UNIVERSITÄT PADERBORN
Die Universität der Informationsgesellschaft

Exploring Cortical Contributions to Postural Control in Patients After Anterior Cruciate Ligament Reconstruction

Cumulative Dissertation

for the academic degree

Doctor rerum medicinalium

(Dr. rer. medic.)

by

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2020

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Paderborn, September 1, 2020

Declaration of Authorship

I declare to have read and accepted the PhD regulations of the Faculty of Sciences, University of Paderborn (no. 50 / 12, 11-12-2012). Furthermore, I declare that the work presented in the present thesis is original and the result of my own work, except as acknowledged, and has not been submitted, neither in parts nor as a whole, for any other degree or qualification at any University. Content and ideas taken from other sources are - to the best of my knowledge and belief - cited correspondingly. As such, I declare that the research presented in the included studies was conducted in absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Acknowledgements

I would like to express my gratitude to everyone who supported me through the course of my present career. Foremost, my sincere thanks goes to my principle supervisor Professor Jochen Baumeister for his aspiring guidance and advice, introducing me to many brilliant scientists & experts, and for giving me the opportunity to develop as a scientist.

I would like to thank my current and former lab-mates of the Exercise Neuroscience Unit for their constructive criticism and stimulating discussions. In particular, my sincere thanks goes to my office buddy Daniel Büchel for all the constructive - but also funny nonsense - discussions, as well as his constant support. Furthermore, I would like to acknowledge with much appreciation all my co-authors and collaborators for their inspiring contributions and the productive teamwork. I also thank Arnd Gebel and Gerrit Stassen for proof-reading this thesis on such a short notice, as well as for their valuable comments and ideas.

A special thanks also goes to all participants volunteering in any of my experiments. These kind people patiently persisted the long-lasting experiments and created a pleasant atmosphere during their lab appointments.

I am sincerely grateful to my parents Renate & Meinolf, my sister Ann-Kristin and my grandparents. Their continuous support and belief always motivated me to achieve my goals. I heartily thank them for encouraging me to go my own way.

Last but not least, there are no proper words to convey my deep gratitude for my girlfriend Johanna. Her relentless support and incredible patience during the journey of the last couple of years was simply priceless. She was literally my dopamine, endorphin, renin and serotonin.

“The mind that opens up to a new idea never returns to its original size.”

– **Albert Einstein**.

Abstract

Although injuries to the anterior cruciate ligament (ACL) have been shown to cause sensorimotor alterations and subsequent postural deficiencies even after ACL reconstruction (ACLR), compensatory mechanisms of the brain are still unknown. Thus, the aim of this work was to explore compensatory cortical mechanisms accompanying the re-establishment of postural control in ACL patients. Initially, study I revealed that traditional center of pressure measures allowed to unveil postural deficits in ACL patients during eyes-open single leg stance. Thereupon, two sequential studies were designed to scrutinize the suitability of cortical measures for capturing cortical contributions to continuous postural control in ACLR patients. Study II found that mobile electroencephalography allowed to describe cortical contributions to postural control during single leg stance in heathy individuals. While postural sway revealed no significant difference between the ACLR and control group in study III, functional connectivity demonstrated distinct leg-dependent patterns in ACLR patients. These exploratory findings indicated that ACLR patients may increasingly incorporate somatosensory and visual information into complex cortical networks to compensate for altered afferent input from the knee. However, while the functional role of these network modulations remains uncertain, further studies are needed to develop neurophysiological assessments for monitoring the functional progress in ACL patients.

Zusammenfassung

Obwohl bereits gezeigt wurde, dass Verletzungen des vorderen Kreuzbandes (VKB) zu sensomotorischen Veränderungen und posturalen Defiziten führen, sind kompensatorische Mechanismen des Gehirns weitestgehend unerforscht. Das Ziel der vorliegenden Arbeit war daher, kompensatorische kortikale Mechanismen bei der Wiederherstellung der posturale Kontrolle zu erforschen. Zuerst zeigte Studie I, dass Parameter des Center of Pressure geeignet sind, um posturale Defizite nach VKB Ruptur im Einbeinstand mit geöffneten Augen aufzuzeigen. Daraufhin zielten zwei aufeinanderfolgende Studien darauf ab die Eignung kortikaler Parameter zur Abbildung posturaler Prozesse bei VKB-Patienten zu untersuchen. Studie II zeigte, dass mobile Elektroenzephalographie kortikale Beiträge zur posturalen Kontrolle im Einbeinstand bei gesunden Probanden abbilden kann. Während Schwankungsparameter keine signifikanten Unterschiede zwischen VKB-Patienten und Gesunden in Studie III aufwiesen, konnten unterscheidbare Muster funktioneller Konnektivität in Abhängigkeit vom Standbein gefunden werden. Dies deutet darauf hin, dass VKB-Patienten möglicherweise vermehrt somatosensorische und visuelle Informationen in kortikale Netzwerke einbeziehen, um so den veränderten afferenten Input vom Knie zu kompensieren. Da die funktionelle Rolle dieser Netzwerk-Modulationen jedoch ungeklärt bleibt, bedarf es weiterer Studien zur Entwicklung neurophysiologischer Assessments des funktionellen Fortschritts bei VKB-Patienten.

Table of contents

List of publications

The present thesis is based on the following papers and manuscript.

Study I — Lehmann T, Paschen L, Baumeister J (2017) Single-Leg Assessment of Postural Stability After Anterior Cruciate Ligament Injury: a Systematic Review and Meta-Analysis. Sport Med Open 3.

Study II — Lehmann T, Büchel D, Cockcroft J, Louw Q, Baumeister J (2020) Modulations of Inter-Hemispherical Phase Coupling in Human Single Leg Stance. Neuroscience 430:63–72.

Study III — Lehmann T, Büchel D, Mouton C, Gokeler A, Seil R, Baumeister J (2021) Exploring Cortical Contributions to Postural Control in Patients Six Weeks Following Anterior Cruciate Ligament Reconstruction

List of figures & tables

List of abbreviations

AC	Alternating current
ACL	Anterior cruciate ligament
ACLR	Anterior cruciate ligament reconstructed
Ag/AgCl	Silver/silver chloride
AMICA	Adaptive mixture independent component analysis
CNS	Central nervous system
CoG	Center of gravity
CoM	Center of mass
CoP	Center of pressure
EEG	Electroencephalography
EMG	Electromyography
FFT	Fast Fourier transformation
FIR	Finite impulse response
fMRI	Functional magnetic resonance imaging
IC	Independent component
ICA	Independent component analysis
PET	Positron emission tomography
PLI	Phase lag index
PSD	Power spectral density
ROI	Region of interest
wPLI	Weighted phase lag index

1. Background

1.1 Introduction

Anterior cruciate ligament (ACL) sprains or tears are some of the most common knee injuries in sports. For those athletes who suffer ACL damage at some point in their career, the injury mostly constitutes a season-ending event with both short- and long-term consequences for knee function and stability (Ageberg, 2002; Tengman et al., 2014). Despite ACL reconstruction (ACLR) and rehabilitation, injured individuals still have a substantially increased risk of developing osteoarthritis (Paschos, 2017), as well as experiencing a second ACL injury after their return to leisure or sporting activity (Paterno et al., 2012, 2014; Wiggins et al., 2016). The underlying functional impairments thereby appear to extend beyond biomechanical alterations and may be induced by modifications in the sensorimotor system (Neto et al., 2019). Adapted neuromuscular strategies such as increased hamstring activation have already been proposed to cope for injury-related knee instability by reducing anterior tibial translation (Boggess et al., 2018). Nevertheless, profound knowledge about the compensatory mechanisms of the sensorimotor system is still lacking. Hence, not only the identification of neurophysiological factors associated with the restoration of knee function in ACL patients, but also the development of suitable methods for evaluating return-to-sports readiness has received more and more scientific attention (Gokeler et al., 2017). Due to technical challenges, neuroscientific research in this field has been confined to stationary motor paradigms in the past. However, recent breakthroughs in mobile brain imaging technology now bear the potential to explore compensatory sensorimotor dynamics in ACL patients during more natural and freely moving motor tasks. Therefore, the aim of the present thesis was to explore compensatory cortical mechanisms accompanying functional deficiencies in ACL patients, exemplarily investigated in the conceptual framework of postural control.

1.2 The anterior cruciate ligament

1.2.1 Anatomy and neuroanatomy

The ACL is a complex band structure of dense connective tissue which plays a major role for the mechanical stabilization of the knee joint. From the origin at the posterior-medial aspect of lateral femoral condyle (**Fig. 1**), the ACL runs to the anterior aspect of the tibial plateau by spanning a length of 22 to 39 mm between the femoral and tibial attachments (Amis and Dawkins, 1991; Beasley et al., 2005). Composed of two bundles, a more proximal anteromedial and a more distal posterolateral bundle, the ACL forms a chord of 10 to 12 mm thickness with a tensile strength of up to 1725 N. Due to these structural and mechanical properties, the ACL is regarded as the primary passive restraint against anterior tibial translation and internal rotation of the knee joint (Beasley et al., 2005).

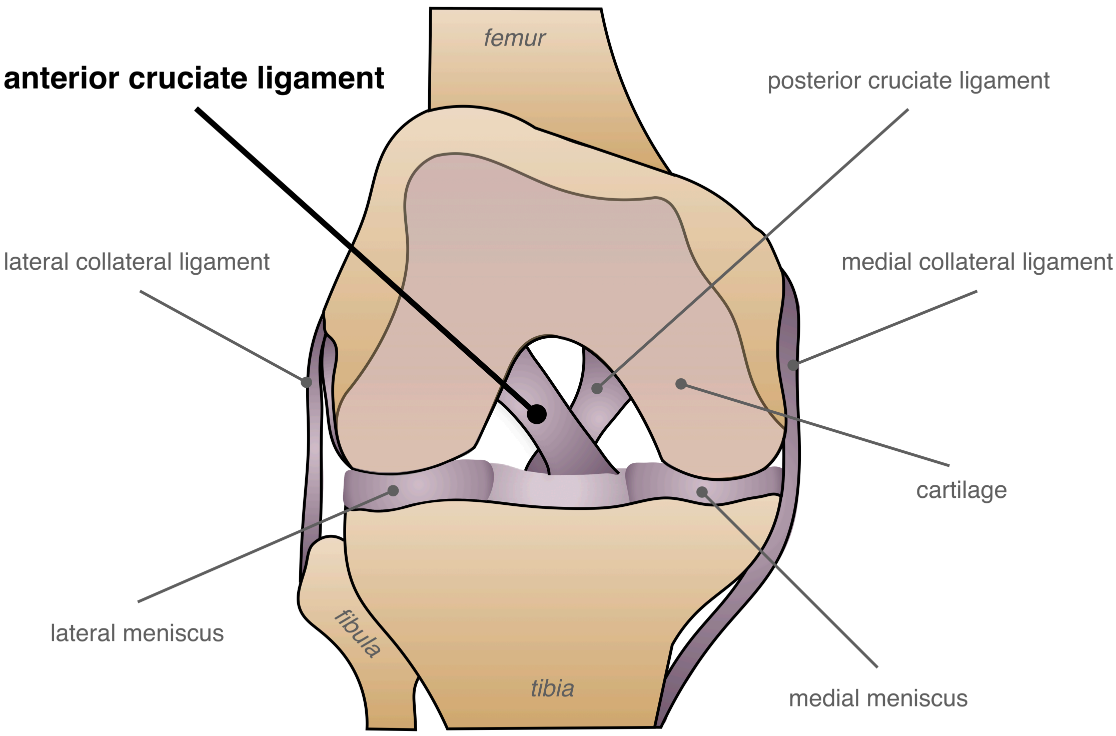


Fig. 1 Anatomy of the knee joint (right knee, patella reflected)

Apart from functioning as a mechanical stabilizer of the knee joint, the ACL is also attributed an important proprioceptive function. Histological studies have shown that posterior branches of the tibial nerve penetrate the ACL. While most of these fibers are sympathetic efferent vasomotor fibers associated with endoligamentous vasculature, a small portion of myelinated and unmyelinated nerve fibers are located in the intrafascicular spaces of the ligament (Duthon et al., 2006). The non-vasomotor fibers were mostly found to constitute fast-conducting, mechanoreceptive sensory afferents with specialized sensory nerve endings. These mechanoreceptors are dispersed throughout the ligament and were predominantly found close to the bone attachments (Çabuk and Kuşku Çabuk, 2016).

Located on the surface of the ACL, Ruffini corpuscles are one group of receptors that are sensitive to axial and tensile loadings. In that way, Ruffini corpuscles detect angular velocity, intra-articular pressure, joint position and displacement. Near the bone insertions of the ligament, Golgi tendon organ-like structures state the largest of the articular mechanoreceptors. They specifically recognize ligamentous tension in extreme positions and provide information about intra-articular forces and joint position. Similar to the Golgi tendon organ-like receptors, Pacini receptors are located at the femoral, but also tibial attachments of the ACL. In contrast to Golgi receptors, Pacini corpuscles have a low threshold for mechanical stress and sense motion on even lower scales. Lastly, free nerve endings are distributed over the entire tissue of the ligament. As the only ligamentous receptors with a non-myelinated fiber structure, free nerve endings are sensitive to abnormal mechanical deformation and therefore constitute the ligamentous nociceptive system (Johansson, 1991; Beasley et al., 2005; Duthon et al., 2006).

1.2.2 The ACL and functional knee joint stability

With its unique anatomical and neuroanatomical properties, the ACL primarily contributes to the static restraint, but also to the dynamic restraint of the knee joint. In principle, the passive restraint of the knee joint is achieved by joint anatomy and geometry, incorporating multiple ligaments, the joint capsule, cartilage friction and bone alignment. Similar to the ACL, these structures mechanically stabilize the knee by guiding the skeletal components of the joint in motion. On the other hand, the attachments of muscles and tendons crossing the knee represent the dynamic restraints, by counteracting synergistic to the static restraint (Riemann and Lephart, 2002a). In this manner, preparatory and reactive muscle activations control the resistance of the joint and its supporting structures against articular displacement (Riemann and Lephart, 2002b). Altogether, the interaction of both static and dynamic components accounts for functional knee joint stability, by maintaining and restoring proper alignment through an equalization of articular forces (Riemann and Lephart, 2002a).

However, adequate responses to perturbations of knee joint homeostasis inherently require the central nervous system (CNS) to flexibly adapt the protective mechanisms of the dynamic stabilization. Therefore, ligaments like the ACL not only passively limit motion within the natural range of the knee joint, but also function as an important source of sensory information for the initiation of synergistic muscle activation (Solomonow and Krogsgaard, 2001). Induced by articular motion and subsequent mechanical deformation within the articulation, mechanoreceptors of the ACL collectively generate proprioceptive information on joint position and acceleration, as well as acting forces within the knee. Through serial and parallel afferent pathways of either the dorsal lateral tracts or spinocerebellar tracts, these polymodal information are integrated into an intricated sensorimotor control system, which encompasses all sensory and motor processes in the CNS to control human movement (Riemann and Lephart, 2002a). As an integrative system, sensorimotor control is comprised of multi-sensory and motor components in the spinal cord, subcortical areas and the cerebral cortex. Hereof, the afferent information provide the sensory neural impulses necessary to mediate motor actions for the regulation of joint stability and posture in higher levels of the CNS (Amaral, 2013).

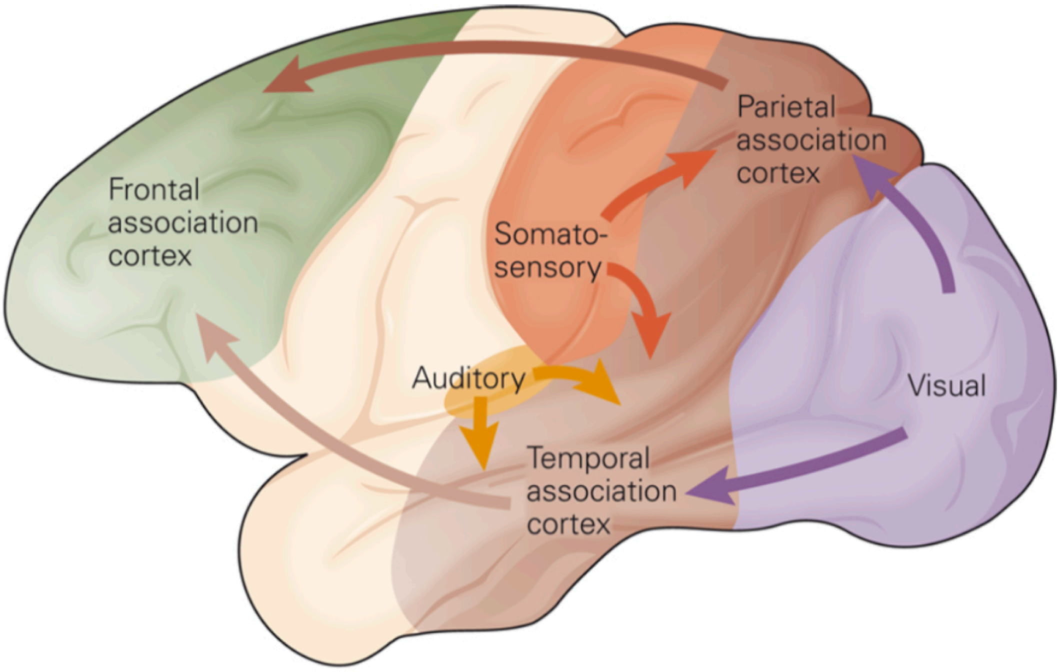


Fig. 2 Cortical sensory information processing (source: Kandel et al., 2013, p. 397).

At the spinal level, a motor signal is instantaneously generated through reflexive stimulation of motor neurons in the ventral aspect of the spinal cord, serving as a direct efferent response to the peripheral sensory input (Ramsey et al., 2003). Travelling cranially through nerval fibers within the spinal cord, the afferent information is conveyed and integrated into complex subcortical and cortical circuits by the thalamic relay. Through distinct nuclei of the thalamus, afferent information from peripheral, but also other somatosensory receptors (visual, vestibular, auditory) reach the primary somatosensory cortex. Neurons in the primary somatosensory cortex are specifically sensitive to sensory stimulation and project to other neurons in adjacent cortical areas like the motor or anterior part of the parietal association cortex (**Fig. 2**). The motor cortex may then directly generate efferent motor impulses, which pass down the spinal cord to initiate a motor response or adapt subcortical motor programs. The anterior parietal association cortex, in turn, projects to the posterior part of the parietal association cortex. While other sensory areas primarily deal with input from a single somatosensory modality, the parietal association cortex receives multimodal sensory information from sensory, visual and auditive areas. The posterior association cortex then projects to the parahippocampal, temporal association and frontal association cortex, which integrate information from multiple somatosensory modalities into complex cortical networks for the guidance of directed movement or action. Eventually, a motor response is mediated through fibers originating in the primary motor cortex and terminating in the ventral horn of the spinal cord, where the motor command is forwarded to the motor neurons of target muscles (Amaral, 2013).

In this way, the resulting motor behavior constitutes a fast and flexible reaction to environmental demands, where automatic reflexive regulation is insufficient to maintain or restore functional knee stability (Lephart et al., 1997). However, alterations in any part of the sensorimotor system, caused by physical harm or damage, will lead to modified sensory information processing and consequently influence the load acting to the structures of the joint (Beasley et al., 2005).

1.3 Injuries to the anterior cruciate ligament

1.3.1 Etiology and mechanism of ACL injury

Partial or complete tears of the ACL are some of the most common knee injuries in sports and cause immediate disability with long-term consequences for athletes. Epidemiological studies of various national registries and insurance databases have reported similar incidence rates of ACL injuries in the general population, spanning the range from 29 to 38 injuries per 100,000 people. In contrast, other studies reported widely varying incidence rates for athlete populations participating in the same sports in different countries (Singh, 2018). Although the mechanisms of ACL injuries are still not completely understood, there is general consensus that most of these injuries appear in situations without direct contact to other players or athletes (Boden et al., 2000; Shimokochi and Shultz, 2008; Hewett et al., 2016; Seil et al., 2016; Kaeding et al., 2017). Kobayashi and colleagues (2010), for instance, reported non-contact injuries in more than sixty percent of ACL patients, followed by accident, contact and collision inciting events at the time of injury. Within the sporting context, the majority of injuries could be traced back to competitive (49.2%) or practice (34.8%) activities, while leisure or other activities only showed minor (8.5%) injury rates (Kobayashi et al., 2010). In that respect, it is generally accepted that vulnerable situations particularly develop in the presence of knee motion beyond the normal physiologic ranges in multiple planes. Thereby, the inciting event is typically associated with a sudden deceleration from running or jumping with a concurrent change of direction. The resulting load on the knee joint is characterized by excessive valgus stress and internal-external rotation in slight flexion of the knee, which leads to severe torsion forces within the articulation. It is further proposed that a weight shift to the back of the heel may mechanically elevate the contraction forces of the quadriceps. In consequence, counteracting hamstring activation may operate less efficient and reduce the dynamic restraint against anterior tibial translation (Boden et al., 2000; Demorat et al., 2004; Shimokochi and Shultz, 2008; Hewett et al., 2016). Although decelerating, cutting and landing maneuvers are frequently performed in many sports, adverse motor behavior within 30 – 100 milliseconds from ground contact will pose an athlete at great risk for suffering an ACL tear, if anticipatory postural adjustments and reflexive strategies are not able to sufficiently stiffen the knee joint (Swanik, 2015; Hewett et al., 2016).

1.3.2 Treatment of ACL injuries

With suspicion of ACL injury, the use of passive accessory movement testing (e.g. Lachmann test) or instrumented arthrometry (KT-2000, Medmetric Corp., San Diego, USA) is typically used to detect abnormal joint laxity and a possible damage of the ligament. Additionally, magnetic resonance imaging is used to prove the initial diagnosis and to further detect concomitant joint damage. Following a positive diagnosis, either non-operative or operative management will then be chosen to treat the ACL injury (Anderson et al., 2016). Even though ACL tears cause significant mechanical and functional impairments, the decision towards surgical reconstruction depends upon individual patient characteristics. Seil and colleagues (2016) reported that patients involved in competitive sports were more likely to undergo arthroscopic reconstruction than patients participating in recreational sports. Furthermore, the probability of operative treatment is higher in young (< 35 years) than older individuals (Seil et al., 2016). Thus, in older or less active individuals without additional intra-articular injury and the simple aim to return to straight plane daily activities, a non-operative treatment may be sufficient to restore (near-) normal knee function. In contrast, younger ACL patients with persistent functional instability, recurrent episodes of giving way or active participation in jumping, cutting and pivoting sports, a surgical reconstruction would be indicative to reduce to the risk of subsequent injury of ligaments, cartilage or menisci (Diermeier et al., 2020). In these patients, the torn ligament is most commonly replaced with an autograft, extracted from endogenous tendon structures, such as the patellar tendon, semitendinosus or quadriceps muscles.

However, apart from a proper diagnosis and treatment decision making, well-designed acute and subacute rehabilitation approaches are crucial for the long-term outcomes after ACL injury (Gokeler et al., 2017). This becomes particularly important given the fact that only half of the patients are able to successfully return to sports at 1 year, as well as only two-thirds at 2 years following ACL injury (Ardern et al., 2014). Therefore, ACL rehabilitation typically aims to progressively decrease symptoms while concurrently reestablishing normal knee function. In the very early phase of rehabilitative treatment, the main goal is to control pain, inflammation and swelling related to the tear or surgical procedures (Gokeler et al., 2017). In the subsequent weeks, full passive knee range of motion and progressive weight-bearing activities are addressed to reestablish independent activities of daily living (Myer et al., 2008). As patients progress in their functional capabilities, the rehabilitation focus is supposed to shift towards a gradual increase of muscular strength, power and endurance. Additionally, the restoration of sensorimotor functions becomes increasingly important in the middle and late course of rehabilitation, aiming to facilitate the transition from patient to athlete status. In the late phase of the rehabilitation program, patients also establish capabilities to further improve and maintain their functional status after their release from therapeutic care (Nyland, 2010; Nyland et al., 2016).

1.3.3 Long-term consequences of ACL injury

Although surgical reconstruction and rehabilitation techniques have continuously improved, ACL injuries treated operatively or non-operatively are associated with long-term consequences and persistent disabilities. Common impairments associated with ACL tear include altered hip rotation moments and altered knee joint loading patterns during walking or jumping, increased frontal plane knee range of motion during landing, as well as sagittal plane knee moment asymmetries at initial contact to the ground (Alkjaer et al., 2003; Paterno et al., 2010; Alkjær et al., 2011). Altogether, as a result of biomechanical alterations, the knee joint is exposed to changed articular stress patterns and poses a high risk for patients of suffering a second ACL injury (Paterno et al., 2014; Wiggins et al., 2016). In line with this, the adapted loading patterns of the knee also raise the prevalence for associated consecutive symptoms that may include degenerative meniscal tears (Jones et al., 2003; Salata et al., 2010), chondral lesions (Jones et al., 2003) or early onset of osteoarthritis (Paschos, 2017). Moreover, biomechanical alterations of the lower limbs in ACL patients are often accompanied by persistent neuromuscular changes. Based on the altered somatosensory information from ACL mechanoreceptors, neuromuscular deficiencies in ACL patients encompass reduced reflex latencies (Bonfim et al., 2003; Melnyk et al., 2007), modified muscle timing and recruitment (Wojtys et al., 1994), decreased muscular strength and force control of lower limb muscles (Keays et al., 2001; Baumeister et al., 2011; Thomas et al., 2013), as well as declined joint position sense and threshold to detect passive motion (Barrett, 1991; Adachi et al., 2002; Ageberg, 2002; Baumeister et al., 2008). In sum, the biomechanical and neuromuscular deficiencies following ACL injury equally affect isolated motor actions and gross motor skills, which may adversely affect chronic dysfunction in the majority of ACL patients (Trulsson et al., 2015; Meyer et al., 2018).

1.4 Neurophysiological alterations and adaptations in ACL patients

With regards to sensorimotor alterations affecting the dynamic restraint of the ACL injured knee, a growing amount of evidence has begun to identify clinically meaningful neural adaptations following ACLR (Neto et al., 2019; Kakavas et al., 2020). Recent studies indicated that a loss of mechanoreceptors from the ACL may consequently lead to diminished afferent input to higher levels of the sensorimotor system (Courtney et al., 2005; Kapreli et al., 2009). Along with changed or even absent somatosensory information from the ACL, a decreased innervation to the primary sensory cortex (Valeriani et al., 1999), as well as diminished corticospinal and motor cortex excitability (Pietrosimone et al., 2015; Grooms et al., 2017; Lepley et al., 2020) have been observed in ACLR patients.

The cumulative neuroplastic and functional alterations observed in ACL patients are likely to impede the restoration of optimal sensorimotor control and can adversely facilitate chronic dysfunction. Consequently, ACL patients are required to develop compensatory strategies in order to cope with altered biomechanical and sensorimotor properties (Neto et al., 2019). It is currently known that these strategies include compensatory loading of the contralateral limb (Butler et al., 2016; Renner et al., 2018), extension of the hip or ankles to countervail a knee extension moment deficit during loading (Ernst et al., 2000), but also adaptations of increased hamstring activation to counteract joint instability (Courtney et al., 2005). Hence, compensatory mechanisms pertain to coordinated motor behavior in favor of the dynamic restraint, which suggests they are likely arising from supraspinal centers which govern the temporal and spatial organization of the motor response (Riemann and Lephart, 2002b).

Lepley et al., (2020), for instance, have suggested that ACLR patients may require higher cortico-cortical stimulation to evoke proper efferent neural signaling for controlling motion and stability of the knee joint. ACLR patients also demonstrate stronger involvement of neurocognitive resources in the frontal cortex to deal with modified proprioceptive information from the knee, when precise control of joint position and lower limb force is demanded (Baumeister et al., 2008, 2011). Hip and knee motor control in ACL patients further show strong activations involving parieto-occipital cortical areas responsible for spatial cognition and orientation, as well as visual-motor processing (Criss et al., 2020). Onate and colleagues (2019) therefore assumed that altered afferent information after ACL injury may entail an increased reliance on visual information processing and cortical motor planning to ensure proper sensorimotor control of the knee joint.

1.5 Postural control in ACL patients

1.5.1 Postural control

A functional deficiency frequently appearing with ACL injury is the impairment of lower limb postural control. As afferent feedback from the knee essentially contributes to the dynamic restraint of the knee joint, altered sensory information on joint position and motion has a substantial effect on the control of standing posture in ACL patients (Howells et al., 2011; Negahban et al., 2014). Postural control is generally defined as the ability to monitor body position and alignment in space, involving multimodal interactions of musculoskeletal and neural systems (**Fig. 3**). It is comprised of two components accomplishing the goals of postural orientation and postural stability. Whereas postural orientation describes the visually and vestibular-guided ability of monitoring the interrelationship between body segments relative to the environment, postural stability predominantly incorporates somatosensory information to control the center of mass (CoM) in relationship to the base of support. With respect to functional deficiencies in ACL patients, postural control constitutes a crucial determinant for the quality of complex full-body movement through predictable and unpredictable, as well as stable and dynamic environments. It reflects multimodal interactions within the sensorimotor system, encompassing the integration of somatosensory, vestibular and visual information in the CNS to properly control COM motion, limb and head position, gaze fixation, as well as acting ground reaction forces. By integrating multimodal sensory information in the process of controlling postural equilibrium, the sensorimotor system enables to compensate deteriorations of single sensory sources and adjusting postural responses to the specific sensory demands of a given task. The neural components of postural control include the brainstem, cerebellum and spinal networks which organize muscle activations throughout the body into neuromuscular synergies. As a result, these structures enable a selective transmission of motor commands to elicit appropriate muscular responses through motor neurons across the body. Within these intricate neural circuits, postural control in healthy individuals therefore allows anticipatory and adaptive motor behavior to effectively control body position in space (Shumway-Cook and Woollacott, 2012).

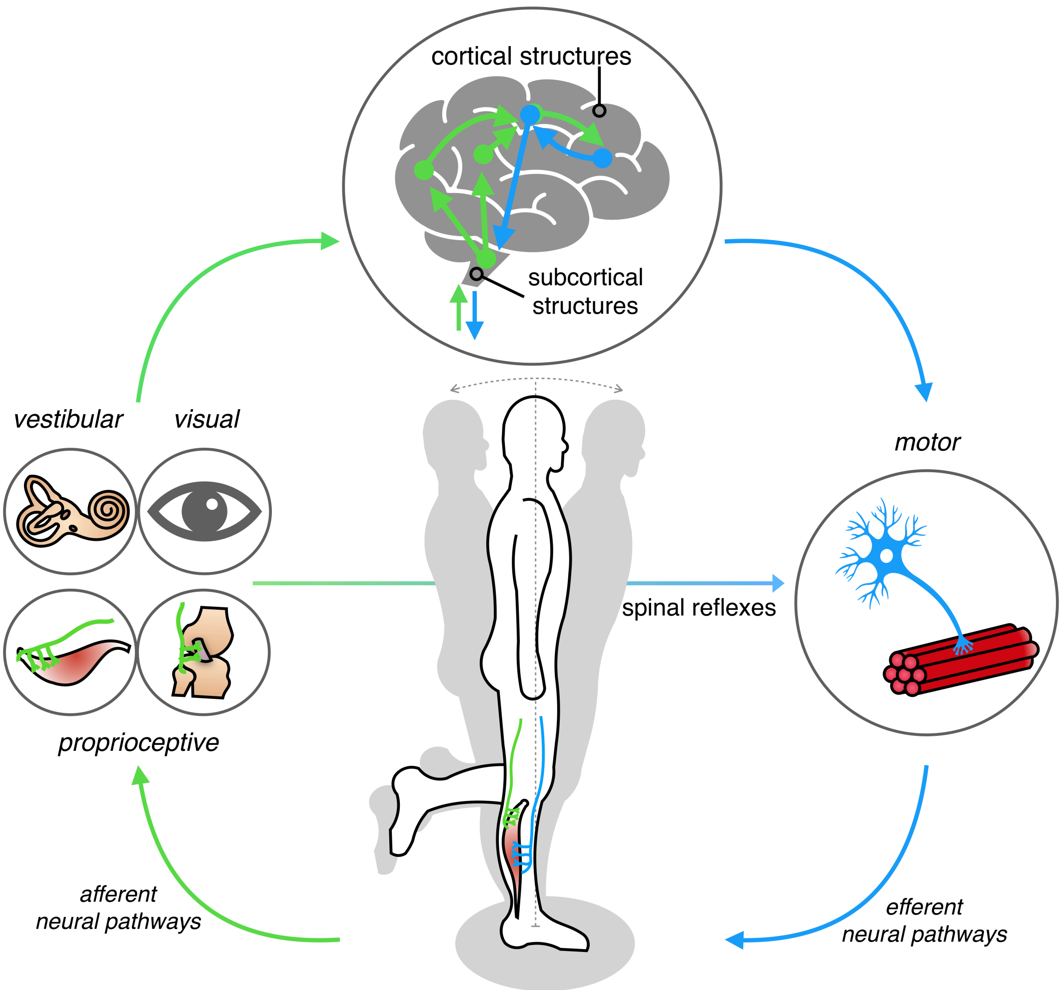


Fig. 3 Schematic model of postural control (adapted from Baumeister, 2013).

Traditionally postural control was associated with automatic processing or a set of postural reflexes in rather lower levels of the CNS, predominantly involving polysynaptic pathways within subcortical areas of the vestibulospinal, tectospinal and reticulospinal tract (Shumway-Cook and Woollacott, 2012). However, more recent findings from neuroimaging studies have already suggested active contributions of the cerebral cortex to maintain and restore postural equilibrium (Jacobs and Horak, 2007; Wittenberg et al., 2017). Cortical activation in the dorsolateral prefrontal cortex, anterior cingulate cortex, supplementary motor areas and posterior parietal cortex has been assumed to actively govern subcortical pathways in response to challenges of static postural stability, as well as to coordinate reactive postural adjustments or to generate compensatory postural responses (Wittenberg et al., 2017).

1.5.2 Postural deficiencies in ACL patients

Although a tear of the ACL is not considered a direct insult to the CNS, the indirect role of ligamentous afferents is proposed to affect the processing of postural responses in ACL injured patients. Indeed, several investigations have already found diminished postural control of both conservatively and surgically treated patients (Howells et al., 2011; Negahban et al., 2014). Patients enrolled in these studies collectively demonstrated increased postural sway and sway velocities, such as worse stability scores in various stance positions compared to healthy individuals. Most interestingly, these deficiencies seem to have a long-term effect on postural control and were found years after injury or reconstruction (Howells et al., 2011; Negahban et al., 2014). In that respect, the altered sensory inputs and insufficient muscle activations reported in ACL patients were held responsible for impairments of postural stability in this population (Bonfim et al., 2003). Moreover, simultaneous execution of a cognitive task during single leg standing has also been shown to induce significant disturbances of postural stability in ACLR patients in comparison to healthy matched controls (Negahban et al., 2013). Thus, declines in postural control during concurrent performance of attentionally demanding tasks in daily-life or sports-related situations may pose an increasing risk of postural instability, insufficient dynamic restraint of the knee joint and consequent re-injury (Mohammadi-Rad et al., 2016). However, as ACLR patients after restoration of the passive restraint still reveal functional impairments, persistent postural deficiencies are likely to go beyond mechanical alterations and point to modifications in sensorimotor neural networks responsible for the dynamic stabilization of the knee joint (Needle et al., 2017).

1.6 The potential of mobile brain imaging in postural control assessments

1.6.1 Mobile electroencephalography

Various techniques used by neuroscientists paved the way to study how the nervous system integrates multiple sources of sensory information, as well as how the brain adapts under different conditions to accurately control motor actions. In the present thesis, non-invasive mobile electroencephalography (EEG) was used to capture brain dynamics associated with sensorimotor processing of continuous postural control. While the EEG has originally been established in clinical applications for the diagnosis of certain neurological conditions (e.g. epilepsy) and in clinical research contexts, this method gained growing importance in applied fields of cognitive and behavioral neuroscience over the last decades. Compared to other brain imaging devices (e.g. fMRI, PET), the high temporal resolution and mobility of the EEG allow to record cortical phenomena associated with conscious cortical processes in freely movable applications and real-world environments (Ladouce et al., 2017).

In general, the human electroencephalogram measures electrical activity arising from simultaneously activated neuronal cell assemblies within the cerebral cortex. The electrical potentials are attributable to the synchronized excitation of thousands of pyramidal neurons in the cerebral cortex, which themselves generate and transmit an electrical current flow through their axons. Distinct neuronal assemblies thereby operate at particular frequencies in which neuronal information is processed. These assemblies form functional units that enable to process a wide range of information in parallel and dispersed over the entire cortex. With respect to the conductive properties of cortical layers and tissues, the EEG electrodes placed on the scalp surface record a summation of the underlying postsynaptic potentials (**Fig. 4**). Thus, the emerging signal is comprised of rhythmic oscillations with specific characteristics depending on the strength of synchronicity of the contributing neuronal populations. The more synchronous the neuronal activity within neuronal patches and at a particular frequency, the stronger the corresponding oscillations appear in the EEG signal (Bear et al., 2016).

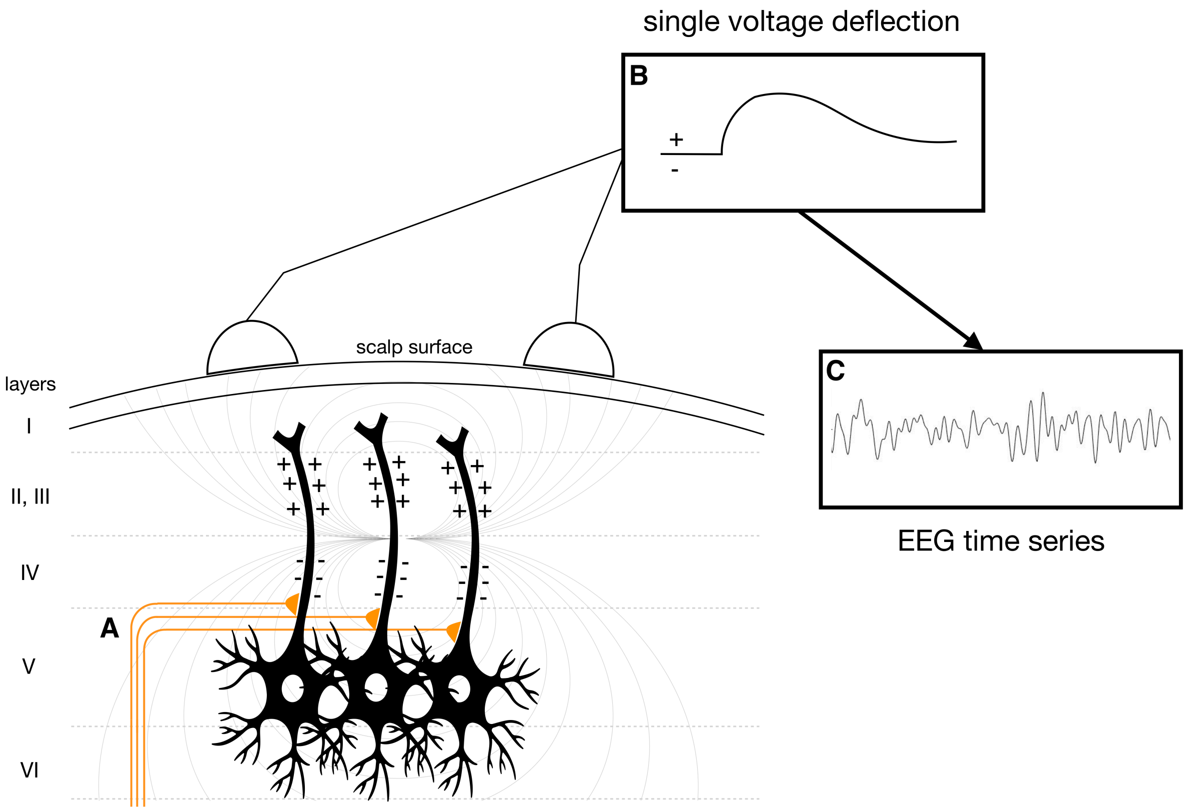


Fig. 4 Generation of the EEG signal (modified from Kandel et al., 2013). In this exemplary illustration, a thalamocortical excitatory input to a patch of pyramidal neurons in layer V (A) causes an upward voltage deflection at the surface (B). Multiple positive and negative deflections in the cortex attenuated in time constitute the typical EEG times series (C).

1.6.2 EEG oscillations and postural control

Although functional human EEG rhythms span the range from 1-90 Hz (Bear et al., 2016), broadband changes of specific frequency bands have been related to functional processing in presumably task-relevant cortical areas of postural control (Wittenberg et al., 2017): theta (4-7 Hz), alpha (8-12 Hz), beta (13-30 Hz) and gamma (31-48 Hz) frequencies. However, particularly the theta and alpha bands were proposed to act in a postural control network for the detection of postural instability and the subsequent generation of postural responses for maintaining upright postural stability (Varghese et al., 2014; Hülsdünker et al., 2015; Mierau et al., 2017). In general, theta band oscillations are suggested to reflect a general brain integrative mechanism related to cognitive processes, which are responsible for short term storage and manipulation of multimodal information for a given operation (Sauseng et al., 2010). Particularly in the frontal regions of the brain, synchronized oscillations in the theta band are associated with working memory processes (Klimesch, 1999; Sauseng et al., 2010), attentional control (Gevins et al., 1997; Haufler et al., 2000; Luchsinger et al., 2016) and movement initiation (Haufler et al., 2000; Perfetti et al., 2011). Moreover, another function of these rhythmic oscillations is the integration of sensorimotor information, which is assumed to be represented by an increase (synchronization) of frontal theta in conjunction to a concurrent decrease (desynchronization) of parietal alpha oscillations (Cruikshank et al., 2012).

Alpha waves are particularly present in a relaxed cortical state and reflect functional modes of different brain areas. More precisely, while the alpha-1 subband (8-10 Hz) is related to global alertness of cortical areas, alpha-2 subband (10-12 Hz) is attenuated by task-specific sensorimotor processing. Here the amplitude of alpha oscillations is inversely related to the activity of neuronal populations and is therefore considered an idling rhythm, which either facilitates or inhibits the transmission and retrieval of sensorimotor information in the brain (Pfurtscheller and Lopes, 1999; Babiloni et al., 2008; Sadaghiani et al., 2012). With regards to postural control, differential modulations within the theta and alpha frequency bands have already been reported with voluntary postural sway and the transition to instability stage during single leg stances (Slobounov et al., 2005, 2008, 2009). Additionally, as Hülsdünker and colleagues (2015) have demonstrated a functional role of both theta and alpha oscillations in fronto-central and centro-parietal areas for postural control processes, these dynamic oscillations may serve as temporal regulators of neuronal activation in order to coordinate sensorimotor processing in task-relevant cortical structures (Palva and Palva, 2011).

1.6.3 Functional brain connectivity and postural control

Cortical neurons are highly interconnected in local cellular circuits and between functionally subdivided brain regions (Nunez and Srinivasan, 2006). These connections together form large-scale neural networks with distinct spatial and temporal properties (Kandel et al., 2013). The interactions within the functional networks correspond to either neuroanatomical links through white matter tracts (structural connectivity), temporally correlating activity of anatomically connected and unconnected regions (functional connectivity), or coupled activity with directed causal influences (effective connectivity) between two distinct neuroanatomical areas (Rubinov and Sporns, 2010). Therefore, not only synchronized local excitations of neuronal patches determine the functions of particular brain areas, but also the global integration of brain processes plays a crucial role for task-related information processing (Friston, 2011). In this framework, the brain is considered a complex large-scale network of functionally interacting subsystems, which are temporally activated for the purpose of governing relevant cortical processes of higher-level cognitive and motor functions (Palva and Palva, 2011). Thus, synchronized neuronal oscillations facilitate intra- and inter-areal interactions of neuronal patches (Palva and Palva, 2011) when processing multisensory information of complex perception-action loops (Sadaghiani et al., 2012).

While brain imaging research has extensively studied whole-brain maps of structural connections within supraspinal networks of the mammalian sensorimotor system (Barker et al., 2012; Feher, 2012), functional connections related to postural control processes in the human brain have just become subject of brain imaging research (Mierau et al., 2017; Solis-Escalante et al., 2019; Varghese et al., 2019). In some reports, adjustments to bodily posture of upright stance were shown to involve cortical dynamics of prefrontal, premotor, supplementary motor and parietal areas (Ouchi et al., 1999; Mihara et al., 2008, 2012), which revealed functional connections distributed across the cortex (Mierau et al., 2017; Varghese et al., 2019). These fronto-parietal functional connections have been investigated in terms of attentional demands or top-down modulations of motor control (Sadaghiani et al., 2012; Cole et al., 2013) and might be of particular relevance in patients with disturbances affecting the structure or function of the CNS.

1.6.4 EEG research in ACLR patients

Differential modulations of cortical activity in ACLR patients have already been observed in joint positioning and force sensation tasks. Baumeister and colleagues (2008) found higher theta power in frontal electrode positions in both limbs of ACLR patients when performing a knee-angle reproduction task, accompanied by higher alpha-2 power only in the ACLR limb at parietal sites. These findings pointed to lower processing in somatosensory areas in the ACLR group, conceivably resulting from changed afferent information. The significantly higher involvement of the frontal cortex in this study may thus function as a compensatory mechanism, integrating multimodal sensory information in the sensorimotor system to achieve a target knee angle. Similarly, this research group also found increased frontal theta power in a force reproduction task with the ACL-reconstructed limb (Baumeister et al., 2011). Therefore, these two initial findings for the first time indicated that ACLR patients may require elevated focussed attention to actively control knee joint motion.

Interestingly, instantaneous cortical activity responses in the alpha-2 frequency band during knee joint loading have also been found by An et al., (2018). Although no substantially increased joint laxity was found, ACLR patients demonstrated greater alpha-2 desynchronization over the somatosensory cortex in response to a controlled passive anterior tibial translation, when compared to a group of healthy controls (An et al., 2018). In contrast to the active task execution in Baumeister et al., (2008, 2011), it may be speculated that the stronger alpha-2 desynchronization during passive knee displacement indicated an increased excitability of the somatosensory cortex to receive proprioceptive information from remaining mechanoreceptors of the knee. Altogether, considering the already stated modifications in central representation (Valeriani et al., 1996), cortical information processing (Baumeister et al., 2008, 2011; An et al., 2018) and a potential reorganization of the CNS (Kapreli and Athanasopoulos, 2006; Kapreli et al., 2009; Grooms et al., 2015, 2017) after ACLR, theta and alpha frequency oscillations may help to understand sensorimotor processing, as well as cortical contributions to postural control in patients after ACL injury.

Furthermore, evidence from clinical studies has already demonstrated changes in structural and functional brain connectivity related to postural control in various deficit models, e.g. multiple sclerosis (Peterson et al., 2016) or traumatic brain injury (Caeyenberghs et al., 2012; Diez et al., 2016). In these patients, a decrease of functional connectivity within the fronto-parietal and cortico-subcortical networks has been associated with poor postural stability (Caeyenberghs et al., 2012; Diez et al., 2016). Moreover, Diekfuss et al. 2018 already demonstrated dampened functional connections between the sensorimotor cortex and cerebellar structures in a prospective study with subjects prior to ACL injury. Thus, functional connections of distributed cortical areas are also likely to play a crucial role for the integration of sensorimotor information in ACL patients. However, brain connectivity among functionally separated cortical areas involved in sensorimotor processing has yet to be investigated in patients after ACL injury and may provide further insights into compensational cortical adaptations appearing with postural deficiencies in the rehabilitation process.

1.7 Rationale

Despite surgical reconstruction of the ACL and the implied mechanical restoration of passive knee stability, many patients are confined to long-term functional deficiencies or risk of secondary injury. The fact that some individuals are able to cope with functional deficiencies after successful ACLR suggests that compensatory strategies in higher levels of the sensorimotor system may facilitate adaptations of the dynamic restraint to reestablish functional knee stability. Although changed afferent sensory pathways and alterations in cortical processing have been observed in patients following ACLR, compensatory mechanisms of the sensorimotor system still remain uncertain.

Current assessments to monitor the restoration of sensorimotor functions after ACLR are typically limited to isolated movements and solely behavioral measures. Most commonly, rehabilitative monitoring describes clinical outcomes and considers motor behavior as a common output, rather focusing biomechanical changes than addressing the underlying mechanisms within the highly complex sensorimotor system. In fact, these current methods enable a reliable behavioral evaluation of the rehabilitation progress but barely provide sufficient information about functional adaptations within the CNS. Especially in the transition from rehabilitation to sporting activity, a failure to achieve optimal sensorimotor recovery following ACLR may place patients at high risk for recurrent injuries to the lower limb. Therefore, advanced neurophysiological assessments are required to detect patients at risk and finally develop strategies for their individual optimal recovery.

Whereas technical difficulties limited the application of neurophysiological measurements to stationary and highly controlled movements in the past, recent breakthroughs in mobile brain and body imaging technology now enable the investigation of the dynamic interplay between motor behavior and neurophysiological functions in freely moving situations. In this light, the modality of postural control offers a suitable solution for the investigation of sensorimotor processes. On the one hand, the relatively controllable and stable measurement situation is feasible for mobile high-density EEG recordings. On the other hand, controlling postural equilibrium and functional knee joint stability constitutes a complex motor task involving top-down regulation of the sensorimotor system. Thus, cortical contributions to the control of upright posture and knee stability in ACLR patients during ordinary postural tasks may provide valuable insights into the neural correlates of postural control and sensorimotor functions in the early stage of recovery. In the long run, compensatory sensorimotor adaptations in ACLR patients may help to understand why some patients are able to cope with functional deficiencies or not and, in turn, detect patients at risk for long-term functional impairments. By this means, cortical correlates of motor behavior may expedite the development of new methods for rehabilitative monitoring with respect to individually tailored approaches.

1.8 Objectives

The overall aim of this thesis was to explore compensatory cortical mechanisms accompanying postural deficiencies in ACLR patients (**Fig. 5**). At first, it was aimed to assign a suitable research paradigm for the detection of postural deficiencies, as well as the description of cortical processing related to postural control in ACLR patients. Subsequently, the conflating experimental design was supposed to provide initial insights into postural and cortical patterns in ACLR patients which may appear differently in comparison to a group of healthy controls.

Study I: The major aim of the systematic literature overview and meta-analysis was to quantify postural deficits in eyes open single-leg stance in patients after ACL injury. Since no gold standard has yet been established to assess postural stability in ACL patients, a second purpose was to examine the potential of traditional CoP measures for identifying postural deficiencies in this group. Thereby, the selection of eligible studies was specifically focussed on postural assessments of single leg standing to provide a comprehensive picture of injury related effects in both limbs.

Study II: The objective of the descriptive laboratory study was to investigate patterns of cortical contributions to postural control in bipedal and single leg stance. It was further aimed to scrutinize the suitability of the phase lag index (PLI) for capturing modulations of functional connectivity among distributed cortical areas, in order to reasonably describe the allocation of cortical contributions appearing with the decreasing base of support and concurrent postural instability.

Study III: The aim of the controlled laboratory study was to examine the potential of functional connectivity measures derived from mobile EEG, in order to finally explore cortical contributions to postural control in the early stage of functional rehabilitation after ACLR.

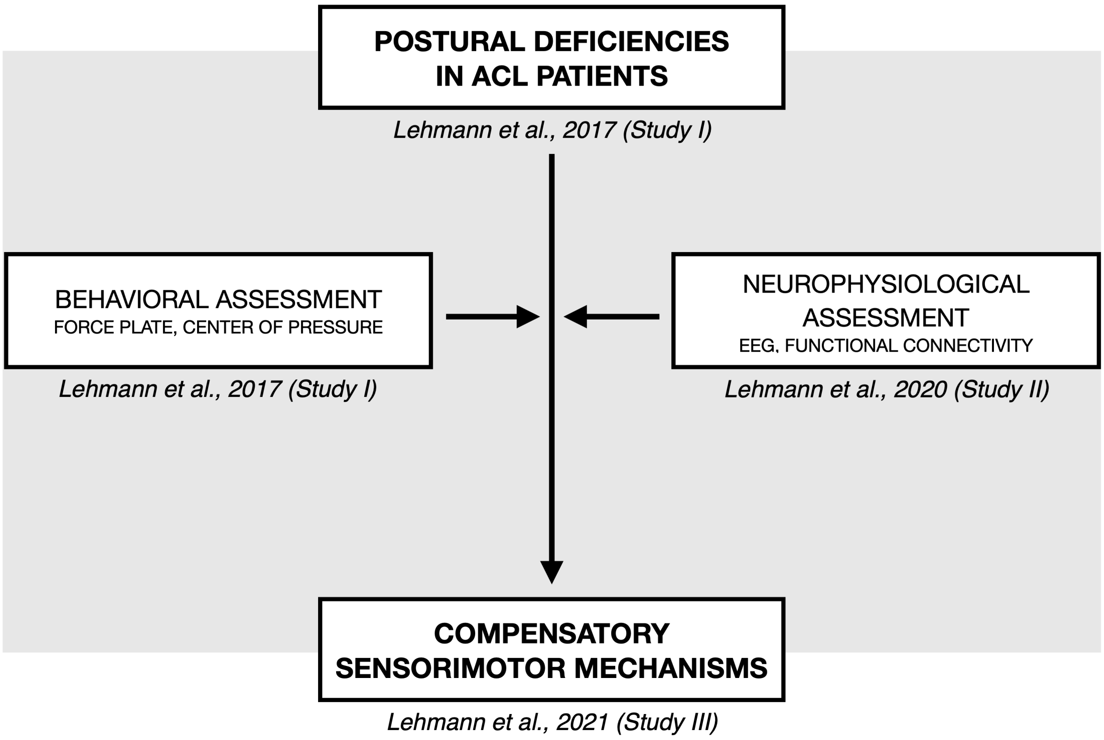


Fig. 5 Research objectives of the present thesis

2. Methods

The three studies included in this thesis followed a consecutive concept of synthesizing findings of a postural deficit following ACL injury, examining the suitability of EEG measures in the respective postural research paradigm and finally applying this approach to a sample of ACLR patients. The studies were carried out at the Exercise Neuroscience & Health Lab of Flensburg University, the FNB-3D Movement Analysis Laboratory of Stellenbosch University and the Exercise Neuroscience Lab of Paderborn University.

2.1 Study designs

With regards to the aims of this thesis, study I was based on secondary data from a systematic literature review, whereas study II and III were premised on experimental designs incorporating primary subject data (**Tab. 1**).

Tab. 1 Study designs, populations and sample sizes of the three studies included in the present thesis.

Design	Population	Sample size
Study I		
Systematic review & meta-analysis	ACL injured patients with conservative or surgical treatment; healthy controls without injuries to the lower limb	11 studies, a total of 594 subjects (329 ACL patients, 265 controls)
Study II		
Descriptive laboratory study	Healthy young adults	12 healthy subjects
Study III		
Controlled laboratory study	ACL injured patients after ACL reconstruction; healthy matched controls without history of lower extremity surgery	12 ACL patients, 12 healthy controls

2.2 Study sample characteristics

The systematic literature review and meta-analysis in study I considered data of ACL non-reconstructed and reconstructed patients involved in 11 controlled trials of postural stability measurements. Subjects of all ages and sexes were eligible for inclusion if no history of lower limb musculoskeletal surgery, neurological or psychological diseases was reported. A total sample of 594 subjects was included in the comprehensive meta-analysis, comprised of 329 ACL patients and 265 healthy controls. The individual trials incorporated an average of 20 ± 7 males and 10 ± 10 females (ratio 66% / 34%) in the ACL group. The respective control groups were composed of 19 ± 8 males and 8 ± 5 females (ratio 70% / 30%). Both the ACL and control subjects were physically active for at least 1–3 days per week and predominantly involved in team sports like soccer and basketball.
According to the type of treatment after injury, 224 patients underwent surgery and 105 patients were treated conservatively. The surgical procedures of the ACLR patients implied patellar tendon allografts/autografts, semitendinosus tendon allografts/autografts and iliotibial tract autografts as substitutes of the torn ACL.

In study II, a total of fifteen healthy male students (21.7 ± 2.8 years, 175.1 ± 7.8 cm, 77.8 ± 15.8 kg) were recruited from Tygerberg Campus at Stellenbosch University. After data processing, twelve subjects were included in further analysis. All subjects were physically active and had no history of musculoskeletal injuries or neurological diseases. The standing leg for the single leg stance condition was determined as the non-kicking, non-dominant leg in soccer (left for all subjects).

In the final controlled laboratory experiment (study III), only patients following ACLR were considered as eligible for participation. This was basically for two reasons:

1. The surgical procedure represents a restoration of the mechanical restraint, which assumes that similar conditions of passive knee joint stability could theoretically be expected across patients.
2. The surgery constitutes an explicit event in time for each single patient, which consequently makes it possible to exactly set and standardize the appointment of investigation across patients.

Therefore, a sample of twelve voluntary ACLR patients (5 female / 7 male, 25.1 ± 3.2 years, 178.1 ± 9.7 cm, 77.5 ± 14.4 kg) was recruited from local rehabilitation and outpatient centers. All patients underwent arthroscopic reconstruction of the ACL (7 left, 5 right) within the past 6-8 weeks (44.4 ± 4.5 days) and were actively participating in rehabilitation practice at the time of recruitment. In all of the patients, a semitendinosus/gracilis tendon autograft was used for the mechanical restoration of knee stability. Six of the patients reported a history of previous ACL injury, while another four reported concomitant meniscal repairs within their current surgical procedures. Three of the patients with persisting complaints after initial conservative treatment underwent surgery within a mean time of 441 ± 347 days from injury to surgery. The remaining nine patients were operated for acute or subacute ruptures within a range of 42.4 ± 25.8 days. All patients actively participated in sports (judo, soccer, fitness, team handball, athletics, vaulting) prior to their injury and had a sporting experience of 17.7 ± 4.8 years. Collectively, the ACL patients declared their left leg as the dominant stance leg. Participants were excluded in degenerative changes of the knee joint, chronic ankle instability, previous surgery to the ankle joint or a history of any neurological / psychological diseases. A sample of twelve healthy (177.0 ± 9.6 cm, 73.7 ± 9.9 kg), sex (5 female / 7 male), age (25.5 ± 3.8 years) and sporting activity / experience (16.6 ± 5.7

years) matched subjects served as the control group. The control subjects were included following the same criteria as the ACLR group, except for any history of previous knee or ankle surgery.

2.3 Ethics

All studies in this thesis were conducted in accordance with the ethics guidelines and regulations established by the Declaration of Helsinki. Thus, participants enrolled in the present investigations were informed about relevant study details and gave written consent to their participation. The investigator, or a person designated by the investigator, asked for the informed consent of any patient meeting the inclusion criteria. The subject information implied all pertinent aspects related to the purpose and requirements of the study, as well as to the rights as a participant. Subjects were given time and opportunity to inquire about details of the investigation and to decide whether or not to participate in the study. In case the volunteers agreed to participate, an informed consent form was dated and signed. A copy of the executed informed consent was given to the participant and the originals were filed in accordance with German data protection regulations. To guarantee the anonymity of the participation, an individual identification code was assigned to each enrolled subject on all data forms and physiological records. Subjects were explicitly informed about their right to withdraw from the study at any time and for any reason. Prior to the beginning of the study, the experimental protocol of study II was approved by the local ethics committee of Stellenbosch University, South Africa [N16/05/068], whereas study III was approved by the local ethics committees of Paderborn University, Germany and the Comité National d'Ethique de Recherche, Luxembourg [DAL-ORTHO-PHCE-ACL1].

2.4 Experimental procedures

The initial start of the research project, namely the systematic review and meta-analysis, was conducted at the Exercise Neuroscience & Health Lab at Flensburg University, Germany, to provide an objective overview of single limb postural stability in patients after ACL injury. To ensure an objective and standardized strategy of literature screening, the procedure followed the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)" provided by Moher et al., (2015). In addition, an independent researcher separately applied the study selection and reviewed the critical appraisal of selected articles.

The following two experimental approaches of study II and study III were comprised of synchronized posturography and mobile EEG, in order to draw a comprehensive picture of sensorimotor processes related to postural control. The investigations of study II were conducted at the FNB-3D Movement Analysis Laboratory of Stellenbosch University. The lab provides a wide range of biomechanical equipment for three-dimensional movement analysis in sports, occupational or rehabilitation settings, with a testing area spatially apart from the experimenter space. For study III, the experiments took place at the similarly equipped Exercise Neuroscience Lab of Paderborn University, Germany. The laboratory is endowed with a variety of equipment commonly used in clinical or sports settings to quantify human performance and neurophysiological parameters in diverse populations, spanning from children to older adults, athletes and patients. In the testing area of the lab, subjects are able to freely move in a neutral environment, while being fully equipped with wireless, mobile brain and body imaging devices. In both experimental studies, posturography and mobile EEG were simultaneously collected during trials. The temporal synchronization of both data streams was realized through synchronous manual starting of the two devices in study II and a fully automated recording process using a custom-built Unity (Unity technologies, San Francisco, USA) program in study III.

2.5 Posturopraphic Assessment

In the present course of studies, the single leg stance was used as the target assessment of postural stability in ACL patients. The single leg stance requires subjects to maintain postural equilibrium while standing on one leg and simultaneously holding the non-weightbearing leg in slight flexion. Many gross motor actions in daily and sporting activities depend on postural stability within certain periods of single leg support. In these situations, the postural control system is required to stabilize the body CoM over a narrow base of support. As a result, single leg postural stability is significantly correlated with the accuracy of suprapostural limb movements such as kicking (Chew-Bullock et al., 2012). Therefore, ACL rehabilitation programs typically incorporate single limb static and dynamic postural exercises to restore functional performance of the knee (Zech et al., 2009; Malempati et al., 2015). Over the last decades, numerous studies have further highlighted the reliability of single leg stance assessments for the quantification of postural deficiencies (Mohammadi et al., 2012; Kouvelioti et al., 2015) and the monitoring of rehabilitative progress in ACL patients (Howells et al., 2011; Negahban et al., 2014).

In clinical research, the evaluation of single limb postural sway is most commonly carried out by instrumented force platforms, which are designed to measure the forces of the standing body acting to the ground (Browne and O'Hare, 2001). Equipped with strain gauged load transducers and built-in digital amplifiers, force plates generate an electrical signal proportional to the ground reaction forces and moments in three-dimensional orientation (**Fig. 6**). From the forces exerted to the triaxial transducers, a broad biomechanical picture can be drawn to map body sway and acceleration (Winter, 2009).

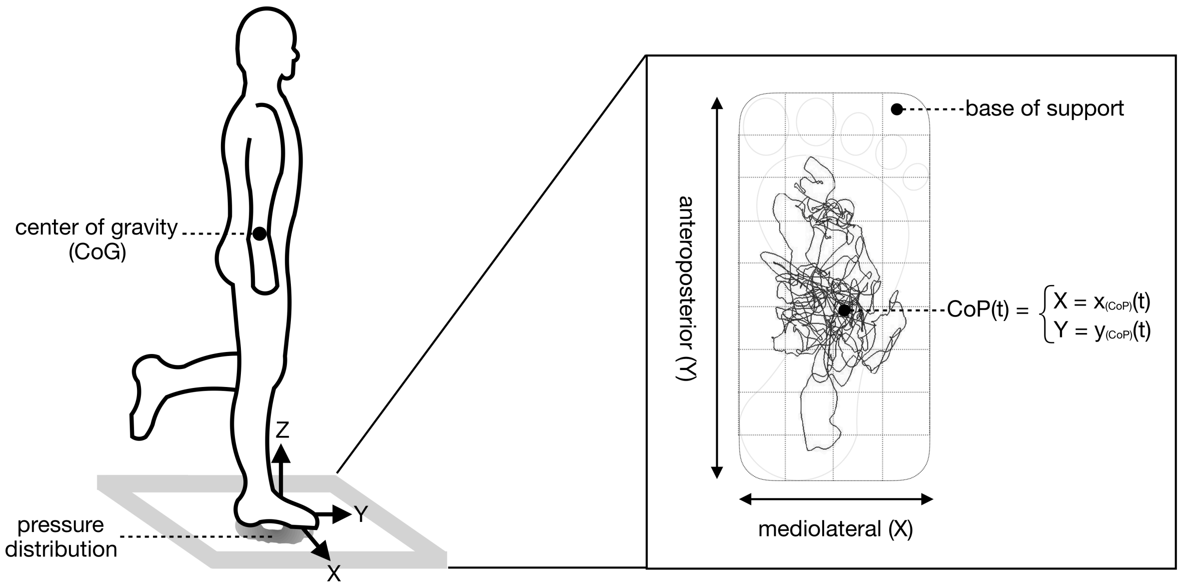


Fig. 6 Illustration of the center of pressure (CoP) trajectory (modified from Haddad et al., 2006). X, Y, Z represent the orthogonal directions to which the ground reaction forces act.

2.5.1 Center of pressure

Assessments of postural stability in quiet stance are based on ground reaction forces, which act directly under the area of the feet in contact with supporting surface. As the body is a dynamic system and synergistic muscular effort is required to sustain a vertical position, quiet stance is inherently characterized by spontaneous oscillations termed postural sway. While the CoM represents the site where the weighted relative position of the distributed mass sums to zero, the center of gravity (CoG) describes the point where gravity acts to the net location of the CoM. Once the CoG moves towards a boundary of the base of support, reflexive muscle contractions generate multi-joint moments that align body segments for maintaining postural equilibrium. Consequently, the sum of all ground reaction forces acting between the body and the supporting surface constitute a vector of total vertical force. The center point through which this vector acts to the force plate is referred to as the center of pressure (CoP) and represents the vertical downward-projection of the CoG. Thereby, the trajectory of the CoP in the anteroposterior and mediolateral directions

(**Fig. 6**) describe the sway of the body in relation to the base of support (Shumway-Cook and Woollacott, 2012). The fact that CoP trajectories are certainly influenced by the collective outcome of compensatory joint movements makes it particularly sensitive to even minimal deviations of postural stability. Therefore, postural assessments based on force plate CoP measures is currently considered the gold standard in many clinical populations (Huurnink et al., 2013).

Among a wide variety of linear CoP parameters established in the field of clinical posturography, the area of sway and mean sway velocity are traditional and widely employed time-domain measures to describe postural stability. Sway velocity is calculated as the total distance tracked by the CoP per sample time, whereas the area of sway represents the 90% or 95% ellipse area of all CoP trajectories in the anteroposterior and mediolateral direction (Paillard and Noé, 2015). In this way the area of sway is regarded as a measure of overall postural performance, whereas sway velocity is rather considered to represent the efficiency of the postural control system during upright stance (Paillard and Noé, 2015). For both measures, smaller mean values are usually associated with better postural stability.

Fundamental non-linear measures have repeatedly been shown to reliably distinguish manifold clinical populations from healthy individuals (Raymakers et al., 2005; Błaszczyk et al., 2007; Salavati et al., 2009; Dauty et al., 2010; Bolbecker et al., 2011; Cimino et al., 2018). In clinical populations, standing still often constitutes a demanding task for the patients and may limit the duration of trials in the postural assessment. In that respect, sampling durations of 30 seconds have already gained proper reliability of both the area of sway and sway velocity with increasing number of trials (Pinsault and Vuillerme, 2009; Ruhe et al., 2010). Moreover, the mean velocity of the CoP excursions in quiet stance has been emphasized for a proper consistency across repetitions (Lafond et al., 2004; Duarte et al., 2011) and reliability for group comparisons (Raymakers et al., 2005). The average of multiple trials has further been shown to limit the influence of random temporary postural responses and instability (Pinsault and Vuillerme, 2009; Scoppa et al., 2013). However, as the area of sway and sway velocity may evolve differently depending on the task and among patients, it is recommended to consider both parameters simultaneously in the assessment of postural stability (Asseman et al., 2004). An unstable stance, characterized by a wide area and / or high velocity of the CoP trajectory, may theoretically increase the probability to contact the boundaries of postural stability and subsequently evoke cortical alertness for the initiation of compensatory postural adjustments (Slobounov et al., 2009). It was therefore assumed that distinct spatial (area of sway) and temporal (sway velocity) properties of the CoP data in ACL patients may appear simultaneously with specific patterns of cortical processing.

2.5.2 CoP data processing

In study II and study III, excursions of the CoP were recorded from triaxial force plates (FP6090-15 / FP4060-05, Bertec, USA) and captured at a sampling rate of 1000 Hz. The processing of the force plate data was conducted using an automated custom-built code in MATLAB (v.R2015b, Mathworks Inc., Natick, USA) with similar processing steps in both studies. To eliminate transition effects from bipedal to single leg stance, the code removed the first and last three seconds of each trial in study II, whereas solely the first and last seconds of data were deleted in study III. Before the data was then downsampled to 100 Hz, as well as detrended in both studies (Scoppa et al., 2013), a fourth-order low-pass Butterworth filter with a cut-off frequency at 6.25 Hz was additionally applied in study III (Clark et al., 2014). Afterwards, postural sway was quantified by the mean area of sway and mean velocity among trials, based on the anteroposterior and mediolateral displacements of the CoP.

2.6 Neurophysiological Assessment

For the quantification of cortical contributions to postural control, mobile EEG was used as a non-invasive way to image brain functions at high temporal resolution. The EEG is one of the primary electrophysiological monitoring methods of neurophysiological research, measuring electrical currents on the scalp that reflect the activity of the human cerebral cortex. Assemblies of perpendicularly oriented pyramidal neurons, located at different spatial scales of the cortex, produce dynamic patterns of electrical potentials which predominantly contribute to the EEG signal. In general, synaptic activity of neuronal cells generates subtle electrical impulses across the membrane of the target neuron. Thus, excitatory or inhibitory postsynaptic potentials change the membrane voltage and correspondingly create a local current source. A summation of these postsynaptic potentials originating from large neuronal populations firing in synchrony eventually possesses the property of propagating through the different cortical layers to the scalp (**Fig. 4**). The superficial electrical potential projected to the scalp can be recorded from EEG electrodes placed on up to 256 distinct positions across the head. Such scalp potentials are characterized by sinusoidal potential fluctuations, so called oscillations, which shape recurring waveforms with specific temporal and spatial features (**Fig. 7**). In this manner, the EEG signal recorded at distinct scalp positions is a mixture of different oscillatory components at multiple frequencies, each representing a dynamic signature of the underlying physiological processes. The amplitude of these frequency components thereby strongly depends on the amount of synchronization among neurons, whereas an amplitude reduction reflects a desynchronization of underlying neuronal patches. While many patterns of neuronal oscillations have already been related to sensorimotor or cognitive functions, many others still have to be decoded (Schomer and Silva, 2011).

2.6.1 Power spectral density

One of the most traditional methods for extracting the features of EEG data is to obtain information from linearly scaled frequency components calibrated in Hertz (Hz). As the EEG signal is a sum of superimposed spiking activities at different frequencies, computational procedures are typically applied to transform the series of discrete data samples from the time domain to the frequency domain. Hereof, fast Fourier transformation (FFT) is used to define the spectrum of a certain time series (Schomer and Silva, 2011). The FFT is basically an efficient mathematical operation for computing the discrete Fourier transformation, which constitutes the actual reversible mapping operations of the time series (Cochran et al., 1967; Baudiquez et al., 2020). For the estimation of power spectral density (PSD) of continuous data, Welch's method is further used to average consecutive spectral estimates from a sequence of time samples of the whole signal (Welch, 1967). The resultant power values then represent the squared amplitudes of the signal (μV^2) in the dimension of intensity per bandwidth (V^2/Hz) and characterize definite contributions of any given frequencies composing the overall EEG signal (Schomer and Silva, 2011).

2.6.2 Functional connectivity

Apart from power properties of an EEG time series, the phase of a frequency specific oscillation represents an important quantity for the delineation of cortical network dynamics. Neural oscillations are naturally characterized as a sine wave with time-dependent variations in an alternating current circuit (**Fig. 7**). Hereby, the wave is performing a full cycle of 360 degrees or 2π radians at the rate of a given oscillatory frequency, while spanning the minimum and maximum amplitudes of both positive and negative polarities. Expressed by degrees or radians, the phase describes the angular position and direction of the signal along the sine wave at any instant (Dorf, 2000; Keil et al., 2014).

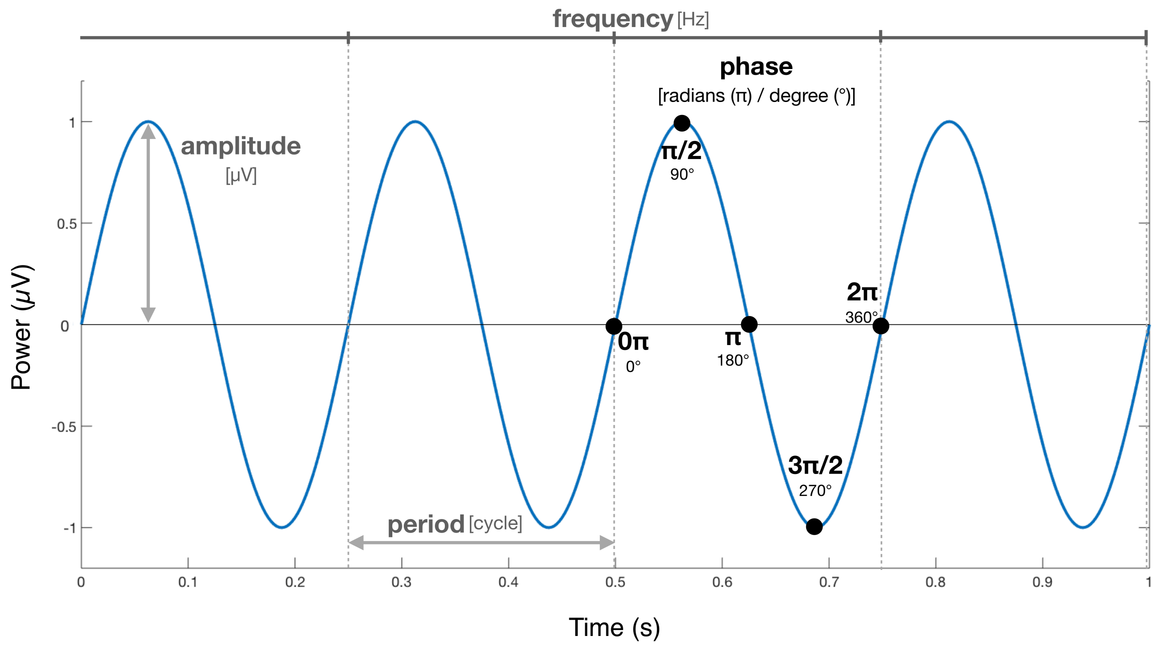


Fig. 7 Characteristics of oscillatory signals, determined by the strength of the signal (amplitude), the full cycles comprising a positive and negative deflection (period), the number of cycles per second (frequency) and the instantaneous position in the oscillation cycle (modified from Ladouce, 2018).

As cortical dynamics are assumed to rely on the interconnectivity of various network components and their corresponding dynamics, phase-locked activations of distant, non-overlapping neuronal brain areas facilitate the resonant interactions between these neuronal assemblies (Fries, 2005). Therefore, different measures for the computation of phase synchrony or phase coherence have been established as estimates of functional connectivity between cortical areas.

For the exploratory purposes of study II, the phase lag index (PLI) was deemed a reliable measure of functional connectivity. It was intended to utilize a robust methodological proceeding to investigate functional brain connectivity within a continuous state of cortical processing (Douw et al., 2014; Tóth et al., 2017; Fraga González et al., 2018). The PLI is a measure of dynamic phase coupling, estimating functional connectivity as the statistical dependencies among neurophysiological events between pairs of EEG channels. In this regard, the Hilbert transform is used to compute the instantaneous phase of each channel and time point. The PLI then depicts dynamical changes of phase synchrony, by calculating the asymmetry of the instantaneous phase difference distribution between the time series (**Fig. 8**). By using the absolute value of the signum function (sign), the PLI disregards phase locking centered around zero phase difference and thus excludes effects of volume conduction. Mathematically, the PLI of two signals can be expressed as

$$PLI = |\mathrm{E}\{\mathrm{sign}(\Delta\phi)\}| \tag{2.1}$$

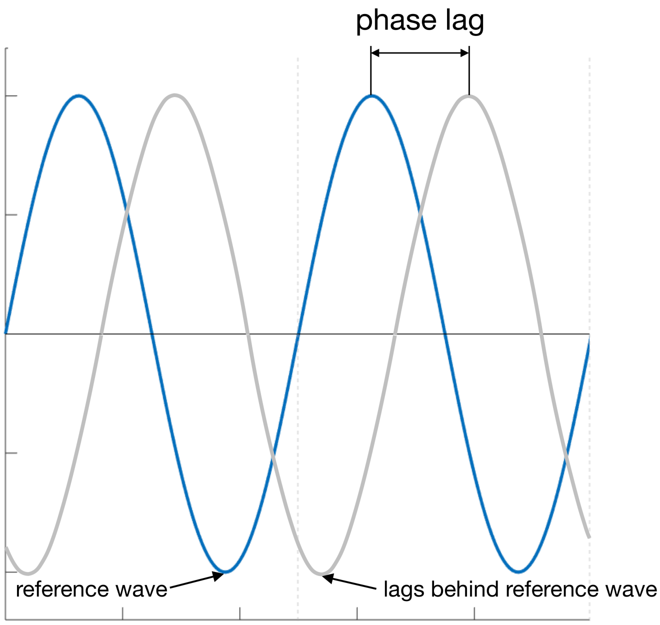
where E is a function computing the mean value and $\Delta\phi$ denotes the instantaneous phase difference. These consistent, non-zero phase lags can be quantified as rather random or synchronized, with PLI values within a range from 0 - 1. While zero indicates no coupling of the two signals, PLIs of 1 indicate perfect phase locking (Stam et al., 2007). Additionally, by ignoring zero-phase interactions, the PLI is assumed to be less sensitive to influences of common sources, amplitude or volume conduction effects, as well as spurious interactions (Stam et al., 2007; Diessen et al., 2015). Simulation data has further shown that the PLI outperformed other functional connectivity measures, such as the imaginary part of coherency, in detecting true changes in phase-synchronization (Stam et al., 2007). Therefore, PLI-based estimates are likely to represent true interactions between the underlying cortical systems in a mobile brain imaging paradigm.

In study III, the weighted phase lag index (wPLI) was used as an extension to the traditional PLI. As Vinck and colleagues (2011) have demonstrated that PLI indices may be biased by the discontinuity of the binarized phase differences, estimating phase synchronization effects of small magnitudes may appear problematic under noisy conditions. Therefore, wPLI as a novel unbiased measure of phase-synchronization has been developed, based on weighting each phase difference with respect to the imaginary part of the cross-spectrum (Vinck et al., 2011). The cross-spectrum here denotes a complex-valued function for the comparison of two time series according to their amplitude and phase differences, with amplitude versus frequency as the real part and phase versus frequency as the imaginary part of the transfer function (Eriksson, 2000; Pereda et al., 2005; Baudiquez et al., 2020). By weighting each phase difference with respect to the magnitude of the phase lag, calculated as

$$wPLI \equiv \frac{|E\{\Delta\phi\}|}{E\{\Delta\phi\}} = \frac{|E\{|\Delta\phi| sign(\Delta\phi)\}|}{E\{|\Delta\phi|\}} , \qquad (2.2)$$

the wPLI is designed to ignore non-brain sources of activity, which would typically generate near-zero lags between the time series of two channels (Vinck et al., 2011; Lau et al., 2012; Choi et al., 2019). It will further reduce the probability of detecting false positive connectivity in the presence of non-brain sources. In this way, the wPLI is considered a robust measure to quantify the dynamic interaction between two recording sites in resting state applications, but also in the context of human movement (Lau et al., 2012).

Fig. 8 Phase lag between two sine oscillations (simplified illustration).



2.6.3 EEG data processing

In both experimental studies, cortical activity was continuously recorded from active Ag/AgCl electrodes (actiCap, Brain Products, Munich, Germany) with impedance conversion at sensor level. The amplification directly at the recording site reduces the influence of cable movements and leads to much lower noise levels compared to conventional passive electrode recordings. Acquisition of EEG data was conducted using high-density wireless transmission systems (MOVE / LiveAmp-64, Brain Products, Munich, Germany) placed in a lightweight backpack. The MOVE system used in study II is comprised of two wireless transmitters, which amplify and digitize the incoming raw analogue signal at a sampling rate of up to 1000 Hz. By replacing the cables between amplifier and electrode cap with a wireless connection, the digital signal is transmitted to a receiver and converted back to analogue before being streamed to the recording computer. On the other hand, the LiveAmp-64 utilized in study III is an even more compact, wearable high-density EEG system. The LiveAmp-64 allows for EEG recordings with a sampling rate of 500 Hz and offers local storage of the EEG data in parallel to wireless data transmission. In contrast to the MOVE system, data obtained from EEG electrodes is directly amplified by the LiveAmp and digitally transmitted to the recording computer through a wireless transmission path. However, with their small dimensions, both ultra-lightweight devices are designed for high subject flexibility with comfortable wearability.

The consequent processing of the acquired EEG data followed a similar procedure in study II and study III. For the preprocessing routine, the EEGLAB open source toolbox (Delorme and Makeig, 2004) was used and complemented by customized MATLAB (v.R2015b, Mathworks Inc., Natick, USA) scripts for the standardization of all possible preprocessing steps.

In a first step of the automated pipeline, sinusoidal artifacts (50 Hz / 100 Hz) from AC power line fluctuations, power suppliers or fluorescent lights were removed by means of an adaptive frequency domain regression technique implemented in the CleanLine plugin for EEGLAB (Mullen, 2012). To further improve the signal-to-noise ratio, a linear finite impulse response (FIR) filter with a bandpass of 2.5 - 30.0 Hz / 3 - 30.0 Hz was used to shape the frequency content of the EEG signal by allowing only the specified frequencies to pass through (Widmann et al., 2015). In order to reduce computational costs of iterative analyses, while still keeping the spectral information of interest, data was downsampled to 128 Hz / 256 Hz at the end preprocessing pipeline (Shannon, 1949).

In study II, the previous data preprocessing was followed by visual inspection of the channel time series. Channels severely affected by bad electrode-skin contact, electrode specific affection of movement or non-stereotypical electromyographic patterns throughout the recording were manually removed by the investigator. On the contrary, the removal of bad channels was standardized in study III. Here, the eBridge plugin for EEGLAB (Alschuler et al., 2014) was used to identify channels linked by low-impedance electrical bridges, in order to avoid unwanted influences on connectivity measures. Additionally, noisy channel detection based on kurtosis, joint probability and spectrum of the recorded channels was included in the script for study III, using the EEGLAB *pop_rejchan* function. In case of any channel rejections in one of the two studies, a spherical spline interpolation of missing channels was applied to maintain a uniform structure of the data array (channels × sample points) across subjects. Furthermore, signal referencing was computed to common average. It is assumed that the average sample points of a high number of electrodes will equal zero and may therefore state a quiet-reference for the entire montage (Nunez and Srinivasan, 2006).

Additionally, non-stereotypical artifacts (e.g. single electrode pops, jawing, chewing or clenching) were initially rejected by visual inspection (Delorme et al., 2012). Any stereotyped artifacts such as eye blinks, muscle activity, external noise or recurrent electrode pops, were removed by an independent component analysis (ICA) based artifact rejection. Hereof, the adaptive mixture independent component analysis (AMICA) algorithm was used (Palmer et al., 2011). The ICA is a common signal processing method which identifies maximally independent sources of electrical activity linearly mixed in multi-channel EEG data. In this manner, the ICA is able to distinguish several classes of stereotyped non-brain signals from real brain sources resting upon their spatio-temporal features (Delorme et al., 2012). Independent components (ICs) exhibiting diverse or scattered topographies with multiple poles, dipole locations extremely superficial or even outside the head model, as well as irregular magnitudes of the frequency spectrum are likely representing non-brain mixed sources. Therefore, ICs were removed from the data if they were clearly attributable to a typical artifact pattern (Onton and Makeig, 2006). While a heuristic approach described by Onton and Makeig (2006) was followed in study II to label artifact ICs, an automated independent component classifier (ICLabel, Pion-Tonachini et al., 2019) was utilized in study III to distinguish between brain and stereotypical non-brain sources. After the artifactual sources were removed in both studies, the remaining ICs were retained and back-projected to the sensor level, in order to create the final artifact free dataset.

For the quantification of cortical network dynamics, the continuous EEG data was divided into 4-seconds epochs (Hardmeier et al., 2014) and exported to Brainwave software (Version 0.9.58, C. J. Stam; available at http://home.kpn.nl/stam7883/brainwave.html) for calculations of functional connectivity. Prior to the computation of the PLI / wPLI, the epoched data was offline band-pass filtered into separate frequency bands (theta, alpha-1 & alpha-2) using a discrete fast Fourier transformation filter. The PLIs / wPLIs were then computed for all possible channel pairs between the predefined regions of interest (ROIs).

Lastly, a custom-built MATLAB script calculated the average PLI / wPLI matrix of all epochs per subject and condition for the corresponding connections of ROIs. A detailed description of the allocation of ROIs can be found in studies II & III.

3. Summary of results

The following section will provide a broad overview of the results from all papers included in the present thesis, as well as unpublished visualizations of the most important findings.

3.1 Study I: Single-Leg Assessment of Postural Stability After Anterior Cruciate Ligament Injury: a Systematic Review and Meta-Analysis

The first aim of the initial study I, the systematic review and meta-analysis, was to synthetize findings of postural deficits in patients following ACL injury, derived from controlled trials of post-injury static postural stability assessments in single-leg stance. Moreover, a second aim was to examine the potential of traditional CoP measures in order to distinguish postural stability in ACL patients and healthy controls.

The systematic literature review of the two databases PubMed and Scopus revealed a total of 535 records. After screening for the predefined inclusion criteria, 11 studies were included in the following meta-analysis, enrolling a total of 594 subjects (329 ACLs / 265 healthy controls). Hereof, 224 subjects of the patient group underwent surgery and 105 patients were treated conservatively. While most of the eligible studies have shown a fair methodological quality, two studies were classified as poor quality. Moreover, the studies further revealed varying characteristics, such as the range between injury and time of measurement (7 days - 7 years), the trial length (10 – 30 s), number of trials (1 - 5) and total recording time (30 – 90 s).

With regards to the findings of the eligible investigations, the quantitative data synthesis revealed that postural stability was significantly decreased in patients after ACL injury. During eyes open single-leg stance, the included studies collectively showed significantly higher sway magnitudes and velocities in the injured limb of the ACL group. No significant differences were found for comparisons of the ACL-injured and non-injured leg, as well as for the ACL-non-injured and matched control leg (**Fig. 9**).

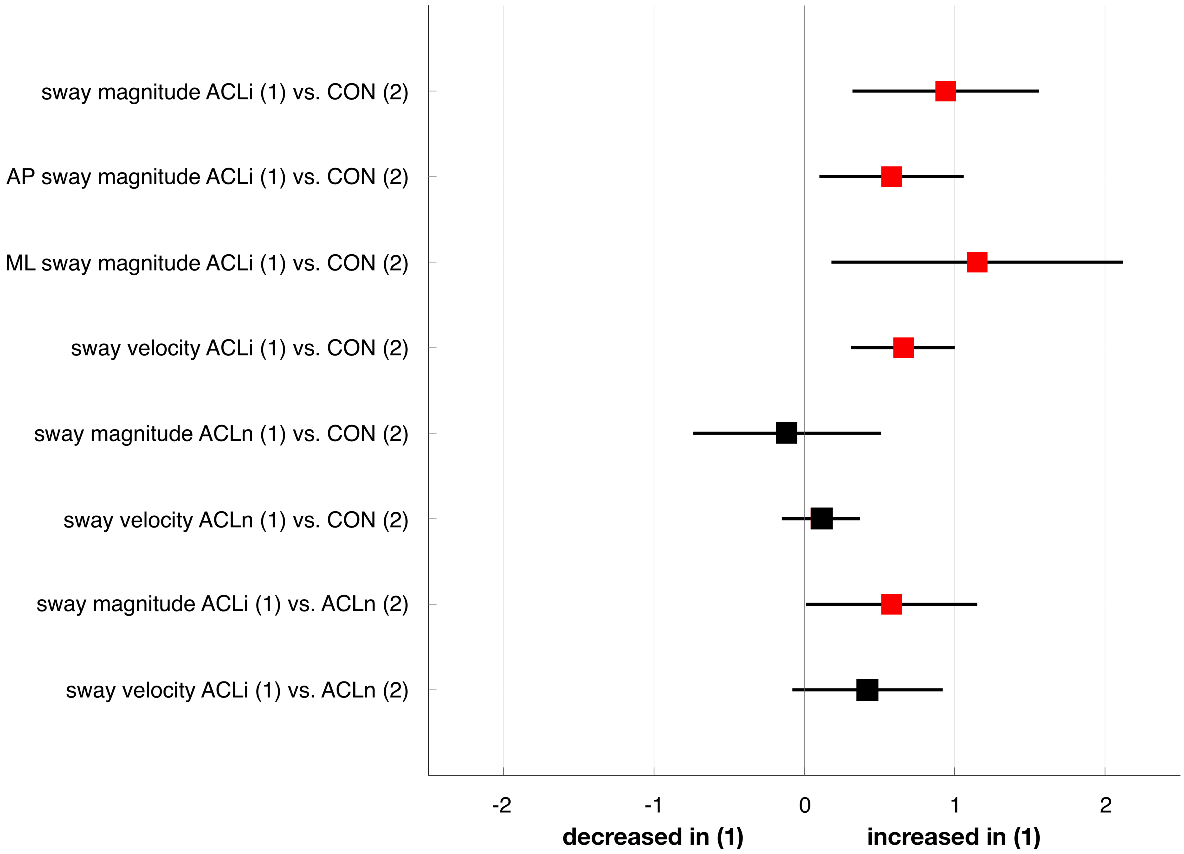


Fig. 9 Major findings of study I. Significant (red box) and non-significant (black box) effects for comparisons of the ACL injured (ACLi), ACL non-injured (ACLn) and control (CON) limb derived from the overall standardized mean difference in sway magnitude and velocity.

3.2 Study II: Modulations of Inter-Hemispherical Phase Coupling in Human Single Leg Stance

The objective of the first laboratory study was to investigate the suitability of the PLI for capturing patterns of cortical contributions appearing with a decreasing base of support from bipedal to single leg stance in healthy individuals.

The force plate data revealed a significantly increased area of sway for single leg stance compared to bipedal stance, although sway velocity was not significantly changed. The cumulative distributions of the power spectra across ROIs indicated different cortical activity in bipedal and single leg stance conditions. While power spectral density demonstrated no statistically significant changes in theta and alpha-1 between conditions, significantly lower alpha-2 power in the single leg condition indicated enhanced cortical excitation in bilateral frontal, motor, parietal and occipital areas. Furthermore, PLIs in the alpha-2 frequency band demonstrated significantly decreased inter-hemispherical functional connectivity of connections predominantly involving the ipsilateral motor ROI to the left standing limb in the single leg stance condition (**Fig. 10**).

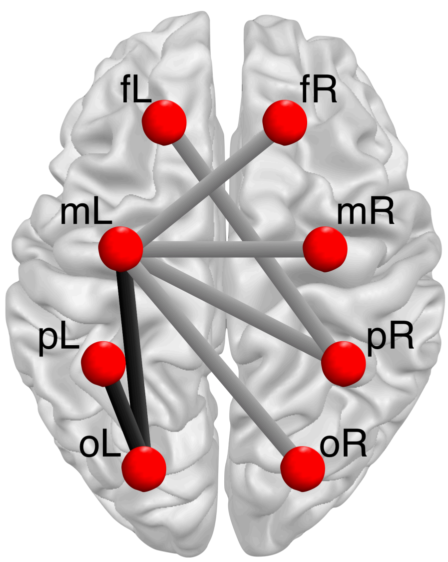


Fig. 10 Major findings of study II. Significantly decreased functional connectivity between frontal (fL / fR), motor (mL / mR), parietal (pL / pR) and occipital (oL / oR) intra- (black) and inter-hemispherical connections (gray) from bipedal to single leg stance, based on PLIs in the alpha-2 frequency band.

The brain model was illustrated with Brain Voyager Brain Tutor commercially available software (http://www.brainvoyager.com).

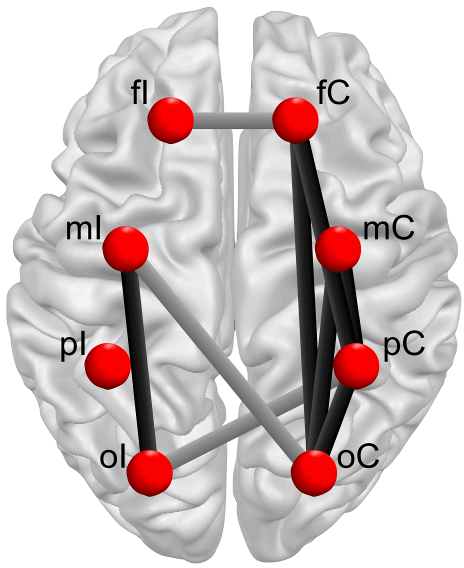
3.3 Study III: Cortical Contributions to Postural Control in Patients Six Weeks Following Anterior Cruciate Ligament Reconstruction

Based on the findings of study I and study II, the experimental study III finally aimed to explore patterns of cortical contributions to postural control during single leg stance in patients six weeks following ACLR.

While the subjective rating of knee function showed significantly lower values in ACLR patients compared to their matched controls, sway area and sway velocity did not show significantly different patterns between groups. Furthermore, wPLIs in the theta frequency band demonstrated no significantly differing patterns of functional connectivity in ACLR patients and healthy controls on either standing leg. However, the alpha network revealed significantly differing patterns of functional connectivity between ROIs (**Fig. 11**). In the alpha-1 frequency band, a significant group × leg interaction effect was found for wPLIs in the connection between the contralateral parietal and ipsilateral occipital ROI. Moreover, alpha-2 connectivity predominantly increased within the contralateral hemisphere to the standing leg in ACLR patients, whereas exhibiting a contrary trend for the matched limb of the controls. In detail, these group × leg interactions were found for functional connections including parieto-frontal, parieto-motor, parieto-occipital, occipito-frontal, occipito-motor and occipito-parietal connections within the contralateral hemisphere, as well as an occipito-motor intra-hemispherical connection on the ipsilateral side. Additionally, functional connectivity within inter-hemispherical connections of fronto-frontal and occipito-motor ROIs also appeared differently in the alpha-2 range among groups.

Fig. 11 Major findings of study III. Significant group × leg interactions indicating differing patterns of functional connectivity in the ACLR and control group within intra- (black) and inter-hemispherical (gray) connections between ROIs (red dots). Ipsilateral (fI, mI, pI, oI) and contralateral (fC, mC, pC, oC) ROIs, exemplarily shown for single leg stance on the left injured leg.

The brain model was illustrated with Brain Voyager Brain Tutor commercially available software (http://www.brainvoyager.com).



4. Discussion

The following chapter will provide a brief interpretation of the findings obtained in the three studies included in the present thesis, whereas a more in-depth discussion of the particular results is presented in each of the corresponding studies. For this reason, the subsequent discussion will mainly place emphasis on the overall significance of the findings, the potential of a combined postural and neurophysiological assessment in ACL research, as well as the implications for future studies to develop more sophisticated methods for monitoring functional recovery of the sensorimotor system after ACL injury.

4.1 Summary of results

The overall aim of the present thesis was to provide a better understanding of the cortical mechanisms accompanying functional impairments of postural control in ACLR patients, by exploring compensational mechanisms of the sensorimotor system for altered afferent information from the ACL. For these purposes, this research initially examined the feasibility of traditional CoP measures and EEG based functional connectivity measures as a potential neurophysiological assessment in ACL rehabilitation. Therefore, a systematic review and meta-analysis was conducted to aggregate available empirical evidence on postural deficiencies in ACL patients during single leg stance. The comprehensive analysis of study I showed that the included reports collectively point to decreased postural stability in the ACL injured limb compared to healthy individuals. In this regard, the traditional CoP measures included for quantifying sway magnitude and velocity appeared applicable to distinguish ACL patients and healthy controls in terms of postural stability. Although the eligible studies were selected for highly specific criteria, included research still exhibited considerable heterogeneity. The variability among investigations was attributed to different characteristics of the enrolled populations, the matching of experimental and control group, the time periods between surgery and measurement, as well as methodological aspects of the postural assessment. Nevertheless, injury to the ACL was associated with increased postural sway magnitude and velocity in standardized single leg stance on the injured limb, which may demonstrate the usability of the selected assessment for the rehabilitative monitoring of functional recovery after ACL injury.

While the included observations in study I solely describe the motor consequences of postural deficiencies, further etiological approaches are needed to assess neurophysiological mechanisms underlying these functional deficits in ACL patients. Building upon this reasoning, two mobile EEG studies were designed to scrutinize the suitability of cortical measures for capturing oscillatory modulations linked to the maintenance of postural equilibrium in ACLR patients. The first experimental study in healthy individuals demonstrated that functional brain connectivity allowed to reasonably describe the allocation of cortical activation appearing with postural instability and changed sensory information induced by a narrowed base of support. Compared to bipedal standing, the single leg stance was characterized by increased inhibition of transcortical connections in conjunction with a global increase in cortical excitability. These findings indicated an enhanced task-specific cortical processing as a consequence of incremental postural sway. Thus, a critical finding of studies I & II was that postural control assessment based on single leg standing may allow to identify postural deficiencies, as this simple balance task already requires increased cortical alertness and selective inhibition of sensorimotor pathways within the cortex to properly control postural stability. While PSD in study II solely allowed to draw broad conclusions regarding cortical excitability, functional connectivity provided a more differentiated and revelatory view into cortical contributions to postural control.

In study III, the final conflating approach was therefore deemed to reveal changes of sensorimotor processing in ACLR patients. This final investigation aimed to explore cortical contributions to postural control in patients six weeks following ACLR. Interestingly, postural sway parameters did not show significantly different patterns in the ACLR group compared to their matched controls. However, functional connectivity allowed to depict differing patterns of cortical contributions to postural control in ACLR patients. While cortico-cortical connectivity predominantly increased in connections within the hemisphere responsible for controlling the injured leg of ACLR patients, these patterns appeared unchanged or even slightly opposed in the control group. The findings showed differing patterns of cortical contributions in ACLR patients, including intra-hemispherical connections between the posterior somatosensory and visual areas to the more anterior frontal and motor areas in the contralateral hemisphere to the injured leg, as well as a visual-motor intra-hemispherical connection on the ipsilateral side. Furthermore, functional connectivity within inter-hemispherical connections of fronto-frontal, visual-motor and visual-somatosensory areas appeared differently among groups. A higher emphasis on occipital connections with the motor areas in the ACLR group may therefore point to stronger functional relationships and interactions between these areas. Although ACLR patients in study III, however, were able to control postural sway, these findings indicate that ACLR patients may probably depend on higher neural drive to motor areas by increasingly incorporating somatosensory and visual information to compensate for altered afferent information from the knee. More cortical contributions may thus be required to coordinate efferent neural signaling for maintaining knee joint stability and postural stability when standing on the injured limb. In turn, an increased dependency on visual and somatosensory information may eventually limit the variability of postural responses in more dynamic and less predictable situations of daily life and in the sporting context.

4.2 Methodological considerations

The present thesis basically employed two different scientific approaches – a literature-based and a data-based methodology – for the identification and application of a combined neurophysiological postural assessment, finally aiming to explore cortical contributions to postural control in ACLR patients. Certainly, both approaches entail their own advantages for the discovery of specific outcomes applied within the general framework and also the specifics of a research question. However, as any scientific issue is inevitably multifactorial in nature, several limitations come along with each of the two approaches when breaking down the complex research question to a single investigation. The following chapter will therefore elucidate the strengths and limitations of the selected methodologies of this thesis.

4.2.1 Strengths & limitations of the systematic review and meta-analysis approach

The initial study of this thesis was conducted to systematically collate the relevant evidence of postural deficiencies in ACL patients quantified by gold standard CoP measures. Systematic reviews provide a reliable syntheses of primary research findings related to a particular topic or research question. By following an explicit and reproducible methodology for the identification, selection and evaluation of eligible studies, systematic reviews constitute an effective scientific approach to provide a comprehensive overview of a broad set of empirical findings. In addition, many systematic reviews incorporate a meta-analysis to combine various statistical results of eligible studies. These statistical techniques use the pooled data of multiple studies to draw new statistical conclusions and providing more precise estimates of a general outcome (Moher et al., 2015). Hence, an essential strength of this literature-based approach is that it collates already peer-reviewed research in a reproducible and standardized way to assess the state of empirical knowledge on a specific research question. Nonetheless, the literature screening requires extensive access to a wide range of databases and peer-reviewed journals, which may lead to an incomplete picture of current evidence in cases of inaccessible articles. Another issue of this approach could be related to the selective reporting of outcomes by the authors. Although the predefined inclusion criteria for studies mainly facilitate an objective screening process, there is still an inevitable subjectivity in the final study selection that needs to be considered. In the present systematic review, the detailed and standardized PRISMA protocol (Moher et al., 2015) was followed to facilitate the appraisal of the applied review procedures. Moreover, to limit subjective inclusion and reporting of studies, two investigators independently applied the study selection on the basis of an identical search term. This, together with the general advantages mentioned above, allowed to include a consistent subset of studies in the qualitative synthesis, which drew a conclusive picture of postural deficiencies in ACL patients. However, the systematic review of study I also illustrated a considerable methodological heterogeneity of postural assessments included in the meta-analysis. Even though all records matched the predefined inclusion criteria, some experimental deviations, for instance, trial lengths or parameter calculations aggravated the interpretation of the pooled data. Furthermore, the applied quality assessment tool for observational studies only revealed a fair methodological quality of the eleven studies that matched the inclusion criteria. In parts of the studies, either the methodological procedures or the results were insufficiently reported and finally led to lower scores in the quality assessment. As such, it is conceivable that further potentially relevant records may have already been excluded in the early stages of the search process, due incomplete reporting of methodological procedures in their abstracts. Furthermore, a possible publication bias must always be taken into consideration, as only publishing significant findings could also distort the distribution of findings and consequently affect conclusions about the existence of postural deficiencies (Van Aert et al., 2019). In this light, the review conducted in study I also emphasizes the importance of a transparent and explicit reporting of experimental procedures and findings for the appraisal of empirical evidence in ACL research.

4.2.2 Strengths & limitations of postural control assessment in ACLR patients

For the purpose of assessing postural control and related cortical processing, the two experimental studies (II & III) of this thesis utilized static posturography on a fixed instrumented force plate. Static force plate posturography is a valuable assessment to quantify postural control in different healthy or clinical populations. This method is frequently used in contemporary clinical settings for the detection of weight-bearing asymmetries, unsteadiness of postural sway or limits of postural stability. Furthermore, it allows for a quantitative analysis and identification of postural abnormalities, as well as the isolated analysis of affected somatosensory systems (e.g. visual / vestibular) in patients with neurological indications or musculoskeletal injuries. Most commonly, the posturopraphic assessments comprise an upright stance where subjects are required to maintain postural equilibrium in a relatively unperturbed state. A varying base of support, stance position or visual feedback can thereby modify the postural requirements and either isolate or accentuate specific somatosensory systems. In contrast to non-instrumented tests of postural assessments, which only provide a gross indicator of postural control function, the instrumented postural assessment offers objectively quantifiable measures of physiological postural responses to naturally or perturbation-evoked instability. In this way, several sway measures based on the CoP are able to find systematic differences between various healthy and clinical populations at both a functional and a physiological level (Visser et al., 2008). Despite the many advantages of instrumented posturography, a lack of universally standardized protocols for the assessment of postural stability, as well as a missing consensus on most suitable measures hamper the comparative consideration of various findings and the collection of normative data. In most instances, the characteristics of CoP measures are strongly dependent on the study-specific experimental design, quality of force sensors, analysis domain (time / frequency) and processing algorithms. Altogether, these features pose the risk of incomparable results among different studies (Scoppa et al., 2013). For this reason, the three studies of this thesis were intentionally premised on the probably most fundamental characteristics of postural sway, namely the magnitude and velocity of body sway. Correspondingly, only studies using at least one parameter were included in the systematic review approach of study I. The subsequent experimental studies then used the area of sway and mean sway velocity as two of the gold-standard measures in static posturography. Although these measures have been shown to detect postural deficiencies in various clinical populations (Raymakers et al., 2005; Błaszczyk et al., 2007; Salavati et al., 2009; Dauty et al., 2010; Bolbecker et al., 2011; Cimino et al., 2018), confounding effects of anthropometric subject characteristics on the vertical ground reaction forces need to be considered. Moreover, different postural strategies may constitute another limitation of the

CoP measures used in this thesis. Whereas the area of sway demonstrated reasonable findings in study I & II, the results of study III did not allow to distinguish ACLR patients and healthy controls based on postural stability metrics. A potential explanation might be that the trial-averaged parameters lacked sensitivity to adaptive compensatory postural strategies in ACLR patients. Despite similar average sway scores in both groups, it is conceivable that these were biased by different postural strategies. From a theoretical standpoint, healthy controls may have used an open-loop strategy based on proprioceptive feedback, which enables to maintain a constant stance position with larger amplitudes at a slow and regular speed. Contrary to this strategy, ACLR patients may hypothetically have tended to a closed-loop strategy heavily reliant on visual information (Clark et al., 2014). In line with visual observations during the corresponding measurements, many patients rather used a knee joint (hyper-) extension of the standing limb, which consequently limited the movement amplitudes, but led to more rapid and irregular oscillations. On average, both the constantly controlled and the irregularly deflecting strategy may have achieved comparable sway scores, even though the actual postural control strategy was potentially different. Considering the free choice of knee angles and position in study III, the ACLR patients may have found a strategy to control the extent of postural sway at the expense of higher cortical processing. As recently demonstrated, a knee joint hyperextension during single leg stance may lack sensitivity to detect postural deficiencies in ACLR patients, whereas single leg stances with slight flexion of the supported limb may appear more suitable to distinguish postural performance of patients and controls (Kirsch et al., 2019). In future studies in ACL rehabilitation, it may therefore be recommended to use a more unstable knee angle in the supporting limb, which increases the degrees of freedom within the joint. Furthermore, following the development of postural strategies and knee angles over the course of treatment may also provide interesting information about naturally chosen lower limb biomechanics for the maintenance of knee stability.

As opposed to the expectations developed from study I and II, the traditional measures area of sway and mean sway velocity may also not necessarily comply with the requirements of sensitivity to altered postural strategies in ACLR populations of experienced athletes. Therefore, a refinement of the postural assessments in athletes at the early stage of rehabilitation after ACLR may be subject to future studies. Modern non-linear CoP measures such as multi-scale wavelet separation or sample entropy analysis assess the frequency, complexity and regularity of the CoP trajectories to separate distinct components of sway (Clark et al., 2014). However, with regards to the amount of studies available (Negahban et al., 2010; Clark et al., 2014; Rhea et al., 2014) these non-linear approaches lag behind a considerable body of evidence based on traditional linear measures of the CoP. Although offering promising insights into the regularity of postural sway, the reliability of non-linear measures in populations with musculoskeletal injuries has not yet been approved. Thus, an extended analysis approach, combining traditional and modern measures of CoP analysis, may provide more conclusive insights into the nature and mechanisms of postural impairments in ACLR patients at the early stage of recovery. Additionally, future approaches may also consider supra-postural, perturbation-based (mechanical / visual) or dynamic postural tasks, in order to progressively develop more natural paradigms to determine whether laboratory-based measures exhibit functional relevance for daily and sporting activities in athletes with ACLR. Thus, the sole use of instrumented posturography may need further advancement, and even more, it may be pertinent to use additional (neurophysiological) measures in order to unveil the underlying postural strategies ACLR patients chose to cope with functional deficiencies.

4.2.3 Strengths & limitations of mobile brain imaging in ACLR patients

Human movement in everyday life or sporting situations is inherently characterized by a considerable number of dynamic processes in the brain, integrating multi-modal sensory information in executive cortical loops to guide a target motor action. Due to technical limitations, traditional attempts of gaining insights into the complex cortical contributions to human movement were limited to the execution of isolated single joint movements in stationary seated or supine positions. Although these approaches offered great experimental control, they restrict real-world dimensionality and natural sensorimotor behavior. However, recent technological developments in mobile brain imaging technology nowadays allow to capture brain dynamics in more complex and mobile situations (Ladouce et al., 2017).

Among a variety of brain imaging modalities, the EEG was attributed a superior suitability for the application in mobile movement protocols (Gramann et al., 2014). While early approaches utilized overhead crane systems carrying the EEG amplifiers above the head of a subject, modern devices replace the cables between electrode system and the recording computer. Hence, these wireless transmission systems have led to free mobility and relatively unrestricted movement of the subjects (Reis et al., 2014). Although offering a precise temporal accuracy, mobile EEG is still lacking a spatial resolution as known from stationary imaging techniques like functional magnetic resonance imaging (fMRI). Moreover, further general challenges of mobile brain imaging arise from the inevitable appearance of movement-related artifacts which affect the signal-to-noise ratio of EEG records. A mobile experimental protocol therefore typically constitutes a critical trade-off between the aspiration to permit maximally natural behavior and simultaneously instructing the subject to suppress movements / muscle contractions affecting the data quality (e.g. rapid head movement or jaw clenching). In line with this, another unnatural aspect of mobile experiments is still ascribed to the necessity to record a certain amount of trials or data points in favor of the robustness of the outcome measures. Signal averaging of many recurrent trials is a common technique in EEG research. It is used to increase the signal-to-noise ratio by removing random noise from the signal. Albeit positively influencing the quality of a signal, repeated trials give rise to possible fatigue, habituation or motivational effects, which may in turn influence the natural aspect of the target motor behavior (Ladouce et al., 2017).

In the present experimental studies (II & III), the single leg stance appeared suitable for mobile brain imaging applications. The upright stance, although mobile, constituted a stable measurement situation with little influences of movement-related artifacts. Furthermore, the selected procedure of ICA-based artifact removal was able to identify and eliminate the few occasionally appearing stereotypical artifacts (eye blinks, lateral eye movement, muscle activity, cardiac pulses, line noise) by means of their characteristic scalp topography, activity power spectrum and actual activity time course. The preliminary pilot testing prior to the start of study II has further demonstrated that no explicit instructions were required to confine upper limb or head movement. Equipped with the wireless EEG systems, subjects were able use their natural motor strategies to maintain and recover postural equilibrium. In this way, the given experimental approaches took advantage of the high mobility of the recording systems but did simultaneously not fully exploit the excellent temporal resolution of the EEG. In both experimental studies, the outcome measures were extracted and averaged within predetermined time windows of the continuous record. The state-based analysis approach has partially not considered that single events, such as instantaneous loss of stability within hundreds of milliseconds, may have influenced cortical processing during the trials. Consequently, a targeted analysis of time-locked deflections in the EEG trace appearing with instantaneous loss of postural stability, as used by Slobounov et al. (2009), may therefore complement the current approach to further describe the cortical processes related to postural deficiencies in ACLR patients. Nevertheless, there is currently no consent about the explicit methodologies (e.g. filtering frequencies) for detecting events of postural instability during the continuous maintenance of postural equilibrium in ACLR patients (Haddad et al., 2006), as existing for non-time-locked CoP measures like the area of sway (Scoppa et al., 2013).

Another limitation of the present approaches may consist in analyzing EEG data on the sensor level. In studies II and III, eight ROIs were created based on previously published reports (Mierau et al., 2017; Tóth et al., 2017; Wittenberg et al., 2017) in order to determine functional connectivity within a network of cortical areas presumably related to postural control. Each ROI was composed of multiple channels located above the frontal, motor, parietal and occipital cortices for each hemisphere. However, the channel-based determination of cortical ROIs may not adequately comply with the exact anatomical location as associated by their scalp positions. In particular, deriving EEG measures from channel data entails methodological limitations, as the electrical potentials are recorded at a distance from their actual source (Rutkove, 2007). Due to the conductive properties of brain tissues and fluids, the electrical currents are propagated to multiple sensors on the scalp. Each particular channel therefore represents a linearly mixed multivariate signal composed of various brain and non-brain sources (Nunez and Srinivasan, 2006). Against this background, the channel approach may limit the probability of representing true functional connectivity of the subjacent cortical areas. To solve this problem, source modeling approaches may help to isolate cortical sources for the analysis of functional brain connectivity (Lai et al., 2018). Advanced signal processing algorithms such as the ICA are able to identify statistically independent components of concurrently active and temporally distinct sources projecting to the scalp. By separating brain source activity from non-brain content, the ICA constitutes a powerful tool to increase the signal-to-noise ratio and simultaneously adds spatial specificity to cortical source activity (Onton et al., 2006).

Whereas the EEG analysis in this thesis solely utilized ICA for the dissociation and effective removal of stereotypical artifacts from the channel data, this method could also be applied to directly analyze temporal and spectral features of distinct independent brain sources. Some initial studies have recently detected particular cortical sources involved in postural control processes (Sipp et al., 2013; Peterson and Ferris, 2018; Solis-Escalante et al., 2019; Gebel et al., 2020). These studies reported cortical phenomena in fronto-central, parietal and occipital sources in response to visually- or physically-evoked postural perturbations during standing and walking. Nonetheless, it must be noted that none of these studies investigated the interaction between sources of related brain activation. As postural control likely relies on topographically delimited functional networks within the cortex (Mierau et al., 2017), source space connectivity analysis may be a potent method to depict connectivity between cortical sources of activity and thus providing a better approximation of the postural network organization in healthy individuals and ACL patients (Lai et al., 2018). Concurrently, the source space approach may also pave the way for more directed ways of connectivity analysis of postural networks (Varghese et al., 2019). In the present sequel of studies, measures of functional connectivity were able to depict differences in cortical communication with a changing base of support, just as between ACLR patients and healthy controls. The PLI and wPLI successfully quantified the interaction between subsets of channel pairs and by this means described functional connectivity between the subjacent brain regions. However, phase-based functional connectivity measures on the channel level solely describe statistical dependencies among neurophysiological processes in resting or acting states. While these static measures of functional connectivity provide knowledge about the functional organization of the brain, they lack information about the causal or effective interactions of areas functioning as a task-related cortical network (Friston, 2011). On the contrary, effective connectivity measures in the source space estimate the causal statistical influences which neural sources exert over each other in a given task-specific cognitive or motor operation (Friston, 2011). Applications of source space effective connectivity measures have already demonstrated to depict cortical network dynamics of human locomotion, revealing differences in sensorimotor network connectivity during walking and standing (Lau et al., 2014). Although source modeling methods are essentially based on computational derivations to estimate the underlying neuronal activity from distant scalp sensors, the advantage of separating brain signals from other electrical sources, together with a more differentiated source-based network representation may pose a great potential to explain interrelations between motor behavior and sensorimotor strategies in future studies. Therefore, data driven approaches of effective connectivity may provide an additional informative value in mobile EEG experiments and could build upon the present findings to further investigate large-scale sensorimotor networks in ACL patients (Bressler and Seth, 2011). However, mobile EEG measurements exhibit different methodological limitations affecting source space analysis. In the presence of multiple non-brain signals, source space components can also contain a mixture of true brain and non-brain signals. In this case, topographically equivalent ICs may not be detectable for every subject. Studying source space connectivity based on non-homologous ICs within or across subjects could therefore limit the statistical analysis through a mismatch of physiologically plausible IC pairs within the model (Artoni et al., 2014). In addition, source space connectivity analysis is prone to spurious or ghost interactions between sources (Palva et al., 2018). Hence, future studies are required to develop sophisticated brain modelling methods which allow to investigate source space connectivity from mobile EEG recordings. In this regard, future mobile EEG approaches will represent a meaningful complement, rather than a competitor to the traditional brain imaging modalities.

4.3 Mobile brain and body imaging in future ACL research

The present thesis demonstrated that mobile EEG appears applicable in a postural control assessment at the early stage of ACLR rehabilitation. Although the final experimental study found no differences of postural sway between ACLR patients and healthy controls, the functional connectivity measures revealed differing patterns of cortical contributions in the two groups. Many concepts of rehabilitation involve postural control as an essential element to restore sensorimotor function after ACLR. Although evidence supports a positive effect of balance exercises in ACL rehabilitation (Onate et al., 2019), the beneficial impact on reestablishing proper sensorimotor functioning in ACL patients is still based on theoretical considerations. This raises the question, why not starting to quantify neurophysiological adaptations in the course of rehabilitative treatment. Repeated assessments at different stages of ACL rehabilitation may help to better understand compensational adaptations of the sensorimotor system accompanying the reestablishment of knee function.

Mobile EEG holds great potential for the quantification of cortical processes within many different occasions in ACL research. While allowing free motion of the patient during the measurement, sensorimotor processes related to complex gross motor tasks could be assessed in realistic and natural situations. Moreover, integrating a simultaneous capturing of the actual motor responses may further facilitate the link between brain and body dynamics. Portable motion capture systems composed of a magnetic sensors, accelerometers and gyroscopes are capable of describing the kinematics of human movement, by tracking the position, orientation and acceleration of single body segments. Furthermore, combined wireless EMG systems, recording the muscular activation related to a target movement, may complete the picture of a multimodal brain and body imaging approach for detecting the underlying dynamics within the sensorimotor system (Ladouce et al., 2017). Correlated phenomena of cortical and muscular activations may help explain how motor behavior is encoded in the electrical signals derived from the sensorimotor system (Enders and Nigg, 2016). This cortico-muscular coherence may also be capable of differentiating to which extent postural control strategies in ACLR patients appears reflex-based or driven by supraspinal centers (Geertsen et al., 2013).

With respect to previous findings in healthy individuals, a multimodal application of a mobile brain and body imaging postural assessment in carefully designed dual-task (Huang et al., 2016), perturbation (Varghese et al., 2017), jumping/landing (Miao et al., 2017), obstacle stepping (Nordin et al., 2019) or beam walking (Sipp et al., 2013) protocols may further the understanding of neurofunctional restoration in ACLR patients. In this way, mobile brain and body imaging postural assessments are not intended to replace the existing and well-established clinical evaluations but may be considered as a new ingredient of the decision-making process in future ACL rehabilitation.

4.4 Clinical implications & future directions

Over the past two decades, a growing amount of evidence has begun to identify clinically meaningful neural alterations in the sensorimotor system following ACL injury (Neto et al., 2019). The associated functional deficiencies observed in ACL patients are likely to impede the recovery of optimal sensorimotor control and may adversely facilitate persistent dysfunction across the lifespan (Lohmander et al., 2004; Øiestad et al., 2013; Tengman et al., 2014; Stensdotter et al., 2016). Consequently, ACL patients are necessarily required to develop compensatory strategies to cope with altered biomechanical and sensorimotor properties in order successfully return to daily or sporting activities. Indeed, neuroimaging studies have shown that ACL patients involve more neurocognitive and sensory resources than healthy controls to execute even simple motor tasks (Neto et al., 2019). Further, these functional deficiencies also seem to affect more complex postural tasks (study I) and may require specific interactions within a distributed cortical network to control gross motor actions (study III). In line with previous findings (Onate et al., 2019; Jiganti et al., 2020), study III conditionally indicated that the integration of visual and somatosensory information may have a particular role for compensatory postural strategies in those after ACLR. As a consequence, targeting the sensorimotor system and its specific subsystems could be one key to effective ACL rehabilitation (Grooms et al., 2015; Onate et al., 2019). Balance-training-induced structural and functional adaptations in brain regions responsible for movement planning and visual perception (Duru and Balcioglu, 2018), as well as for the generation of motor impulses (Taubert et al., 2016) may positively influence the reestablishment of postural control in ACL patients. Moreover, training interventions with high postural demands may also show additional effects on neuromuscular features, such as neuromuscular drive or rate of force development (Gruber and Gollhofer, 2004). However, although postural control is a frequently used element in ACL rehabilitation with hypothetically promising effects (Myer et al., 2008), study I demonstrated that ACL patients exhibit postural deficiencies even long after returning to sports practice. By now it remains uncertain why some individuals are able to cope with these deficiencies, while others experience long-term impairments of postural stability. Additionally, the impact of different rehabilitation programs and interventions on functional recovery has not been clarified. Thus, validated models for a combined behavioral and neurophysiological monitoring of sensorimotor recovery are needed to better understand the underlying mechanisms of persistent postural deficiencies in those with ACL injury, and to finally address individually appropriate therapeutic consequences. Therefore, study II & III proposed that cortical network measures may bear the potential to yield insights into compensatory sensorimotor processes in the human brain and further disentangle the reliance on specific sensory information in ACLR patients. While the current neuroimaging evidence only permits initial assumptions on the feasibility of cortical measures or the adaptative neural strategies appearing after ACL injury, future studies in this area are required to extensively prove the reliability of these findings and their actual functional relevance for therapeutic treatment. In this regard, it is of vital importance to minimize the impact of the confounding variables and methodological issues mentioned in the previous chapters. It may also be important to prove the actual neurophysiological effects of the ligamentous tear on the one hand, as well as the invasive surgical procedures on the other hand. Furthermore, it might be crucial to ascertain whether postural deficiencies manifest at specific time points after reconstruction or if the impairments ultimately appear after ligamentous injury. Longitudinal studies accompanying the entire rehabilitative process until the time of return-to-sports may further the understanding of developing sensorimotor strategies and their definite impact on functional outcomes after ACL rehabilitation. Therefore, further studies are needed i) to investigate the clinical role of altered brain connectivity for the functional recovery in ACLR patients, ii) to prove the reliability of these measures in repeated measurements and more complex postural tasks, as well as iii) to apply the suggested assessments at different stages of the rehabilitation process under consideration of clinical patient characteristics and treatment properties. Looking ahead, the knowledge gained from those investigations may, in the future, allow to identify patients at risk of persistent functional impairments, providing support for the decision-making in the rehabilitation process and, beyond that, developing therapeutic interventions for individually tailored rehabilitative strategies.

5. Conclusion

Although changed afferent sensory pathways have already been observed in patients with ACL injury, compensatory sensorimotor mechanisms in these patients still remain uncertain. Therefore, the overall aim of this thesis was to examine the applicability of mobile EEG based functional connectivity measures to finally explore compensatory cortical mechanisms accompanying postural deficiencies in ACLR patients at the early stage of functional rehabilitation. While the present thesis has on the one hand shown that investigations in ACL patients collectively report deficiencies of postural stability, it is important to acknowledge that posturographic examinations need to be carefully designed in order to facilitate sufficient sensitivity for the detection of postural incongruencies. Although posturography could lack sensitivity to unveil postural deficits in specific populations of ACLR patients (e.g. experienced athletes), functional brain connectivity may allow to reasonably describe the allocation of cortical contributions to postural control appearing with simple postural tasks in the course of rehabilitation. In ACLR patients, functional connectivity indicated that compensational cortical mechanisms underlying postural control may rely on a selective involvement of transient cortical connections in different states of synchrony and with oscillations at particular frequencies. ACL patients may further depend on higher neural drive to motor areas by increasingly incorporating somatosensory and visual information to compensate for altered afferent information from the knee joint. However, while the functional role of these network modulations remains unclear, further studies are needed to investigate the definite impact of cortical connectivity on the functional outcomes of ACL rehabilitation. Beyond this work's theoretical implications for rehabilitation and applied neuroscience, the present findings offer new perspectives for the development of multifaceted, comprehensive brain and body imaging assessments to monitor functional progress in ACL patients and other musculoskeletal deficit models.

6. Scientific dissemination

6.1 Peer-reviewed publications

1. Lehmann T, Paschen L, Baumeister J (2017) Single-Leg Assessment of Postural Stability After Anterior Cruciate Ligament Injury: a Systematic Review and Meta-Analysis. Sport Med Open 3.

2. An YW, Di Trani Lobacz A, Lehmann T, Baumeister J, Rose WC, Higginson JS, Rosen J, Swanik CB (2018) Neuroplastic changes in anterior cruciate ligament reconstruction patients from neuromechanical decoupling. Scand J Med Sci Sport.

3. Lehmann T, Büchel D, Cockcroft J, Louw Q, Baumeister J (2020) Modulations of Inter-Hemispherical Phase Coupling in Human Single Leg Stance. Neuroscience 430:63–72.

4. Gebel A, Lehmann T, Granacher U (2020) Balance task difficulty affects postural sway and cortical activity in healthy adolescents. Exp Brain Res

5. Lehmann T, Büchel D, Mouton C, Gokeler A, Seil R, Baumeister J (2021) Exploring Cortical Contributions to Postural Control in Patients Six Weeks After Anterior Cruciate Ligament Reconstruction

6.2 Oral presentations

1. Lehmann T, Paschen L, Baumeister J (2018) Comparison of postural stability in the ACL-deficient and -reconstructed leg: a meta-analysis. Deutscher Olympischer Sportärtzekongress. Sport Orthop Traumatol 34:198–199

6.3 Poster presentations

1. An YW, Lobacz AD, Lehmann T, Baumeister J, Swanik CB (2017) Altered Brain Activity During Joint Loading After Anterior Cruciate Ligament Reconstruction. Annual Meeting of the American College of Sports Medicine 2017. Med Sci Sport Exerc 49:360.

2. Büchel D, Lehmann T, Cockcroft J, Louw Q, Baumeister J (2018) Effect of a cognitive dual-task on electrocortical activation during single leg stance. Proceedings of the 3rd International Mobile Brain/Body Imaging Conference, Berlin, 69-70

3. Lehmann T, Büchel D, Cockcroft J, Louw Q, Baumeister J (2018) Exploring Functional Brain Connectivity of Postural Control in Upright Stance. Proceedings of the 3rd International Mobile Brain/Body Imaging Conference, Berlin, 69-70

4. Lehmann T, Büchel D, Cockcroft J, Louw Q, Baumeister J (2019) Phase Coupling of Bilateral Motor Areas Decreases From Bipedal to Single Leg Stance. In: 2019 OHBM Annual Meeting, Rome, Italy. Rome.

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