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Unilateral Handgrip Holds to Failure Result in Sex-Dependent Contralateral Facilitation

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ABSTRACT

International Journal of Exercise Science 15(4): 782-796, 2022. This study examined changes in maximal voluntary isometric contraction (MVIC) force following dominant (Dm) and nondominant (NDm) unilateral, handgrip isometric holds to failure (HTF) for the exercised ipsilateral (IPS) and non-exercised contralateral (CON) limbs and determined if there are sex- and hand- (Dm vs NDm) dependent responses in the HTF time, performance fatigability (PF) for the exercised IPS limb, and changes in MVIC force for the CON limb after unilateral fatigue. Ten men and 10 women (Age = 22.2 years) completed an isometric HTF at 50% MVIC for the Dm and NDm hand on separate days. Prior to, and immediately after the HTF, an MVIC was performed on the IPS and CON limbs, in a randomized order. The Dm (130.3 ± 36.8 s) HTF (collapsed across sex) was significantly longer (p = 0.002) than the NDm (112.1 ± 34.3 s). The men (collapsed across hand) demonstrated IPS (%Δ = 22.9 ± 10.8%) PF and CON facilitation (%Δ = -6.1 ± 6.9%) following the HTF, while the women demonstrated differences in PF between the Dm and NDm hands for the IPS (%Δ Dm = 28.0 ± 9.4%; NDm = 32.3% ± 10.1%; *p* = 0.027), but not the CON limb (%Δ Dm = -1.6 ± 5.7%; NDm = 1.7 ± 5.9%). The cross-over facilitation of the CON limb for men, but not women, following a unilateral, isometric handgrip HTF may be related to post-activation potentiation.

KEY WORDS: Neuromuscular, fatigue, sex differences

INTRODUCTION

The nature and magnitude of fatigue across exercise modalities have been demonstrated to occur both centrally and peripherally and is commonly quantified by performance fatiguability, defined as a ‘decline in an objective measure of performance over a discrete period of time’ (8). Most commonly, fatigue is expressed as an ‘exercise-induced decline in maximal voluntary force’ (12) and is typically measured from changes in maximal voluntary isometric contraction (MVIC) force (8) that reflect global fatigue (i.e. including central and peripheral factors). Central fatigue commonly includes the mechanisms and processes of fatigue, proximal to the neuromuscular junction where the central nervous system modulates the drive required to produce a desired force or performance outcome based on feedback from group III/IV afferents (6, 7). Peripheral fatigue, conversely, has been defined as mechanisms of fatigue in the working muscle, distal to the neuromuscular junction, such as ischemia and metabolic byproduct accumulation (8, 39). Such effects of fatigue, which share a common point of overlap near the neuromuscular junction as metabolic byproduct elicit type III/IV afferents signaling to reduce the central drive to the muscles, have been noted to occur at different rates based on the intensity and mode of exercise (8, 28, 39). The decrement in force production measured by MVIC force has been common in literature to quantify the combined peripheral and central factors eliciting performance fatiguability (21).

Examination of the systemic effect of unilateral fatigue on the force production of the non-exercised contralateral, homologous muscle groups has demonstrated varying responses of no change (15, 18), decreases (1, 2, 18, 25), or facilitation in the MVIC force or torque (29, 38) produced by an individual. These changes in MVIC of the non-exercised, contralateral limb have been termed “cross-over fatigue” or “cross-facilitation” for decreases or increases, respectively (1, 28). No defined mechanism has been identified as the primary factor responsible for these phenomena, but it has been suggested that they may occur due to a combination of central and peripheral factors of exercise performance modulation (1, 7, 17, 29). The “cross-over” inhibition has been proposed to arise from group III/IV afferent feedback from metabolic and mechanical perturbations within the exercised ipsilateral (IPS) limb (1, 2). This afferent feedback ultimately decreases central drive to both the exercised IPS and non-exercised contralateral (CON) limb (2). Fatigue elicited through the aforementioned central and peripheral mechanisms explain the decreases seen in the CON limb performance, but the presence of contralateral facilitation in some groups (29, 37) suggests an additional mechanism may be influencing the performance of the CON limb following fatiguing exercise. Central factors, or factors proximal to the cortical and subcortical structures, of this “cross-facilitation” phenomenon have been suggested to be due to interhemispheric communication through the transcallosal connection or the mutual pathways of the exercising and non-exercising limb in the spinal cord or brain stem (1). A peripheral factor or a factor proximal to the exercising muscle and distal to the cortical processes includes the post-activation potentiation (10, 11, 23, 27, 29, 39) or post-activation performance enhancement (PAPE) (43). The central mechanisms provide evidence for the facilitation demonstrated in the CON, homologous, non-exercising limb through excitatory signaling ‘spilling over’ into the contralateral hemisphere providing excitation to the non-exercising muscle, while peripheral mechanisms involve increased calcium concentrations that elicit conformational changes through phosphorylation of myosin essential and light chain proteins (1,5,7,17,25,29,39). These central and peripheral mechanisms may explain changes in the force-generating capacity of the non-exercised, contralateral limb following unilateral fatigue.

It is of importance to note that exercise responses may be influenced by hand dominance. Differences in handgrip strength have been suggested to exist between the dominant (Dm) and non-dominant (NDm) hand (3, 4, 20, 31, 41). Specifically, the Dm hand has been suggested to produce 10% greater strength than the NDm limb (3). Greater Dm limb strength has been demonstrated in right limb dominant individuals, but this finding has been reduced or negated in individuals who are left limb dominant (4, 20, 31, 41). Continual favoring of the dominant limb to perform daily tasks has been suggested to be the principal influence on this phenomenon in right limb dominant individuals and the prevalence of right limb dominant devices may counteract this phenomenon in left limb dominant individuals (16, 19, 33). Thus, the hand dominance should also be considered in the examination of "cross-over fatigue" and "cross-over facilitation" to determine if there are differences in Dm and NDm strength that influence the exercised, ipsilateral, and/or non-exercised CON limb performance fatigability.

The nature and magnitude of exercise-induced fatigue have also been demonstrated to be sex-dependent (24, 26). For example, performance of low intensity (20% to 50% MVIC) isometric and intermittent muscle actions to failure have demonstrated less performance fatigability in women compared to men (24, 26). In addition, women have demonstrated a greater fatigue resistance compared to men, reflected by longer times to task failure as well as the completion of more repetitions to failure at submaximal intensities (26). Despite these reported differences between men and women during the examination of fatiguing tasks (24, 26), the effect of fatigue on the non-exercised, CON homologous muscle groups has not been widely examined in literature outside of a study by Martin & Rattey (24), which demonstrated a greater effect of CON performance fatigability in men than women. Thus, there are currently limited data available to describe changes in the non-exercised, CON limb after unilateral fatigue in men and women. Therefore, the purposes of this study were to: 1) examine changes in the MVIC force following Dm and NDm unilateral, handgrip isometric holds to failure at 50% MVIC for the exercised IPS and non-exercised CON limb, and 2) determine if there are sex- and hand- (Dm vs NDm) dependent responses in the HTF time, performance fatiguability for the exercised IPS limb and MVIC force for the non-exercised CON limb after unilateral fatigue. Therefore, it was hypothesized that: 1) the Dm hand would produce a greater pre-HTF and post-HTF MVIC force and a longer time to failure for the HTF than the NDm hand; 2) the IPS limb would demonstrate significant performance fatiguability following the HTF that would be hand specific (Dm > NDm) and the non-exercised CON limb would demonstrate no change or a small performance fatiguability effect due to a cross-over in fatigue response; 3) the women would demonstrate a longer HTF time at the relative 50% pre-HTF MVIC value and would have a lower degree of performance fatigability for the IPS limb than the men; and 4) there would be no difference between men and women in the relative changes in MVIC force for the CON limb.

METHODS

Participants

Ten men (Mean: Age: 22.6 yrs; Height: 182.0 cm; Weight: 82.9 kg) and 10 women (Age: 21.7 yrs; Height: 166.8 cm; Weight: 67.1 kg) between 18 and 35 years of age were recruited for this study. The number of participants selected was similar to Keller et al. (21) and was determined from an a priori power analysis using the G*Power3 (9). From the power analysis, it was determined that a minimum of 16 subjects (8 per group) were required to demonstrate mean differences between independent groups using mixed model ANOVAs, a large effect size ($p\eta^2$) of 0.14, a power of 0.80, and an alpha of 0.05. The subjects were familiar with resistance training exercise and had been resistance training at least 3 times per week for the past year. In addition, subjects were only included if they had no known cardiovascular, metabolic, or musculoskeletal diseases or disorders, particularly in the shoulder, arm, elbow, forearm, or wrist. The subjects were asked to maintain their current level of physical activity, but to abstain from upper body resistance exercise at least 24 hours prior to their testing session. Subjects were only included if they met the criteria above regarding age, training status, and health history. All subjects completed a health history questionnaire and signed a written informed consent document before participation in this study. This study was approved by the University's Institutional Review Board for Human Subjects. This research was carried out fully in accordance with the ethical standards of the International Journal of Exercise Science (28).

Protocol

During visits 1-3 of this study, the subjects performed 2-4, 6-sec pre-HTF MVIC with the IPS and CON side using a handgrip dynamometer (FT-220 hand dynamometer, iWorks, Dover, NH 03820). The handgrip MVIC holds and HTF were performed in a 90° forearm flexion position with the hand supinated. Only two MVIC tests were performed per hand if the MVIC force (kg) values are within 5% of one another. Additional MVIC tests were performed until two values were recorded that did not differ by greater than 5%. All of the subjects obtained 2 MVIC values within 5% of one another within 4 tests. The highest instantaneous force value for the 2 MVIC holds within 5% of one another were averaged and used as the pre-HTF MVIC value. The pre-HTF MVIC values for visits 1-3 were used to determine reliability. The pre-HTF MVIC values measured for visits 2 and 3 were used to examine performance fatigability. A 5-min rest was provided after the MVIC tests. The subjects then performed a single, HTF for the Dm or NDm hand at 50% of the IPS MVIC force until volitional fatigue or until the force dropped by greater than 5% of the target force for more than 5 seconds. Immediately following the HTF, the post-HTF MVIC force was determined for the IPS and CON hands. The HTF test (Dm or NDm) was randomized between visits 2 and 3 and the side tested first (IPS and CON) was randomized for pre-and post-HTF tests within each visit. The highest instantaneous force value for the IPS and CON MVIC as well as the total time for the HTF at 50% of MVIC were recorded and used in subsequent analyses. The performance fatigability was defined as a percent change (%Δ) from the pre-test to the post-test MVIC values. Test-retest reliability data for the MVIC (kg) measurements for this laboratory demonstrated an intraclass correlation coefficient ($ICC_{2,1}$) of 0.936, standard error of the measurement (SEM) of 2.7 kg, and coefficient of variation (CoV) of 6.6%.

Statistical Analysis

Independent samples t-tests were used to examine age, height, and weight between men and women. A 2 (hand [Dm, NDm]) x 2 (limb [IPS, CON]) x 2 (time [pre-HTF, post-HTF]) x 2 (sex [men, women]) mixed-model ANOVA was used to examine the MVIC kg force and a 2 (hand [Dm, NDm]) x 2 (sex [men, women]) mixed-model ANOVA was used to examine time for the HTF. Follow-up analyses consisted of 3-, and 2-way mixed models and repeated measure ANOVAs, and pairwise comparisons. *A priori* planned comparisons of the performance fatigability (%Δ = ((pre-HTF MVIC – post-HTF MVIC) / pre-HTF MVIC)*100)) following the

HTF between men and women were examined based on the 2 (hand [Dm, NDm]) x 2 (limb [IPS, CON]) x 2 (time [pre-HTF, post-HTF]) x 2 (sex [men, women]) mixed-model ANOVA used to examine the MVIC kg force. The 95% confidence intervals for mean comparisons were constructed and measures of effect size were calculated using partial eta squared ($p\eta^2$) and Cohen's *d*. The alpha level was set at $p \leq 0.05$ for all analyses. Analyses were performed using IBM SPSS Statistics 24 software (IBM SPSS Inc., Chicago, Illinois, USA) and Microsoft Excel® (Microsoft Corp., Redmond, Washington, USA).

RESULTS

Hold to Failure: The descriptive characteristics of the subjects are presented in Table 1. There was no significant hand x sex interaction ($F(1,18) = 1.940$; $p = 0.181$; $p\eta^2 = 0.097$) and no main effect for sex ($F(1,18) = 0.620$; $p = 0.441$, $p\eta^2 = 0.033$), but there was a main effect for hand ($F(1,18) = 12.638$; $p = 0.002$; $p\eta^2 = 0.412$) for the total time for the HTF. The mean time (collapsed across sex) for Dm hand HTF (130.3 ± 36.8 s) was significantly longer ($p = 0.002$; mean diff = 18.3 ± 23.52s; 95% CI = 7.5s – 29.0s; $d = 0.50$) than the NDm hand HTF (112.1 ± 34.3 s) (Table 2).

Table 1. Individual and composite anthropometric characteristics (age, height, and weight) and limb dominance.

Subject	Age (years)	Height (cm)	Body Mass (kg)	Hand Dominance
1 (W)	27	165.9	66.0	R
3 (W)	21	163.0	65.3	R
5 (W)	22	167.5	51.4	R
6 (W)	18	176.1	62.0	R
7 (W)	18	172.0	67.9	R
8 (W)	21	161.0	61.2	R
9 (W)	19	168.7	60.2	R
10 (W)	25	163.0	99.7	R
18 (W)	18	159.6	60.4	R
20 (W)	28	170.8	76.7	R
Mean	21.7	166.8	67.1	
SD	3.8	5.3	13.2	
2 (M)	30	172.0	77.1	R
4 (M)	20	186.8	94.6	R
11 (M)	21	184.3	71.5	R
12 (M)	20	189.4	93.8	R
13 (M)	28	177.8	78.0	L
14 (M)	25	179.7	65.8	R
15 (M)	19	177.1	74.4	R
16 (M)	21	190.6	117.4	R
17 (M)	22	188.5	82.5	L
19 (M)	20	174.0	74.0	L
Mean	22.6	182.0*	82.9*	
SD	3.8	6.8	15.2	

Composite			
Mean	22.2	174.4	75.0
SD	3.7	9.8	16.0

* Indicates the mean for the men was significantly greater than the women.

Table 2. Individual and composite dominant limb (Dm) and nondominant (NDm) hold to failure (HTF) time (seconds) for all subjects (n = 20).

Subjects	Dm HTF	NDm HTF
1 (W)	91	93
2 (M)	154	154
3 (W)	159	150
4 (M)	126	81
5 (W)	148	137
6 (W)	115	92
7 (W)	74	79
8 (W)	111	92
9 (W)	177	182
10 (W)	113	111
11 (M)	112	72
12 (M)	89	72
13 (M)	113	99
14 (M)	131	103
15 (M)	140	151
16 (M)	120	62
17 (M)	87	93
18 (W)	207	154
19 (M)	207	138
20 (W)	132	126
Mean	130.3*	112.1
(SD)	36.8	34.3

*Indicates the Dm HTF was significantly longer than the NDm HTF

There was no significant four-way interaction for MVIC force, but there was a significant interaction for hand x limb x sex (F(1,18) = 4.511, p = 0.048, pη^2 = 0.200). Additionally, there was a significant interaction for limb x time (F(1,18) = 162.697, $p \leq 0.001$, pη^2 = 0.900). Because all four factors were involved in an interaction, the model was decomposed with separate 2 (hand [Dm vs NDm]) x 2 (limb [IPS vs CON]) x 2 (time [Pre vs Post]) repeated measures ANOVAs for the men and women. There was also a main effect for sex (F(1,18) = 22.626, $p < 0.001$, pη^2 = 0.557) that indicated the MVIC was greater ($p \leq 0.001$, mean diff: 15.552 ± 3.269) for the men (46.07 ± 10.64 kg; 95% CI [41.214, 50.928]) than the women (30.52 ± 6.93 kg; 95% CI [25.662, 35.376]), when collapsed across hand, limb, and time.

The follow-up three-way hand x limb x time repeated measures ANOVA for the men (n = 10) demonstrated no significant three-way interaction (F(1,9) = 1.498, p = 0.252, pη^2 = 0.143), but there was a significant interaction for limb x time (F(1,9) = 76.2, $p \leq 0.001$, pη^2 = 0.000). The IPS pre-HTF MVIC force (collapsed across hand) (48.4 ± 9.0 kg) was greater than (t = 6.891; $p \leq 0.001$; mean diff: 10.7 ± 5.0; 95% CI [7.2, 14.2]; d = 0.99) than the IPS post-HTF MVIC (37.6 ± 10.2 kg) (%Δ = 22.9 ± 10.8%). The CON pre-HTF MVIC (47.9 ± 9.5 kg) was less than (t = -2.676; p = 0.025; mean diff: -2.8 ± 3.0; 95% CI [-4.7, -0.4]; d = -0.29) the CON post-HTF MVIC (50.4 ± 8.7 kg) (%Δ = -6.1 ± 6.9%). There was no difference (t = 0.726; p = 0.486; mean diff: 0.5 ± 2.1; 95% CI [-1.0, 2.0]; d = 0.05) between the IPS pre-HTF MVIC and the CON pre-HTF MVIC, but the IPS post-HTF MVIC was less than (t = -8.822; $p \leq 0.001$; mean diff: -12.1 ± 4.6; 95% CI [-16.1, -9.5]; d = -1.13) the CON post-HTF MVIC (Figure 1).

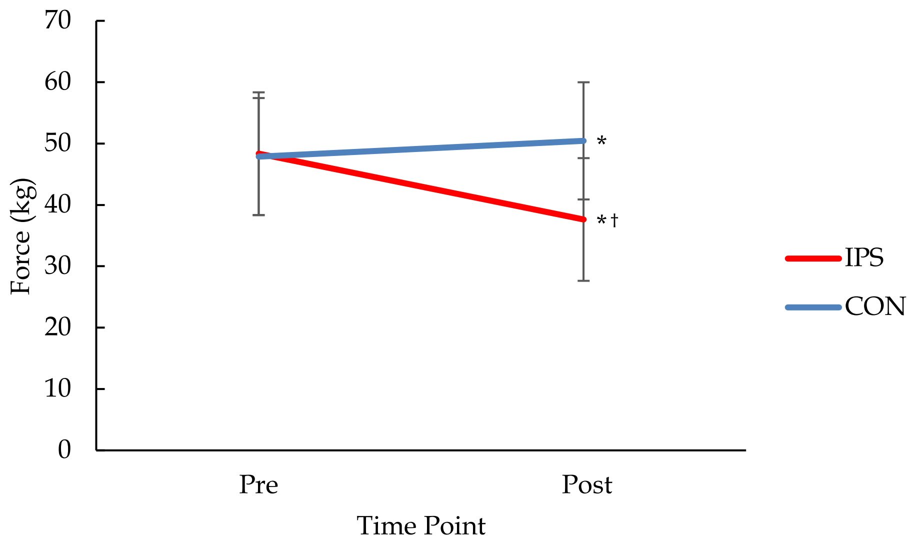

Figure 1. The mean maximal voluntary isometric contraction (MVIC) force in kilograms (kg) for the unilateral, pre- and post-handgrip hold to failure (HTF) for the men on the ipsilateral (red) and contralateral (blue) limb (collapsed across hand). An asterisk (*) indicates that the data point was significantly different from the pre-test MVIC force for the respective limb. A † indicates the ipsilateral (Dm) post-test MVIC force was significantly less than the contralateral (NDm) post-test MVIC force.

The follow-up three-way hand x limb x time repeated measures ANOVA for the women (n = 10) demonstrated no significant three-way (F(1,9) = 0.002, p = 0.968, pη^2 = 0.000) interaction. However, there were significant two-way interactions for side x time (F(1,9) = 98.631, $p \leq 0.001$, pη^2 = 0.916) and hand x limb (F(1,9) = 12.003, p = 0.007, pη^2 = 0.571). Because all three factors were involved in an interaction, the model was decomposed with separate 2 (limb [IPS vs CON]) x 2 (time [Pre vs Post]) repeated measures ANOVAs for the Dm and NDm hand.

For the Dm hand, there was a significant limb x time interaction (F(1,9) = 79.975, $p \leq 0.001$, pη^2 = 0.899). The IPS pre-HTF MVIC (34.1 ± 5.0 kg) was greater than (t = 7.424; $p \leq 0.001$; mean diff: 9.7 ± 4.1; 95% CI [6.7, 12.6]; d = 1.43) the IPS post-HTF MVIC (24.4 ± 4.3 kg) (%Δ = 28.0 ± 9.4%), but the CON pre-HTF MVIC (31.6 ± 6.7 kg) was not different (t = -0.619; p = 0.551; mean diff: -0.33 ± 1.7; 95% CI [-1.6, 0.9]; d = -0.05) from the CON post-HTF MVIC (32.0 ± 5.9 kg) (%Δ = -1.6 ± 5.7%). The IPS (i.e., Dm hand) pre-HTF MVIC was greater than (t = 2.575; p = 0.030; mean diff:

2.4 ± 3.0; 95% CI [0.297, 4.59]; *d* = 0.41) the CON (i.e., NDm hand) pre-HTF MVIC. In addition, the IPS post-HTF MVIC was less than (t = -5.829; $p \leq 0.001$; mean diff: -7.55 ± 4.09; 95% CI [-10.48, -4.62]; *d* = -1.2) the CON post-HTF (Figure 2).

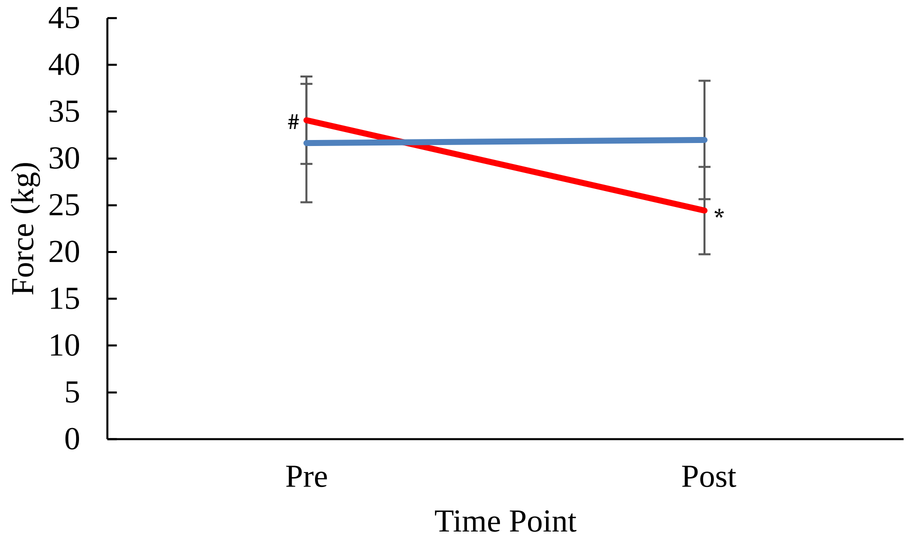

Figure 2. The mean maximal voluntary isometric contraction (MVIC) force in kilograms (kg) for the unilateral, pre- and post-handgrip hold to failure (HTF) of the dominant (Dm) hand for the women on the ipsilateral (red) and contralateral (blue) limb. An asterisk (*) indicates that the data point was significantly less than the pre-test MVIC force for the respective limb. A number sign (#) indicates the ipsilateral (Dm) pre-test MVIC force was significantly greater than the contralateral (NDm) side.

For the NDm hand, there was a significant limb x time interaction ($F(1,9) = 99.91$, $p \leq 0.001$, $p\eta^2 = 0.917$). The IPS pre-HTF MVIC (32.3 ± 6.5 kg) was greater than (t = 7.073; $p \leq 0.001$; mean diff: 10.61 ± 4.74; 95% CI [7.21, 13.998]; *d* = 1.38) the IPS post-HTF MVIC (21.7 ± 4.6 kg) (%Δ = 32.3% ± 10.1%). The CON pre-HTF MVIC (34.3 ± 5.6 kg) was not different from (t = 0.939; p = 0.373; mean diff: 0.64 ± 2.16; 95% CI [-0.91, 2.19]; *d* = 0.12) the CON post-HTF MVIC (33.7 ± 5.3 kg) (%Δ = 1.7 ± 5.9%). The IPS (i.e., NDm hand) pre-HTF MVIC was less than (t = -2.537; $p \leq 0.001$; mean diff: -1.95 ± 2.43; 95% CI [-3.69, -0.219]; *d* = -0.33) the CON (i.e., Dm hand) pre-HTF MVIC. In addition, the IPS post-HTF MVIC was less than (t = -16.25; $p \leq 0.001$; mean diff: -11.92 ± 2.32; 95% CI [-13.57, -10.26]; *d* = -1.54) the CON post-HTF (Figure 3).

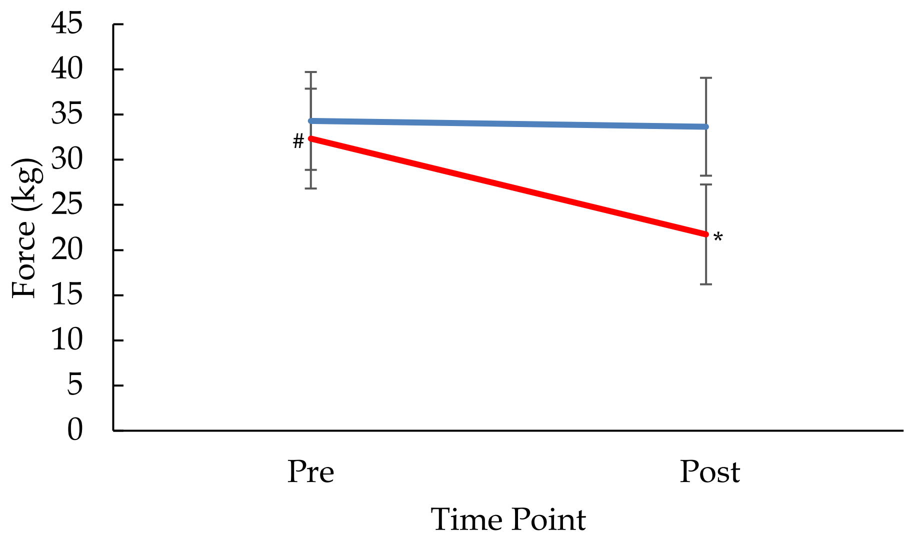

Figure 3. The mean maximal voluntary isometric contraction (MVIC) force in kilograms (kg) for the unilateral, pre- and post-handgrip hold to failure (HTF) of the nondominant (NDm) hand for the women on the ipsilateral (red) and contralateral (blue) limb. An asterisk (*) indicates that the data point is significantly less than the pre-test MVIC force for the respective limb. A number sign (#) indicates the ipsilateral (NDm) pre-test MVIC force was significantly less than the contralateral (Dm) side.

The *a priori* planned comparisons for the performance fatigability (%Δ) indicated that there was no difference in the %Δ between the men (22.9 ± 10.8%; collapsed across Dm and NDm hand HTF) and the women for the IPS limb, Dm hand HTF (28.0 ± 9.4%; t = -1.12; p = 0.277; mean diff: -5.1 ± -4.55; 95% CI [-14.65, 4.55]; d = -0.50) or for the IPS limb, NDm hand HTF (32.3 ± 10.1%; t = -2.01; p = 0.060; mean diff: -9.43 ± -4.70; 95% CI [-19.29, 0.44]; d = -0.69). The IPS limb performance fatigability for the women for the Dm hand (28.0 ± 9.4%) was less than (t = -2.634; p = 0.027; mean diff: -4.33 ± -5.20 ; 95% CI [-8.05, -0.61]; d = -0.44) the NDm hand (32.3 ± 10.1%). In addition, for the %Δ on the non-exercised, CON limb, there was no difference between the men (-6.1 ± 6.9%; collapsed across Dm and NDm hand HTF) and the women (-1.57 ± 5.74%) for the Dm hand (t = -1.62; p = 0.123; mean diff: -4.65 ± 2.87; 95% CI [-10.69, 1.39]; d = 0.10). Alternatively, the men (-6.1 ± 6.9%) demonstrated a greater %Δ (facilitation of the CON limb) compared to the women (1.7 ± 5.9%) for the NDm hand (t = -2.72; p = 0.014; mean diff: -7.90 ± 2.90; 95% CI [-13.998, -1.80]; d = -0.23).

DISCUSSION

In this study, the absolute MVIC force was greater for the men (46.1 ± 10.6 kg) compared to the women (30.5 ± 6.9 kg). These findings were consistent with previous studies that have demonstrated greater absolute strength for men compared to women (20). Interestingly, the women, but not the men, demonstrated greater MVIC force for the Dm hand compared to the NDm hand, consistent with the findings of Thorngren & Werner (41). There were no differences between men and women in the 50% MVIC HTF time, however, the Dm hand demonstrated a greater time to task failure (130.3 ± 36.8 sec) compared to the NDm hand (112.1 ± 34.3 sec). The differences in fatigue resistance between the Dm and NDm limbs were consistent with our hypothesis and may be attributed to activities of daily living wherein individuals will favor their Dm limb rather than their NDm limb (16). However, the lack of sex differences in time to task failure was not consistent with our hypothesis and there were no sex differences in performance fatigability for the exercised, IPS side. There is some evidence (26) that sex differences in fatigability become smaller or are not present for fatiguing isometric exercise performed at intensities that are greater than or equal to 50% MVIC, potentially related to occlusion in blood flow to the working muscle(s). It is possible that the isometric HTF, performed at 50% MVIC in the current study, was at an intensity high enough to cause increases in intramuscular pressure for both the men and the women that occluded blood flow within the muscle and created similar performance limitations. Thus, the current findings showed no difference between the men and the women in HTF time or performance fatigability, contrary to our hypothesis, and this may be related to the relative intensity (50% MVIC) and the mode (i.e., isometric, intermittent isometric, or dynamic) of the fatiguing task.

In the current study, there was a facilitation (6% increase) in force in the CON limb following the 50% MVIC HTF for the men but no change in CON limb force for the women. Thus, the hypothesis that the non-exercising CON limb would demonstrate no change or a small performance fatigability effect due to a cross-over in fatigue response was supported for the women but not the men. Unilateral fatiguing tasks have been reported most frequently to cause no change (2, 15) or decreases (1, 18) in force production of the non-exercise CON limb which has been attributed to the "cross-over" inhibitory phenomenon (1). This "cross-over" inhibition is thought to be caused by group III/IV afferent feedback of metabolic and mechanical perturbations from the exercised limb (2). This afferent feedback, in turn, leads to central fatigue by limiting the central drive to both the IPS and CON limbs (2). However, the presence and magnitude of this "cross-over" inhibitory effect may be related to the mode and intensity of the fatiguing task (2, 15, 29, 38). Thus, for the women in this study, the 50% isometric HTF may not have been at an intensity high enough to elicit alterations in CON strength.

The CON limb facilitation demonstrated for the men in this study was consistent with the findings of Neltner et al. (29), where 4 to 5% increases in torque were demonstrated in the non-exercised CON limb following unilateral, dynamic leg extensions. Strang et al. (38) also reported a significant increase in the quadriceps force of the CON limb of 13.4% and a nonsignificant increase of 2.7% in the CON limb hamstring following fatiguing, dynamic leg extension exercise. The facilitation of force/torque in the CON limb demonstrated in these studies may be due to a combination of central mechanisms that lead to increased central (i.e., cortical) drive to the non-exercised CON limb (1). Changes in the cortical-spinal pathways may be responsible for the increase in performance in the contralateral limb, defined as "cross-facilitation" (1, 29). Contralateral activation has been reported in homologous intrinsic muscle groups of the hand during the performance of unilateral exercise at intensities of 20-40% MVIC in tonic pinch grips (22) and greater than or equal to 50% MVIC in isometric thumb abductions (1, 7). This contralateral activation may have been produced via excitatory signaling through the transcallosal connection or shared pathways in the brain stem or spinal cord, influencing both hemispheres of the brain and subsequent exercised IPS and non-exercised CON muscle groups (1). Interhemispheric inhibition (IHI) is a mechanism in which this shared excitatory signaling pathway is inhibited to prevent mirror movements in a CON limb during a unilateral task (5, 7). Depolarized inhibitory neurons at the cortical level signal further depolarization in the distal decussating pyramidal neurons which project to the homologous, contralateral muscle fibers (5, 7). Despite the presence of this IHI, muscle actions at higher intensities (≥ 50% MVIC) have been demonstrated to decrease its inhibitory effects (1, 7). Higher intensity muscle actions will elicit excitatory signaling in the trans-colossal fibers, mediated by the collaterals of corticospinal neurons via the corpus callosum, producing the cross-facilitation effect despite inhibitory signaling in the interneurons (5, 7). The activation of additional brain regions from this excitatory signaling may subsequently elicit greater motor evoked potential (MEP) amplitude, as amplitude is contingent upon the balance of both the excitation and inhibition of supraspinal and spinal anatomy leading to increased neural drive to the muscle (1, 13).

During fatiguing muscle actions, increased neural drive, regulated by the motor cortex to compensate for the decreased spinal motoneuron excitability elicited by fatiguing muscle actions, may produce these greater force productions associated with facilitation (1, 29). Thus, the results of the current study in conjunction with others (25, 29), suggest that the central nervous system does not selectively control neural drive to the exercising muscle only, possibly to provide overall coordination to maintain cellular homeostasis due to anticipatory regulation between shared neural networks of the IPS and CON limbs (17). The 50% MVIC HTF in this study was at an intensity similar to or greater than the intensity demonstrated to produce a sum of excitatory signaling that is greater than the inhibitory signaling from IHI, eliciting activation at the cortical level, leading to activation in the non-exercising CON limb (1, 7, 29). The effect of this signaling may have additionally increased the neural drive to compensate for the reduction in the spinal motoneuron activity following the fatiguing HTF and may have produced this facilitation that was demonstrated in the men (1, 29). The cross-over facilitation effect may have been elicited by a combination of these central mechanisms, however, the lack of change for the women suggested an alternative mechanism may help further explain these findings.

The facilitation demonstrated by the men, but not the women, may also be the result of a combination of central and peripheral mechanisms related to PAPE. During unilateral muscle actions, the increased neural drive to the exercised muscle travels through crossed and shared neural pathways of the IPS and CON homologous muscles during exercise performance. It has been reported that this shared pathway results in a 10-15% activation in the homologous, non-exercised CON muscle (29, 30, 32). This CON limb activation during IPS exercise may lead to increased myosin light chain phosphorylation through calcium ions eliciting a PAPE response (33). Two protein subunits that wrap themselves around the myosin rod region that connect the myosin head to the thick filament, termed the essential light chain and regulatory light chain, provide a type of mechanical support to the myosin rod region (23, 39). Calcium release to the sarcomeres may phosphorylate the essential and regulatory light chains, resulting in a movement in the myosin head closer to the actin filament subsequently resulting in a greater number of possible cross-bridge formations or increased cycling rates (23, 39). The PAPE phenomenon has been demonstrated in plantar flexor muscles following various 6-second conditioning contractions at 40, 60, 80, and 100%, with the 80% MVIC increasing force production by 6.1 ± 5.5% and 100% MVIC increasing force production by 7.4 ± 6.8% in the IPS limb (11), which was similar to the 6.1 ± 6.9% increase in the CON limb MVIC force demonstrated for the men in the current study. Fukutani et al. (10) demonstrated similar findings in the thumb adductor muscles, as performance of 10-second contractions at 20, 40, and 60%MVIC significantly increased the PAPE effect in the MVIC torque production and demonstrated greater PAPE effects for each increasing intensity. Mettler & Griffin (27) supported these findings, as the potentiation effect of performing 25%, 50%, and 100% MVIC in the adductor pollicis muscle increased as the intensity of the hold increased. The subjects in the current study performed a 50% MVIC HTF at a similar intensity to these aforementioned studies, suggesting that the mechanisms underlying PAPE may have played a role in the facilitation effect seen in the men (10, 11, 27).

The PAPE phenomenon and its subsequent effect on force generation have been suggested to occur during tasks that require smaller motor units similar to the handgrip muscles used in the current study (35, 37). In addition to motor unit size, the muscle fiber type may impact the PAPE phenomenon (36). Type II fibers have been suggested to demonstrate a greater PAPE response as the phosphorylation of myosin regulatory light chains occurs more rapidly in these fibers (36). In a study conducted by Gervasi et al. (14), following a 40-minute run at the lactate threshold, the countermovement jump height increased and subjects subsequently recruited greater numbers of type II fibers to perform the movement. The men in the current study demonstrated a CON facilitation effect while the women demonstrated no significant change, possibly due to the differences in muscle fiber type distributions between men and women (42). It is possible the men in the current study possessed a greater number of type II muscle fibers that are more sensitive to the mechanisms associated with the PAPE phenomenon and may explain the sex differences in CON limb MVIC force production. (42). Thus, it is hypothesized that the central factors of shared neural pathways and the interhemispheric influence of excitatory and inhibitory signaling may have produced a 'cross-facilitation' effect that was demonstrated in the current study, however, a greater emphasis is placed upon the peripheral influence of the post-activation performance enhancement phenomenon.

This study was limited by the inability to complete measurements to distinguish central and peripheral factors of fatigue. This study did not examine the metabolic byproduct accumulation, neuromuscular responses, or fiber type distribution patterns of the subjects. These measures may explain the mechanisms underlying the responses observed in the current study and may better inform future studies examining the fatigue response in the CON and IPS limb following a unilateral, isometric HTF in both men and women.

In summary, the results of this study demonstrated sex- and limb-dependent responses during unilateral, isometric handgrip exercise to failure. Despite the differences in absolute grip strength, the isometric (50% MVIC) handgrip HTF time was not different between the men and women but the Dm hand (130.3 ± 36.8 seconds) demonstrated a greater fatigue resistance than the NDm hand (112.1 ± 34.3 seconds). Similar performance fatigability was demonstrated in the IPS limb following the HTF in both men (22.9 ± 10.8%) and women; however, this effect was demonstrated to be greater in the NDm (32.3 ± 10.1%) than the Dm (28.0 ± 9.4%) hand for the women. The limb dependent performance fatigability for the women may have been related to the greater absolute strength in the Dm relative to the NDm hand. Interestingly, CON limb facilitation was demonstrated in the men (-6.1 ± 6.9%) but not the women. The existence of such a phenomenon may be due to central factors of facilitation such as shared neural pathways at the cortical and spinal cord levels and the summation of excitatory and inhibitory signaling eliciting interhemispheric influences. However, as this facilitation was not demonstrated for the women, it is hypothesized that the peripheral PAPE phenomenon may have played a larger role as it is demonstrated more frequently in type II muscle fibers (23, 25, 29, 39, 42). Thus, the results of this study demonstrated that relative 50% MVIC handgrip holds to failure produced similar levels of IPS performance fatiguability in men and women, but despite similar times to failure, CON limb facilitation was observed in the men and not the women.

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REFERENCES

1. Aboodarda SJ, Šambaher N, Behm DG. Unilateral elbow flexion fatigue modulates corticospinal responsiveness in non-fatigued contralateral biceps brachii. Scand J Med Sci Sports 26(11): 1301–12, 2016.

2. Amann M, Venturelli M, Ives SJ, McDaniel J, Layec G, Rossman MJ, et al. Peripheral fatigue limits endurance exercise via a sensory feedback-mediated reduction in spinal motoneuronal output. J Appl Physiol 115(3): 355–64, 2013.

3. Bechtol CO. Grip test; The use of a dynamometer with adjustable handle spacings. J Bone Joint Surg Am 36-A(4): 820–4, 1954.

4. Bohannon RW. Grip strength: A summary of studies comparing dominant and nondominant limb measurements. Percept Mot Skills 96(3): 728–30, 2003.

5. Carson RG. Neural pathways mediating bilateral interactions between the upper limbs. Brain Res 49(3): 641–62, 2005.

6. Davis JM, Bailey SP. Possible mechanisms of central nervous system fatigue during exercise. Med Sci Sports Exerc 29(1): 45–57, 1997.

7. Derosiere G, Alexandre F, Bourdillon N, Mandrick K, Ward TE, Perrey S. Similar scaling of contralateral and ipsilateral cortical responses during graded unimanual force generation. Neuroimage 85: 471–7, 2014.

8. Enoka RM, Duchateau J. Translating fatigue to human performance. Med Sci Sports Exerc 48(11): 2228-38, 2016.

9. Faul F, Erdfelder E, Lang A-G, Buchner A. G* Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods 39(2): 175–91, 2007.

10. Fukutani A, Hirata K, Miyamoto N, Kanehisa H, Yanai T, Kawakami Y. Effect of conditioning contraction intensity on postactivation potentiation is muscle dependent. J Electromyogr Kinesiol 24(2): 240–5, 2014.

11. Fukutani A, Miyamoto N, Kanehisa H, Yanai T, Kawakami Y. Influence of the intensity of a conditioning contraction on the subsequent twitch torque and maximal voluntary concentric torque. J Electromyogr Kinesiol 22(4): 560–5, 2012.

12. Gandevia SC. Spinal and supraspinal factors in human muscle fatigue. Physiol Rev 81(4): 1725-89, 2001.

13. Gandevia SC, Macefield G, Burke D, McKenzie DK. Voluntary activation of human motor axons in the absence of muscle afferent feedback: The control of the deafferented hand. Brain 113(5): 1563–81, 1990.

14. Gervasi M, Calavalle AR, Amatori S, Grassi E, Benelli P, Sestili P, et al. Post-activation potentiation increases recruitment of fast twitch fibers: A potential practical application in runners. J Hum Kinet 65: 69–78, 2018.

15. Grabiner MD, Owings TM. Effects of eccentrically and concentrically induced unilateral fatigue on the involved and uninvolved limbs. J Electromyogr Kinesiol 9(3): 185–9, 1999.

16. Habibi E, Kazemi M, Dehghan H, Mahaki B, Hassanzadeh A. Hand grip and pinch strength: Effects of workload, hand dominance, age, and body mass index. Pak J Med Sci 29(1 suppl): 363-7, 2013.

17. Halperin I, Chapman DW, Behm DG. Non-local muscle fatigue: Effects and possible mechanisms. Eur J Appl Physiol 115(10): 2031–48, 2015.

18. Halperin I, Copithorne D, Behm DG. Unilateral isometric muscle fatigue decreases force production and activation of contralateral knee extensors but not elbow flexors. Appl Physiol Nutr Metab 39(12): 1338–44, 2014.

19. Helbig CR, Gabbard C. What determines limb selection for reaching? Res Q Exerc Sport 75(1): 47–59, 2004.

20. Kamarul T, Ahmad TS, Loh WYC. Hand grip strength in the adult Malaysian population. J Orthop Surg 14(2): 172–7, 2006.

21. Keller JL, Housh TJ, Hill EC, Smith CM, Schmidt RJ, Johnson GO. Are there sex-specific neuromuscular or force responses to fatiguing isometric muscle actions anchored to a high perceptual intensity? J Strength Cond Res 36(1): 156–61, 2022.

22. Liepert J, Dettmers C, Terborg C, Weiller C. Inhibition of ipsilateral motor cortex during phasic generation of low force. Clin Neurophysiol 112(1): 114–21, 2001.

23. Lowey S, Trybus KM. Common structural motifs for the regulation of divergent class II myosins. J Biol Chem 285(22): 16403–7, 2010.

24. Martin PG, Rattey J. Central fatigue explains sex differences in muscle fatigue and contralateral cross-over effects of maximal contractions. Pflügers Archiv - Eur J Physiol 454(6): 957–69, 2007.

25. Matkowski B, Place N, Martin A, Lepers R. Neuromuscular fatigue differs following unilateral vs bilateral sustained submaximal contractions. Scand J Med Sci Sports 21(2): 268–76, 2011.

26. Maughan RJ, Harmon M, Leiper JB, Sale D, Delman A. Endurance capacity of untrained males and females in isometric and dynamic muscular contractions. Eur J Physiol 55(4): 395–400, 1986.

27. Mettler JA, Griffin L. Postactivation potentiation and muscular endurance training. Muscle Nerve 45(3): 416–25, 2012.

28. Navalta JW, Stone WJ, Lyons TS. Ethical issues relating to scientific discovery in exercise science. Int J Exerc Sci 12(1): 1-8, 2019.

29. Neltner TJ, Anders JPV, Keller JL, Smith RW, Housh TJ, Schmidt RJ, et al. Ipsilateral and contralateral torque responses to bilateral and unilateral maximal, fatiguing, isokinetic leg extensions. Int J Kinesiol Sports Sci 8(4): 25–33, 2020.

30. Nyberg-Hansen R, Rinvik E. Some comments on the pyramidal tract, with special reference to its individual variations in man. Acta Neurol Scand 39(1): 1–30, 1963.

31. Petersen P, Petrick M, Connor H, Conklin D. Grip strength and hand dominance: challenging the 10% rule. Am J Occup Ther 43(7): 444–7, 1989.

32. Phillips CG, Porter R. The pyramidal projection to motoneurones of some muscle groups of the baboon's forelimb. Prog Brain Res 12: 222–45, 1964.

33. Przybyla A, Good DC, Sainburg RL. Dynamic dominance varies with handedness: Reduced interlimb asymmetries in left-handers. Exp Brain Res 216(3): 419–31, 2012.

34. Rassier DE, Macintosh BR. Coexistence of potentiation and fatigue in skeletal muscle. Braz J Med Biol Res 33(5): 499–508, 2000.

35. Sale D. Postactivation potentiation: Role in performance. Br J Sports Med 38(4): 386–7, 2004.

36. Sale DG. Postactivation potentiation: Role in human performance. Exerc Sport Sci Rev 30(3): 138–43, 2002.

37. Sonne MW, Hodder JN, Wells R, Potvin JR. Force time-history affects fatigue accumulation during repetitive handgrip tasks. J Electromyogr Kinesiol 25(1): 130–5, 2015.

38. Strang AJ, Berg WP, Hieronymus M. Fatigue-induced early onset of anticipatory postural adjustments in non-fatigued muscles: Support for a centrally mediated adaptation. Exp Brain Res 197(3): 245–54, 2009.

39. Stull JT, Kamm KE, Vandenboom R. Myosin light chain kinase and the role of myosin light chain phosphorylation in skeletal muscle. Arch Biochem Biophys 510(2): 120–8, 2011.

40. Thomas K, Goodall S, Howatson G. Performance fatigability is not regulated to a peripheral critical threshold. Exerc Sport Sci Rev 46(4): 240–6, 2018.

41. Thorngren K-G, Werner CO. Normal grip strength. Acta Ortho Scand 50(3): 255–9, 1979.

42. Thorstensson A, Carlson H. Fibre types in human lumbar back muscles. Acta Physio Scand 131(2): 195–202, 1987.

43. Zimmermann HB, MacIntosh BR, Dal Pupo J. Does postactivation potentiation (PAP) increase voluntary performance? Appl Physiol Nutr Metab 45(4): 349–56, 2020.