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Differential modulation of corticomotor excitability in older compared to young adults following a single bout of strength -exercise

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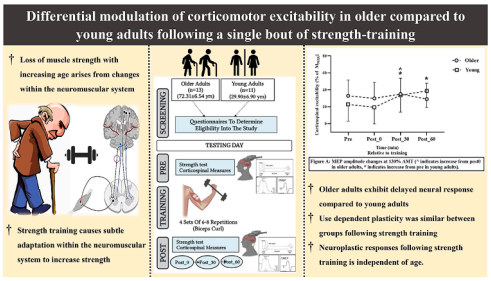
HIGHLIGHTS

- Corticomotor responses to a single bout of strength exercise vary between younger and older adults.
- Following a single bout of strength exercise, older adults exhibit a prolonged reduction in neural drive.
- There was no effect of a single bout of strength exercise on intracortical facilitation or inhibition.

GRAPHICAL ABSTRACT



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ABSTRACT

Evidence shows corticomotor plasticity diminishes with age. Nevertheless, whether strength-training, a proven intervention that induces corticomotor plasticity in younger adults, also takes effect in older adults, remains untested. This study examined the effect of a single-session of strength-exercise on corticomotor plasticity in older and younger adults. Thirteen older adults (72.3 ± 6.5 years) and eleven younger adults (29.9 ± 6.9 years), novice to strength-exercise, participated. Strength-exercise involved four sets of 6–8 repetitions of a dumbbell biceps curl at 70–75% of their one-repetition maximum (1-RM). Muscle strength, cortical, corticomotor and spinal excitability, before and up to 60-minutes after the strength-exercise session were assessed. We observed significant changes over time ($p < 0.05$) and an interaction between time and age group ($p < 0.05$) indicating a decrease in corticomotor excitability (18% $p < 0.05$) for older adults at 30- and 60-minutes post strength-exercise and an increase (26% and 40%, all $p < 0.05$) in younger adults at the same time points. Voluntary activation (VA) declined in older adults immediately post and 60-minutes post strength-exercise (36% and 25%, all $p < 0.05$). Exercise had no effect on the cortical silent period (cSP) in older adults however, in young adults cSP durations were shorter at both 30- and 60- minute time points (17% 30-minute post and 9% 60-minute post, $p < 0.05$). There were no differences in short-interval cortical inhibition (SICI) or intracortical facilitation (ICF) between

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groups. Although the corticomotor responses to strength-exercise were different within groups, overall, the neural responses seem to be independent of age.

1. Introduction

The decline in force production accompanying ageing can be attenuated through strength-training, as evidenced by various studies (Caserotti et al., 2008; Häkkinen et al., 2001; Hortobágyi et al., 2001; Marques et al., 2022). Notably, in its initial phase, strength-training augments force production without inducing significant muscle hypertrophy (Sale, 1988). These enhancements stem from early adaptations within the central nervous system (CNS), spanning cortical, corticomotor, and spinal levels (Carroll et al., 2002; Kidgell et al., 2017; Mason et al., 2019b; Muellbacher et al., 2001; Nuzzo et al., 2017). The objective of this study is to assess the impact of strength training-related on neuromotor adaptations and to differentiate between (training) effects exerted at cortical, corticomotor and/final common pathways.

In older adults, there is a well-documented reduction in corticomotor excitability, supported by various studies (Hortobágyi & DeVita, 2006; Oliviero et al., 2006; Sale & Semmler, 2005; Woldeamanuel et al., 2022). Transcranial magnetic stimulation (TMS) studies consistently report an age-related decline in motor-evoked potentials (MEPs), indicating a reduced ability to activate corticomotoneuronal cells (Eisen et al., 1991). Paired-pulse TMS paradigms also reveal age-related reductions in cortical inhibitory mechanisms (Kossev et al., 2002; Wassermann, 2002) and shortened silent period durations (Eisen et al., 1996; Prout & Eisen, 1994; Sale & Semmler, 2005). Insights from motor training studies further support these findings, suggesting a delayed emergence of use-dependent corticomotor plasticity in older adults, particularly following a single session of ballistic motor training (Semmler et al., 2021).

Research examining the effects of acute strength-exercise in young adults has shown increased corticomotor excitability, such as intracortical facilitation (ICF) (Latella et al., 2017) and corticomotor excitability (Hendy & Kidgell, 2014; Latella et al., 2016, 2017; Leung et al., 2015; Nuzzo et al., 2016), evident in increased MEPs and reduced silent periods (Latella et al., 2017). While a single session of strength-exercise induced sustained corticomotor plasticity for two weeks in young adults (Mason et al., 2019a), these responses remain untested in older adults. To date, only one two-week training study in older adults reported reduced MEP amplitude and shorter silent period duration targeting the ankle dorsiflexor muscles (Christie & Kamen, 2014). Therefore, a comprehensive understanding of the acute corticomotor responses to strength-exercise in older adults is warranted (Siddique et al., 2022).

Furthermore, voluntary activation (VA), an electrophysiological technique assessing neural transmission from the motor cortex to muscles, declines with age (Clark & Taylor, 2011; Harridge et al., 1999; Jakobi & Rice, 2002; Shinohara et al., 2003). However, research on VA improvements post strength-exercise in older and younger adults has produced inconclusive results (Cannon et al., 2007; Walker & Häkkinen, 2014). Additionally, adaptations within the spinal cord that may contribute to increased force production after strength-exercise have been explored using cervicomedullary evoked potentials (CMEPs) in younger adults (Nuzzo et al., 2016). However, there is a lack of research on acute spinal responses post a single strength-exercise session in older adults.

Understanding the acute neural responses to strength-exercise, specifically, a the cortical, corticomotor (assessed via TMS and VA), and spinal levels (evaluated through CMEPs) is important for understanding the long-term neural adaptations to strength-training. Therefore, the primary aim of this investigation focuses on exploring the immediate neural responses, following metronome-paced strength-exercise training (MPST), in older adults. Existing evidence suggests that variations in corticomotor responses are task-dependent (Tinazzi et al., 2003). Distinguished by its synchronization with an external metronome, MPST differs from self-paced strength-training (SPST) (Leung et al., 2017). Recent findings propose its potential to augment corticomotor excitability compared to SPST (Gómez-Feria et al., 2023). Given that older adults often manifested reduced use-dependent plasticity, implying potential disparities compared to younger individuals (Rogasch et al., 2009), our study aimed to evaluate the immediate responses at the cortical, corticomotor, and spinal levels following MPST in young and older adults. We anticipated subtle alterations in corticomotor plasticity after MPST, potentially showing delayed or diminished effects in the older participants. Additionally, we sought to compare these responses between age groups to identify differences in corticomotor excitability, inhibition, and neural drive

2. Methods

2.1. Subjects and experimental approach

Thirteen older adults (6 males and 7 females, aged 72 ± 6 years, stature 162 ± 19 cm, mass 69 ± 14 kg, BMI 26.95 ± 6.80) and eleven younger adults (5 males and 6 females, aged 29 ± 6 years, stature 168 ± 10 cm, mass 67 ± 14 kg, BMI 23.65 ± 5.54) volunteered to participate in the study. All participants were screened for neurological (TMS safety questionnaire) and musculoskeletal diseases or injuries and confirmed their sedentary status through self-report. Among the older adults, 6 were taking blood pressure medications (Avapro, Olmetec, Irbesartan, Olmesartan, Co-Diovan, Karvezide) and had their condition under control. Additionally, participants completed the Physical Activity Readiness Questionnaire (PAR-Q) and the International Physical Activity Questionnaire (IPAQ). Notably, both the older and younger group were categorized as inactive, with MET-min values below 600 (583 MET-min for the older group and 587 MET-min for the younger group) based on their IPAC scores (Committee, 2005). Furthermore, none of the participants had engaged in strength-training over the past 12 months. Hand dominance was assessed through the Edinburg Handedness Inventory, yielding mean Laterality Scores of 89 ± 17 for the older group and 80 ± 50 for the younger group (Oldfield, 1971). The study received approval from Monash University Human Research Ethics Committee (Project ID: 29887) and prior to the commencement of testing, each participant provided written informed consent. All experiments were conducted in strict adherence to the ethical standards set forth by the Helsinki Declaration.

Participants made two separate visits to the laboratory, allowing for a maximum seven-day interval between visits. During the first visit, participants underwent a familiarization session that encompassed the following procedures: (a) Measurement of stature (in centimetres) and weight (in kilograms); (b) Introduction and orientation to TMS, peripheral electrical nerve stimulation (PNS), and surface electromyography (sEMG). The subsequent visit involved the testing phase, which included the investigation of various neuromuscular outcome measures (Fig. 1) both before and after a single session of strength-exercise. It is important to note that both the older and younger participant groups engaged in strength-exercise during the testing phase only.

2.2. Strength-exercise protocol

All participants completed a single strength exercise session comprising standard unilateral bicep curls synchronized to a metronome (3 sec arm flexion and 4 sec arm extension) (Kidgell et al., 2010). Participants were instructed to maintain this tempo consistently throughout the entire exercise session, ensuring uniformity and standardization

across all participants. To allow for recovery, a 2-minute interval was allocated between sets, and continuous verbal encouragement was provided throughout the exercise session. Each participant completed four sets, with each set comprising 6 to 8 repetitions. The resistance was adjusted to 70–75% of their one-repetition maximum (1-RM). Additionally, surface electromyography (sEMG) data was collected during both the concentric and eccentric phases of the exercise to monitor muscle activation throughout each set.

2.3. Surface electromyography

Surface electromyography (sEMG) was recorded from the dominant biceps brachii muscle using bipolar Ag-AgCl electrodes. The electrodes were placed according to SENIAM recommendations (Hermens et al., 2000). Prior to electrode placement, the skin was abraded and cleaned with 70% isopropyl alcohol to minimise skin impedance (Gilmore & Meyers, 1983). The electrodes were positioned approximately 2 cm apart over the muscle belly, along the line connecting the medial acromion to the cubital fossa, specifically at a distance of one-third from the cubital fossa. The ground electrode was placed on the lateral epicondyle of the Humerus. sEMG signals were amplified (×1000), bandpass filtered (high pass at 13 Hz, low pass at 1000 Hz), digitized online at 2 kHz for 1 s, recorded and analysed using Power lab 4/26 (AD Instruments, Bella Vista, Australia). The sEMG signals were recorded at baseline and at post-time points of 0, 30, and 60 minutes following a single bout of strength-exercise for all measures.

2.4. Voluntary strength testing

Voluntary dynamic strength of the biceps brachii muscle was assessed via the one-repetition maximum (1-RM) test. This test established the training load for the single strength-exercise session i.e., 70–75% of the 1-RM (Leung et al., 2017). This procedure has been shown to be highly reliable (Kidgell et al., 2010; ICC = 0.980, CV% = 4.5) and 1-RM testing in the biceps brachii has been shown to be just as reliable as large muscle group actions e.g., bench press (ICC = 0.998 versus 0.999 in Seo et al., 2012) in both males and females. Participants initially identified the maximum weight dumbbell they could lift and then stood against a wall with their nondominant hand behind the back. Next, with the dumbbell in their dominant hand, elbow fully extended and forearm supinated, the participant was instructed to flex their arm to perform a standard biceps curl. A 3-minute recovery period between each curl minimized muscle fatigue (Kidgell et al., 2010). After successful completion of a curl, the dumbbell weight was increased (0.5 kg increments) until the participant could no longer complete a complete curl. The heaviest weight lifted was recorded as the participant's 1-RM.

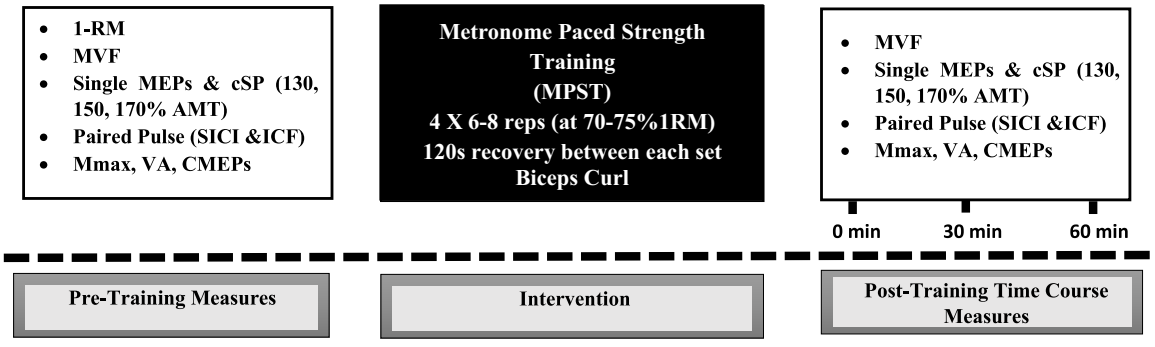
2.5. Maximum voluntary force

Maximum voluntary isometric force (MVF) of the biceps brachii was recorded for each participant. Participants were seated in a chair with their shoulders relaxed and their elbow flexed at 90°. Participants were instructed to maintain a supinated hand position under the force transducer (Futek Force Transducer LSB302, Melbourne), which was positioned at the forearm level corresponding to the wrist. Subsequently, participants were asked to exert force against the transducer for a duration of three seconds and the maximum force achieved was recorded. Three consecutive trials were performed, with three minutes of rest between each trial to minimize fatigue. Each trial was required to have a difference of no more than 5% from one another. The highest force amongst the three trials was documented as the participant's MVF. MVF testing was conducted at baseline and at all subsequent time points (0, 30, and 60 minutes) following a single bout of strength-exercise.

2.6. Transcranial magnetic stimulation

Motor cortical responses were investigated via single- and paired-pulse TMS paradigms, administered using a Magstim 200^2 stimulator (Magstim Co., Ltd, Whitland, UK). The localisation of the motor hotspot pertaining to the biceps brachii muscle within the primary motor cortex (M1) was determined utilising the international 10–20 system (Jasper, 1958). A circular coil measuring 90 mm in diameter was positioned over this cortical region with a posterior-to-anterior current flow orientation. The objective was to elicit motor-evoked potentials (MEPs) in the biceps brachii. The motor hotspot was precisely determined at the optimal scalp location where the largest MEP response in the biceps brachii was generated during a 10% MVF contraction. To ensure consistent coil placement during the testing session, this optimal scalp position was marked as the motor hotspot. The active motor threshold (AMT) for each participant was established as the minimum threshold intensity necessary to evoke MEP amplitudes exceeding 200μV, a criterion previously established (Kidgell et al., 2010), in at least five out of ten stimulus presentations. The AMT was reassessed and adjusted if necessary following the single session of strength-exercise at time points immediately post, 30-and 60 minutes post.

Single-pulse TMS was used to determine corticomotor excitability (MEP amplitude) and corticomotor inhibition (silent period duration) by constructing stimulus-response curves. Five pulses were delivered at 130%, 150% and 170% of AMT during a 10% low-level isometric contraction of their predetermined MVF (Rogasch et al., 2009). The TMS pulses were delivered with a 10-second interval using a metronome (Kidgell et al., 2010). Additionally, 10 paired-pulse stimuli were administered to assess corticocortical excitability (ICF, glutamatergic



1RM one repetition maximum, *MVF* maximum voluntary force, *MEPs* motor-evoked potentials, *cSP* cortical silent period, *AMT* active motor threshold, *SICI* short interval intracortical inhibition, *ICF* intracortical facilitation, *Mmax* maximum M_{wave}, *VA* voluntary activation, *CMEPs* cervicomedullary evoked potentials.

Fig. 1. Schematic representation of the experimental design with measures obtained before and following single session metronome-paced strength training (MPST).

activity) and inhibition (SICI, GABA-$_A$ mediated neurotransmission). In the assessment of SICI, the stimulator output intensity was configured at 130% of AMT for the test response and 80% of AMT for the conditioning stimulus, employing an interstimulus interval of 3 ms. In the case of ICF, the interstimulus interval was set at 10 ms with test and conditioning pulses configured identically. TMS was administered both before and after the single session of strength-exercise, occurring at three distinct time points: immediately post strength-exercise, 30 minutes post strength-exercise, and 60 minutes post strength-exercise. In order to eliminate the possibility of pre-existing fluctuations in rmsEMG (root mean square electromyography) immediately prior to and following the strength-exercise session, we additionally gathered rmsEMG data during the 100 ms interval preceding the administration of each TMS pulse. All data was collected and analysed using LabChart™ v8.1.24 software (ADInstruments, Bella Vista, Australia).

2.7. Maximum compound action potential

Supramaximal electrical stimulation (pulse width 200μs) was administered at Erb's point (brachial plexus) using a constant current electrical stimulator (DS7A, Digitimer, Hertfordshire, UK) to elicit the maximal compound action potential (M-wave). Stimulating electrodes (3.2 cm round, Axelgaard Manufacturing Co., LTD) were utilized, with the cathode placed over the supraclavicular fossa and the anode over the acromion, to elicit direct muscle responses from the biceps brachii muscle. Initially, low-level electrical stimuli were delivered while the participant isometrically contracted at 10% of their MVF. The stimulation intensity was gradually increased (5 mA) until there was no further increase in the peak-to-peak amplitude sEMG response. To ensure maximal muscle responses, the threshold intensity was increased by an additional 20%, and the maximal M-wave (M_{MAX}) was recorded. Three trials were performed with 6–8 s of rest between each trial.

We started the data collection process with baseline M_{MAX} recordings. Subsequent M_{MAX} measurements were then captured at specific time intervals: immediately post strength-exercise, at the 30-minute time point, and at the 60-minute time point following a single bout of strength-exercise. This approach aimed to document and assess any alterations in peripheral muscle excitability that might potentially impact MEP amplitude.

2.8. Cervicomedullary evoked potentials

Cervicomedullary evoked potentials (CMEPs) were also recorded from the participants by stimulating the cervicomedullary junction (Taylor & Gandevia, 2004). Transmastoid electrical stimulation (200 μs duration, DS7A, Digitimer, Hertfordshire, UK) was delivered using neurostimulation electrodes (3.2 cm round, Axelgaard Manufacturing Co., LTD), with the cathode placed on the left and the anode on the right side of the mastoid processes (Nuzzo et al., 2016). The participants underwent stimulation at their individual M_{MAX} intensities (ranging from 72 to 264 mA). This was done while they engaged in isometric contractions at 50% of their MVF level, resulting in responses characterised by peak-to-peak amplitudes of 70% of M_{MAX} in the biceps brachii muscle. We also analysed latencies of CMEPs. We conducted a meticulous analysis of each response latency, excluding any latencies that deviated from the predetermined range of 6 to 8 ms. CMEPs were recorded both before and after a single session of strength-exercise, with data collection occurring at three specific time points: immediately post strength-exercise, at 30-minutes post, and at 60-minutes post.

2.9. Central activation ratio

In the assessment of the central activation ratio (CAR), participants first completed an MVF test of the dominant bicep brachii muscle. Once the participant's MVF was determined, participants received supramaximal electrical stimulation administered using a pulse width of 200 μs (DS7A, Digitimer, Hertfordshire, UK) delivered at Erb's point within the brachial plexus whilst they executed a near maximal contraction (i.e., > 90% MVF) (Gauche et al., 2009). CAR measurements were obtained both prior to and following the single session of strength-exercise, capturing data at distinct time points: immediately post strength-exercise, at the 30-minute time point, and at the 60-minute time point, to assess changes over time and to measure VA.

3. Data analysis

In the recorded TMS data, we extracted pre-stimulus rmsEMG activity from the biceps brachii muscle, occurring 100 ms prior to the application of the TMS pulse, at various experimental time points. Any trials in which the pre-stimulus rmsEMG exceeded 8±1% of the maximal rmsEMG were excluded and repeated. The peak-to-peak amplitude of MEPs were quantified within the dominant biceps brachii muscle, which was contralateral to the stimulated primary motor cortex. This measurement was conducted within the timeframe of 10–50 ms post-stimulation. The resultant MEP values, expressed in mV, were normalized to M_{MAX} and scaled by a factor of 100. Data analysis was executed using Lab Chart Software (ADInstruments, Bella Vista, Australia).

The duration of the cSP was determined through visual inspection. To ensure consistency and accuracy, the initiation of the silent period was computed from the stimulus onset, and the conclusion of the silent period was assessed upon the return of sEMG activity to pre-stimulus levels. This was achieved by positioning horizontal cursors on the maximum and minimum pre-stimulus sEMG levels and identifying the moment when the sEMG crossed these threshold levels subsequent to the silent period (Wilson et al., 1993).

To assess paired-pulse data at different time points, SICI and ICF ratios were computed. This involved dividing the MEP elicited by paired-pulse stimulation by the MEP induced by single-pulse stimulation (set at 130% of AMT) and then multiplying the result by 100.

To evaluate the overall neural drive to the elbow flexors, we calculated the CAR (Knight & Kamen, 2001). This comparison involved measuring the MVF that was achieved during maximal isometric testing and then comparing to the MVF achieved via supramaximal electrical stimulation. CAR was calculated using the following formula (Knight & Kamen, 2001):

$$\mathrm{CAR}(\%) = (\mathrm{VoluntaryForce} \,/\, \mathrm{MaximalForce})\mathrm{x}100$$

Peak-to-peak amplitude of CMEPs was calculated utilising the cursor and normalised to M_{MAX} amplitude using the formula:

$$[(\mathrm{CMEPsamplitude} \,/\, M_{MAX})\mathrm{x}100].$$

Finally, relative strength was also calculated for each participant by dividing their respective body weight by their individual baseline MVF. Moreover, 1-RM rmsEMG was also recorded while assessing 1-RM strength. Additionally, training load-volume for each participant was computed using the formula:

$$(\mathrm{sets} \times \mathrm{repetitions} \times \mathrm{load})$$

4. Statistical analysis

The sample size for our study was determined using G*Power software. Given the limited number of studies investigating the effects of a single session of strength exercise on corticomotor responses in older adults, our calculation was based on the research by Christie and Kamen (2014). Their study reported an effect size of 1.02 for the change in cSP following a two-week training regimen targeting the ankle dorsiflexor muscle. For sample size calculation, we set the statistical power (β) to 0.80 and the significance level (α error probability) to 0.05, employing the observed effect size of 1.02 from prior analysis. This indicated a requirement of 12 participants per group. Subsequently, 13 older and 11 young volunteers were entered to the study.

We also conducted a normality assessment of all collected data using the Shapiro-Wilk test (all data were normally distributed). In order to investigate the influence of a single session of strength-exercise on the cortical, corticomotor, and spinal responses, we employed a Linear Mixed Model with repeated measures (LMM_{RM}) (Wilkinson et al., 2023). This model served as a robust framework for analysing our data considering both fixed and random effects simultaneously. Corticomotor excitability and inhibition (MEPs and cSP at 130%, 150%, 170% AMT), intracortical inhibition (SICI) and facilitation (ICF), CMEPs and CAR were assessed using the LMM_{RM}. The model included time (Pre, Post0, Post30, Post60) and age group (older and younger) as main effects, and an interaction between age group (younger and older) and time with participants as the random effect within the model. Post-hoc comparisons were conducted using the least significant difference (LSD) correction method.

We also performed unpaired *t*-tests to report baseline and between group differences among younger and older adults. In all comparisons, effect sizes (ES) of 0.2, 0.5 and 0.8 were used to indicate a small, moderate and large effect respectively (Cohen's *d;* Cohen, 1973). All analyses were conducted using SPSS Statistics v28.0 (SPSS, IBM, New York) and graphs were constructed using GraphPad Prism Software. The significance level was set at 0.05; all data reported in text are mean differences, whilst figures and tables are reported as mean ± SD.

5. Results

No participants withdrew or reported any negative effects from participating in the study. No significant differences were observed between groups at baseline for the following variables: MVF ($p = 0.06$), AMT ($p = 0.18$), relative strength ($p = 0.13$), CAR ($p = 0.63$), SICI ($p = 0.25$), ICF ($p = 0.053$), one-repetition maximum (1-RM) rmsEMG ($p = 0.39$), or MVF rmsEMG ($p = 0.95$). At baseline, differences were observed in the duration of the cSP when all stimulator intensities were pooled together. Specifically, the older group exhibited a significantly shorter cSP duration compared to the younger group ($p = 0.002$, $d = 0.41$), as well as reduced CMEP amplitudes ($p = 0.03$, $d = 0.19$). There were also differences in 1-RM strength ($p = 0.02$; $d = 0.79$), 1RM relative strength ($p = 0.03$; $d = 0.99$ and training volume ($p = 0.005$, $d = 0.64$) when comparing the older and younger groups (refer to Table 1). Table 2 displays the mean ± SD for AMT stimulus intensity, M_{MAX} amplitude, electrical stimulator output (ESO) to elicit M_{MAX}, single-pulse TMS pre-stimulus rmsEMG and paired-pulse TMS pre-stimulus rmsEMG prior to and following the single bout of strength-exercise for the biceps brachii (Tables 1 and 2).

5.1. Maximal voluntary force

Following strength-exercise, we showed a significant main effect for Time ($F_{1,3} = 3.1$, $p < 0.003$), with post hoc analysis showing that there was a significant decrease in MVF from pre to post (MD = 7.5, $p = 0.01$, 95% CI [1.72 to 13.3], $d = 0.56$) in the older adults. There were no main effects for Age Group or Time by Age Group (all $p > 0.05$, Table 1).

5.2. Corticomotor excitability (MEPs)

We showed a significant main effect for Time ($F_{1,\ 3} = 29.5$, $p < 0.001$), maximal stimulator output (MSO) ($F_{1,\ 2} = 126.92$, $p < 0.001$) and a significant Time by Age Group interaction for corticomotor excitability ($F_{1,\ 3} = 21.5$, $p < 0.001$). However, the main effect of Age Group was not statistically significant ($p = 0.89$; refer to supplementary Table 1 for details). In older adults, corticomotor excitability at 130% AMT remained unchanged immediately following strength-exercise ($p > 0.05$). However, corticomotor excitability increased at 30-minutes post strength-exercise (MD = 5.11, $p = 0.026$, 95% CI [0.598 to 9.615], $d = 0.27$). Subsequently, at 150% of the AMT, corticomotor excitability decreased immediately post strength-exercise (MD = −7.167, $p = 0.005$, 95% CI [−11.565 to −2.008], $d = 0.36$). Interestingly, corticomotor excitability increased at 30-minutes (MD = 5.715, $p = 0.021$, 95% CI [0.855 to 10.574], $d = 0.38$) and 60-minutes (MD = 7.17, $p = 0.004$, 95% CI [2.346 to 11.987], $d = 0.30$) post strength-exercise. However, at 170% of AMT, corticomotor excitability decreased at all post-exercise time points (0, 30, and 60 minutes) (MD = −16.57 to −13.51, all $p < 0.001$, $d = 0.56$ to 0.87; Fig. 2).

For the younger adults, corticomotor excitability at 130% of AMT increased across the post strength-exercise time points (MD = 10.74 to 19.39, all $p < 0.001$, $d = 0.54$ to 0.98). Additionally, at 150% of AMT, corticomotor excitability decreased immediately following strength-exercise (MD = −6.351, $p = 0.015$, 95% CI [−11.448 to −1.254], $d = 0.32$). However, at 30- and 60-minutes following strength-exercise corticomotor excitability increased (MD = 6.14 to 17.03, all $p < 0.05$, $d = 0.51$ to 0.71, Table 3). Interestingly, similar to the older adults, at 170% of AMT, corticomotor excitability decreased immediately post strength-exercise (MD = −5.832, $p = 0.02$, 95% CI [−10.929 to −0.735], $d = 0.30$), and then recovered, with increases at 30-and 60-minutes following the strength-exercise (MD = 5.89 to 13.74, $p < 0.05$, $d = 0.30$ to 0.69, Fig. 2 and supplementary Fig. 1).

5.3. Cortical silent period (cSP)

For corticomotor inhibition, we showed a significant main effect for Time ($F_{1,\ 3} = 3.9$, $p = 0.008$), MSO ($F_{1,\ 2} = 58.4$, $p < 0.001$), and a Time by MSO interaction ($F_{1,\ 6} = 2.4$, $p = 0.023$). There were no main effects for Age Group ($p = 0.59$). For the main effect of time by MSO, post hoc analyses showed that corticomotor inhibition remained unchanged post strength-exercise for the older adults at all stimulus intensities. However, corticomotor inhibition was reduced in the young adults at 150%

Table 1
Mean ± SD values for 1RM, 1RM rmsEMG(%M_{MAX}), MVF, Relative Strength, MVF rmsEMG and Training Load-volume for biceps brachii prior to and following a single session of strength exercise.

	Older				Young			
Measure	Pre	Post0	Post30	Post60	Pre	Post0	Post30	Post60
1RM (kg)	**10.4±2.7***				12.5±4.4			
1RM Range (kg)	8.8				12			
1RM Relative Strength	**0.15±0.03***				0.19±0.05			
1-RM rmsEMG (%M_{MAX})	11.6±7.2				9.8±3.7			
MVF (N)	58.0±16.3	**50.41±11.5#**	53.1±12.6	53.6±16.3	68.0±23.3	65.6±21.8	61.5±21.2	63.0±23.0
MVF Range (N)	73				92			
Relative Strength(N/kg)	0.9±0.2				1.2±0.3			
MVF rmsEMG (% M_{MAX})	8.6±4.3	6.8±3.3	7.7±4.7	8.9±5.0	8.5±4.9	5.9±3.6	6.9±3.8	8.4±5.0
Training Load-Volume (Au)	**932.5±246.7***				1154.3±440.6			

* denotes $P<0.05$ baseline in older group compared with young adults for the same variable. # denotes $P<0.05$ for reduced MVF in the older group following strength exercise. *Au*, arbitrary unit; *1RM*, one repetitions maximum; *N*, newton; *MVF*, maximum voluntary force; M_{MAX}, maximum M-wave; *rmsEMG*, root-measure square electromyography

Table 2
Mean±SD for AMT Stimulus Intensity, M_{MAX} amplitude, ESO M_{MAX}, single-pulse TMS pre-stimulus rmsEMG and paired-pulse TMS pre-stimulus rmsEMG prior to and following the single bout of strength exercise for the biceps brachii.

	Older				Young			
Measure	Pre	Post0	Post30	Post60	Pre	Post0	Post30	Post60
AMT SI (%)	51±12	51±1	50±1	50±1	48±7	48±7	47±7	47±7
M_{MAX} (mV)	5.8±2.6	6.00±2	4.9±1.2	4.8±1.3	8.7±4.7	8.9±4.0	7.2±4.0	7.2±3.4
ESO M_{MAX} (mA)	136.1±65.4				112.9±19.8			
SPrmsEMG (%M_{MAX})	1.9±1.6	1.5±1.6	1.8±2.2	1.5±2.6	1.0±0.8	0.8±0.6	0.9±0.7	1.5±1.2
PPrmsEMG (%M_{MAX})	1.5±1.1	1.6±2.1	1.8±2.4	2.0±3.0	0.7±0.4	0.6±0.4	0.9±0.9	1.3±1.3

AMT active motor threshold, *ESO* electrical stimulator output, *EMG* electromyography, *mA* milliamps, maximum compound action potential, *PPrmsEMG* paired-pulse root-mean-squared EMG, *SI* stimulator intensity, *SPrmsEMG* single-pulse root-mean-squared EMG.

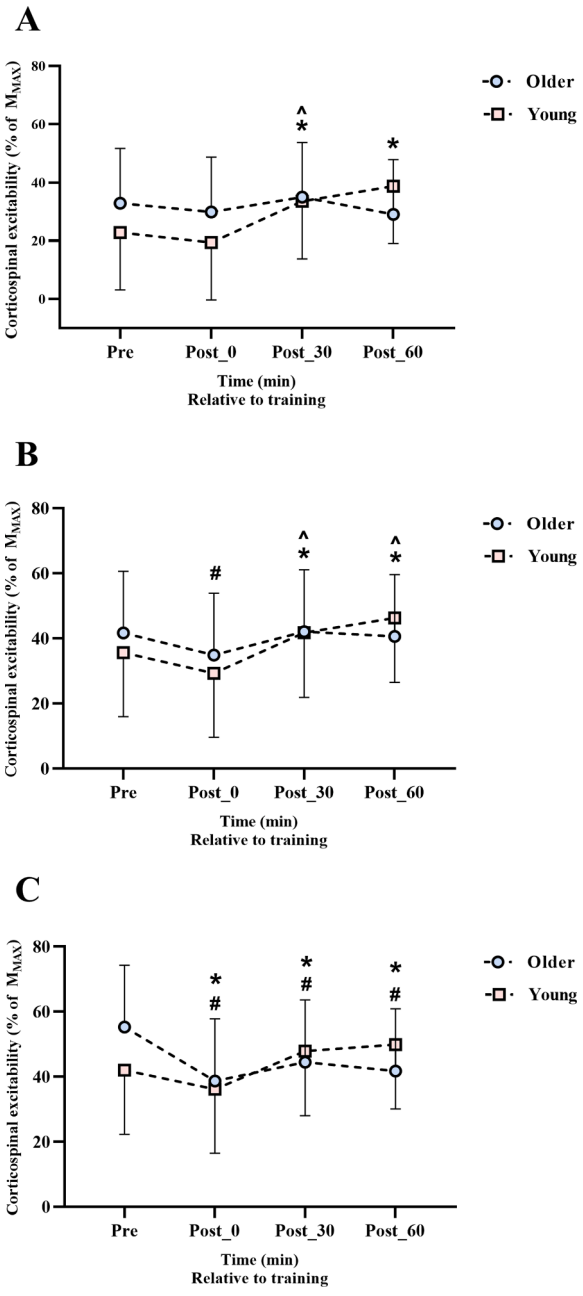


Fig. 2. MEP amplitude at (A)130% AMT (B)150% AMT and (C)170% AMT of the biceps brachii, expressed as $M_{MAX.}$ (Mean±SD). ^ indicates a significant increase in MEP amplitude from Post 0 in older adults, while * indicates a significant increase from baseline in young adults. # indicates a significant decrease in MEP amplitude at various time points (0, 30, and 60 minutes) from baseline in both older and young adults.

AMT at 30-minutes post strength-exercise (MD = −15.63, p = 0.044, 95% CI [−30.839, −0.427], d = 0.47). This reduction remained at 30-minutes (MD = −31.14, $p < 0.001$, 95% CI [−46.268, −16.016], d = 0.31) and 60-minutes post strength-exercise (MD = −19.86, p = 0.010, 95% CI [−34.909, −4.813], d = 0.60); at 170% of AMT (Fig. 3, Supplementary Table 2).

5.4. SICI and ICF

There were no main effects for Time ($F_{3, 53} = 0.62$, $p = 0.61$), Age Group ($F_{1, 21} = 0.15$, $p = 0.70$) or Time by Age Group interactions ($F_{1, 3} = 5.31$, $p = 0.01$). Notably, there were no main effects for Time ($F_{3, 47} = 0.41$, $p = 0.74$), Age Group ($F_{1, 22} = 3.7$, $p = 0.06$), or Time by Age Group interactions ($F_{3, 47} = 0.84$, $p = 0.48$) in the context of intracortical facilitation.

5.5. CAR and CMEP

Significant main effects were observed for Time ($F_{3, 48} = 6.8$, p = 0.006), and a Time by Age Group interaction ($F_{3, 48} = 2.8$, $p = 0.006$). there were no significant main effects for Age Group ($p = 0.35$). Post-hoc comparisons for the Time by Group interaction indicated a 36% decrease in CAR immediately post strength-exercise for the older adults (MD = 34, $p = 0.0005$, 95% CI [8.2, 60], $d = 2.05$). Furthermore, this reduction was sustained at the 60-minute post-assessment time point, with a 35% decrease (MD = 33, p = 0.01, 95% CI [5.6, 59], d =1.81, Fig. 4). In contrast, there were no differences in neural drive following strength-exercise for the younger adults. There were no significant main effects for Time (p = 0.30), Age Group (p = 0.43), or any Time by Age Group Interactions (p = 0.21) for spinal excitability (CMEPs).

5.6. Muscle activation during exercise

During the single session of strength-exercise, we recorded sEMG activity during each repetition and set for both the concentric and eccentric phases. There was a significant main effect for Muscle Action ($F_{1, 20} = 15.7$, $p < 0.0001$), whereby post-hoc analysis revealed that the sEMG activity (as % of the maximum rmsEMG obtained during 1-RM testing) during the concentric muscle action (M = 90) was significantly higher than during the eccentric muscle action (M = 19), with a mean difference of 71% (95% CI: 59 to 83). This result indicates that there was a substantial increase in sEMG activity during the concentric phase of each repetition. However, there was no significant main effect for Group on sEMG activity ($F_{1, 22} = 1.0$, $p = 0.32$). The predicted mean sEMG activity for the older group was 58%, while it was 51% for the younger group, with a small mean difference of 7.3% (95% CI: −7.6 to 22). Therefore, no significant differences were found between the two age groups in terms of sEMG activity during exercise. The interaction effect between Muscle Action and Age Group was also not significant ($F_{1, 20} = 0.50$, $p = 0.48$). This suggests that the relationship between Muscle Action and sEMG activity did not differ significantly between the older and younger groups (Fig. 5).

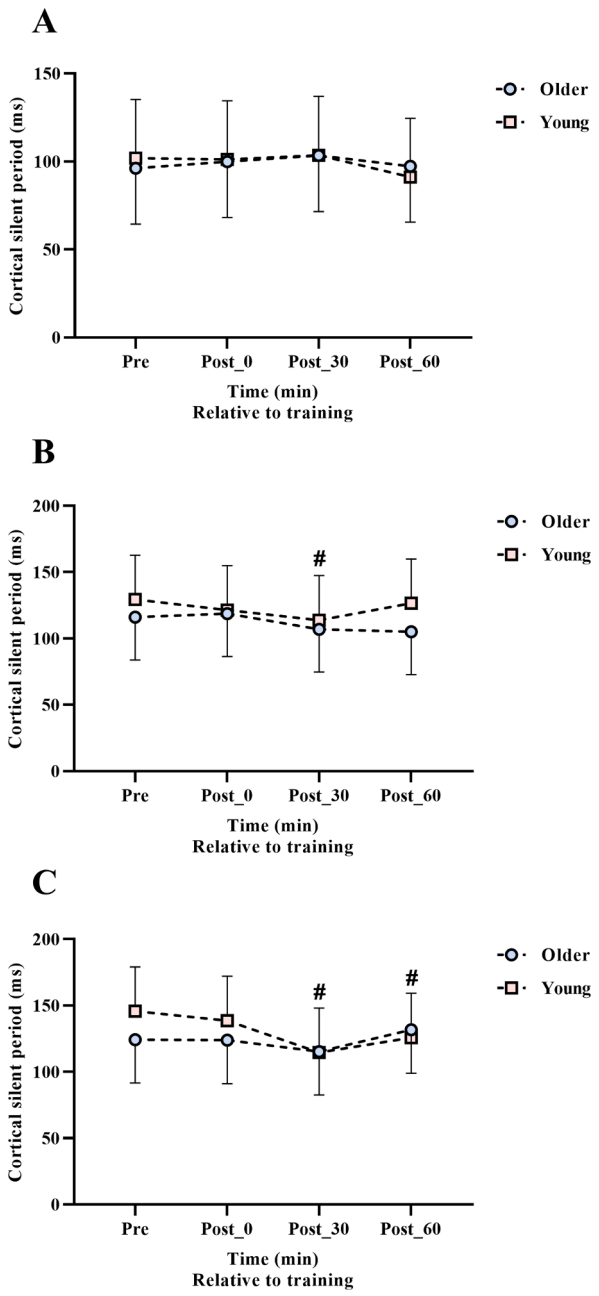


Fig. 3. cSP duration (Mean ± SD) at (A) 130 % AMT, (B) 150 % AMT, and (C) 170 % AMT of the biceps brachii in both older and young adults. # indicates a significant decrease in the silent period from baseline at 30- and 60-minutes post-exercise in young adults.

6. Discussion

The primary objective of this study was to investigate the immediate neurological responses in older individuals following a single session of high-intensity MPST, focusing on cortical, corticomotor, and spinal excitability. Specifically, we aimed to assess the neural drive towards the targeted muscles and explore potential effects at the spinal level by examining corticomotor axon excitability (CMEPs). To contextualize our findings, we conducted comparative analyses with younger cohorts to discern any differential responses to MPST. It is important to note, that our study cohorts were deliberately not matched based on their baseline 1RM strength. This intentional decision was taken to enable the investigation of age-related reductions in muscle strength and their effect on different corticomotor outcomes. We recognise that solely matching groups based on 1RM strength may not adequately address the diverse aspects of ageing, such as changes in muscle structure, neuromuscular function, and other physiological adaptations. In light of this, the primary findings of this study are as follows:

1. Our observations suggest a decrease in corticomotor excitability immediately post strength-exercise in older as compared to young sedentary adults. The distinction in the neural response to strength exercise in older vs younger adults is suggestive of a delayed response mechanism.
2. A noteworthy finding was the observed decrease in neural drive among older adults after strength-exercise. This indicates the potential induction of central fatigue in this age group, impacting their corticomotor responses.
3. No age-related differences were observed in intracortical excitability before or after strength-exercise in both young and older adults, suggesting that differences in corticomotor responses are unlikely to be attributed to variations in GABAergic or glutamatergic activity

6.1. Changes in corticomotor excitability and cortical silent period following MPST

Previous research has documented a decline in TMS-induced MEPs and alterations in plasticity within the motor cortex among older adults (Müller-Dahlhaus et al., 2008; Tecchio et al., 2008; Todd, 2010). Our findings are somewhat in line with this existing body of literature, as we observed a reduction in corticomotor excitability immediately after exercise. However, we noted a subsequent increase in MEP response following this initial decline. In contrast, we observed increases in corticomotor excitability in younger adults, persisting for up to 60-minutes post MPST. At the very least, our data support the existence of delayed neural responses due to reduced motor cortex excitability in older adults, consistent with previous studies (Bhandari et al., 2016; Freitas et al., 2013; Semmler et al., 2021; Zimerman & Hummel, 2010).

The observed post-initial-decline in corticomotor excitability is a noteworthy finding. While the exact mechanisms that modulate post exercise MEP depression are likely to vary among individuals, it is probable that some degree of central fatigue occurred in the older adults as a result of the high-intensity nature of the strength-exercise. First, the older adults completed considerably less volume-load of exercise when compared to the younger group (i.e., less repetitions in total) as the sets progressed, suggesting central fatigue may have occurred. Second, neural drive was reduced following MPST in the older adults, even at the post assessment time point of 60-minutes. Third, the cumulative effect seems to have resulted in a reduced ability of the CNS to activate motoneurons due to reduced excitability of the motor cortex. Various exercise protocols targeting different muscle groups have demonstrated variations in the duration of MEP depression. For instance, research has indicated varying durations of MEP depression in the elbow flexors (Tergau et al., 2000) and the wrist flexors (Samii et al., 1997). Notably, it appears that short-duration and high-intensity exercise tends to elicit more pronounced MEP depression compared to light-intensity exercise (Höllge et al., 1997). Also, studies have reported that the duration of MEP depression is correlated with the intensity of the exercise, with higher intensities being linked to more prolonged MEP depression (Sacco et al., 2000). These findings agree with the current study, whereby high-intensity strength-exercise led to MEP depression.

It is important to note that the observed immediate MEP depression was transient and may represent a physiological response to the acute stress induced by the strength-exercise session, particularly in older adults who exhibited comparatively lower strength levels than the young adults. Interestingly, this depression in MEP was then followed by a period of recovery and a subsequent increase in corticomotor excitability. The post strength-exercise increases in corticomotor excitability may reflect the activation of mechanisms related to use-dependent

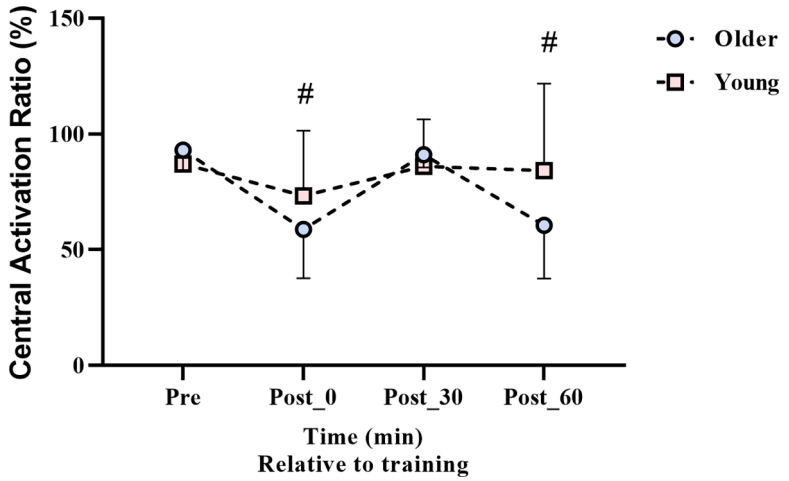


Fig. 4. Central activation ratio (Mean ± SD). # indicates a significant decrease in neural drive at post 0 and 60-minutes post-exercise in older adults compared to pre.

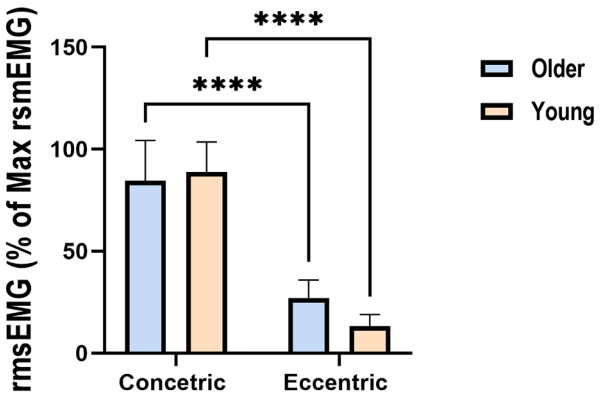


Fig. 5. Muscle activation ((Mean ± SD [% of rmsEMG]). **** indicates a significant increase in muscle activation between concentric and eccentric muscle actions during strength exercise for both the older and younger groups.

plasticity, whereby the nervous system adapts to the new training stimulus. Alternately, the increase may have been a compensatory response to account for the reduced neural drive observed.

Our findings also differ from those of the only other TMS strength-exercise study conducted in older adults by Christie and Kamen (2014), where significant changes in MEP amplitude were not observed after a two-week ankle dorsiflexor strength-exercise program. Furthermore, our prior research in younger adults demonstrated that the most significant TMS responses occur after a single session of strength-exercise and remain consistent throughout the training program (Mason et al., 2019a). The outcomes in younger adults align with our earlier research. However, the results in older adults agree with other studies (Rogasch et al., 2009), where MEPs were found to be suppressed in older adults compared to their younger counterparts following ballistic thumb training, a form of strength-exercise (Taube et al., 2020). This observation strongly implies a reduction in use-dependent plasticity associated with the normal-ageing process. Our study offers initial evidence of distinct acute neural responses to MPST in older adults compared to their younger counterparts. An important distinction between ballistic training and MPST appears to lie in the training intensity, with the latter involving significantly higher training intensities, specifically at 70–75% of their 1-RM. Recent research also supports the idea that there is a threshold for training intensity required to stimulate use-dependent plasticity in the elbow flexors (Colomer-Poveda et al., 2020). It is important to note that a single session of MPST may not be sufficient to overcome delayed and reduced responses, but sustained, long-term training efforts may potentially achieve this goal. Nevertheless, the facilitation of MEP amplitude in older adults following the initial post-exercise depression suggests that MPST has the potential to effectively induce use-dependent plasticity over time.

The current study did not observe any significant change in cSP following MPST in older adults. Previous research has established that cSP duration tends to increase following exercise (Ruotsalainen et al., 2014) and during fatigue (Gandevia et al., 1994; Gruet et al., 2014). However, our findings in older adults are unique and are not in alignment with a short-term training study which reported a decrease in cSP duration (Christie & Kamen, 2014). However, it is important to note that there was no baseline difference in cSP duration between the younger and older adults in the Christie and Kamen (2014) study. In the current study, we showed a 13.5 ms difference between older and younger adults. Further, this shortening in cSP is also similar to the difference that Sale and Semmler (2005) reported, which likely reflect an adaptive response (i.e., reduction) of $GABA_B$ neurotransmission related to advancing age.

The younger adults demonstrated reduced cSP durations post strength-exercise, which supports previous findings (Latella et al., 2017). This finding suggests that strength-exercise differentially modulates $GABA_B$ neurotransmission, with a release of inhibition in younger adults which may explain why neural drive was not different in the younger group. Further, it appears that strength-exercise in the older population does not exhibit a direct influence on $GABA_B$ neurons. The decline in motoneuron activation (i.e., reduced CAR) subsequent to strength-exercise likely involves mechanisms beyond the detection capabilities of TMS, such as enhanced presynaptic inhibition, which could potentially diminish motor output (Nielsen & Petersen, 1994), despite the concurrent elevation in corticomotor excitability. The increase in corticomotor excitability (and lack of change in cSP) following strength-exercise may be temporary in nature and related to mechanisms that differ from the processes associated with MPST. Alternatively, it is plausible that an increased number of training sessions is necessary for older adults to show a noticeable effect on $GABA_B$-mediated inhibition (Christie & Kamen, 2014).

6.2. *Changes in intra-cortical inhibition and facilitation following MPST*

We did not observe any significant physiological changes in the excitability of various intracortical circuits responsible for regulating corticomotor excitability. However, this study marks the first investigation into SICI during strength-exercise in older adults, and the results suggest that a single training session does not influence SICI. Several lines of evidence have pointed to a decrease in SICI among older adults

(Peinemann et al., 2001). However, contrasting studies have reported either no differences (Oliviero et al., 2006; Wassermann, 2002) or, in some instances, an increase in SICI (Kossev et al., 2002) with advancing age. However, interpreting these findings is challenging, given the existing evidence that indicates motor training can indeed induce changes in corticomotor plasticity (Muellbacher et al., 2001). It remains unclear why strength-exercise had no impact on SICI. Our strength-exercise regimen involved controlling elbow flexion in time with a metronome, which should have increased the motor tasks focus. However, our exercise engaged a large muscle with significant synergist input (Mason et al., 2017), possibly reducing the task specificity and, consequently, failing to modulate SICI.

Changes in ICF following MPST have received limited attention in both acute and chronic strength-exercise literature (Colomer-Poveda et al., 2020; Latella et al., 2017; Mason et al., 2019a). In our study, we observed that an acute session of MPST did not produce any noticeable effect on ICF in both older and younger adults. Our findings align with previous research involving younger adults which also reported no significant changes in ICF (Colomer-Poveda et al., 2020; Latella et al., 2016). Nevertheless, it is important to highlight that generating intracortical measures, such as ICF, has been demonstrated to be rather inconsistent, as evident from the lack of studies reporting on it (Kidgell et al., 2017), and none have investigated this phenomenon in older adults.

6.3. Changes in voluntary drive and spinal excitability following MPST

Neural drive, as assessed via the CAR, serves as an indicator of the overall efferent drive to the motoneuron pool (Gandevia et al., 1998; Knight & Kamen, 2001). Age-related variations in VA or CAR seem to exhibit discrepancies across different muscle groups. In individuals aged over 70 years, there is a notable reduction in CAR (i.e., VA) observed in the knee extensors and elbow flexors. Several studies have reported a 1–5% lower neural drive in elbow flexors among older adults compared to their younger counterparts (De Serres & Enoka, 1998; Hunter et al., 2016; Jakobi & Rice, 2002).

Interestingly, we observed a reduction in neural drive immediately following strength-exercise in older adults and 60 minutes post, whereas no changes were observed in younger adults. Considering the limited examination of acute changes in neural drive, our findings in younger adults align somewhat with some studies in the chronic strength-exercise literature that observed no changes in neural drive (Cannon et al., 2007; Harridge et al., 1999; Herbert et al., 1998; Scaglioni et al., 2002, Walker et al., 2013). However, some studies have reported increases in neural drive following training in both younger and older adults (Knight & Kamen, 2001; Walker & Häkkinen, 2014). The mechanism decreasing neural drive in older adults likely emanates from the reduction in MVF obtained post exercise during the CAR calculation. That is, older adults had consistently lower MVF values post strength-exercise compared to pre. Indeed, immediately post strength-exercise, MVF was reduced by 12% in the older adults and this decrease was sustained at 60-minutes (8% decrease with an average effects size of 0.6). The reduction in neural drive in the older adults is an important new finding that seems to follow the decrease in corticomotor excitability, the reduction in dynamic strength (i.e., 1-RM strength), the reduced training volume-load and the overall delay in corticomotor plasticity following strength-exercise.

One important objective of our current study was to examine the specific sites of adaptations (neural responses) subsequent to a single-session of strength-exercise. CMEPs are responses elicited through subcortical stimulation of corticomotor axons at the cervicomedullary junctions (Nuzzo et al., 2017). Importantly, they display significant monosynaptic components in the biceps brachii muscle (Petersen et al., 2002), and neurons targeted by corticospinal volleys do not exhibit presynaptic inhibition (Jackson et al., 2006; Nielsen & Petersen, 1994). The facilitation of CMEPs signifies an increase in the efficiency of corticomotor synapses or an increase in motoneuronal excitability. Our findings indicate that there was no notable facilitation of CMEPs following a single-session of strength-exercise in both younger and older adults. This study marks the first attempt to examine spinal changes after an acute strength-exercise session in older adults, and our observations revealed no significant differences. This finding alone warrants further investigation for future studies examining the neural adaptations to strength exercise in older adults.

6.4. Limitations

The present investigation introduces original findings elucidating synaptic adjustments at the cortical, corticomotor, and spinal levels subsequent to a single session of strength-exercise. However, certain limitations warrant acknowledgment. Firstly, while our adherence to fundamental strength training guidelines utilised a traditional mode of dynamic strength-training, known to enhance corticomotor excitability, other strength training modalities using high-velocity actions, such as velocity-based training, may induce different neural responses. Thus, for older adults, examining different modalities is warranted. Secondly, although our sample size aligns with comparable studies examining neural responses to a single session of strength-exercise, expanding it would have strengthened our statistical power. Additionally, the limited availability of studies that have examined the corticomotor response to strength-exercise in older adults requires cautious consideration in our power analysis. Regrettably, our restricted statistical power precluded an exploration of potential sex differences. Additionally, it is important to acknowledge that the measures employed in this study only provide information regarding the sedentary nature of the included participants, and outcomes may vary if participants with high physical activity levels were included. Another noteworthy limitation pertains to the absence of documentation concerning the menstrual cycle phase among young female participants, a factor potentially influencing the observed neural responses in our younger female participants. For example, we did identify some unreported patterns of response in our data, that indicate future research should be dedicated to this line of inquiry. Thus, our findings should be interpreted within the context of the study limitations.

6.5. Conclusion

In summary, the most pronounced increase in corticomotor excitability immediately after strength-exercise was observed in younger adults, while older adults displayed a delayed potentiation in corticomotor excitability. Older adults had reduced neural drive following strength-exercise, but younger adults displayed no changes. Importantly, because we only observed within group differences, the induction of use-dependent plasticity, at least for the corticomotor responses are not different between older and younger adults. At a minimum, this implies that corticomotor plasticity following strength-exercise may be relatively independent of age. Further research is required to elucidate the neurophysiological mechanisms that govern corticomotor plasticity following strength-exercise in older adults. Understanding the mechanism that drive cortical plasticity has important clinical implications for improving muscle function through the ageing process.

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CRediT authorship contribution statement

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draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation. **Ashlyn K. Frazer:** Writing – review & editing, Validation, Supervision, Methodology, Investigation, Formal analysis, Conceptualization. **Janne Avela:** Writing – review & editing, Visualization, Validation. **Simon Walker:** Writing – review & editing, Visualization, Validation, Methodology. **Juha P. Ahtiainen:** Writing – review & editing, Visualization, Validation. **Meghan Tanel:** Writing – review & editing, Visualization, Validation. **Sergio Uribe:** Writing – review & editing, Supervision. **Yonas Akalu:** Writing – review & editing, Methodology, Investigation, Data curation. **Mohamad Rostami:** Writing – review & editing, Visualization, Validation, Investigation, Data curation. **Jamie Tallent:** Writing – review & editing, Visualization, Validation, Supervision, Methodology, Investigation, Conceptualization. **Dawson J. Kidgell:** Writing – review & editing, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors do not declare any conflicts of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.archger.2024.105384.

References

Bhandari, A., Radhu, N., Farzan, F., Mulsant, B. H., Rajji, T. K., Daskalakis, Z. J., & Blumberger, D. M. (2016). A meta-analysis of the effects of aging on motor cortex neurophysiology assessed by transcranial magnetic stimulation. *Clinical Neurophysiology, 127*, 2834–2845.

Cannon, J., Kay, D., Tarpenning, K. M., & Marino, F. E. (2007). Comparative effects of resistance training on peak isometric torque, muscle hypertrophy, voluntary activation and surface EMG between young and elderly women. *Clinical Physiology and Functional Imaging, 27*, 91–100.

Carroll, T. J., Riek, S., & Carson, R. G. (2002). The sites of neural adaptation induced by resistance training in humans. *The Journal of Physiology, 544*, 641–652.

Caserotti, P., Aagaard, P., Buttrup Larsen, J., & Puggaard, L. (2008). Explosive heavy-resistance training in old and very old adults: Changes in rapid muscle force, strength and power. *Scandinavian Journal of Medicine & Science in Sports, 18*, 773–782.

Christie, A., & Kamen, G. (2014). Cortical inhibition is reduced following short-term training in young and older adults. *Age, 36*, 749–758.

Clark, B., & Taylor, L. (2011). Age-related changes in motor cortical properties and voluntary activation of skeletal muscle. *Current Aging Science, 4*, 192–199.

Committee, I.R., 2005. Guidelines for data processing and analysis of the International Physical Activity Questionnaire (IPAQ)-short and long forms. http://www.ipaq.ki.se/scoring.pdf.

Cohen, J. (1973). Eta-squared and partial eta-squared in fixed factor ANOVA designs. *Educational Psychological Measurement, 33*(1), 107–112.

Colomer-Poveda, D., Hortobágyi, T., Keller, M., Romero-Arenas, S., & Márquez, G. (2020). Training intensity-dependent increases in corticospinal but not intracortical excitability after acute strength training. *Scandinavian journal of Medicine & Science in Sports, 30*, 652–661.

De Serres, S. J., & Enoka, R. M. (1998). Older adults can maximally activate the biceps brachii muscle by voluntary command. *Journal of Applied Physiology, 84*, 284–291.

Eisen, A., Entezari-Taher, M., & Stewart, H. (1996). Cortical projections to spinal motoneurons: Changes with aging and amyotrophic lateral sclerosis. *Neurology, 46*, 1396.

Eisen, A., Siejka, S., Schulzer, M., & Calne, D. (1991). Age-dependent decline in motor evoked potential (MEP) amplitude: With a comment on changes in Parkinson's disease. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section, 81*, 209–215.

Freitas, C., Farzan, F., & Pascual-Leone, A. (2013). Assessing brain plasticity across the lifespan with transcranial magnetic stimulation: Why, how, and what is the ultimate goal? *Frontiers in Neuroscience, 7*, 42.

Gandevia, S., Butler, J., Allen, G., & Taylor, J. (1994). Prolongation of the silent period following transcranial magnetic stimulation during human muscle fatigue. *The Journal of Physiology, 10011-4211*, P110.

Gandevia, S., Herbert, R., & Leeper, J. (1998). Voluntary activation of human elbow flexor muscles during maximal concentric contractions. *The Journal of Physiology, 512*, 595–602.

Gauche, E., Couturier, A., Lepers, R., Michaut, A., Rabita, G., & Hausswirth, C. (2009). Neuromuscular fatigue following high versus low-intensity eccentric exercise of biceps brachii muscle. *Journal of Electromyography and Kinesiology, 19*, e481–e486.

Gilmore, K. L., & Meyers, J. E. (1983). Using surface electromyography in physiotherapy research. *Australian Journal of Physiotherapy, 29*, 3–9.

Gómez-Feria, J., Martín-Rodrígue, J. F., & Mir, P. (2023). Corticospinal adaptations following resistance training and its relationship with strength: A systematic review and multivariate meta-analysis. *Neuroscience and Biobehavioral Reviews, 152*, Article 105289.

Gruet, M., Temesi, J., Rupp, T., Levy, P., Verges, S., & Millet, G. Y. (2014). Dynamics of corticospinal changes during and after high-intensity quadriceps exercise. *Experimental Physiology, 99*, 1053–1064.

Häkkinen, K., Pakarinen, A., Kraemer, W. J., Häkkinen, A., Valkeinen, H., & Alen, M. (2001). Selective muscle hypertrophy, changes in EMG and force, and serum hormones during strength training in older women. *Journal of Applied Physiology, 91*, 569–580.

Harridge, S. D., Kryger, A., & Stensgaard, A. (1999). Knee extensor strength, activation, and size in very elderly people following strength training. *Muscle & Nerve: Official Journal of the American Association of Electrodiagnostic Medicine, 22*, 831–839.

Hendy, A. M., & Kidgell, D. J. (2014). Anodal-tDCS applied during unilateral strength training increases strength and corticospinal excitability in the untrained homologous muscle. *Experimental Brain Research, 232*, 3243–3252.

Herbert, R., Dean, C., & Gandevia, S. (1998). Effects of real and imagined training on voluntary muscle activation during maximal isometric contractions. *Acta Physiologica Scandinavica, 163*, 361–368.

Hermens, H. J., Freriks, B., Disselhorst-Klug, C., & Rau, G. (2000). Development of recommendations for SEMG sensors and sensor placement procedures. *Journal of electromyography and Kinesiology, 10*, 361–374.

Höllge, J., Kunkel, M., Ziemann, U., Tergau, F., Geese, R., & Reimers, C. (1997). Central fatigue in sports and daily exercises. A magnetic stimulation study. *International Journal of Sports Medicine, 18*, 614–617.

Hortobágyi, T., & DeVita, P. (2006). Mechanisms responsible for the age-associated increase in coactivation of antagonist muscles. *Exercise and Sport Sciences Reviews, 34*, 29–35.

Hortobagyi, T., Tunnel, D., Moody, J., Beam, S., & DeVita, P. (2001). Low-or high-intensity strength training partially restores impaired quadriceps force accuracy and steadiness in aged adults. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 56*, B38–B47.

Hunter, S. K., McNeil, C. J., Butler, J. E., Gandevia, S. C., & Taylor, J. L. (2016). Short-interval cortical inhibition and intracortical facilitation during submaximal voluntary contractions changes with fatigue. *Experimental Brain Research, 234*, 2541–2551.

Jackson, A., Baker, S., & Fetz, E. (2006). Tests for presynaptic modulation of corticospinal terminals from peripheral afferents and pyramidal tract in the macaque. *The Journal of Physiology, 573*, 107–120.

Jakobi, J. M., & Rice, C. L. (2002). Voluntary muscle activation varies with age and muscle group. *Journal of Applied Physiology, 93*, 457–462.

Jasper, H. H. (1958). Ten-twenty electrode system of the international federation. *Electroencephalography and Clinical Neurophysiology, 10*, 371–375.

Kidgell, D. J., Bonanno, D. R., Frazer, A. K., Howatson, G., & Pearce, A. J. (2017). Corticospinal responses following strength training: A systematic review and meta-analysis. *European Journal of Neuroscience, 46*, 2648–2661.

Kidgell, D. J., Stokes, M. A., Castricum, T. J., & Pearce, A. J. (2010). Neurophysiological responses after short-term strength training of the biceps brachii muscle. *The Journal of Strength & Conditioning Research, 24*, 3123–3132.

Knight, C., & Kamen, G. (2001). Adaptations in muscular activation of the knee extensor muscles with strength training in young and older adults. *Journal of Electromyography and Kinesiology, 11*, 405–412.

Kossev, A. R., Schrader, C., Däuper, J., Dengler, R., & Rollnik, J. D. (2002). Increased intracortical inhibition in middle-aged humans; a study using paired-pulse transcranial magnetic stimulation. *Neuroscience Letters, 333*, 83–86.

Latella, C., Hendy, A. M., Pearce, A. J., VanderWesthuizen, D., & Teo, W. P. (2016). The time-course of acute changes in corticospinal excitability, intra-cortical inhibition and facilitation following a single-session heavy strength training of the biceps brachii. *Frontiers in Human Neuroscience, 10*, 607.

Latella, C., Teo, W. P., Harris, D., Major, B., VanderWesthuizen, D., & Hendy, A. M. (2017). Effects of acute resistance training modality on corticospinal excitability, intra-cortical and neuromuscular responses. *European Journal of Applied Physiology, 117*, 2211–2224.

Leung, M., Rantalainen, T., Teo, W. P., & Kidgell, D. (2015). Motor cortex excitability is not differentially modulated following skill and strength training. *Neuroscience, 305*, 99–108.

Leung, M., Rantalainen, T., Teo, W. P., & Kidgell, D. (2017). The corticospinal responses of metronome-paced, but not self-paced strength training are similar to motor skill training. *European Journal of Applied Physiology, 117*, 2479–2492.

Mason, J., Frazer, A., Horvath, D. M., Pearce, A. J., Avela, J., Howatson, G., & Kidgell, D. (2017). Adaptations in corticospinal excitability and inhibition are not spatially confined to the agonist muscle following strength training. *European Journal of Applied Physiology, 117*, 1359–1371.

Mason, J., Frazer, A. K., Jaberzadeh, S., Ahtiainen, J. P., Avela, J., Rantalainen, T., Leung, M., & Kidgell, D. J. (2019a). Determining the corticospinal responses to single bouts of skill and strength training. *The Journal of Strength & Conditioning Research, 33*, 2299–2307.

Mason, J., Frazer, A. K., Pearce, A. J., Goodwill, A. M., Howatson, G., Jaberzadeh, S., & Kidgell, D. J. (2019b). Determining the early corticospinal-motoneuronal responses to strength training: A systematic review and meta-analysis. *Reviews in the Neurosciences, 30*, 463–476.

Marques, D. L., Neiva, H. P., Marinho, D. A., & Marques, M. C. (2022). Velocity-monitored resistance training in older adults: The effects of low-velocity loss threshold on strength and functional capacity. *Journal of Strength and Conditioning Research, 36*(11), 3200–3208.

Muellbacher, W., Ziemann, U., Boroojerdi, B., Cohen, L., & Hallett, M. (2001). Role of the human motor cortex in rapid motor learning. *Experimental Brain Research, 136*, 431–438.

Müller-Dahlhaus, J. F. M., Orekhov, Y., Liu, Y., & Ziemann, U. (2008). Interindividual variability and age-dependency of motor cortical plasticity induced by paired associative stimulation. *Experimental Brain Research, 187*, 467–475.

Nielsen, J., & Petersen, N. (1994). Is presynaptic inhibition distributed to corticospinal fibres in man? *The Journal of Physiology, 477*, 47–58.

Nuzzo, J. L., Barry, B. K., Gandevia, S. C., & Taylor, J. L. (2016). Acute Strength Training Increases Responses to Stimulation of Corticospinal Axons. *Medicine and Science in Sports and Exercise, 48*, 139–150.

Nuzzo, J. L., Barry, B. K., Jones, M. D., Gandevia, S. C., & Taylor, J. L. (2017). Effects of Four Weeks of Strength Training on the Corticomotoneuronal Pathway. *Medicine and Science in Sports and Exercise, 49*, 2286–2296.

Oldfield, R. (1971). Edinburgh handedness inventory. *Journal of Abnormal Psychology*.

Oliviero, A., Profice, P., Tonali, P., Pilato, F., Saturno, E., Dileone, M., Ranieri, F., & Di Lazzaro, V. (2006). Effects of aging on motor cortex excitability. *Neuroscience Research, 55*, 74–77.

Peinemann, A., Lehner, C., Conrad, B., & Siebner, H. R. (2001). Age-related decrease in paired-pulse intracortical inhibition in the human primary motor cortex. *Neuroscience Letters, 313*, 33–36.

Petersen, N. T., Taylor, J. L., & Gandevia, S. C. (2002). The effect of electrical stimulation of the corticospinal tract on motor units of the human biceps brachii. *The Journal of Physiology, 544*, 277–284.

Prout, A. J., & Eisen, A. A. (1994). The cortical silent period and amyotrophic lateral sclerosis. *Muscle & Nerve: Official Journal of the American Association of Electrodiagnostic Medicine, 17*, 217–223.

Rogasch, N. C., Dartnall, T. J., Cirillo, J., Nordstrom, M. A., & Semmler, J. G. (2009). Corticomotor plasticity and learning of a ballistic thumb training task are diminished in older adults. *Journal of Applied physiology, 107*, 1874–1883.

Ruotsalainen, I., Ahtiainen, J. P., Kidgell, D. J., & Avela, J. (2014). Changes in corticospinal excitability during an acute bout of resistance exercise in the elbow flexors. *European Journal of Applied Physiology, 114*, 1545–1553.

Sacco, P., Thickbroom, G. W., Byrnes, M. L., & Mastaglia, F. L. (2000). Changes in corticomotor excitability after fatiguing muscle contractions. *Muscle & Nerve: Official Journal of the American Association of Electrodiagnostic Medicine, 23*, 1840–1846.

Sale, D. G. (1988). Neural adaptation to resistance training. *Medicine and Science in Sports and Exercise, 20*, S135–S145.

Sale, M. V., & Semmler, J. G. (2005). Age-related differences in corticospinal control during functional isometric contractions in left and right hands. *Journal of Applied Physiology, 99*, 1483–1493.

Samii, A., Wassermann, E. M., & Hallett, M. (1997). Post-exercise depression of motor evoked potentials as a function of exercise duration. *Electroencephalography and Clinical Neurophysiology/Electromyography and Motor Control, 105*, 352–356.

Scaglioni, G., Ferri, A., Minetti, A. E., Martin, A., Van Hoecke, J., Capodaglio, P., Sartorio, A., & Narici, M. V. (2002). Plantar flexor activation capacity and H reflex in older adults: Adaptations to strength training. *Journal of Applied Physiology, 92*, 2292–2302.

Semmler, J. G., Hand, B. J., Sasaki, R., Merkin, A., & Opie, G. M. (2021). Age-related changes in motor cortex plasticity assessed with non-invasive brain stimulation: An update and new perspectives. *Experimental Brain Research, 239*, 2661–2678.

Seo, D., Kim, E., Fahs, C. A., Rossow, L., Young, K., Ferguson, S. L., Thiebaud, R., Sherk, V. D., Loenneke, J. P., Kim, D., Lee, M. K., Choi, K. H., Bemben, D. A., Bemben, M. G., & So, W. Y. (2012). Reliability of the one-repetition maximum test based on muscle group and gender. *Journal of Sports Science and Medicine, 11*(2), 221–225.

Shinohara, M., Keenan, K. G., & Enoka, R. M. (2003). Contralateral activity in a homologous hand muscle during voluntary contractions is greater in old adults. *Journal of Applied Physiology, 94*, 966–974.

Siddique, U., Frazer, A. K., Avela, J., Walker, S., Ahtiainen, J. P., Howatson, G., Tallent, J., & Kidgell, D. J. (2022). Determining the cortical, spinal and muscular adaptations to strength-training in older adults: A systematic review and meta-analysis. *Ageing Research Reviews*, Article 101746.

Taube, W., Gollhofer, A., & Lauber, B. (2020). Training-, muscle-and task-specific up-and downregulation of cortical inhibitory processes. *European Journal of Neuroscience, 51*, 1428–1440.

Taylor, J., & Gandevia, S. (2004). Noninvasive stimulation of the human corticospinal tract. *Journal of Applied Physiology, 96*, 1496–1503.

Tecchio, F., Zappasodi, F., Pasqualetti, P., De Gennaro, L., Pellicciari, M., Ercolani, M., Squitti, R., & Rossini, P. (2008). Age dependence of primary motor cortex plasticity induced by paired associative stimulation. *Clinical Neurophysiology, 119*, 675–682.

Tergau, F., Geese, R., Bauer, A., Baur, S., PAULUS, W., & Reimers, C. D. (2000). Motor cortex fatigue in sports measured by transcranial magnetic double stimulation. *Medicine & Science in Sports & Exercise, 32*, 1942–1948.

Todd, A. J. (2010). Neuronal circuitry for pain processing in the dorsal horn. *Nature Reviews Neuroscience, 11*, 823–836.

Walker, S., & Häkkinen, K. (2014). Similar increases in strength after short-term resistance training due to different neuromuscular adaptations in young and older men. *The Journal of Strength & Conditioning Research, 28*, 3041–3048.

Wassermann, E. M. (2002). Variation in the response to transcranial magnetic brain stimulation in the general population. *Clinical Neurophysiology, 113*, 1165–1171.

Wilkinson, R. D., Mazzo, M. R., & Feeney, D. F. (2023). Rethinking the statistical analysis of neuromechanical data. *Exercise and Sport Sciences Reviews, 51*, 43–50.

Wilson, S., Lockwood, R., Thickbroom, G., & Mastaglia, F. (1993). The muscle silent period following transcranial magnetic cortical stimulation. *Journal of the Neurological Sciences, 114*, 216–222.

Woldeamanuel, G., Frazer, A. K., Lee, A., Avela, A., Tallent1, J., Ahtiainen, J. P., Pearce, A. J., & KidgeLL, D. J. (2022). Determining the corticospinal responses and cross-transfer of ballistic motor performance in young and older adults: A systematic review and meta-Analysis. *Journal of Motor Behavior, 54*, 763–786.

Zimerman, M., & Hummel, F. C. (2010). Non-invasive brain stimulation: Enhancing motor and cognitive functions in healthy old subjects. *Frontiers in Aging Neuroscience, 2*, 149.