enhance neuroplasticity in patients after ACL injury*	*With integration of motor learning principles physiotherapists can optimize rehabilitation and transfer of skills gained during gym training to sport specific environment.*
Sheurer et al. 2019	*Aim of the study was to investigate functional implications of altered corticomotor pathways.*	*Authors found increased upper motor neuron threshold. Second finding was increased intracortical inhibition with lowered ability to generate torque in later temporal intervals of limb movement.*
Baumeister et al. 2011	*Aim of the study was to investigate impact of ACL reconstruction motor control and brain activation pattern.*	*They found increased Theta frontal brain waves, which shows increased neurocognitive demand of simple motor task in patients after ACL reconstruction.*
Pietrosimone et al. 2015	*Aim of the study was to investigate if excitability of spinal reflex and coritoco-motor pathways differs between patients after ACL reconstruction compared to control group.*	*They found increased motor cortex activation threshold, increased excitability of spinal reflex pathways in patients after ACL reconstruction compared with control group.*

DISCUSSION

NEUROPHYSIOLOGY OF ANTERIOR CRUCIATE LIGAMENT

In addition to its passive mechanical role, ACL has neurophysiological function. Along with other knee ligaments and capsulo-ligamentous tissue ACL via numerous mechanoreceptors transmit affetent information to the CNS, thus underllying various important neuromuscular functions. According to immunohistochemical studies, the ACL has all kind of mechnoreceptors (Ruffini ending, Pacinian corpuscles and Golgi tendon organs) (Banios et al., 2022). These enable perception of pain and inflammation, the sense of torque, changes in knee joint position and positions of the knee joint at the extremes of end ranges of motions (Banios et al., 2022). Neurophysiological role of ACL is even more significant given the fact that ACL contains disproportionally more mechanoreceptors in its content compared to other ligaments in the knee and other joints (Çabuk & Kuşku Çabuk, 2016). Anterior cruciate ligament via its neuro-anatomical organization supports numerous neuromuscular reflexes (Solomonow & Krogsgaard, 2001). Beside its role as passive stabilizer, ligament such as ACL also plays a role as dynamic sensory organ (Solomonow & Krogsgaard, 2001). During anterior translation of the tibia, significant forces are transmitted to the ACL, triggering numerous mechanoreceptors that convey sensory stimuli to the dorsal horn of the spinal cord. This process trigger ligamentomuscular protective reflex, which triggers the contraction of the hamstring muscles, preventing further anterior translation of the tibia and preventing supraphysiological loading of the ACL (Solomonow & Krogsgaard, 2001). There is also a flexor reflex which occurs upon stimulation of free nerve endings or nociceptors. High loading of ACL triggers these neurons, causing refelxive flexion of the knee and hip, therby withdrawing limb from potentially dangerous situation (Solomonow in Krogsgaard, 2001). Beside the previously described reflexes, ACL has also role in the gamma motor loop (Sjolander, n.d.). System of gamma motor neuron and muscle spindles is constantly influenced by descending neural pathways as well as afferent signals from ACL (Sjolander, n.d.).

COORDINATIVE ERROR AS MEChANISM OF NON-CONTACT ACL INJURY

Non contact ACL injury occurs within the 40 milliseconds after initial ground contact (Koga et al., 2010). All evidence shows that ACL injury happens in complex multidimensional environment, that requires high level of distributed and divided attention over multiple segments, optimal working memory, minimal reaction time, precise decison making and inhibitory coortical control over emotion, behaviour, motor action and cognition (D. Grooms et al., 2015), (Gokeler et al., 2021). According to research ACL injury occurs extremely fast after first contact, which indicates that the cause of injury is possibly a coordinative error, which happens in CNS (McLean et al., 2010). Most sports are random and unpredictable and require a feedforward type of motor control (McLean et al., 2010). Divided attention, double tasking and complex visuomotor demands can overload the neurocognitive system of athlete and cause coordinative errors and decreaseing movement variability which can cause aberrant biomechanical patterns and ACL injury (C. “Buz” Swanik, 2015). Individual interaction with other players can lead to disrupted attention and increased risk of coordinative errorors and ACL injuries (D. Grooms et al., 2015). Neurocognitive factors such as reaction time, information processing speed, dual tasking ability, attention and visual-motor control are all closely related to biomechanical factors associated with ACL injury (D. R. Grooms & Onate, 2016). Overloading of neurocognitive resources can cause loss of situational awareness which lead to disrupted neuromuscular control (C. B. Swanik et al., 2007). Visual system also plays significant role as it enables the direction of attention toward relevant cues. Worse visual and oculomotor abilities in ahtletes are associated with elevated risk for ACL injury (Chen et al., 2022) (Avedesian, McPherson, et al., 2022).

NEUROCOGNITIVE RISK FACTORS FOR NON CONTACT ACL INJURY

Neurocognitive factors such as reaction time, processing speed and visual and verbal memory are important indirect markers of cerebral capability (C. B. Swanik et al., 2007). Situational attention and attentional capacity can also affect above aspects, thus influencing the integration of vestibular, visual, and somatosensory information and consequently neuromuscular control of movement (C. B. Swanik

et al., 2007). Integration of most relevant sensory information from the environment and ignoring less relevant is important aspect of neurocognitive processing which enable athletes to effectivelly coordinate and execute precise movements (C. “Buz” Swanik, 2015)(C. B. Swanik et al., 2007). C. B. Swanik et al., (2007) Indicated that slower reaction time, slower processing speed as well as poorer visual and verbal memory are significant neurocognitive risk factors for the occurence of non – contact ACL injuries. Thus, neurocognitive risk factor such as slower reaction time can negatively affect coordination in unexpected sport situations and increase the ahtlete's susceptibility to judgement errors (C. B. Swanik et al., 2007). Visual and verbal memory are essential processes for selective processing of environmental information, they also play role in interpreting informational conflicts. Deficits in both types of memory can lead to loss of spatial awareness, resulting in disorientation and coordination errors (Avedesian, Forbes, et al., 2022), (C. “Buz” Swanik, 2015), (C. B. Swanik et al., 2007). Both Avedesian, Forbes, et al., (2022) and Bertozzi et al., (2023) identified an association between poorer cognitive abilities and biomechanical movement patterns known to occur during ACL injury and thus increase the risk for non-cntact ACL injury. Athletes with slower reaction times and information processing speeds, demonstrate higher ground reaction forces, greater anterior shear forces on the tibia and increased abduction angle in the knee joint (Bertozzi et al., 2023). A higher incidence of errors during landing in response to unexpected stimulus is also associated with poorer working memory (Bertozzi et al., 2023). In this case slower athlete's responses to unexpected stimulus reduce the time interval within which athlete can react and plan the neccessary movement. Poorer visual-spatial memory can also lead to worse performance in dual tasking which is often present and crucial in sports (Bertozzi et al., 2023). Above-mentioned changes in neurocognition are indirect markers of potentially altered functioning of neural netrworks and pathways within the CNS, that for instance support reaction time. The cited literature is also a basis for exploring the factors of the CNS that contribute to the occurence of non – contact ACL injury (Diekfuss et al., 2019).

NEUROLOGICAL BIOMARKERS FOR ACL INJURY

Diekfuss et al., (2019) investigated functional neurological connections within the CNS and found that individuals who went on to injurye their ACL exhibited altered functional connectivity between various parts of the CNS. Specifically weaker conenctions between left primary sensory cortex (S1) and the posterior lobe of the cerebellum. S1 is crucial for sensory information processing and the initiation of the motor programs, whereas the cerebellum plays significant role in postural stability and detection of discrepancies between planned and executed movements. These results show potential functional neurological dysfunctions predisposing athletes to ACL injury (Diekfuss et al., 2019). The sensory and cerebellar areas are highly involved in navigating temporal and spatial demands of sport environment, which is why optimal functinoal connectivity between these areas is crucial (Diekfuss et al., 2019). This study supports the notion that ACL injuries are more complex than mere mechanical failures and may reflect neurophysiological dysfunction (Diekfuss et al., 2019). In addition, this study also support previous findings regarding poorer neurocognitive abilities in individuals who torn their ACL during non – contact scenarios (C. B. Swanik et al., 2007). The same group examined structural and functional changes in neural pathways within male population, comparing functional brain conenctivity in athletes who went on to injurying their ACL to those who did not (Diekfuss et al., 2020). Similar to previous study they found altered and decreased connectivity between sensorimotor areas critical for knee control in males. Specifically weaker connections were found between the left secondary somatosensory cortex (SII) and the left and right supplemenetary motor areas, the right premotor cortex, the left primary motor cortex (M1) and the left S1 (Diekfuss et al., 2020). These findings furhter reinforce the idea of altered CNS function as a risk factor for ACL injuries (Diekfuss et al., 2020). Diminished functional connectivity within specific sensorimotor regions may lead to coordination errors and poorer neuromuscular control in temporally and spatially complex sport situations, increasing ACL injury risk (Diekfuss et al., 2020). Besides the above mentioned findings, which show changes in neurological functional connectivity of the CNS and diminished neurocognitive abilities as risk factor for ACL injuries, many authors have recently considered non-contact ACL injury as an error

in sensorimotor integration caused by a mismatch in perception-action coupling or continious regulatory loop between perception and movement output (Avedesian, 2024) (C. B. Swanik et al., 2007). Frequently during sport, increased cognitive load, can narrow athelte's visual field, slow reaction time and alter muscular activities during the coordination tasks (Kim et al., 2016). Dynamic knee stiffness and electromyographic activity of muscles are significanlty decreased during visuospatial tasks compared to control group (Kim et al., 2016). Increased sensory complexity and stressfull situations narrows athletes attention span and ability to process information, which leads to decreased knee joint stifness and slower neuromuscular responses (Kim et al., 2016). Reduction in neuromuscular control is also commonly present when athletes must visually attend to various environmental stimulus while performing high risk sport maneuvers (Hughes & Dai, 2023). D. R. Grooms et al., (2022) identified associations between aberrant biomechanical patterns during drop jump and leg press movement like increased frontal plane knee movement and increased bilateral motor control (D. R. Grooms et al., 2022). Greater knee abduction was associated with increased activity in several brain areas: precuneus (area integrating sensorimotor coordination when visual attention is required), posterior cingulate gyrus (area processing spatial awareness and attention for motor control) and lingual gyrus and intercalcarine cortex (areas processing spatial awareness and attention for motor control). Individual with increased risk of injury also showed increased activity in primary and secondary sensorimotor cortex activity when compared to those classified as low injury (D. R. Grooms et al., 2022). This injury – risk biomechanis are manifestation of reduced neural crossmodal sensory integration for knee spatial awareness, contributing to the inability of knee abduction control during motion and loading (D. R. Grooms et al., 2022). Increased visuo – spatial information processing while engaging in motor control task could disrupt one's ability to maintain safer knee position during complex dynamic sport skills (D. R. Grooms et al., 2022). Those athletes may lack neurological resources to maintain both neuro – muscular coordination and engage in complex sport situations that require visuospatial and sensory processing (D. R. Grooms et al., 2022). This altered brain activation may be important link between visuo-spatial and cognitive attention deficits that increase ACL injury risk (D. R. Grooms et al., 2022). Futhermore increased cross modal processing (increased lingual gyrus activation) is present in those who exhibit poor neuromuscular coordination and injury – risk loading (D. R. Grooms et al., 2022). Given the fact that those with elevated injury – risk loading had increased primary and pre - motor cortex activity during loading tasks, those neurocognitive resources might be disproportionally taxed, which could lead to increased ACL injury risk in complex sport situations (D. R. Grooms et al., 2022). This pattern of brain activation during motor task is similar to »novice« athletes who depend significantly more on increased brain activity for motor planning and rely more on visuo-cognitive strategy for movement control (D. R. Grooms et al., 2022).

Another neurological risk factor for ACL injury is increased reaction time in attention network task, which measures athletes ability to direct visual attention to a specific region of space within the environment to detect further information more quickly (Avedesian, McPherson, et al., 2022). Every 10 milliseconds increase in orienting network rection time is associated with 15% elevated risk for ACL injury (Avedesian, McPherson, et al., 2022).

Based on these neurological risk factors ACL injury is not simple mechanical injury. Biomechanical patterns seen during injury event, could be manifestation of altered sensorimotor and visual – cognitive processing during complex sport situations, wihich can lead to motor control error and non – contact ACL injury (D. R. Grooms et al., 2022). Complex sport environment and pressing situations put high demands on athletes selective visual attention and inhibitory control of less relevant information (Gokeler et al., 2024). Athletes who injured their ACL during non contact situation displayed significant reduction in cortical inhibitory control (Gokeler et al., 2021). A sport situation while player is immersed in a dynamic environment often demands quickly inhibiting already planned motor commands and executing new motor program all within very short period of time (Gokeler et al., 2024). This study shows us another potential neurological risk factor for ACL injury which is reduced cortical inhibitory ability (Gokeler et al., 2024)

Chen et al., (2022) investigated potential risk factors for ACL injury. They found that degree of visual fusion in the visual cortex is an important risk factor for ACL injury (Chen et al., 2022). Two different images fall onto our retinas and they are projected through two different visual pathways through the lateral geniculate bodies to the visual cortex, where more complex processing begins (Chen et al., 2022). In layer 4 of the visual cortex two images from two retinas merge and start creating the basis for depth perception (Chen et al., 2022). Depth perception is one of the most important visual functions that enable high level of sport performance performance. The study study by Chen et al., (2022) found that reduced visual fusion is associated with higher risk of ACL injury.

ARTHROGENIC MUSCLE INHIBITION AFTER ACL INJURY

ACL injury triggers deafferentiation and onset of neuroplastic changes in CNS. Damaging the mechanoreceptors within the ACL can trigger neurochemical and neurophysiological responses similar to other neurological injuries, causing long lasting widespread neurological changes in various CNS regions (Navarro et al., 2007). ACL injury leads to abnormal sensitivity of muscle spindles due to altered gamma motor loop activity and regulation of intrafusal muscle fibers which leads to significatn quadriceps inhibition (Sjolander, n.d.), (Konishi et al., 2002). In addition to deafferentiation, inhibition can also arise due to tissue injury, inflammation, and pain, which happen after injury and reconstruction, leading to neuroplastic changes at the peripheral part of nervous system, spinal cord, and cortex level (Criss et al., 2021). Thre combination of inflammation, cytokine infiltration, inflammation, deafferentiation and nerve ending damage can all lead to extensive adaptation of the CNS (Criss et al., 2021). It is important to consider the reconstruction of ACL which represents additional trauma, with further intra-articular damage of afferent axons and activation of hypothalamic- pituitariy axis causing a strong stress response which is strong stimulus for CNS neuroplastic change (Criss et al., 2021). Arthrogenic muscle inhibition emerges as consequence of above factors happening after injury and ACL reconstruction. AMI is caused by altered afferent neuron firing which changes the activity and excitability of many spinal and supraspinal reflex pathways (Rice & McNair, 2010). Afferent neurons project to many spinal and supraspinal motor control circuits, influencing alpha motor neurons via various neuronal pathways (Rice & McNair, 2010). Quadriceps inhibition, weakness and atrophy happen mainly due to altered function of three reflexive pathways (Rice & McNair, 2010). Non – reciprocal IB interneurons receive dominant afferent input from Ib afferent fibers originating in Golgi tendon organs and other peripheral mechanireceptors (Rice & McNair, 2010). Ib inhibitory interneurons connect synaptically with alpha motor neurons, which are inhibited upon acitivation of Ib interneurons (Rice & McNair, 2010). Swelling and increased activation of II neurons due to inflammation can increase activaiton of Ib inhibitory interneurons, inhibiting alpha motor neurons and thus quadriceps musculature (Rice & McNair, 2010). Wide dynamic range neurons are located in lamina V and mediate flexion reflex which inhibits quadriceps musculature (Rice & McNair, 2010). Intra – articular state after ACL injury icnreases firing of many afferent axons that increase activation of WDR which become hypersensitive with increased receptive fields (Rice & McNair, 2010). This state lowers threshold for activation of the flexion reflex and causes futher increase in quadriceps inhibition via reciprocal inhibition (Rice & McNair, 2010). The third cause of AMI describes abnormal functioning of gamma motor loop. Gamma motor neurons are essential for normal muscle activation. After injury there is disruption of Ia afferent transmission due to damaged mechanoreceptors and increased presynpatic inhibition in spinal cord which causes increased excitation threshold and diminished activation of alpha and gamma motor neurons (Rice & McNair, 2010),(Konishi et al., 2003), (Konishi et al., 2002). Gamma motor neuron dysfunction is also possibly caused by corticospinal inhibition and increased nociceptive activity which causes further presynaptic inhibition and AMI (Rice & McNair, 2010), (Konishi et al., 2003). Interestingly, gamma motor loop dysfunction occurss bilaterally (Konishi et al., 2003), affecting both the injured and uninjured sides (Konishi et al., 2003). The cause of bilateral gamma motor loop dysfunction is probably supraspinal inhibitory effect on alpha motor neurons and inhibitory effect of interneurons which can affect the alpha motor neurons on both sides of the spinal cord (Konishi et al., 2002),(Konishi et al., 2003).

Arthrogenic muscle inhibition as we can see, seriously affeects spinal reflex circuits, which leads to quadriceps inhibition, loss of strength and atrophy (Rodriguez et al., 2021). Arthrogenic muscle inhibition leads to further disruptions in neuromuscular function (Sherman et al., 2023). Sherman et al., (2023) have also identified quadriceps weakness; however, their sample was 2.4 years from surgery so underlying mechanism for persistent weakness was different (Sherman et al., 2023). They found insufficient recovery of strenght, failure to recruit motor units and inability to upregulate firing rates of recruited motor units during high volitional efforts (Sherman et al., 2023). They also did not find impairment of motor neuron pool excitability as it is evident in the acute phase after injury. Their findings suggest catabolism of motor units rather than inability to activate all motor units, which resulted in smaller motor neuron pools (Sherman et al., 2023). The above-described process of AMI leads to reduction and disruption of neuromuscular junctions after ACL injury, which leads to accumulation of denervated fibers in the involved quadriceps (Sherman et al., 2023), (Hunt et al., 2022). These findings suggest that due to inability to recruit all motor units, especially larger ones, anabolism would occur just in motor units activated during rehabilitation while catabolism occurs in non-activated motor units (Hunt et al., 2022). Re-conditioning of just small amplitude, low threshold motor units while larger amplitude, high threhsold motor units remain untrained is catastrophic as all sport require expression of large forces at short time intervals (Sherman et al., 2023).

BRAIN NEUROPLASTICITY AFTER ACL INJURY

In recent years, many researchers have identified changes in brain function, activation and structure after ACL injury. Valeriani et al., (1996) were the first to demonstrate brain neuroplastic changes after ACL injury. They demonstrated abnormal patterns of somatosensory evoked potential (SEP) in individuals after ACL injury, indicating central somatosensory dysfunction loacted above medial lemniscus (Valeriani et al., 1996). These findings point to central neuroplastic changes following ACL injury, likely resulting from deafferentiation. Altered or absent SEPs may arise from modification in cortical and thalamocortical neurons, progressive occupation of other neurons in somaotopic representaiton of ACL, reorgansiaiton of spinal somatotopic representations and absence of afferent informations from previously intact ACL (Valeriani et al., 1996).

Baumeister et al., (2011) investigated if altered central processing of information exist following ACL injury. They found a significantly higher number of errors in reproducing the target angle of the knee joint in individuals after ACL injury (Baumeister et al., 2011). Reduced precision and kinesthetic awareness were due to deafferentiation which lead to lack of afferent information that provide basis for perception (Baumeister et al., 2011). Besides that, patients also exhibited significant alternation in brain wave patterns measured by electroencephalograpy (Baumeister et al., 2011). Patients exhibited increased frontal theta wave activity compared to the control group indicating higher level of focused attention required after ACL injury, along with an increased cognitive load. Increased theta activity was also observed during movement on the uninjured side (Baumeister et al., 2011). Additionally, the injured individuals demonstrated significantly lower alpha wave activity in the parietal cortex. These shifts in brain wave patterns indicate a higher cognitive load on central executive fuctions and working memory following ACL injury (Baumeister et al., 2011). Theta activity plays a crucial role in processes such as working memory, information processing and attention in cognitive and sensorimotor tasks (Baumeister et al., 2008),(Baumeister et al., 2011). Most theta activity is generated in anterior cingulate cortex, which is part of the neural network responsible for attention. These findings indicate a higher level of focused attention and greater neurocognitive load in individuals following ACL injury (Baumeister et al., 2011). Elevated cognitive load in individuals after ACL injury can significantly affect neuromuscular performance in demanding sports environments characterised by rapid movements, unexpected situations and the need for divided attention, which can lead to motor control error and injury of the ACL (Baumeister et al., 2011). A characteristic of individuals after ACL injury is the reliance on explicit knowledge for specific motor tasks which requires conscious control. This leads to cortical descending control over subcortical areas, consequently diminishing the ability to automatically regulate motor programs and decreased variability of motor commands which is necessary for

movement adaptation during complex sport situations (Bosch and Cook, 2015). An already burdened neurocognitive system can become overwhelmed during unexpected sport situations and demands of sport environments which can lead to reduced capacity to regulate stiffness of muscle-tendon system, visuo – spatial disorientation as well as poorer coordination and risky biomechanical profile (C. "Buz" Swanik, 2015). Above situation can also cause startle reflex and attentional blindness, resulting in diminished ability to perceive relevant information for motor planning and coordination error (C. "Buz" Swanik, 2015). Kapreli et al., (2009) were first to investigate altered activation patterns within the brain following ACL injury. They found decreased activity across numerous areas, including the contralateral thalamus, post-parietal cortex, primary somatosensory area, globus pallidus, secondary somatosesnroy area (SII), cingualte motor area, premotor cortex and ipsilateral cerebellum. Conversely there was inreased activity observed in contralteral presupplementary motor area, the contralateral posterior secondary somatosensory area and ipsilateral posterior inferior temporal gyrus (pITG) (Kapreli et al., 2009). These findings indicate that ACL injury isn't simple mechanical injury but complex neurophysiological dysfunction (Dingenen et al., 2016). Elevated activity in pITG indicated greater need for visualization of intended movements and visual feedback during movement due to reduced inflow of proprioceptive information (Kapreli et al., 2009). Increased pre-supplementary motor area activity reflects a heightened need for planning of simple movements, which can overload neurocognitive system in more complex movement tasks and increase risk for ACL injury (Kapreli et al., 2009). D. R. Grooms et al., (2017) observed specific changes in activation of sensory, motor and visuo-sensory-motor areas of the CNS (D. R. Grooms et al., 2017). They found increased activation of primary motor cortex (M1), indicating a hightened need for cortical activation during quadriceps muscle contraction (D. R. Grooms et al., 2017). Reduced excitability of motor neurons within motor cortex along with increased influx of signals from other areas of CNS may explain elevated activation of M1 (D. R. Grooms et al., 2017). Furthermore they observed increased activation of SII, suggesting functional cortical sensory processing reorganization. An interesting finding was increased activation of medial occipito-tempotaral gyrus which is responsible for cross-modal processing of visual and sensory feedback necessary for limb movment control, sensory-visual-spatial navigation, attention, memory and perception of movement (D. R. Grooms et al., 2017). This again indicates that individuals after ACL injury rely more heavily on visual strategies for controlling knee joint movement (D. Grooms et al., 2015), having important implications for rehabilitation after ACL injury. Additionally, diminished activation was observed in cerebellum which may be due to increased activation of contralateral motor cortex, suggesting a higher cortical descending control of movement following ACL injury. This increased cortical control of movement can diminish allocation of cognitive resources to processes like decision making, double tasking and visuo-spatial orientation and increase the risk of motor control error and potentially ACL injury (D. R. Grooms et al., 2017). Neto et al., (2019), (Needle et al., 2017) and (Rodriguez et al., 2021) also found changes in brain activation patterns, different electroencephalographic activity in certain brain regions, altered excitability of brain areas, altered function of spinal reflexes as well as reduced ability to voluntarily activate the quadriceps musculature. In addition to the above changes, a decreased volume of corticospinal pathways and altered microstructure of the white matter in CNS are observed following ACL injury (Lepley et al., 2020). This includes changes in axon myelination and alternations in architecture of cell membranes on the side of brain corresponding to the injured limb (Lepley et al., 2020). This study (Lepley et al., 2020) also explains the cause of reduced excitability in the corticospinal pathways, which is attributed to decreased volume and altered microstructure of white matter.

NEUROSCIENCE STRATEGIES AND ACL INJURY REHABILITATION

Traditional rehabilitation process doesn't address neurocognitive and neuroplastic changes that occur after ACL injury. Gokeler et al., (2019) described several important concepts of motor learning that can improve rehabilitation. Instructions that utilize externally focused attention are more effective compared to internally oriented attention. Externally focused attention facilitates motor learning by promoting automaticity, while internally oriented attention encourages conscious motor control of

movement (Gokeler et al., 2019). Externally focused attention promotes balance between intracortical inhibition and excitation, which can help restore better activaiton of quadriceps (Gokeler et al., 2019). Implicit learning enables lower awareness of movement allowing athletes to allocate cognitive resources more efficiently to other aspects of movement execution. This is important for sport-specific environment where athletes must maintain motor control while navigating through complex environment (Gokeler et al., 2019). Differential learning allows application of variable training which promotes self-organization of movement and enhances learning and transfer to sport (Gokeler et al., 2019). Increased parieto-occipital activation after differential learning indicated strengthened somatosensory memory trace, which explains enhanced motor learning (Gokeler et al., 2021). We can also upgrade traditional rehabilitation strategies with contextual interference where individuals perform a specific motor task within the contex of another task (Gokeler et al., 2019). These described procedures facilitate neuroplasticity and provide us with tools to reduce the development of characteristic changes that occur in the CNS following ACL injury (Gokeler et al., 2019).

We can also change constraints like task, organism (individual strength, fatigue and level of arousal), and environment and thereby promote self – organisation of movement without verbal feedback (Kadlec et al., 2023). By that we are manipulating athlete's »solution space« within which execution is successful, this variability also promotes motor learning and preparing athlete for worse case scenarios which are omnipresent in sport (Kadlec et al., 2023). Strength training is a crucial aspect of ACL injury rehabilitation; nevertheless rate of force development (RFD) which is aspect of neuromuscular system to quickly produce force is more sport specific (Buckthorpe and Roi, 2017). Rate of force development is dependent on neurological aspects such as rate coding of motor units. This aspect of neuromuscular function (RFD) is affected to a greater degree than absolute strength in patients after ACL injury. Deficits in RFD as high as 30% could be present after ACL injury, while maximal strenght is fully restored (Buckthorpe and Roi, 2017). Given the fact that earliest recovery of RFD is 12 months after ACL injury and that decifit in RFD is significant risk factor for primary and secondary ACL injury, rehabilitation must be focused on this neuromuscular aspect (Buckthorpe and Roi, 2017). Scheurer et al., (2020) showed that there is significant deficit in initiation of force production, ability to quickly produce force (RFD) and controlling force production. Above occurs as a result of diminished recruitment and firing of motor neurons (Scheurer et al., 2020). Reduced excitability of corticospinal pathways after ACL injury is therefore associated with diminished ability to produce force in early phase of RFD (0-100ms) (Scheurer et al., 2020). This has important implications for rehabilitation after ACL injury and therefore calls for action to integrate more explosive training strategies, such as ballistic training and plyometrics in rehabilitation after ACL injury (Scheurer et al., 2020), (Buckthorpe in Roi, 2017).

One of the most clinically significant neurological change after ACL injury is increased reliance on the visual information and feedback which occurs as compensation for diminished somatosensory function due to deafferentiation and cortical neuroplastic changes (D. Grooms et al., 2015). Individuals after ACL injury exhibit poor neuromuscular control in motor tasks where additional visual-cognitive load is applied (Gholipour Aghdam et al., 2024). The higher cognitive load in patients after ACL injury also leads to the emergence of risky biomechanical patterns (D. Grooms et al., 2015). Rehabilitation procedures that allow complete conscious control of movement are insufficient to address and prepare athletes for the chaotic nature of interactions occuring within the sport environment (Gokeler et al., 2019). Intermittent visual obstruction with stroboscopic glasses is by increasing neurocognitive load during exercises an effective strategy for enhancing rehabilitation after ACL injury (Gokeler et al., 2019). It can improve anticipation, attention level and short term memory. Additionally, stroboscopic glasses add complexity to simple agility drills and thus improve transfer of physical and percpetual abilites to sport (Avedesian, 2024). Integration of components like reaction time, ball tracking, engagement with other players, decision-making demands and dual task performance as well as dissociations between upper and lower limb tasks facilitates a more effective transfer of skills to complex environment of sport (Avedesian, 2024). Adding components like small sided games where athletes experience increased spatio-temporal demands and frequency of opportunities for anticipation and decision making (Kadlec et al., 2023). Virtual reality training represents an additional

innovative rehabilitation strategy following ACL injury, enabling attention dissociation that distracts individuals from the motor task they are performing (Gokeler et al., 2016). This reduces internally directed attention, alter movement patterns and brings them closer to those of uninjured athletes (Gokeler et al., 2016).

We can also add neurocognitive components into return to sport phase after ACL injury. By integrating concepts of situational awareness and progressive application of tactical, tactical-reactive and reactive components to exercises and drills in this late phase of rehabilitation, we ensure the athlete is exposed to enough sport specific neurocognitive and physical stressors before returning to full participation (Porter & Hoch, 2023). Classical return to sport tests like the single leg hop for distance are not specific enough and lack neuro-cognitive elements, typically present in a sport environment (D. R. Grooms et al., 2023). Application of neurocognitive challanging hop test can improve rehabilitation outcomes and identify athletes who express excessive neurocognitve reliance during performance test such as single hop for distance (D. R. Grooms et al., 2023), (Farraye et al., 2022).

CONCLUSION

Noncontact ACL injury is common musculoskeletal injury that was until recently mostly researched as a common ligament injury with mechanical consequences on joint stability. In recent years, more and more authours have found neurological alternations after this msuculoskeletal injury. Besides neuroplastic changes after ACL injury, there are also neuro-cognitive, visual and neurological risk factors for non contect injury of ACL. After injury there is a cascade of significant neuroplastic changes on different levels of CNS. Initially there are changes in motor reflex loops within the spinal cord, followed by changes in the higher levels of CNS, which causes long term neuromuscular, visuo – motor and neurocognitive deficits. Therefore non contact ACL injury is more than just injury affecting mechanical and passive aspects of the musculoskeletal system but is also neurophysiological dysfunction. There are several strategies based on neuroscience principles that can enhance our rehabilitation protocols. Visuo-motor training, principles of motor learning, virtual reality and neurocognitive return to sport tests are few of strategies that can make rehabilitation after non contect ACL injury more sport specific.

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