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Transfer of ballistic motor skill between bilateral and unilateral contexts in young and older adults: neural adaptations and behavioral implications

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Hinder MR, Carroll TJ, Summers JJ. Transfer of ballistic motor skill between bilateral and unilateral contexts in young and older adults: neural adaptations and behavioral implications. *J Neurophysiol* 109: 2963–2971, 2013. First published March 27, 2013; doi:10.1152/jn.00535.2012.—Bilateral movement rehabilitation is gaining popularity as an approach to improve the recovery not only of bimanual function but also of unilateral motor tasks. While the neural mechanisms mediating the transfer of bilateral training gains into unimanual contexts are not fully understood, converging evidence from behavioral, neurophysiological, and imaging studies suggests that bimanual movements are not simply the superposition of unimanual tasks undertaken with both (upper) limbs. Here we investigated the neural responses in both hemispheres to bilateral ballistic motor training and the extent to which performance improvements transferred to a unimanual task. Since aging influences interhemispheric interactions during movement production, both young ($n = 9$; mean age 19.4 yr; 6 women, 3 men) and older ($n = 9$; 66.3 yr; 7 women, 2 men) adults practiced a bilateral motor task requiring simultaneous “fast-as-possible” abductions of their left and right index fingers. Changes in bilateral and unilateral performance, and in corticospinal excitability and intracortical inhibition, were assessed. Strong transfer was observed between bimanual and unimanual contexts for both age groups. However, in contrast to previous reports of substantial bilateral cortical adaptations following unilateral training, increases in corticospinal excitability following bilateral training were not statistically reliable, and a release of intracortical inhibition was only observed for older adults. The results indicate that the neural mechanisms of motor learning for bilateral ballistic tasks differ from those that underlie unimanual ballistic performance improvement but that aging results in a greater overlap of the neural mechanisms mediating bilateral and unilateral ballistic motor performance.

motor learning; bilateral training; transcranial magnetic stimulation; transfer; aging; motor cortex

BECAUSE COORDINATED BIMANUAL actions cannot be viewed simply as the superposition of two independent actions, bilateral movement therapy has recently been applied in rehabilitation environments with the aim of promoting faster, and more complete, motor recovery (e.g., after stroke; Cauraugh and Summers 2005; Stewart et al. 2006). Moreover, it is believed that bimanual practice may also result in improved unilateral performance (Waller and Whittall 2008), perhaps because of releases in intracortical inhibition in both hemispheres (Waller et al. 2008). However, it is not fully understood to what extent the neural mechanisms governing bimanual and unimanual actions overlap, and whether improvements in motor performance during bimanual tasks result in commensurate behav-

ioral gains when the task is subsequently undertaken in a unimanual context. Providing answers to these questions is critical so that rehabilitation programs can be tailored to maximize the recovery of an individual at both the behavioral (task) and neural levels. However, because of the complications in assessing a relative novel paradigm in stroke survivors, who are known to respond differently to therapies depending on the site of the lesion and the severity of paresis, age, motivation, etc., it is important to first undertake studies in healthy volunteers.

A limited number of behavioral studies have investigated transfer of motor skill between bimanual and unimanual contexts. Nozaki and colleagues (Nozaki et al. 2006) reported that after adaptation of bimanual reaches to an external force field performance gains were only partly transferred to unimanual reaches in the same dynamic environment. A greater degree of bimanual-unimanual between-task transfer was observed after adaptation of bimanual reaches to a visuomotor rotation (Wang and Sainburg 2009). It was postulated that although distinct neural processes may govern unilateral and bilateral movements, the visuomotor adaptation process itself may occur upstream of the sites that distinguish between unilateral and bilateral adaptation. On the basis of these studies, it appears that although some benefits may be conferred in unilateral movements as a result of bilateral training protocols, further unilateral training would be required to obtain performance levels reached during the bimanual setting. The neural mechanisms mediating the transfer between different task contexts has not, to date, been directly assessed. This fact was highlighted in a recent review by Waller and Whittall (2008), who, on assessing the bimanual training literature with a view to stroke recovery, called for more studies investigating the neurophysiological mechanisms of bilateral training.

As indicated above, adaptation to complex visual and dynamic environments often involves a distributed network of visual and motor regions within the brain, and it is not clear how principles of transfer obtained from these sensorimotor adaptation studies may relate to other contexts, such as transfer of strength gains. Moreover, all of the aforementioned studies were conducted on young adults, and it cannot be assumed that these results would generalize to older populations given age-related changes in intracortical and interhemispheric inhibitory mechanisms that may affect interhemispheric communication during movement (Talelli et al. 2008). An interesting question is therefore how the neural mechanisms thought to be responsible for mediating strength gains might generalize between bimanual and unimanual tasks across the life span. This is an important consideration, as loss of strength (due to both muscle

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atrophy and degeneration of neural pathways) is common after stroke. Moreover, Barker et al. (2008) reported that a 4-wk training program specifically designed to increase upper limb strength not only led to the expected strength gains but also engendered improvements in clinical (functional) markers of motor ability (e.g., modified Ashworth score and Motor Assessment Scale). Furthermore, Byblow and colleagues (Byblow et al. 2012) observed better motor learning of fine motor tasks such as a grooved pegboard task (resembling activities of daily living) after a bilateral movement “priming.” As such, assessing the mechanisms mediating strength gain (in bilateral tasks), and its subsequent transfer, is of clear importance for rehabilitation.

We have recently conducted a number of studies investigating cross-limb transfer of ballistic finger movements (e.g., Carroll et al. 2008; Hinder et al. 2011; Lee et al. 2010). Importantly, it has been shown that these high-force tasks induce neural adaptations akin to those that are thought to mediate strength gains following resistance training (Selvanayagam et al. 2011) and that occur within a single session (<1 h) of training. Accordingly, such tasks provide an appropriate laboratory model to study the neural mechanisms associated with strength training: a limitation of actual strength training protocols for assessing the neural mechanisms thought to underpin transfer of strength is that many weeks is required to evoke a strength (behavioral) gain, rendering the changes undetectable via transcranial magnetic stimulation (TMS). Performance improvements in these ballistic tasks can result in posttraining increases in excitability of the corticospinal pathways projecting from the primary motor cortex representation of the trained muscle (Baraduc et al. 2004; Muellbacher et al. 2002) and its homolog in the untrained hemisphere (Carroll et al. 2008; Hinder et al. 2011; Lee et al. 2010) as well as releases of intracortical inhibition in the trained, and untrained, hemisphere (Hinder et al. 2011). Muellbacher and colleagues (Muellbacher et al. 2002) reported that repetitive TMS (rTMS), applied to the trained motor cortex after a period of motor practice, reduced those performance gains that were observed immediately prior to the stimulation, while rTMS applied to the untrained hemisphere (Lee et al. 2010) reduced performance gains in the untrained limb. Accordingly, evidence exists that changes within M1 play a crucial role in mediating performance gains in both the trained and untrained limbs after unilateral ballistic training. To our knowledge, studies investigating the neural mechanisms associated with bilateral ballistic movements and the subsequent transfer to unilateral ballistic tasks (in young or older adults) have not been undertaken.

It is well known that bilateral movements require extensive interhemispheric communication and interactions between left and right M1 (see Carson 2005 and Swinnen 2002 for reviews), as well as between other nonprimary cortical regions such as the supplementary motor area (SMA) (Donchin et al. 2002). The present experiment used TMS to assess whether, in young and older adults, performance gains associated with bilateral motor training are accompanied by changes in corticospinal excitability and intracortical inhibition in both motor cortices, and assessed whether these training gains are subsequently manifested in a unilateral task context.

METHODS

Participants

A total of 18 right-handed (Laterality Index ≥ 90 ; Oldfield 1971) adults volunteered to participate in the study and were enrolled into “young” ($n = 9$, mean \pm 95% confidence interval: 19.4 ± 0.9 yr) and “older” ($n = 9$, 66.3 ± 4.0 yr) groups. All participants gave their written informed consent before beginning the experiment, which had received ethical approval from the University of Tasmania’s Human Research Ethics Committee. Participants were screened for contraindications to TMS, had normal or corrected-to-normal vision, and were free from neurological and neuromuscular disorders.

Movement Task and Experimental Design

The experiment was designed to investigate the effect of bilateral ballistic motor training (rapid abductions of the index fingers) on the same task but undertaken with each hand in isolation (unilateral performance). Our particular interest was the proportion (or percentage) of any behavioral gains in the trained bilateral task subsequently exhibited during an untrained unilateral task (defined as between-task transfer) and the neural mechanisms mediating this transfer. Participants were seated comfortably with their forearms pronated (palms down) and resting on a horizontal board mounted onto a table. The elbows were bent at $\sim 120^\circ$. Participants were instructed to make discrete abductions of both index fingers simultaneously (bilateral condition) or of one of the index fingers in isolation (unilateral condition) with the goal of maximizing peak abduction acceleration of the finger(s). Pegs inserted into the horizontal board helped to maintain a constant hand position throughout the experiment and also aimed to restrict movements to the second metacarpo-phalangeal joint (Carroll et al. 2008; Hinder et al. 2011). Triaxial accelerometers (Dytran Instruments, Chatsworth, CA; Endevco, San Juan Capistrano, CA), which were mounted to plastic splints and taped to the top of the left and right index fingers, were used to measure finger abduction.

Initially we established baseline performance in both the left and right hands unilaterally and bilaterally (PRE tests of performance). These tests involved 10 discrete ballistic movements (in each of the left unilateral, right unilateral, and bilateral conditions). Performance feedback and verbal encouragement were not provided; participants were simply instructed at the start of the test trials to make isolated abduction movements as quickly as possible (i.e., to maximize their accelerations). An audio tone was used to prompt subjects to perform a discrete ballistic movement every 2 s (0.5 Hz)—speeded reaction times were not required. After the PRE tests, participants underwent bilateral training in which both index fingers were required to make simultaneous discrete movements. Training consisted of 2 blocks of 150 movements at 0.5 Hz (300 movements total). Short breaks (~ 30 s) were provided every 10 movements to minimize any possible effects of fatigue; thus each block lasted ~ 12 min. During bilateral training participants were provided with visual feedback of the combined peak acceleration attained in each bilateral movement (calculated by summing acceleration traces from either hand on a point-by-point basis: positive acceleration was in the direction of finger abduction for each digit). The combined acceleration from each movement was represented on a computer screen as a point on a graph on which the y -axis represented peak (combined) acceleration (i.e., “performance score”) and the x -axis represented movement number. Participants were verbally encouraged to improve on each movement such that the line created by joining all feedback points gradually rose up the screen. A prerequisite for attaining peak performance (because of the manner in which feedback score was calculated) was that both index fingers attained their peak acceleration simultaneously. Upon completion of the first and second bilateral training blocks, we assessed performance in the left and right hands unilaterally, and bilaterally, in the absence of feedback or encouragement (MID and POST tests; 10 movements per condition). The order of testing (i.e.,

bilateral, unilateral right hand, unilateral left hand) was pseudorandomized across time points (PRE, MID, POST) and participants.

Recording of Muscle Activity

Electromyography (EMG) was recorded from the first dorsal interosseus (FDI)—the primary agonist during index finger abduction—in both hands with Ag/AgCl electrodes (Meditrace 130, Tyco Healthcare, Mansfield, MA) in a belly-tendon montage. EMG was recorded during execution of the task and during magnetic stimulation (see below). Data were fed into a CED 1401 amplifier (Cambridge, UK) where a notch filter (50 Hz) was applied prior to amplification (gain 300–1,000).

Transcranial Magnetic Stimulation

TMS was used to investigate neural adaptations that may have occurred in conjunction with changes in performance as a result of the bilateral training. TMS was administered while participants relaxed both arms with their hands in the same posture as that assumed during the movement task with two Magstim 200 units (Magstim, Dyfed, UK) connected via a Bistim unit and a single figure of eight coil (external diameter of each loop 70 mm). Optimal locations for eliciting motor evoked potentials (MEPs) and resting motor thresholds (RMTs) for the left and right FDI were determined with well-described techniques used in our previous studies (Carroll et al. 2001, 2008; Hinder et al. 2011).

Measures of corticospinal excitability and short-interval intracortical inhibition (SICI) (Kujirai et al. 1993) were obtained from blocks of TMS stimulation conducted in conjunction with the tests of performance. However, TMS testing at each time point (i.e., PRE, MID, POST) always preceded performance testing so that we could be sure that any changes in excitability and/or inhibition were a result of the bilateral motor training phase (and not due to the bilateral/unilateral test phases). Each TMS block consisted of 20 stimulations (at 0.2 Hz) to each cortex (the order of which was counterbalanced across participants). Accordingly, the MID and POST TMS blocks commenced ~1.5 (first cortex tested) or 4 (second cortex tested) min after completion of the preceding training block. Ten of the twenty stimulations within each block consisted of a single “test” stimulus, applied to the predetermined FDI motor hot spot at 130% RMT. These trials provided a measure of corticospinal excitability. In the other 10 trials, we used a paired-pulse paradigm (first pulse 70% RMT 3 ms prior to the 130% RMT test stimulus) (see Kujirai et al. 1993). SICI was determined as the ratio of the mean MEP evoked after paired-pulse stimulation to the MEP amplitude evoked in the single-pulse stimulation. SICI ratios < 1 indicate inhibition, with lower values (closer to 0) indicating greater inhibition. Values > 1 indicate facilitation, rather than inhibition. The order of single- and paired-pulse trials within each block was randomized.

Data Acquisition and Analysis

Movement data were sampled at 2 kHz from 500 ms before the “go” tone for 1,500 ms with Signal (CED) programs, and subsequent analysis was performed with custom-written Signal routines. Acceleration data were low-pass filtered at 20 Hz prior to analysis. For each movement, peak abduction acceleration was determined as the first peak in the horizontal acceleration. Peak acceleration was determined in the 10 movements of the PRE, MID, and POST unilateral tests for the left and right hands and then averaged across the 10 movements. Values were then normalized (for each participant) to the corresponding PRE acceleration for each hand. Bilateral test performance was assessed by determining the first acceleration peak in the combined acceleration trace (calculated by summing the acceleration traces of each hand). Averaging and normalizing were undertaken as above. The performance of each hand within the bilateral tests was also

determined by calculating the left and right hands’ contributions to the combined acceleration trace (i.e., the instantaneous acceleration of the left and right hands at the same time point where the overall bilateral acceleration peak was determined). The contribution of the left and right hands to the bilateral performance was then normalized to PRE test values of each hand within the bilateral task. In this manner we were able to determine how each hand performed within the bilateral task, and how this translated to performance improvements when each hand was required to make unilateral movements.

We wished to determine whether bilateral training affected the nature of muscle activation patterns when each hand was required to make unilateral movements. For each left and right hand unilateral test movement, EMG data were rectified and low-pass filtered (20 Hz) prior to determination of the average EMG activity in the FDI executing the movement and the contralateral FDI (i.e., mirror activation). Movement onset was defined as the time when the muscle activity in the FDI undertaking the movement first increased above 4 times background EMG, and movement offset was determined as the time at which FDI activity dropped below 20% of the peak (rectified) EMG amplitude. This enabled us to determine a movement offset even in circumstances in which cocontraction was present when the finger movement had ceased (Carroll et al. 2008). Average EMG within this window was then calculated, from which background EMG (50–100 ms prior to the “go” signal) was subtracted. Average activity was then calculated in a similar manner in the contralateral FDI within this same time window. EMG values for both hands were then averaged over the 10 movements of the PRE, MID, and POST tests. The values for the right FDI (in left and right hand unilateral tests) were normalized to the EMG value obtained for the right FDI during the unilateral right hand PRE test. Values for left FDI activity (during left and right hand unilateral tests) were normalized to the left FDI EMG value obtained for the left hand unilateral PRE test. As such, mirror activity was expressed as a proportion of the level of activity exhibited when that hand was required to make the volitional ballistic movement.

Responses to the cortical stimulations were sampled at 10 kHz from 3 s before to 2 s after the suprathreshold TMS pulse. The peak-to-peak amplitude of the MEP was measured in the period 15–50 ms after stimulation. Average MEP amplitudes were derived for the 10 single-pulse and 10 paired-pulse stimulations of each TMS block. MEP amplitudes (elicited in single-pulse trials) were then normalized to the PRE value prior to statistical analyses. Normalized MEP amplitudes are referred to as nMEP and used as an indication of training-induced changes in corticospinal excitability of pathways to the trained and untrained FDI muscle. The SICI ratio was determined as the average (nonnormalized) MEP amplitude in the paired-pulse stimulations divided by the average MEP amplitude in the single-pulse stimulations in the same test block (SICI < 1 indicates inhibition). To assess training-induced changes in SICI, we divided the SICI ratio in the MID and POST test trials by the SICI ratio in the PRE test and refer to this value as nSICI (Hinder et al. 2011).

Finally, we note that the normalization procedures for all dependent variables employed here remove possible confounds in the statistical results that may otherwise arise as a result of inherent intergroup variability in the PRE test values. That is, statistical analyses of normalized values are not biased by the data of any one participant who has a particularly low or high nonnormalized PRE test value (Hinder et al. 2011).

Statistical Analysis

Task performance. The efficacy of the bilateral training was assessed by considering changes in normalized combined bilateral acceleration (i.e., the performance variable that participants aimed to maximize during training). To this end, we conducted analysis of variance (ANOVA) on normalized bimanual acceleration with time as a (repeated) within-group factor (MID and POST tests) and age group

Table 1. Raw peak accelerations in unilateral test phases for young and older groups

Unilateral Testing: Peak Accelerations, m/s ²	PRE	MID	POST
Young—R hand	11.53 ± 0.68	18.53 ± 1.38	23.05 ± 2.04
Young—L hand	15.46 ± 1.09	19.83 ± 1.76	22.19 ± 1.98
Older—R hand	13.45 ± 1.52	15.07 ± 1.91	16.75 ± 2.49
Older—L hand	13.38 ± 1.30	15.24 ± 1.49	18.03 ± 2.21

Values are average (±95% confidence intervals) raw peak accelerations in the unilateral test phases for the young and older groups.

(young, older) as a between-group factor. To determine the extent to which bilateral training resulted in changes in performance of both hands during the bilateral and the unilateral tasks, we undertook ANOVA using normalized accelerations (of each hand, see above) with task type (bilateral, unilateral), hand (left, right), and time (MID test, POST test) as within-group factors (repeated measures on time) and age group (young, older) as a between-group factor. Between-task transfer (i.e., performance improvement in the unilateral task as a proportion of that performance improvement in the trained bilateral task) was specifically assessed by way of the main effect of task, with any age-related differences in transfer assessed via the interaction between task and age. Finally, the relative timing of peak accelerations of the left and right hands within the context of the bimanual task was analyzed with a time × age group ANOVA to determine the simultaneity of the movements of each hand.

Muscle activity during unilateral tests. We wished to determine whether bilateral training affected the intensity of EMG burst when a unilateral task was subsequently undertaken, and whether bilateral training resulted in a change in the extent of mirror activity exhibited during unilateral tasks. Accordingly, we assessed normalized muscle activity in the FDI muscle of the hand instructed to undertake the unilateral task, using ANOVA with hand (left, right) and time (MID, POST; repeated measures) as within-subjects factors and age group as a between-subjects factor. The extent of the mirror activity in FDI of the contralateral hand during the unilateral test was assessed by ANOVA with hand (left, right) and time (PRE, MID, POST; repeated measures) as within-subjects factors and age (young, older) as a between-subjects factor.¹

Corticospinal excitability and intracortical inhibition. Baseline levels of corticospinal excitability and intracortical inhibition were assessed by comparing nonnormalized MEP amplitudes and SICI values in both hands and both age groups prior to any training (PRE values). Normalized MEP amplitudes (nMEP) were used to assess changes in corticospinal excitability of projections to the FDI muscle (i.e., the muscle primarily engaged in index finger abductions) in both hands as a result of bilateral training. Changes in intracortical inhibition (SICI) were assessed in the right and left FDI by evaluating nSICI. For both measures we undertook ANOVA with hand (right, left) and time (MID, POST; repeated measures) as within-subjects factors and age group as a between-subjects factor.

For all ANOVAs, Huynh-Feldt corrections were applied if the assumption of sphericity was violated ($\epsilon < 0.7$). Partial η^2 (η_p^2) values are presented as a measure of effect size to aid the interpretation of the tests of significance. Statistical significance was set at $P < 0.05$. Data are presented as group means ± 95% confidence intervals.

¹ Because the extent of mirror activity is reported relative to the level of activity in that same hand when it undertook the task (i.e., mirror activity in the left hand during right hand movements is reported relative to the activity in the left hand during left hand movements), PRE values are not unity and, as such, are included in the ANOVA.

RESULTS

A full set of TMS data was not collected from one of the older participants who, after initial stimulations, did not relish the prospect of numerous TMS stimulations throughout the experiment. This participant happily continued with the full behavioral protocol with electromyographic recordings.

Task Performance

Both participant groups undertook the bilateral task well, producing time-locked accelerations of both index fingers that increased in amplitude over the course of training. In the bilateral test trials, the mean time lag between the peak accelerations in the left and right hands was not significantly different between groups [$F_{(1,16)} = 2.61, P = 0.126, \eta_p^2 = 0.14$] and did not differ significantly from zero (i.e., perfectly time-locked) across both groups [young: -3.3 ± 4.3 ms; older: 1.85 ± 4.3 ms; $F_{(1,16)} = 0.21, P = 0.652, \eta_p^2 = 0.01$; negative number indicates left hand acceleration occurred first]. The time-locking between hands did not vary across PRE, MID, and POST tests [$F_{(2,16)} = 0.05, P = 0.954, \eta_p^2 < 0.01$]. The interaction between group and time was also not statistically significant ($P = 0.798$).

Raw peak accelerations for the left and right hands in the PRE, MID, and POST unilateral and bilateral test phases, as well as the peak values of the raw combined acceleration trace during the bilateral test phases, are shown in Tables 1 (unilateral tests) and 2 (bilateral tests). Trends in performance, and statistical outcomes, for these raw data are very similar to those that we report here for the normalized data.

Figure 1 shows normalized bilateral (combined) acceleration (i.e., the variable that participants attempted to maximize during training) in the PRE, MID, and POST bilateral tests. By completion of the training the young group had increased combined acceleration to 2.08 times that exhibited in the PRE test (significant increase, $P < 0.01$), while for the older group combined acceleration had increased to 1.41 times PRE test levels ($P < 0.05$). The increase in combined acceleration was greater for the young group [age main effect: $F_{(1,16)} = 8.21, P = 0.011, \eta_p^2 = 0.34$], and increases in the POST test outweighed those in the MID test [time main effect: $F_{(1,16)} = 11.52, P = 0.004, \eta_p^2 = 0.42$], suggesting a progressive improvement throughout training. The nonsignificant interaction between age and time [$F_{(1,16)} = 0.09, P = 0.772, \eta_p^2 = 0.01$] indicates that the degree of improvement between MID and POST tests did not differ between groups.

Figure 2 shows normalized peak accelerations for each hand in both the bilateral and unilateral tests for the young and older

Table 2. Raw peak accelerations in bilateral test phases for young and older groups

Bilateral Testing: Peak Accelerations, m/s ²	PRE	MID	POST
Young—combined	22.26 ± 1.88	36.66 ± 2.93	42.38 ± 2.14
Young—R hand component	12.50 ± 0.87	19.17 ± 1.63	21.95 ± 1.10
Young—L hand component	13.95 ± 1.26	21.40 ± 1.61	23.68 ± 0.94
Older—combined	23.43 ± 2.56	23.35 ± 2.51	33.06 ± 4.02
Older—R hand component	13.79 ± 1.63	13.82 ± 1.64	18.09 ± 2.51
Older—L hand component	13.07 ± 1.29	13.28 ± 1.37	18.09 ± 2.17

Values are average (±95% confidence intervals) raw peak accelerations in the bilateral test phases for the young and older groups.

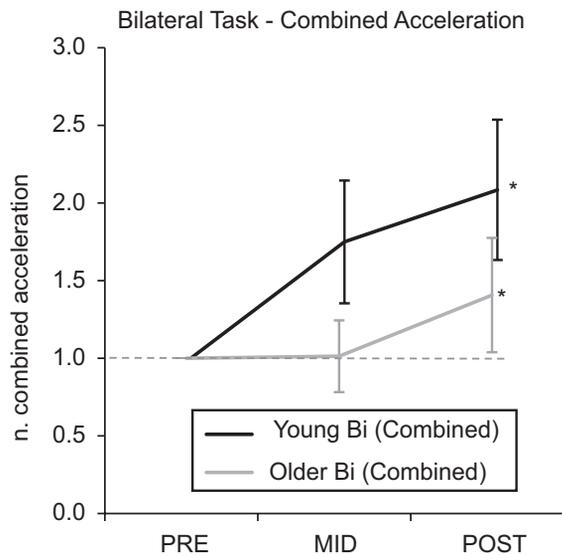


Fig. 1. Normalized peak of the combined acceleration trace during bilateral (Bi) test phases. Young and older adults both exhibited a significant increase in combined acceleration in the POST test. Error bars represent 95% confidence intervals. *Significant change relative to PRE test ($P < 0.05$).

groups. Qualitatively, it can be observed that peak accelerations of both hands in both the bilateral and unilateral tests increased as a result of bilateral training but that these increases were larger for the younger adults. Acceleration increases were greater for the young (66%) group compared with the older (21%) group [age main effect: $F_{(1,16)} = 7.87$, $P = 0.013$, $\eta_p^2 = 0.33$] and increased between MID (31%) and POST (56%) tests [time main effect: $F_{(1,16)} = 13.6$, $P = 0.002$, $\eta_p^2 = 0.46$]. The absence of a significant main effect of task [$F_{(1,16)} = 0.15$, $P = 0.705$, $\eta_p^2 = 0.01$] suggests that acceleration increases of each hand in the bilateral context as a result of bilateral training (44% increase) were not significantly different from those increases observed in each hand during the unimanual task context (42% increase). This particular result therefore suggests almost complete between-task transfer of peak acceleration gains. The main effect of hand was not significant [$F_{(1,16)} = 1.21$, $P = 0.288$, $\eta_p^2 = 0.07$]. The significant hand \times age interaction [$F_{(1,16)} = 5.03$, $P = 0.039$, $\eta_p^2 = 0.24$] indicates that acceleration increases (across both tasks) were comparable in both hands in the older group but that the younger group exhibited larger acceleration increases in their right, compared with their left, hand (see Fig. 2). All other two-way interactions were not significant. Importantly, the statistically nonsignificant age \times task interaction [$F_{(1,16)} = 1.46$, $P = 0.245$, $\eta_p^2 = 0.08$] indicates that although young adults exhibited greater acceleration increases than the older group (evidenced by the age main effect), this age difference was not further influenced by task type, i.e., the greater improvements in the trained bilateral task (Fig. 1, Fig. 2A) are mirrored by commensurately larger improvements (for both hands and at both time points) in the untrained unilateral task (Fig. 2B). This finding indicates that the between-task transfer did not differ between age groups. The only other significant interaction was the three-way interaction of hand \times age \times time [$F_{(1,16)} = 6.86$, $P = 0.019$, $\eta_p^2 = 0.30$], but all post hoc tests were not significant. The interaction of hand \times age \times task was marginal [$F_{(1,16)} = 3.66$, $P = 0.074$, $\eta_p^2 = 0.19$].

Electromyographic Data

We assessed whether bilateral training affected the volitional FDI muscle bursts exhibited in the left and right hands during unilateral testing. Furthermore, we wished to determine whether bilateral training affected the degree of mirror activation exhibited in unilateral movements. Averaged over both hands and age groups, and across MID and POST tests, there was a 13% increase in volitional EMG burst intensity relative to PRE test bursts (Fig. 3A), which was statistically significant [$F_{(1,16)} = 9.78$, $P = 0.007$, $\eta_p^2 = 0.38$]. This suggests that at least some of the increase in acceleration in the unilateral test phases may have been due to greater recruitment of muscle fibers within the task-specific FDI. The main effects of age, time, and hand and all two-way interactions were nonsignificant (all $P > 0.342$, $\eta_p^2 < 0.06$). The three-way interaction of hand \times time \times age was, however, significant [$F_{(1,16)} = 6.98$, $P = 0.016$, $\eta_p^2 = 0.30$]—post hoc tests to further investigate this interaction revealed a significant PRE-POST increase in EMG in the right hand for younger adults (Fig. 3A); all other POST test values did not differ reliably relative to the PRE test, nor were there between-group differences at any time point.

With respect to mirror activity (Fig. 3B), older adults exhibited greater mirror activation than young adults averaged over all time points [age main effect: $F_{(1,16)} = 4.53$, $P = 0.049$, $\eta_p^2 = 0.22$]. There was a significant main effect of time [$F_{(1,16)} = 6.74$, $P = 0.004$, $\eta_p^2 = 0.30$], indicating that mirror activity in the unilateral tasks increased as a result of bilateral training averaged across both groups. The main effect of hand and all interactions were not significant (all $P > 0.178$, all $\eta_p^2 < 0.11$), indicating that the degree of increase in mirror activity as a

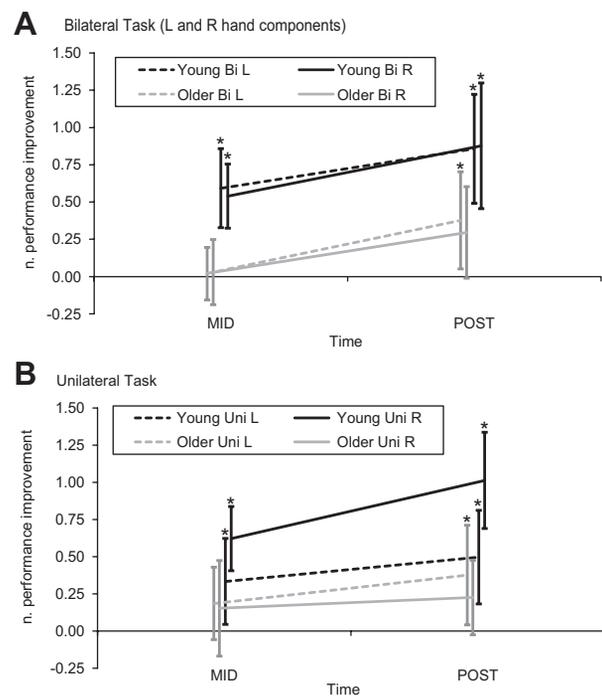


Fig. 2. Normalized performance improvements in the MID and POST testing (relative to PRE testing) in the left (L) and right (R) hands for the bilateral (Bi; A) and unilateral (Uni; B) tasks. Data are shown for young and older groups. Error bars show 95% confidence intervals. *Significant change relative to PRE test ($P < 0.05$).

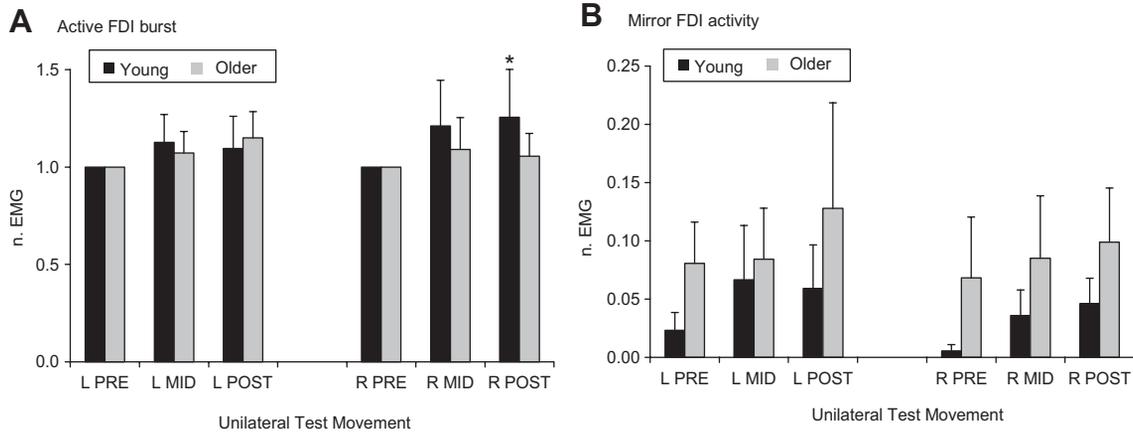


Fig. 3. Magnitude of EMG activity in the volitional index finger burst [first dorsal interosseus (FDI); A] and homologous muscle in the contralateral hand (i.e., mirror activity) (B) during unilateral task testing. Data are shown for left and right hand movements and for young and older groups. Error bars show 95% confidence intervals. *Significant change relative to PRE test ($P < 0.05$).

function of time due to bilateral training was similar for older and young participants.

Corticospinal Excitability and Intracortical Inhibition

RMTs, measured as a percentage of maximum stimulator output, for the young group were $46.9 \pm 3.5\%$ and $44.0 \pm 3.8\%$ for the left and right FDI, respectively. For the older group, RMTs were $49.6 \pm 3.2\%$ (left) and $49.3 \pm 2.6\%$ (right). ANOVA revealed that the effect of hand [$F_{(1,15)} = 4.0$, $P = 0.063$, $\eta_p^2 = 0.17$] and age [$F_{(1,15)} = 2.93$, $P = 0.096$, $\eta_p^2 = 0.16$] and the interaction of hand \times age [$F_{(1,15)} = 3.25$, $P = 0.106$, $\eta_p^2 = 0.17$] did not reach statistical significance. MEPs measured in the FDI during PRE testing were 1.2 ± 0.51 mV (left hand) and 1.42 ± 0.74 mV (right hand) for the young group. For the older group, MEPs were 0.85 ± 0.99 mV and 0.91 ± 0.48 mV for the left and right hands, respectively. ANOVA indicated that the effect of hand [$F_{(1,15)} = 0.18$, $P = 0.678$, $\eta_p^2 = 0.01$] and age [$F_{(1,15)} = 1.15$, $P = 0.299$, $\eta_p^2 = 0.07$] and the two-way interaction [$F_{(1,15)} = 0.06$, $P = 0.805$, $\eta_p^2 < 0.01$] were all not statistically significant.

To determine whether any changes in MEP amplitudes occurred as a result of the bilateral training protocol, we conducted ANOVA using nMEP. Averaged over all variables, MEP amplitudes increased by 21% relative to the PRE test excitability; this increase, however, did not reach the a priori level of statistical significance [$F_{(1,15)} = 3.34$, $P = 0.087$, $\eta_p^2 = 0.18$]. All main effects and two-way interactions were not significant (all $P > 0.224$). The statistically marginal three-way interaction, while not significant [$F_{(1,15)} = 3.26$, $P = 0.091$, $\eta_p^2 = 0.18$], can be seen to be driven by the significant PRE-POST increase in excitability in the right hand for the older group (Fig. 4).

SICI ratios (1 = no inhibition, 0 = complete inhibition) measured in the FDI during PRE testing were 0.48 ± 0.14 (left hand) and 0.32 ± 0.16 (right hand) for the young group. For the older group, SICI was 0.56 ± 0.15 and 0.45 ± 0.17 for the left and right hands, respectively. Overall, MEPs following paired-pulse stimulation were significantly suppressed relative to MEPs from single-pulse stimulation, i.e., intracortical inhibition was apparent [$F_{(1,15)} = 200.54$, $P < 0.001$, $\eta_p^2 = 0.93$]. ANOVA to assess baseline SICI indicated that the effect of hand [$F_{(1,15)} = 2.48$, $P = 0.136$, $\eta_p^2 = 0.14$] did not reach

statistical significance. Furthermore, the main effect of age [$F_{(1,15)} = 1.81$, $P = 0.198$, $\eta_p^2 = 0.11$] and the two-way interaction of hand \times age [$F_{(1,15)} = 0.11$, $P = 0.750$, $\eta_p^2 < 0.01$] were not statistically significant.

To determine whether the bilateral training protocol resulted in any changes in SICI within each hemisphere (relative to PRE test values), we conducted ANOVA using normalized SICI values (nSICI) that were calculated with respect to SICI in the PRE test (Fig. 5). Averaged over all variables (time, hand, and age), SICI was released by 20% at the MID and POST tests relative to the PRE tests [$F_{(1,15)} = 9.19$, $P = 0.008$, $\eta_p^2 = 0.38$]. A significant main effect of age [$F_{(1,15)} = 8.59$, $P = 0.010$, $\eta_p^2 = 0.36$] indicates that, averaged across the other variables, a significant release of inhibition was apparent for the older (39% reduction) but not the young (1% reduction) group. The main effect of hand [$F_{(1,15)} = 0.30$, $P = 0.590$, $\eta_p^2 = 0.02$] was not statistically significant, and the main effect of time [$F_{(1,15)} = 2.19$, $P = 0.160$, $\eta_p^2 = 0.13$] did not reach statistical significance. The only statistically significant interaction was that of hand \times time [$F_{(1,15)} = 6.43$, $P = 0.023$, $\eta_p^2 = 0.30$], indicating (averaged across both age groups) a significant release of SICI in the left hand during POST (48% release) but not MID (1% release) testing, while release of

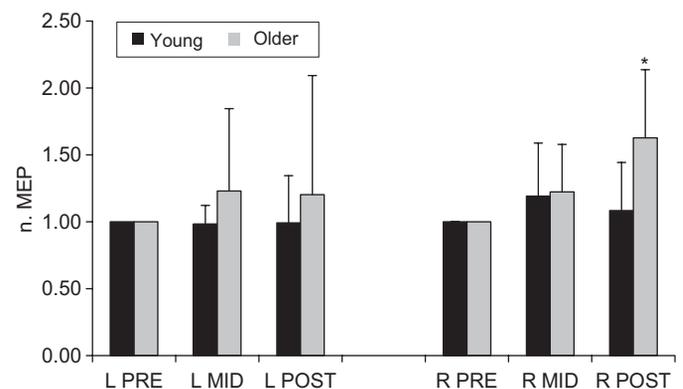


Fig. 4. Normalized corticospinal excitability [normalized motor evoked potential amplitude (nMEP)] in the left and right FDI in the PRE, MID, and POST tests. Data are shown for the young and older groups. Error bars show 95% confidence intervals. *Significant change relative to PRE test ($P < 0.05$).

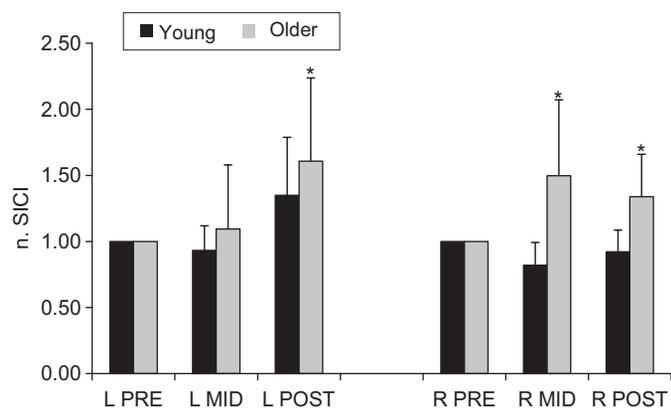


Fig. 5. Normalized short-interval intracortical inhibition (nSICI) in the left and right FDI in the PRE, MID, and POST tests. Data are shown for the young and older groups. Error bars show 95% confidence intervals. *Significant change relative to PRE test ($P < 0.05$).

inhibition in the right hand was not dissimilar in MID (16% release) and POST (13% release) tests.

DISCUSSION

The present study was designed to assess whether behavioral gains exhibited in a bilateral ballistic motor task are transferred to a situation in which the same motor actions are required to be undertaken in a unilateral task context. Importantly, the neural mechanisms that mediate peak acceleration increases during ballistic motor training are akin to those that mediate strength gains following a strength training protocol (Selvanayagam et al. 2011). Moreover, because recovery of strength gains after paresis is an important step in regaining functional movements (Barker et al. 2008), the present study provides valuable information as to how those training gains and neural adaptations exhibited in each arm after a bilateral strength training protocol (during stroke rehabilitation, for example) might transfer to subsequent situations in which each limb is required to undertake the trained action but in a unilateral context. While we acknowledge that the extent to which the present results can be generalized to other tasks and muscle groups is limited [at least in part because of differences in the degree of interhemispheric inhibition between proximal and distal muscle groups (Harris-Love et al. 2007) and our relatively small sample size, which may limit the statistical power of some statistical outcomes], they nonetheless represent an important step in determining the neural changes associated with bilateral training.

Behavioral gains manifested (by young and older adults) in each limb as a result of a bilateral training task were fully transferred to a task that requires each hand to undertake the same movement unilaterally (Fig. 1 and associated ANOVA). Muscle activity recorded during unilateral tests revealed that at least some of the acceleration increases during the unilateral tasks for both participant groups (in both hands) as a result of bilateral training are likely due to greater recruitment of muscle fibers within the task-specific FDI. Furthermore, accompanied with the increase in burst intensity in the “active” hand, we observed an increase in mirror activity in the contralateral FDI muscle. However, such increases in mirror activity have also been observed after unilateral ballistic training in our previous work (Hinder et al. 2011) and therefore cannot be assumed to

represent bilateral entrainment (i.e., increased bilateral activations during actions intended to be unilateral) due to the current bilateral training protocol. Accordingly, no specific degradation in the ability to execute unilateral activations (while maintaining quiescence in the contralateral limb) can be assumed to occur as a result of ballistic bilateral training. Consistent with previous work (Baliz et al. 2005; Bodwell et al. 2003; Hinder et al. 2011), mirror activity during the unilateral tasks was greater for older compared with young adults, supporting the view that older adults exhibit greater bilateral activity of motor cortices during unilateral tasks (Ward et al. 2008), which may be due to the breakdown of interhemispheric inhibitory mechanisms (see, e.g., Talelli et al. 2008, but also see Hinder et al. 2010, 2012) mediating unilateral actions.

With respect to the neurophysiological data, generalized training-induced increases in excitability (i.e., across both hands and both age groups and averaged over MID and POST tests) failed to reach statistical significance (Fig. 4); however, a tendency for excitability increases in the dominant right limb was present for the older adults. The magnitude of the overall change (21% increase) and associated effect size ($\eta_p^2 = 0.18$) are perhaps indicative of a tendency for increased excitability, though smaller than the training-induced increases in bilateral excitability that we have observed after unilateral ballistic motor training, where excitability increases of up to 60% have been observed (Carroll et al. 2008; Hinder et al. 2011; Lee et al. 2010). Overall it appears that unilateral motor training may evoke greater increases in excitability of the corticospinal projections (innervating both the trained muscle and its homolog in the contralateral untrained limb) than bilateral training, especially with regard to younger adults. This suggests that differences in the nature of the neural adaptations induced by the two forms of training may exist, despite the motor action itself being identical. With respect to intracortical inhibition, in the present task we observed a bilateral release of inhibition for the older adults but not for the young group (Fig. 5), indicating that alterations in motor cortical inhibitory circuits in response to the present bilateral training protocol are most prominent in older adults. Bilateral releases of SICI have previously been reported after bilateral upper limb training in young/middle-aged adults (Waller et al. 2008) and after unilateral training in young and older adults (Hinder et al. 2011).

Previous research has shown that bilateral tasks cannot simply be viewed as the superposition of unilateral tasks undertaken simultaneously with both upper limbs (e.g., Duque et al. 2010), with evidence indicating that distinct brain regions such as SMA are recruited in coordinated bilateral movements (Duque et al. 2010). That said, Donchin et al. (1998) challenged the view that bimanual movements are principally governed by the SMA: neurons within monkey primary motor cortex showed specific “bimanual related” activity that was distinctly different from that of the same cells during unilateral movements. Furthermore, cells within SMA were equally active in unimanual and bimanual tasks (Donchin et al. 1998). If a substantial component of the motor procession for bimanual actions occurs in circuits upstream of M1, one might predict that the bilateral increase in the excitability of corticospinal projections and release in intracortical inhibition within M1 observed after unilateral ballistic motor learning (Carroll et al. 2008; Hinder et al. 2011; Lee et al. 2010) would be less pronounced, or absent, after bimanual training. The present

data are consistent with this postulation. Interestingly, any changes induced by bilateral training in the motor cortex or corticospinal tract appear predominantly for the older, and less so for the young, adults.

Taken together, the present neurophysiological and behavioral data are consistent with a postulation that a more significant “crossover” exists between the mechanisms mediating unilateral and bilateral ballistic motor tasks in older adults, compared with younger adults, at least those residing within primary motor cortex. That is, for older adults, bilateral training results in more significant neural adaptations that occur at least in part within M1 and that are accessed when the task is subsequently undertaken in a unilateral context. This finding does not preclude the possibility that there may be a greater between-task overlap of mechanisms mediated within non-M1 sites in younger adults, which are not probed by TMS. It is also interesting to note that bilateral ballistic accelerations improved much less for older adults (35% improvement across both limbs) (Fig. 1) than for young subjects (87% improvement across both limbs), which may suggest reduced neural adaptations that are specifically associated with the bilateral movement context in the older brain; indeed, as noted above, the neural adaptation that does occur for older adults more closely resembles that observed following unilateral training, suggesting at least some degree of overlap of the mechanisms mediating unilateral and bilateral motor adaptation. In contrast, it is conceivable that acceleration increases in the bilateral task exhibited by the younger adults are mediated more strongly by regions other than primary motor cortex, e.g., SMA, that represent more bimanual-specific neural adaptations.

As noted above, the training-induced gains exhibited in the bilateral and unilateral contexts of the present study were larger at completion of training for the young compared with the older adults. Previous work investigating unilateral ballistic movements is inconclusive with respect to whether healthy aging impacts on the extent of training-induced performance improvements (Cirillo et al. 2010; Hinder et al. 2011). In an attempt to more fully understand the nature of the training-related increases in peak acceleration in the bilateral task used in the present study, we conducted further analyses on raw (nonnormalized) acceleration measurements. We assessed the between-task (unimanual vs. bimanual) difference in peak acceleration at the PRE, MID, and POST testing for both hands and both age groups. Across all factors (time, age, and hand), the between-task difference was not significantly different from zero ($P = 0.987$). Furthermore, all main effects and interactions associated with this ANOVA were not statistically significant (all $P > 0.221$). These analyses reveal that both young and older participants were able to accelerate both fingers as quickly in the bimanual task as they did in the unimanual tasks during each testing phase. Accordingly, training-induced improvements in the bilateral task for both groups were not primarily a result of a reduction in a “bilateral deficit” (Howard and Enoka 1991), which could conceivably have limited peak acceleration in each hand during the bilateral task relative to the performance of each hand when performing unilaterally. It may be that the limited improvements observed for older people in the bilateral task occurred because they were unable to access specific mechanisms to promote bilateral motor output during training. Thus the adaptations induced in the older group may have been more generic to the production

of ballistic movement per se (i.e., irrespective of whether one or both limbs were involved).

In summary, the present data add to the recent literature investigating the transfer of learning between bimanual and unimanual tasks by demonstrating a greater degree of overlap in the mechanisms mediating acceleration increases during ballistic finger accelerations in unilateral and bilateral task contexts in older compared with younger adults. Because the neural mechanisms mediating ballistic motor tasks share many characteristics with the neural adaptations thought to occur as a result of strength training (Selvanayagam et al. 2011), the present findings have implications for recovery after brain injury (e.g., stroke) that primarily affects one side of the body and where recovery of strength is associated with reduction of motor impairment (Barker et al. 2008). More work is warranted to consider the mechanisms of transfer in different movement tasks and muscles, for example, forearm flexor and extensors, which are often severely affected after stroke. Furthermore, determining what other factors may affect the degree of transfer between task contexts—including more salient measures of performance feedback during bilateral training (e.g., feedback of each limb’s performance within the bilateral task as opposed to feedback of only the combined performance)—is important, so that the maximum rehabilitative benefit can subsequently be conferred during unimanual tasks.

GRANTS

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: M.R.H. conception and design of research; M.R.H. performed experiments; M.R.H. analyzed data; M.R.H. prepared figures; M.R.H. drafted manuscript; M.R.H., T.J.C., and J.J.S. approved final version of manuscript; T.J.C. and J.J.S. interpreted results of experiments; T.J.C. and J.J.S. edited and revised manuscript.

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