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Quadriceps cortical adaptations in individuals with an anterior cruciate ligament injury

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ABSTRACT

Background: Altered quadriceps corticomotor excitability has been demonstrated following anterior cruciate ligament (ACL) injury and reconstruction, however only the single joint vasti muscles have been assessed. There is no current data on rectus femoris corticomotor excitability following ACL injury, the biarticular quadriceps muscle also critical for force attenuation and locomotion. The purpose of this study was to examine rectus femoris corticomotor excitability, intracortical inhibition and cortical motor representation in individuals with and without an ACL injury.
Methods: A cross-sectional design was used to evaluate corticomotor excitability bilaterally in individuals with a physician confirmed ACL injury (12 males, six females; mean ± SD age: 29.6 ± 8.4 years; BMI: 24.8 ± 2.3 kg·m^2; 69.5 ± 42.5 days post-injury) compared to a healthy control group (12 males, six females; age: 29.2 ± 6.8 years; BMI: 24.6 ± 2.3 kg·m^2). Single-pulse transcranial magnetic stimulation (TMS) was used to assess corticomotor excitability and cortical motor representation, and paired-pulse TMS used to assess intracortical inhibition for rectus femoris while participants maintained a knee extension force at 10% of body weight.
Results: The cortical silent period (cSP) duration was longer in the injured limb of the ACL group compared to the uninjured limb ($P = 0.004$). No significant differences were found for corticomotor excitability, intracortical inhibition or cortical motor representation center position and size ($P > 0.05$).
Conclusions: There is preliminary evidence that the cSP is longer, but changes in rectus femoris corticomotor excitability and cortical motor representation are not present following ACL injury.

1. Introduction

Quadriceps muscle weakness is common in people who have sustained an anterior cruciate ligament (ACL) injury or undergone ACL reconstruction (ACLR) [1–3]. There is evidence that quadriceps weakness contributes to disability [4], and potentially influences the onset and progression of post-traumatic knee osteoarthritis in these individuals [5,6]. Understanding the causes of quadriceps muscle dysfunction is critical for developing interventions to effectively treat persistent muscle weakness following ACL injury [1,3]. There is evidence that persistent quadriceps muscle weakness is a consequence of alterations within the central nervous system (CNS), more specifically alterations in the excitability of the primary motor cortex of the brain and associated descending pathways [7–9] contribute to persistent quadriceps muscle weakness.

The excitability of the cortex and associated pathways can be measured with transcranial magnetic stimulation (TMS) by evaluating the motor threshold, or the amplitude of the muscle response evoked by the TMS [10]. The motor threshold is defined as the minimum stimulus intensity required to elicit a muscle response (motor evoked potential; MEP) of a predefined size. A higher motor threshold is considered indicative of reduced corticomotor excitability, requiring higher levels of stimulation or neural drive to create excitation and neuronal depolarization [11].

Previous studies have demonstrated alterations in quadriceps corticomotor excitability in individuals with ACL injury [7] and ACLR [2,12], and in individuals with chronic anterior knee pain [13]. Following ACLR, the active motor threshold of the primary motor cortex is higher in the involved versus uninvolved limb and uninjured healthy controls, indicating reduced corticomotor excitability in the involved limb [2,12]. However, there were no changes in the MEP amplitude following ACLR indicating that although a greater stimulus is required for excitation and depolarization, the amplitude of the motor response is similar within the target muscle of individuals with an ACLR and uninjured individuals [2,11]. The research suggests a role for the CNS in quadriceps neuromuscular dysfunction, as higher quadriceps active

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motor threshold (AMT) was found in conjunction with reduced voluntary muscle activation and quadriceps strength deficits in individuals with an ACLR [2].

Transcranial magnetic stimulation (TMS) during an active muscle contraction produces an interruption in voluntary electromyography (EMG) known as the cortical silent period (cSP). The cSP is mediated by both spinal and cortical mechanisms, with the latter part of the cSP (>50 ms) mediated by inhibitory γ-aminobutyric acid receptor B ($GABA_B$) activity in the cortex [14]. The inhibitory system within the human brain can be more specifically assessed using paired-pulse TMS.

Paired-pulse TMS utilizes a conditioning stimulus and a test stimulus at varying inter-stimulus intervals (ISI). Subthreshold conditioning stimuli will preferentially excite the interneurons, which will suppress or facilitate the subsequent MEP generated from the test stimulus depending on the duration of the ISI. Subthreshold conditioning stimulus coupled with a supra-threshold stimulus using an ISI of one to six milliseconds produces short-interval intracortical inhibition (SICI), and is thought to represent γ-aminobutyric acid receptor A ($GABA_A$) activity [15,16]. Alternatively, long interval intracortical inhibition (LICI) is the result of two suprathreshold stimuli at an ISI of 50 to 200 ms and is thought to represent $GABA_B$ activity [15,16]. Intracortical inhibition has been assessed in this manner to examine changes in neuromuscular function associated with aging [17], and in clinical populations [18–20]. Physiological changes in the intracortical inhibitory circuits may be contributing to higher quadriceps AMT, and quadriceps neuromuscular dysfunction previously demonstrated in individuals with an ACL injury and ACLR [2,7,12]. Although SICI does not appear to differ between healthy individuals and those with knee osteoarthritis [18], intracortical inhibition has yet to be investigated in individuals with an ACL injury or ACLR.

Spatial reorganization within the CNS in terms of changes in size, shape and center of the cortical motor representation of the target muscle can occur following injury [21–23]. Although traditionally examined following neurological injury [24], cortical motor representation mapping has more recently been used in musculoskeletal injury research examining the effects of spatial reorganization on neuromuscular function. Alterations in cortical representation position and size have been found for forearm extensors in individuals with lateral elbow pain [22] and in the transversus abdominus in individuals with recurrent low back pain [23], but have yet to be investigated in relation to the quadriceps following ACL injury.

Identifying and understanding CNS adaptations contributing to quadriceps dysfunction would provide novel therapeutic targets within the motor cortex that may lead to improved quadriceps muscle function following ACL injury. Previous corticomotor excitability studies following ACL injury or reconstruction have focused primarily on evaluation of the single joint vasti muscles [2,4,7,12]. However, there is value in exploring changes in rectus femoris following ACL injury as it has been shown that all portions of the quadriceps work to enable knee extension and loading control [25]. Given that the rectus femoris spans two joints, it is possible that it is under differential cortical control compared to the single joint vasti and thus may not be affected to the same extent as the vasti following ACL injury.

Therefore, the aims of this study were: 1) to examine rectus femoris corticomotor excitability and intracortical inhibition in individuals with an ACL injury compared to healthy uninjured individuals, and 2) to determine the calculated center position and area of the rectus femoris cortical motor representation following ACL injury compared to healthy uninjured individuals. We hypothesized that there would be a significant reduction in rectus femoris active motor threshold (AMT), MEP amplitude and cortical motor representation area (size) (H_1), and that there would be a significant increase in intracortical inhibition (SICI, LICI and cSP) in those with an ACL injury compared to healthy uninjured individuals (H_2).

2. Methods

2.1. Study design

This was a cross-sectional laboratory study examining rectus femoris corticomotor excitability, intracortical inhibition and cortical motor representation in a group of individuals with ACL injury, as well as a group of healthy control participants. All main outcome measures were collected during a single data collection session. All participants gave written informed consent, and the study was approved by the Ethics Committee of the University of Melbourne (ID: 1340551).

2.2. Participants

All ACL injured participants were recruited from two orthopedic surgeons within the Melbourne metropolitan area. We included individuals between the ages of 18 to 50 years old, within eight months of an initial isolated ACL injury and no meniscal trauma requiring meniscectomy. Those with multi-ligament trauma, chondral defects (grades III to IV), and previous ACL injury and/or surgery on either limb were excluded. In addition to the ACL group, a control group of healthy, recreationally active men and women with no history of lower limb musculoskeletal injury in the past year that limited function for more than one week, or required surgical intervention were recruited from the university community. Each participant completed a 15-item questionnaire to assess for any contraindications to non-invasive brain stimulation [26]. No participant in either group reported any neurological or medical condition that would contraindicate TMS. Leg dominance was self-reported and determined by the foot preferred for kicking a ball [27].

2.3. Instrumentation

Quadriceps contraction intensity during TMS was measured via a force transducer (Sensortronics 60001 Scale Components, Australia), attached to the distal shin one centimeter proximal to the malleoli using a soft Velcro cuff. All participants were securely seated for testing in a supportive chair, to keep the hip joint at 90° and knee joint at 60° of flexion.

A Bi-Stim^2 magnetic stimulator (Magstim Co, UK) producing a monophasic pulse shape, with a figure-of-eight 70 mm coil (Magstim Co, UK) held tangential to the skull was used to examine corticomotor excitability, intracortical inhibition and the cortical motor representation. A custom designed form-fitting cap (EasyCap, Germany), with stimulus sites marked at one centimeter spacing in latitude and longitude, was fitted to the participant's head with the vertex aligned with the center of the cap co-ordinates [28]. The placement of the cap was continuously monitored during testing to ensure consistency of the site of stimulation.

A Trigno wireless electromyography (EMG) sensor (Delsys, USA) was affixed to the skin with double-sided tape over the rectus femoris muscle belly halfway between the anterior superior iliac spine and patella in the direction of muscle fiber orientation [29]. The rectus femoris muscle was identified via palpation during manually resisted knee extension in a seated position. Prior to attaching the EMG sensor the skin site was prepared by shaving, debriding, and cleaning with alcohol wipes [30]. EMG signals were sampled at 2000 Hz for 500 ms, and EMG amplification was set at a gain of 1000 (PowerLab 4/35 ADInstruments, USA) with a 10 Hz highpass filter. The common mode rejection ratio of the EMG amplifier was 100 dB with an input impedance of one megaohm.

2.4. Knee function

The Knee Injury and Osteoarthritis Outcome Score (KOOS) was used to assess self-reported knee function, and is a valid measure of function following knee injury [31]. A Visual Analogue Scale (VAS), a