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Bilateral motor priming for post stroke upper extremity hemiparesis: A randomized pilot study

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Abstract

Background: Bilateral priming, device assisted bilateral symmetrical wrist flexion/extension, is a noninvasive neuromodulation technique that can be used in the clinic.

Objective: We examined the additive effect of bilateral motor priming and task specific training in individuals with severe upper limb hemiparesis.

Methods: This is a parallel assignment, single-masked, randomized exploratory pilot study with three timepoints (pre-/post-intervention and follow up). Participants received either bilateral motor priming or health care education followed by task specific training. Sixteen participants who were at least 6 months post-stroke and had a Fugl Meyer Upper Extremity (FMUE) score between 23 and 38 were randomized. Our primary and secondary measures were Chedoke Arm & Hand Activity Index 9 (CAHAI-9) and the FMUE respectively. We determined changes in interhemispheric inhibition using transcranial magnetic stimulation. We hypothesized that improvement in the priming group would persist at follow up.

Results: There was no between-group difference in the CAHAI. The improvement in the FMUE was significantly greater in the experimental group at follow up ($t = 2.241$, $p = 0.045$).

Conclusions: Both groups improved in the CAHAI. There was a significant between-group difference in the secondary outcome measure (FMUE) where the bilateral priming group had an average increase of 10 points from pre-intervention to follow up.

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Keywords

Stroke; upper extremity; hemiparesis; priming; bilateral; task specific training; interhemispheric inhibition

1. Introduction

Upper extremity (UE) hemiparesis is the most common post-stroke disability. Constraint-induced movement therapy is an effective intervention but is only appropriate for those with mild UE impairment who are in the upper quartile of residual function (Wolf et al., 2006). Treatments described in the stroke rehabilitation literature for individuals with moderate to severe impairment include various types of robotic therapy (Gandolfi et al., 2018; Gandolfi et al., 2019; Lo et al., 2010), mirror therapy (Colomer, E, & Llorens, 2016), and virtual reality therapy (Perez-Marcos et al., 2017). Although many of these studies include impressive technology, careful review of the study results show modest changes in the Fugl Meyer Test of Upper Extremity Function (FMUE) (Gandolfi et al., 2018; Gandolfi et al., 2019; Lo et al., 2010); and limited numbers of participants experiencing clinically significant gains (Perez-Marcos et al., 2017). There is no well-established clinical treatment that has demonstrated efficacy for the 75% of individuals who have chronic moderate to severe UE hemiparesis. Thus, treatments that are easily translated to the clinic are needed to target the 75% of individuals with moderate to severe upper limb impairment whose prognosis for motor recovery is less favorable.

Task specific training (TST), used in both research and clinical settings, has shown modest benefits for individuals with more severe impairment (Nishimoto et al., 2018). To date, only one other randomized clinical trial (Kimberley et al., 2018) has demonstrated results that exceed the estimated clinically important difference (CID) of 4.25–7.25 in the Fugl-Meyer Test of Upper Extremity Function (Fugl-Meyer, Jaasko, Leyman, Olsson, & Steglind, 1975) for individuals with severe upper limb hemiparesis. The clinically important difference is an estimate of the amount of improvement in arm movement that is considered by a clinician to be meaningful (Page, Fulk, & Boyne, 2012).

Bilateral motor priming (BMP) is a neuromodulation technique and not a therapy in itself. It consists of mirror symmetric, bilateral, wrist flexion and extension movements using a device with a mechanical linkage so the less affected hand and affected one move in exact symmetry (Stinear, Barber, Coxon, Fleming, & Byblow, 2008). Unlike bilateral training, in which the bilateral movements are the training, the bilateral symmetrical movements in BMP are considered a neuromodulation technique. In a case controlled study, BMP prior to Wii-based therapy (Shiner, Byblow, & McNulty, 2014) improved the results of therapy in post-stroke individuals, some of whom were severely impaired. This raised the question of whether BMP could be used to enhance the benefits of TST.

In this pilot study, we examined the efficacy of BMP as a non-invasive, cost-effective neuromodulation technique (Stinear et al., 2008). We conducted a six week intervention study with pre-/post-intervention and follow up time points to investigate the additive effect of bilateral priming in conjunction with a task specific training protocol previously shown to

be efficacious (Levy et al., 2016). We hypothesized that individuals assigned to the bilateral priming group would demonstrate greater improvements in motor function and motor impairment relative to a comparator group that received healthcare education in addition to the same training protocol. We also hypothesized that the difference between the two groups would be greater at follow up. Consistent with a previous study (Stinear et al., 2008), we hypothesized that the experimental group would have a greater magnitude of change in transcallosal inhibition persistence (TCI) from ipsilesional hemisphere to contralesional hemisphere at post-intervention and follow up.

2. Materials and methods

2.1. Trial design and setting

This was a parallel group, single masked study with two intervention arms and three time points for data collection: baseline, post-intervention and follow up at 6 weeks post cessation of treatment ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study?term=NCT02277028) identifier: [NCT02277028](https://clinicaltrials.gov/ct2/show/study?term=NCT02277028)). Only the rater was masked to group assignment, and assessments did not occur in the same room as treatment sessions. The study took place at Rush University Medical Center (RUMC) in Chicago. The RUMC IRB approved the study protocol.

2.2. Participants

All potential participants who visited the lab signed a consent form according to the declaration of Helsinki. Participants were consented and enrolled by the principal investigator (MES). Eligibility criteria included: (a) no orthopedic conditions of the contralateral or ipsilateral wrist; (b) 55 years of age and over; (c) at least 6 months post-stroke; (d) unilateral stroke; and (e) a Fugl-Meyer Test of Upper Extremity Function (FMUE) score between 23 and 38 (inclusive). A transcranial magnetic stimulation (TMS) safety checklist was administered as part of the screening (Rossi, Hallett, Rossini, & Pascual-Leone, 2011). Participants were deemed ineligible if they had contraindications to TMS including: (a) metal implants of any size in the head or neck area; (b) history of epilepsy, seizures, or convulsions; (c) previous head trauma or concussion with loss of consciousness; (d) cochlear implants; (e) history of ongoing headaches; and (f) presence of a pacemaker (Rossi et al., 2011).

2.3. Randomization

Participants were stratified according to their FMUE score. More severely impaired participants had scores of 23 to 29, while relatively less severely impaired participants had scores of 30 to 38. The primary investigator enrolled participants. Two computer-generated number lists, (one for each level of severity) created by a statistician, were used for group assignment. A research assistant, who assigned participants prior to the first day of treatment, was responsible for the lists. See Fig. 1 for the study flow diagram.

2.4. Motor Function and motor impairment measures

Motor outcome measures were administered at baseline, post-intervention, and at a 6-week follow-up appointment by a rater masked to treatment assignment. The Chedoke Arm and Hand Activity Index 9 (CAHAI-9) (Barreca, Stratford, Lambert, Masters, & Streiner, 2005)

was chosen as the primary outcome measure because it is a test of bimanual function, has established reliability and validity, and is relevant to everyday life. In addition, our participants had moderate to severe impairment and were more able to perform tasks from the CAHAI rather than unilateral measures of function such as those studied in the Action Research Arm Test (ARAT) (Yozbatiran, Der-Yeghiaian, & Cramer, 2008). Activities in the CAHAI include opening a jar, dialing 911, pouring water, drawing a line with a ruler, buttoning a shirt, drying one's back, putting toothpaste on a tooth brush, cutting simulated food with fork and knife, and wringing out a washcloth, all using both hands. Test item scores are based on the incorporation of the affected limb during a bimanual task. The affected hand can be used as a stabilizer or manipulator, and scores are not diminished if the affected arm is used in a stabilizer role. The FMUE was the secondary motor outcome measure (Fugl-Meyer et al., 1975). The FMUE is a well-known impairment scale with established interrater and intra-rater reliability. The FMUE test addresses both synergy and isolated movements of the upper limb. The total score ranges from 0 to 66.

2.5. Neurophysiological measure

Transcallosal inhibition persistence (TCI), a measure of tonic interhemispheric inhibition, was determined at baseline, post-intervention, and follow up using the MagStim 200 and a focal figure-of-eight coil (wing diameter 9 cm). Maximal voluntary contraction (MVC) of the less affected extensor carpi radialis (ECRL) was determined prior to assessing TCI. To identify the hotspot for the ipsilesional ECRL, the highest stimulation intensity that the participant could tolerate was used to identify a facilitatory EMG response (Harris-Love, Morton, Perez, & Cohen, 2011). After identification of the hotspot, 12 stimuli were delivered in blocks of four at 80% maximal stimulator output (MSO) over the site for eliciting motor evoked potentials (MEPs) in the affected ECRL. During this time, both hands of the participant were positioned in pronation, and participants were instructed to extend their less affected wrist and generate 50% of the previously calculated MVC using a computerized visual target (Stinear et al., 2008). Transcallosal inhibition persistence was defined as the number of trials (out of a maximum of 12) that resulted in an ipsilateral silent period of the less affected ECRL in which the EMG trace dropped to less than 50% of the pre-trigger value during a 30 to 60 milliseconds window post-stimulus. This protocol was replicated from the 2008 study by Stinear and colleagues with one exception; the criteria for an ipsilateral silent period in the Stinear et al, 2008 study was below 1/3 of the pre-trigger value while our criteria was set at below 1/2 (Stinear et al., 2008).

2.6. Intervention

Participants received a total of 30 hours of intervention over 15 sessions. They were scheduled two to three times per week for two hours of treatment per session.

Treatment arm 1: bilateral motor priming plus task specific training: Participants in the BMP group performed 15 minutes of continuous, symmetrical wrist flexion and extension using the Exsurgo Bilateral Priming Device (Exsurgo Rehabilitation, Auckland, New Zealand). Both hands are strapped in place between two vertically oriented plates. A mechanical linkage in the device allows the less affected arm to drive the affected one in wrist flexion and extension at a frequency of 1 Hz paced by a metronome (See Fig. 2). If

participants became too tired, the occupational therapist would assist the participant so that the entire 15 minutes was completed prior to task specific training.

Treatment arm 2: healthcare education plus task specific training: Participants in the HCE+TST group played computerized jeopardy games that facilitated their knowledge about stroke prevention based on the American Heart Association website. Participants were encouraged to use their affected hand to operate the computer keyboard or mouse during the jeopardy games. Total time for healthcare education was 15 minutes and was followed by the same task specific training protocol provided to the bilateral priming group.

Task specific training: Following BMP or HCE, the first 45 minutes of the TST protocol was dedicated to activities facilitating the transport phase of reach, grasp, release, and reach to grasp. This was followed by a 30 to 60 minute break. Bilateral motor priming or HCE were then repeated prior to 45 minutes of practice of self-selected ADLs identified by the Canadian Occupational Performance Measure (COPM) (Law et al., 1990). The first author designed the TST protocol during the Everest trial that examined epidural electrical stimulation (invasive brain stimulation) paired with task specific training and compared it to task specific training alone (Levy et al., 2016). Versions of this task specific training protocol have been used in other training studies as well (Fischer et al., 2016; Harvey et al., 2018; Thielbar et al., 2017)

2.7. Adverse events monitoring

We requested that study participants notify the principal investigator of any adverse events through-out the course of the study.

2.8. Statistical analysis

We did not conduct a formal sample size calculation for this pilot study. We aimed to recruit 16 participants to generate a preliminary estimate of effect for the intervention. For the motor outcome tests, we analyzed between-group change scores including post – pre and follow up – pre using independent t-tests. Within-group changes were analyzed using separate paired t-tests for each group. Due to equipment failure of the MagStim at follow-up testing, we were not able to obtain TMS follow up results for three subjects. Thus, for TCI persistence, we are presenting the between group analysis of post-pre change scores only. The Mann Whitney Test was used to analyze the post- pre changes in TCI. Statistical analysis was performed using SPSS, version 25 (Chicago IL), SAS version 9.4 and Excel.

3. Results

3.1. Participants

Sixty-three individuals from Chicago, Illinois and the surrounding neighborhoods were contacted and underwent an initial phone screen. Thirty individuals were excluded over the phone. Thirty-three participants were further evaluated for eligibility in the laboratory using the Fugl-Meyer Upper Extremity Test. Twelve individuals that came for the lab screen were ineligible due to their Fugl-Meyer score. One individual was ineligible because she was

enrolled in another study, one declined to participate, and one was not certain about specific TMS precautions. Two participants were found to be ineligible after enrollment. One of the participants was deemed ineligible due to complete sensory loss that was not determined at screening. The second participant was ineligible due to age. Though enrolled, they were not randomized, and their data were not included.

A final 16 participants were stratified by FMUE scores and then randomized as previously described. During the course of the study, one participant was hospitalized for unrelated reasons. An additional participant was lost to follow up due to a co-morbidity. The recruitment period was from July 2014 to July 2015. The last follow up session was in February of 2016. Demographics are presented in Table 1.

3.2. Motor outcome measure results

CAHAI Results: There were no significant differences between groups for post -pre change scores ($t=-0.584$, $p=0.57$) or follow up – pre change scores ($t=0.717$, $p=0.487$). The BMP group did not significantly change from pre- to post-intervention ($t=1.86$, $p=0.11$). However, they had a statistically significant change from pre to follow up ($t=2.909$, $p=0.027$). There were no significant within group changes in the HCE group from pre to post-intervention ($t=1.58$, $p=0.163$) or from pre to follow up ($t=1.83$, $p=0.116$). At the end of the study, the mean CAHAI 9 score was 28.42 for BMP and 26.4 for HCE. Although statistics were calculated using the change scores, we present the pre, post and follow up means and standard errors for the graph below (Fig. 3).

FMUE Results: There was no significant between-group difference in the post – pre change scores ($t=0.878$, $p=0.397$). There was a significant between group difference for the follow up – pre change scores ($t=2.241$, $p=0.045$) indicating greater improvement in the BMP group than the HCE+TST group. While the HCE+TST group had a follow up – pre change score of 4.4, the BMP+TST had a follow up – pre change of 10 points. At the end of the study, the group mean FMUE score was 39 for the BMP and 33.4 for the HCE group. Although statistics were calculated using the change scores, Fig. 4 presents the group means and standard errors for the FMUE scores at pre, post and follow up. In addition to presenting the data based on the means, we also present group medians and IQRs as well as median change scores and IQRs for both the FMUE and the CAHAI in Table 2. The median data demonstrate a slightly larger follow up – pre change of 11 points, which is one point larger than the mean difference of 10 points. We have chosen to present the median data as well as the mean data since a recent study by Ward et al. (N. S. Ward, Brander, & Kelly, 2019) reported their results using the median score, and this enables us to directly compare our results.

3.3. Neurophysiological measure

Mann-Whitney U test was used to analyze the between group change score (post – pre) in TCI persistence. There was a significant between- groups effect indicating that the BMP +TST group had significantly greater increase in TCI persistence from pre to post ($p=0.03$). The median change score from pre- to post-intervention was 4 (IQR 5). The control group

had a median change score of -1.5 (IQR -3). Figure 5 presents the medians and interquartile ranges of the change scores for both groups.

3.4. Adverse events

We had two adverse events. The first occurred when a participant fell outside of the hospital. This fall was not related to the research protocol. The participant was transported to the emergency room but had no serious injuries. The second event involved a participant in the BMP group who needed to be hospitalized for a reason unrelated to the study.

4. Discussion

For chronic post stroke individuals with moderate to severe upper limb impairment, this is one of the first studies with a training schedule of 30 hours to document a follow up – pre change score that exceeds the estimated clinically important difference on the FMUE (4.25–7.25). The bilateral priming group had a change of 10 points at 6-weeks post-discharge and a between-groups difference score of 5.6. Although the changes in the CAHAI did not reach statistical significance between the groups, both groups exceeded the Minimal Clinically Important Difference (MCID) of 6.3. The MCID is the minimal score needed for a patient or research participant to perceive a change. Interestingly, the HCE+TST reached the MCID at post with a change score of 7.6, which was not retained at follow up. The bilateral motor priming group continued to improve from post-intervention to follow up and exceeded the MCID of the CAHAI at follow up. This continued progress, even after the training has ended, is consistent with previous studies using bilateral priming (Shiner et al., 2014; Stinear et al., 2008; Stoykov & Corcos, 2013; Stoykov & Stinear, 2010). The bilateral priming group also demonstrated significantly greater improvement on persistence of TCI at post-intervention compared to the HCE+TST group.

As noted earlier, the estimated clinically important difference of the FMUE has been established as a change score of 4.25–7.25. The functional picture associated with this change is not well described in the literature. In our study, several individuals had pre- to follow up changes of 10 points. For one participant in the priming group, the significance of a 10-point change was reflected in the perceived performance scores of the COPM. The identified goals on the COPM included tying sweatpants, tying shoes, two-handed typing, playing cards, and bridging with the affected hand to play billiards. On the initial rating of perceived performance (ranging from 1–10, 1 = not able to do it at all, 10 = able to do it extremely well), the participant rated tying shoes and tying sweatpants as a “1.” Two-handed typing, dealing cards, and bridging with the affected hand to play billiards were also rated low in performance (5, 3, and 3 respectively). At post-intervention, all performance scores (except two-handed typing) improved considerably as did all scores in satisfaction with performance. Although the participant’s typing performance score did not improve, his satisfaction with performance for the two-handed typing improved to a 10 (extremely satisfied). The disparity between satisfaction and performance scores was due to the participant being able to incorporate the affected hand in typing but at a reduced speed.

Priming studies, which include a neuromodulation technique as well as training, are well documented in the literature. In a review on priming (Stoykov & Madhavan, 2015), the

authors define the most common priming paradigms as: 1) stimulation-based priming (Kimberley et al., 2018; Madhavan & Shah, 2012; Pomeroy et al., 2007); 2) motor imagery and action observation (Gaggioli, Meneghini, Morganti, Alcaniz, & Riva, 2006; Simmons, Sharma, Baron, & Pomeroy, 2008); 3) sensory based priming (Carrico et al., 2016; Muellbacher et al., 2002); 4) pharmacology- based priming (A. Ward et al., 2017); and movement-based priming (Linder, Rosenfeldt, Dey, & Alberts, 2017; Stinear et al., 2008). Many of these priming plus training studies have demonstrated the greatest gains in the experimental (priming) group at a follow up time point after the training is finished (Carrico et al., 2016; Kimberley et al., 2018; Linder et al., 2017; Linder, Rosenfeldt, Rasanow, & Alberts, 2015; Shiner et al., 2014; Stinear et al., 2008; Stoykov & Stinear, 2010).

In a recent study using peripheral nerve stimulation as the priming technique with severely impaired participants (baseline FMUE score of 29), the authors found a within-group pre- to follow up FMUE change score of 7.2, which is in the upper range of the estimated clinically important difference (Carrico et al., 2016). The difference between the two groups was 4.4 (change score of experimental group – change score of control group). Another promising priming study paired vagus nerve stimulation with upper limb rehabilitation and had a large pre- to follow up change (30 days post end of treatment) of 8 points and a between-groups difference in the FMUE score of 2.3 (Kimberley et al., 2018). There are a number of differences between our study and the Kimberley et al. study that are worth considering in the context of clinical applicability. First, some of the participants in the latter study were less impaired in comparison to our participants. Second, the Kimberley et al. participants continued a structured, task-specific training therapy in the home following post-intervention evaluation. Our study did not include an intense post-clinic home protocol. Notably, in the Kimberley et al. study, there were 21 adverse events recorded in the experimental group ($n = 8$), three of which were designated as serious adverse events related to implantation surgery (Kimberley et al., 2018). It is important to remember that, when compared to other priming methods, BMP, as used in our study, has no known safety issues, does not require a skilled operator, and is cost effective (Byblow et al., 2012). This speaks to its ability to be easily adapted to clinical practice.

Our study had a within group (BMP+TST) pre- to follow-up change of 10 points in the FMUE that is well above the estimated clinically important difference. Our between-group difference from pre- to follow-up was 5.6, the largest between group difference that we are aware of. A medication-based priming study did have a large between-group difference of 6.1 at follow-up (A. Ward et al., 2017). However, retention of the experimental group was poor, and, at follow up, only three experimental participants remained in the study, potentially reducing the clinical relevance of the results.

We are encouraged by the results of the recent study by Ward and colleagues (N. S. Ward et al., 2019). While this study did not use priming techniques, it did administer a large dose (90 hours) of task specific training and a variety of other techniques used in upper limb neurorehabilitation. Ward and colleagues showed a 8-point median change FMUE score (post – pre) that was followed by an 9-point median change score (6-week follow up – pre). Our median scores for the bilateral priming group were comparable to the Ward et al. study with median change scores of 5 (post – pre) and 11 (follow-up – pre). Table 2 presents

medians and interquartile ranges in our study. Our protocol was delivered in one third of the time (30 hours) compared to the Ward et al. study (90 hours). Similar to the Ward et al. study, a previous study by McCabe and colleagues also showed large FMUE changes after 300 hours of TST training over 12 weeks (McCabe, Monkiewicz, Holcomb, Pundik, & Daly, 2015). In a recent commentary on the Ward et al. study, Cramer states that 32 hours of therapy does not result in significant gains in arm function (Cramer, 2019). While we agree that more therapy can produce better outcomes, it is also the case that 30–36 hours of therapy (or less) can improve chronic upper limb outcomes. Indeed, our findings as well as the findings of others have shown that various types of priming plus training have yielded significant changes in the FMUE that are comparable to the results of the Ward et al. study (Harvey et al., 2018; Kimberley et al., 2018; Linder et al., 2017; Linder et al., 2015; Shiner et al., 2014; A. Ward et al., 2017). The large clinical trial by Harvey et al. with patients 3–12 months post-stroke using the same training protocol as the one in our study, found a mean FMUE improvement of 8.5 and 8.1 in both control (sham priming) and experimental (primed with rTMS) groups respectively at 6 months post end of treatment (Harvey et al., 2018). Although there was no evidence for the effect of priming, overall results of Harvey et al. were certainly comparable to the Ward study, again with 1/3 of the training time. In the United States, 24 – 30 hours is the typical amount of treatment allotted for outpatient physical or occupational therapy, and large increases in therapy coverage are unlikely to change in the near future. However, the data of Ward and colleagues are certainly supportive of increased therapy coverage, especially for individuals who clearly have not reached a plateau in their therapy (N. S. Ward et al., 2019).

In a previous study, sub-acute post-stroke participants who received bilateral priming plus training were three times more likely than control participants to reach their clinical endpoint at 12 weeks post-stroke, indicating that bilateral priming accelerates subacute post-stroke recovery (Stinear, Petoe, Anwar, Barber, & Byblow, 2014). Our findings and the findings of others suggest that, in the chronic post-stroke phase, bilateral priming amplifies the positive effect of therapy and provides similar improvement as studies which provide much higher doses of training (Shiner et al., 2014). Bilateral priming could be beneficial to other training protocols with documented efficacy for individuals with post-stroke arm impairment. For example, impairment oriented training (IOT) has shown efficacy in the subacute post-stroke phase. Thus, the addition of bilateral priming to IOT could augment the documented positive effects (Platz et al., 2005; Platz et al., 2009).

The studies by Ward et al, and McCabe et al, studies both show considerable ongoing improvement as training continues (McCabe et al., 2015; N. S. Ward et al., 2019). In our study, improvement in the FMUE did not plateau in either group. We can extrapolate from our data that continuing the treatment past the 15 sessions would likely bring even greater improvement.

It was not expected that the secondary outcome measure (FMUE) would demonstrate a larger between-group difference when compared to the primary outcome measure (CAHAI). However, it did. This may be because the FMUE measures motor recovery, not motor compensation (Prabhakaran et al., 2008). The scoring of the CAHAI, however, measures the ability to use the affected arm as either a stabilizer or manipulator during object related

bimanual tasks. Improvements in the CAHAI could indicate both motor recovery and/or motor compensation that is specific to the individual. Since the largest change occurred in the FMUE in the experimental group, we speculate that bilateral priming may aid in true biologic recovery.

Our finding of significantly increased TCI persistence from pre- to post-intervention suggests a positive neuroplastic change indicating more normalized inhibition in chronic stroke survivors. Transcallosal inhibition persistence from ipsilesional to contralesional hemisphere requires elicitation of the ipsilateral silent period and is measured using the less affected arm, making it an ideal measure of neuroplasticity for our participants. Further, TCI is important for complex dexterous movement. An increase in TCI depth (percentage of inhibition compared to pre-stimulus EMG) in elderly participants has been associated with improved manual skill (Davidson & Tremblay, 2013). There is growing evidence that increase in TCI (whether in duration or depth) coincides with improved motor control (He et al., 2018). In bimanual movement, TCI may be responsible for finely tuned variation of force modulation between the hands (Tazoe, Sasada, Sakamoto, & Komiyama, 2013). In our study, there were very few stimulation trials at pre-intervention that resulted in ipsilateral silent periods. Thus, persistence, rather than depth or duration, was a better measure for our participants.

Increases in corticomotor excitability following bilateral priming in healthy adults have been documented in the literature (Byblow et al., 2012; Jordan & Stinear, 2018). A recent study examined possible underlying intracortical neural mechanisms influencing bilateral priming. Although the study did find increased cortical excitability after bilateral priming, the authors concluded that these increases were not the result of intracortical mechanisms. Instead, the authors suggest that bilateral priming may modulate interhemispheric facilitatory pathways (Jordan & Stinear, 2018).

Our pilot clinical trial has several limitations. The first limitation is that due to equipment malfunction, we have no TCI data at follow up. The second limitation is that the study was only conducted at one site using a small number of treatment therapists (two at any given time). The third limitation is that only one female was studied in the bilateral motor priming group and two females were studied in the HCE+TST group limiting our ability to generalize to women. A fourth limitation is that the mechanism that underlies bilateral priming is not clear.

5. Conclusion

In conclusion, both groups improved at post-intervention in both the primary and secondary measures. The bilateral priming group experienced a greater magnitude of improvement in the FMUE that continued after post-treatment and was most notable at follow up. The results of this study strongly suggest that further mechanistic studies are warranted that determine, 1) whether it is priming that causes the benefit post-treatment or whether it is just performing movements for 15 minutes that cause improved retention; and 2) whether there are other neurophysiological changes that occur in addition to increases in transcallosal persistence. These preliminary results support a clinical trial that replicates the finding of a

10-point change in the FMUE and the extent to which this difference can be increased by using a longer period for treatment. The duration of daily treatment and the number of weekly sessions administered is the maximum that can be tolerated by individuals with this severity of upper limb impairment. As such, the only way to increase dose is to increase the time over which therapy is applied.

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Fig. 1.
Participant Flow through the Study.

Fig. 2.
Picture of Exsurgo Rehabilitation Primer (Auckland, NZ).

Fig. 3.

Group means and standard errors for the Chedoke Arm Hand Activity Index, Version 9 (CAHAI 9) scores at each time point for healthcare education (HCE) with task specific training and bilateral motor priming (BMP) with task specific training (TST). $*=p < 0.05$ within group significance for BMP group.

Fig. 4.

Group means and standard errors for the Fugl Myer Upper Extremity Test of Function (FMUE) scores and at each time point for healthcare education (HCE) plus task specific training (TST) or bilateral motor priming (BMP) plus task specific training (TST). ** $p < 0.05$ between group significance.

Fig. 5. Median transcallosal inhibition persistence (TCI) change scores (Post-Pre) and interquartile ranges for the healthcare education (HCE) and bilateral motor priming (BMP) paired with task specific training (TST). ** $p < 0.05$ between group significance.

Table 1.**Participant Demographics**

Characteristics	BMP	HCE
Age (SD)	61 (7.60)	63 (5.21)
Months post-stroke, mean (SD)	62.9 (50.00)	68.13 (51.11)
Lesioned hemisphere (Right/Left)	5R/3L	5R/3L
Baseline FMUE score, mean (SD)	29 (4.6)	29 (5.42)
Male	7	6
Female	1	2
Race		
Caucasian	3	1
African American	4	6
Asian	1	1

Abbreviations; BMP: bilateral priming group; HCE: health care education group; SD: standard deviation; FMUE: Fugl-Myer Motor Function Test; *R* = right; *L* = left.

Table 2.

CAHAI 9 and FMUE group medians (IQR) for all time points & median change scores (IQR)

	CAHAI 9 (scale is 9–63)				FMUE (scale is 0–66)			
	Pre	Post	Follow up	Post-Pre	Follow up	Post	Follow up	Post-Pre
BMP								
Median (IQR)	19 (1)	26 (5.5)	28 (6.5)	5 (8)	9 (8.5)	28 (6)	37 (14)	43 (10.5)
HCE								
Median (IQR)	18.5 (7.2)	22 (15.7)	22 (16.2)	3.5 (10)	4 (6.5)	28 (8)	31.7(14)	–0.5 (5.7)

Abbreviations: CAHAI: Chedoke Arm & Hand Activity Index; FMUE: Fugl-Meyer Motor Function Test; IQR: interquartile range (quartile 3 – quartile 1); Post-Pre: change score from pre-intervention to post; Follow up – Pre: change score from pre-intervention to follow up.