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## RESEARCH PAPER

# Task-specific strength increases after lower-limb compound resistance training occurred in the absence of corticospinal changes in vastus lateralis

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## Abstract

Neural adaptations subserving strength increases have been shown to be task-specific, but responses and adaptation to lower-limb compound exercises such as the squat are commonly assessed in a single-limb isometric task. This two-part study assessed neuromuscular responses to an acute bout (Study A) and 4 weeks (Study B) of squat resistance training at 80% of one-repetition-maximum, with measures taken during a task-specific isometric squat (IS) and non-specific isometric knee extension (KE). Eighteen healthy volunteers ( $25 \pm 5$  years) were randomised into either a training ( $n = 10$ ) or a control ( $n = 8$ ) group. Neural responses were evoked at the intracortical, corticospinal and spinal levels, and muscle thickness was assessed using ultrasound. The results of Study A showed that the acute bout of squat resistance training decreased maximum voluntary contraction (MVC) for up to 45 min post-exercise ( $-23\%$ ,  $P < 0.001$ ). From 15–45 min post-exercise, spinally evoked responses were increased in both tasks ( $P = 0.008$ ); however, no other evoked responses were affected ( $P \geq 0.240$ ). Study B demonstrated that following short-term resistance training, participants improved their one repetition maximum squat ( $+35\%$ ,  $P < 0.001$ ), which was reflected by a task-specific increase in IS MVC ( $+49\%$ ,  $P = 0.001$ ), but not KE ( $+1\%$ ,  $P = 0.882$ ). However, no training-induced changes were observed in muscle thickness ( $P = 0.468$ ) or any evoked responses ( $P = 0.141$ ). Adjustments in spinal motoneuronal excitability are evident after acute resistance training. After a period of short-term training, there were no changes in the responses to central nervous system stimulation, which suggests that alterations in corticospinal properties of the vastus lateralis might not contribute to increases in strength.

## KEYWORDS

adaptation, corticospinal excitability, exercise, intracortical inhibition, squat

## 1 | INTRODUCTION

Adaptations of neural function in response to resistance training play an important role in the development of strength, particularly in the early stages (<4 weeks) of training (Carroll, Riek, & Carson, 2001;

Sale, 1988). Previous research has demonstrated a number of neural adaptations concurrent with increased strength, including decreased intracortical inhibition (Weier, Pearce, & Kidgell, 2012), increased corticospinal (Weier et al., 2012) and motoneuronal excitability (Nuzzo, Barry, Jones, Gandevia, & Taylor, 2017), as well as increased

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firing rates and decreased recruitment thresholds of motor units (Del-Vecchio et al., 2019). In recent years, transcranial magnetic stimulation (TMS) of the primary motor cortex and electrical stimulation of the corticospinal tract at subcortical levels have been performed to assess these adaptations (for reviews see Mason et al., 2019; Siddique et al., 2020), with the change in evoked electromyographical (EMG) responses used as indices of adaptation.

The neural adaptations to resistance training are considered, by some, to be a form of motor learning, as the individual learns to produce specific patterns of muscle recruitment (Carroll et al., 2001). Indeed, motor learning and resistance training share similar patterns of adaptation, such as a reduction in motor cortex inhibition and an increase in corticospinal excitability (Leung, Rantalainen, Teo, & Kidgell, 2017; Ljubisavljevic, 2006; Weier et al., 2012), and it is well established that the adaptations to motor training are specific to the trained task (Beck et al., 2007; Schubert et al., 2008; Taube, Gollhofer, & Lauber, 2020). Specific to resistance training, when two distinct tasks are employed (ballistic vs. sustained contractions), neural adaptations are only demonstrated when the corticospinal tract is stimulated during the trained task (Giboin, Weiss, Thomas, & Gruber, 2018). The notion of utilising a task-specific testing task has been echoed throughout the past decade, with researchers highlighting the need to assess neurophysiological variables during the motor task used as in the intervention (Avela & Gruber, 2011; Kalmar, 2018; Sidhu, Cresswell, & Carroll, 2013).

Despite the requirement for task-specific neural assessment, adaptation in response to lower-limb compound resistance training has not been assessed in a task-specific manner. For instance, Weier et al. (2012) assessed corticospinal responses in a single-limb isometric task following 4 weeks of squat resistance training. Similarly, following an acute bout of squat training, Thomas et al. (2018) demonstrated no changes in measures of corticospinal function when assessed in a single-limb isometric task. Thus, a common approach in the literature is to assess corticospinal adaptations to squat training by evoking responses in the knee extensors during a single-limb isometric testing task, with considerably different neuromechanical characteristics to the squat exercise. Indeed, our laboratory recently demonstrated poor agreement between measures of short-interval intracortical inhibition (SICI) and corticospinal excitability when measured during isometric squat (IS) and knee extension (KE) tasks at the same relative intensity (Brownstein et al., 2018a). Given the disparities in neural activity between the two tasks, it is possible that neural adaptations to squat resistance training could be masked when measuring responses during isometric KE. As such, investigating neural changes to squat exercise using a task that more closely replicates the squat is warranted.

Considering that improving bilateral lower-limb force production is a goal of neurorehabilitation and athletic training programmes (Baker & Nance, 1999; Carr & Shepherd, 2010; Ng & Shepherd, 2000), understanding the mechanisms of neural adaptations in response to lower-limb compound interventions is necessary to inform exercise prescription in a range of populations. Consequently, determining appropriate testing methodologies in order to capture these neural

### New Findings

- **What is the central question of the study?**  
Are corticospinal responses to acute and short-term squat resistance training task-specific?
- **What is the main finding and its importance?**  
A single bout of resistance training increased spinal excitability, but no changes in corticospinal responses were noted following 4 weeks of squat training despite task-specific increases in strength. The present data suggest that processes along the corticospinal pathway of the knee extensors play a limited role in the task-specific increase in strength following resistance training.

adaptations is imperative in obtaining valid results. Therefore, the present two-part study aimed to quantify the corticospinal responses to acute (Study A) and short-term (4 weeks; Study B) squat resistance training in a task-specific IS (Brownstein et al., 2018a) for the first time and compare it with responses to single-limb isometric KE. It was hypothesised that (1) acute resistance training would result in an increase in corticospinal and spinal excitability; (2) short-term resistance training would result in increased dynamic strength and corticospinal excitability and a reduction in intracortical inhibition; and (3) in both Study A and B, the IS task would demonstrate greater changes in evoked corticospinal responses, due to the task-specific nature of assessment.

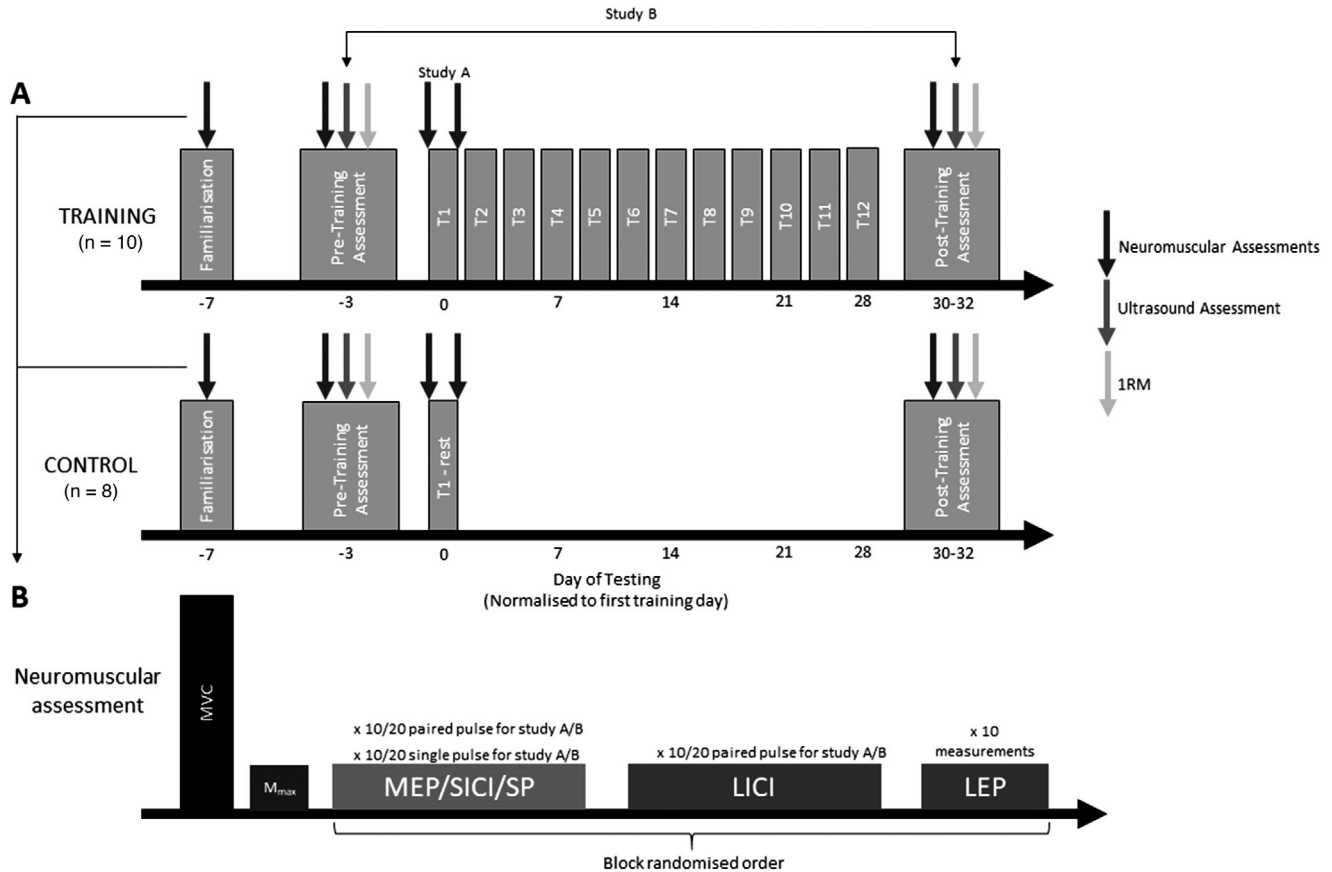
## 2 | METHODS

### 2.1 | Ethical approval

The study received institutional ethical approval from the Northumbria University Health and Life Sciences Research Ethics Committee (submission reference: 9610) and was conducted according to all aspects of the *Declaration of Helsinki*, apart from registration in a database. Participants provided written, informed consent to volunteer for the study.

### 2.2 | Participants

Based on the effect sizes reported in Weier et al. (2012), four participants per group were needed to detect statistically significant group  $\times$  time interactions in CNS function (corticospinal excitability, short intracortical inhibition) following 4 weeks of squat resistance training ( $\alpha = 0.05$ ,  $1 - \beta = 0.80$ ). To increase statistical power ( $\alpha = 0.001$ ,  $1 - \beta = 0.99$ ), 18 healthy young participants (mean  $\pm$  SD age  $25 \pm 5$  years; height  $176 \pm 9$  cm; mass  $76.4 \pm 9.5$  kg; five females) were recruited for the study and were randomised into either training ( $n = 10$ ; 4 females) or control ( $n = 8$ ; 1 female) groups. All participants were considered recreationally active, defined as meeting the World



**FIGURE 1** Overview of the experimental design for both squat and control groups. (a) Schedule of the training/control period. (b) Details of the neuromuscular assessment. All neuromuscular assessments were conducted in both specific (isometric squat) and non-specific (isometric knee extensor) tasks. Participants were randomly allocated to experimental and control groups

Health Organization's recommendation of 150 min moderate activity per week (World Health Organisation, 2010), but were untrained with regards to lower-body resistance training (i.e. had not performed lower-body resistance training more than once per week prior to the study). Of the five female participants, four were eumenorrhoeic, reporting average menstrual cycle durations between 26 and 30 days and no use of hormonal contraceptives for >6 months, and were tested in the early follicular phase (day 1–7) of the menstrual cycle. The remaining female was utilising a contraceptive implant (Nexplanon®). This permitted the testing of neural adaptation without the influence of endogenous hormone changes on neuromuscular function (Ansdell et al., 2019). Participants were instructed to refrain from alcohol (24 h), caffeine consumption (12 h), and strenuous lower-body physical activity (48 h) before experimental visits. All participants completed a TMS safety screening questionnaire (Rossi, Hallett, Rossini, & Pascual-Leone, 2011).

### 2.3 | Experimental design

Participants in the training group visited the laboratory 15 times in total, including a familiarisation visit, pre-training assessment, 12 training sessions (separated by a minimum of 24 h), and a post-training assessment (see Figure 1 for details). Participants in the

control group visited the laboratory four times (familiarisation, pre- and post-4 weeks of habitual activity, and for the acute visit; see below). Neuromuscular function was assessed during non-specific isometric KE, and a task-specific IS. Electromyographic responses were assessed in the vastus lateralis (VL) as this muscle is heavily implicated in knee extension, while the knee extensors are prime movers in the squat exercise (Delgado, Drinkwater, Banyard, Haff, & Nosaka, 2019; Lahti, Hegyi, Vigotsky, & Ahtiainen, 2019) and were considered an appropriate muscle group for the investigation. Moreover, we selected the VL as opposed to the rectus femoris (RF) since we have previously shown that at submaximal contraction intensities, the EMG activity and evoked responses in the RF exhibit poorer agreement between the IS and KE tasks compared to the VL (Brownstein et al., 2018a), which could potentially make the RF less sensitive to changes. Also, the VL is a monoarticular muscle involved solely in knee extension, thus functionally playing a similar role in IS and KE. Furthermore, unlike in the RF, no differences were noted previously in the EMG activity measured in the VL during both tasks (Brownstein et al., 2018a), and thus we deemed the VL more suitable for comparison of responses between tasks. The familiarisation session took place 7 days before the first training session, and involved habituation with the neurostimulation procedures, squat exercise and the neuromuscular assessment protocols.

## 2.4 | Study A: responses to an acute training session

Responses to acute lower-body compound resistance exercise were assessed during the first training session for Study B. Neuromuscular function was assessed before, immediately post (i.e. began within 60 s of finishing exercise), and 15, 30, 45 min post a bout of free-weight back squat exercise in order to discern the immediate neural adjustments to a session of resistance training. These time points were chosen as the acute corticospinal adjustments after resistance exercise appear to peak within the hour post-exercise (Latella, Hendy, Vanderwesthuizen, & Teo, 2018; Nuzzo, Barry, Gandevia, & Taylor, 2016). A baseline neuromuscular assessment (PRE) was performed in both IS and KE tasks, in a randomised order, with 10 min rest between assessments. Initially, two (3 s) maximal isometric voluntary contractions (MVC) were performed. If participants MVC values were >5% apart, a third MVC was performed. Following this, all stimuli were delivered during a 10% contraction as it has been shown that resistance training-induced changes in CNS are only observable when assessed during contraction (Siddique et al., 2020). Briefly, one percutaneous nerve stimulation was delivered to elicit a maximal compound action potential ( $M_{max}$ ), 10 electrical stimuli were delivered to the lumbar spinal tract to evoke lumbar evoked potentials (LEPs; Škarabot et al., 2019b), and 10 single and 20 paired-pulse TMS were delivered during IS and KE to assess corticospinal excitability, SIC1, long-interval intracortical inhibition (LICI) and TMS silent periods (SPs) in a pseudorandomised order. Subsequently, the training group performed the first training session (see 'Training protocol'), while the control group rested for 25 min. Immediately upon completion of the last set of training or rest, the neuromuscular assessment was performed again in both testing tasks (POST0) and again at 15 (POST15), 30 (POST30) and 45 min (POST45) after completion of the last set. The neuromuscular assessments involving electrical stimulation of the femoral nerve and lumbar spinal tract, and single- and paired-pulse TMS (pseudorandomised order) lasted 5 min per task (pseudorandomised, counterbalanced order), and were performed consecutively at each time point.

## 2.5 | Study B: responses to short-term training

The baseline visit began with a resting ultrasound assessment to discern VL thickness (see 'Ultrasound'). Subsequently, the neuromuscular assessments (in both IS and KE tasks, pseudorandomised order) were performed with 20 min rest between the two in order to negate the influence of fatigue (Carroll, Taylor, & Gandevia, 2017). Participants performed three MVCs separated by 30 s. The greatest instantaneous force of the three was used to set a target guideline at 10% MVC, whereby all subsequent stimulations were performed. Next, SIC1 was assessed from 20 conditioned and 20 unconditioned TMS pulses, of which the unconditioned pulses were also used as an index of corticospinal excitability (expressed relative to  $M_{max}$ ), and the TMS silent periods were used as an index of neural inhibition. LICI was then assessed using 20 conditioned and 20 unconditioned pulses, and 10 LEPs were evoked to assess spinal motoneuron excitability.

Following the neuromuscular assessments, participants were given 20 min rest, then performed a warm-up followed by a dynamic one repetition maximum (1RM) squat. The warm-up consisted of 5 min cycling at 1.5 W ( $\text{kg body mass}^{-1}$ ), followed by warm-up sets of one to five repetitions of back squats (high bar position), beginning with an unloaded barbell and progressing to 50, 70, 80 and 90% of their estimated 1RM. The load on the bar was then incremented by 2–5% until participants could not complete one repetition. A maximum of three attempts at each weight were permitted, and participants were required to descend to a depth corresponding to 90 deg of knee flexion. Squat depth was verified by tracking the position of the barbell (GymAware, Kinetic Performance, Canberra, Australia). Participants performed a testing visit 2–4 days following the final training session to permit recovery of exercise-induced neuromuscular dysfunction (Howatson, Brandon, & Hunter, 2016) and TMS-evoked responses (Škarabot et al., 2019c). Post-training assessments were performed at absolute (10% of pre-training MVC) and relative (10% of post-training MVC) intensities.

## 2.6 | Training protocol

The training protocol for Study B was similar to that used in Weier et al. (2012), which showed large changes in corticospinal excitability and SIC1 following 4 weeks of resistance training. Participants performed three supervised training sessions per week for 4 weeks. Following a warm up consisting of 5 min on a cycle-ergometer at 1.5 W ( $\text{kg body mass}^{-1}$ ), participants performed three to five back squat repetitions, with the load gradually increased from an unweighted bar to 25, 50, 75, then 90% of the target weight (5, 5, 3 and 3 repetitions, respectively), after which they completed four sets of six to eight repetitions with the target weight (80% 1RM), with 5 min of rest between sets. This training protocol was previously shown to be effective in eliciting maximum strength improvements (Weier et al., 2012). The velocity of each repetition was controlled using an audible electronic metronome and visual feedback of bar displacement (GymAware) to ensure a 3 s eccentric phase, 3 s concentric phase, and adequate squat depth (90 deg knee flexion; Weier et al., 2012). The metronome paced approach to strength training was utilised as previous research has demonstrated that corticospinal adaptations are apparent only after externally paced, and not self-paced, strength training (Ackerley, Stinear, & Byblow, 2011; Leung et al., 2017). Once participants could complete four sets of eight repetitions at the target load, the load was increased by 5%, whereas the load was maintained if participants were unable to complete all repetitions (see Figure 4a for depiction of progression in training load). In Study A, five participants were able to successfully perform four sets of eight repetitions, and five participants performed three sets of eight and one set of six. All participants performed the 12 training sessions in Study B.

## 2.7 | Isometric knee extension

Isometric knee extension force (N) was measured using a calibrated load cell (MuscleLab force sensor 300; Ergotest Technology,

Prosrgrunn, Norway). The load cell was fixed to a custom-built chair and strapped with a non-compliant cuff to the participant's right leg, superior to the ankle malleoli. Hip and knee angles were set at 90 deg flexion measured using a goniometer at the beginning of the trial and visually inspected by the investigators throughout the trial to ensure consistency. Participants were instructed to maintain the same posture throughout trials. Verbal encouragement was provided by the investigators during MVCs, and real-time force feedback was provided to the participants on a computer screen directly in front of them (Spike2 v8; Cambridge Electronic Design (CED), Cambridge, UK). During stimulation procedures, a horizontal line corresponding to 10% MVC was provided on the screen and participants were instructed to try to match the line as closely as possible.

## 2.8 | Isometric squat

A detailed procedure for the isometric squat assessment task has been previously published (Brownstein et al., 2018a). A force plate placed directly under the right foot of the participants (Type 9286B; Kistler Group, Winterthur, Switzerland) was used to measure isometric squat force, with a sampling frequency of 5 kHz. Participants were seated on a bench placed directly under a fixed barbell to provide support during isometric contraction. The barbell height was adjusted according to individual torso length and positioned on the shoulders. Knee and hip angle were kept at 90 deg as measured by the goniometer at the beginning of the trial. Participants were instructed to keep their feet at hips width apart with the toes pointing forwards. The position of the foot was marked on the force plate with tape to ensure consistent placement throughout the trials and maintenance of knee and hip joint angles. Additionally, the position of the hip and knee were visually inspected by the investigators throughout the trial to ensure consistency. This knee and hip position also ensured similar VL muscle length in both IS and KE tasks and thus avoided the muscle length-related differences in neural recruitment (Doguet et al., 2017). Participants had freedom in choosing their hand position on the bar, but were instructed to keep it consistent throughout the protocol. Participants were instructed to keep the neck in an anatomical zero (neutral) position and orient their gaze on the screen in front of them where force feedback was provided. This indirectly ensured consistency of head position throughout TMS trials. During contractions, participants were instructed to exert force upwards against the bar using their whole body (Bishop et al., 2017). Similar to KE, verbal encouragement was provided by the investigators and real-time force feedback was provided to the participants on a computer screen directly in front of them, including a horizontal guideline at 10% MVC for stimulations (Spike2 v8).

## 2.9 | Electromyography

Surface bipolar EMG activity was recorded using self-adhesive surface electrodes (8 mm diameter, 20 mm inter-electrode distance; Kendall 1041PTS, Henley's Medical, Welwyn Garden City, UK) placed over VL muscle according to SENIAM recommendations (Hermens, Freriks,

Disselhorst-Klug, & Rau, 2000), with the reference electrode placed over the patella. Prior to electrode placement, the skin was thoroughly prepared including shaving, abrading with preparation gel and wiping with an alcohol swab. The EMG signal was amplified ( $\times 1000$ ), band pass filtered (20–2000 Hz; Neurolog System, Digitimer Ltd, Welwyn Garden City, UK), digitised (4 kHz; CED 1401), acquired and analysed off line (Spike2 v8).

## 2.10 | Percutaneous nerve stimulation

Electrical stimuli were delivered over the femoral nerve via a constant-current stimulator (1 ms pulse duration; Digitimer DS7AH) using self-adhesive surface electrodes (CF3 200; Nidd Valley Medical Ltd, Harrogate, UK). The cathode was placed over the femoral nerve in the femoral triangle with the anode positioned between the greater trochanter and iliac crest. The intensity of stimulation was increased in 20 mA stepwise increments until  $M_{\max}$  plateaued, upon which the intensity was increased by 30% to ensure the stimulation was supra-maximal. The same procedure was employed during IS ( $164 \pm 81$  mA) and KE ( $167 \pm 86$  mA).

## 2.11 | Electrical spinal tract stimulation

Lumbar evoked potentials were elicited with a constant-current stimulator (1 ms pulse duration; Digitimer DS7AH) via self-adhesive electrodes (Nidd Valley Medical Ltd, Bordon, UK) during a contraction at 10% MVC. The cathode ( $5 \times 9$  cm) was centred over the first lumbar ( $L_1$ ) spinous process, with the long axis of the electrode aligned to the centre of the vertebral column. The surface area of the cathode covered two spinous processes above and below the centre point ( $T_{11}$ – $L_3$ ). The bottom of the anode (circular shape; 3.2 cm diameter) was placed in the midline of the vertebral column 5 cm above the upper edge of the cathode, corresponding to the level of the eighth thoracic spinous process ( $T_8$ ). These electrode positions were chosen based on modelling studies that showed the greatest electrical field magnitude was induced between  $T_{10}$  and  $T_{12}$  spinous processes as the electric field is highest between the stimulating electrodes (Kuck, Stegeman, & van Asseldonk, 2017). As a result, the site of the greatest spinal cord activation is likely to occur between  $L_1$  and  $L_5$  spinal cord segments, corresponding to the motoneuron pool of the quadriceps (Sayenko et al., 2015). This stimulating site has been shown to activate corticospinal axons at the level of lumbar spinal segments (Škarabot et al., 2019b). Latency of the response was constantly monitored for an abrupt change with increases in stimulus intensity, to minimise the possibility of dorsal roots being activated (Taylor & Gandevia, 2004). To ensure ventral roots were not activated, a change in LEP size with increased contraction strength was ensured before the testing protocol (Martin, Butler, Gandevia, & Taylor, 2008). The electrodes remained in place throughout Study A ensuring consistency of stimulating site. In Study B, the electrodes were repositioned following 4 weeks of resistance training using anatomical landmarks as reference points (Nuzzo et al., 2017). The intensity of stimulation was standardised to  $\sim 15$ – $25\%$   $M_{\max}$  evoked at

10% MVC, and remained constant from PRE to POST45 in Study A (IS:  $184 \pm 59$  mA, KE:  $168 \pm 59$  mA), and from pre- to post-training during Study B (IS:  $173 \pm 54$  mA, KE:  $156 \pm 54$  mA).

## 2.12 | Transcranial magnetic stimulation

Single- and paired-pulse TMS were delivered over the motor cortex via a concave double-cone coil using a Magstim 200<sup>2</sup> magnetic stimulator (Magstim Co., Ltd, Whitland, UK). Initially, the junction of the double-cone coil was placed 1–2 cm left of the vertex and oriented to induce posterior-to-anterior cortical current. After that, the optimal location ('hotspot') was determined by locating the coil position that elicited the greatest MEP amplitude in the VL muscle at 50% stimulator output during a 10% MVC and was subsequently marked with indelible ink. After that, active motor threshold (AMT) was determined during a 10% MVC and defined as the intensity that elicited a MEP amplitude in the VL muscle of  $>200$   $\mu$ V in three out of five trials (Kidgell, Stokes, Castricum, & Pearce, 2010). The 'hotspot' and AMT were both determined separately for KE and IS. For single-pulse TMS, the stimulus intensity was set at 120% AMT as it corresponds to the ascending portion of the stimulus–response curve and is thus sensitive to changes in corticospinal excitability (Han, Kim, & Lim, 2001) and has previously been shown to increase following resistance training (Weier et al., 2012). For SICI, a conditioning stimulus intensity of 70% AMT was delivered prior to the test stimulus with an interstimulus interval (ISI) of 2 ms (Brownstein et al., 2018b). For LICI, a conditioning stimulus of 120% AMT and an ISI of 100 ms were used (O'Leary, Morris, Collett, & Howells, 2015). In Study A, AMT was determined at the beginning of the experimental session (IS:  $46 \pm 8\%$ , KE:  $45 \pm 8\%$  of stimulus output;  $P = 0.274$ ) and the stimulus intensities were consistently kept the same throughout the trial. In Study B, AMT was assessed before (KE:  $47 \pm 8\%$ , IS:  $47 \pm 7\%$ ;  $P = 0.335$ ) and after the 4-week period (KE:  $44 \pm 8\%$ , IS:  $44 \pm 8\%$ ;  $P = 0.902$ ). Ten paired and 10 single stimuli were delivered in Study A, and 20 paired and 20 single stimuli were delivered in Study B. A lower number of stimuli were used in Study A since measures were performed on both tasks every 15 min. A reduction in the number of stimuli thus allowed for a sufficient break between testing points to minimise the possibility of assessment-induced declines in neuromuscular function (Dekerle, Greenhouse-Tucknott, Wrightson, Schäfer, & Ansdell, 2019). However, as suggested by Brownstein et al. (2018b), 10 measurements could be used when time was constrained, and have been shown to exhibit similar levels of reliability compared to 20 for both single (ICC: 0.90 vs. 0.91) and paired-pulse (ICC: 0.78 vs. 0.84) responses (Brownstein et al., 2018b).

No evidence exists in the lower limbs regarding the optimal stimulus variables for LICI, and whilst it is noted that the responses to paired-pulse TMS using 100 ms ISI might represent both spinal and intracortical inhibition (McNeil, Martin, Gandevia, & Taylor, 2011), pilot testing on 10 participants determined that, in the VL, using an ISI of 100 ms elicits the smallest unconditioned to conditioned MEP ratio ( $59.5 \pm 26.8\%$ ) compared to 150 and 200 ms ( $151.5 \pm 70.4$  and  $105.6 \pm 24.2\%$ , respectively,  $F_{1,2,10.6} = 10.8$ ,  $P = 0.001$ ). Therefore, 100 ms ISI was used in the present study.

## 2.13 | Ultrasound

Vastus lateralis muscle thickness was measured using a real-time B-mode ultrasound (AU5 Harmonic, Esaote Biomedica, Genoa, Italy). Muscle thickness has been shown to be highly associated with resistance training-induced changes in anatomical cross-sectional area (Franchi et al., 2018). Prior to the measurement of VL thickness, participants lay supine for 20 min to allow for fluid distribution to equilibrate (Berg, Tender, & Tesch, 1993). With the participant laid supine and their non-dominant leg fully extended, the distal and proximal insertions sites and the medial and lateral borders of the VL were identified using an ultrasound probe (7.5 MHz linear array probe, 55 mm wide). Muscle length and width were measured using an anthropometric tape measure, and muscle thickness was then measured at 50% of VL length and width. The distance between the superficial and deep aponeurosis was used for muscle thickness. Digitizing software (ImageJ 1.45, National Institutes of Health, Bethesda, MD, USA) was used for image analysis, with the average of three measurements taken across the width of the image recorded.

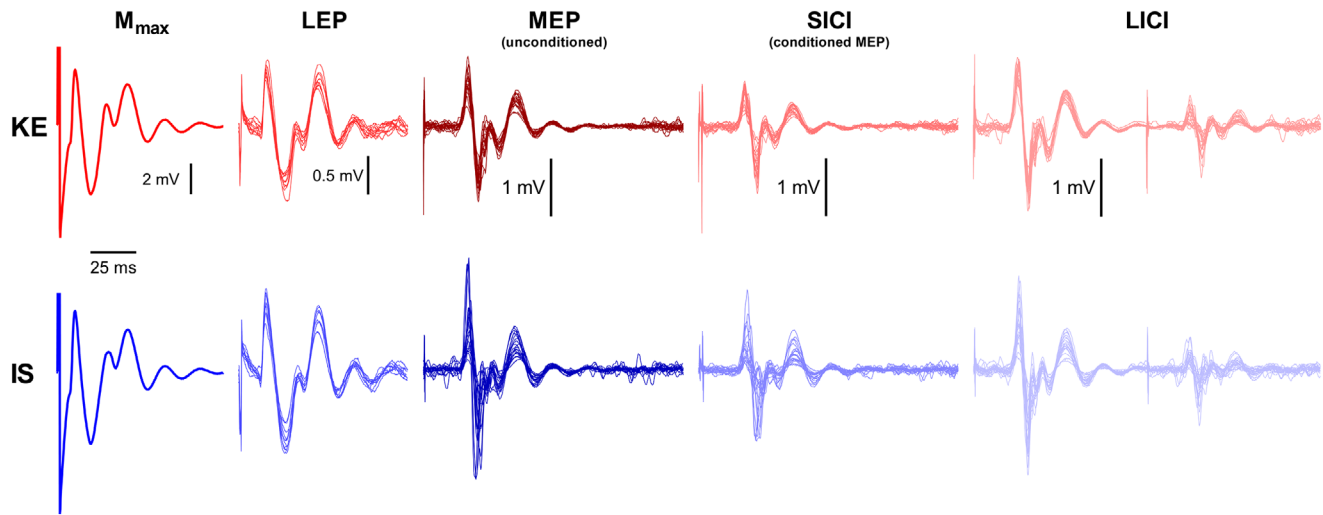
## 2.14 | Data analysis

All analyses were performed offline using Spike2 software. The greatest instantaneous MVC force was assessed in both tasks. Peak-to-peak amplitudes of evoked potentials ( $M_{\max}$ , LEP, conditioned and unconditioned MEP) were calculated as an average of all stimulations. LEPs and unconditioned MEPs were expressed relative to  $M_{\max}$  to quantify spinal motoneuronal and corticospinal excitability, respectively. The SP duration for unconditioned MEPs was calculated between the stimulus artefact and resumption of voluntary EMG (Damron, Dearth, Hoffman, & Clark, 2008). To quantify SICI and LICI, the size of the conditioned paired-pulse MEP was expressed relative to the size of the unconditioned MEP. Representative traces of evoked responses during KE and IS are shown in Figure 2. Background EMG activity was calculated as the root mean square (RMS) EMG activity in the 100 ms epoch prior to stimulus delivery and expressed relative to  $M_{\max}$  ( $\text{RMS}/M_{\max}$ ). EMG activity during MVC before and after 4 weeks of squat resistance training was calculated in the 500 ms around peak force (from 250 ms before to 250 ms after peak force) and expressed relative to  $M_{\max}$  ( $\text{RMS}_{\text{MVC}}/M_{\max}$ ).

## 2.15 | Statistical analysis

All data are reported as means  $\pm$  standard deviation. Normality and sphericity of the data were assessed using Shapiro–Wilks and Mauchly's test, respectively. All data were normally distributed.

Within- (Study A) and between-session (Study B) test–retest reliability was calculated from control group data using multiple indexes (Atkinson & Nevill, 1998; Hopkins, 2000), including bias (using repeated measures ANOVA for Study A and paired-samples Student's *t* test for Study B) and within-participant variation as typical error (standard deviation of the mean differences divided by the square root



**FIGURE 2** Raw traces of evoked responses during knee extension (KE; shades of red) and the isometric squat (IS; shades of blue) in one participant. Superimposed responses to supramaximal electrical stimulation over the femoral nerve ( $M_{\max}$ , one trace), electrical stimulation of lumbar spinal segments (LEP; 10 traces), single pulse transcranial magnetic stimulation (MEP; 20 traces) and paired-pulse transcranial magnetic stimulation at short (2 ms; SICI;  $n = 20$ ) and long interstimulus intervals (LICI;  $n = 20$ ) are shown from left to right. The representative data are from a single subject in the training group obtained in the pre-training assessment

of 2). Typical error was expressed as absolute raw values and as a percentage of the mean (coefficient of variation, CV).

For Study A, a three-way ( $2 \times 2 \times 5$ ; group (training and control), task (IS and KE), and time (PRE, POST0, POST15, POST30 AND POST 45)) ANOVA was used to assess whether acute changes (MVC,  $M_{\max}$ , RMS/ $M_{\max}$ , MEP/ $M_{\max}$ , LEP/ $M_{\max}$ , MEP/LEP, SICI, LICI, SP) associated with squat training were task-specific.

For Study B, a three-way ( $2 \times 2 \times 2$ ; group (training and control), task (IS and KE), and time (PRE, POST)) ANOVA was used to assess whether responses to short-term squat training were task-specific. To assess training induced changes in 1RM, a two-way ( $2 \times 2$ ; group (training and control) and time (PRE and POST)) ANOVA was used. If significant interactions or main effects were found, analysis was continued using pairwise comparisons with Bonferroni correction. Analyses were performed on both absolute and relative intensity post-training data, but the results were similar for both, and therefore for simplicity only the relative data are reported. Statistical significance was determined as an  $\alpha$  of 0.05. Hedge's  $g$  with correction for small sample sizes was calculated to estimate effect sizes of between-group differences (<0.2 is a small, 0.2–0.8 is a medium, >0.8 is a large effect).

### 3 | RESULTS

#### 3.1 | Test-retest reliability of measures

Variability of measures was lower in Study A compared to Study B, and tended to be lower in the KE task in Study A, whereas it was lower in the IS task in Study B (Table 1). Variability was low for mechanical variables (MVC and 1RM; CV <10%). Electromyographical data displayed greater variability, but similar to that reported by our

group (Ansdell et al., 2019; Brownstein et al., 2018b; Goodall, Romer, & Ross, 2009; Škarabot et al., 2019c) and others (O'Leary et al., 2015) previously. The random error of LEP/ $M_{\max}$  in Study B was high (CV: 59% for KE and 39% for IS).

#### 3.2 | Study A: responses to an acute training session

Following squat exercise, MVC force was reduced at all time points for both tasks, with no change in MVC in the control group ( $F_{4,64} = 7.96$ ,  $P < 0.001$ ,  $g = 1.21$ ; Figure 3a,b). There was no difference in the reduction in MVC during KE compared to IS ( $F_{2,7,43,6} = 1.33$ ;  $P = 0.276$ ;  $g = 0.50$ ).

No acute changes in  $M_{\max}$  were observed following squat exercise in either testing task ( $F_{4,64} = 1.02$ ,  $P = 0.403$ ,  $g = 0.44$ ), with no differences between the training and control groups ( $F_{4,64} = 0.28$ ,  $P = 0.893$ ,  $g = 0.23$ ; Table 2). No change in RMS/ $M_{\max}$  was observed following squat exercise when measured during KE or IS, and no difference was found between the squat and control group, as demonstrated by no time  $\times$  group ( $F_{4,64} = 1.33$ ,  $P = 0.269$ ,  $g = 0.50$ ) and no time  $\times$  task  $\times$  group interactions ( $F_{4,64} = 1.70$ ,  $P = 0.162$ ,  $g = 0.56$ ; Table 2).

No change in corticospinal excitability (MEP/ $M_{\max}$ ) was observed during KE or IS ( $F_{4,64} = 0.65$ ,  $P = 0.627$ ,  $g = 0.34$ ), or between the training and control groups ( $F_{4,64} = 0.60$ ,  $P = 0.751$ ,  $g = 0.33$ ; Figure 3c,d). A significant time  $\times$  group interaction was found for spinal excitability ( $F_{4,64} = 3.75$ ,  $P = 0.008$ ,  $g = 0.83$ ). *Post-hoc* analysis revealed an increase in LEP/ $M_{\max}$  at 15 ( $P = 0.027$ ), 30 ( $P = 0.005$ ) and 45 min ( $P = 0.030$ ) following squat exercise, with no differences immediately post (Figure 3e;  $P = 0.654$ ). The increase in spinal excitability occurred irrespective of testing task ( $F_{4,64} = 0.84$ ,  $P = 0.507$ ,  $g = 0.39$ ).

No change in neural inhibition in response to squat exercise was observed in either task (Figure 4). For SICI, no time  $\times$  group



**TABLE 1** Test–retest reliability for Study A and B

Measure	Study A				Study B			
	Bias	P	TE	CV	Bias	P	TE	CV
Knee extension								
MVC (N)	18	0.345	32	6%	33	0.139	39	7%
M <sub>max</sub> (mV)	0.5	0.260	1	15%	1.6	0.229	2.4	31%
RMS/M <sub>max</sub>	0.003	0.170	0.001	11%	0.002	0.024	0.003	43%
MEP/M <sub>max</sub>	0.20	0.208	0.1	33%	0.01	0.676	0.06	46%
LEP/M <sub>max</sub>	0.01	0.754	0.06	35%	0.06	0.363	0.13	59%
SICI (/unconditioned MEP)	0.02	0.209	0.09	12%	0.05	0.548	0.17	21%
LICI (/unconditioned MEP)	0.07	0.381	0.19	30%	0.12	0.079	0.12	20%
SP (ms)	6	0.051	7	5%	1	0.937	22	15%
Isometric squat								
MVC (N)	53	0.462	79	9%	31	0.636	127	15%
M <sub>max</sub> (mV)	0.3	0.236	0.9	14%	1.5	0.274	2.6	32%
RMS/M <sub>max</sub>	0.001	0.197	0.002	22%	0.002	0.004	0.002	22%
MEP/M <sub>max</sub>	0.01	0.327	0.05	26%	0.00	0.895	0.06	29%
LEP/M <sub>max</sub>	0.02	0.071	0.04	22%	0.00	0.940	0.07	39%
SICI (/unconditioned MEP)	0.02	0.779	0.06	8%	0.01	0.824	0.11	15%
LICI (/unconditioned MEP)	0.01	0.973	0.09	17%	0.14	0.063	0.13	25%
SP (ms)	4	0.727	10	8%	8	0.352	15	11%
1RM (kg)	1	0.628	5	4%				

1RM, 1 repetition maximum; CV, coefficient of variation; LEP, lumbar evoked potential normalised to M<sub>max</sub>; LICI, long-interval intracortical inhibition; MEP/M<sub>max</sub>, motor evoked potential normalised to M<sub>max</sub>; M<sub>max</sub>, maximal compound action potential; MVC, maximal isometric voluntary contraction; P, significance pertaining to bias; RMS/M<sub>max</sub>, root-mean-square EMG activity prior to stimulation normalised to M<sub>max</sub>; SICI, short-interval intracortical inhibition; SP, silent period; TE, typical error.

( $F_{4,64} = 1.41, P = 0.240, g = 0.51$ ) or time  $\times$  task  $\times$  group interaction was found ( $F_{4,64} = 0.01, P = 0.605, g = 0.05$ ), and no time  $\times$  group ( $F_{4,64} = 0.77, P = 0.573, g = 0.38$ ) or time  $\times$  task  $\times$  group interaction ( $F_{4,64} = 0.73, P = 0.578, g = 0.37$ ) was found for LICI. Similarly, for SP, there was no time  $\times$  group interaction ( $F_{2,7,42,9} = 0.54, P = 0.403, g = 0.31$ ) or time  $\times$  task  $\times$  group interaction ( $F_{2,5,42,9} = 0.29, P = 0.403, g = 0.23$ ).

### 3.3 | Study B: responses to short-term training

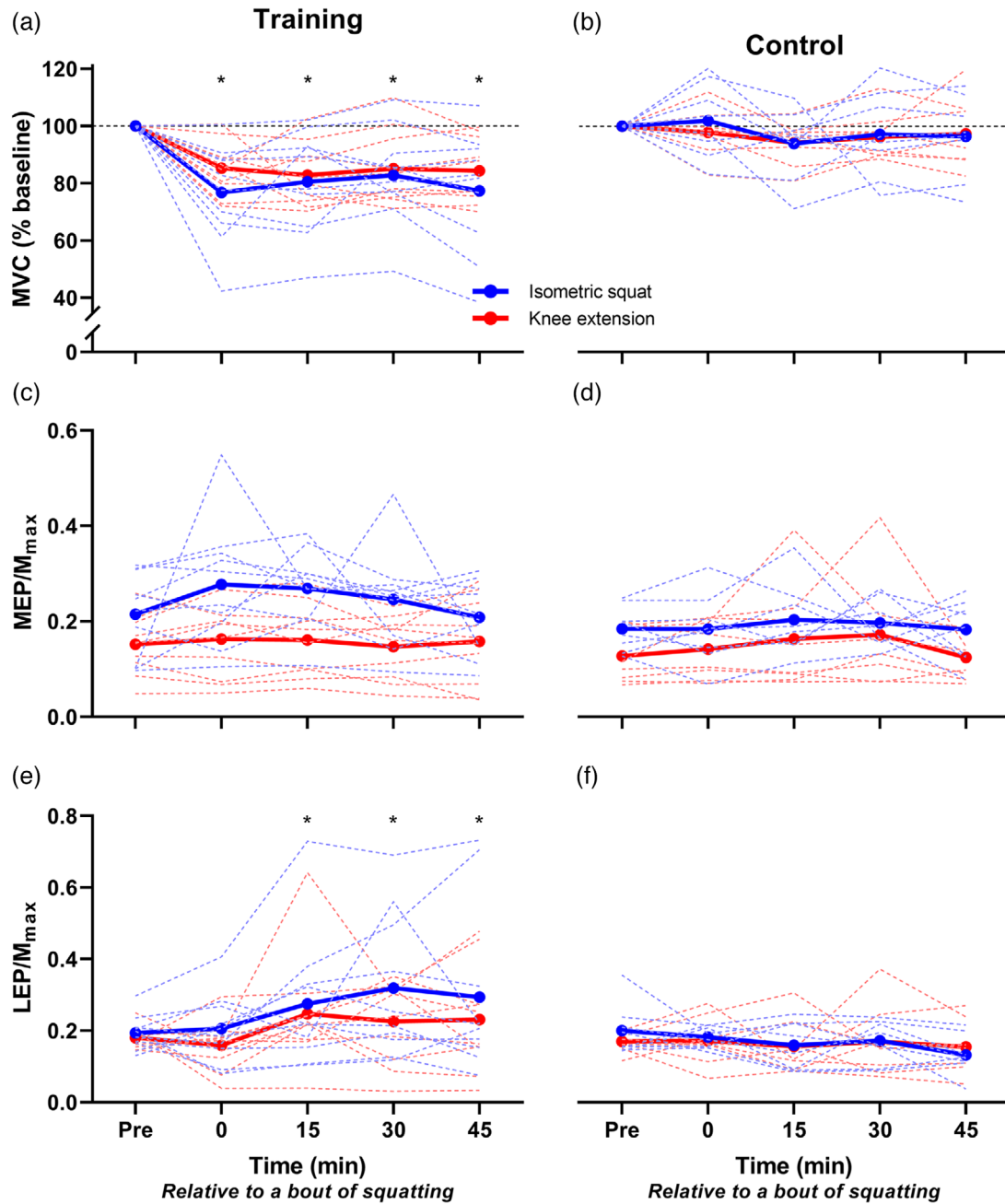
There were no between-group differences in 1RM at baseline ( $P = 0.330$ ). Throughout the 12 training sessions across 4 weeks of squat resistance training, participants increased their training load by  $36 \pm 15\%$  (Figure 5a;  $F_{11,99} = 120.43, P < 0.001, g = 4.62$ ). A main effect of time ( $F_{1,16} = 45.64, P < 0.001, g = 2.90$ ) and a significant group  $\times$  time interaction was found for 1RM ( $F_{1,16} = 39.72, P < 0.001, g = 2.71$ ). *Post hoc* comparisons showed an increase in 1RM by  $35 \pm 16\%$  for the training group only (Figure 5b;  $P < 0.001$ ). This occurred without a change in the VL muscle thickness measured at 50% of muscle length (training group:  $22.2 \pm 2.3$  vs.  $23.0 \pm 3.1$  mm; control:  $22.8 \pm 2.3$  vs.  $22.8 \pm 3.5$  mm;  $F_{1,16} = 0.55, P = 0.468, g = 0.32$ ).

A task-specific increase in MVC measured during the IS was found in the training group, with no improvement in the control group (Figure 6a,b). Although no time  $\times$  group interaction was found

( $F_{1,16} = 3.73, P = 0.071, g = 0.83$ ), the time  $\times$  task  $\times$  group interaction ( $F_{1,16} = 6.37, P = 0.023, g = 1.09$ ) revealed an improvement in MVC measured during IS in the training group (+49%;  $P < 0.001$ ; Figure 6a), with no improvement in KE MVC (+1%;  $P = 0.882$ ).

No change in M<sub>max</sub> was observed following short-term squat training measured in either task ( $F_{1,16} = 0.43, P = 0.521, g = 0.28$ ), or between the training and control group ( $F_{1,16} = 0.86, P = 0.311, g = 0.40$ ; Table 2). No change in either RMS/M<sub>max</sub> ( $F_{1,16} = 0.33, P = 0.573, g = 0.25$ ) or RMS<sub>MVC</sub>/M<sub>max</sub> ( $F_{1,16} = 0.12, P = 0.736, g = 0.15$ ) was found following short-term squat training (Table 2), or between the training and control groups (RMS/M<sub>max</sub>:  $F_{1,16} = 1.39, P = 0.255, g = 0.51$ ; RMS<sub>MVC</sub>/M<sub>max</sub>:  $F_{1,16} = 0.25, P = 0.623, g = 0.22$ ).

The stimulus intensity at AMT did not differ in either task or between the training and control groups, with no time  $\times$  group ( $F_{1,16} = 0.05, P = 0.820, g = 0.10$ ) and time  $\times$  task  $\times$  group interaction ( $F_{1,16} = 0.11, P = 0.745, g = 0.14$ ) observed. No change in cortico-spinal excitability was observed following short-term squat training measured in either task, or between the training and control groups (Figure 6c,d), as displayed through the lack of time  $\times$  group interaction ( $F_{1,16} = 0.44, P = 0.560, g = 0.29$ ) or time  $\times$  task  $\times$  group interaction ( $F_{1,16} = 1.37, P = 0.258, g = 0.50$ ). No change in spinal motoneuron excitability was found following short-term squat training measured in either task ( $F_{1,16} = 0.35, P = 0.564, g = 0.25$ ), or between the training and control group ( $F_{1,16} = 1.37, P = 0.258, g = 0.50$ ; Figure 6e,f).



**FIGURE 3** Maximal voluntary contraction (MVC) force (a,b), motor (MEP/M<sub>max</sub>; c,d) and lumbar (LEP/M<sub>max</sub>; e,f) evoked potentials normalised to maximal muscle response before and in the 45 min following a bout of squat resistance exercise (training; a,c,e) or the equivalent duration of rest (control; b,d,f) assessed in the isometric squat and knee extension. Continuous and dashed lines denote the sample mean and individual responses, respectively. \* $P < 0.001$  compared to 'Pre' in both tasks

Neural inhibition did not change in response to short-term squat training measured in either KE or IS (Figure 7). For SIC1, there was no time  $\times$  group interaction ( $F_{1,16} = 0.01$ ,  $P = 0.683$ ,  $g = 0.04$ ) or time  $\times$  task  $\times$  group interaction ( $F_{1,16} = 0.02$ ,  $P = 0.215$ ,  $g = 0.05$ ). For LIC1, a time  $\times$  group interaction was found ( $F_{1,16} = 5.73$ ,  $P = 0.029$ ,  $g = 1.00$ ), with *post hoc* test revealing that LIC1 ratio was significantly decreased in the control group between baseline and 4 weeks ( $P = 0.024$ ). No time  $\times$  task  $\times$  group interaction for LIC1 was observed ( $F_{1,16} = 0.71$ ,  $P = 0.412$ ,  $g = 0.36$ ). Similarly, for the SP, there was

no time  $\times$  group interaction ( $F_{1,16} = 2.39$ ,  $P = 0.141$ ,  $g = 0.67$ ) or time  $\times$  task  $\times$  group interaction ( $F_{1,16} = 2.04$ ,  $P = 0.172$ ,  $g = 0.61$ ).

## 4 | DISCUSSION

The present study aimed to assess whether the neuromuscular responses to acute (Study A) and short-term (Study B) squat resistance training were task-specific, using a comprehensive assessment of the

**TABLE 2** Background EMG activity, EMG activity during MVC and maximal compound action potential

	Study A						Study B							
	Training			Control			Training			Control				
	PRE	POST0	POST15	POST30	POST45	PRE	POST0	POST15	POST30	POST45	POST	PRE	POST	
RMS <sub>EMG</sub> (% M <sub>max</sub> )	0.7 ± 0.2	0.7 ± 0.2	0.7 ± 0.3	0.7 ± 0.2	0.7 ± 0.3	0.7 ± 0.2	0.8 ± 0.3	0.9 ± 0.3	0.9 ± 0.5	0.7 ± 0.2	0.6 ± 0.2	0.6 ± 0.3	0.8 ± 0.3	0.6 ± 0.3
IS	0.8 ± 0.4	1.1 ± 0.4	1.0 ± 0.3	0.9 ± 0.3	0.9 ± 0.3	0.9 ± 0.4	0.9 ± 0.3	1.0 ± 0.3	0.9 ± 0.2	0.8 ± 0.3	0.9 ± 0.4	0.7 ± 0.2	1.0 ± 0.5	0.8 ± 0.4
RMS <sub>MVC</sub> (% M <sub>max</sub> )	-	-	-	-	-	-	-	-	-	-	7.6 ± 2.4	8.9 ± 2.6	6.4 ± 2.4	7.8 ± 4.1
IS	-	-	-	-	-	-	-	-	-	-	6.0 ± 2.1	6.0 ± 2.9	7.3 ± 2.8	8.1 ± 6.1
M <sub>max</sub> (mV)	6.3 ± 2.0	5.9 ± 1.6	5.8 ± 1.6	5.9 ± 1.9	5.9 ± 1.9	6.7 ± 1.8	6.2 ± 2.5	5.9 ± 2.3	6.4 ± 2.5	6.8 ± 2.5	6.2 ± 1.5	8.3 ± 2.9	6.9 ± 3.7	8.5 ± 3.5
IS	6.1 ± 2.1	5.4 ± 3.1	5.3 ± 1.8	5.6 ± 2.0	5.7 ± 1.5	6.8 ± 2.5	6.4 ± 2.0	6.3 ± 2.0	6.4 ± 1.8	7.3 ± 2.6	5.9 ± 1.6	8.8 ± 2.2	7.4 ± 4.6	8.9 ± 4.3

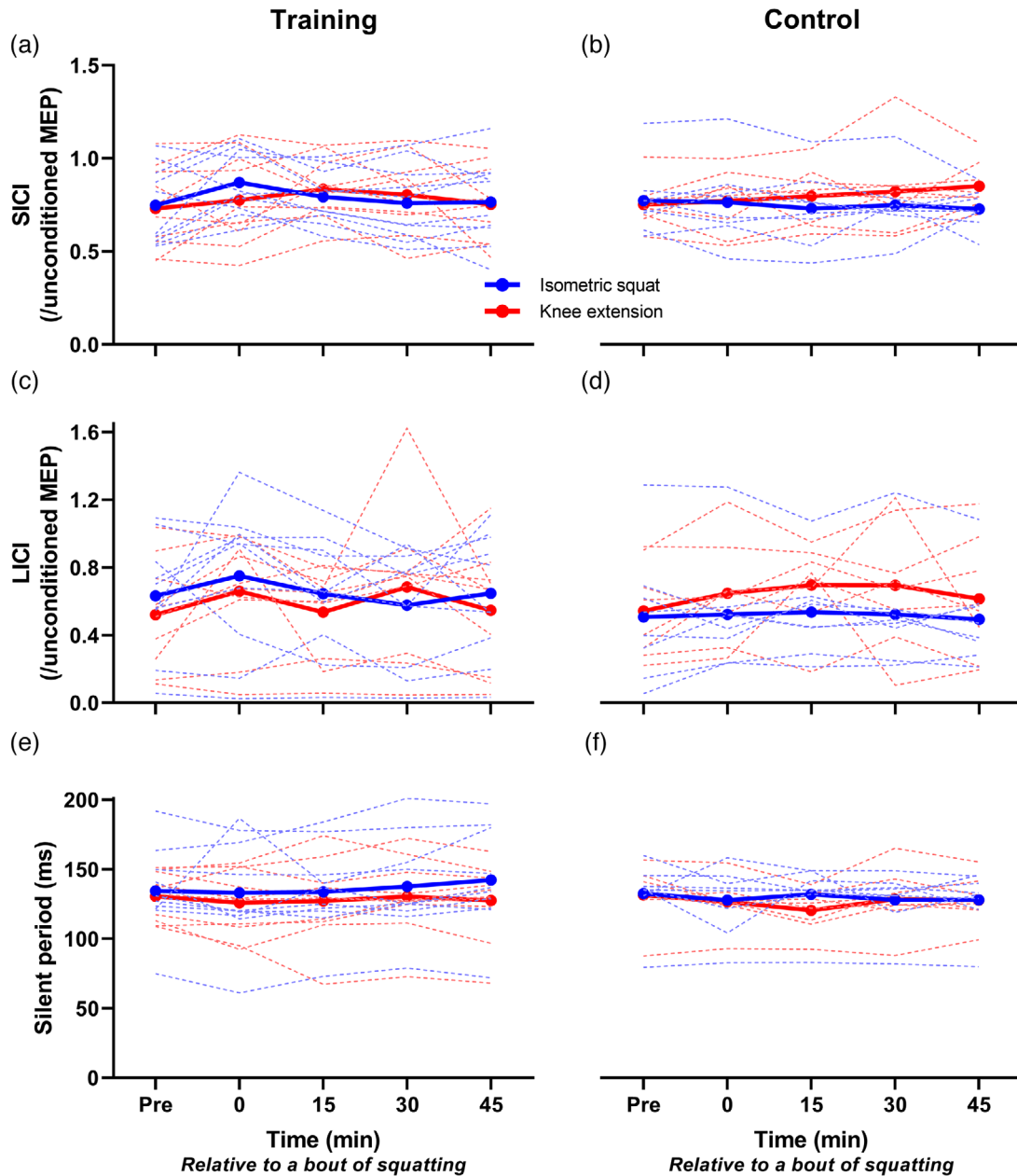
M<sub>max</sub>: maximal compound action potential; RMS<sub>EMG</sub> (% M<sub>max</sub>), root mean square EMG activity normalised to maximal muscle response in the 100 ms prior to stimulations; RMS<sub>MVC</sub> (% M<sub>max</sub>), root mean square EMG activity normalised to maximal muscle response in the 500 ms at peak MVC force.

corticospinal pathway, in a novel isometric squat task compared to a non-specific single-limb isometric knee extension, in a randomised control trial. The results from Study A demonstrated that an acute bout of squat resistance training increased spinal excitability 15–45 min following exercise. However, the spinal response was not task-specific, and occurred in both tasks. In Study B, the training group demonstrated a 35 ± 16% improvement in 1RM strength, and a task-specific increase in maximum strength, with MVC force increasing in the IS task only. Despite the substantial improvement in 1RM and maximal strength in the training group, in contrast to previous findings, no changes in measures of intracortical, corticospinal, or spinal motoneuronal excitability were observed. These results suggest that the task-specific increase in isometric maximum strength observed following 4 weeks of squat resistance training was not related to changes in the properties of intracortical and corticospinal neurons measured in the VL during both task-specific and non-specific tasks.

#### 4.1 | Responses to acute resistance training

The acute bout of squat exercise caused an immediate decrease in MVC force in the training group and remained decreased for up to 45 min, with no associated change in cortical excitability. Conflicting evidence exists regarding the acute effect of resistance training on corticospinal excitability (Colomer-Poveda, Romero-Arenas, Lundbye-Jensen, Hortobágyi, & Márquez, 2019; Kidgell & Pearce, 2010; Latella, Hendy, Pearce, VanderWesthuizen, & Teo, 2016; Nuzzo et al., 2016; Ruotsalainen, Ahtiainen, Kidgell, & Avela, 2014; Thomas, Toward, West, Howatson, & Goodall, 2017, 2018), but a recent systematic review (Mason et al., 2019) concluded that a single session of resistance training increases corticospinal excitability (MEP amplitude), a conclusion not supported by the present study. This discrepancy in the literature could be due to differences in several experimental factors, including differences between exercised muscles (i.e. upper versus lower limbs, due to differences in intracortical circuits and corticospinal projections; Brouwer & Ashby, 1990; Chen et al., 1998), the characteristics of the resistance exercise protocol (explosive versus slow sustained strength tasks (Giboin et al., 2018), or self-paced versus externally paced (Leung et al., 2017)), and, as previously highlighted, differences in the assessment task. Indeed, the aforementioned studies assessed single-limb models of exercise, and therefore might not be comparable to the multi-joint, squat exercise and assessment used in the present study. Previous studies assessing the acute effects of squat exercise on corticospinal excitability have similarly displayed no change in MEP amplitude when assessed during single-limb KE (Thomas et al., 2017, 2018), and combined with the present responses measured in a task-specific IS, suggest that lower-body compound resistance exercise has no acute effects on corticospinal excitability of the VL.

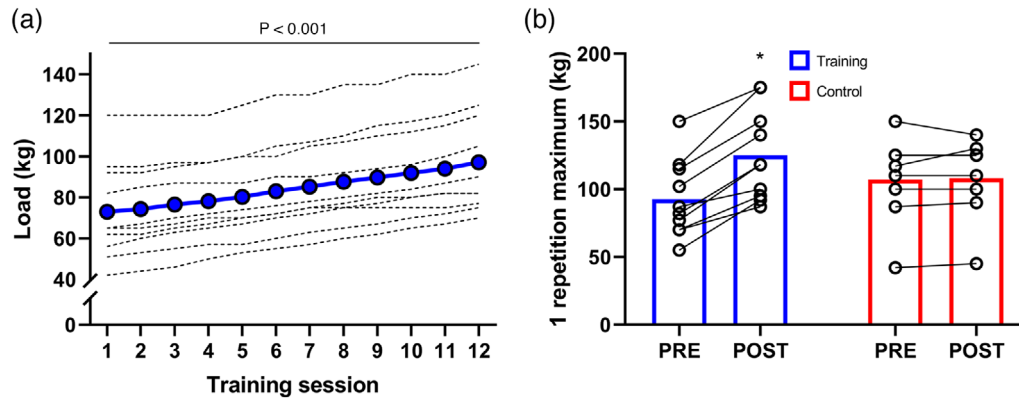
This study is the first to measure the spinal response to acute and short-term resistance training of the lower limbs. Lumbar evoked potentials measured in the VL increased from 15 to 45 min following an acute bout of resistance training, suggesting modulation in neural function at the spinal level. However, the observed increase in spinal



**FIGURE 4** Short-interval intracortical inhibition (SICI; a,b), long-interval intracortical inhibition (LICI; c,d) and transcranial magnetic stimulation-evoked silent period (SP; e,f) before and in the 45 min following a bout of squat resistance exercise (training; a,c,e) or the equivalent duration of rest (control; b,d,f) assessed in the isometric squat and knee extension. Continuous and dashed lines denote the sample mean and individual responses, respectively

excitability was not task-specific. The increase in spinal excitability following a single bout of resistance training is in agreement with previously published data following ballistic concentric training with the index finger (Giesebrecht, van Duinen, Todd, Gandevia, & Taylor, 2012), and strength training of the elbow flexors (Colomer-Poveda et al., 2019; Nuzzo et al., 2016), demonstrating increases in the response to cervicomedullary stimulation (CMEP) in the acute period post-exercise. Nuzzo et al. (2016) suggested that potentiation of corticospinal-motoneuronal synapses could cause this augmented response to subcortical stimulation. Support for this suggestion stems from studies investigating the effects of repeated paired pre- and

postsynaptic stimuli aimed at potentiating these synapses through spike timing-dependent plasticity, which transiently augmented voluntary force production and evoked potentials (Taylor & Martin, 2009). Therefore, the increase in LEP amplitude following acute squat training could also be due to improved efficacy of corticospinal-motoneuronal synapses. Indeed, LEPs exhibited a delayed facilitation following exercise (only observed from POST15 onwards), which is the hallmark of improved efficacy of corticospinal-motoneuronal synapses (Taylor & Martin, 2009), and is in agreement with Nuzzo et al. (2016). Alternatively, the delayed facilitation could be due to the dissipation of the neuromodulatory effects of exercise-induced fatigue, which has



**FIGURE 5** Squat load throughout 12 training sessions across 4 weeks (a) and squat one repetition maximum pre- and post-4 weeks of squat resistance training (b). The blue line with circles in (a) denotes the sample mean, whilst each black line represents an individual participant; in (b)  $*P < 0.001$  compared to 'PRE'

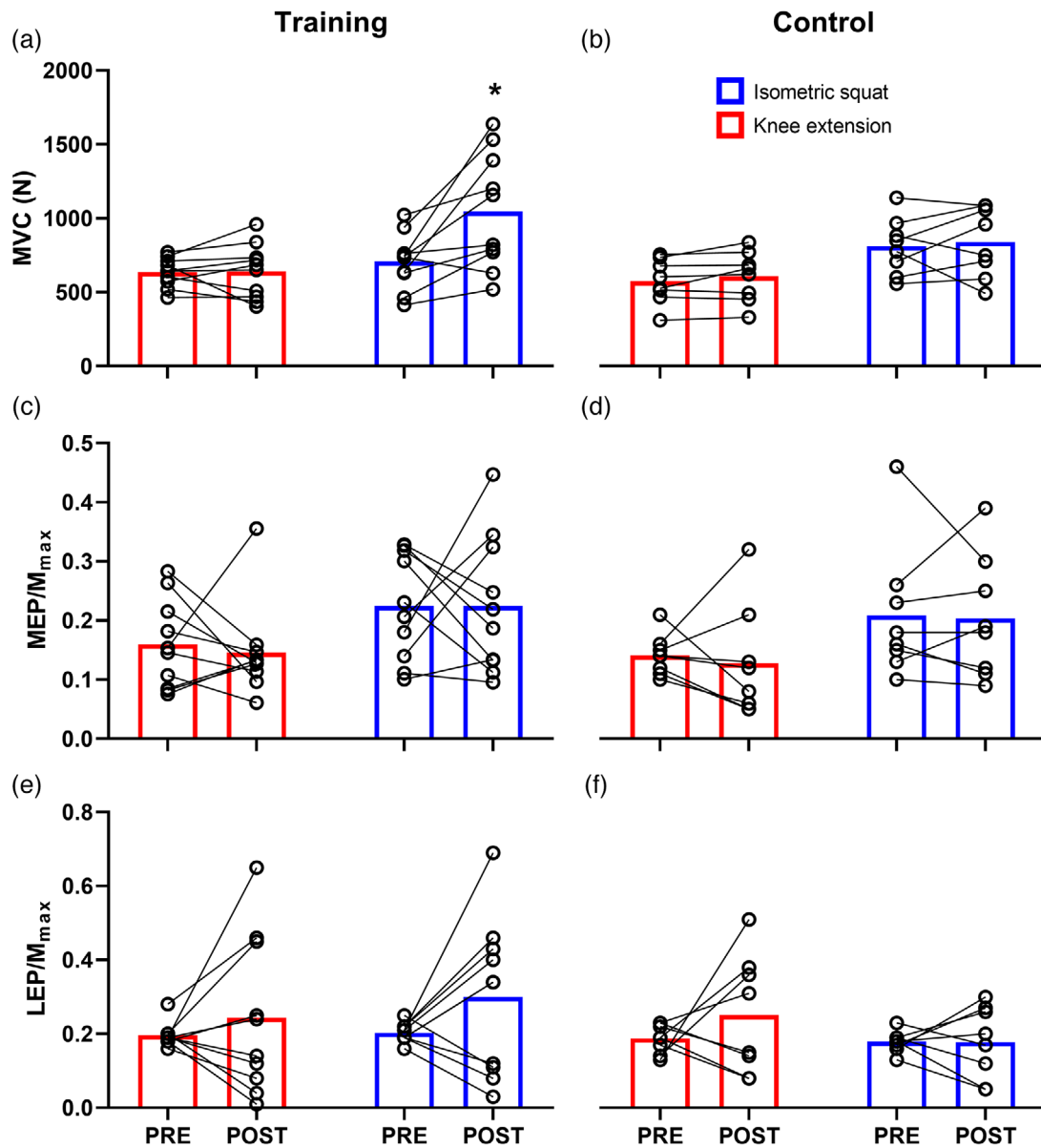
previously been shown to reduce spinal motoneuron excitability (Finn, Rouffet, Kennedy, Green, & Taylor, 2018). Nevertheless, the present data corroborate previous findings in other muscle groups showing increased spinal motoneuron excitability following an acute bout of resistance training (Nuzzo et al., 2016).

The indices of inhibition (SICI, LICI, SP) remained unchanged following an acute bout of lower-limb compound resistance training. This is in agreement with similar data following a bout of heavy strength training in the elbow flexors that demonstrated no change in SICI or LICI (Latella et al., 2016), but in contrast to Latella et al. (2018), who reported reduced SP duration in RF up to 1 h following acute resistance training in the knee extensors. Similar to the discrepancies with acute changes in MEP amplitude, no change in SP could be due to the muscle(s) trained, the training protocol and the assessment task. Furthermore, measures of SP might be significantly constrained by differences in the methods employed to evoke this measure (Škarabot, Mesquita, Brownstein, & Ansdell, 2019d). Using a similar squat exercise protocol to the present study, Thomas et al. (2018) showed no change in SICI following an acute bout of squatting when assessed in the non-specific KE. Using a task-specific assessment, this study provided further evidence that lower-limb compound resistance training does not induce immediate adjustments in neural inhibition when measured in VL.

#### 4.2 | Responses to short-term lower-limb compound resistance training

The present training protocol improved the 1RM squat of participants in the training group (+35%). This increase in 1RM was only reflected in the MVC in the IS (+49%) and not the KE (+1%) task. Due to no change in muscle thickness, the changes in strength cannot be explained by adaptations in muscle cross-sectional area (Franchi et al., 2018). The lack of change in muscle thickness is in agreement with previous findings (Weier et al., 2012), which showed no change in muscle thickness and isometric KE strength following 4 weeks of squat resistance training. It is important to note, however, that ultrasound

measures were confined to a single site on the VL and thus potential changes in hypertrophy at other, e.g. distal (Häkkinen et al., 2001), muscle sites cannot be entirely excluded without additional measuring sites or the use of more sensitive measures (e.g. magnetic resonance imaging). Although no changes in muscle thickness suggest that the strength adaptations might be underpinned by alterations within the CNS, the present study found no effect of short-term squat training on corticospinal excitability or intracortical inhibition when measured during either KE or the more task-specific IS, at absolute or relative contraction intensities. These results are in contrast to that of Weier et al. (2012), who demonstrated a substantial increase in corticospinal excitability (+116%) and reduction in intracortical inhibition (-32%) following the same training protocol and similar experimental design to that of the present study. While the results differ from that of Weier et al. (2012), discrepancies between studies in this area have been previously highlighted (Kidgell, Bonanno, Frazer, Howatson, & Pearce, 2017), with inconsistencies suggested to be a result of factors such as different strength training tasks (e.g. static vs. dynamic or tonic vs. ballistic training), the duration of the training intervention, the muscle(s) investigated and/or different methodological techniques. Indeed, Weier et al. (2012) measured responses in the RF and not the VL. Furthermore, Weier et al. (2012) assessed responses during 60 deg of knee flexion, whereas the present study did so at 90 deg, making it possible that differences in muscle length could have affected the observed responses (Doguet et al., 2017). Alternatively, Weier et al. (2012) employed a smaller range of motion during both 1RM testing and the training protocol, which permitted a substantially greater tolerable absolute load compared to full-depth squats (Pallarés, Cava, Courel-Ibáñez, González-Badillo, & Morán-Navarro, 2020). In turn, it has been demonstrated that neural adaptations are enhanced following resistance training involving high compared with lower loads (Jenkins et al., 2017). Indeed, the group mean increase in 1RM was greater in Weier et al. (2012) compared to the present data (87 vs. 35%, respectively), possibly due to smaller range of motion used in their study. This could indicate that vast improvements in strength augmentation are required to detect modulations in corticospinal

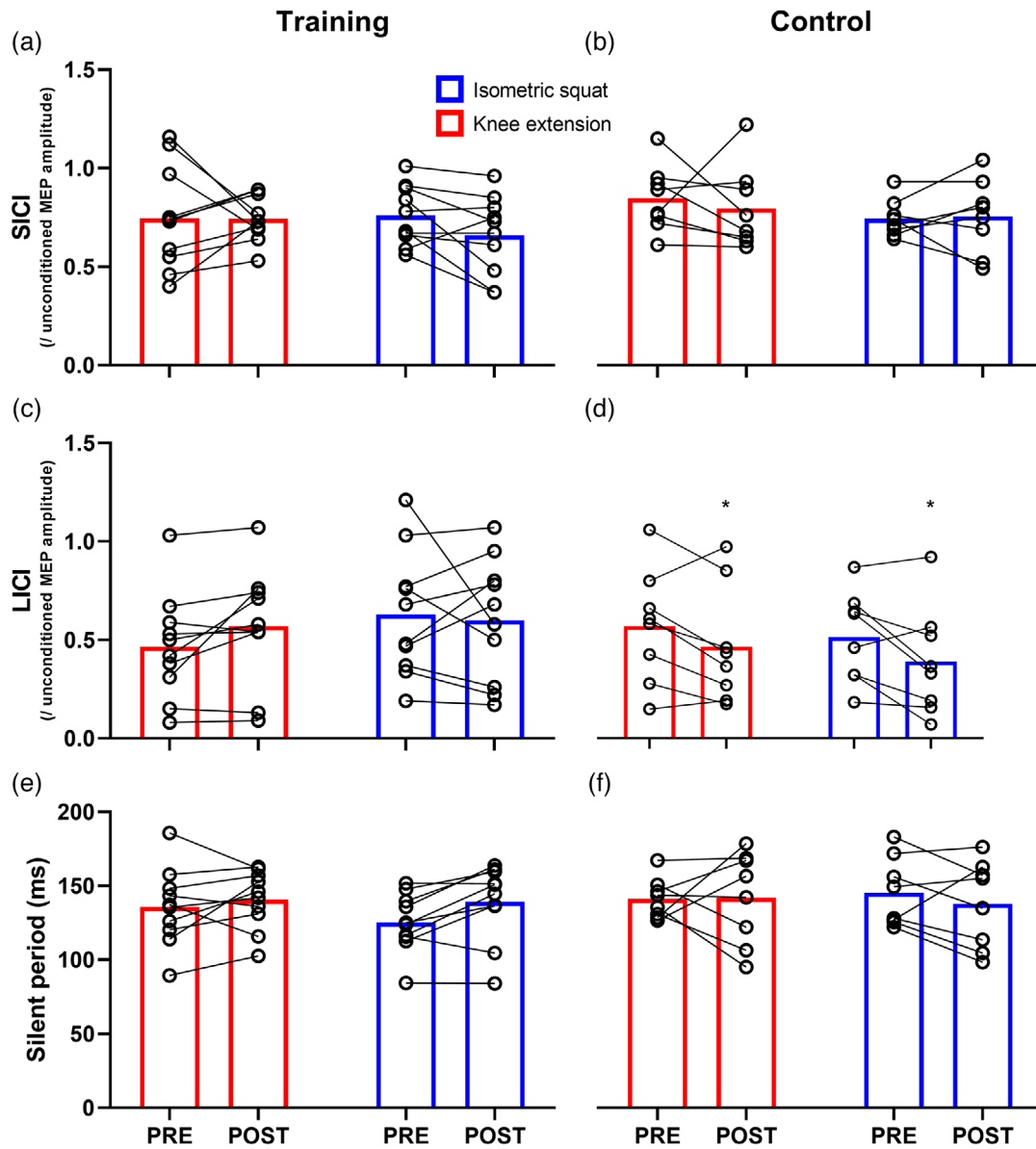


**FIGURE 6** Maximal voluntary contraction (MVC; a,b) force, motor (MEP/M<sub>max</sub>; c,d) and lumbar (LEP/M<sub>max</sub>; e,f) evoked potentials normalised to maximal muscle response before and after 4 weeks of squat resistance training (a,c,e) compared to control (b,d,f) assessed in the isometric squat and knee extension. \**P* < 0.001 compared to 'PRE' in the same assessment task

and intracortical function. Overall, the present data are in contrast to reported changes in intracortical inhibition following strength training (Siddique et al., 2020), but in agreement with numerous other studies (Carroll, Barton, Hsu, & Lee, 2009; Christie & Kamen, 2014; Coombs et al., 2016), and the conclusions of Kidgell et al. (2017), who in their systematic review suggested that the change in MEP amplitude following strength training is negligible.

To investigate any potential alterations in the corticospinal tract at a segmental level, the present study compared responses to subcortical stimulation before and after the training protocol. No difference was observed following the 4 weeks of training, which agrees with the only other study to employ this type of investigation (Nuzzo et al., 2017). While Nuzzo et al. (2017) elicited CMEPs in

the elbow flexors at rest to avoid differences in muscle activity, the present study aimed to recreate the training task as best as possible to maximise aspects of task specificity (i.e. posture, joint angles, bilateral force production), and because resistance training-induced changes have been shown to be only detectable in an active muscle (Siddique et al., 2020). No difference in pre-stimulus RMS EMG was observed between assessments, implying that background muscle activity was not altered, and therefore allowing a valid pre-post training comparison. Despite the difference in muscle activity during assessment between the present study and that of Nuzzo et al. (2017), both demonstrated no training-induced changes in the spinal contribution to corticospinal excitability following a period of resistance training. Contrary to our hypothesis, no change in evoked



**FIGURE 7** Short-interval intracortical inhibition (SICI; a,b), long-interval intracortical inhibition (LICI; c,d) and transcranial magnetic stimulation-evoked silent period (SP; e,f) before and after 4 weeks of squat resistance training (a,c,e) compared to control (b,d,f) assessed in isometric squat and knee extension tasks. \* $P < 0.05$  compared to 'PRE'

responses were observed during either task. In light of the lack of change in evoked responses during the more task-specific IS, it is unsurprising that no change in responses was observed during the less task-specific KE. Furthermore, the lack of change in evoked responses during KE could also be considered unsurprising given that KE MVC was unchanged. It should be noted, however, that the unchanged KE MVC does not necessarily indicate that adaptations to the knee extensors did not contribute to improvements in squat 1RM and IS MVC. Rather, the considerable differences in the characteristics of force production during squat exercise and KE could explain the unchanged KE MVC. Accordingly, although no changes in evoked responses were observed, the greater increase in IS compared with KE further highlights the importance of utilising task-specific testing tasks to assess neuromuscular adaptations to strength training.

### 4.3 | Further considerations

Despite the observed task-specific increase in strength following squat resistance training, and in contrast to our hypothesis, no changes were demonstrated in the evoked corticospinal responses. However, it should be noted that the corticospinal tract during multi-joint, lower-limb compound contractions acts in an integrated and dynamic neural network for execution of the required movement (Capaday, Ethier, Van Vreeswijk, & Darling, 2013; Devanne, Cohen, Kouchtir-Devanne, & Capaday, 2002; Mason et al., 2017). Indeed, individual muscle groups involved in the movement might not be controlled by distinct areas within the motor cortex, but are more likely interconnected by intrinsic collaterals involved in the integrated control of muscle synergies (Capaday et al., 2013). Regarding the IS, the knee extensors act as the

primary agonists, but these muscles are supported by other agonist and synergist muscles, including spine stabilising muscles (e.g. rectus abdominis, the obliques and erector spinae; Nuzzo, McCaulley, Cormie, Cavill, & McBride, 2008; Willardson, Fontana, & Bressel, 2009). Thus, given the overlapping and intertwined nature of muscle representation in the motor cortex (Devanne et al., 2006), it is plausible that the changes in activation patterns of synergists could have contributed to the task-specific expression of strength in the present study. This is consistent with the lack of change in isometric knee extension strength, whereby the quadriceps act as an agonist without significant contribution of synergist muscles.

Furthermore, the present study demonstrated that LEP size was increased following the acute session, but remained unchanged following the 4-week training period. One possible explanation for this is that the acute increase in LEP was a result of 'reactive plasticity', in which general, possibly compensatory, changes at the spinal cord occur due to a change in the activity of surrounding networks directly implicated in the task, i.e. those involved in 'primary plasticity' (Giboin, Tokuno, Kramer, Henry, & Gruber, 2020; Wolpaw, 2010). In turn, this could induce secondary changes in spinal pathways not directly implicated in the task, in our case leading to an increase in LEP amplitude during both the IS and KE. Subsequently, time-dependent, task-specific neural reorganisation might have occurred throughout the training period, meaning that spinal alterations could only be observed during the task itself (Giboin et al., 2020). Despite the more task-specific nature of the IS, the differences in characteristics of the dynamic squats involved in the task (see 'limitations' section) could have precluded the detection of these neuroplastic changes in response to the intervention.

Future research should also consider potential alterations in other descending tracts. For example, the reticulospinal tract is implicated in force generation during gross and forceful motor tasks (Baker & Perez, 2017; Zaaimi, Edgley, Soteropoulos, & Baker, 2012), and its neurons have been shown to synapse onto  $\alpha$ -motoneurons in primates (Riddle, Edgley, & Baker, 2009), and are activated bilaterally within the spinal cord (Davidson, Schieber, & Buford, 2007). It is conceivable that this descending tract is implicated in force production during the squat, a gross bilateral motor task, but any adaptations within this tract in the present study would have gone undetected with the methodology employed.

#### 4.4 | Limitations

As acknowledged previously (Brownstein et al., 2018a), whilst the present IS squat set-up provides means to assess neuromuscular responses in a task that more closely replicates the characteristics of the squat, it still exhibits differences compared to a conventional dynamic squat. These differences include, but are not limited to, the contraction type, being supported versus unsupported, stability requirements and joint angle. These differences could potentially lead to deviations in the motor commands required for the training and assessment tasks, implying that the IS does not recreate the biomechanical and contextual demands of dynamic squatting. Further

limitations relate to fundamental limitations associated with TMS and electrical stimulation. For example, the highly synchronised neural responses evoked by these measurements are likely to deviate considerably from the pattern of neural activity associated with dynamic strength training. Moreover, not all descending connections contributing to human movement are equally excited by TMS, which preferentially excites monosynaptic fast-conducting corticospinal projections (Bestmann & Krakauer, 2015), though these are likely implicated during strength training. In addition, the requirement to evoke measures in a controlled and reproducible environment means that measures must be evoked during isometric contractions, thus deviating from the training task and reducing ecological validity. Due to these inherent limitations, it should be acknowledged that corticospinal adaptations to dynamic strength training can go undetected using TMS and electrical spinal stimulation. Nevertheless, our approach offers a reasonable compromise when attempting to measure corticospinal adaptations to lower-body compound resistance exercise which improves on previous methodologies using less task-specific single-limb KE. The challenge for this line of research in the future will be designing an experimental set-up that replicates the characteristics of the dynamic squat more accurately, whilst recreating the demands of training and working within the constraints of measuring stimulation responses during different contraction types and muscle lengths, and potential differences in neural activation patterns that can arise from those (Doguet et al., 2017; Škarabot et al., 2019a).

To assess spinal excitability following 4 weeks of resistance training, electrode position over the spinal cord was replicated and intensity of stimulation kept the same as during pre-training assessments. Whilst this approach has been used previously in a similar investigation utilising magnetic CMEPs (Nuzzo et al., 2017), it should be noted that factors other than adaptations within the spinal cord might have contributed to the response, namely subtle difference in electrode location (both stimulating and EMG), or changes in skin resistance. Whilst subtle difference in EMG electrode location or changes in skin resistance were minimised with normalisation of the evoked responses to  $M_{\max}$  (Lanza, Balshaw, & Folland, 2017), any slight difference in stimulation electrode location might have resulted in subtle differences in the activation site of lumbar spinal segments and be responsible for greater variability of LEPs observed (Table 1). Presumably, however, these factors would have affected both the training and the control group, such that had there been any observable changes in spinal excitability following 4 weeks of training, they would have been greater than the variability observed by the control group.

The present study utilised a low contraction intensity during TMS and lumbar stimulation, using stimulus intensities which evoked responses of 15–25%  $M_{\max}$  in order to prevent fatigability induced by the measurements and because this stimulus paradigm has been shown to be sensitive to strength training-induced alterations in corticospinal excitability (Griffin & Cafarelli, 2007; Siddique et al., 2020). Nevertheless, given the low contraction/stimulus intensities used when evoking neural responses, it is likely that these measurements reflect the excitability of low-threshold motor units,



and adaptations to high-threshold motor units could thus have gone undetected. However, there is currently little evidence to suggest that motor unit adaptations which occur during strength training are threshold-specific (Enoka, 2019), with studies displaying similar adaptations to both low- and high-threshold motor units following strength training interventions (Del-Vecchio et al., 2019; Van Cutsem, Duchateau, & Hainaut, 1998), though these interventions differed to our own. Thus, while we believe our methods were sufficient to detect corticospinal alterations in the VL had they occurred, further work is required to determine whether motor unit adaptations following lower-body compound resistance exercise are threshold-specific. Future studies should also consider constructing the stimulus-response curves using a range of stimulation intensities (Rosenkranz, Williamon, & Rothwell, 2007), as limited evidence suggests higher intensities might be required to detect changes in neural function following skill learning (Kleim, Kleim, & Cramer, 2007).

## 5 | SUMMARY AND CONCLUSION

This study assessed the acute and short-term neural responses to whole body resistance training at multiple levels of the corticospinal pathway, in non-specific and, for the first time, task-specific tasks. We hypothesised measuring responses in a novel task-specific assessment task would allow for a more sensitive assessment of the corticospinal adaptation to resistance training, but this hypothesis was rejected. For the immediate response to resistance exercise, an increase in spinal excitability was demonstrated, but this was not task-specific. After a period of resistance training, there were marked increases in task-specific strength, but no change in muscle thickness. This absence of increase in muscle thickness of VL in the presence of a task-specific strength increase implies that neural adaptation was responsible, but surprisingly there were no changes in intracortical, corticospinal, or spinal responses in both specific and non-specific tasks. The results of the present study therefore suggest that alterations in the corticospinal tract, when measured in the VL, might not contribute to task-specific improvements in strength following lower-body compound resistance exercise. Further work is required, including concomitant assessment of synergist muscles and consideration for other descending tracts, to gain a more holistic understanding of CNS adaptations to lower-limb compound resistance training.

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### CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

### AUTHOR CONTRIBUTIONS

The experiments were performed in the Integrated Physiology Laboratory at Northumbria University. P.A., C.G.B., J.Š., D.K., A.F., K.M.H., R.D., G.H., S.G. and K.T. conceived and designed the study; P.A., C.G.B., J.Š. and K.M.H. acquired the data; P.A., C.G.B., J.Š., K.M.H. and L.A. analysed the data; P.A., C.G.B. and J.Š. drafted the manuscript; all authors edited and revised the manuscript. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work ensuring that questions related to the accuracy and integrity of any part of the work are appropriately investigated and resolved; all persons designated as authors qualify for authorship, and all those who qualify for authorship are listed.

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