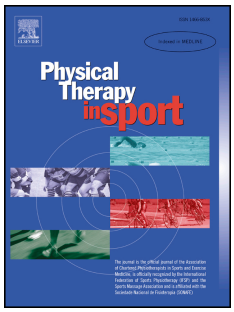
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Corticospinal and spinal neuromuscular function in physically active adults after unilateral primary anterior cruciate ligament reconstruction: A systematic review and meta-analysis.

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TITLE: Corticospinal and spinal neuromuscular function in physically active adults after unilateral primary anterior cruciate ligament reconstruction: A systematic review and meta-analysis.

Abstract:

Objectives: To (1) characterise prevalence of technical methods and neuromuscular variables assessed with transcranial magnetic stimulation (TMS) following anterior cruciate ligament reconstruction (ACLR); (2) quantify differences between ACLR leg, contralateral non-ACLR, and healthy control legs using TMS and peripheral nerve stimulation (PNS); (3) determine changes in neuromuscular variables across post-operative time.

Design: Systematic review and meta-analysis.

Setting: Systematic searches were conducted across PubMed, Web of Science, CINAHL, and Google Scholar from database inception until September 2025.

Participants: Thirty-six studies with physically active adults (18–45 years) with ACLR were included.

Outcome measures: Neuromuscular outcomes assessed using TMS and PNS including active motor threshold (AMT), motor evoked potential, short-interval intracortical inhibition, H-reflex, quadriceps voluntary activation (CAR), and quadriceps strength.

Results: Most studies (72.2%) assessed quadriceps isometric actions at 90° knee flexion. AMT was higher in the ACLR leg versus contralateral (SMD=0.16) and healthy legs (SMD=0.47); other TMS variables were unchanged. Quadriceps strength (SMD=−0.60 to −0.78) and CAR (SMD=−0.18 to −0.49) were reduced in the ACLR leg. Meta-regression showed no temporal changes in quadriceps neuromuscular function.

Conclusion: Methodological variability highlights the need for standardized TMS and PNS protocols. Ongoing corticospinal deficits and quadriceps weakness emphasize targeted rehabilitation of quadriceps neuromuscular pathways.

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INTRODUCTION:

Anterior cruciate ligament (ACL) sprains are common sports injuries, particularly in football[1] and basketball[2], often necessitating ACL reconstruction (ACLR) and prolonged rehabilitation.[3,4] Approximately 52,000 ACL injuries and 27,000 ACLR surgeries occur annually in the United Kingdom.[5] Quadriceps strength is a critical treatment target following ACLR due to its influence on landing biomechanics,[6] perceived function,[7] and functional outcomes.[8–10] Patients with ACLR often exhibit bilateral quadriceps weakness[11,12] - this highlights the need to understand the neural contributors to quadriceps weakness by comparing both the reconstructed limb to the contralateral limb and to healthy controls.

Quadriceps weakness after ACLR has been linked to altered central nervous system (CNS) and peripheral nervous system function[13,14] via several approaches (e.g., corticospinal excitability (CSE), spinal reflex excitability, voluntary muscle activation). Existing research has reported altered corticospinal responses, impaired spinal reflexes, and reduced voluntary activation in people with ACLR.[14,15] Reduced central voluntary activation (CAR) after ACLR is often attributed to arthrogenic muscle inhibition (AMI), a reflex inhibition of the quadriceps driven by altered joint afferent input.[16] Because ACL injury typically occurs during eccentric quadriceps loading (e.g., decelerating during cutting),[17] eccentric muscle actions are also of particular interest, yet remains understudied with neurophysiological techniques such as transcranial magnetic stimulation (TMS). Transcranial magnetic stimulation is a common method for assessing corticospinal function, using variables such as active motor threshold (AMT), motor evoked potentials (MEP), and short interval intracortical inhibition (SICI).[13,18,19] In addition, measures of spinal pathway excitability, including the Hoffman reflex (H-reflex), and volitional output such as maximum voluntary effort (MVE) and the central activation ratio (CAR) also provide insight into neuromuscular status after ACLR[13,15]. Separating these supraspinal and spinal measures clarifies the mechanisms potentially driving quadriceps weakness and supports the development of targeted post-operative rehabilitation.

Despite the importance of the above methods and measures, the technical approaches used to obtain them vary widely across studies.[13,20] Changes in corticospinal function have been reported in previous studies during early,[21] middle,[22] and late[14] stage of rehabilitation after primary unilateral ACLR. How these neural changes evolve with time since surgery remains unclear, which motivates our third aim. Differences in equipment configuration, knee joint position, and muscle action type likely influence the values reported for variables such as AMT, MEP, and H-reflex.[14,21,23] As a result, findings appear inconsistent and, therefore, it is difficult to form a clear understanding of quadriceps neuromuscular status after ACLR or how it changes across rehabilitation. Previous systematic reviews and meta-analyses provide initial syntheses to this end; Rodriguez et al.[13] and Rush et al.[20] examined corticospinal and spinal excitability after ACLR. Rush et al.[20] compared outcomes before and after 24 months from the surgery. Santana et al.[24] included ACL deficient and ACLR participants.[24] However, to our knowledge, none of these reviews quantified how frequently different TMS and peripheral nerve stimulation techniques and outcome variables were

used across their included studies, or modelled time since surgery as a continuous variable using meta-regression. The present study extends the past work in adults with unilateral primary ACLR as the above methods and measures are increasingly relevant because altered corticospinal function may contribute to reinjury risk and to the development of post-trauma osteoarthritis.[13,14,20]

Given the clinical importance of neuromuscular recovery for optimising quadriceps strength and knee joint health,[9,25,26] and given the methodological inconsistency across studies, a consolidated synthesis of the literature is required. Therefore, the first aim of this study was to identify the technical methods and outcome variables used in studies employing TMS to assess quadriceps neuromuscular function in physically active male and female adults with unilateral primary ACLR. It was hypothesised that studies will demonstrate heterogeneity in technical methods and variables. The second aim was to quantify differences in quadriceps neuromuscular function as assessed by TMS and peripheral nerve stimulation (PNS) between the reconstructed limb, contralateral non-ACLR leg, and healthy controls. It was hypothesised that individuals with unilateral primary ACLR would demonstrate a decrease in corticospinal and spinal reflex excitability, as well as a reduction in quadriceps voluntary activation and strength relative to non-ACLR leg and healthy control. The third aim was an exploratory analysis of how these corticospinal and spinal neuromuscular variables changed across post-operative time. It was hypothesised that neuromuscular function would improve as time from surgery increased.

METHODS:

Review development, registration, and reporting

Consistent with recommendations for the development and reporting of systematic reviews[27] this review included a multi-disciplinary team of physiotherapists and physiologists. The review was pre-registered on PROSPERO (CRD42024562633) and followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2021 guidelines.[27]

Eligibility criteria

Studies were included for analysis if they fulfilled the following criteria: (i) physically active male and female adults, minimum mean age 18 years, maximum mean age 45 years, who have undergone unilateral primary ACLR; (ii) analytical studies (e.g., experimental, observational); (iii) analytical studies that quantify quadriceps neuromuscular function using single or paired pulse TMS and associated variables alone (e.g., AMT, MEP, SICI) or with PNS and associated variables (e.g., H-reflex), and/or knee extensor muscle strength via dynamometry and associated variables (e.g., MVE, CAR, peak torque); (iv) studies published in English language peer-reviewed journals.

Exclusion criteria included: (i) studies with children: mean age < 18 years; (ii) descriptive studies (e.g., case study); (iii) studies with participants who experienced a tibiofemoral or patellofemoral dislocation; (iv) studies with participants who underwent a revision ACLR; (v) studies with

participants with a primary knee problem that is gradual onset in nature (e.g., osteoarthritis); (vi) no maximum time since surgery was applied as an eligibility criterion, in order to capture the full range of post-operative recovery and permit the exploratory analysis of neuromuscular change over time (vii) studies not published in English language or in peer-reviewed journals.

Information sources

An electronic search of the literature was conducted in the following databases from inception until 12th September 2025: PubMed, Web of Science, and CINAHL.[28] To ensure the entire field of literature had been reached, a final search was conducted via Google Scholar using the relevant key terms. Following these processes, the reference lists of all included studies were screened for additional relevant papers. As a sensitivity check, the reference lists of three previous systematic reviews and meta-analyses (Rodriguez et al.[13], Rush et al.[20] and Santana et al.[24]) were cross-checked against the final list of included studies."

Search strategy

Electronic databases were searched using discipline-specific free-text key terms and associated synonyms (Table 1).

Selection process

All studies identified from the literature search were exported onto a Covidence software.[29] One researcher performed the initial search and screened all retrieved articles to remove duplicates and any items that were deemed outside the scope of the meta-analysis. Two researchers then independently screened and reviewed the remaining titles and corresponding abstracts. Full-text articles that satisfied the inclusion criteria were read, with eligible studies then included within the meta-analysis. Next, the two researchers met to discuss and resolve any discrepancies across the included studies. No automation tools were used.

Data collection process and data items

Data from included studies were extracted from the available text to a custom-made Excel spreadsheet. For purpose 1, information on participant characteristics (e.g., age, sex, height, mass), technical methods (e.g., knee angle, type of muscle action), and variables (e.g., AMT, H-reflex; Table 3) were catalogued.

For purpose 2, data were extracted as means and standard deviation (SD) for each variable in both the ACLR (operated leg, contralateral leg) and control groups (healthy control leg). Where SDs were presented across multiple time points, data were pooled into a single value and subsequently used for analysis.[13] The following equations were used to calculate between group pooled SDs.

$$SD_{pooled} = \sqrt{\frac{({SD_1}^2 - {SD_2}^2)}{2}}$$

Where, SD_1 = standard deviation for group 1 and SD_2, = standard deviation for group 2.[13]

For three or more groups, the denominator was changed to reflect the number of samples, k:

$$S_{pooled=} \sqrt{\frac{(n_1 - 1)S_1^2 + (n_2 - 1)S_2^2 + \ldots (n_k - 1)S_k^2}{n1 + n2 + \ldots + n_k - k}}$$

Where, n_1 = sample size for group 1, n_2 = sample size for group 2 and S = SD[13]

For equal sample sizes, the formula was simplified to:

$$S_{pooled} = \sqrt{\frac{S_1^2 + S_2^2 + \ldots + S_k^2}{k}}$$

For the experimental studies, baseline means and SDs were used for analyses. Corresponding authors were contacted via email to request original data if missing. Any data missing from any study were classed as 'not examined/not reported'. For purpose 3, range of time from surgery data for the time analysis (in months) were extracted. No automation tools were employed.

Quality assessment and risk of bias: The modified Downs and Black quality checklist[30] was used for broader quality assessment and Egger's regression test was performed specifically for risk of bias assessment.

Statistical analysis:

For the first aim, prevalence estimates were calculated by converting frequency counts of experimental techniques and variables to proportions (%). For the second aim, a meta-analysis was performed on Review Manager (RevMan) software using a random-effects model, with standardized mean difference (SMD) and 95% confidence intervals used to measure effect size. Heterogeneity was assessed using the I^2 statistic, with cut-offs for low (25%), moderate (50%), and high (75%) heterogeneity. The sensitivity analysis (exclusion of RMT studies, with studies not stating the condition treated as AMT) and the leave-one-out analysis. For the third aim, an exploratory meta-regression was conducted. After the meta-regression, a sensitivity analysis was carried out to evaluate the strength of the observed association. To identify whether the statistical

significance and direction of the association remained constant, the meta-regression model was re-run under altered circumstances, by stepwise elimination of significant studies. Finally, a quality analysis was performed using a modified Downs and Black checklist[31] (total=13 items), with study quality being graded low (0-6/13), moderate (7-9/13), and high (≥10/13). Cohen's kappa (κ) assessed inter-rater agreement,[32] values of 0.00-0.20, 0.21-0.40, 0.41-0.60, 0.61-0.80 and 0.81-1.00 were considered slight, fair, moderate, substantial, and almost perfect agreement, respectively.[32] Publication bias was assessed using funnel plots and Egger's regression test. R Studio (R Foundation for Statistical Computing, Vienna, Austria) was used for all analyses with alpha set at 0.05.

RESULTS:

Literature search, study selection and study characteristics-

A total of 2,008 articles were identified with 1,970 retained after the removal of duplicates. Eight additional studies were identified from the reference list of the identified studies. After screening titles and abstracts, 40 articles were further evaluated. Table 2 cross-references the 36 studies included in the present review against those included in Rodriguez et al.[13], Rush et al.,[20] and Santana et al.[24], indicating study overlap and newly captured studies. A PRISMA flowchart for the literature search and selection is shown in Figure 1. Four studies were excluded; Heroux et al.[33] and Ward et al.[21] had considered ACL degeneration populations along with ACLR populations; data was not relevant from the study by Rosenthal et al.,[34] and Zarzycki et al.[15,35] presented the same data in two publications - therefore, only one study was used here.[35] A total of 36 studies were selected for the final analyses.

A) Proportion analysis:

Individual study characteristics including study design, technical methods and variables are presented in Table 3, which shows 88.9% and 11.1% assessed quadriceps isometric and concentric muscle actions, respectively. No study assessed quadriceps eccentric muscle actions. Quadriceps assessment angle was 90° knee flexion in 72.2% of included studies. For TMS variables, 66.7% assessed AMT, 36.1% assessed MEP/M_{MAX} ratio (MEP divided by M_{MAX}), and 13.9% assessed SICI. For PNS variables, 41.1% assessed H-reflex, 66.6% assessed MVE, and 61.1% assessed CAR.

B) Meta-analysis:

1.1- Corticospinal excitability (AMT)

Data from 18 studies[14,35–51] were used to assess changes in AMT in the between-leg analysis (n=415, I^2=0%) (Figure 2a) and from 12 studies[18,27,30–33,33,34,36,55,57–59,67] for the between-group analysis (n=546, I^2=81%) (Figure 2b). In the between-leg analysis, mean AMT was 47.0 ± 10.9 %

MSO in the ACLR leg and 45.2 ± 11.0 % MSO in the non-ACLR leg. In the between-group analysis, it was 45.9 ± 10.9 % MSO in the ACLR leg and 42.1 ± 8.9 % MSO in healthy controls. Pooled data indicated that CSE decreases when compared with the non-ACLR leg (SMD=0.21, 95% CI: [0.07, 0.34], p=0.003) (Figure 2) as well as when compared with a healthy control leg (SMD=0.48, 95% CI: [0.06,0.9], p<0.01) (Figure 2).

1.2- Corticospinal excitability (MEP/M_{MAX})

A total 11 studies[14,35,36,39,42–44,44,45,47,51] were included in the between-leg analysis (n=186, I^2=80%) (Figure 3a) and five[14,35,39,42,51] studies were included in the between-group analysis (n=167, I^2=87%) (Figure 3b). In the between-leg analysis, mean MEP/M_{MAX} was 0.04 ± 0.04 in the ACLR leg and 0.05 ± 0.04 in the non-ACLR leg. In the between-group analysis, it was 0.16 ± 0.11 in the ACLR leg and 0.16 ± 0.21 in healthy controls. No statistically-significant differences were observed for the ACLR leg in comparison with the non-ACLR leg (SMD=-0.21, 95% CI: [-0.64, 0.22], p=0.34) (Figure 3) as well as with the healthy control leg (SMD=0.44, 95% CI: [-0.24, 1.11], p=0.21) (Figure 3).

1.3- Intracortical inhibition (SICI)

Data from four studies[35,47,50,51] were used to assess changes in SICI in the between-leg analysis (n=81, I^2=0%) (Figure 4a) and from four studies[23,35,42,51] for the between-group analysis (n=140, I^2=0%) (Figure 4b). In the between-leg analysis, mean SICI was 57.3 ± 26.7 % in the ACLR leg and 63.2 ± 33.5 % in the non-ACLR leg. In the between-group analysis, it was 60.7 ± 27.6% in the ACLR leg and 62.4 ± 25.2% in healthy controls. Pooled data indicated no changes in intracortical inhibition when compared with the non-ACLR leg (SMD =-0.18, 95% CI: [-0.49, 0.13], p=0.26) (Figure 4) as well as when compared with a healthy control leg (SMD =-0.07, 95% CI: [-0.40, 0.26], p=0.68) (Figure 4).

1.4- Spinal reflex excitability

A total of 17 studies[14,35,37–41,43–45,48–52] were included in the between-leg analysis (n=406, I^2=0%) (Figure 5a) and 12 studies[14,35,37–41,48,49,51,52] were included in the between-group analysis (n=549, I^2=70%) (Figure 5b). In the between-leg analysis, mean H:M ratio was 0.25 ± 0.27 in the ACLR leg and 0.22 ± 0.17 in the non-ACLR leg. In the between-group analysis, it was 0.25 ± 0.16 in the ACLR leg and 0.21 ± 0.15 in healthy controls. There was no statistically-significant change in H:M ratio of the ACLR leg when compared with the non-ACLR leg (SMD =-0.11, 95% CI: [-0.03, 0.25], p=0.95) (Figure 5) as well as with a healthy control leg (SMD =-0.17, 95% CI: [-0.12, 0.46], p=0.25) (Figure 5).

1.5- Quadriceps strength (MVE)

Data from 12 studies[14,23,37–39,41,48,50,53–55] were used to assess changes in quadriceps strength in the between-leg analysis (n=297, I^2=24%) (Figure 6a) and from 10 studies[7,14,23,37–41,48] for the between-group analysis (n=441, I^2=34%) (Figure 6b). In the between-leg analysis, mean MVE was 2.34 ± 0.64 Nm/kg in the ACLR leg and 2.75 ± 0.70 Nm/kg in the non-ACLR leg. In the between-

group analysis, it was 2.34 ± 0.67 Nm/kg in the ACLR leg and 3.03 ± 0.75 Nm/kg in healthy controls. Pooled data indicated a statistically-significant reduction in quadriceps strength of the ACLR leg when compared with the non-ACLR leg (SMD=-0.60, 95% CI: [-0.79, -0.40], p<0.001) (Figure6) as well as when compared with a healthy control leg (SMD =-0.78, 95% CI: [-1.03, -0.52], p<0.001) (Figure 6).

1.6- Quadriceps voluntary activation (CAR)

Data from 15 studies[23,37–39,41,47–50,52–56] were used to assess changes in quadriceps voluntary activation in the between-leg analysis (n=424, I^2=0%) (Figure 7a) and from 11 studies[7,23,37–41,48,49,52] for the between-group analysis (n=512, I^2=63%) (Figure 7b). In the between-leg analysis, mean CAR was 88.9 ± 9.3 % in the ACLR leg and 90.3 ± 8.9 % in the non-ACLR leg. In the between-group analysis, it was 88.7 ± 9.9 % in the ACLR leg and 93.4 ± 5.8 % in healthy controls. Pooled data indicated a statistically-significant reduction in quadriceps voluntary activation of the ACLR leg when compared with the non-ACLR leg (SMD=-0.18, 95% CI: [-0.32, -0.05], p=0.009) (Figure 7) as well as when compared with a healthy control leg (SMD=-0.49, 95% CI: [-0.80, -0.18], p=0.002) (Figure 7).

C) Meta-regression:

Studies that reported the outcome data of interest and the time since surgery at which it was assessed were included in the meta-regression.[14,29,32–34,40,42,43,46,48,49,51,54,58,59,61] However, a lack of sufficient studies (fewer than the recommended eight)[31,57] prevented this analysis for MEP and SICI comparisons between the ACLR and healthy control legs, as well as SICI between the ACLR and non-ACLR legs. Findings indicated a statistically-significant increase (p<0.05) in AMT of the ACLR leg when compared with the non-ACLR leg from the time of surgery (Table 4). Although the full analysis showed a statistically-significant relationship, after performing a sensitivity analysis, the relationship was no longer statistically-significant.

No statistically-significant changes were observed in AMT for the ACLR leg from the time of surgery when compared with healthy controls (Table 4). In addition, no statistically-significant changes were observed in CSE (MEP/M_{MAX}) in the ACLR leg when compared with the non-ACLR leg.

Findings also indicated no change in H-reflex, MVE, and CAR values in the ACLR leg across post-operative time when compared with the non-ACLR leg or healthy controls (Table 5).

Study quality and risk of publication bias– Results of the modified Downs and Black checklist are presented in Table 6. Overall, the majority of studies were graded as high quality. Inter-rater agreement was k=0.78, p<0.01, indicating substantial agreement.

Visual inspection of the funnel plots and the Egger's test output indicated no statistically-significant publication bias (p>0.05). (Supplementary documents).

DISCUSSION:

This review aimed to characterise the technical methods and variables used in studies assessing quadriceps neuromuscular function with TMS in adults with unilateral primary ACLR. The analysis revealed heterogeneity in the assessment methods, with most studies focusing on isometric muscle actions at 90° knee flexion. The review also found that individuals with ACLR exhibited decreased central motor drive and quadriceps strength in the ACLR leg compared to the non-ACLR or healthy control leg. Despite an initial finding of decreased CSE across post-operative time, this effect was not statistically-significant after a sensitivity analysis. In addition, there were no other statistically-significant changes in neuromuscular function over time.

Our proportion analysis shows heterogeneity in TMS and PNS variables used to assess quadriceps neuromuscular function in physically active males and females post-ACLR, and that existing studies fail to fulfil the specificity principle for neuromuscular assessment relative to noncontact injury mechanisms.[58] Anterior cruciate ligament tears happen typically when an athlete is landing from a jump or decelerating and abruptly slowing down to change direction in a noncontact situation.[17] During such manoeuvres, the knee flexes, abducts, and internally rotates with the quadriceps muscles working eccentrically.[17] However, we found no study that examined the quadriceps muscles using eccentric muscle actions. It is also noted that most ACL injuries take place when the knee joint is in 0°-60° of flexion.[3] Eccentric exercise interventions have shown promise for enhancing neuroplasticity and quadriceps function after ACLR in small case-series and trial work though neither study incorporated the neurophysiological outcomes considered here.[59,60] It is important to consider the specificity principle for neuromuscular assessments relative to knee noncontact injury mechanisms,[58] e.g., quadriceps eccentric muscle actions in an arc of 0-60° knee flexion.[61] As corticospinal and spinal excitability can vary with joint angle and background muscle length, this discrepancy between the injury-relevant range and the angles actually assessed may limit the clinical applicability of current findings. The 60° versus 90° variation between studies may itself contribute to between-study inconsistency in reported outcomes.

The meta-analysis found that AMT is higher in the ACLR leg compared to both the non-ACLR and healthy control legs, representing decreased CSE that requires greater stimulation for muscle activation.[18] This finding of elevated AMT in the ACLR leg is consistent with Rush et al.[20] and Rodriguez et al.[13], both of whom also reported reduced CSE post-ACLR. The present review extends these findings by incorporating additional studies and a broader range of outcomes, allowing a more precise pooled estimate and the exploratory analysis time since surgery. The exploratory meta-regression also indicated that CSE decreases as post-operative time increases, which points to persistent quadriceps activation impairment post-reconstruction (Table 4). The AMT measures the minimum stimulation needed to activate a muscle, reflecting the excitability of motor pathways.[13,20] A lower AMT reflects increased CSE, whereas a higher AMT indicates decreased CSE due to a greater depolarization threshold of pyramidal cells in the primary motor cortex, thereby reducing their efficiency to transmit impulses to muscles and contributing to persistent

muscle weakness.[43,18,62] The reduction in excitability may also be due to neuroplastic restructuring of the CNS at supraspinal level.[13,20] These changes in CSE are linked not only to quadriceps muscle weakness but also to suboptimal central drive after ACLR.[63]

No statistically-significant changes in MEP amplitudes were observed in the ACLR leg relative to the non-ACLR leg. These findings may be attributed to several factors. First, MEP amplitudes and AMT measure distinct aspects of CSE as MEPs reflect the magnitude of stimulus transmission, while AMT represents the excitability of pyramidal cell membranes.[18,19] Therefore, it is possible that while a stronger stimulus is required to activate pyramidal cells, the subsequent signal transmission remains unchanged.[18, 36] Secondly, included studies often measured MEP amplitude at a predetermined percentage of AMT (e.g., 120%), which may have obscured true between-group differences in CSE by normalising stimulation intensity across participants, rather than characterising the full stimulus response relationship using input-output (recruitment) curves.[13] Recruitment curves are more sensitive to differences in CSE and gain and can, therefore, reveal group differences that single intensity measures fail to detect.[64,65] A third possibility is the low statistical power and high heterogeneity among the small number of studies included in the meta-analysis, which limits the ability to draw firm conclusions.

Analysis of the included studies found no statistically-significant changes in intracortical inhibition (SICI) when comparing the ACLR leg to either the non-ACLR or healthy control legs. After ACLR, increased intracortical inhibition (lower SICI amplitudes) from the brain's intracortical areas has been linked to decreased CSE, slower force development, and reduced voluntary activation[52], ultimately contributing to persistent quadriceps weakness.[40] Methodological differences in how SICI is collected may also contribute to the mixed SICI findings. SICI is weaker during voluntary contraction than at rest,[66] and studies that determine AMT typically collect SICI during light background contraction, whereas studies that determine RMT typically collect it at rest. Because the number of studies reporting SICI was small (four per comparison), and active and resting conditions were not analysed separately, we could not test whether collection state explains the variability between studies. Future studies should report threshold type and collection state and analyse them separately. More longitudinal research is needed to fully understand the effects of SICI on quadriceps neuromuscular function due to the limited and inconsistent findings.

While no statistically-significant differences were observed in spinal reflex excitability between the ACLR leg, non-ACLR leg, and healthy control legs, individual studies revealed mixed findings. Some studies showed increased excitability in the ACLR leg,[45,51] while others found a decrease.[49,50] This inconsistency may be linked to the varied post-operative time, although the exploratory meta-regression found no change in spinal reflex excitability over time (Table 5). Our null finding for spinal reflex excitability (H:M ratio) is consistent with Rush et al.[20], who similarly reported no significant between-leg difference. It contrasts, however, with Rodriguez et al.[13], who reported a significant increase in H:M ratio in both the reconstructed and non-reconstructed limbs relative to healthy controls. This three-way discrepancy across independent reviews of overlapping

literature may reflect differences in the included study samples. It may also reflect differences in PNS stimulation parameters and electrode placement across the underlying primary studies, which underscores the need for greater methodological standardisation of H-reflex assessment in this field. These results suggest that acute changes in joint afference from pain, effusion, and loss of mechanoreceptors after ACL injury and ACLR surgery may alter CNS function,[67,68] leading to a reflexive suppression of adjacent musculature.[69] This has been demonstrated by a decrease in H-reflex amplitude after ACLR and in artificial models of effusion and pain.[70,71,72] Conversely, some meta-analyses suggest that a general increase in spinal reflex excitability may serve as a compensatory mechanism for reduced CSE.[13,49] These findings are consistent with arthrogenic muscle inhibition (AMI), a neural-mediated phenomenon whereby altered joint afferent input due to pain, effusion, and disrupted mechanoreceptors following ACLR induces reflexive inhibition of periarticular muscles through spinal and supraspinal mechanisms,[73] and is evidenced by reductions in H-reflex amplitude and reflects altered CNS excitability rather than intrinsic muscle dysfunction.[69,70] The conflicting evidence suggests that AMI may not be uniform across all ACLR patients and could be influenced by factors such as pain levels, effusion levels, and pre-injury activity.

The present analyses identified moderate-to-strong evidence of quadriceps strength deficits when comparing the ACLR leg to both the non-ACLR and healthy control legs. These persistent impairments are likely due to a combination of factors, such as a period of inactivity or decreased muscle activation immediately after surgery due to pain, swelling, or restricted movement,[72] leading to muscle atrophy, particularly of type-2 fibres, which are not used as frequently post-injury.[74] Secondly, post-ACLR knee instability may result in compensatory strategies that hinder effective quadriceps recruitment, which contributes to weakness.[54,75] Thirdly, surgical trauma and potential damage to sensory afferents can compromise proprioceptive feedback from the knee joint, leading to impaired quadriceps motor control.[68,76] Finally, variations in motor cortex excitability can diminish the signal from the corticospinal tract to the quadriceps, resulting in weaker muscle actions.[36] The current findings on quadriceps strength impairments corroborate previous literature and underscore the importance of restoring these deficiencies after reconstruction.

Despite a lack of change in quadriceps voluntary activation over time since surgery, likely due to early post-operative pain and swelling, this meta-regression revealed moderate-to-weak evidence of differences in quadriceps voluntary activation when comparing the operated (ACLR) leg to the non-ACLR leg. Furthermore, there was moderate evidence of a change in quadriceps voluntary activation when comparing the ACLR leg to a healthy control leg. Before considering physiological explanations for this mixed evidence, a methodological explanation is that CAR values are known to differ systematically depending on whether the superimposed burst or interpolated twitch technique is used, with the former generally overestimating voluntary activation. Because included studies used both techniques without distinction in our pooled analysis, some of

the apparent inconsistency in voluntary activation findings may be attributable to this methodological heterogeneity, in addition to, or instead of, the physiological mechanisms. Quadriceps voluntary activation (CAR) showed a similar pattern, with lower activation in the ACLR leg than in the non-ACLR leg (SMD = −0.18) and healthy controls (SMD = −0.49), suggesting that incomplete central drive contributes to the strength deficits. CAR values depend on the collection method: the superimposed burst technique gives higher activation estimates than the interpolated twitch technique, so CAR values from studies using different techniques are not directly comparable. One possible explanation for the decreases in voluntary activation in the early stages following injury and surgery is altered spinal reflex excitability.[52] Although spinal reflex excitability may increase in the acute phase following injury or surgery, this does not necessarily translate to improved voluntary activation.[39] Altered afferent input from pain and effusion can promote AMI, reflexively reducing alpha-motoneuron output and limiting motor unit recruitment despite heightened reflex responsiveness.[49] Concurrent supraspinal adaptations, such as reduced CSE and increased intracortical inhibition, may further impair descending drive, resulting in decreased voluntary activation. The gamma loop is a sensorimotor feedback system in which gamma motor neurons regulate muscle spindle sensitivity, thereby influencing Ia afferent input to the spinal cord and stimulation alpha motor neurons.[77] This loop plays an important role in maintaining normal voluntary muscle activation.[77] A disturbed quadriceps gamma loop function is a neurological mechanism that is thought to cause patients to have diminished voluntary quadriceps activation following ACLR.[77,78] It is, therefore, hypothesised that injured ACL mechanoreceptors and altered ligamentous afferent feedback are the source of quadriceps gamma loop dysfunction, which occurs following ACLR.[77] Since the recruitment of high threshold motor units depends on intact afferent feedback, gamma loop dysfunction could also be the cause of decreased voluntary quadriceps activation.[77]

The substantial inter-rater agreement (k=0.78) supports the consistency of the quality assessment process, indicating that the checklist was applied in a robust and reproducible manner. Furthermore, absence of statistically-significant publication bias, by both funnel plot symmetry and Egger's test, minimises concerns about selective reporting influencing the results. Overall, these factors strengthen the validity of the present analyses.

Our exploratory meta-regression modelled AMT as a continuous function of time since surgery. In contrast to Rush et al.[20], who dichotomised studies into <24 and >24 months post-operative and reported significantly greater motor threshold in the involved limb specifically beyond 24 months. The present study also differs to Tayfur et al.[79], who reported neural and strength outcomes at monthly intervals for the first six months and every 6-12 months thereafter across multiple knee injury types. A continuous regression approach, while allowing analysis across the full available time range, may not capture a threshold-type effect reported by Rush et al.[20], which may explain why our AMT meta-regression finding did not remain statistically significant following

sensitivity analysis. This highlights that the choice of analytic approach for modelling time since surgery can materially affect conclusions, and future reviews, ideally with a larger pool of eligible studies should consider both continuous and time-stratified approaches to more fully characterise the trajectory of neuromuscular recovery after ACLR. This review has several limitations. Active and resting motor threshold were pooled under a single AMT variable, although they reflect distinct physiological states, and the small number of studies reporting each separately precluded a subgroup analysis. Studies that did not report the motor threshold condition were assumed to have used AMT. Pooling may, therefore, have obscured the CSE effect. The MEP amplitude was not consistently normalised to M_{MAX} across studies despite being pooled under one MEP label, and CAR was obtained with both superimposed burst and interpolated twitch techniques, which yield systematically different values. One included study (Bodkin et al., 2021) was an intervention study; only baseline data were extracted for analysis, but differences in study design may still contribute to between-study heterogeneity. Furthermore, not all included studies assessed the full range of TMS and PNS variables, which limited the ability to explore relationships between these variables that may be relevant for ACLR rehabilitation, highlighting the need for more cross-sectional and longitudinal research in this area. Also, eligibility was determined by group mean age (18–45 years) rather than individual participant age; as a result, a small number of individual participants under 18 years cannot be ruled out in studies that did not report individual ages. Finally, studies published in English language were included, potentially introducing a language bias and limiting the broader relevance of the findings. Future reviews should consider incorporating studies published in other languages.

CONCLUSION:

This study revealed substantial heterogeneity in technical methods and outcome variables across TMS and PNS research, restricting comparability of findings. Meta-analysis and meta-regression revealed reduced CSE following ACLR, indicated by increased AMT, which persisted over time without moderation by post-operative duration. In contrast, spinal reflex excitability did not differ between reconstructed limbs and non-ACLR or healthy controls. These findings are consistent with reported deficits in quadriceps strength and voluntary activation, suggesting that persistent corticospinal dysfunction, rather than alteration in the spinal reflex pathways, may cause neuromuscular impairment following ACLR.

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1

Journal Pre-proof

Table 1: Boolean chart of search strategies.

TERM	SEARCH STRATEGY
	"Anterior cruciate ligament" OR "anterior cruciate ligament injury" OR "anterior cruciate ligament reconstruction" OR "anterior cruciate ligament surgery" OR "ACL" OR "ACLR" OR "ACL-R" OR "ACLS" OR "ACLI" OR "post anterior cruciate ligament reconstruction" OR "post ACLR" OR "anterior cruciate ligament deficiency" OR "ACLD" OR "anterior cruciate ligament degeneration" OR "post traumatic knee osteoarthritis" OR "post traumatic knee OA" OR "tibiofemoral joint"
AND	"Neural adaptation" OR "neuromuscular changes" OR "neuromuscular adaptations" OR "cortical connectivity" OR "neuromuscular function" OR "neuronal plasticity" OR "corticospinal plasticity" OR "neuroplasticity" OR "neural plasticity"
AND	"Transcranial magnetic stimulation" OR "TMS" OR "TMS measures" OR "TMS parameters" OR "transcranial magnetic nerve stimulation" OR "TMNS" OR "motor evoked potential" OR "MEP" OR "corticospinal excitability" OR "neural excitability" OR "cortical excitability" OR "spinal reflex" OR "H-reflex" OR "Hoffmann reflex" OR "spinal excitability" OR "H:M ratio" OR "MVC" OR "MVIC" OR "maximum voluntary contraction" OR "maximum voluntary isometric contraction" OR "corticospinal inhibition"
NOT	"Posterior cruciate ligament injury" OR "lateral collateral ligament injury" OR "medial collateral ligament injury" OR "knee meniscus" OR "knee cartilage injury" OR "knee fracture"

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Table 2: Comparison of studies included in past systematic reviews and meta-analyses and the present study.

No.	Author	Rodriguez et al 2021	Rush et al 2021	Santana 2025	Present Study
1.	Baumeister et al.[32] (2011)	X	X	X	✓
2.	Bodkin et al.[33] (2021)	X	X	X	✓
3.	Bodkin et al.[34] (2019)	✓	✓	✓	✓
4.	Burland et al.[35] (2021)	X	✓	X	✓
5.	Burland et al.[36] (2019)	X	✓	X	✓
6.	Davis et al.[37] (2023)	X	X	X	✓
7.	Fukunaga et al.[38] (2019)	X	X	X	✓
8.	Garcia et al.[39] (2022)	X	X	X	✓
9.	Harkey et al.[40] (2016)	✓	✓	X	✓
10.	Johnson et al.[41] (2018)	X	X	X	✓
11.	Kuenze et al.[7] (2017)	X	X	X	✓
12.	Kuenze et al.[42] (2015)	✓	✓	✓	✓
13.	Kuenze et al.[43] (2014)	X	X	X	✓
14.	Lepley et al.[14] (2019)	✓	✓	✓	✓
15.	Lepley et al.[44] (2019)	✓	✓	✓	✓
16.	Lepley et al.[45] (2015)	✓	✓	✓	✓
17.	Lepley et al.[46] (2014)	✓	✓	✓	✓
18.	Lepley et al.[47] (2018)	✓	✓	X	✓
19.	Leung et al.[48] (2023)	X	X	X	✓
20.	Luc-Harkey et al.[49] (2017)	✓	✓	✓	✓
21.	Norte et al.[50] (2018)	✓	✓	✓	✓
22.	Norte et al.[51] (2018)	✓	✓	✓	✓
23.	Pietrosimone et al.[52] (2013)	X	✓	X	✓
24.	Pietrosimone et al.[53] (2015)	✓	✓	✓	✓
25.	Rodriguez et al.[54] (2024)	X	X	X	✓
26.	Rodriguez et al.[55] (2022)	X	X	X	✓
27.	Scheurer et al.[21] (2020)	✓	✓	✓	✓
28.	Sherman et al.[56] (2023)	X	X	X	✓
29.	Sherman et al.[57] (2023)	X	X	X	✓
30.	Sherman et al.[58] (2023)	X	X	X	✓
31.	Thomas et al.[59] (2016)	X	X	X	✓
32.	Ward et al.[60] (2016)	X	✓	✓	✓
33.	Ward et al.[61] (2018)	✓	✓	✓	✓
34.	Zarzycki et al.[15] (2020)	X	✓	X	✓
35.	Zarzycki et al.[31] (2018)	✓	✓	✓	✓
36.	Zech et al.[62] (2009)	X	X	X	✓

(✓= Present, X= Absent)

Table 3: Proportional analysis of methodologies and variables used in included studies:

Author	Study design	Isometric action	Concentric action	Eccentric action	Knee angle/ arc	AMT	MEP	SICI	H-reflex	MVE	CAR
Baumeister et al.[32] (2011)	Case-control study	✓	X	X	90°	X	X	X	X	✓	X
Bodkin et al.[33] (2021)	Single blinded, sham controlled, crossover randomized trial	X	✓	X	90°	✓	✓	X	X	✓	✓
Bodkin et al.[34] (2019)	Cross-sectional study	X	✓	X	Arc of 0-90°	✓	✓	X	✓	X	X
Burland et al.[35] (2021)	Cross-sectional study	✓	X	X	90°	✓	✓	X	✓	✓	✓
Burland et al.[36] (2019)	Longitudinal-case series	✓	X	X	90°	✓	✓	X	✓	X	X
Davis et al.[37] (2023)	Cross-sectional study	✓	X	X	90°	X	X	X	X	✓	✓
Fukunaga et al.[38] (2019)	Prospective cohort study	✓	X	X	30°	X	X	X	X	✓	✓
Garcia et al.[39] (2022)	Experimental study	✓	X	X	85°	X	X	X	X	✓	✓

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Harkey et al.[40] (2016)	Cross-sectional case-control study	✓	X	X	90°	X	X	X	✓	X	✓
Johnson et al.[41] (2018)	Cross-sectional study	X	✓	X	90°	X	X	X	X	X	✓
Kuenze et al.[7] 2017)	Clinical trial	✓	X	X	90°	X	X	X	X	✓	✓
Kuenze et al.[42] (2015)	Descriptive laboratory study	✓	X	X	90°	✓	X	X	✓	✓	✓
Kuenze et al.[43] (2014)	Descriptive laboratory study	✓	X	X	60°	X	X	X	X	✓	✓
Lepley et al.[14] (2019)	Case-control study	✓	X	X	90°	✓	✓	X	✓	✓	X
Lepley et al.[44] (2019)	Cross-sectional study	✓	X	X	90°	✓	✓	X	X	X	X
Lepley et al.[45] (2015)	Longitudinal case-control	✓	X	X	90°	✓	✓	X	✓	✓	✓
Lepley et al.[46] (2014)	Cross-sectional study	✓	X	X	90°	✓	X	X	✓	✓	✓
Lepley et al.[47] (2018)	Descriptive laboratory study	✓	X	X	90°	X	X	X	X	✓	✓
Leung et al.[48] (2023)	Cross-sectional observational analysis	✓	X	X	60°	✓	X	X	X	X	X

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Luc-Harkey et al.[49] (2017)	Case-control study	✓	X	X	90°	✓	✓	✓	X	X	✓
Norte et al.[50] (2018)	Cross-sectional study	✓	X	X	90°	✓	X	X	✓	✓	✓
Norte et al.[51] (2018)	Cross-sectional study	X	✓	X	Arc of 0-110°	✓	X	X	✓	✓	✓
Pietrosimone et al.[52] (2013)	Case-control experiment	✓	X	X	90°	✓	X	X	X	✓	X
Pietrosimone et al.[53] (2015)	Case-control study	✓	X	X	90°	✓	X	X	✓	X	✓
Rodriguez et al.[54] (2024)	Randomized controlled laboratory study	✓	X	X	60°	✓	✓	X	X	✓	X
Rodriguez et al.[55] (2022)	Reliability study	✓	X	X	60°	✓	✓	X	X	✓	X
Scheurer et al.[21] (2020)	Cross-sectional study	✓	X	X	90°	✓	X	✓	X	✓	✓
Sherman D et al.[56] (2023)	Cross-sectional study	✓	X	X	90°	X	X	X	✓	✓	✓
Sherman et al.[57] (2023)	Cross-sectional study	✓	X	X	90°	✓	X	X	X	X	X
Sherman et al.[58] (2023)	Cross-sectional study	✓	X	X	90°	✓	X	X	X	✓	✓

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Thomas et al.[59] (2016)	Case series	✓	X	X	90°	X	X	X	X	✓	✓
Ward et al.[60] (2016)	Cross-sectional study	✓	X	X	60°	✓	✓	✓	X	X	X
Ward et al.[61] (2018)	Cross-sectional study	✓	X	X	90°	✓	X	X	✓	✓	✓
Zarzycki et al.[15] (2020)	Longitudinal observational study	✓	X	X	90°	✓	✓	✓	✓	X	X
Zarzycki et al.[31] (2018)	Case-control study	✓	X	X	90°	✓	✓	✓	✓	X	X
Zech et al.[62] (2009)	Prospective longitudinal study	✓	X	X	90°	X	X	X	X	✓	X
Proportion (%)		88.9% (*n* = 32)	11.1% (*n* = 4)	0% (*n* = 0)	90° = 72% (*n* = 26) Other= 28%	66.7 % (*n* = 24)	36.1% (*n* = 13)	13.9% (*n* = 5)	41.1% (*n* = 15)	66.6% (*n* = 24)	61.1% (*n* = 22)

(AMT= active motor threshold, MEP= motor evoked potential, SICI= short interval cortical inhibition, MVE= maximum voluntary effort, CAR= central activation ratio)

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Table 4: Changes in TMS variables across post-operative time.

	TMS variables	Adjusted R-squared	*β* value	*p* value
1.	AMT (ACLR vs non-ACLR)	0.23	0.51	0.02
2.	AMT (ACLR vs healthy control)	0.08	0.02	0.92
3.	MEP (ACLR vs non-ACLR)	0.09	0.42	0.18
4.	MEP (ACLR vs healthy control)	-	-	-
5.	SICI (ACLR vs non-ACLR)	-	-	-
6.	SICI (ACLR vs healthy control)	-	-	-

(TMS = transcranial magnetic stimulation, AMT = active motor threshold, ACLR = anterior cruciate ligament reconstruction, MEP = motor evoked potential, SICI = short-interval intra-cortical inhibition).

Table 5: Changes in the values of PNS and knee strength variables across post-operative time.

	PNS and knee strength variables	Adjusted R-squared	*β* value	*p* value
1.	H-reflex (ACLR vs non-ACLR)	0.06	0.31	0.18
2.	H-reflex (ACLR vs healthy control)	0.09	0.1	0.76
3.	MVE (ACLR vs non-ACLR)	0.18	0.13	0.68
4.	MVE (ACLR vs healthy control)	0.0	0.33	0.34
5.	CAR (ACLR vs non-ACLR)	0.002	0.27	0.33
6.	CAR (ACLR vs healthy control)	0.07	0.17	0.61

(PNS = peripheral nerve stimulation, ACLR = anterior cruciate ligament reconstruction, MVE= maximum voluntary effort, CAR = central activation ratio).

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Table 6: Scores of modified Down's and Black scale

	Author	Items in modified Downs and Black scale													
		Reporting						External validity		Internal validity (bias)		Internal validity (confounding)		Power	**Total score (13)**
		1	2	3	6	7	10	11	12	18	20	21	22	27	
1.	Baumeister et al.[32] (2011)	1	1	1	1	1	1	1	0	1	1	0	0	1	**10**
2.	Bodkin et al.[33] (2021)	1	1	1	1	1	1	1	0	1	1	0	1	0	**10**
3.	Bodkin et al.[34] (2019)	1	1	1	1	1	1	1	0	1	1	1	1	0	**11**
4.	Burland et al.[35] (2021)	1	1	1	1	1	1	1	0	1	1	1	1	0	**11**
5.	Burland et al.[36] (2019)	1	1	1	1	1	1	1	0	1	1	1	1	0	**11**
6.	Davis et al.[37] (2023)	1	1	1	1	1	1	0	0	1	1	1	1	0	**10**
7.	Fukunaga et al.[38] (2019)	1	1	1	1	1	1	0	0	1	1	0	1	0	**9**
8.	Garcia et al.[39] (2022)	1	1	1	1	1	1	1	0	1	1	1	0	0	**10**
9.	Harkey et al.[40] (2016)	1	1	1	1	1	1	1	0	1	1	1	1	0	**11**
10.	Johnson et al.[41] (2018)	1	1	1	1	1	1	0	0	1	1	0	0	0	**8**
11.	Kuenze et al.[7] (2017)	1	1	1	1	1	1	0	0	1	1	0	0	1	**9**
12.	Kuenze et al.[42] (2015)	1	1	1	1	1	1	1	0	1	1	1	1	0	**11**
13.	Kuenze et al.[43] (2014)	1	1	1	1	1	1	1	0	1	1	1	0	0	**10**
14.	Lepley et al.[14] (2019)	1	1	1	1	1	1	1	0	1	1	1	0	0	**10**
15.	Lepley et al.[44] (2019)	1	1	1	1	1	1	1	0	1	1	1	0	0	**10**

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16.	Lepley et al.[45] (2015)	1	1	1	1	1	1	1	0	1	1	1	0	0	**10**
17.	Lepley et al.[46] (2014)	1	1	1	1	1	1	0	0	1	1	1	1	0	**10**
18.	Lepley et al.[47] (2018)	1	1	1	1	1	1	1	0	1	1	0	0	0	**9**
19.	Leung et al.[48] (2023)	1	1	1	1	1	1	1	0	1	1	1	1	0	**11**
20.	Luc-Harkey et al.[49] (2017)	1	1	1	1	1	1	1	0	1	1	0	0	1	**10**
21.	Norte et al.[50] (2018)	1	1	1	1	1	1	1	0	1	1	1	1	1	**12**
22.	Norte et al.[51] (2018)	1	1	1	1	1	1	0	0	1	1	1	0	0	**9**
23.	Pietrosimone et al.[52] (2013)	1	1	1	1	1	1	1	0	1	1	1	1	0	**11**
24.	Pietrosimone et al.[53] (2015)	1	1	1	1	1	1	1	0	1	1	1	1	0	**11**
25.	Rodriguez et al.[54] (2024)	1	1	1	1	1	1	1	0	1	1	1	1	1	**12**
26.	Rodriguez et al.[55] (2022)	1	1	1	1	1	1	1	0	1	1	1	1	0	**11**
27.	Scheurer et al.[21] (2020)	1	1	1	1	1	1	1	0	1	1	0	0	0	**9**
28.	Sherman et al.[56] (2023)	1	1	1	1	1	1	0	0	1	1	1	1	0	**10**
29.	Sherman et al.[57] (2023)	1	1	1	1	1	1	1	0	1	1	0	0	0	**9**
30.	Sherman et al.[58] (2023)	1	1	1	1	1	1	1	0	1	1	1	1	0	**11**
31.	Thomas et al.[59] (2016)	1	1	1	1	1	1	0	0	1	1	1	0	0	**9**
32.	Ward et al.[60] (2016)	1	1	1	1	1	1	1	0	1	1	1	1	1	**12**
33.	Ward et al.[61] (2018)	1	1	1	1	1	1	0	0	1	1	0	0	0	**8**
34.	Zarzycki et al.[15] (2020)	1	1	1	1	1	1	1	0	1	1	0	0	0	**9**

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35.	Zarzycki et al.[31] (2018)	1	1	1	1	1	1	1	0	1	1	1	0	1	**11**
36.	Zech et al.[62] (2009)	1	1	1	1	1	1	1	0	1	1	1	0	0	**10**

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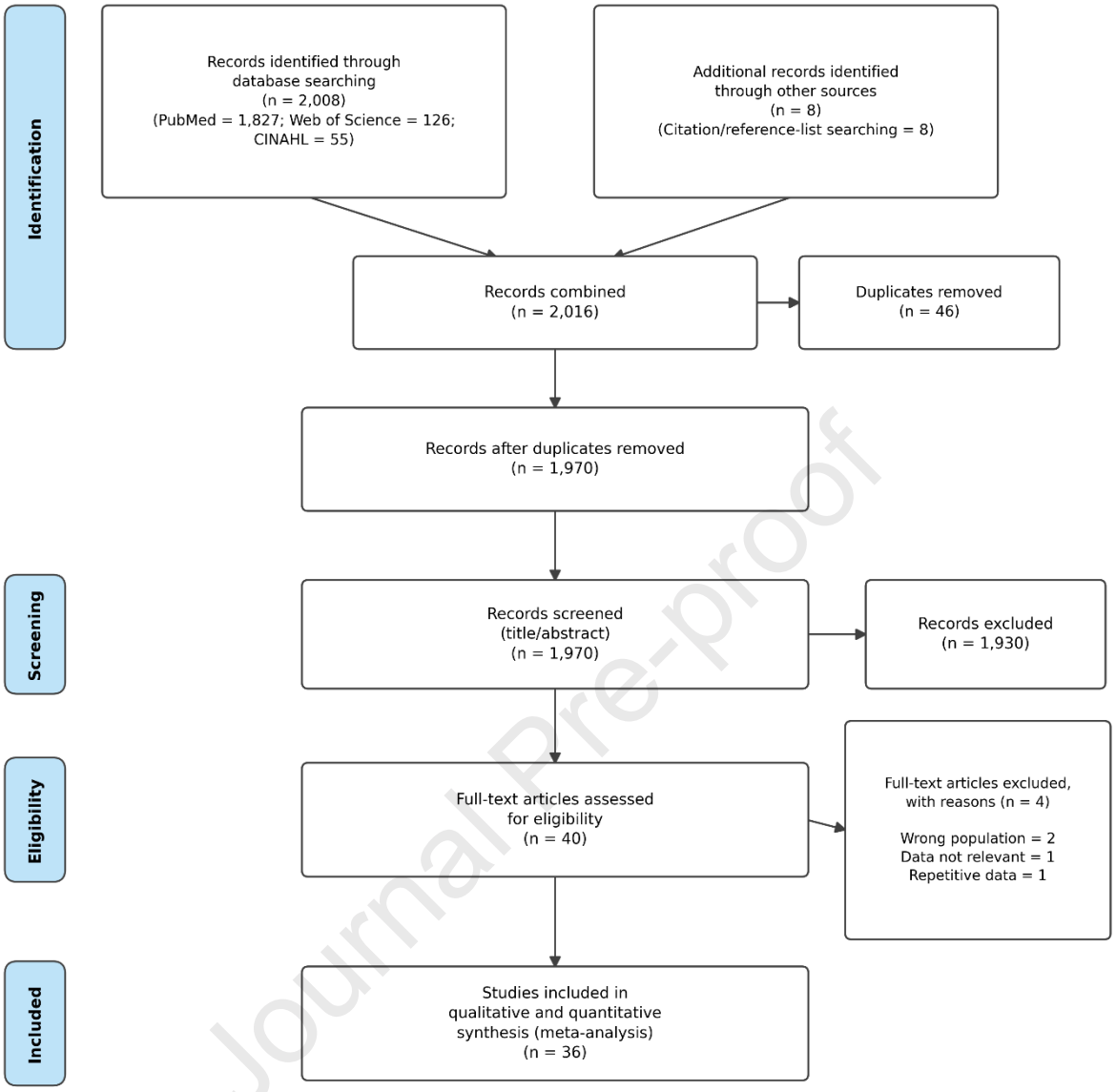
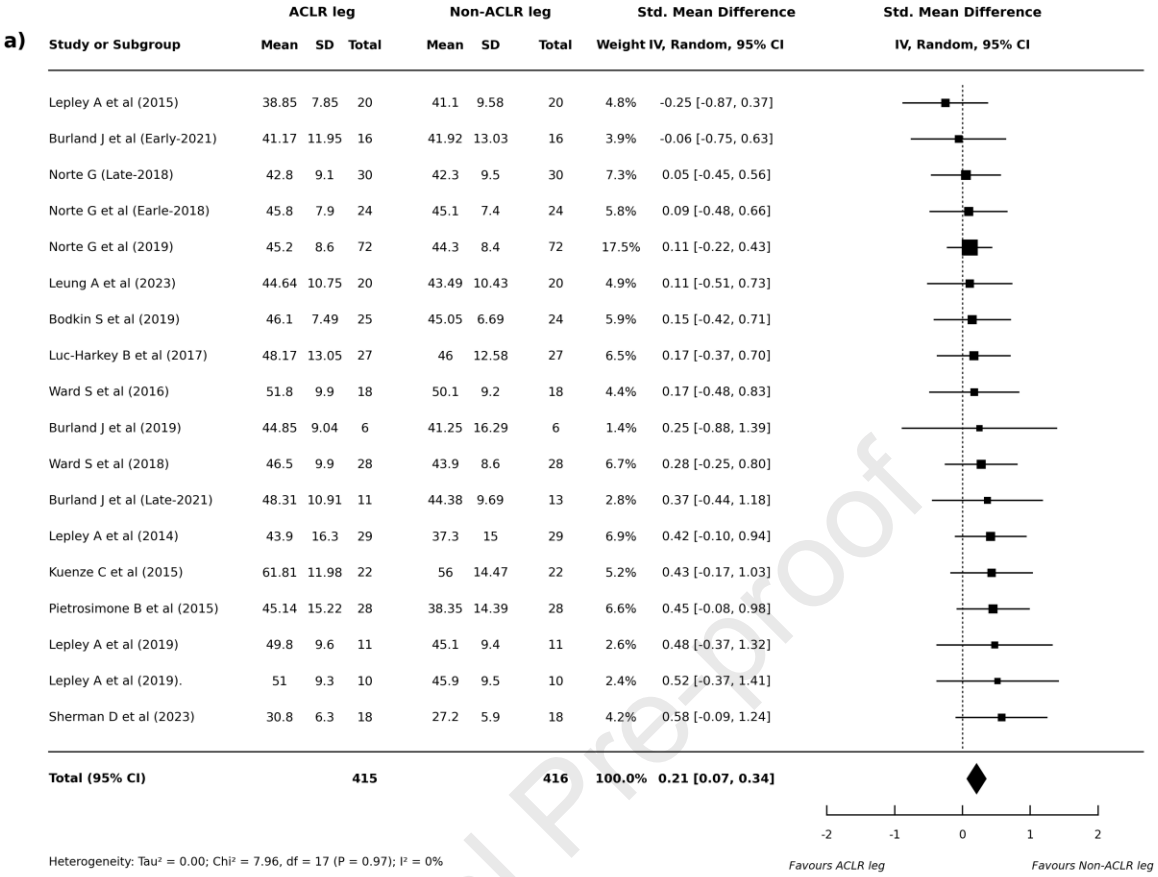


Figure 1: A schematic of PRISMA flow diagram of the identification and selection of the studies included in study.



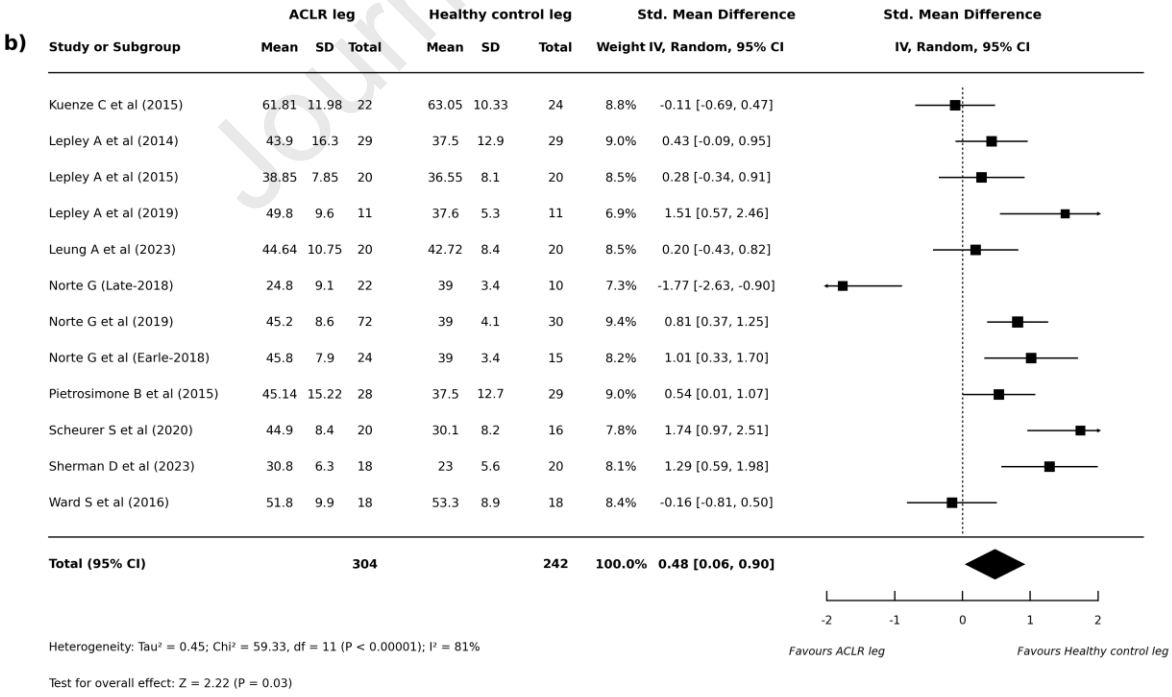


Figure 2: Forest plots depicting the pooled standardized mean difference (95% CI) of quadriceps AMT

(AMT = active motor threshold)

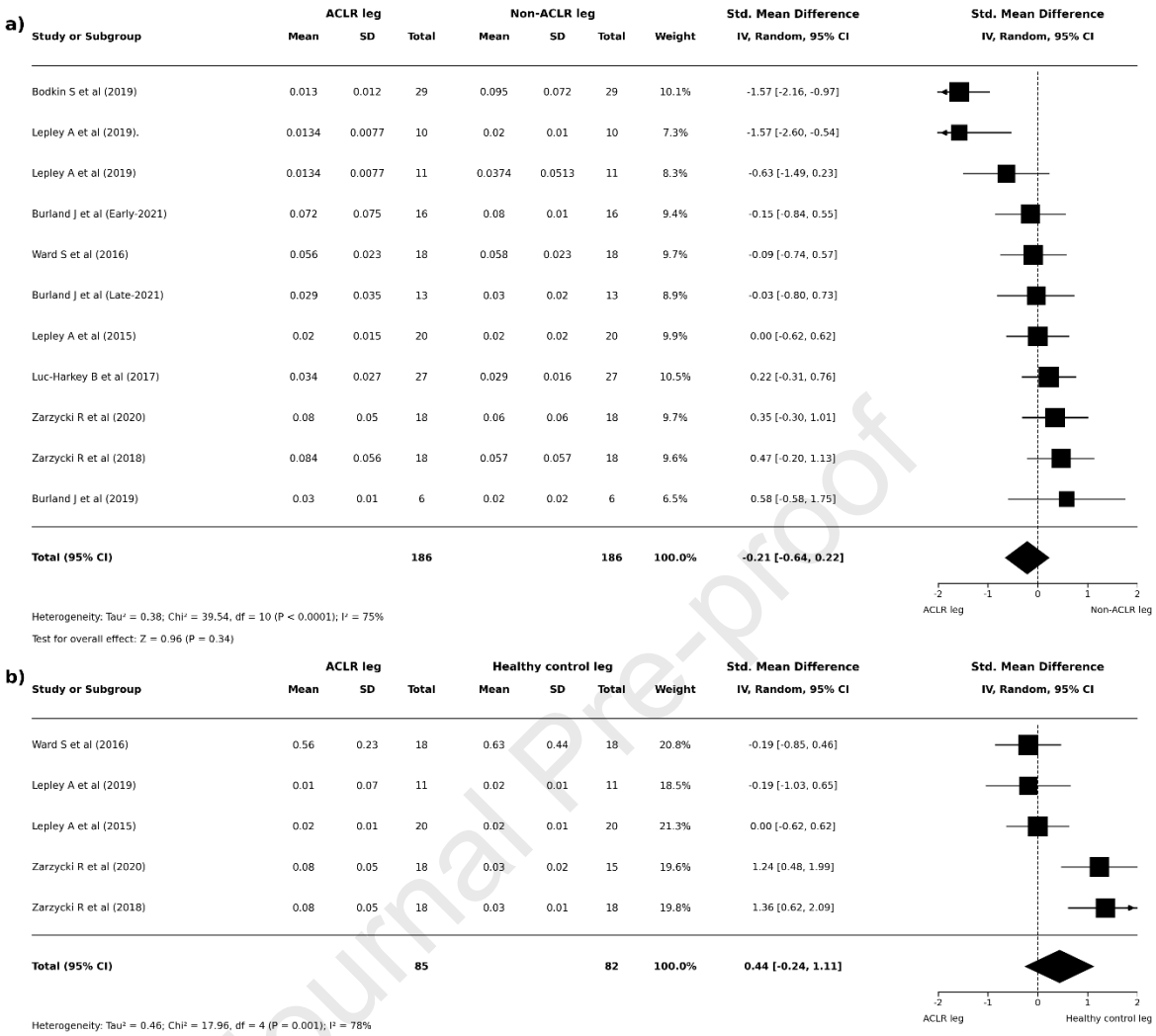


Figure 3: Forest plots depicting the pooled standardized mean difference (95% CI) of quadriceps MEP/M_{MAX}

(MEP/M_{MAX} = motor evoked potential/Maximal M-wave)

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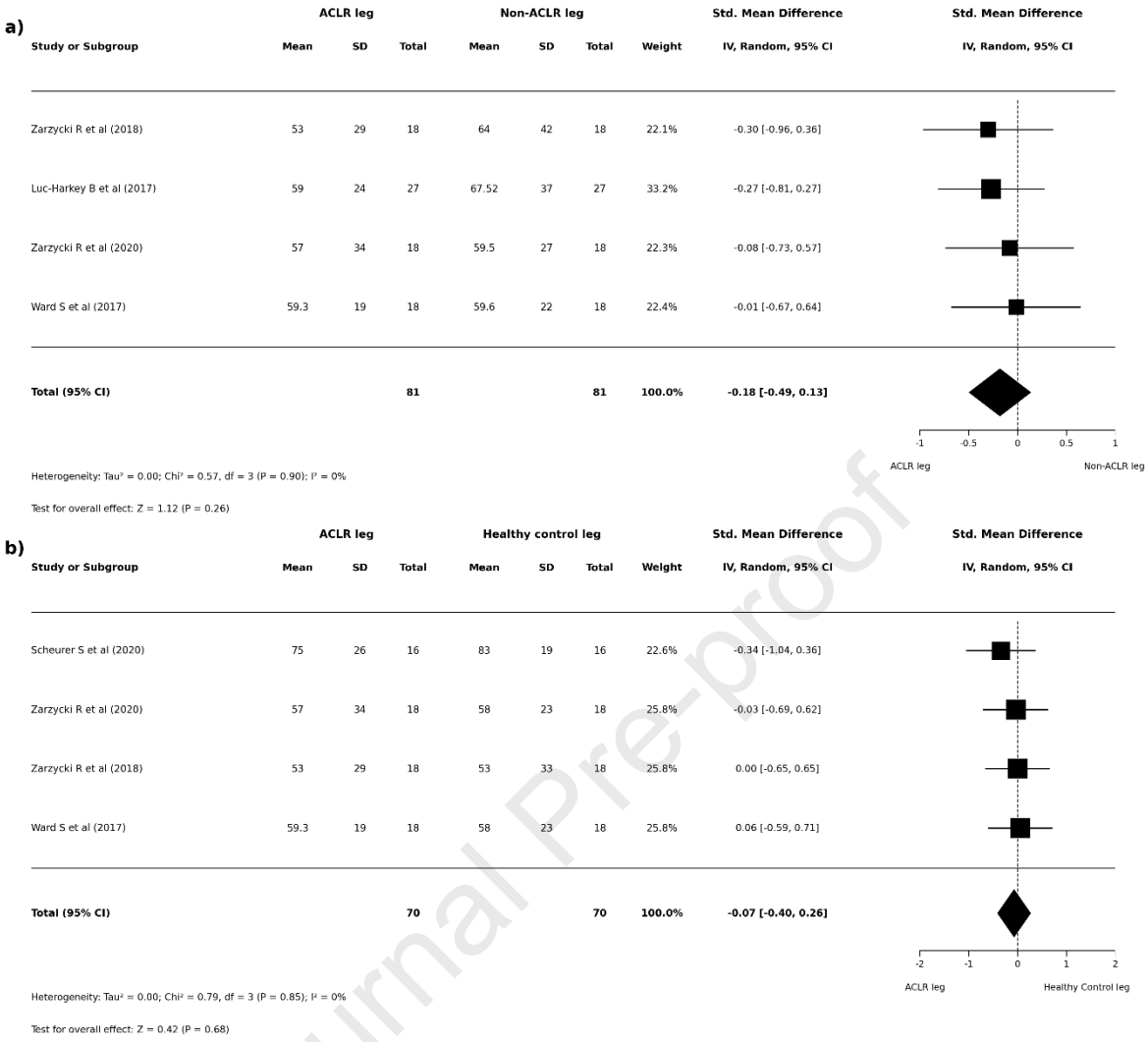


Figure 4: Forest plots depicting the pooled standardized mean difference (95% CI) of quadriceps SICI (SICI = short interval cortical inhibition)

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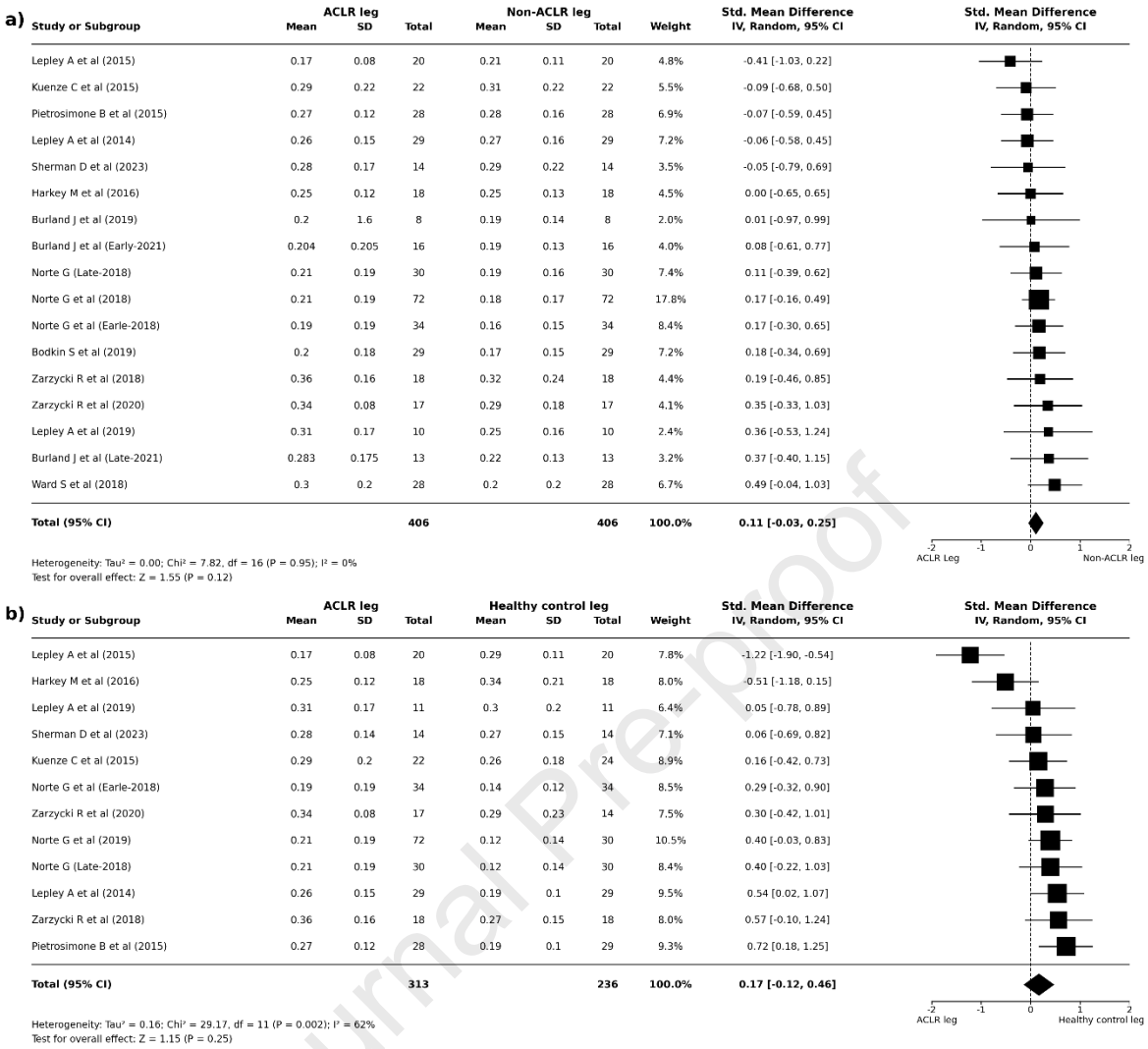


Figure 5: Forest plots depicting the pooled standardized mean difference (95% CI) of quadriceps H-reflex

(H-reflex = Hoffmann reflex)

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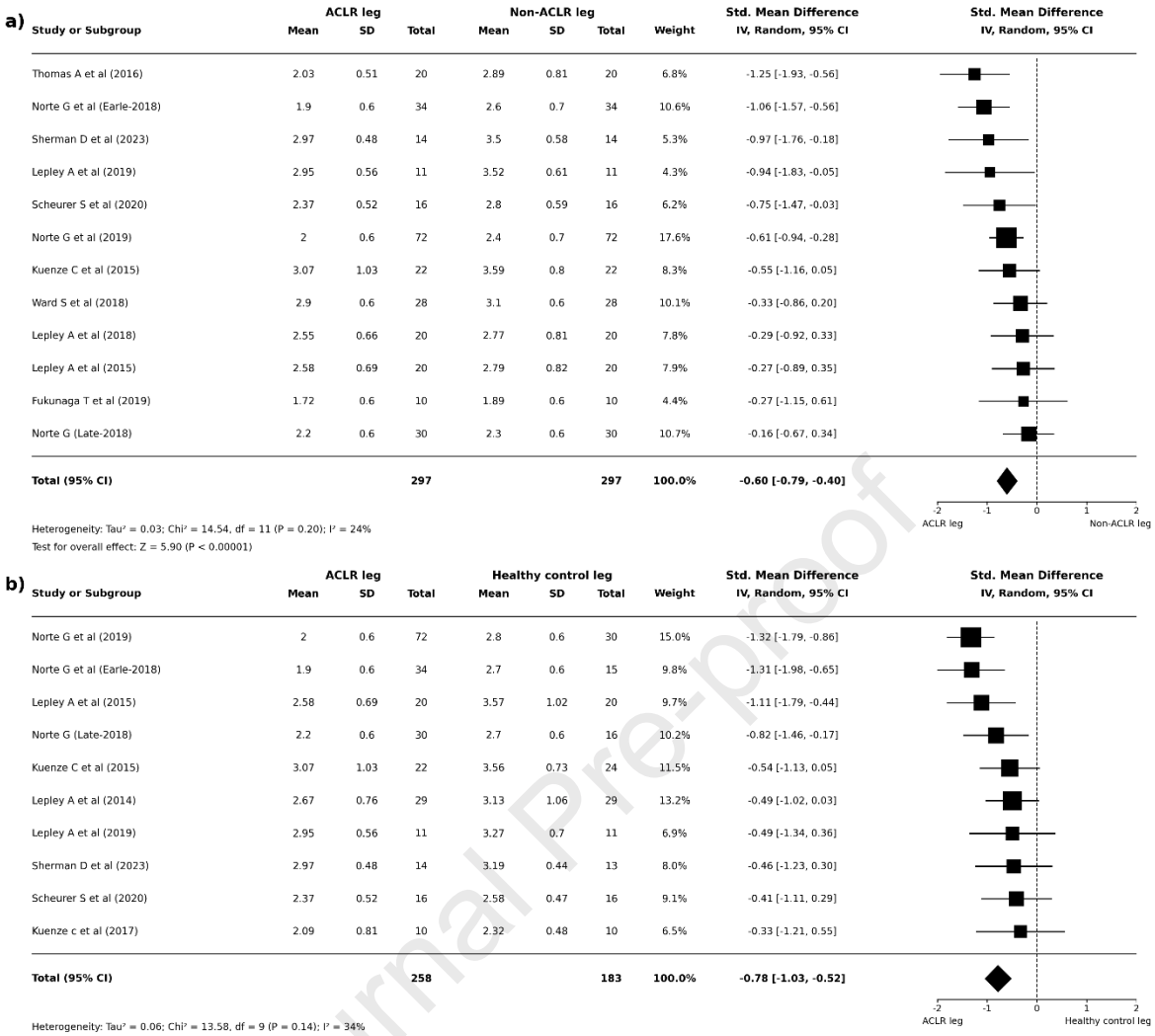


Figure 6: Forest plots depicting the pooled standardized mean difference (95% CI) of quadriceps MVE (MVE = maximum voluntary effort)

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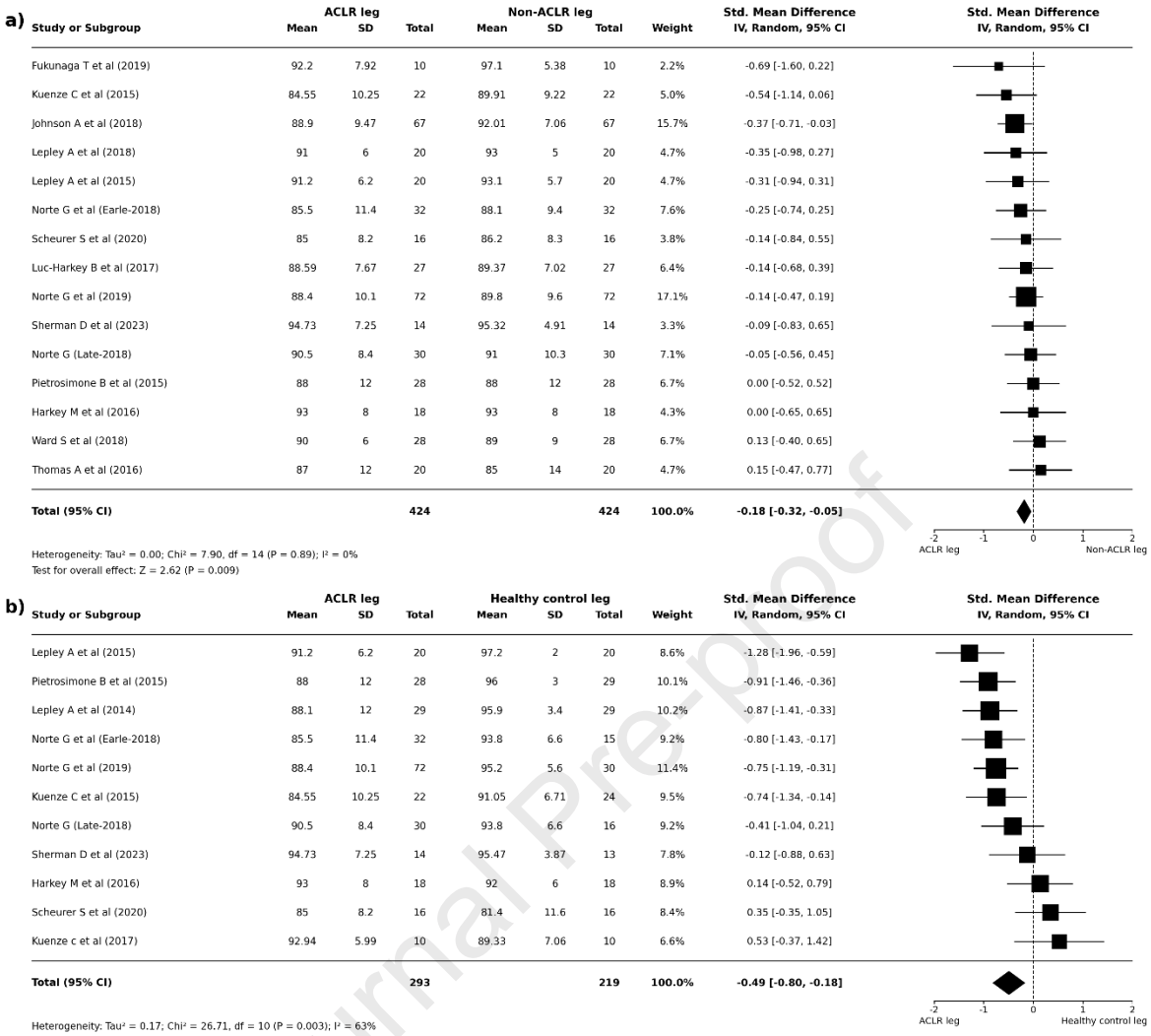


Figure 7: Forest plots depicting the pooled standardized mean difference (95% CI) of quadriceps CAR

(CAR = central activation ratio)

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Highlights:

- Corticospinal excitability is reduced following unilateral Anterior Cruciate Ligament reconstruction (ACLR).
- Persistent quadriceps weakness and reduced voluntary activation were identified after ACLR.
- Substantial heterogeneity exists in transcranial magnetic stimulation (TMS) and peripheral nerve stimulation (PNS) assessment methodologies.
- Spinal reflex excitability did not differ between ACLR and healthy control limbs.
- Findings support targeted rehabilitation of quadriceps neuromuscular pathways.

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Statement for studies in humans/animals:

This study is a systematic review and meta-analysis of previously published studies and did not involve direct experimentation on humans or animals. Therefore, ethical approval and informed consent were not required. The review protocol was registered in PROSPERO, and the registration number is provided in the manuscript.

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Declaration of competing interests:

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The authors declare no conflict of interest.

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