



Sex comparisons of the bilateral deficit in proximal and distal upper body limb muscles



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ARTICLE INFO

Keywords:

Maximal voluntary contraction
Isometric
Sex difference
Muscle activity
Interhemispheric interaction

ABSTRACT

Bilateral deficit (BLD) describes a phenomenon that the force produced during maximal simultaneous bilateral contraction is lower than the sum of those produced unilaterally. The aim of this study was to examine the potential sex-related differences in BLD in upper body proximal and distal limb muscles. Ten men and eight women performed single-joint maximal contractions with their elbow flexors and index finger abductors at separate laboratory visits, during which the maximal isometric voluntary contractions (MVICs) were performed unilaterally and bilaterally with a randomized order in the designated muscle group. Surface electromyographic (EMG) signals were recorded from the prime movers of the designated muscle groups (biceps brachii and first dorsal interosseous) during the maximal contractions. Both men and women demonstrated BLD in their elbow flexors (deficit: men = $-11.0 \pm 6.3\%$; women = $-10.2 \pm 5.0\%$). Accompanied by this force deficit was the reduced EMG amplitude from the dominant biceps brachii (collapsed across sex: $p = 0.045$). For the index finger abductors, only men (deficit = $-13.7 \pm 6.1\%$), but not women showed BLD. Our results suggested that the BLD in the proximal muscle group is likely induced by the decreased maximal muscle activity from the dominant prime mover. The absence of BLD in women's index finger muscle is largely due to the inter-subject variability possibly related to the sex hormone flux and unique levels of inter-hemispheric inhibition.

1. Introduction

Daily physical activities are composed of a large number of bilateral movements, with the unilateral and contralateral homologous limbs producing the same or the coordinated muscle actions simultaneously. The force production and control during unilateral or bilateral muscle contractions are regulated through the human neuromuscular system. One particularly interesting fact found in this system is that the activation of a unilateral limb muscle can influence the contralateral homologous muscle. For example, the rested contralateral homologous muscle often becomes inadvertently active during a high or maximal intensity unilateral muscle contraction (Sars, Prak, Hortobagyi, & Zijdwind, 2018; Zijdwind & Kernell, 2001). Additionally, when homologous muscle pairs are simultaneously contracting with maximal effort: the force output from the bilateral contraction is usually less than the sum of those from individual unilateral muscle contractions performed separately. This latter phenomenon is referred to as the bilateral deficit (BLD) and was originally observed by Henry and Smith (1961).

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<https://doi.org/10.1016/j.humov.2019.02.017>

Received 20 October 2018; Received in revised form 26 February 2019; Accepted 27 February 2019

Available online 02 March 2019

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Even though some research studies were not able to demonstrate the BLD (Hakkinen, Pastinen, Karsikas, & Linnamo, 1995; Jakobi & Cafarelli, 1998), and some even reported the bilateral facilitation (BLF: the force produced during the maximal bilateral contraction is greater than the sum of those produced unilaterally) (Howard & Enoka, 1991; Skarabot, Cronin, Strojnik, & Avela, 2016), the BLD has been reported in the majority of the previous research for different types of muscle actions across a variety of upper and lower limb muscles (Skarabot, Cronin et al., 2016). While psychological, task-specific, and biomechanical factors all could affect the variability of the results, factors originated from different sites of the neuromuscular system seem to serve as intrinsic contributors to the existence of BLD (see the review article by Skarabot, Alfonso et al. (2016)). For example, findings from brain imaging research favor the potential mechanisms from the supraspinal level by showing evidence of interhemispheric inhibition through the transcallosal pathway (Ferber et al., 1992). Specifically, both hemispheres mutually inhibit each other by limiting the cortical activation intensity, thereby reducing maximal muscle force output during a maximal bilateral muscle contraction (DeJong & Lang, 2012). Interestingly, the potential force reductions (deficit) from individual unilateral limb muscle during a bilateral contraction are not necessarily equal. It was proposed by Henry and Smith (1961) that the BLD is due to force reduction in the dominant limb. However, this has not been consistently reported through different research studies (Skarabot, Cronin et al., 2016).

Anatomically, transcallosal fibers connect both hemispheres through the corpus callosum in primates. In addition, the number of transcallosal projections that link proximal muscle representations in the primary somatosensory cortex (S1) and primary motor cortex (M1) areas is larger than those of the distal muscles (Gould, Cusick, Pons, & Kaas, 1986; Pandya & Vignolo, 1971; Rouiller et al., 1994). Thus, the number of corticospinal projections is greater in distal compared to more proximal muscles (Kuypers, 1978; Palmer & Ashby, 1992). Such morphological differences support the findings of recent studies (Aune, Aune, Ettema, & Vereijken, 2013; Aune, Ettema, & Vereijken, 2016): the BLD is more prominent in the proximal shoulder muscle than in the distal index finger muscle, while the bilateral asymmetry is larger for the index fingers than for the shoulders. In addition to the body part location-dependent transcallosal projection size as mentioned, sex-related differences in hemispheric connectivity have also been reported previously. For example, women overall demonstrate greater connectivity between the two hemispheres than men do (Ingahlilkar et al., 2014). In addition, during fine motor tasks such as finger tapping, men and women showed significantly different bilateral activation patterns at the cortical and subcortical regions (Lissek et al., 2007). These differences potentially account for the sex-related differences in motor skill performance (Hall & Kimura, 1995; Nicholson & Kimura, 1996). Furthermore, it has been suggested that the magnitudes of the interhemispheric inhibition could differ during different phases of the menstrual cycle, potentially due to the hormonal fluctuations across the ovarian cycle (Hausmann et al., 2006). Thus, if interhemispheric inhibition serves as an important role accounting for the BLD, then women may respond differently by showing more variation, when compared to men. Interestingly, very limited information is available regarding the potential sex-related differences in BLD, especially for the more distal finger muscles that are primarily responsible for fine motor skills. In the past, studies have examined BLD in distal finger muscles with both sexes mixed (Aune et al., 2013; Herbert & Gandevia, 1996; Post et al., 2007; Van Dieen, Ogita, & De Haan, 2003; Zijdewind & Kernell, 2001). However, a relatively small female sample size made the between-group comparison impossible.

Therefore, the purpose of this investigation was to examine the potential BLD in proximal elbow flexors and distal index finger abductors during maximal bilateral and unilateral contractions for both sexes. In addition, to examine the potential changes in individual muscle activity between the bilateral and unilateral contractions, surface electromyographic (EMG) signals were recorded in the prime movers (biceps brachii and first dorsal interosseous) of the designated muscle groups. Based on the hypothesis and results from Aune et al. (2013), we expected to see a greater magnitude of BLD in the elbow flexors than that in the index finger abductors. In addition, compared to men, women may demonstrate different force and muscle activity responses when maximally contracting distal index finger muscles bilaterally. The results of this investigation could potentially help understand the sex-related differences in bimanual motor functions. In addition, they could also provide important insights into the clinical or rehabilitation field. For example, emerging evidence (DeJong & Lang, 2012; Kang & Cauraugh, 2018) have suggested that high-intensity bilateral muscle contractions facilitate the paretic limb (neurologically more affected) muscle force production than unilateral contraction does in post-stroke and chronic stroke patients. Thus, if the sex factor indeed influences bilateral interactions, then it is important to take this into consideration when developing related rehabilitative interventions for clinical populations.

2. Methods

2.1. Participants

Ten men (mean \pm SD: age = 25 \pm 4 years, height = 178.9 \pm 7.8 cm, weight = 81.4 \pm 8.2 kg) and eight women (age = 21 \pm 1 years, height = 163.9 \pm 6.9 cm, weight = 66.4 \pm 12.8 kg) voluntarily participated in this study. All participants were healthy and recreationally active (engaged in aerobic exercise for 2 h, resistance exercise for 1 h, or recreational activities for 1 h per week at least 6 months prior to this investigation) based on the pre-health and exercise questionnaire they completed. In addition, they did not have any current or recent neuromuscular or musculoskeletal disorders. The experimental procedures of this investigation were in accordance with the Declaration of Helsinki and were approved by the University Institutional Review Board (protocol number: 17–070). During the consenting process, the participants were instructed to maintain their normal habits in terms of dietary intake, hydration status, and sleep during the investigation. Extra effort was made to conduct testing at the same time of the day. In addition, the participants were instructed to refrain from any vigorous physical activity 72 h prior to the beginning of this investigation and throughout the entire investigation. Before any experimental testing or procedures, all participants signed a written informed consent.

2.2. Experimental design

This study used a within-subject crossover design to examine the potential BLD in maximal elbow flexion and index finger abduction contractions. Three separate visits to the laboratory were required to complete this investigation, with a minimum of 24 h of rest provided between visits. The first visit served as the familiarization, and the following two visits were the experimental visits. During the experimental visits, the elbow flexor (EF) muscles and the index finger abductor (FA) muscles were examined separately with the randomly sequenced order.

2.3. Procedures

2.3.1. Familiarization

During the familiarization visit (Visit 1), all participants visited the laboratory to receive instructions and to participate in a familiarization trial specifically to practice maximal voluntary isometric contractions (MVICs) with their EF and FA muscles in the designated strength testing apparatuses. Extra time was provided for each participant to practice both muscle strength testing until they could conformably and properly produce the maximal voluntary contractions in the apparatuses. In addition, the hand-dominance tests were conducted using the Edinburgh Handedness Inventory (Oldfield, 1971), where all women and nine men were right-handed (Laterality Index mean \pm standard deviation = 71.47 ± 20.44), and one man was left-handed (Laterality Index = -60.00).

2.3.2. Isometric strength testing

At least 24 h after the familiarization session, the participant returned to the laboratory for one of the experimental testing visits (EF Visit or FA Visit). Upon arrival at the EF Visit, the participant was asked to sit in front of a custom-built table with both elbow joints laying onto the table with a distance of his/her shoulder width. The research staff adjusted the seat height, so the participant's upper arms were parallel to the floor, and the padded edge of the testing table was firmly contacted with the participant's chest and armpits. For the unilateral contraction, one of the participant's wrists was wrapped with a padded cuff connecting to one end of a load cell (Model SM-500; Interface, Scottsdale, AZ, USA), with the other end of the load cell attaching to an immovable steel frame in front of the participant. The participant placed the forearm with the upright position, and extra care was taken to ensure the load cell was attached at the same height as the wrist (Fig. 1a). For the bilateral contraction, the participant's both wrists were attached to the two ends of a light stiff metal bar, with the center of the bar connecting to the load cell from the same immovable steel frame (Fig. 1b). During both unilateral and bilateral contractions, the participant maintained the same posture (both elbow joints placed on the same spots with the shoulder width), and a goniometer (EMI Plastic 12" Goniometer; Elite Medical Instruments, Fullerton, CA, USA) was utilized to ensure the elbow joint angle(s) was (were) 90 degrees during the maximal voluntary isometric contractions (MVICs). With the hand(s) supinated, the participant performed several brief submaximal (i.e., 50% of the perceived maximal effort) contractions

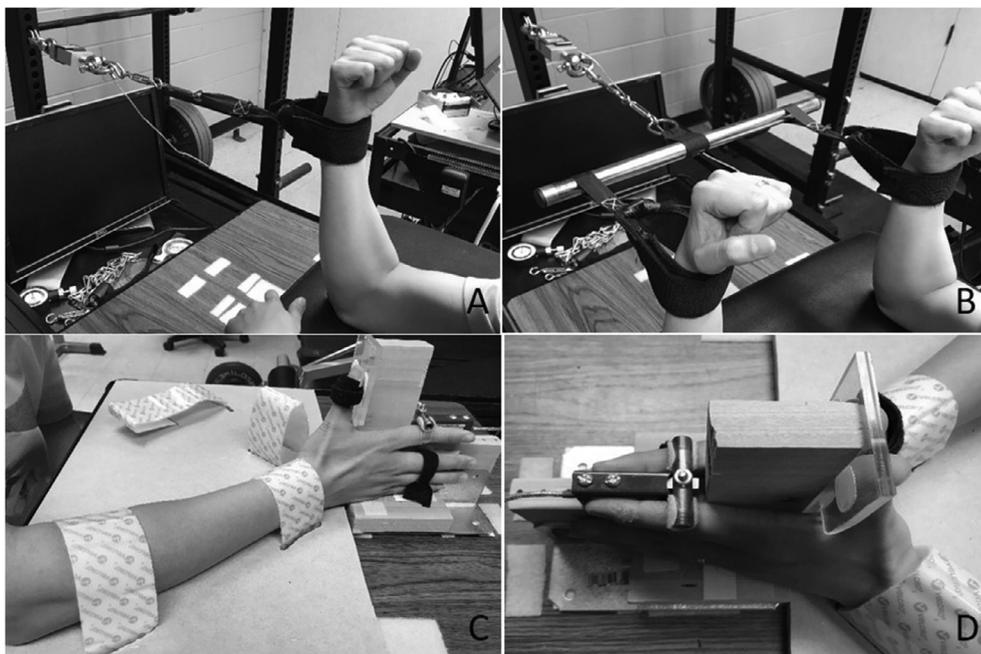


Fig. 1. A. The demonstration for unilateral (right arm) isometric elbow flexion; B. The demonstration for bilateral isometric elbow flexion; C. The demonstration for unilateral (right hand) isometric index finger abduction; B. The demonstration for bilateral isometric index finger abduction.

for sufficient warm-up, followed by three separate 5-second MVICs for each (left (UL_L) and right (UL_R)) and both (bilateral) elbow flexors in a randomized order. One-minute rest interval was provided between consecutive MVICs of the same muscle group, and at least a 2-minute rest interval was provided between different muscle groups.

During the FA Visit, the participant first positioned both elbows onto a table with the shoulder width. The forearms and the wrists were placed in neutral position so both the palms were perpendicular to the surface of the table. The research staff then placed a custom-made index finger abduction device in front of the participant. With both hands placed onto the abduction device and the palms facing each other, extra care was taken to ensure both elbow joint angles were 135 degrees. In addition, two Velcro® straps were used to immobilize the forearms and the wrists to minimize unwanted movements. The little, ring, and middle fingers were extended away from the index finger and rest on the support surface. The thumb was secured at an approximately 60-degree angle to the index finger. The index finger was placed in line with the second metacarpal, which created a zero-degree metacarpophalangeal joint angle. The proximal interphalangeal joint of the index finger was then placed under a brass tube attached perpendicularly to a Mini Beam force transducer (Model MB-100; Interface, Scottsdale, AZ, USA). Thus, both unilateral and bilateral index finger abduction contractions exerted force against the brass tube (Fig. 1c and d). With the same testing procedures described in the EF Visit, three 5-second index finger abduction MVICs were performed with the bilateral, UL_L, and UL_R conditions in a randomized order.

2.4. Measurements

2.4.1. Force output

The force produced during all maximal EF and FA isometric contractions was detected by the tension applied to the force transducers. The force signal was then sampled at 1000 Hz and digitized with a 12-bit analog-to-digital converter (National Instruments, Austin, TX, USA). The maximal isometric force for each muscle (left EF, right EF, bilateral EF, left FA, right FA, and bilateral FA) was quantified based on the highest 1-s portion from the three 5-second MVICs.

2.4.2. Surface EMG signal acquisition and processing

During the EF maximal isometric contractions, bipolar surface EMG signals were recorded through a bipolar surface electrode (DE 2.1 Single Differential Surface EMG sensor, 5-mm interelectrode distance, Delsys, Inc., Natick, MA) from the biceps brachii muscle. Specifically, the electrodes were attached over the biceps brachii muscle belly based on the recommendations from SENIAM (Hermens et al., 1999). For the FA contractions, a five-pin surface array EMG sensor (dEMG sensor, Delsys, Inc., Natick, MA) was utilized due to the relatively small surface area of the first dorsal interosseous muscle. This special sensor array comprised five cylindrical probes (0.5 mm diameter) located at the center and the corners of a 5 × 5 mm square. Thus, 4 separate bipolar EMG signals were detected based on the pairwise differences in the five probes, and only one of the four channels (Channel 1) was selected for subsequent analyses. The reference electrode (Model USX2000; Axelgaard, Fallbrook, CA, USA) was placed on the seventh cervical vertebrae (C7). Prior to any electrode placements, the investigator shaved and cleaned the skin surface with rubbing alcohol, and medical tapes were used to firmly fixate the electrodes on the skin sites.

All analog bipolar EMG signals were collected and amplified (gain = 1000) with a modified Bagnoli 16-channel EMG system (Delsys, Inc., Natick, MA, USA) and filtered with high and low pass filters set at 20 Hz and 450 Hz, respectively. The filtered signals were then digitized at a sampling rate of 20000 Hz with a 12-bit analog-to-digital converter (National Instruments, Austin, TX). Synchronized with the maximal force signal (highest 1-s portion from the three 5-second MVICs), the amplitude of each selected EMG signal was calculated as the root mean square (RMS).

2.5. Data analysis

The bilateral index (BI) of the maximal isometric force from this investigation was calculated based on the formula from Howard and Enoka (1991):

$$BI(\%) = 100 \times [\text{Bilateral}/(\text{UL}_L + \text{UL}_R)] - 100.$$

The “Bilateral” is the force produced during the simultaneous contractions of the right and left muscles, and the “UL_L” and “UL_R” represent the maximal forces from left and right unilateral contractions, respectively. Thus, a negative value indicates the presence of the bilateral deficit (BLD), while a positive value indicates the bilateral facilitation (BLF).

2.6. Statistical analyses

Separate two-way (condition [UL_L + UL_R vs. bilateral] × sex [men vs. women]) mixed factorial analyses of variance (ANOVAs) were used to examine if the maximal isometric force values differed between the two conditions for both sexes. In addition, to compare the potential differences in the relative magnitude of the BI in EF and FA for both sexes, a two-way (muscle [EF vs. FA] × sex [men vs. women]) mixed factorial ANOVA was conducted. For each individual designated muscle (e.g., dominant biceps brachii, non-dominant biceps brachii, dominant first dorsal interosseous, and non-dominant first dorsal interosseous), separate two-way (sex [men vs. women] × condition [unilateral vs. bilateral]) mixed factorial ANOVAs were performed to examine if the EMG amplitudes were different when the muscle was working alone (unilateral condition) or with the contralateral limb (bilateral condition). When appropriate, the follow-up tests included independent samples *t*-tests, and paired samples *t*-tests with Bonferroni adjustments. All statistical tests were conducted using statistical software (IBM SPSS Statistics 22.0, IBM, Armonk, NY) with alpha set

Table 1

Mean ± Standard Deviation (SD) of the maximal isometric force (Newton) for the elbow flexion and finger abduction contractions during unilateral left (UL_L), unilateral right (UL_R), and bilateral conditions for men and women.

| Elbow Flexion | UL _L | UL _R | Bilateral | UL _L + UL _R |
|------------------|-----------------|-----------------|---------------|-----------------------------------|
| Men | 375.3 ± 53.8 | 402.4 ± 60.5 | 691.6 ± 131.0 | 777.7 ± 107.2 |
| Women | 190.9 ± 39.9 | 202.2 ± 49.3 | 353.4 ± 84.6 | 393.2 ± 87.6 |
| Finger Abduction | UL _L | UL _R | Bilateral | UL _L + UL _R |
| Men | 231.2 ± 53.1 | 240.7 ± 64.5 | 410.5 ± 112.4 | 471.9 ± 106.1* |
| Women | 124.4 ± 27.2 | 142.8 ± 40.0 | 285.5 ± 74.6 | 267.2 ± 63.3 |

* Significant difference between bilateral condition and UL_L + UL_R condition.

at 0.05. In addition, effect sizes were calculated using Cohen’s *d*, with 0.20, 0.50, and 0.80 as small, medium, and large effect sizes, respectively (Cohen, 1992). All data were reported as mean ± standard deviation (SD) in the text and tables, and displayed as mean ± standard error of the mean (SE) in the figures.

3. Results

3.1. Force

Table 1 shows the Mean (SD) of the maximal isometric force for the EF and FA contractions during UL_L, UL_R, and Bilateral conditions for both men and women. For the EF, the two-way mixed factorial ANOVA did not show an interaction, but there were main effects for condition ($p = 0.002$) and sex ($p < 0.001$). Thus, after collapsing across sex, the paired samples *t*-test showed that the marginal mean of the bilateral condition was significantly less than that of the UL_L + UL_R condition ($p = 0.001$, $d = 0.31$). The two-way ANOVA for the isometric forces of FA indicated a condition × sex interaction ($p < 0.001$). The follow-up simple main effect tests showed a significant difference between the bilateral condition and UL_L + UL_R condition for men ($p < 0.001$, $d = 0.56$), but not for women ($p = 0.158$, $d = 0.26$).

The two-way ANOVA for the BI indicated a muscle × sex interaction ($p = 0.013$). The follow-up simple main effect tests showed that there was a significant difference for the BI of the FA between men and women (men vs. women = $-13.7 \pm 6.1\%$ vs. $7.7 \pm 18.1\%$; $p = 0.012$, $d = 1.66$). In addition, the BIs of EF and FA were also significantly different for women (EF vs. FA = $-10.2 \pm 5.0\%$ vs. $7.7 \pm 18.1\%$; $p = 0.017$, $d = 1.35$; Fig. 2).

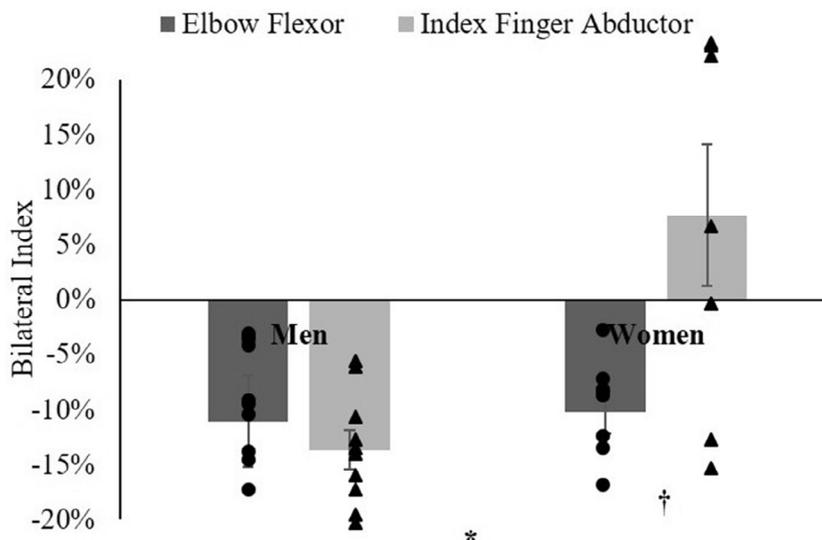


Fig. 2. Individual data and mean of the bilateral indices (%) of proximal elbow flexors and distal index finger abductors during maximal isometric contractions in men and women. Round dot represents the bilateral index of elbow flexors for each individual, and triangular dot represents the bilateral index of index finger abductors for each individual. Negative percentage indicates bilateral force deficit. *Indicates significant sex difference between the bilateral indices of index finger abductors. †Indicates significant difference between the bilateral indices of elbow flexors and index finger abductors in female participants.

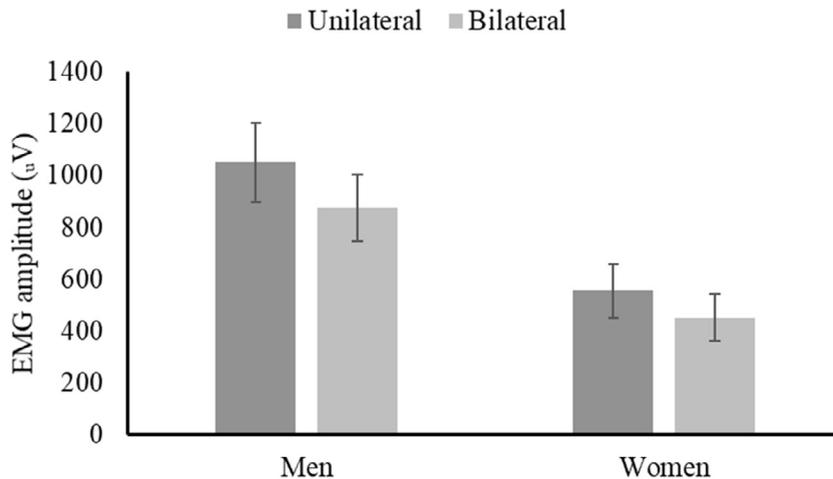


Fig. 3. The maximal mean electromyographic (EMG) amplitude (uV) of the dominant biceps brachii during unilateral and bilateral contraction conditions.

3.2. EMG amplitude

The two-way ANOVA for the non-dominant biceps brachii EMG amplitude indicated that there was no two-way interaction. However, there was a main effect for sex ($p = 0.024$), indicating significantly greater biceps brachii EMG amplitude for men than that for women (collapsed across condition, men vs. women = $833.05 \pm 357.37 \mu\text{V}$ vs. $453.38 \pm 297.67 \mu\text{V}$, $p = 0.012$, $d = 1.14$). Fig. 3 illustrated both men's and women's dominant biceps brachii muscle EMG amplitude during both conditions (unilateral and bilateral). Similar to the non-dominant muscle, the two-way ANOVA for the dominant biceps brachii did not detect an interaction, but there were main effects for condition ($p = 0.045$) and sex ($p = 0.015$). Thus, after collapsing across sex, the follow-up paired samples t -test indicated that the marginal mean of the dominant biceps brachii EMG amplitude was significantly greater in the unilateral condition, when compared with the bilateral condition (unilateral vs. bilateral = $830.61 \pm 472.82 \mu\text{V}$ vs. $687.64 \pm 399.51 \mu\text{V}$, $p = 0.023$, $d = 0.33$). In addition, after collapsing across condition, the follow-up independent t -test indicated that the marginal mean of the men's biceps brachii EMG amplitude was significantly greater than that of the women's (men vs. women = $963.79 \pm 442.76 \mu\text{V}$ vs. $503.29 \pm 269.34 \mu\text{V}$, $p = 0.008$, $d = 1.22$).

The two-way ANOVA for the non-dominant first dorsal interosseus EMG amplitude did not show any interaction or main effects. For the dominant first dorsal interosseus EMG amplitude, the two-way ANOVA indicated a condition \times sex interaction ($p = 0.046$). The follow-up simple main effect tests showed significantly greater EMG amplitude for the unilateral condition than for the bilateral condition in men (unilateral vs. bilateral = $395.05 \pm 193.27 \mu\text{V}$ vs. $330.46 \pm 162.01 \mu\text{V}$, $p = 0.044$, $d = 0.23$; Fig. 4), but not in women.

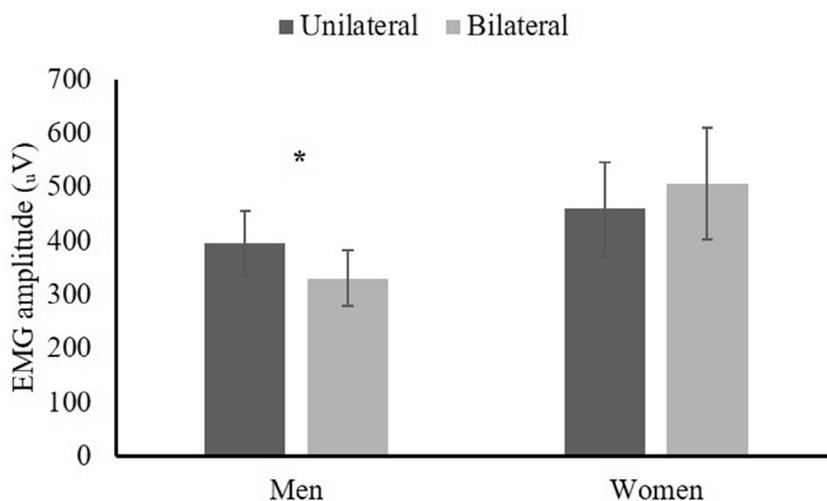


Fig. 4. The maximal mean electromyographic (EMG) amplitude (uV) of the dominant first dorsal interosseus during unilateral and bilateral contraction conditions. *Indicates significant difference between two conditions (unilateral vs. bilateral) in male participants.

4. Discussion

The main purpose of this investigation was to examine the potential sex-related differences in bilateral deficit phenomenon (BLD) in human upper limb proximal muscles (elbow flexors) and distal muscles (index finger abductors). In addition, the surface EMG was used to examine the unilateral individual muscle activity during both the maximal unilateral and bilateral contractions. The main findings of this study showed that: 1) men and women demonstrated BLD for the maximal isometric elbow flexion, 2) only men but not women showed BLD for the maximal isometric index finger abduction, and 3) the magnitudes of BLD of the elbow flexors and index finger abductors in men were comparable, and were accompanied by the lower EMG amplitude from the right biceps brachii and from the right first dorsal interosseous during the simultaneous bilateral contractions, respectively.

The existence of the BLD in isometric elbow flexion from the current investigation is generally consistent with the findings from previous studies (Hernandez, Nelson-Whalen, Franke, & McLean, 2003; Oda & Moritani, 1994; Ohtsuki, 1983). In addition, the current magnitudes of elbow flexion bilateral index (men = $-11.0 \pm 6.3\%$; women = $-10.2 \pm 5.0\%$) also fall into the range (-3.4% to -20.1%) from these reports. Thus, with the positive finding of BLD in maximal isometric elbow flexion, we intended to examine whether the force deficit during simultaneous contractions were due to the similar force deficits from both limbs, or primarily from one specific limb. Henry and Smith (1961) proposed that BLD is due to the force reduction in the dominant limb. However, this remains to be controversial since different results have been reported (Cornwell, Khodiguian, & Yoo, 2012; Skarabot, Cronin et al., 2016). With the current setup, it was impossible for us to quantify force productions from individual limbs during the bilateral contraction, due to the fact that only one load cell was used to measure the force output. As an alternative, we examined the individual muscle (dominant and non-dominant) activity during both bilateral and unilateral contractions. Indeed, it is important to acknowledge that using EMG amplitude to predict or explain force responses could be problematic (Solomonow, Baratta, Shoji, & D'Ambrosia, 1990), due to the curvilinear force-EMG relationship (Lawrence & De Luca, 1983). Our results on individual biceps brachii EMG amplitude suggested that the dominant biceps muscle showed reduced maximal muscle activity during the bilateral condition, when compared with the unilateral condition. A decline in the EMG amplitude may be due to changes within the muscle fibers, changes in the spinal level (motoneuron excitability), or changes in the supraspinal level (motor cortex excitability). However, it was not our intention and was beyond our capability to examine the exact site(s) in the neuromuscular system accounting for this muscle activity decrement. Based on previous experiments, it is possible that the primary underlying mechanism of BLD is supraspinal, evidenced by the decreased symmetrical movement-related cortical potentials (Oda & Moritani, 1995, 1996), the decreased input to the precentral gyrus (Post et al., 2007), as well as the increased interhemispheric inhibition during the simultaneous contractions of homologous muscles. In addition, Oda (1997) proposed that the decrement of cortical activity in the right hemisphere (projecting to the non-dominant side) is smaller than that in the left hemisphere (projecting to the dominant side). Therefore, comparing to the non-dominant muscle, our data suggested that the decrements of muscle activity in the dominant biceps brachii during the simultaneous contractions of both limbs seemed to serve as a greater contributing factor potentially accounting for the BLD in isometric elbow flexion.

Previously, a few research studies have directly examined the BI (%) in different finger muscle contractions (e.g., index finger flexion, thumb adduction, index finger abduction) (Aune et al., 2013; Herbert & Gandevia, 1996; Post et al., 2007; Van Dieen et al., 2003; Zijdwind & Kernell, 2001). Overall, the majority of these studies reported a relatively small magnitude of BLD (e.g., $BI \leq -5\%$) (Aune et al., 2013; Post et al., 2007; Zijdwind & Kernell, 2001), except Van Dieen et al. (2003) ($BI = -20\%$). It was proposed by Aune et al. (2013) that due to the neuroanatomical difference of the proximal and distal muscles (e.g., the number of transcallosal projections connecting proximal muscles are significantly larger compared to those for distal muscles, thereby inducing more pronounced interhemispheric inhibition for the proximal than distal muscles during maximal bilateral contractions), the magnitude of BLD in distal muscles (e.g., finger muscles) would be smaller when compared to the proximal muscles (e.g., upper arm muscle, shoulder muscles). The authors (Aune et al., 2013) confirmed this hypothesis by examining the BLD in shoulder and finger muscles. In the current investigation, our overall data (men and women combined) showed an index finger abduction BI of -4.2% , generally in agreement with the above-mentioned finger contraction BI values. However, different from any previous studies, our data also showed an interesting finding that the bilateral force deficit in index finger abduction is sex-dependent, with only men demonstrating the BLD ($BI = -13.7 \pm 6.1\%$). Thus, the men's BI results (EF: $-11.0 \pm 6.3\%$ vs. FA: $-13.7 \pm 6.1\%$) did not strictly follow the hypothesis of proximal vs. distal limb muscle BLD difference proposed by Aune et al. (2013). In fact, a previous experiment used the transcranial magnetic stimulation (TMS) technique to measure interhemispheric inhibition in distal and proximal arm muscles, and showed comparable values between the biceps brachii and the first dorsal interosseous muscles (Harris-Love, Perez, Chen, & Cohen, 2007). This finding suggested that the magnitude of interhemispheric inhibition between different arm muscles may not follow the proximal-to-distal gradient, thereby supporting our results of BIs in men.

Our female participants did not demonstrate a statistically significant bilateral deficit or facilitation in the finger abductors. Interestingly, half of the women showed a positive bilateral index. As far as we know, sex-related differences in bilateral deficit have never been reported. The only study that has examined potentially related mechanistic variables was from a recent experiment by Sars et al. (2018), where the researchers found that the unintentional activity in the contralateral rested first dorsal interosseous was generally lower in women during a 2-min maximal isometric unilateral index finger abduction, when compared with men. However, an earlier study by the same group of researchers (Zijdwind & Kernell, 2001) found no relationship between BLD and contralateral motor irradiation. Thus, this sex-related difference in contralateral unintentional activity does not seem to contribute to the sex difference in finger abduction BLD. Regarding the BLF, it has been previously reported in the limited literature (Skarabot, Cronin et al., 2016). Howard and Enoka (1991) examined BI in three groups of men with different training statuses (untrained, cyclists, and weightlifters), and found bilateral force facilitation in the weightlifters. However, this specific group was not different from the

untrained group in another study (Secher, Rube, & Elers, 1988). In a recent study by Skarabot, Alfonso et al. (2016) where the participants were grouped into bilateral, unilateral, and control based on the sporting events they competed (e.g., powerlifters and weightlifters were in the bilateral group, whereas high jumpers and long jumpers were in the unilateral group), greater voluntary activation level and motor evoked potential amplitude were found during bilateral, rather than unilateral maximal isometric knee extensions without significant group difference. In the current investigation, the women were only physically active but not undergoing any specific training. Thus, it is also unlikely that the participants' training statuses could have influenced the results. Instead, the only possible explanation for the large inter-individual variability of the women's index finger abduction BI might be the variations of interhemispheric inhibition due to the fluctuations of sex hormones across the menstrual cycle (Weis & Hausmann, 2010). Specifically, by applying TMS on the left motor cortex and measuring the EMG of the ipsilateral first dorsal interosseous muscle in 13 women during their menstrual, follicular and midluteal phases, Hausmann et al. (2006) found significantly shorter ipsilateral silent period (ISP, an indication of interhemispheric inhibition) during the follicular phase than that during the midluteal phase. In addition, the reduced ISP during the follicular phase and the midluteal phase were associated with high levels of estradiol and progesterone, respectively. It is reasonable to speculate that the hormonal flux across the ovarian cycle influenced our results and contributed to the large degree of inter-individual differences in the responses for the women. However, cycle phase data was not collected.

The obvious question then is how to account for the muscle-dependent inter-individuality for the bilateral index in the women. If hormonal flux did indeed influence the magnitude of interhemispheric inhibition, then why did the elbow flexors not show a similar response (women's elbow flexion BI = $-10.2 \pm 5.0\%$)? This inconsistency potentially suggests that BLD in women is muscle-dependent, meaning that the distal finger muscles are more likely influenced. It is unknown why such a difference exists. However, from a functionality perspective, the prime mover of the elbow flexors, biceps brachii muscle, is mainly responsible for producing gross motor activities; whereas the prime mover of the index finger abductors, first dorsal interosseous, is usually involved in complicated fine motor skills. In a study where brain activation patterns were examined during simple (only index finger tap) and complex (index, middle, ring, and pinky finger taps) motor tasks, greater levels of activation were shown in the cortical and subcortical striatal regions in women and men, respectively (Lissek et al., 2007). These findings indicate differential neural processing and hemispheric recruitment for finger movement/contraction in the supraspinal level between men and women. Such sex differences are probably diminished or not evident during gross motor activities with larger, proximal muscle groups. Therefore, maximal bilateral proximal limb muscle contractions may be minimally influenced by factors such as sex hormone concentrations.

5. Conclusions

The current investigation showed a few novel findings regarding the sex- and muscle-related differences in BLD. However, it is important to be cautious when interpreting the findings from the study. Specifically, a major limitation includes the lack of interhemispheric inhibition measurements, as well as the recording of our female participants' cycle information with the sex hormone concentration measurements. Thus, we are still not able to identify the specific mechanism(s) responsible for the sex-related difference in BLD for index finger abduction. In closing, the current experiment suggested comparable bilateral deficit indices in the maximal isometric elbow flexion for both sexes. The reduced force production during maximal bilateral elbow flexion contraction was likely caused by the decreased maximal EMG amplitude from the dominant prime mover biceps brachii muscle. The BLD in index finger abduction was only evident in men, but not in women, due to the large inter-subject variability in female participants. We believe that this variability may potentially be caused by the different interhemispheric inhibitions due to fluctuations in sex hormones across the menstrual cycle. Future studies may continue this research line by examining the distal fine motor skill-based muscle interhemispheric inhibition during different menstrual cycles in women.

Acknowledgements

The authors would like to thank all participants for their time and effort. There were no conflicts of interest declared from authors for the completion of this project and manuscript.

Funding information

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.humov.2019.02.017>.

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