Investigating the Cortical and Subcortical Contributions to Unimanual and Bimanual Wrist Extension

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Statement of Contribution of Collaborators

I, Faven Teku, hereby declare that I am the sole author of this master's thesis. The conception and design of the experiment, data collection and analysis, statistical analyses, and production of this document were completed in collaboration with my thesis supervisor, Dr. Anthony Carlsen, and with input from my thesis committee consisting of Dr. Erin Cressman and Dr. Dana Maslovat.

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Abstract

When exploring movement production, motor control researchers have been interested in investigating the relative contributions to different types of movement. In a research setting, a startling acoustic stimulus (SAS) can be used as a tool to explore the neural processes that are occurring when preparing and initiating a movement. Additionally, suprathreshold TMS is another tool which can induce a suppression of the cortical region of the brain, resulting in RT delays which provides us with the ability to assess the corticospinal contributions to a particular movement. The aim of the current study was to investigate potential differences in the planning and execution of bimanual versus unimanual wrist extension movements. It was of particular interest as to whether bimanual coupling occurs at the cortical level or in lower parts of the output pathway (reticulospinal). Participants (N=6) were instructed to complete a unimanual or bimanual wrist extension following a control go-signal or a SAS. For subset of trials, in order to explore the level of corticospinal excitability of the movement, suprathreshold TMS was applied over the left M1 during the task to induce a cortical silent period (CSP). Results revealed that the impact of TMS on response initiation was not significantly different for unimanual task versus a bimanual task. Furthermore, the SP (silent period) only had an impact on the right limb and not the left during the bilateral task. Lastly, SAS did lead to shorter RTs for both the unimanual and bimanual wrist extension task, but the RT delay induced by TMS in the right limb was not shorter in SAS trials compared to control. The findings of the present study suggest that bimanual coupling may be occurring at the cortical level and in lower parts of the output pathway as there may be correlated neural activity in the two hemispheres occurring during bimanual wrist extension movements.

Glossary of Terms

CSP: Cortical Silent Period

ECR: Extensor carpi radialis

FCR: Flexor carpi radialis

EMG: Electromyography

M1: Primary motor cortex

MEP: Motor evoked potential

MVF: Maximum voluntary force

OOc: Orbicularis orsi muscle

PMT: Premotor RT

RM ANOVA: Repeated measures analysis of variance

rMT: Resting motor threshold

RT: Reaction time

SAS: Startling acoustic stimulus

SCM: Sternocleidomastoid muscle

SP: Silent period

TMS: Transcranial magnetic stimulation

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Chapter I: Literature Review

1. Introduction

On a daily basis, humans regularly prepare and initiate responses to engage in activities of daily living. From waiting for the traffic light to turn green before pushing the gas pedal, to sprinters waiting for the 'go' signal in a race, many tasks require advance preparation of an intended movement. Motor control researchers are particularly interested in the neural processes underlying human movements. One area of exploration is the processes that are occurring across different types of movement. The corticospinal tract in particular has been associated with voluntary movements, as well as fine movements such as a precision grip (Lawrence & Kuypers, 1968). The reticulospinal tract is predominately involved in more gross movement such as locomotion (Schepens & Drew, 2004). Although the neural processes outlined are separate, there is a coordination that occurs and there is a more distributed approach to the neural networks involved in a particular movement. One way of exploring the corticospinal and reticulospinal contributions in a lab setting is by using a startling acoustic stimulus (SAS) to explore the movement initiation processes that are occurring. Transcranial Magnetic Stimulation (TMS) can also be used in conjunction with SAS as TMS can induce a disruption in the cortical region in the brain, which allows exploration in the activity that is occurring for initiating different movements. Smith et al. (2019) explored the contributions of corticospinal and reticulospinal regions to flexion and extension movements and found that the contributions may be impacted differently depending on the particular movement involved.

Recent studies have suggested that the reticulospinal tract may be involved with bilateral movements (Davidson & Buford, 2006). Bimanual finger movements have been shown to have

an increased reticulospinal drive compared to unimanual finger movements (Maslovat et al., 2020). As such, it is of particular interest to explore if TMS would have any implications on unimanual and bimanual wrist extension movements, and what is the impact on movement initiation.

2. **Response Programming**

When exploring the preparation of an intended movement, various functional areas of the brain are innervated leading to an increase in neural activity to prepare and eventually execute the movement. The brain's various areas engage in information processing to perform the movement. When engaging in a task, information processing is broken down into 3 stages: stimulus identification, response selection, and response programming (Schmidt & Lee, 2011). The first stage, stimulus identification, requires one to detect and identify a stimulus. The second stage, response selection, requires the individual to then make an appropriate response to the stimulus identified. Lastly, the response programming stage is when the individual prepares and initiates the movement they had selected. Reaction time (RT) is often used as an indicator of the time required for the central processes involved in information processing (Schmidt & Lee, 2011). The response programming stage is when the motor program is said to be prepared and ready to be released for execution. Additionally, response initiation is said to occur once the decision has been made to execute the prepared movement. To gather a better understanding of the processes involved in movement preparation, researchers can modify the number and type of stimuli involved and examine how response time is affected. For example, simple RT tasks require the individual to perform a task as quickly and accurately as possible in response to a single imperative stimulus. Choice RT involves two or more stimuli, with each stimulus

requiring a distinct response. It has been shown that as the number of stimuli and associated responses increase, RT also increases. It has been reasoned that in choice RT tasks, individuals must detect and identify the stimulus, select the appropriate response and then program and execute that response. Since there is an increased requirement in the response selection phase and subsequent response programming, choice RT is generally slower than simple RT.

Advance preparation (prior to the stimulus) can occur in simple RT paradigms in which participants are to respond as quickly as possible to a stimulus with a predetermined response. In simple RT tasks, typical RTs for single limb responses range from 150-200 ms. RT is often measured using electromyography (EMG) and can be fractionated into 2 components: premotor RT and motor RT. Premotor RT (PMT) is the time from stimulus presentation to the onset of EMG activity of the muscle, whereas motor RT is the time between the onset of EMG activity and the start of the required movement. In the case of simple RT tasks, participants are required to complete a single movement as fast and accurately as possible in response to the imperative stimulus. Additionally, since the response is predetermined, subjects are able to program the response prior to the 'go' signal resulting in a decrease in RT (Donders, 1969). As such, simple RT latencies provide an objective measure of response detection and initiation processing speeds across a variety of populations (Jensen, 2011). On the other hand, choice RT tasks require the subject to respond to one or more stimuli and requires additional processing related to stimulus identification and response selection, and thus increases the RT interval. Therefore, in the case of choice RT tasks there is the inability to store the movement prior to the stimulus, resulting in an increase in RT due to the central processing that is required compared to a simple RT task.

3. **Motor Programs**

The "motor program" responsible for producing a movement has been described as a series of motor commands that are stored in a region of the brain until movement execution is required (Keele, 1968). While originally intended to act as a metaphor for how actions are planned, motor programs have been argued to be a more literal construct (Morris et al., 1994). Motor programs involve a sequence of muscle commands that are prepared prior to a movement beginning and once the program is released it is not impacted by peripheral feedback (Keele, 1968). Alternatively, closed-loop theorists of the motor program argue that in order for a successful performance of an intended movement, somatosensory information is required (Adams, 1971; James, 2007; Keele, 1968). Open-loop models have been most often used to explain motor programs as further research has demonstrated that sensory feedback was not necessary for the movement to occur. From a neural perspective, it has also been suggested that cortical cell assemblies explain the neural mechanisms behind the ability to store the movement. Cortical assemblies consist of associated groups of cortical neurons that form when neurons have worked together resulting in both structural and functional changes at the synaptic level (Wickens et al., 1994). The particular cell assembly is argued to be the motor cortical representation of a movement (Wickens et al., 1994). The group of cells in the cortical assembly is argued to have the ability to activate more neurons than other cell groups. As such, one question of particular interest to motor control researchers concerns where this motor program is "stored."

4. StartReact Effect Mechanisms

In the laboratory, one way of further understanding where these motor programs are stored is by using a startling acoustic stimulus (SAS) in replacement of a normal go-signal in a RT task. Highly prepared movements can be triggered early when a SAS is presented, presumably due to increased subcortical activation from the startle reflex. Presenting a SAS results in a substantial reduction in RT (mean RTs <80 ms) while still producing the intended movement, which has been termed the Start React effect. Yet, a distinguishing aspect of the phenomenon is that there is little difference in the temporal and spatial characteristics of the triphasic burst pattern of the normal response compared to those triggered by the SAS (Carlsen et al., 2004a).

4.1 Sub-Cortical Storage Hypothesis

Further investigation has tried to understand which mechanisms in the brain lead to the early and involuntary release of a prepared movement when startled. The sub-cortical storage hypothesis indicates that when presented with a SAS, the release of a sub-cortically stored motor program is directly triggered (Valls-Solé et al., 1999). More specifically, the reduction of RT and the unaffected response characteristics following a SAS was originally suggested to be a result of subcortical involvement, which implies that at least part of the motor plan may be represented in reticular centres during the preparation and initiation of the movement. Releasing the movement from subcortical areas would enable cortical processing typically associated with voluntary movements to be bypassed, resulting in a faster reaction time (Carlsen et al., 2004b). Valls-Solé et al. (1999) argued that responses following a SAS with premotor RTs that were <70ms were unlikely to include cortical processing as more time is required to convert the acoustic stimulus

to neural signals and for processes involving cortical neural transmission resulting in the movement to occur. Furthermore, the StartReact response is typically only seen when associated with sternocleidomastoid (SCM) and orbicularis oculi (OOc) startle response EMG activity (Carlsen et al., 2007), both of which are startle indicators that are sub-cortically driven (Yeomans & Frankland, 1995). Although it has been traditionally accepted that in general, movements are primarily organized and executed via cortical regions such as premotor cortex and primary motor cortex (Lawrence & Kuypers, 1968), recent evidence demonstrates that some types of movements involve a certain degree of involvement from reticulospinal centres (Baker, 2011). For example, recent evidence has indicated that the reticular formation may contribute more to wrist flexion as compared to wrist extension, and that more drive is present from reticular formation during SAS triggered movements (Smith et al., 2019).

Additional evidence for the subcortical involvement in the StartReact effect has been found in patients with hereditary spastic paraplegia (HSP). HSP is a group of disorders as a result of degeneration of the corticospinal tract (McDermott et al, 2000) and presents with delayed RTs. Nonnekes et al. (2014) examined the StartReact effect in HSP patients where participants were instructed to complete either dorsiflexion at the ankle, or flexion in the wrist when presented with an audible stimulus. Results revealed that in control trials, RT was significantly slower in the HSP patients, but in response to SAS they exhibited similar RT to the control group. Because the “startle driven” actions were performed as quickly by the patients, this further supports the notion presented in the subcortical storage and triggering hypothesis that prepared movements are released via the reticulospinal tract.

4.2 Cortical Storage Hypothesis

Another hypothesis which has been used to explain the StartReact effect is the cortical storage hypothesis. One way of examining the contributions of the cortical region in the StartReact effect is through the use of TMS which will induce a silent period. Alibiglou and MacKinnon (2012) administered suprathreshold TMS on both control and SAS trials in a simple RT task. Results revealed that for TMS trials there was an RT delay in control trials, but there was also a delay on SAS trials. Because the TMS silent period is thought to primarily impact cortical drive, the significant delay being present in the SAS trials provides evidence that there is involvement of the cortical regions in StartReact trials.

Support of the cortical involvement in the StartReact also comes from studies that have employed this paradigm when participants completed a vocalization task. Speech execution has been shown to involve the cortical regions projecting on subcortical pathways (Simonyan & Horwitz, 2011). Stevenson et al. (2014) had participants prepare to produce a single syllable, “ba” in a simple RT task. On a portion of the trials, the go signal was replaced with a SAS. Findings revealed that even in a vocalization task, SAS led to a reduction in RT, likely due to the cortical contributions in the task. When examining the contributions to the StartReact effect, it is important to note that it is not exclusively one region over the other. Rather it is likely that both the cortical and subcortical regions play a role in the StartReact effect.

5. Bimanual Movement

It has been suggested that bimanual movements, particularly symmetrical bimanual actions, may involve greater reticulospinal drive compared to unimanual actions (Baker, 2011). It is thought that the corticospinal tract plays the predominant role in fine actions such as

individual finger movements (Lawrence & Kuypers, 1968). When analyzing the hand movements of macaque monkeys that experienced a lesion on their corticospinal tract, their ability to grasp was significantly impaired. However, they eventually regained gross motor functioning (Lawrence & Kuypers, 1968). In finger abduction tasks, unimanual finger movement do not demonstrate a decrease in RT caused by startle (Carlsen et al., 2009), further suggesting a predominantly cortical origin. However, Littlemore & Carlsen (2016) found that when individuals completed a bimanual finger abduction tasks, there was a decrease in RT when presented with a SAS. The nature of these results indicates that contrary to previous findings (Carlsen et al., 2009), intrinsic hand movements involving finger abduction movements are susceptible to the StartReact effect, but only when performed bimanually. Therefore, these findings suggest a greater innervation via subcortical connections.

6. **Transcranial Magnetic Stimulation**

Transcranial magnetic stimulation (TMS) is a non-invasive neurostimulation technique that can provide information on the neural processes that occur when humans are preparing and executing movements (Terao & Ugawa, 2002). The tool was constructed as a method for stimulating the brain without the use of external electrodes to the skin which would often lead to discomfort of the participant. The device typically consists of a main unit, which generates a high voltage current, and a handheld “coil” through which the current is rapidly discharged. Since the coil consists of plastic encased windings of copper wire, the TMS creates a powerful electromagnetic field perpendicular to the orientation of the coil. This magnetic field can be delivered through a “figure-8 coil” over the scalp, which impacts superficial layers of the brain,

about 1.5–2 cm deep from the skull. Figure-8 shaped coils are more focal than other coil types, producing maximal current at the intersection of the two round components.

Through the use of electromagnetic induction, TMS induces electrical currents which typically fall perpendicular to the coil when held against the scalp (Klomjai et al., 2015). TMS results in a series of descending neural volleys. The first volley is termed the D-wave, as it is assumed to be evoked by direct excitation of pyramidal tract neurons, whereas the subsequent I-waves appear to be generated by indirect excitation of the pyramidal tract neurons via cortical interneurons (Fuhr et al., 1991). The individual's motor threshold is to be considered when selecting the TMS intensity to use. An individual's motor threshold is the minimum intensity that is required for TMS to generate a motor evoked potential (MEP). A MEP occurs when the M1 is stimulated with a single-pulse TMS, resulting in a twitch in the targeted muscle. The response is measured using surface EMG electrodes placed over the targeted muscle, and the size of the MEP (its peak-to-peak amplitude) can be indicative of the degree of cortico-spinal excitability. At particularly high intensities, single pulse suprathreshold TMS can evoke a prolonged suppression of EMG activity, termed the "silent period" (SP). While the first part of the SP is due to the refractory period of neurons, the latter part is due to the stimulation of inhibitory interneurons in the motor cortex leading to cortical inhibition (Day et al., 1989). Therefore, TMS can be used as a tool to investigate the relationship between brain activity and behaviour, specifically cortical and sub-cortical contributions to different movements.

Previous research has demonstrated that the flexors have greater connections from subcortical regions compared to extensor muscles, which have greater input from the corticospinal tract (Cheney et al., 1991; McKiernan et al., 1998). Smith et al. (2019) further

explored the role of the reticulospinal drive on various movement types and acoustic stimuli by interrupting corticospinal drive using high-intensity TMS. As described above, high intensity (>140% of motor threshold) TMS can be used to elicit a cortical silent period, which results in a suppression of muscle activity for approximately 100-200ms. When utilized in conjunction with a simple RT task, one's RT is delayed as a result of the cortical suppression, presumably as a result of inhibition of the cortical contributions and M1 output involved in voluntary movement. Smith et al. (2019) applied suprathreshold TMS during a simple RT task where participants were required to complete a wrist flexion or extension movement in response to an auditory control go-signal or SAS. On a portion of the trials, suprathreshold TMS was applied over the motor cortex region responsible for the particular movements to induce a SP in order to determine whether contributions varied based on movement type and different muscles innervated. Results showed that TMS led to increased RT in all conditions. However, there was a greater TMS-induced RT delay for extension movements compared to flexion. In terms of SAS, there was a greater RT delay in conditions involving the control go-signal compared to the SAS. The authors suggested that conditions where RT was less affected (delayed), they were likely driven more by subcortical (reticular) structures (Smith et al., 2019). As such, these findings demonstrate the utilization of supra-threshold TMS in addition to SAS further contribute to the understanding of varying cortical and corticospinal contributions to various movements.

Chapter II: Research Article

1. Introduction

Different types of movements often engage various different regions of the brain which can result in a diversity of neural processes underlying those particular movements. In life-

threatening scenarios, the brain must quickly analyze the environment and decide what to do next to avoid a potentially dangerous situation. For example, to avoid an accident while driving, one may have to brake while simultaneously adjusting their steering. In these cases, oftentimes inter-limb or bimanual movements occur which may require integration of sensory and motor processes from the two hemispheres. Although these movements often appear to be coordinated efficiently, there remains a high degree of complexity in their execution. In particular, there remains much uncertainty regarding the neural processes underlying the pre-planning of bimanual movements and just how integrated are the motor plans and associated brain regions that contribute to the coordination of the movements. For example, interlimb coupling effects for bimanual movements have been observed, whereby the two limbs are constrained by one another either temporally or spatially (See Swinnen 2002 for a review). An example of bimanual movement having similar initiation processes can be found in instances where coupling effects have been shown to occur for both the spatial and temporal aspects of movements (Garbarini & Pia, 2013). When participants were asked to complete a bimanual, asynchronous finger tapping task, they were unable to complete the tapping task without interference from the opposite finger (Peters, 1977). For spatial components of a bimanual movement, when each hand is to draw two different shapes, each drawing is influenced by the opposing hands drawing (Franz et al., 1991). In particular Kelso et al. (1979) employed a reaction time (RT) task requiring bimanual reaches to different size or distance targets for each limb. In the case where the complexity of only one limb was manipulated, the other limb was constrained temporally such that the two limbs tended to start and end their movements together.

The neurophysiology underpinning the common initiation processes in bimanual movements is a matter of ongoing research into whether this coupling arises at the cortical level

or in lower parts of the output pathway. It has been shown that correlated neural activity in the two hemispheres is associated with bilaterally symmetric movements (Gribova et al., 2002). On the other hand, evidence from studies involving unilateral stroke patients have shown that aspects of interlimb coupling are preserved in these individuals, suggesting that a substantial part of the coupling may be attributed to lower structures such as brainstem and spinal pattern generators (Arya & Pandian, 2014; Harris-Love et al., 2005). Other research has implicated the increased role of brainstem/reticulospinal drive in bilateral movements. While the reticulospinal system has long been thought to contribute to locomotion and postural control, it has been shown to also include bilateral output to upper limb muscles (Riddle et al., 2009). Indeed, the reticular formation has also been implicated in upper limb voluntary action (Baker, 2011; Baker & Perez, 2017; Carlsen & Maslovat, 2019; Smith et al., 2019). Due to the strong bilateral output (Davidson et al., 2007; Davidson & Buford, 2006), it may contribute much more strongly when voluntary actions are performed bimanually.

One way to assess the common preparation elements between limbs is through the use of transcranial magnetic stimulation (TMS). At high intensities, single-pulse suprathreshold TMS can impart a prolonged (100 – 200 ms) suppression of EMG activity, termed a cortical "silent period" (CSP). EMG suppression following the first 50 ms has been attributed to interruption of cortical motorneuronal drive (Chen et al., 1999). Importantly, when high intensity TMS is applied following a go-signal, but prior to the response output in a simple RT task, RT is delayed due to the interruption of voluntary output caused by the TMS (Day et al., 1989). Therefore, TMS can be used as a tool to investigate the relationship between brain activity and behaviour. One's response to a SAS can also reveal information related to the neural output as movements that are innervated by the reticulospinal tract have been shown to be involuntarily triggered (see

Carlsen and Maslovat 2019 for a review). In particular, Smith et al. (2019) used TMS along with a SAS to investigate whether flexion and extension movements involved different contributions of corticospinal and reticulospinal drive. Participants were required to complete a simple RT task where they were required to complete a wrist flexion or extension following a control tone or SAS. For a subset of trials, suprathreshold TMS was applied over the M1 representation of the wrist muscles. When examining the TMS induced RT delay, the wrist extension movements revealed a longer RT delay compared to flexion and these delays were greater in control compared to SAS trials. These findings suggest that when looking at wrist flexion and extension movements, there appears to be a greater reticulospinal contribution to wrist flexion as indicated by the decrease in TMS induced RT delay. Additionally, the decrease in TMS induced RT delays in the SAS trials in particular reveal an increase in reticulospinal tract drive.

The aim of the current study was to investigate potential differences in the planning and initiation of bimanual versus unimanual wrist extension movements. In order to elucidate the neural structures underlying bilateral actions, supra-threshold single pulse transcranial magnetic stimulation (TMS) was used to induce a transient disruption of cortical activity in the left primary motor cortex (M1) during a simple RT task involving a standard auditory go-signal or a SAS. In particular it was of interest whether 1) the impact of TMS on response initiation was different for a unimanual task versus a bimanual task, 2) whether the SP would impact the initiation of one limb or both limbs during bilateral task, and 3) if any differences observed would be modulated based on whether the action was initiated voluntarily following a control go-signal, or involuntarily following a SAS. It was hypothesized that a TMS induced CSP would delay the initiation of the right limb in both unimanual and bimanual conditions, but that the delay would be smaller in the bimanual conditions. Also, it was predicted that there would be a

delay in RT for only the right wrist as a result of the CSP, but differences would not be present in the left. Furthermore, it was hypothesized that a SAS would lead to shorter RTs for both the unimanual and bimanual wrist extension tasks, and that the RT delay induced by TMS in the right limb would be shorter in SAS conditions. On SAS trials it was predicted that the RT asymmetry between the limbs would be smaller than that observed on non-SAS trials.

2. Methods

2.1 Participants

Nine participants with no self-reported upper body sensory or motor dysfunctions were recruited for this study. Prior to the testing session, participants had provided informed consent and completed the required TMS safety questionnaire (Appendix A) and only those whose answers indicated they had no contraindications were allowed to participate (Rossi et al., 2009). The data of three participants was excluded from the analyses as they did not show a consistent startle reflex (<50%) when presented with a SAS. As such, the final sample size consisted of 6 participants (5 female, 1 male; mean age 28, SD = 8.11). The experiment was completed in one session which lasted approximately 1.5 hours. The study was completed within the ethical guidelines established by the University of Ottawa and conformed to the seventh revision of the Declaration of Helsinki.

2.2 Experimental Setup and Task

All participants were seated at a height-adjustable chair approximately 1.5 m in front of a computer monitor (Figure 1). Both the left and right arms were rested parallel to the floor on the fixed armrest portion of a custom manipulandum that allowed isolated flexion/extension of the wrist. The shoulder was abducted and flexed approximately 30˚ and the elbow flexed 70˚ with

the forearms partially supinated such that the palms of the hands faced inwards. Participants performed blocks of a simple RT task requiring unimanual extension of the right wrist, unimanual extension of the left wrist, or synchronous bimanual wrist extension. Participants were instructed to complete the task as quickly and accurately as possible in response to the auditory go-signal. Following each trial, feedback regarding RT and movement accuracy was displayed on the monitor in front of the participant. Points were allocated on a sliding scale presented to participants along with their RT feedback. Participants were rewarded points if movement RT was below 170 ms and were penalized if movement RT was above 270 ms. These points were not analyzed but were included as a source of motivation and also assisted in ensuring the movement was completed as accurately and rapidly as possible.

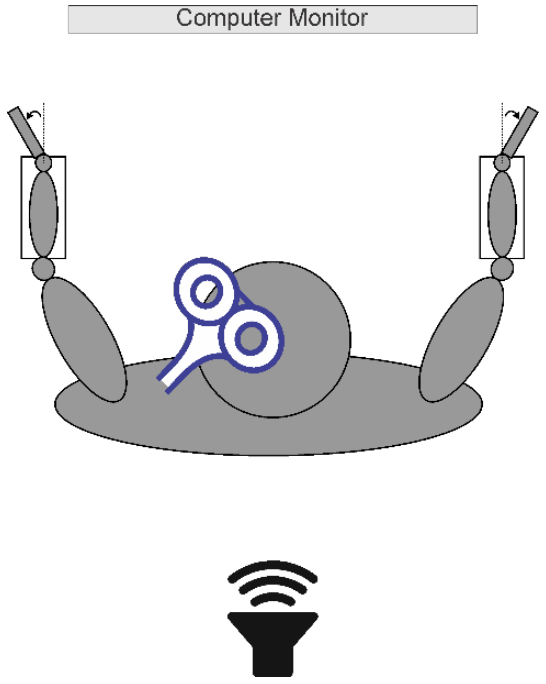


Figure 1. Experimental Set-up. Participants were seated in a chair facing a computer monitor. Both arms were harnessed with a Velcro strap to allow 20˚ extension of the wrists. EMG data was collected from bilateral sternocleidomastoid, and both right and left extensor carpi radialis (ECR) and flexor carpi radialis (FCR). For a subset of trials, TMS was applied over the left primary motor cortex representation for the wrist extensor muscles.

2.3 Transcranial Magnetic Stimulation

TMS was delivered using a MagStim 200^2 stimulator with a figure-8 coil. TMS was applied over the M1 representation of the right extensor carpi radialis (ECR) muscle region. This area was first estimated by finding the midpoint between the nasion and inion, and the midpoint between the right and left preauricular notches. Once those two points were located, another location 4 cm lateral and 1 cm anterior from this intersection was marked. The mark was then used as a starting point to determine the best location by moving the coil in small increments (~0.5 cm) to find the location that generated the largest motor evoked potential (MEP) in the right ECR muscle. Once this "hotspot" was determined, this specific location was saved using a neuro-navigation system (ANT Visor 2) to aid in targeting the delivery of the suprathreshold TMS for the remainder of the trials.

The resting motor threshold (rMT) of the right ECR was then determined (to the nearest 1% of stimulator output) as the minimum intensity required to elicit a peak-to-peak MEP of 100μV in 5 of 10 trials (Rossini et al., 2015). Throughout the TMS trials in the experiment, suprathreshold TMS (140% of participant rMT) was applied 70 ms prior to each participant's median RT for each RT task condition, as determined during a preliminary block of control trials (i.e., with no TMS; see section 2.6 below).

2.4 Recording Equipment

Surface EMG data was collected bilaterally from the wrist extensor (ECR) and wrist flexor (flexor carpi radialis; FCR) muscles, as well as bilaterally from the sternocleidomastoid (SCM). The recording sites were cleansed and prepared prior to the attachment of the EMG surface electrodes to help decrease electrical impedance. Ag/AgCl surface EMG electrodes

(Delsys Bagnoli DE-2.1) were attached to the middle of the muscle bellies. The electrodes were then attached to an external amplifier (Delsys Bagnoli-8). A reference electrode (Dermatrode HE-R) was attached to the individual's right medial epicondyle. Linear potentiometers were attached to the pivot point of the manipulanda and were used to measure the angular displacement of the wrists. Raw EMG and potentiometer data were sampled at 4 kHz (National Instruments PCIe-6321) for 3 s using a customized LabVIEW program beginning 1 s prior to the go-signal/SAS.

2.5 Maximum Voluntary Force and Baseline TMS Silent Period

A schematic depiction of the experimental timeline (i.e., blocks of trials) can be found in Figure 2. Prior to testing, participants completed 2 maximum voluntary force (MVF) trials for each movement type: unilateral left, unilateral right, bilateral. For these trials participants were required to complete a wrist extension movement as forcefully as possible against the force transducer(s) for 3 seconds. The MVF for each movement type was the average peak force of the two trials for the particular movement type.

Upon determining participants resting motor threshold and MVF, participants completed a force production task while TMS was applied over the M1 representation of the right ECR region (i.e., hotspot) in order to determine the baseline TMS silent period (SP) elicited in each task. Participants performed 3 blocks (unimanual right, unimanual left, bimanual) of 10 trials where participants were instructed to hold a constant wrist extension force at 10% of their MVF for the entire block of trials. During these trials the participants were presented with a scale which displayed their force in order to ensure they were maintaining the required force. While

holding the constant wrist extension force, suprathreshold TMS pulses were applied at approximately 5 s intervals (controlled manually by the experimenter).

2.6 Task and Procedure

Following the MVF and baseline SP blocks, all participants performed 3 familiarization/practice trials of each reaction time (RT) task (unimanual right, unimanual left, and bimanual). Practice trials required participants to complete a simple RT task to an auditory go-stimulus. Once the practice trials were completed, participants moved onto the baseline blocks.

The baseline RT measurement consisted of 3 baseline blocks (one block for each RT task), consisting of 12 control trials and 4 SAS trials, pseudorandomly distributed such that none of the first 3 trials and no 2 consecutive trials contained a SAS. Premotor RT was determined by the experimenter on each baseline trial by placing a marker at the point of agonist EMG onset that was displayed using a custom LabVIEW program. Median onset time for each task and auditory stimulus type was then calculated to provide baseline RT values. Task order was counterbalanced across participants, and each phase of the experiment used the same task order for that particular participant.

Once baseline blocks were completed, participants performed nine experimental testing blocks (three blocks of each task). All three blocks of each task were completed before moving to the next task. Each block consisted of 8 control trials, 4 control trials with TMS, 2 SAS trials, and 2 SAS trials with TMS, totalling 16 trials per block (i.e., 48 total trials per task, including 12 SAS trials per task).

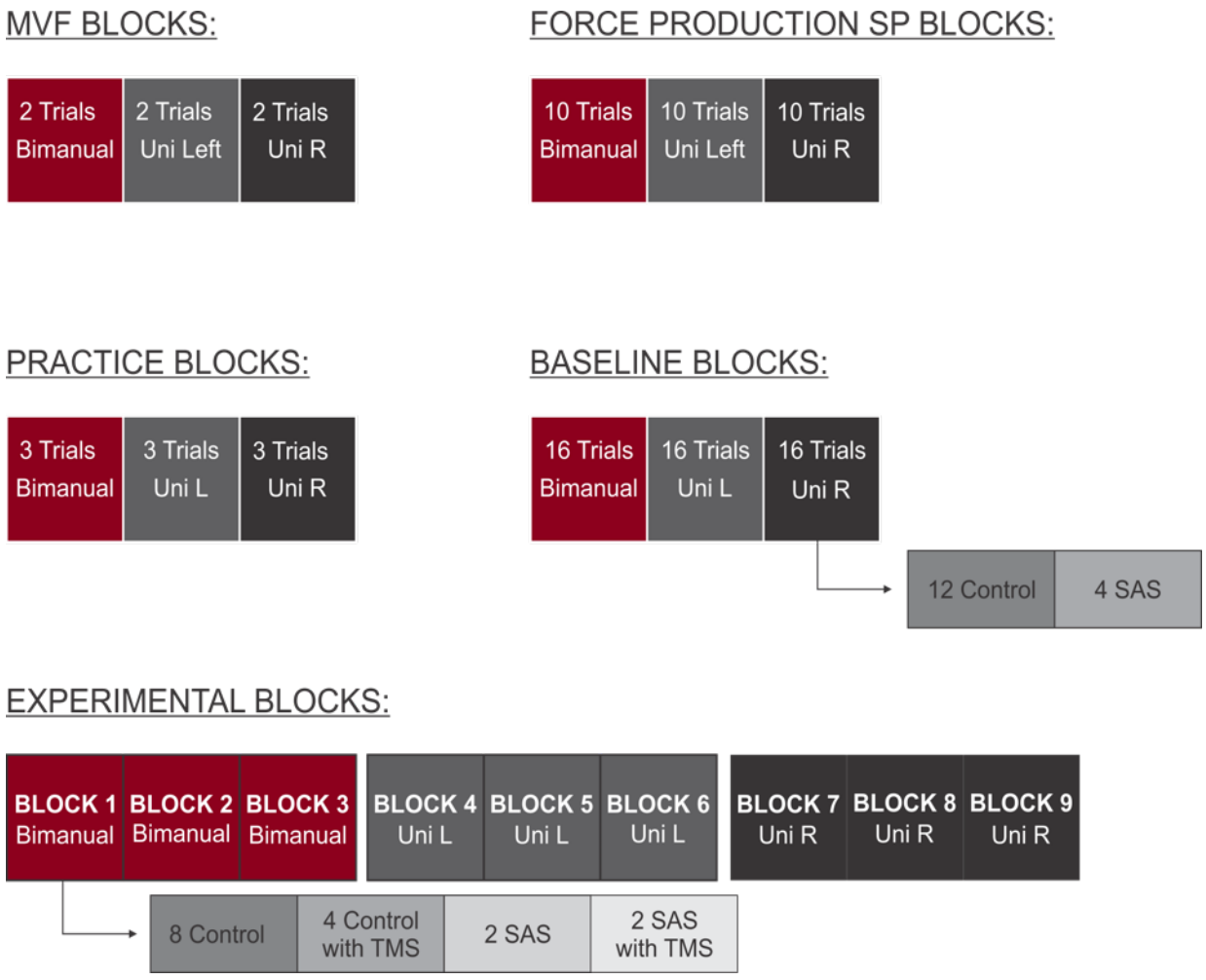


Figure 2. Order of experimental blocks. Participants completed 3 MVF blocks followed by the force production SP blocks. Once completed, participants completed 3 practice blocks (3 control trials) followed by 3 baseline blocks (12 control, 4 SAS trials). After the baseline blocks participants completed the 3 experimental of each movement types (9 blocks total).

Each experimental trial began with the words 'Get Ready' and a fixation cross being displayed on the computer monitor for 1000 ms, followed by a primary auditory warning signal (100 ms, 200 Hz, 82 dB). After presentation of the warning signal, the computer screen displayed a blank screen, followed by a variable foreperiod of 1500 – 2500 ms. Following this, the control auditory imperative stimulus (82 dB, 25 ms, 1000 Hz) or SAS (120 dB,25 ms, broadband 300 Hz – 11 kHz white noise) was presented, which indicated to participants to

execute the prepared movement as quickly and accurately as possible. All acoustic stimuli were generated using digital-analog output, amplified using a home amplifier, and delivered by a loudspeaker (MG Electronics M58-H) located 30 cm behind the participant. Stimulus intensity was confirmed using a precision sound level meter (Cirrus Research Optimus, CR:162C; A-weighted, impulse setting) placed at the location of the participant's left ear during testing.

On control+TMS trials, supra-threshold TMS was applied 70 ms prior to each participant's median control trial baseline RT for each task as determined from the baseline block. On SAS+TMS trials, the control stimulus was replaced with a SAS and supra-threshold TMS was applied 70 ms prior to each participant's median SAS trial baseline RT for each task as determined from the baseline block.

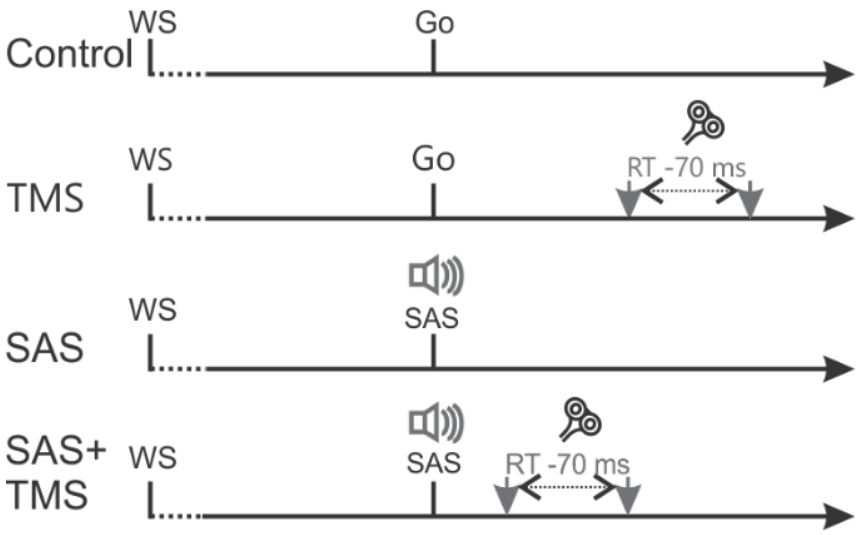


Figure 3. Timeline of experimental trials. All trials will begin with an auditory warning signal (WS) followed by a variable foreperiod of 1500-2500ms and an auditory go signal (82dB). On selected trials, the go signal will be replaced with a 120dB startling acoustic stimulus (SAS). In trials with transcranial magnetic stimulation (TMS), TMS will be applied 70 ms prior to each participant's median baseline RT for control and SAS trials respectively.

3. Data Analysis

3.1 EMG

EMG onset for left and right ECR was defined as a sustained rise in rectified, filtered (zero-lag, 2nd order, 25 Hz, low pass elliptic filter) EMG of more than 2 SD above baseline (mean of 100 ms EMG activity preceding the go-signal). The EMG data was computed and marked using a custom LabView program. These markers were displayed on the raw EMG traces on a computer monitor, which allowed manual correction to any possible errors due to the strictness of the algorithm (Hodges & Bui, 1996). On SAS trials, EMG onset in right and left SCM was calculated in a similar fashion, with a startle reflex defined as the observation of SCM activity in either the left or right SCM muscle between 25 and 120 ms following the SAS. In addition, EMG parameters and kinematic measures were calculated for each limb. Peak EMG amplitude was defined as the highest amplitude calculated from the rectified and filtered trace within the first 100 ms of EMG burst onset. Integrated EMG in time intervals of 0-30 ($iEMG_{30}$) and 0-100 ($iEMG_{100}$) ms after EMG onset were also quantified from the rectified raw EMG data. Peak velocity was measured as the maximum angular velocity occurring before peak displacement. Peak displacement was defined as the greatest displacement achieved during the movement. Lastly, final position was defined as the point at which angular velocity fell below 8˚/s for a minimum of 150 ms. As a result of a technical issue, kinematic data from a single participant were not available and thus this participant has been removed from analyses involving kinematic measures.

3.2 Data Reduction

The main dependent measure was premotor RT, defined as the time interval between stimulus onset and agonist EMG onset. In order to examine the bimanual symmetry that occurred in the bimanual movements across all conditions, the average onset asynchrony was calculated between the right and left limbs. Reasons for discarding trials included premotor RT below 50ms (i.e., anticipation), RT more than 2.5 standard deviations above median control RT for the particular task (i.e., not paying sufficient attention), and incorrect movement. SAS trials where there were no observable SCM activity in the EMG were discarded. 3 Participants showed SCM activation in less than 50% of SAS trials, and in remaining participants a startle reflex was observed in 93.4% of trials (SD=5.7). In retained participants, 7 trials were removed as a result of anticipation, 4 were removed due to a slow RT, 14 trials were removed due to movement error, and 17 trials were removed due to a lack of startle reflex in SCM resulting in a 95.1% trial inclusion rate. Trials that were discarded due to movement error include: no movement was performed, moving both limbs in the unimanual condition and vice versa, and moving the incorrect limb.

3.3 Statistical Analysis

To ensure all data meet the assumptions for parametric test statistics, Shapiro-Wilk's test of normality was conducted on all variables. To determine if the presentation of TMS led to differences in the onset asymmetry between the limbs in the bimanual task, RT symmetry was compared using a 2 (TMS: no TMS, TMS) x 2 (Stimulus: control, SAS) repeated measures analysis of variance (RM ANOVA). In order to determine if any RT delays induced by the TMS was different between unimanual and bimanual conditions and between limbs, RT differences

between noTMS and TMS trials were compared using a 2 (Limb: right, left) x 2 (Task: unimanual, bimanual) x 2 (TMS: noTMS, TMS) x 2 (Stimulus: control, SAS) RM ANOVA. To determine if the presentation of TMS led to differences in the SCM EMG onset between tasks was compared using a 3 (Task: Uni L, Uni R, Bimanual) x 2 (TMS: No, Yes) x 2 (SCM: Left, Right) RM ANOVA.

Secondary analyses were carried out on the remaining dependent variables using a 2 (Limb: right, left), x 2 (Task: unimanual, bimanual) x 2 (TMS: no TMS, TMS) x 2 (Stimulus: control, SAS) RM ANOVA to determine if there were any differences as a result of limb, SAS or TMS. Lastly, any differences as a result of TMS and SAS on the left limb in the bimanual task were analyzed using a 2 (TMS: no TMS, TMS) x 2 (Stimulus: control, SAS) RM ANOVA to determine if there were any differences as a result of TMS and SAS on the left limb in the bimanual task.

The significance value for all statistical values was set at $p < .05$, and where appropriate, partial eta-squared (η_p^2) is reported to give an estimate of effect size for ANOVAs. All significant differences were analyzed using post-hoc tests with a Holm -Bonferroni correction for multiple comparisons to determine the locus of significant differences. All analyses were carried out using the JASP statistical software package (version 0.14.1).

4. Results

4.1 Premotor RT

Premotor RT across all conditions can be found in figure 3. A 2 (Limb: right, left), x 2 (Task: unimanual, bimanual) x 2 (TMS: no TMS, TMS) x 2 (Stimulus: control, SAS) repeated measures ANOVA revealed main effects for all factors (all main effects <.015). The highest

order effect was a 3-way Limb by Stimulus by TMS interaction (F (1,5) = 7.675, P = .039, η_p^2 =.606). There was also a significant interaction between Limb and TMS (F (1,5) = 31.814, P = .002, η_p^2 = .864). These interactions are further decomposed in the following analyses. Only the analyses related to the primary hypotheses are presented here. Secondary analyses can be found in Appendix 2.

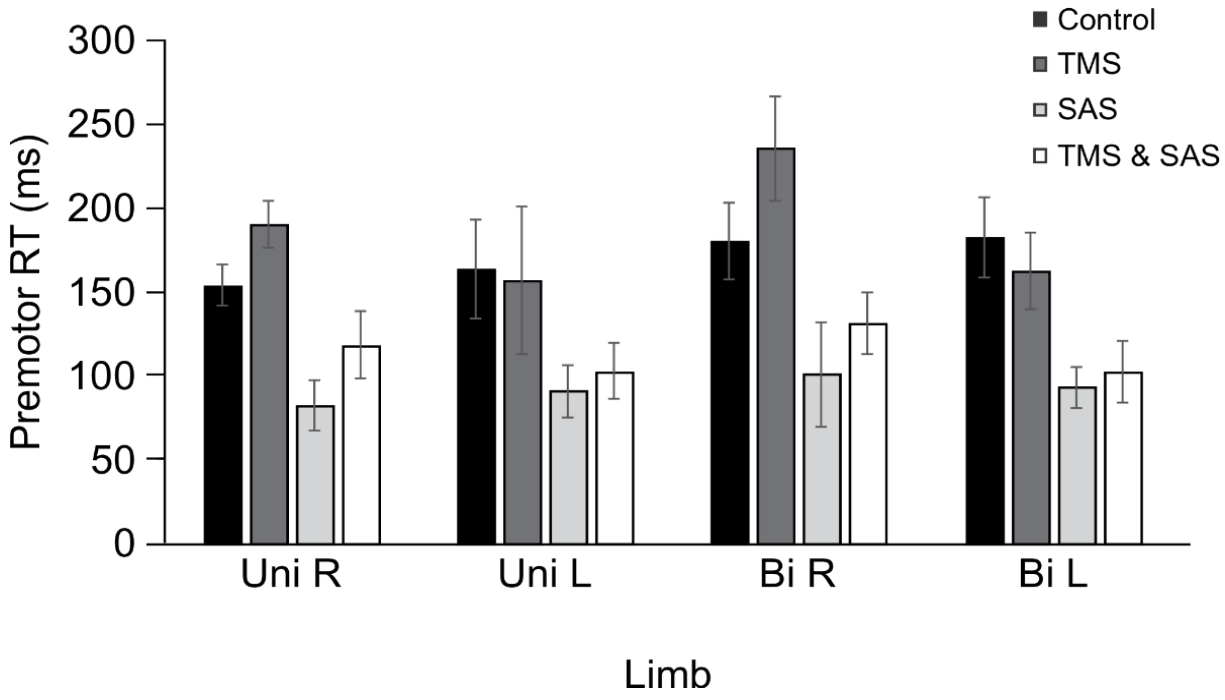


Figure 4. Mean (SD) premotor reaction time observed across limb and task conditions.

Premotor RT onset asymmetry values of the right and left limb for the bimanual conditions are shown in figure 4. A 2 (TMS: no TMS, TMS) x 2 (Stimulus: control, SAS) RM ANOVA revealed a significant main effect of TMS, indicating that bimanual asymmetry for TMS trials was greater than no TMS trials (F (1,5) = 18.093, P = .008, η_p^2 = 0.783). The main effect of Stimulus was not significant (P =.262); however, these effects were superseded by a significant interaction between the factors (F (1,5) = 6.793, P = .048). Post hoc tests indicated

that there was a significant difference between TMS and no TMS trials for control trials (P = .004), but not for SAS trials (P = .393).

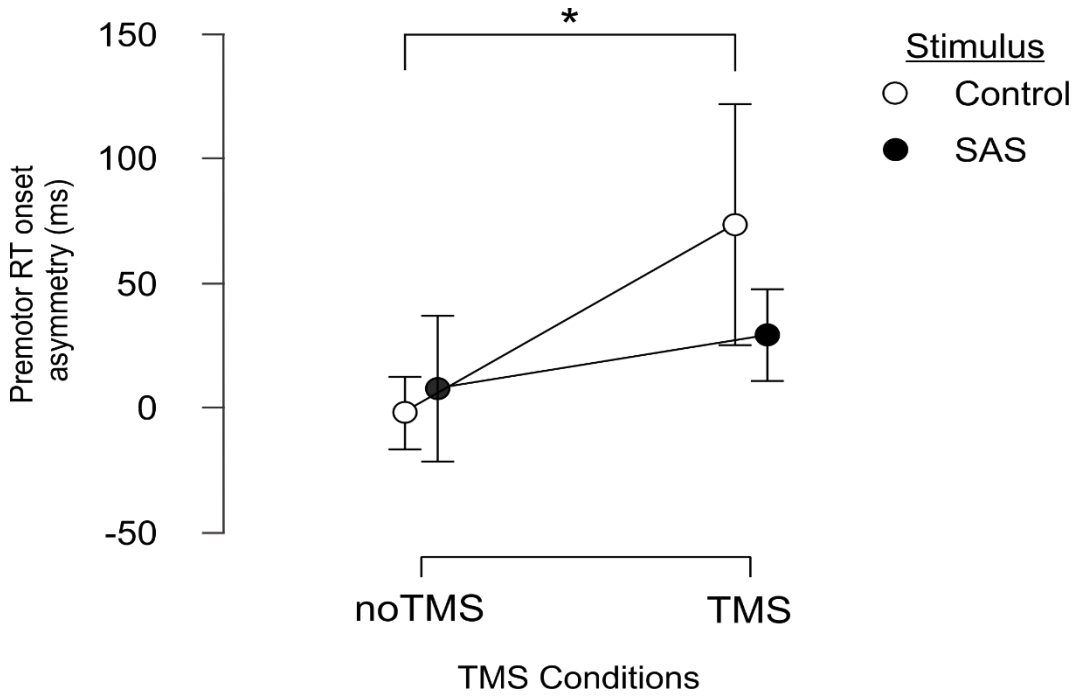
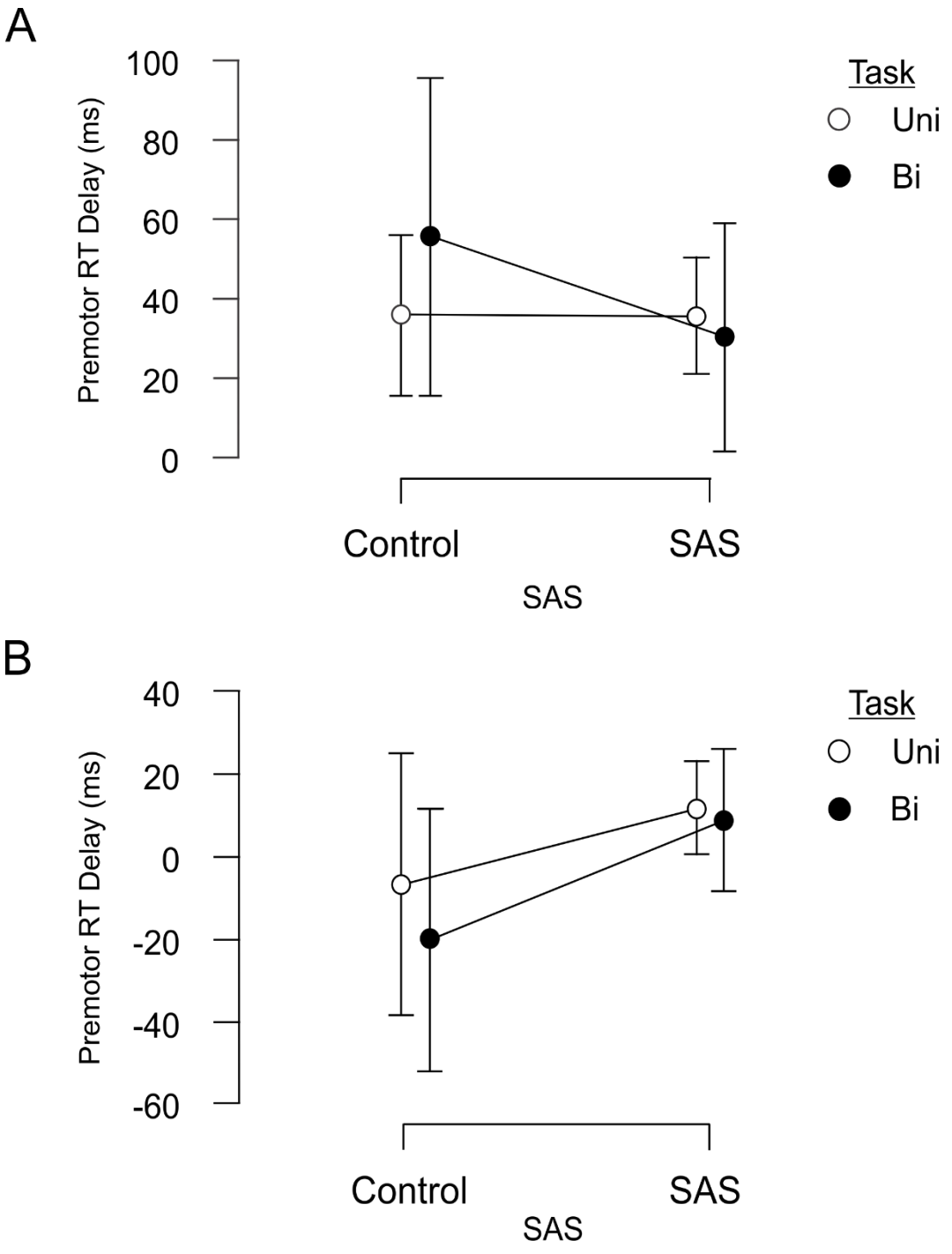


Figure 5. Mean (95% CI) premotor reaction time onset asymmetry observed between the right and left limbs in the bimanual conditions. Asterisk (*) denotes significant (p<.05) differences between control trial TMS conditions.

Premotor RT delay in both limbs following TMS applied to the left hemisphere can be found in figure 5. A 2 (Limb: right, left) x 2 (Task: unimanual, bimanual) x 2 (Stimulus: control, SAS) RM ANOVA revealed a main effect of Limb ($F(1,5) = 34.814$, $P = 0.002$, $\eta_p^2 = 0.864$) as well as a significant interaction between Limb and Stimulus ($F(1,5) = 7.675$, $P = 0.039$, $\eta_p^2 = 0.606$). There was no main effect of Task (P = .946) or interactions involving task (all p-values > .218). Post hoc tests indicated that there was a significant difference between the limbs in the delay induced by TMS on control trials (Mean difference = 59.4 ms, SE = 9.8; P < .001), but this between limb difference was not significant for SAS trials (Mean difference = 22.8 ms, SE = 9.8;

P = .130). Furthermore, in the right limb, there was no difference between control and SAS trials in terms of the delay induced by the TMS (Mean difference = 12.9 ms, SE = 11.7; P = .298). When looking at SCM EMG onset, a 3 (Task: Uni L, Uni R, Bimanual) x 2 (TMS: No, Yes) x 2 (SCM: Left, Right) RM ANOVA revealed no main effects or interactions across all conditions (P > 0.05).



F*igure 6.* Mean (95% CI) premotor reaction time (RT) delay observed across stimulus and task conditions. Premotor RT delay in the control and SAS conditions are displayed as a function of task (unimanual vs. bimanual), for the right (A) and left (B) limbs. Note negative values denote faster responses following TMS.

5. **Discussion**

The purpose of the present experiment was to investigate the potential differences in the initiation of unimanual and bimanual wrist extension movements. Specifically, the experiment explored whether 1) the impact of TMS on response initiation would be different for unimanual task versus a bimanual task, 2) whether the SP would impact the initiation of one limb or both limbs during bilateral task, and 3) if a difference observed would be modulated based on whether the action was voluntarily initiated following a control go-signal, or involuntarily following a SAS. In order to explore the preparation and initiation of the movements, suprathreshold TMS was applied over the left primary motor cortex (M1) during a simple RT task to induce a cortical silent period (CSP). In line with the hypotheses, the TMS induced silent period significantly delayed the right limb in both the unimanual and bimanual tasks. However, the RT delays were not smaller for the bimanual condition as initially expected. Additionally, there was a significant RT delay exclusively in the right limb due to the CSP while there were no differences were evident in the left limb (Figure 5). When examining the impact of SAS on the TMS-induced RT delays the results demonstrated that SAS did lead to significantly shorter RTs in both unimanual and bimanual wrist extension tasks but the TMS induced delays in the right limb were not significantly shorter in SAS conditions. In line with the hypothesis, asymmetry results revealed that RT asymmetry on TMS trials was smaller for SAS trials compared to control. Some secondary analyses showed trends toward significance in 4-way interactions, but due to the exploratory nature of the study and low sample size it is difficult to interpret these findings due to the lack of power. Overall, these results seem to suggest that when performing bimanual movements, there may be an increased role of subcortical structures that contribute to movement initiation.

A technique used to explore the different corticospinal and reticulospinal contributions to movement initiation is suprathreshold TMS which can be used to induce a CSP. When applied over the M1, this can cause a disruption of ongoing muscle activity due to a suppression of output from M1 and interruption of voluntary corticospinal drive (Chen et al., 1999). When applied prior to voluntary RT, delays in response output are often observed (Day et al., 1989). The suppression seen in voluntary movements due to the CSP lasts approximately 100-200 ms. Any suppression that exceeds 50 ms is representative of the delay as a result of the disruption of voluntary cortical processing that is occurring (Day et al., 1989). The results of the present experiment revealed that application of TMS resulted in a significantly delayed RT in the right limb for both the unimanual and bimanual tasks. Additionally, the TMS induced RT delays were only present in the right limb and the differences were not present in the left (Figure 6). This result supports previous findings that reveal the suprathreshold TMS over the M1 region lead to an increase in RT due to the disruption of cortical output specific to the targeted effector, but also indicates that a cortical disruption on one limb has little if any impact on the other limb during a bimanual movement.

While the reticular formation has traditionally been associated with postural control of axial muscles, it also has been shown to be involved in the control of upper limb voluntary actions (Baker, 2011). Due to its strong bilateral output (Davidson & Buford, 2006) the reticulospinal tract has been recently been shown to play a stronger role in the production of bimanual movements (Maslovat et al., 2020). Because the RT delay induced by suprathreshold TMS is thought to result from disruption of cortical drive, it was reasoned that a supposed increase in reticulospinal activation for bimanual movements would lead to a diminished impact from the TMS. Specifically, it was hypothesized that the RT delay in the right wrist on TMS

trials would be smaller during the bimanual movements as compared to unimanual movements. Although a RT delay occurred in the contralateral wrist following the TMS application for both the unimanual and the bimanual extension, there were no differences in the magnitude of the RT delay induced by TMS between the unimanual and bimanual tasks in control trials (Figure 6). The lack of RT delay differences between the two tasks despite the increase in reticulospinal innervation in a bimanual movement may be due to a stronger lateralization in the primary motor cortex for distal bimanual movements (Gribova et al., 2002). Previous work exploring proximal bimanual movements have revealed that representations of both arms are more interconnected in the cortical hemispheres than distal movements (Rouiller et al., 1994).

Presenting a SAS in replacement of a control go-signal has been previously used as a tool to investigate motor preparation in simple RT tasks. When presented with a SAS, prepared movements are typically triggered involuntarily alongside SCM activation resulting in a reduction in RT, which has been termed the StartReact effect. There have been conflicting accounts regarding the cortical and subcortical contributions to the StartReact effect. The subcortical storage hypothesis states that sufficient details of the planned movement are stored in reticulospinal areas so that when the startle response is apparent, these subcortical areas can then release the prepared movement without the normal cortical involvement (Valls-Solé et al., 1999). More recently it has been suggested that cortical and subcortical drive contribute to the response production, with relative contributions depending on the movement type (Carlsen & Maslovat, 2019). Given that bimanual responses in particular appear to involve reticulospinal activation (Davidson & Buford, 2006), it was expected that the StartReact effect would not only be present, but interlimb coupling might be strengthened when driven by StartReact. Previous work looking at unimanual and bimanual finger movements reported that the StartReact effect was present for

bimanual movements and not unimanual (Maslovat et al., 2020), which is indicative of greater reticulospinal contributions in bimanual movements than unimanual. Furthermore, the StartReact effect was not present in unimanual individuated finger movements but was present in coordinated grasps which has greater reticulospinal contributions compared to the latter (Honeycutt et al., 2013). In the present study, SAS led to shorter RTs for both the unimanual and bimanual wrist extension tasks (Figure 4). Furthermore, while not significant, it appears that the RT delay in the right limb was marginally smaller in the bimanual task when triggered by startle (Figure 6). This, coupled with the significantly smaller RT asymmetry seen between the limbs on TMS trials with startle compared to control (Figure 5) suggests marginally larger subcortical activation drove the response initiation on SAS trials. Secondary analyses on the remaining dependent variables revealed that peak velocity was also significantly faster for SAS trials compared to control. Furthermore, peak displacement was larger for SAS trials compared to control. Cumulatively, the results indicate that the StartReact effect was present for both the unimanual and bimanual movements, and that increased subcortical drive was present in the right limb during SAS trials during the bimanual wrist extension compared to unimanual. Although previous literature has demonstrated the increase in corticospinal activation in unimanual movements, the present findings may be a further indication that bimanual upper limb movements have slightly stronger innervation from reticulospinal structures (Riddle et al., 2009).

The RT asymmetry between the limbs when engaged in bimanual movements allowed further investigation of the impacts of SAS. RT asymmetry was explored as it provides information on the RT differences between the two limbs for the various TMS and go-signal conditions. As hypothesized, results revealed that RT asymmetry was smaller for SAS compared to control trials. It was expected that RT asymmetry would be smaller for SAS trials due to the

hypothesised increase in reticulospinal contributions on StartReact trials. The presence of the smaller RT asymmetry would also provide additional evidence of the subcortical region's involvement in bimanual movements. One way of explaining the potential decrease in RT asymmetry is the neural coupling which has been explored in post stroke patients where it is evident that despite the neural coupling being disrupted, they are still able to transfer the movement effects from one limb to the other through involvement of the lower brain regions. (Arya & Pandian, 2014).

In the present study there was an apparent conflict between the RT asymmetry findings and the RT delay results (see Figure 5 and Figure 6). When examining the RT change induced by TMS on left limb, it is evident that on control trials TMS had led to a decrease in RT (i.e., negative RT delay). This may be due to TMS having a facilitatory effect on the left hand when engaged in control trials (Figure 6B). However, a RT delay *was* evident in the TMS+SAS trials for the left limb. This, coupled with the modest decrease in RT delay for the right limb on bimanual SAS trials (Figure 6A), appears to have driven the RT asymmetry effect seen in Figure 5. Therefore, on SAS trials the bimanual movements appeared to be more symmetrical in terms of onset time, particularly following TMS. This may provide additional evidence that when acting bimanually, the two limbs are more "interconnected" in terms of their initiation. Overall, these findings provide some evidence that when completing a bimanual movement, there may be an increase in bimanual coupling occurring at the subcortical level when the action is involuntarily triggered by a SAS.

6. General Discussion

The purpose of the present study was to explore the varying neural contributions to unimanual and bimanual wrist extension movements. Consistent with previous literature, the TMS induced silent period significantly delayed onset of the effector muscle (right limb) in both the unimanual and bimanual RT tasks. As expected, a SAS lead to shorter RTs for both movements. Movement kinematic data also revealed that peak displacement was larger, and peak velocity was faster for SAS trials compared to control.

To my knowledge, previous research has not explored the impacts of TMS on the opposing limb in a bimanual movement and as such provided a novel area of exploration in motor control research. The results revealed that TMS application did cause a significant delay in the right limb, but the delay was not present in the left limb for the bimanual task. Therefore, these findings suggest that the cortical disruption on one limb does not have an effect on the other limb when engaged in a bimanual movement. Stronger bimanual neural coupling may have occurred when the response was triggered by SAS as RT asymmetry induced by the TMS between the two limbs in in the bimanual task was smaller for SAS trials compared to control. This suggests that increased subcortical activation was driving the limbs in these conditions. Although the experiment looked to examine the cortical and subcortical contributions using SAS and TMS on bimanual movements, it is important to note that the neural activity involved in a particular movement is vast and not solely the contribution of one particular region.

6.1 Limitations

There are two major limitations in this study that could be addressed in future research. Firstly, participant recruitment was severely impacted as a result of Covid-19 restrictions in

place. As such, the current experiment had an insufficient sample size, thus impacting the power of the presented research findings. One of the main findings of the experiment is the trend towards premotor RT being impacted by TMS, depending on the limb. Insufficient data in the current study may have led to the inability to detect statistically significant differences between conditions. An increase in sample size would ensure statistical power is met to detect true effects. Secondly, the modification of the timing of the TMS pulse would ensure more accurate application as the experiment progresses. With the current study design, TMS application may have occurred too early in the RT interval, as the time was based on each participant baseline early on in the experimental session. Incorporating this in the current study design would require an additional experimenter in the room to adjust the mean in the program, which is not recommended given the current Covid-19 protocols in place.

6.2 Future Direction

In the present study, MVF data was collected for both unimanual and bimanual wrist extension movements in conjunction to suprathreshold TMS. A future study may examine the result of the TMS application on the peak force while engaged in a bimanual task. Additionally, the current study examined a bimanual gross movement and the impacts of TMS on the two limbs. A future direction would be to examine the impacts across various movements. The current study examined a wrist extension movement, but future experiments could investigate the cortical and subcortical contributions using TMS and SAS on bimanual finger movements, which are more strongly driven by the corticospinal tracts (Lawrence & Kuypers, 1968), as bimanual finger movements have been shown to have greater reticulospinal involvement than unimanual (Maslovat et al., 2020). Lastly, another avenue of exploration would be to analyze the

size of the MEPs as well as the length of the cortical silent periods as another way of exploring the level of corticospinal excitability in bimanual movement preparation.

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Appendix A: TMS Safety Questionnaire

Safety Screening Questionnaire for Transcranial Magnetic Stimulation

Please answer the following questions by putting a check mark (√) in the appropriate YES or NO box.

1.	Have you ever had an adverse reaction to transcranial magnetic stimulation?	YES □ NO □
2.	Had a seizure?	YES □ NO □
3.	Had an EEG (electroencephalogram)?	YES □ NO □
4.	Had a stroke?	YES □ NO □
5.	Had a head injury (include neurosurgery)?	YES □ NO □
6.	Do you have any metal in your head (outside the mouth) such as shrapnel, surgical clips, or fragments from welding or metalwork?	YES □ NO □
7.	Do you have any implanted devices such as cardiac pacemakers, medical pumps, or intracardiac lines?	YES □ NO □
8.	Do you suffer from frequent or severe headaches?	YES □ NO □
9.	Have you ever had any other brain-related condition?	YES □ NO □
10.	Have you ever had illness that caused brain injury?	YES □ NO □
11.	Are you taking any medications?	YES □ NO □
12.	Does anyone in your family have epilepsy?	YES □ NO □
13.	Are you pregnant?	YES □ NO □

PARTICIPANT NAME: _____

PARTICIPANT SIGNATURE: _____

DATE: _____ OR SIGNATURE OF LEGALLY AUTHORIZED INDIVIDUAL

APPENDIX B: Secondary Analyses

1. Peak EMG Amplitude

Peak EMG amplitude showed no main effects or interactions across all conditions ($P > 0.05$). There was a trend towards a main effect of Task ($F(1,5) = 6.075$, $P = 0.057$, $\eta_p^2 = 0.549$). Furthermore, there was a trend towards an interaction between Limb and TMS ($F(1,5) = 6.549$, $P = 0.051$, $\eta_p^2 = 0.567$). For exploratory purposes, post-hoc analyses correcting for multiple comparisons showed that there were no significant differences between the conditions ($P > .05$).

2. Integrated EMG Amplitude

Repeated measures ANOVA revealed no main effects or interactions across all conditions ($P > 0.05$) for either iEMG30 or iEMG100.

3. Peak Velocity

Analysis revealed a main effect of Stimulus ($F(1,4) = 54.235$, $P = 0.002$, $\eta_p^2 = 0.931$), where SAS trials had significantly faster peak velocity (Mean = 542.1 deg/s, SE = 58.4), compared to control (Mean = 429.5.1 deg/s, SE = 52.4). In addition, there was a significant interaction between Task and TMS ($F(1,4) = 159.208$, $P < .001$, $\eta_p^2 = 0.975$). Post-hoc analyses correcting for multiple comparisons revealed no significant differences between conditions ($P > .05$), however, looking at the plotted data, it appears that in the unimanual condition, TMS may have led to marginally higher peak velocity, whereas this does not appear to be the case for the bimanual condition (Figure 7).

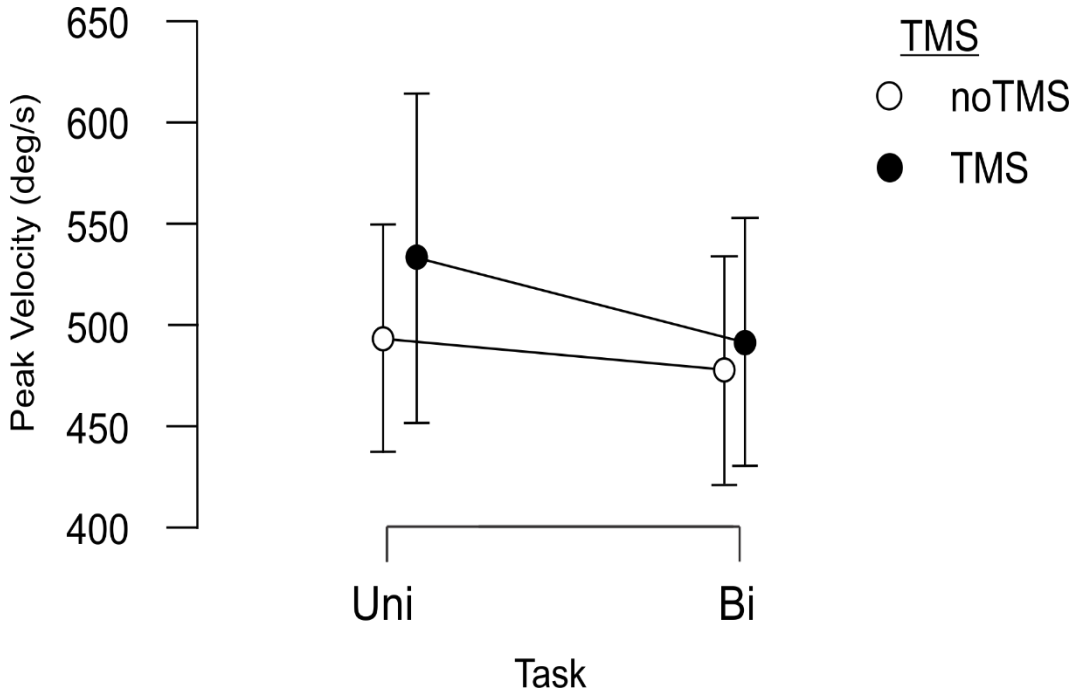

Figure 7. Mean (95% CI) peak velocity observed across Task and TMS conditions. Peak velocity in unimanual and bimanual conditions are displayed as a function of TMS (no TMS and TMS).

4. Peak Displacement

Analysis of peak displacement revealed a trend towards main effect of Stimulus ($F(1,4) = 7.037$, $P = 0.057$, $\eta_p^2 = 0.638$), where SAS trials had a marginally larger peak displacement (Mean = 34.2 deg, SE = 4.2), compared to control (Mean = 31.6 deg, SE = 3.8). In addition, there was a significant interaction between Task and TMS ($F(1,4) = 46.427$, $P = .002$, $\eta_p^2 = 0.921$). Post-hoc analyses correcting for multiple comparisons revealed no significant differences between conditions ($P > .05$), however, looking at the plotted data, it appears that, similar to peak velocity, in the unimanual condition, TMS may have led to marginally larger peak displacement, whereas this does not appear to be the case for the bimanual condition (Figure 8).

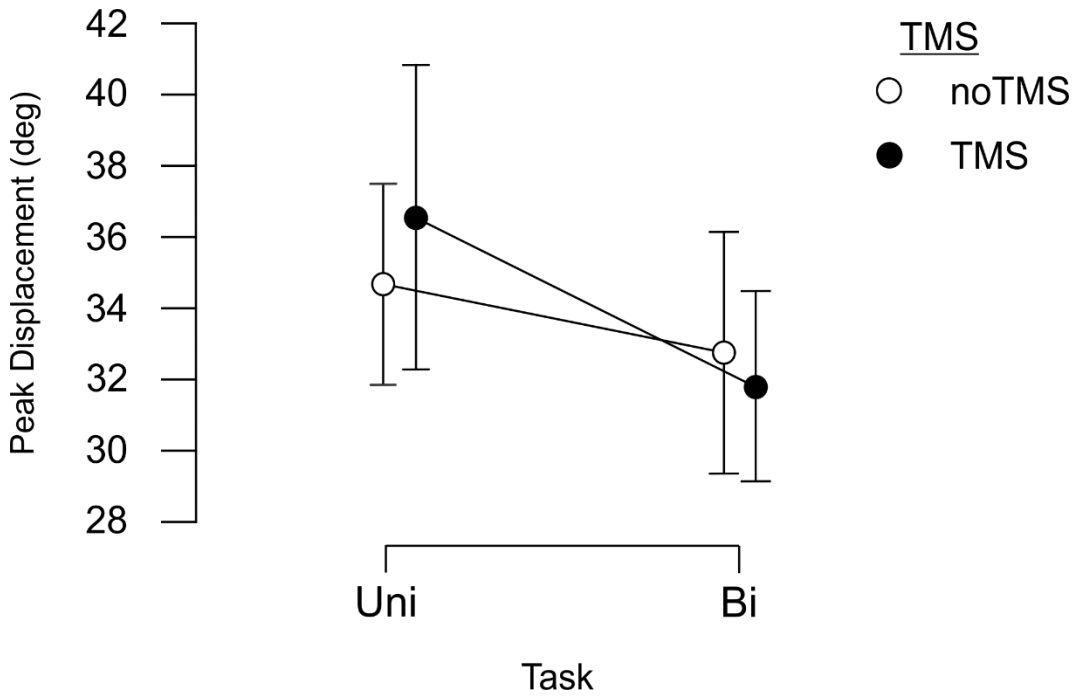

Figure 8. Mean (95% CI) peak displacement observed across Task and TMS conditions. Peak displacement in unimanual and bimanual conditions are displayed as a function of TMS (no TMS and TMS).

5. Final Position

Analysis of final position revealed a significant interaction between Task and TMS ($F(1,4) = 30.620$, $P = .002$, $\eta_p^2 = 0.921$). Post-hoc analyses correcting for multiple comparisons revealed no significant differences between conditions ($P > .05$), however, looking at the plotted data, it appears that final position in the bimanual condition was marginally smaller following TMS compared to the unimanual condition, but little difference existed between the conditions with no TMS (Figure 9).

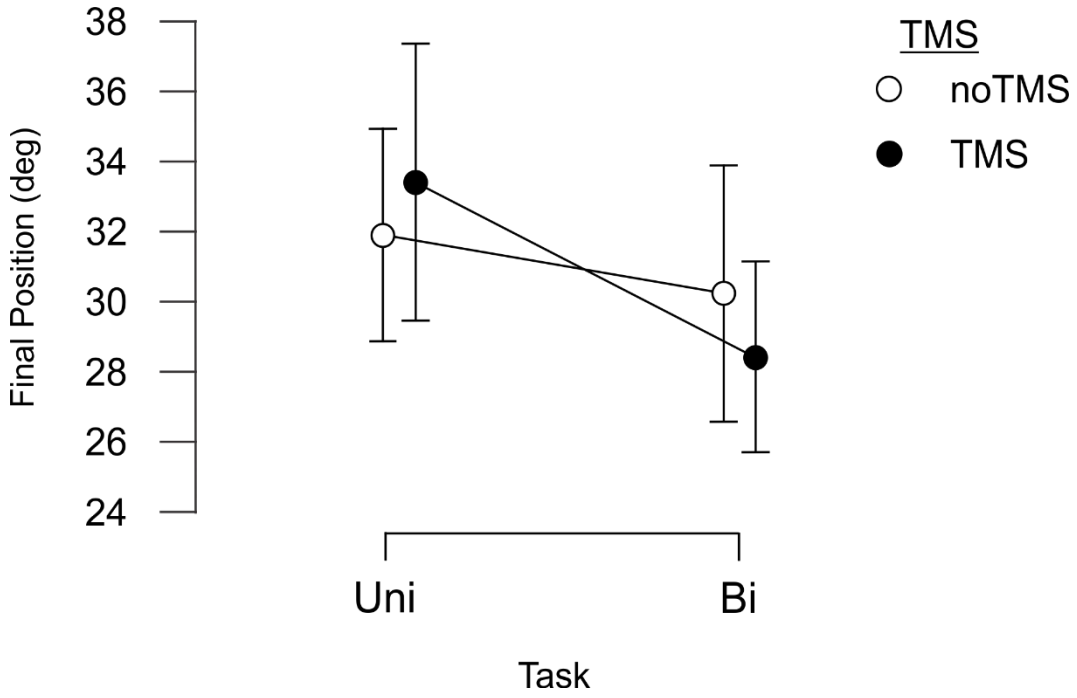

Figure 9. Mean (95% CI) final position observed across Task and TMS conditions. Final position in unimanual and bimanual conditions are displayed as a function of TMS (no TMS and TMS).